PBRER Appendix 3 Tabular Summary of Validated Safety Signals	
Medicinal Product	VAXZEVRIA (ChAdOx1-S [recombinant])
Period covered	29 June 2022 to 28 December 2022
Date	17 February 2023

Appendix 3

Tabular Summary of Validated Safety Signals

1 GENERAL CONSIDERATIONS

The tabular summary of validated safety signals presented here presents validated signals that were ongoing and closed during the reporting period.

The column headings in the tabular summary have the following meanings:

- **Signal term**: A brief descriptive name of the medical concept for the validated signal. The description may evolve and be refined as the signal is evaluated. The concept and scope may, or may not, be limited to specific Medical Dictionary for Regulatory Activities (MedDRA) term(s), depending on the source of the signal. Where applicable, the tabulation refers to the specific MedDRA terms (eg, Preferred Terms [PTs], High Level Terms [HLTs], System Organ Classes [SOCs], etc) or Standardised MedDRA Queries (SMQs) that were reviewed.
- **Date detected:** This is the month and year when AstraZeneca became aware of the signal.
- **Status:**
  - Ongoing: A validated signal that was under evaluation at the data lock point. An anticipated completion date is provided, if known
  - Closed: A validated signal whose evaluation was completed before the data lock point of the PBRER

Note: A new validated signal of which AstraZeneca became aware during the reporting period will be classified as closed or ongoing, depending on the status of signal evaluation at the end of the PBRER reporting period.

- **Date closed**: The month and year when the signal evaluation was completed.
- **Source of signal**: The data or information source from which a signal arose. Examples include, but may not be limited to, spontaneous adverse event reports, clinical trial data, scientific literature, non-clinical study results, or information requests or enquiries from a regulatory authority.
- **Reason for evaluation and summary of key data**: A brief summary of key data and the rationale for further evaluation.
- **Method of signal evaluation**: A brief description of the method(s) used for evaluating the signal, including data sources.
- **Action(s) taken or planned**: A statement regarding whether or not a specific action has been taken or is planned for all closed validated signals that have been classified as potential or identified risks; refer to PBRER Section 16.2, Signal evaluation for further detail. Any further actions planned for newly or previously identified signals under evaluation at the data lock point are listed; otherwise this will be left blank for ongoing signals

Table 1 Tabular summary of validated safety signals that were ongoing or closed during the reporting period

Signal term	Date detected	Status (ongoing or closed)	Date closed (for closed signals)	Source of signal	Reason for evaluation and summary of key data	Method of signal evaluation	Action(s) taken or planned
Cutaneous vasculitis	05 April 2022	Closed	31 August 2022	Literature Article, Regulatory Authority	Regulatory Authority Enquiry or Request. GSP or SSaMT Leader consider signal requires evaluation.	Quantitative Signal Detection System (Observed versus expected analysis), External Quantitative Signal Detection System (EVDAS), Literature review. Qualitative data analysis (Individual Case Safety Report or Case Series)	Change to Reference Safety Information and Product Labelling. Summary: CDS Section 4.8 (undesirable effects) was updated to include cutaneous vasculitis as an ADR (frequency: not known)
Immune thrombocytopenia	06 July 2022	Closed	08 November 2022	Qualitative data analysis (Individual Case Safety Report or Case Series), Literature cases	GSP or SSaMT Leader consider signal requires evaluation based on new well-documented spontaneous case reports and also published literature	Quantitative Signal Detection System (Observed versus expected analyses), Literature review, Preclinical review, Clinical review, Qualitative data analysis (Individual Case Safety Report or Case Series), Epidemiology analyses	Change to Reference Safety Information and Product Labelling Summary: Update to 4.4 Special warnings and special precautions for use. Addition of ITP to 4.8 in summary of post-authorization data

Table 1 Tabular summary of validated safety signals that were ongoing or closed during the reporting period

Signal term	Date detected	Status (ongoing or closed)	Date closed (for closed signals)	Source of signal	Reason for evaluation and summary of key data	Method of signal evaluation	Action(s) taken or planned
Feeling hot[a]	22 December 2022	Closed	17 January 2023	AZ clinical trial	GSP or SSaMT Leader consider signal requires evaluation	Qualitative data analysis (Individual Case Safety report or Case Series) Literature Quantitative Signal detection system	No signal
Decreased appetite[a]	22 December 2022	Ongoing		AZ clinical trial	GSP or SSaMT Leader consider signal requires evaluation	Qualitative data analysis (Individual Case Safety report or Case Series) Literature Quantitative Signal detection system	Change to Reference Safety Information and Product Labelling: CDS Section 4.8 (Undesirable effects) to be updated to include Decreased appetite as an ADR (frequency: uncommon)

[a] Signal of Decreased appetite was ongoing and Feeling hot was closed after the data lock point on 17 January 2023

ADR Adverse Drug Reaction; AZ AstraZeneca; CDS Core Data Sheet; EVDAS External Quantitative Signal Detection System; GSP Global Safety Physician; ITP Immune Thrombocytopenia; SSaMT Safety Strategy and Management Team

PBRER Appendix 4 Listings of All Post-Authorisation Safety Studies	
Medicinal Product	VAXZEVRIA (ChAdOx1-S [recombinant])
Period covered	29 June 2022 to 28 December 2022
Date	17 February 2023

Appendix 4

Listings of All Post-Authorisation Safety Studies

Table 1 Listing of all non-interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI / LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
D8111R00010	An assessment of a relationship between the exposure to COVID-19 vaccines and risk of thrombotic thrombocytopenia syndrome	A retrospective study using linked secondary databases in England	All patients, in England who are present in the integrated health records of NHS Digital TRE and/or ORCHID	Not applicable	Final study report Q2 2023	Ongoing	Association between COVID-19 vaccine exposure and the TTS. voluntary PASS
D8111R00007	Real-world effectiveness of the Oxford/AstraZeneca COVID-19 vaccine in England	Observational retrospective cohort study	English population greater or equal to 16 years of age		Final study report: Q1 2023	Ongoing	Effectiveness of the AZD1222 in England
D8110C00003	Pregnancy Registry of Women Exposed to AZD1222 Immediately Before or During Pregnancy as Part of the C-VIPER Registry Consortium.	An international, prospective, observational cohort study of pregnant women	Women aged ≥ 18 years old, who receive the AZD1222 vaccine at any time while they are pregnant or who become pregnant within a predefined period (eg, 30 days pre-LMP) after being vaccinated		July 2026	ongoing	Pregnancy Registry of Women Exposed to AZD1222 Immediately Before or During Pregnancy as Part of the C-VIPER Registry Consortium.

Table 1 Listing of all non-interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI / LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
D8111C00004	A Phase IV Non-interventional Enhanced Active Surveillance Study of Adults Vaccinated with AZD1222; conducted by the Drug Safety Research Unit (DSRU, UK))	Phase IV Non-interventional Enhanced Active Surveillance Study	Adult volunteers from UK		Jan 2024	ongoing	To monitor the safety and utilisation of the COVID-19 vaccine AstraZeneca (AZD1222) administered to vaccinees under real world use in the UK. Primary objective is to examine the safety of COVID-19 vaccine AstraZeneca (AZD1222) through active surveillance of all vaccinee reported adverse events and assessment of incidence.
D8111R00006	A Post-authorisation/Post-marketing Observational Study to Evaluate the Association Between Exposure to AZD1222 and Safety Concerns Using Existing	A multinational, retrospective cohort study using secondary data sources in the UK, Spain, the Netherlands, and Italy	All individuals registered in each of the five included healthcare data sources during the study period		June 2024	Ongoing	The study aims to compare the incidence of AESIs after receiving AZD1222 with that in three different matched comparator cohorts: concurrent unvaccinated comparators, active comparators, and historical comparators

Table 1 Listing of all non-interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI / LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
	Secondary Health Data Sources						

COVID-19 Corona Virus Disease of 2019; CSR Clinical Study Report; DSUR Development Safety Update Report; FSI First Subject In; LSO Last Subject Out. LMP Last Menstrual Period; NHS National Health Service; PASS Post-Authorisation Safety Study; TTS Thrombosis with Thrombocytopenia Syndrome; TRE Trusted Research Environment; UK United Kingdom

Table 2 Listing of all interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI/LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
D8111C00010	Immunogenicity and Safety Study of AZD1222 Vaccine in Immunocompromised Adults	Interventional Clinical pharmacology	Immunocompromised Adults in the US and South America.	Study protocol submission: 24 April 2021	NA	Withdrawn	Immunogenicity of a 2 dose primary vaccination.
COV001	Phase I/II Study of Efficacy, Safety, and Immunogenicity of the Candidate Coronavirus Disease (COVID-19) Vaccine ChAdOx1	Interventional Phase I/II Study	Healthy Adult Volunteers in the UK		Final report: 31 March 2023	Ongoing	Efficacy and safety

Table 2 Listing of all interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI/LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
	nCoV-19 in UK Healthy Adult Volunteers						
COV002	Phase II/III Study of Efficacy, Safety, and Immunogenicity of the Candidate Coronavirus Disease (COVID-19) Vaccine ChAdOx1 nCoV-19	Interventional A Phase II/III Study	Adults aged 18 years and older in the UK		Final report: 31 March 2023	Ongoing	Efficacy and safety
COV003	Randomized, Controlled, Phase III Study of Safety, Efficacy, and Immunogenicity of the Non-Replicating ChAdOx1 nCoV19 Vaccine	Interventional Randomized, Controlled, Phase III Study	Adults aged 18 years and older in the UK		Final report: 31 March 2023	Ongoing	Efficacy confirmed with PCR

Table 2 Listing of all interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI/LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
COV005	Adaptive Phase I/II Randomized Placebo-controlled Study of Safety, Immunogenicity and Efficacy of Non-Replicating ChAdOx1 SARSCoV-2 Vaccine in South African Adults Living Without HIV, and Safety and Immunogenicity in Adults Living with HIV	Interventional An Adaptive Phase I/II Randomized Placebo-controlled Trial	Adults in South Africa living with and without HIV+		Final report: 31 March 2023	Ongoing	Safety, tolerability, and reactogenicity profile of AZD1222 in people living with HIV; cellular and humoral immunogenicity of AZD1222 after one and two doses of vaccine
COV004	Phase IB/II Single-Blinded, Randomized, Controlled Study of Safety, Immunogenicity and Efficacy of the Candidate Coronavirus Disease (COVID-19)	Interventional Phase IB/II Single-Blinded, Randomized, Controlled Study	Adults in Kenya		Final report: 31 March 2023	Ongoing	Safety, tolerability and reactogenicity, and immunogenicity profile of ChAdOx1 nCoV-19

Table 2 Listing of all interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI/LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
	Vaccine ChAdOx1 nCoV-19 in Adults in Kenya						
D8111C00002	A Phase I/II Randomized, Double-blind, Placebo-controlled Multicenter Study in Participants Aged 18 Years or Older to Determine the Safety and Immunogenicity of AZD1222, a Non-replicating ChAdOx1 Vector Vaccine, for the Prevention of COVID-19	Interventional Phase I/II Randomized, Double-blind, Placebo-controlled Multicenter Study	2 cohorts: Healthy participants aged 18 to 55 years and healthy elderly participants aged ≥ 56 years.		Primary analysis: Q2 2021 Final CSR addendum : 11 April 2022	Completed	Antibody response to AZD1222 Spike antigen following 2 IM doses of AZD1222 or placebo and safety, tolerability, and reactogenicity profile of AZD1222. *Specific obligation.*
D8110C00001	Phase III Randomized, Double-blind, Placebo-controlled	Interventional Phase III Randomized, Double-blind, Placebo-	Adults ≥18 years of age who are healthy or have medically stable chronic diseases and are at increased risk for	Primary efficacy analysis 2021	Final report: Q4 2023	Ongoing	Efficacy, safety, tolerability, and reactogenicity (substudy) of 2 IM doses of

Table 2 Listing of all interventional studies with the primary aim of post-authorisation safety monitoring

Study no.	Study title	Study type	Population studied	FSI/LSO (actual/ planned)	CSR (actual/ planned)	Status (ongoing/ completed)	Comments
	Multicenter Study in Adults for Safety, Efficacy, and Immunogenicity of AZD1222, a Non-replicating ChAdOx1 Vector Vaccine, for the Prevention of COVID-19	controlled Multicenter Study	SARS-CoV-2 acquisition and COVID-19.				AZD1222 compared to placebo *Specific obligation*
MS1222-0003*	Are HIT antibodies increased in the sera of vaccinated individuals	Interventional (in vitro) Platelet activation	Vaccinated patients		Final report: 01 August 2021	Closed	Presence if HIT antibodies in the sera of vaccinated individuals and mechanisms and possible triggers of platelet activation after vaccination. *Additional requirement* for thrombosis in combination with thrombocytopenia

COVID-19 Corona Virus Disease of 2019; CSR Clinical Study Report; FSI First Subject In; LSO Last Subject Out. ChAdOx1 Chimpanzee Adenovirus; HIT Heparin-induced thrombocytopenia; HIV Human Immunodeficiency Virus; IM Intramuscular; NA not applicable; PCR Polymerase chain reaction; SARSCoV-2 Severe Acute Respiratory Coronavirus 2; UK United Kingdom; US United States

COV001/002/003/004/005 studies are completed after the DLP of this PBRER

PBRER Appendix 6 Post-marketing Exposure Data	
Medicinal Product	VAXZEVRIA (ChAdOx1-S [recombinant])
Period covered	29 June 2022 to 28 December 2022
Date	17 February 2023

Appendix 6

Post-marketing Exposure Data

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1 THE EUROPEAN UNION DISTRIBUTION DATA

Interval and Cumulative post-marketing exposure based on doses distributed at the country level, for specified countries in the European Union are presented in Table 1.

Table 1 VAXZEVRIA exposure based on Doses Distributed in the European Union

Country	Interval (01 July 2022 to 31 December 2022)[a]	Cumulative (Up to 31 December 2022)[a]
Austria	0	5519600
Belgium	0	32008240
Bulgaria	0	4518400
Croatia	0	1458100
Cyprus	0	452000
Czech Republic	0	1081400
Denmark	0	1387500
Estonia	0	818300
Finland	0	648000
France	0	12156000
Germany	0	22398900
Greece	0	4324800
Hungary	0	6513800
Iceland	0	87200
Ireland	0	1433600
Italy	0	15209400
Latvia	0	663800
Lithuania	0	1355300
Luxembourg	0	186600
Malta	0	926300
Netherlands	0	4503400
Norway	0	58400
Poland	0	20001200
Portugal	0	5267500
Romania	0	4478000
Slovakia	0	1552800
Slovenia	0	823800
Spain	0	14031800

Table 1 VAXZEVRIA exposure based on Doses Distributed in the European Union

Country	Interval (01 July 2022 to 31 December 2022)[a]	Cumulative (Up to 31 December 2022)[a]
Sweden	0	1413700
Total	**0**	**165277840**

[a] Information included in this table reflects the dispatch of vaccine by AstraZeneca up to 31 December 2022.

2 GLOBAL ADMINISTRATION DATA

2.1 Doses Administered by Country

Interval and cumulative post-marketing patient exposure to doses administered at the country level is provided in Table 2. The information in the table has either been provided to AstraZeneca directly from Government bodies or has been sourced from country specific websites.

Table 2 VAXZEVRIA exposure based on Doses Administered by Country, as of 28 December 2022

Country	Interval (29 June 2022 to 28 December 2022)	Cumulative (Up to 28 December 2022)
European Union		
Austria	4720	1592242
Belgium	1222	2848907
Bulgaria	0	478524
Croatia	590	568422
Cyprus	0	254531
Czech Republic	336	886117
Denmark	432	155991
Estonia	2849	238876
Finland	421	553820
France	5378	7859124
Germany	10386	12795088
Greece	1732	1557233
Hungary	5600	1252978
Iceland	9	115475
Ireland	25432	1215415

Table 2 VAXZEVRIA exposure based on Doses Administered by Country, as of 28 December 2022

Country	Interval (29 June 2022 to 28 December 2022)	Cumulative (Up to 28 December 2022)
Italy	476	11974868
Latvia	692	259771
Lithuania	32	536313
Luxembourg	-105	105059
Malta	56	227551
Netherlands	-5282	2473242
Norway	527	147948
Poland	3326	5292338
Portugal	14480	2272232
Romania	6	852295
Slovakia	1414	844168
Slovenia	-1024	323078
Spain	2200	9794915
Sweden	-7130	1322066
United Kingdom		
England	0	0
Scotland	0	0
Wales	0	0
Northern Ireland	0	0
North America		
Canada	4525	2815503
Rest of the World		
Afghanistan	0	975338
Argentina	6662043	26769473
Australia	120392	13833921
Brazil	31911308	151574297
Bangladesh	16560063	56241743
Chile	2656618	3206288
Colombia	3006605	11687143
Ecuador	5115297	8273662
Ghana	448113	10545038
Guatemala	847446	4487824

Table 2 VAXZEVRIA exposure based on Doses Administered by Country, as of 28 December 2022

Country	Interval (29 June 2022 to 28 December 2022)	Cumulative (Up to 28 December 2022)
India	165833251	1745211297
Iran	3790687	14426537
Iraq	0	717233
Lebanon	2077	722870
Malaysia	1634910	5707489
Mexico	0	49783383
Nepal	5026073	14999238
New Zealand	2106	9039
Peru	3762254	8102808
Philippines	3313684	22135134
Uruguay	182	91320
Saint Lucia	0	72660
South Korea	29597	20348873
Taiwan	62973	15297711
Thailand	5965036	48704094
Total	**256868734**	**2354582258**

2.2 Doses Administered split by Dose number, Age group and/or Gender

The following tables present vaccine dose administration, split by Dose number, Age group and/or Gender, where provided for the following regions/countries.

- European Union - Table 3
- United Kingdom - Table 4 (Please note: The format of this Table reflects interval and cumulative exposure across the whole of UK instead of England, Scotland and Wales only as presented in earlier reports)
- Australia Table 5

For the remaining countries that are listed in Table 2, dose administration data split by Dose number, Age group and/or Gender is not available to AstraZeneca.

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
Austria	18-24	197	44966	89	41109	286	86075	5.41
	25-49	987	269994	559	249362	1546	519356	32.65
	50-59	356	170439	232	161569	588	332008	20.87
	60-69	320	157980	226	152562	546	310542	19.52
	70-79	300	141976	241	138285	541	280261	17.62
	80+	-127	32100	-139	30421	-266	62521	3.93
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**2033**	**817455**	**1208**	**773308**	**3241**	**1590763**	**100.00**
Belgium	18-24	41	20273	32	20023	73	40296	1.41
	25-49	308	295297	286	291760	594	587057	20.61
	50-59	84	355792	77	352808	161	708600	24.87
	60-69	128	285465	123	283108	251	568573	19.96
	70-79	56	292641	58	290226	114	582867	20.46
	80+	12	182646	17	178868	29	361514	12.69
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**629**	**1432114**	**593**	**1416793**	**1222**	**2848907**	**100.00**
Bulgaria	18-24	0	6026	0	5398	0	11424	2.39
	25-49	0	66088	0	59872	0	125960	26.32
	50-59	0	43590	0	40170	0	83760	17.50
	60-69	0	60594	0	56860	0	117454	24.55
	70-79	0	55067	0	52411	0	107478	22.46
	80+	0	16215	0	15507	0	31722	6.63

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
	Unknown	0	582	0	144	0	726	0.15
	All Ages	**0**	**248162**	**0**	**230362**	**0**	**478524**	**100.00**
Croatia	18-24	4	3732	2	3420	6	7152	1.26
	25-49	36	41735	36	39600	72	81335	14.32
	50-59	4	38319	4	36781	8	75100	13.22
	60-69	12	80236	11	78166	23	158402	27.89
	70-79	3	80550	3	78783	6	159333	28.05
	80+	4	43635	3	42997	7	86632	15.25
	Unknown	30	30	26	26	0	0	0.00
	All Ages	**93**	**288237**	**85**	**279773**	**122**	**567954**	**100.00**
Cyprus	18-24	0	1614	0	1448	0	3062	1.20
	25-49	0	38043	0	35279	0	73322	28.81
	50-59	0	21114	0	20208	0	41322	16.23
	60-69	0	30647	0	29861	0	60508	23.77
	70-79	0	34116	0	33255	0	67371	26.47
	80+	0	4663	0	4283	0	8946	3.51
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**0**	**130197**	**0**	**124334**	**0**	**254531**	**100.00**
Czechia	18-24	0	2496	88	2496	88	4992	0.28
	25-49	1	45212	875	45212	876	90424	5.06
	50-59	1	43010	518	43010	519	86020	4.81
	60-69	0	95264	1033	95264	1033	190528	10.66

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
	70-79	0	188732	2709	188732	2709	377464	21.12
	80+	1	72041	2503	72041	2504	144082	8.06
	Unknown	446755	446755	446755	446755	893510	893510	50.00
	All Ages	**446758**	**893510**	**454481**	**893510**	**901239**	**1787020**	**100.00**
Denmark	18-24	-1336	8873	-47	179	-1383	9052	2.91
	25-49	-593	77473	44	1728	-549	79201	25.45
	50-59	-25	41089	16	514	-9	41603	13.37
	60-69	1838	24845	51	376	1889	25221	8.11
	70-79	38	326	21	113	59	439	0.14
	80+	11	51	4	15	15	66	0.02
	Unknown	152656	152656	2922	2921	155578	155577	50.00
	All Ages	**152589**	**305313**	**3011**	**5846**	**155600**	**311159**	**100.00**
Estonia	18-24	0	3077	-7	3009	-7	6086	2.58
	25-49	3	32921	-62	32293	-59	65214	27.64
	50-59	8	25159	-32	24841	-24	50000	21.19
	60-69	10	38952	-32	38473	-22	77425	32.82
	70-79	5	16212	-10	15996	-5	32208	13.65
	80+	3	2528	-1	2451	2	4979	2.11
	Unknown	6	6	4	4	10	10	0.00
	All Ages	**35**	**118855**	**-140**	**117067**	**-105**	**235922**	**100.00**
Finland	18-24	2	3392	1	36	3	3428	0.62
	25-49	23	31791	9	231	32	32022	5.78

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
	50-59	27	46574	1	341	28	46915	8.47
	60-69	46	228940	51	144984	97	373924	67.55
	70-79	5	48195	11	43714	16	91909	16.60
	80+	2	2836	0	2543	2	5379	0.97
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**105**	**361728**	**73**	**191849**	**178**	**553577**	**100.00**
Greece	18-24	17	870	14	495	31	1365	0.09
	25-49	182	266916	165	260382	347	527298	33.87
	50-59	69	65648	63	64364	132	130012	8.35
	60-69	164	372011	156	364520	320	736531	47.32
	70-79	115	63914	114	62520	229	126434	8.12
	80+	40	18029	36	16967	76	34996	2.25
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**587**	**787388**	**548**	**769248**	**1135**	**1556636**	**100.00**
Hungary	18-24	0	29989	0	27496	0	57485	4.61
	25-49	0	240307	0	226782	0	467089	37.44
	50-59	0	181770	0	176335	0	358105	28.71
	60-69	0	103934	0	100727	0	204661	16.41
	70-79	0	60733	0	59595	0	120328	9.65
	80+	0	20225	0	19597	0	39822	3.19
	Unknown	14	0	98	0	112	0	0.00
	All Ages	**14**	**636958**	**98**	**610532**	**112**	**1247490**	**100.00**

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
Iceland	18-24	0	1918	0	1444	0	3362	2.91
	25-49	0	9676	1	8033	1	17709	15.34
	50-59	0	13918	0	12511	0	26429	22.89
	60-69	0	20003	0	18967	0	38970	33.75
	70-79	0	14544	0	14232	0	28776	24.92
	80+	0	118	0	103	0	221	0.19
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**0**	**60177**	**1**	**55290**	**1**	**115467**	**100.00**
Ireland	18-24	-1316	18258	-1474	17822	18537	36080	2.97
	25-49	7493	126412	5629	123232	133517	249644	20.54
	50-59	-1953	71258	-2381	70411	73041	141669	11.66
	60-69	-9536	342884	-9621	340676	340818	683560	56.25
	70-79	19185	52141	18995	51777	56025	103918	8.55
	80+	153	218	139	207	371	425	0.03
	Unknown	-1	4	0	0	-6	4	0.00
	All Ages	**14030**	**611175**	**11287**	**604125**	**622313**	**1215300**	**100.00**
Italy	18-24	0	103625	0	47126	0	150751	0.63
	25-49	0	1148673	0	805803	0	1954476	8.16
	50-59	0	848768	1	600518	1	1449286	6.05
	60-69	1	2035520	0	1909413	1	3944933	16.47
	70-79	0	2215212	0	2109869	0	4325081	18.06
	80+	1	77927	0	72449	1	150376	0.63

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
	Unknown	6429725	6429715	5545178	5544680	11974903	11974395	50.00
	All Ages	**6429727**	**12859440**	**5545179**	**11089858**	**11974906**	**23949298**	**100.00**
Latvia	18-24	0	3251	0	3006	0	6257	2.42
	25-49	0	21776	0	21317	0	43093	16.63
	50-59	0	14430	0	14081	0	28511	11.00
	60-69	0	28272	0	27692	0	55964	21.60
	70-79	0	40426	0	39467	0	79893	30.84
	80+	0	22682	0	22679	0	45361	17.51
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**0**	**130837**	**0**	**128242**	**0**	**259079**	**100.00**
Lithuania	18-24	0	18227	0	16833	0	35060	6.54
	25-49	0	101795	0	97478	0	199273	37.16
	50-59	0	44890	0	43137	0	88027	16.41
	60-69	0	47002	0	45342	0	92344	17.22
	70-79	0	43014	0	41721	0	84735	15.80
	80+	0	18591	0	18251	0	36842	6.87
	Unknown	0	5	0	0	5	5	0.00
	All Ages	**5**	**273524**	**0**	**262762**	**5**	**536286**	**100.00**
Luxembourg	18-24	-4	728	-6	608	-10	1336	1.27
	25-49	-97	21840	-91	18313	-188	40153	38.22
	50-59	3	4647	-1	4507	2	9154	8.71
	60-69	-638	6580	-637	6498	-1275	13078	12.45

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
	70-79	575	19298	573	19074	1148	38372	36.53
	80+	103	1489	100	1462	203	2951	2.81
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**-58**	**54582**	**-62**	**50462**	**-120**	**105044**	**100.00**
Malta	18-24	0	5586	1	5662	1	11248	4.95
	25-49	4	48485	10	47292	14	95777	42.11
	50-59	0	25564	2	25923	2	51487	22.64
	60-69	0	31888	1	32285	1	64173	28.21
	70-79	1	2565	1	2046	2	4611	2.03
	80+	2	77	0	74	2	151	0.07
	Unknown	-10	0	-60	0	-70	0	0.00
	All Ages	**-3**	**114165**	**-45**	**113282**	**-48**	**227447**	**100.00**
Norway	18-24	16	14022	14	385	30	14407	9.76
	25-49	59	73514	51	2151	110	75665	51.25
	50-59	14	35859	14	1095	28	36954	25.03
	60-69	24	18962	17	599	41	19561	13.25
	70-79	8	594	8	207	16	801	0.54
	80+	3	187	4	78	7	265	0.18
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**124**	**143138**	**108**	**4515**	**232**	**147653**	**100.00**
Poland	18-24	37	113598	86	108115	123	221713	4.18
	25-49	274	959005	927	941576	1201	1900581	35.86

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
	50-59	110	457942	444	448567	554	906509	17.11
	60-69	191	1127092	1196	1133546	1387	2260638	42.66
	70-79	14	1247	33	1322	47	2569	0.05
	80+	4	176	7	149	11	325	0.01
	Unknown	3382	3382	3594	3594	6976	6976	0.13
	All Ages	**4012**	**2662442**	**6287**	**2636869**	**10299**	**5299311**	**100.00**
Portugal	18-24	438	13423	313	8507	751	21930	0.97
	25-49	2865	132066	1742	93104	4607	225170	9.94
	50-59	906	112034	252	89303	1158	201337	8.88
	60-69	1026	489484	93	442317	1119	931801	41.12
	70-79	557	433946	-137	412751	420	846697	37.36
	80+	179	23066	22	16007	201	39073	1.72
	Unknown	164	164	152	152	316	316	0.01
	All Ages	**6135**	**1204183**	**2437**	**1062141**	**8572**	**2266324**	**100.00**
Romania	18-24	0	31550	0	29923	0	61473	7.22
	25-49	0	241876	0	232399	0	474275	55.69
	50-59	0	103600	0	100041	0	203641	23.91
	60-69	0	35801	0	35182	0	70983	8.34
	70-79	0	16456	0	15905	0	32361	3.80
	80+	0	4538	0	4341	0	8879	1.04
	Unknown	-239	0	-438	0	-677	0	0.00
	All Ages	**-239**	**433821**	**-438**	**417791**	**-677**	**851612**	**100.00**

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
Slovakia	18-24	2674	11459	2090	10700	4764	22159	2.62
	25-49	14705	193066	11705	187570	26410	380636	45.09
	50-59	296	129800	612	128871	908	258671	30.64
	60-69	-5388	90470	-4153	90789	-9541	181259	21.47
	70-79	-11194	154	-9963	1241	-21157	1395	0.17
	80+	11	21	16	24	27	45	0.01
	Unknown	14	14	11	11	25	25	0.00
	All Ages	**1118**	**424984**	**318**	**419206**	**1436**	**844190**	**100.00**
Slovenia	18-24	-1	9623	0	8933	-1	18556	5.74
	25-49	-6	65258	-8	59303	-14	124561	38.56
	50-59	-72	39885	-69	37876	-141	77761	24.07
	60-69	-205	47299	-195	45987	-400	93286	28.88
	70-79	-47	2791	-48	2607	-95	5398	1.67
	80+	-221	1824	-202	1642	-423	3466	1.07
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**-552**	**166680**	**-522**	**156348**	**-1074**	**323028**	**100.00**
Spain	18-24	57	96235	35	78997	92	175232	1.79
	25-49	421	1024301	247	860561	668	1884862	19.24
	50-59	280	419163	106	350529	386	769692	7.86
	60-69	1380	3566446	-110	3390445	1270	6956891	71.03
	70-79	-62	3927	-31	3816	-93	7743	0.08
	80+	-61	282	-62	213	-123	495	0.01

Table 3 VAXZEVRIA interval and cumulative exposure in EEA based on Doses Administered, by Country and split by Age group as of 28 December 2022

Country	Age groups (in years)	Dose 1		Dose 2		Total doses		Percentage (%)
		Interval	Cumulative	Interval	Cumulative	Interval	Cumulative	Cumulative
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**2015**	**5110354**	**185**	**4684561**	**2200**	**9794915**	**100.00**
Sweden	18-24	6	15331	-16	5205	-10	20536	1.55
	25-49	0	110762	-6	42942	-6	153704	11.63
	50-59	-62	54979	-16	23123	-78	78102	5.91
	60-69	-618	189707	-569	168476	-1187	358183	27.09
	70-79	-2224	327269	-2114	318835	-4338	646104	48.87
	80+	-787	33298	-740	32123	-1527	65421	4.95
	Unknown	0	0	0	0	0	0	0.00
	All Ages	**-3685**	**731346**	**-3461**	**590704**	**-7146**	**1322050**	**100.00**

The weekly administered data from European Centre for Disease Prevention and Control (ECDC) is stratified by age and an 'unknown' category which is subject to change every week. The administered data for the PBRER reporting interval is derived by subtracting the previous report's cumulative from current cumulative values (Current Cumulative - Previous Cumulative = Current Interval) across all the Countries. Therefore, the negative values here is due to a greater cumulative value (from respective age groups) from previous report in comparison to current report.

Table 4 VAXZEVRIA interval and cumulative exposure for UK based on Doses Administered, split by Age group, Dose number and Gender as of 28 December 2022

Vaccination Events By Cohort (Age Group)	United Kingdom	
	Interval	Cumulative
80+ 1st Dose Female	-137096	816042
80+ 2nd Dose Female	-114606	807226
80+ 1st Dose Male	-82313	513629
80+ 2nd Dose Male	-67911	508562
80+ 1st Dose Unspecified	-1	10
80+ 2nd Dose Unspecified	-1	9
75-79 1st Dose Female	-43860	780996
75-79 2nd Dose Female	-39144	774970
75-79 1st Dose Male	-46893	683876
75-79 2nd Dose Male	-41430	679328
75-79 1st Dose Unspecified	-3	10
75-79 2nd Dose Unspecified	-3	10
70-74 1st Dose Female	-72681	959846
70-74 2nd Dose Female	-68922	952289
70-74 1st Dose Male	-75272	888364
70-74 2nd Dose Male	-70635	882151
70-74 1st Dose Unspecified	2	25
70-74 2nd Dose Unspecified	2	23
65-69 1st Dose Female	-54021	1053850

Table 4 VAXZEVRIA interval and cumulative exposure for UK based on Doses Administered, split by Age group, Dose number and Gender as of 28 December 2022

Vaccination Events By Cohort (Age Group)	United Kingdom	
	Interval	Cumulative
65-69 2nd Dose Female	-51162	1043276
65-69 1st Dose Male	-57583	1041024
65-69 2nd Dose Male	-53763	1031401
65-69 1st Dose Unspecified	1	26
65-69 2nd Dose Unspecified	3	23
60-64 1st Dose Female	-61825	1347739
60-64 2nd Dose Female	-58928	1330938
60-64 1st Dose Male	-68795	1437890
60-64 2nd Dose Male	-64844	1420774
60-64 1st Dose Unspecified	1	42
60-64 2nd Dose Unspecified	4	37
55-59 1st Dose Female	-79303	1523422
55-59 2nd Dose Female	-76425	1501114
55-59 1st Dose Male	-93981	1680361
55-59 2nd Dose Male	-89533	1654629
55-59 1st Dose Unspecified	-8	58
55-59 2nd Dose Unspecified	3	53
50-54 1st Dose Female	-90025	1469180
50-54 2nd Dose Female	-86957	1443357

Table 4 VAXZEVRIA interval and cumulative exposure for UK based on Doses Administered, split by Age group, Dose number and Gender as of 28 December 2022

Vaccination Events By Cohort (Age Group)	United Kingdom	
	Interval	Cumulative
50-54 1st Dose Male	-111560	1602136
50-54 2nd Dose Male	-106244	1570393
50-54 1st Dose Unspecified	-26	69
50-54 2nd Dose Unspecified	-12	64
45-49 1st Dose Female	-75244	1197055
45-49 2nd Dose Female	-72513	1170685
45-49 1st Dose Male	-91066	1270420
45-49 2nd Dose Male	-86170	1236426
45-49 1st Dose Unspecified	-24	76
45-49 2nd Dose Unspecified	-4	72
40-44 1st Dose Female	-84439	1034446
40-44 2nd Dose Female	-81208	1005609
40-44 1st Dose Male	-105109	1033782
40-44 2nd Dose Male	-99061	999512
40-44 1st Dose Unspecified	-29	85
40-44 2nd Dose Unspecified	-4	74
35-39 1st Dose Female	-34900	534169
35-39 2nd Dose Female	-33107	515550
35-39 1st Dose Male	-32071	404797

Table 4 VAXZEVRIA interval and cumulative exposure for UK based on Doses Administered, split by Age group, Dose number and Gender as of 28 December 2022

Vaccination Events By Cohort (Age Group)	United Kingdom	
	Interval	Cumulative
35-39 2nd Dose Male	-29540	390760
35-39 1st Dose Unspecified	-17	65
35-39 2nd Dose Unspecified	-11	58
30-34 1st Dose Female	-31780	429896
30-34 2nd Dose Female	-29758	411237
30-34 1st Dose Male	-29050	315597
30-34 2nd Dose Male	-26551	302791
30-34 1st Dose Unspecified	-19	85
30-34 2nd Dose Unspecified	-10	77
25-29 1st Dose Female	-22610	311794
25-29 2nd Dose Female	-21108	298492
25-29 1st Dose Male	-21374	226232
25-29 2nd Dose Male	-19605	216655
25-29 1st Dose Unspecified	-1	120
25-29 2nd Dose Unspecified	6	110
20-24 1st Dose Female	-19978	235487
20-24 2nd Dose Female	-18796	226277
20-24 1st Dose Male	-18182	171350
20-24 2nd Dose Male	-16748	164091

Table 4 VAXZEVRIA interval and cumulative exposure for UK based on Doses Administered, split by Age group, Dose number and Gender as of 28 December 2022

Vaccination Events By Cohort (Age Group)	United Kingdom	
	Interval	Cumulative
20-24 1st Dose Unspecified	-14	101
20-24 2nd Dose Unspecified	-10	94
16-19 1st Dose Female	-10109	20273
16-19 2nd Dose Female	-9716	19277
16-19 1st Dose Male	-8108	17158
16-19 2nd Dose Male	-7729	16238
16-19 1st Dose Unspecified	2	9
16-19 2nd Dose Unspecified	1	9
10-15 1st Dose Female	-12	101
10-15 2nd Dose Female	-2	71
10-15 1st Dose Male	-16	134
10-15 2nd Dose Male	-10	87
10-15 1st Dose Unspecified	0	0
10-15 2nd Dose Unspecified	0	0
5-9 1st Dose Female	-2	17
5-9 2nd Dose Female	-1	10
5-9 1st Dose Male	-1	25
5-9 2nd Dose Male	0	22
5-9 1st Dose Unspecified	0	0

Table 4 VAXZEVRIA interval and cumulative exposure for UK based on Doses Administered, split by Age group, Dose number and Gender as of 28 December 2022

Vaccination Events By Cohort (Age Group)	United Kingdom	
	Interval	**Cumulative**
5-9 2nd Dose Unspecified	0	0
1-4 1st Dose Female	-11	3
1-4 2nd Dose Female	-3	1
1-4 1st Dose Male	-13	3
1-4 2nd Dose Male	-3	0
1-4 1st Dose Unspecified	1	1
1-4 2nd Dose Unspecified	0	0
Age Unknown 1st Dose Female	-1	61
Age Unknown 2nd Dose Female	1	39
Age Unknown 1st Dose Male	-1	30
Age Unknown 2nd Dose Male	1	25
Age Unknown 1st Dose Unspecified	1652537	1723434
Age Unknown 2nd Dose Unspecified	1534648	1566374
TOTAL 1st Dose	**-6883**	**24725401**
TOTAL 2nd Dose	**-7519**	**24141350**

The administered data for the PBRER reporting interval is derived by subtracting the previous report's cumulative from current cumulative values (Current Cumulative - Previous Cumulative = Current Interval) across all the Countries. Therefore, the negative values here is due to a greater cumulative value (from respective age groups) from previous report in comparison to current report.

Table 5 VAXZEVRIA cumulative exposure in Australia based on Doses Administered, split by Age group, Dose number as of 28 December 2022

State	Dose 1	Dose 2	Total
Australia			
Under 40 Years	846717	827315	1674032
40-49 Years	304146	297337	601483
50-59 Years	987525	977732	1965257
60-69 Years	1960465	1946075	3906540
Above 70 Years	2611829	2595613	5207442
Total	**6710682**	**6644072**	**13354754**

Gender wise data for Australia was not available for current report.

Table 6 VAXZEVRIA cumulative exposure in Brazil based on Doses Administered, split by Age group, Dose number as of 28 December 2022

State	Dose 1	Dose 2	Additional Dose	Booster dose	2nd Booster Dose	Single dose	Total
Brazil							
6 months–2 years	399	260	27	165	122		973
3-4 Years	615	391	32	127	165		1330
5-11 Years	3281	4234	152	1695	869		10231
12-17 Years	16021	14168	4695	51949	3763	6	90602
18-19 Years	894950	647108	32503	761167	124646	5	2460379
20-24 Years	2880580	2387773	80248	1869163	480919	10	7698693
25-29 Years	3590718	3065455	82263	1916073	613910	16	9268435
30-34 Years	4815940	4173090	84390	1924014	916528	15	11913977
35-39 Years	6645716	5764651	87549	2021593	1204245	14	15723768

Table 6 VAXZEVRIA cumulative exposure in Brazil based on Doses Administered, split by Age group, Dose number as of 28 December 2022

State	Dose 1	Dose 2	Additional Dose	Booster dose	2nd Booster Dose	Single dose	Total
40-44 Years	7388907	6576635	103357	2019739	1861823	20	17950481
45-49 Years	6880964	6254642	87317	1692306	1807664	23	16722916
50-54 Years	7627614	6889022	81920	1458055	1805291	23	17861925
55-59 Years	8421501	7896680	77485	1235881	1899117	33	19530697
60-64 Years	7277048	7107516	50888	714812	1443003	14	16593281
65-69 Years	2797365	2865864	37107	401389	1145846	11	7247582
70-74 Years	536493	528069	31342	199430	849913	4	2145251
75-79 Years	597458	547708	21391	124904	557328	6	1848795
≥80 years	1894259	1717736	36732	192299	663952	3	4504981
Total	**62269829**	**56441002**	**899398**	**16584761**	**15379104**	**203**	**151574297**

Table 7 VAXZEVRIA cumulative exposure in Brazil based on Doses Administered, split by gender 28 December 2022

Gender	Dose
Male	70436607
Female	81073593
Others	64097
Total	**151574297**

PBRER Appendix 7 SMQ & MedDRA list used for AESIs & Safety Concerns in the RMP	
Medicinal Product	VAXZEVRIA (ChAdOx1-S [recombinant])
Period covered	29 June 2022 to 28 December 2022
Date	17 February 2023

Appendix 7

Standardised MedDRA Queries (SMQ) and MedDRA search term (MST) lists used for Adverse Events of Special Interest (AESIs) and Safety Concerns in the VAXZEVRIA Risk Management Plan (RMP)

1 GENERAL CONSIDERATIONS

Table 1 below provides a list of the Adverse Events of Special Interest (AESI) and Safety concerns in the latest approved VAXZEVRIA Core Risk Management Plan (RMP) Version 8 and European Union (EU) RMP Version 6 together with the associated MedDRA Preferred Terms (PTs).

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
Other system	***Vaccine associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)*** [a]	Respiratory system: Acute lung injury; Acute respiratory failure; Coronavirus pneumonia; COVID-19 pneumonia; Immune-mediated lung disease; Mechanical ventilation; Pneumonia; Pneumonitis; Post-acute COVID-19 syndrome; Pulmonary haemorrhage; Respiratory failure; SARS-CoV-2 sepsis (Acute respiratory distress syndrome listed under ARDS below); Vaccine associated enhanced disease; Vaccine associated enhanced respiratory disease; Vaccine derived SARS-CoV-2 infection Cardiovascular system: All events covered under cardiovascular system and Embolic and thrombotic events Hematopoietic and Immune system: Coagulopathy; Fibrinogen degradation products increased; ISTH score for disseminated intravascular coagulation; Septic cerebral embolism; Septic coagulopathy; (Other terms are covered under Embolic and thrombotic events) Inflammatory markers: Cytokine abnormal; Cytokine release syndrome; Cytokine storm; Cytokine increased Renal system: PTs covered under acute kidney injury Gastrointestinal and hepatic system: PTs covered under acute liver injury Central Nervous System: Terms are covered under immune mediated neurological conditions Other: Multiple organ dysfunction syndrome; Organ failure; Immune-mediated myositis (PT: Muscle necrosis and Necrotising myositis will covered under AESI Rhabdomyolysis); Autoimmune myositis (Death covered under sudden death; Arthritis-covered under Rheumatoid arthritis; Polyarthritis)
	Sudden death	Sudden death; Sudden cardiac death; Sudden unexplained death in epilepsy
	Multisystem inflammatory syndrome in children/adults (MIS-C/A)	Multisystem inflammatory syndrome in children; Kawasaki's disease; Conjunctivitis viral; Conjunctivitis; Hypotension; Distributive shock; Endotoxic shock; Hypovolaemic shock; Septic shock; Toxic shock syndrome; Hypotensive crisis; Post procedural hypotension; Procedural hypotension; Systemic inflammatory response

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		syndrome; Multisystem inflammatory syndrome in adults; Multisystem inflammatory syndrome; Haemophagocytic lymphohistiocytosis
	Anosmia/ageusia	Anosmia; ageusia
Respiratory	Acute respiratory distress syndrome (ARDS)	Acute respiratory distress syndrome
Neurologic	***Immune mediated neurological conditions*** [a] Guillain-Barré syndrome Peripheral neuropathy and polyneuropathy Multiple sclerosis, transverse myelitis and other demyelinating disorders Optic neuritis/neuromyelitis optica spectrum disorder Encephalitis (inc. acute disseminated encephalomyelitis [ADEM]) / Non-infectious encephalopathy	Immune-mediated neurological disorder; Acute disseminated encephalomyelitis; Acute haemorrhagic leukoencephalitis; Acute motor axonal neuropathy; Acute motor-sensory axonal neuropathy; Acute painful neuropathy of rapid glycaemic control; Acute polyneuropathy; Amyotrophy; Angiopathic neuropathy; Anti-myelin-associated glycoprotein associated polyneuropathy; Autoimmune demyelinating disease; Autoimmune neuropathy; Axonal and demyelinating polyneuropathy; Axonal neuropathy; Bickerstaff's encephalitis; Biopsy peripheral nerve abnormal; Chronic inflammatory demyelinating polyradiculoneuropathy; Clinically isolated syndrome; Concentric sclerosis; Decreased vibratory sense; Demyelinating polyneuropathy; Demyelination; Encephalitis periaxialis diffusa; Encephalomyelitis; Expanded disability status scale score decreased; Expanded disability status scale score increased; Guillain-Barre syndrome; Hypergammaglobulinaemia benign monoclonal; Immune-mediated neuropathy; Ischaemic neuropathy; Joint position sense decreased; Leukoencephalomyelitis; Leukoencephalopathy; Lewis-Sumner syndrome; Loss of proprioception; Marburg's variant multiple sclerosis; Marchiafava-Bignami disease; MELAS syndrome; Miller Fisher syndrome; Multifocal motor neuropathy; Multiple sclerosis; Multiple sclerosis relapse; Multiple sclerosis relapse prophylaxis; Myelitis; Myelitis transverse; Myelopathy; Myoclonic epilepsy and ragged-red fibres; Nerve conduction studies abnormal; Neuralgia; Neuritis; Neuromyelitis optica pseudo relapse; Neuromyelitis optica spectrum disorder; Neuronal neuropathy; Neuropathic muscular atrophy; Neuropathy peripheral; Neuropathy, ataxia, retinitis pigmentosa syndrome; Noninfectious myelitis; Noninfective encephalomyelitis; Notalgia paraesthetica; Optic neuritis; Osmotic demyelination syndrome; Paroxysmal extreme

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		pain disorder; Peripheral motor neuropathy; Peripheral nervous system function test abnormal; Peripheral sensorimotor neuropathy; Peripheral sensory neuropathy; Polyneuropathy; Polyneuropathy chronic; Polyneuropathy idiopathic progressive; Primary progressive multiple sclerosis; Progressive multifocal leukoencephalopathy; Progressive multiple sclerosis; Progressive relapsing multiple sclerosis; Radiation neuropathy; Relapsing multiple sclerosis; Relapsing-remitting multiple sclerosis; Secondary progressive multiple sclerosis; Sensorimotor disorder; Sensory disturbance; Sensory loss; Small fibre neuropathy; Subacute inflammatory demyelinating polyneuropathy; Tick paralysis; Toxic leukoencephalopathy; Tumefactive multiple sclerosis; Zika virus associated Guillain Barre syndrome; Acute encephalitis with refractory; repetitive partial seizures; Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids; Encephalitis; Encephalitis allergic; Encephalitis autoimmune; Encephalitis brain stem; Encephalitis haemorrhagic; Encephalitis post immunisation; Encephalitis toxic; Immune-mediated encephalitis; Limbic encephalitis; Noninfective encephalitis; Panencephalitis; Paraneoplastic encephalomyelitis; Rasmussen encephalitis; Autoimmune encephalopathy; Encephalopathy; Encephalopathy allergic; Encephalopathy neonatal; Gerstmann Straussler Scheinker syndrome; Hashimoto's encephalopathy; Hypertensive encephalopathy; Hypoxic-ischaemic encephalopathy; Immune-mediated encephalopathy; Labrune syndrome; Mitochondrial encephalomyopathy; Mitochondrial neurogastrointestinal encephalopathy; Opsoclonus myoclonus; Periventricular leukomalacia; Posterior reversible encephalopathy syndrome; Postresuscitation encephalopathy; Purpura cerebri; Septic encephalopathy; Subacute myelo-opticoneuropathy; Lumbosacral radiculoplexus neuropathy; Acute necrotising myelitis; Myelin oligodendrocyte glycoprotein antibody-associated disease; Progressive encephalopathy; Hypsarrhythmia and optic atrophy syndrome; Large fibre neuropathy; Ischaemic demyelination; Polyradiculoneuropathy; Ascending flaccid paralysis

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
	Myasthenia gravis	Myasthenia gravis; Myasthenia gravis crisis; Myasthenic syndrome; Immune-mediated myasthenia gravis
	Bell's palsy	Bell's palsy; Facial paralysis; Facial paresis
	Generalised convulsions (seizures)	Clonic convulsion; Epilepsy; Febrile convulsion; Generalised tonic-clonic seizure; Myoclonic epilepsy; Seizure; Status epilepticus; Tonic convulsion; Epilepsia partialis continua; Photosensitive seizure; PURA syndrome; Febrile status epilepticus; New onset refractory status epilepticus; Vertiginous epilepsy
	Narcolepsy	Cataplexy; Narcolepsy
Eye disorder	Acute Macular neuroretinopathy (AMN) / Acute macular outer retinopathy (AMOR)/Paracentral acute middle maculopathy (PAMM)	Acute macular neuroretinopathy
Cardiovascular system	Myocardial infarction	Acute cardiac event; Acute coronary syndrome; Angina unstable; Blood creatine phosphokinase MB abnormal; Blood creatine phosphokinase MB increased; Kounis syndrome; Myocardial reperfusion injury; Myocardial stunning; Periprocedural myocardial infarction; Postinfarction angina; Troponin I increased; Troponin increased; Troponin T increased (other events covered under Embolic and thrombotic events)
	Postural orthostatic tachycardia syndrome	Postural orthostatic tachycardia syndrome
	Myocarditis/pericarditis	Myocarditis; Pericarditis; Autoimmune myocarditis; Eosinophilic myocarditis; Giant cell myocarditis; Hypersensitivity myocarditis; Immune-mediated myocarditis; Lupus myocarditis; Myocarditis; Myocarditis post infection; Autoimmune pericarditis; Pericarditis; Pericarditis adhesive; Pericarditis constrictive; Pericarditis lupus; Pericarditis uraemic; Pleuropericarditis; Myopericarditis; Chronic myocarditis; Immune-mediated pericarditis

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
	Acute cardiac injury including microangiopathy, cardiogenic shock, heart failure, stress cardiomyopathy	Acute left ventricular failure; Acute pulmonary oedema; Acute right ventricular failure; Cardiac asthma; Cardiac failure; Cardiac failure acute; Cardiac failure chronic; Cardiac failure congestive; Cardiac failure high output; Cardiogenic shock; Cardiohepatic syndrome; Cardiopulmonary failure; Cardiorenal syndrome; Chronic left ventricular failure; Chronic right ventricular failure; Congestive hepatopathy; Cor pulmonale; Cor pulmonale acute; Cor pulmonale chronic; Ejection fraction decreased; Hepatojugular reflux; Left ventricular failure; Low cardiac output syndrome; Neonatal cardiac failure; Obstructive shock; Pulmonary oedema; Pulmonary oedema neonatal; Radiation associated cardiac failure; Right ventricular ejection fraction decreased; Right ventricular failure; Ventricular failure; Stress cardiomyopathy; Microangiopathy
Circulatory system/ Haematological	***Thrombosis with thrombocytopenia*** syndrome (TTS) [a]	Co-reported PTs from HLT of "Thrombocytopenias"; Standardised MedDRA Queries (SMQ) of "Hematopoietic Thrombocytopenia-Narrow" and SMQ of "Embolic and thrombotic events
	Embolic and thrombotic events (Thrombosis) [a]	**Embolic and thrombotic events, arterial** Acute aortic syndrome; Acute myocardial infarction; Arterial thrombosis; Cerebellar artery occlusion; Cerebellar artery thrombosis; Cerebral artery embolism; Cerebral artery occlusion; Cerebral artery thrombosis; Coronary artery embolism; Coronary artery occlusion; Coronary artery reocclusion; Coronary artery thrombosis; Coronary vascular graft occlusion; Embolism arterial; Femoral artery embolism; Hepatic artery embolism; Hepatic artery occlusion; Hepatic artery thrombosis; Iliac artery embolism; Iliac artery occlusion; Ischaemic cerebral infarction; Ischaemic stroke; Mesenteric arterial occlusion; Mesenteric arteriosclerosis; Mesenteric artery embolism; Mesenteric artery thrombosis; Myocardial infarction; Myocardial necrosis; Opthalmic artery occlusion; Papillary muscle infarction; Peripheral artery occlusion; Peripheral artery thrombosis; Peripheral embolism; Post procedural myocardial infarction; Precerebral artery embolism; Pulmonary artery occlusion; Pulmonary artery thrombosis; Renal artery occlusion; Renal artery thrombosis; Renal embolism; Renal-

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		limited thrombotic microangiopathy; Retinal artery embolism; Retinal artery occlusion; Retinal artery thrombosis; Silent myocardial infarction; Spinal artery embolism; Spinal artery thrombosis; Splenic artery thrombosis; Splenic embolism; Subclavian artery embolism; Subclavian artery occlusion; Subclavian artery thrombosis; Thromboembolectomy; Thrombotic microangiopathy; Thrombotic thrombocytopenic purpura; Transient ischaemic attack; Vertebral artery occlusion; Vertebral artery thrombosis; Vertebrobasilar stroke; Aneurysm thrombosis; Aortic aneurysm thrombosis **Embolic and thrombotic events, venous** Aseptic cavernous sinus thrombosis; Budd-Chiari syndrome; Cavernous sinus thrombosis; Cerebral venous sinus thrombosis; Cerebral venous thrombosis; Deep vein thrombosis; Embolism venous; Hepatic vein occlusion; Hepatic vein thrombosis; Iliac vein occlusion; Inferior vena caval occlusion; Jugular vein occlusion; Jugular vein thrombosis; Mesenteric vein thrombosis; Mesenteric venous occlusion; Ophthalmic vein thrombosis; Pelvic venous thrombosis; Portal vein occlusion; Portal vein thrombosis; Pulmonary embolism; Pulmonary infarction; Pulmonary microemboli; Pulmonary thrombosis; Pulmonary vein occlusion; Pulmonary venous thrombosis; Renal vein occlusion; Renal vein thrombosis; Retinal vein occlusion; Retinal vein thrombosis; Splenic vein occlusion; Splenic vein thrombosis; Superior sagittal sinus thrombosis; Superior vena cava occlusion; Transverse sinus thrombosis; Venous thrombosis; Peripheral vein thrombosis; Sigmoid sinus thrombosis; Ophthalmic vascular thrombosis; Mesenteric vein embolism; Spermatic vein thrombosis **Embolic and Thrombotic events, vessel type unspecified and mixed arterial and venous** Basal ganglia stroke; Brain stem infarction; Brain stem stroke; Benedikt's syndrome; Cerebellar infarction; Cerebral infarction; Cerebellar stroke; Cerebral ischaemia; Cerebral microembolism; Cerebral microinfarction; Cerebral thrombosis; Cerebral vascular occlusion; Cerebrovascular accident; Choroidal infarction; Coronary bypass

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		thrombosis; Disseminated intravascular coagulation; Embolic cerebellar infarction; Embolic cerebral infarction; Embolic stroke; Haemorrhagic adrenal infarction; Haemorrhagic cerebral infarction; Haemorrhagic infarction; Haemorrhagic stroke; Haemorrhagic transformation stroke; Heparin-induced thrombocytopenia; Lacunar stroke; Microembolism; Pituitary infarction; Post procedural stroke; Spinal stroke; Stroke in evolution; Strokectomy; Thrombotic stroke; Thrombosis with thrombocytopenia syndrome; Weber's syndrome; Metabolic stroke; Thalamic stroke
	Thrombocytopenia including immune thrombocytopenia	Acquired amegakaryocytic thrombocytopenia; Autoimmune heparin-induced thrombocytopenia; Immune thrombocytopenia; Non-immune heparin associated thrombocytopenia; Platelet production decreased; Spontaneous heparin-induced thrombocytopenia syndrome; Thrombocytopenia; Thrombocytopenia neonatal; Thrombocytopenic purpura; Megakaryocytes decreased; Platelet count decreased; Platelet maturation arrest; Platelet toxicity; Megakaryocytes abnormal; Platelet count abnormal; Platelet disorder; Plateletcrit abnormal; Plateletcrit decreased; Dysmegakaryopoiesis; Radiation thrombocytopenia (Heparin-induced thrombocytopenia, Thrombotic thrombocytopenic purpura, and Thrombosis with thrombocytopenia syndrome are included under Embolic and thrombotic events)
	Capillary leak syndrome	Capillary leak syndrome
Gastrointestinal	Acute liver injury	Hepatic necrosis; Acute yellow liver atrophy; Coma hepatic; Hepatic encephalopathy; Hepatitis; Hepatitis toxic; Hepatic failure; Acute hepatic failure; Hepatitis acute; Subacute hepatic failure; Liver injury; Autoimmune hepatitis; Allergic hepatitis; Drug-induced liver injury; Immune-mediated hepatic disorder; Immune-mediated hepatitis; Hepatotoxicity; Hepatocellular injury; Hepatitis fulminant
	Acute pancreatitis	Cullen's sign; Grey Turner's sign; Haemorrhagic necrotic pancreatitis; Hereditary pancreatitis; Immune-mediated pancreatitis; Ischaemic pancreatitis; Oedematous pancreatitis; Pancreatic abscess; Pancreatic cyst drainage; Pancreatic haemorrhage;; Pancreatic phlegmon; Pancreatic pseudoaneurysm; Pancreatic pseudocyst; Pancreatic pseudocyst drainage; Pancreatic pseudocyst haemorrhage; Pancreatic pseudocyst

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		rupture; Pancreatitis; Pancreatitis acute; Pancreatitis haemorrhagic; Pancreatitis necrotising; Pancreatitis relapsing; Pancreatorenal syndrome; Subacute pancreatitis; Walled-off pancreatic necrosis
Renal	Acute kidney injury	Acute kidney injury; Haemolytic uraemic syndrome; Anuria; Crush syndrome; Nephropathy; Hypertensive nephropathy; Renal injury; Nephritic syndrome; Nephritis; Hepatorenal failure; Hepatorenal syndrome; Nephropathy toxic; Renal tubular necrosis; Tubulointerstitial nephritis; Oliguria; Renal failure; Hyperphosphataemia; Hypermagnesaemia; Metabolic acidosis; Renal impairment
Musculoskeletal system	Acute aseptic arthritis	Acute aseptic arthritis; Rheumatoid arthritis; Polyarthritis; Arthritis viral; Arthritis allergic; Autoimmune arthritis; Immune-mediated arthritis; Crystal arthropathy; Gout; Chondrocalcinosis; Gouty arthritis; Paradoxical psoriatic arthritis
	Fibromyalgia	Fibromyalgia
	Rhabdomyolysis	Muscle necrosis; Myoglobin blood increased; Myoglobin blood present; Myoglobin urine present; Myoglobinaemia; Myoglobinuria; Myopathy; Myopathy toxic; Muscle infarction; Necrotising myositis; Rhabdomyolysis; Thyrotoxic myopathy
Immunological	Autoimmune thyroiditis	Autoimmune thyroiditis; Immune-mediated thyroiditis; Silent thyroiditis; Thyroiditis; Thyroiditis acute; Thyroiditis subacute
	Anaphylaxis [a]	Hypersensitivity; Anaphylactic reaction; Anaphylactic shock; Anaphylactic transfusion reaction; Anaphylactoid reaction; Anaphylactoid shock; Circulatory collapse; Dialysis membrane reaction; Procedural shock; Shock; Shock symptom; Type I hypersensitivity; Acquired C1 inhibitor deficiency; Allergic oedema; Angioedema; Circumoral oedema; Circumoral swelling; Conjunctival oedema; Corneal oedema; Epiglottic oedema; Eye oedema; Eye swelling; Eyelid oedema; Face oedema; Gingival oedema; Gingival swelling; Gleich's syndrome; Hereditary angioedema; Hereditary angioedema with C1 esterase inhibitor deficiency; Idiopathic angioedema; Idiopathic urticaria; Intestinal angioedema; Laryngeal oedema; Laryngotracheal oedema; Limbal swelling; Lip oedema; Lip swelling; Mouth

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		swelling; Oculorespiratory syndrome; Oedema mouth; Oropharyngeal oedema; Oropharyngeal swelling; Palatal oedema; Palatal swelling; Periorbital oedema; Periorbital swelling; Pharyngeal oedema; Pharyngeal swelling; Scleral oedema; Swelling face; Swelling of eyelid; Swollen tongue; Tongue oedema; Tracheal oedema; Urticaria; Urticaria cholinergic; Urticaria chronic; Urticaria papular
	Type III hypersensitivity reactions	Glomerulonephritis; Glomerulonephritis acute; Cryoglobulinaemia; Type III immune complex mediated reaction; Henoch-Schonlein purpura; Henoch-Schonlein purpura nephritis; Polyarteritis nodosa; Hypersensitivity vasculitis
	Giant Cell Arteritis	Giant cell arteritis
General	Chronic Fatigue Syndrome/ME/PVFS	Chronic fatigue syndrome; Post viral fatigue syndrome
Pregnancy /Foetal /Neonatal	Pregnancy outcome - Maternal	Premature labour; Gestational Diabetes; Preeclampsia; Eclampsia; Placenta praevia; Maternal death affecting foetus; Abortion spontaneous; Foetal-maternal haemorrhage; Threatened uterine rupture; Uterine rupture; Vasa praevia; Caesarean section; Amniotic cavity infection; Maternal death
	Pregnancy outcome - Neonates	Foetal distress syndrome; Acrocephalosyndactyly; Amniotic band syndrome; Amniotic cavity infection; Anencephaly; Lissencephaly; Annular pancreas; Anomalous pulmonary venous connection; Anophthalmos; Anorectal malformation; Anotia; Aortic valve stenosis; Aorticopulmonary septal defect; Arnold-Chiari malformation; Arteriovenous malformation; Atrial septal defect; Atrioventricular septal defect; Auditory neuropathy spectrum disorder; Brain malformation; Breast malformation; Cardiac septal defect; Cataract congenital; Cerebral arteriovenous malformation haemorrhagic; Cerebral cavernous malformation; Cerebrovascular arteriovenous malformation; Choanal atresia; Cleft lip; Cleft lip and palate; Cleft palate; Cloacal exstrophy; Coarctation of the aorta; Congenital absence of bile ducts; Congenital arterial malformation; Congenital cerebral haemangioma; Congenital coronary artery malformation; Congenital cystic kidney disease; Congenital diaphragmatic hernia; Congenital ectopic bladder; Congenital eye disorder; Congenital eyelid malformation; Congenital foot malformation; Congenital genital

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		malformation; Congenital genital malformation female; Congenital genital malformation male; Congenital hand malformation; Congenital hearing disorder; Congenital heart valve disorder; Congenital heart valve incompetence; Congenital hydrocephalus; Congenital hydronephrosis; Congenital intestinal malformation; Congenital jaw malformation; Congenital joint malformation; Congenital large intestinal atresia; Congenital lymphoedema; Congenital megacolon; Congenital mitral valve incompetence; Congenital mitral valve stenosis; Congenital nose malformation; Congenital oesophageal stenosis; Congenital oral malformation; Congenital pulmonary artery anomaly; Congenital pulmonary valve atresia; Congenital rubella infection; Congenital rubella syndrome; Congenital skin disorder; Congenital small intestinal atresia; Congenital syphilis; Congenital tricuspid valve atresia; Congenital vesicoureteric reflux; Conjoined twins; Constricted ear deformity; Craniorachischisis; Craniosynostosis; Cryptorchism; Cystic lymphangioma; Deaf mutism; Deafness congenital; Death neonatal; Developmental glaucoma; Developmental hip dysplasia; Double outlet right ventricle; Duodenal atresia; Dysmorphism; Ear malformation; Ebstein's anomaly; Encephalocele; Epispadias; Exomphalos; Foetal alcohol syndrome; Foetal anticonvulsant syndrome; Foetal growth restriction; Foetal malformation; Gastrointestinal arteriovenous malformation; Gastrointestinal malformation; Gastroschisis; Genitalia external ambiguous; Haemangioma congenital; Haemangioma of retina; Haemorrhagic arteriovenous malformation; Hepatic arteriovenous malformation; Heterotaxia; Holoprosencephaly; Hydrops foetalis; Hypoplastic left heart syndrome; Hypoplastic right heart syndrome; Hypospadias; Iniencephaly; Interruption of aortic arch; Intestinal atresia; Kidney malformation; Limb reduction defect; Low birth weight baby; Malformation biliary; Malformation venous; Microcephaly; Microencephaly; Microphthalmos; Microtia; Mitral valve atresia; Mitral valve hypoplasia; Multiple gastrointestinal atresias; Neural tube defect; Oesophageal atresia; Parachute mitral valve; Patent ductus arteriosus; Polydactyly; Porencephaly; Premature baby; Pulmonary aplasia; Pulmonary artery atresia; Pulmonary artery stenosis congenital; Pulmonary malformation; Pulmonary valve

Table 1 Preferred Terms (PTs) for the AESI and Safety concerns in the VAXZEVRIA Core/EU RMP Safety Concerns

Body System/ Classification	Medical Concept	PTs
		stenosis congenital; Pyloric stenosis; Rectal atresia; Renal aplasia; Renal arteriovenous malformation; Renal dysplasia; Renal failure neonatal; Renal hypoplasia; Respiratory tract malformation; Retinal arteriovenous malformation; Schizencephaly; Skeletal dysplasia; Skin malformation; Spina bifida; Spina bifida cystica; Spina bifida occulta; Spleen malformation; Stillbirth; Syndactyly; Talipes; Fallot's tetralogy; Thyroid malformation; Tracheo-oesophageal fistula; Transposition of the great vessels; Truncus arteriosus persistent; Umbilical malformation; Univentricular heart; Urethral valves; Urinary tract malformation; VACTERL syndrome; Vascular malformation; Vein of Galen aneurysmal malformation; Venolymphatic malformation; Ventricular septal defect; Vallecular cyst; Foetal vascular malperfusion; Congenital musculoskeletal disorder of limbs; Congenital musculoskeletal disorder of skull; Congenital musculoskeletal disorder of spine; Congenital female genital tract fistula; Oculo-digito-oesophageal-duodenal syndrome; Congenital musculoskeletal disorder of head and neck; Macrophthalmos; Congenital female reproductive tract disorder; Congenital musculoskeletal disorder; Congenital laryngeal malformation; Athelia; Congenital vocal cord paralysis; Congenital subglottic stenosis; Congenital vena cava stenosis; Aphallia; Congenital connective tissue disorder; Congenital musculoskeletal disorder of trunk; Congenital anisocoria; Congenital lip pits; Pleural malformation; Arhinencephaly; Beaver tail liver; Congenital ectopic spleen; Congenital pulmonary airway malformation; Vertebral artery fenestration; Foetal cardiac function test abnormal
Skin	Erythema multiforme	Erythema multiforme
	Chilblain – like lesions	Chillblains

[a] Medical concepts in bold italics are also considered as safety concerns in Core/EU RMP for VAXZEVRIA.

ADEM Acute Disseminated Encephalomyelitis, AESI Adverse Events of Special Interest, AMN Acute Macular Neuroretinopathy, AMOR Acute macular outer retinopathy; ARDS Acute Respiratory Distress Syndrome, COVID-19 coronavirus disease of 2019; HLT High-Level Terms, ISTH The International Society on Thrombosis and Haemostasis, MB Myocardial Band, ME Myalgic Encephalomyelitis, MedDRA Medical Dictionary for Regulatory Activities; MELAS Mitochondrial Encephalopathy Lactic Acidosis and Stroke-like episodes, MIS-C/A Multisystem Inflammatory Syndrome In Children/Adults, PAMM Paracentral acute middle maculopathy, PTs Preferred Terms, PVFS Post Viral Fatigue Syndrome, RMP Risk Management Plan, SARS-CoV-2 Severe Acute Respiratory Coronavirus 2, SMQ Standardised MedDRA Queries, TTS Thrombosis with thrombocytopenia syndrome; VAED Vaccine Associated Enhanced Disease, VAERD Vaccine-Associated Enhanced Respiratory Disease.

PBRER 8 Observed versus Expected Analyses	
Medicinal Product	VAXZEVRIA (ChAdOx1-S [recombinant])
Period covered	29 June 2022 to 28 December 2022
Date	17 February 2023

Appendix 8

Observed versus Expected Analyses

1 OBSERVED VERSUS EXPECTED ANALYSES

Methodology

Observed versus Expected (O/E) analyses is conducted on a weekly basis for the Adverse Event of Special Interest and Safety Concerns listed in the VAXZEVRIA Risk Management Plan (RMP).

The analyses involve establishing exposure in terms of 'Person-Years per Risk Period' by taking the number of vaccine doses distributed or administered and multiplying with the risk period in days.

- For the O/E analyses in this report the actual exposure data for the United Kingdom (UK), EU/European Economic Area (EEA), Brazil, New Zealand, Canada, Australia, Philippines, Mexico, Taiwan, Malaysia, Argentina, Colombia and Thailand were used. However, if this data is unavailable or cannot be provided vaccine distribution data from a Global Batch Traceability system will be used, which provides actual vaccine distribution at the country level.

A risk period is determined for each Adverse Event of Special Interest (AESI) and Safety Concern, and a conservative approach using the longest known risk period post-vaccination will be used. This risk period is provided for each AESI in Table 1, which summarises the O/E analyses. The risk window for each AESI topic was determined through review of multiple sources:

- Brighton Collaboration
- World Health Organization (WHO) COVID-19 Vaccines: Safety Surveillance Manual
- Vaccines Europe AESI Working Group

The 'Incidence Rate' for the AESI and Safety Concerns is derived through medical review and assessment of published literature or epidemiologic program outcome data that most accurately reflect the background rate for the exposed population. Where possible the rates provided from the ACCESS program are used but if data is not available for the AESI or there is significant variability of the rates, published literature sources are utilized. The published literature is obtained through a structured search of the following sources:

- Medline
- Embase
- Brighton Collaboration
- Centres for Disease Control and Prevention
- WHO
- Incidence and Prevalence Database

The articles identified are medically reviewed, to determine the methodology and relevance of the data collected to the vaccinated population, and the rate that most closely matches is selected. If ACCESS incidence rates are not used, a reference to the source article(s) for the incidence rate is provided in this report. References for background estimates obtained from the literature are provided in Appendix 9.

The number of events expected to occur for each AESI and Safety Concern is established by multiplying the 'Incidence Rate' by the 'Person-Years per Risk Period'. The expected number of cases determined up to 28 December 2022 can be found presented in Table 1 below.

The O/E analyses provided is based on the most recent and available data but there is a level of assumption made and changes in the data would impact the results. The following are some of the limitations of the data used:

1 **Doses administered for determination of exposure:** The data used for exposure is solely based on the data provided to AstraZeneca from the providing Country or Health Authority. Currently we are only able to obtain exposure data from the UK, EU/European Economic Area (EEA), Brazil, New Zealand, Canada, Australia, Philippines, Mexico, Taiwan, Malaysia, Argentina, Colombia and Thailand and the level of stratification varies across these sources, and so stratification by age and gender is not feasible. To date it has not been possible to obtain administration data in all countries where the vaccine is being administered, which does reduce the overall Person-Years per Risk Period in our calculations. However, since the majority of safety data obtained is from the countries listed, it is considered appropriate to continue to use only vaccine administration data, which most accurately reflects exposure, versus reliance on distribution data, which would grossly over represent exposure and significantly impact the number of expected cases. This will be reconsidered as additional countries increase their exposure and additional AE reports are received in those regions. It should be noted that exposure data for the UK is available at weekly intervals. For this report, the most recent data from the UK, was through 12 September 2022, EU/EEA was through 11 December 2022, Australia 21 December 2022, Philippines 30 November 2022, Taiwan 25 December 2022, Malaysia and Argentina was through 28 December 2022, Colombia 27 December 2022, Thailand was through 25 November 2022, New Zealand was through 06 December 2022, Brazil was through 25 December 2022, Canada was through 04 December 2022 and Mexico was through 01 October 2022. 48925906 (UK), 68798587 (EU/EEA) and 348391153 collectively for Brazil, New Zealand, Canada, Australia, Philippines, Mexico, Taiwan, Malaysia, Argentina, Colombia and Thailand doses administered. The total exposure data used for O/E analysis was 466115644.

2 **The background incidence rate used for the calculation is the same as the population vaccinated:** The identification of incidence rates can vary tremendously depending on the source of the data, when it was obtained, where it was obtained, how the disease has been defined, method of collection, patient population and calculation. Also, all of the incidence rates used reflect a patient population that has not been exposed to the pandemic and it will take some time to see how these rates change as more recent information becomes available. Changes in the Incidence Rates can have a dramatic impact on the results of the analysis. An overall incidence rate for the adult population was used and could be an over-estimation of the incidence rate in certain AESI groups.

3 **The number of observed events are spontaneously reported:** Spontaneously reported events only represent a fraction of the events that have actually occurred. It is widely acknowledged and accepted that AEs are under-reported in previous vaccination and drug programs. For the vaccination programs associated with this pandemic however there is a level of stimulated reporting not previously seen with other vaccination programs. In addition, media coverage has heightened awareness of certain events and may lead to reporting bias. This has resulted in higher levels of reporting than initially estimated. Over-reporting may also occur where multiple versions of the same case are counted. This occurs when large volumes of cases are received with a limited amount of information available to identify duplicates or the same case is received from different sources with the same scant level of information provided.

4 **The risk period reflects the period of time an event would occur post-vaccination**: The estimation of risk time is complex as it depends on the dosing schedule, route of administration and mechanism of action. This must be considered in the context of each medical topic or event under analysis. Over-estimating the risk window would increase the Person-Years at Risk period and include events that are outside the actual period of time a true event would occur. Under-estimating the risk window will result in reduced sensitivity making it difficult to reach statistical significance. All the risk period/window for each AESI is provided in Appendix 9.

Due to the variability and level of assumption made on the data used to conduct an O/E analyses, the ratio score calculated is sensitive to changes in the data used to conduct the analysis. A sensitivity analyses is conducted for each AESI to determine how much variation is required to alter the conclusions of the analysis. The sensitivity analyses is conducted on two factors, reporting fraction and incidence rate. The sensitivity analyses for each AESI and Safety Topic is available in Appendix 9.

All cumulative processed and unprocessed cases within the risk window for the AESI and Safety Concern are included in the O/E analyses in Table 1. The O/E analyses for all the AESI

and Safety Concerns that are noted in Appendix 7 are presented in Table 1, except for Pregnancy outcome – Neonates, which is discussed in Section 16.3.3.1 of the PBRER document.

Incidence rate for thrombocytopenia narrow was updated in Version 1.2 (dated 30 April 2021) of the ACCESS protocol (Willame et al 2021) to include secondary thrombocytopenia. IRs ranged between 20 and 64/100,000 PYs (CPRD (UK;2019) = 20.12; ARS (Italy; 2019) = 29.86; BIFAP PC/HOSP (Spain, 2018) = 63.07). BIFAP subpopulations rates show that the inclusion of hospital based events increases the event rates. Also data from ADVANCE study (ITP-Broad, General practitioners based;(Willame C et al 2021) showed the IR was 23.62 (95%CI: 19.72-28.29), which is similar to the IR from CPRD and ARS mentioned above; hence both the rates from CPRD and ARS were used for observed /expected analyses along with hospitalisation rate from BIFAP PC/HOSP.

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Acute Aseptic Arthritis	476	2095.74	42	3.91	0.23 (0.21 - 0.25)	Observed significantly < expected
Acute Aseptic Arthritis	522	8981.76	180	3.91	0.06 (0.05 - 0.06)	Observed significantly < expected
Acute Aseptic Arthritis (RW42+Unk TTO)	764	2095.74	42	3.91	0.36 (0.34 - 0.39)	Observed significantly < expected
Acute Aseptic Arthritis RW (RW180+Unk TTO)	810	8981.76	180	3.91	0.09 (0.08 - 0.1)	Observed significantly < expected
Acute Aseptic Arthritis	476	61639.56	42	115	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis	522	264169.53	180	115	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis (RW42+Unk TTO)	764	61639.56	42	115	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis (RW180+Unk TTO)	810	264169.53	180	115	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis	476	13399.9	42	25	0.04 (0.03 - 0.04)	Observed significantly < expected
Acute Aseptic Arthritis	522	57428.16	180	25	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis (RW42+Unk TTO)	764	13399.9	42	25	0.06 (0.05 - 0.06)	Observed significantly < expected
Acute Aseptic Arthritis (RW180+Unk TTO)	810	57428.16	180	25	0.01 (0.01 - 0.02)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Acute Aseptic Arthritis (Extended RW)	533	11776.09	236	3.91	0.05 (0.04 - 0.05)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW+Unk TTO)	821	11776.09	236	3.91	0.07 (0.07 - 0.07)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW)	533	346355.6	236	115	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW+Unk TTO)	821	346355.6	236	115	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW)	533	75294.7	236	25	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW+Unk TTO)	821	75294.7	236	25	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute cardiac injury	332	354871.34	42	688.38	0 (0 - 0)	Observed significantly < expected
Acute cardiac injury (including unknown TTO)	671	368969.02	42	688.38	0 (0 - 0)	Observed significantly < expected
Acute kidney injury	225	106327.34	14	595.12	0 (0 - 0)	Observed significantly < expected
Acute kidney injury (including unknown TTO)	506	106327.34	14	595.12	0 (0 - 0.01)	Observed significantly < expected
Acute liver injury	95	9853.4	14	55.15	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute liver injury (including unknown TTO)	229	9853.4	14	55.15	0.02 (0.02 - 0.03)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Acute Pancreatitis	109	30015.78	42	56	0 (0 - 0)	Observed significantly < expected
Acute Pancreatitis (including unknown TTO)	163	30015.78	42	56	0.01 (0 - 0.01)	Observed significantly < expected
Acute respiratory distress syndrome – ARDS	177	412564.52	365	88.57	0 (0 - 0)	Observed significantly < expected
Acute respiratory distress syndrome – ARDS (including unknown TTO)	215	412564.52	365	88.57	0 (0 - 0)	Observed significantly < expected
Acute respiratory distress syndrome ARDS (Extended RW)	177	475862.1	421	88.57	0 (0 - 0)	Observed significantly < expected
Acute respiratory distress syndrome ARDS (Extended RW + Unk TTO)	215	475862.1	421	88.57	0 (0 - 0)	Observed significantly < expected
Anaphylaxis						
Anaphylaxis type reactions [b]	1478	576.83	2	22.6	2.56 (2.43 - 2.7)	Observed significantly > expected
Anaphylaxis type reactions [b] (including unknown TTO)	2280	576.83	2	22.6	3.95 (3.79 - 4.12)	Observed significantly > expected
Angioedema – Hypersensitivity [c]	10545	2552.36	2	100	4.13 (4.05 - 4.21)	Observed significantly > expected
Angioedema – Hypersensitivity[c] (including unknown TTO)	15589	2552.36	2	100	6.11 (6.01 - 6.2)	Observed significantly > expected
Anosmia – Ageusia	2530	7059.07	42	13.17	0.36 (0.34 - 0.37)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Anosmia – Ageusia (including unknown TTO)	3358	7059.07	42	13.17	0.48 (0.46 - 0.49)	Observed significantly < expected
Autoimmune thyroiditis	117	42879.69	42	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (including unknown TTO)	175	42879.69	42	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis	137	183770.11	180	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (including unknown TTO)	195	183770.11	180	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (Extended RW)	140	240943.03	236	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (Extended RW + Unk TTO)	198	240943.03	236	80	0 (0 - 0)	Observed significantly < expected
Chilblain - like lesions	100	4068.21	42	7.59	0.02 (0.02 - 0.03)	Observed significantly < expected
Chilblain - like lesions (including unknown TTO)	136	4068.21	42	7.59	0.03 (0.03 - 0.04)	Observed significantly < expected
Chronic fatigue syndrome / Post viral fatigue syndrome						
Chronic fatigue syndrome	157	7932.74	42	14.8	0.02 (0.02 - 0.02)	Observed significantly < expected
Chronic fatigue syndrome (including unknown TTO)	272	7932.74	42	14.8	0.03 (0.03 - 0.04)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Chronic fatigue syndrome	167	33997.47	180	14.8	0 (0 - 0.01)	Observed significantly < expected
Chronic fatigue syndrome (including unknown TTO)	282	33997.47	180	14.8	0.01 (0.01 - 0.01)	Observed significantly < expected
Chronic fatigue syndrome (Extended RW)	168	44574.46	236	14.8	0 (0 - 0)	Observed significantly < expected
Chronic fatigue syndrome (Extended RW + Unk TTO)	283	44574.46	236	14.8	0.01 (0.01 - 0.01)	Observed significantly < expected
Post viral fatigue syndrome	139	6539.15	42	12.2	0.02 (0.02 - 0.03)	Observed significantly < expected
Post viral fatigue syndrome (including unknown TTO)	217	6539.15	42	12.2	0.03 (0.03 - 0.04)	Observed significantly < expected
Post viral fatigue syndrome	151	28024.94	180	12.2	0.01 (0 - 0.01)	Observed significantly < expected
Post viral fatigue syndrome (including unknown TTO)	229	28024.94	180	12.2	0.01 (0.01 - 0.01)	Observed significantly < expected
Post viral fatigue syndrome Extended RW	152	36743.81	236	12.2	0 (0 - 0)	Observed significantly < expected
Post viral fatigue syndrome (Extended RW + Unk TTO)	230	36743.81	236	12.2	0.01 (0.01 - 0.01)	Observed significantly < expected
Erythema multiforme	86	3768.05	42	7.03	0.02 (0.02 - 0.03)	Observed significantly < expected
Erythema multiforme (including unknown TTO)	114	3768.05	42	7.03	0.03 (0.02 - 0.04)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Fibromyalgia	226	17848.67	42	33.3	0.01 (0.01 - 0.01)	Observed significantly < expected
Fibromyalgia (including unknown TTO)	478	17848.67	42	33.3	0.03 (0.02 - 0.03)	Observed significantly < expected
Fibromyalgia	233	76494.31	180	33.3	0 (0 - 0)	Observed significantly < expected
Fibromyalgia (including unknown TTO)	485	76494.31	180	33.3	0.01 (0.01 - 0.01)	Observed significantly < expected
Fibromyalgia (Extended RW)	235	100292.54	236	33.3	0 (0 - 0)	Observed significantly < expected
Fibromyalgia (Extended RW + Unk TTO)	487	100292.54	236	33.3	0 (0 - 0.01)	Observed significantly < expected
Immune-mediated neurological conditions						
Encephalitis Overall	214	4877.56	42	9.1	0.04 (0.04 - 0.05)	Observed significantly < expected
Encephalitis Overall (including Unknown TTO)	346	4877.56	42	9.1	0.07 (0.06 - 0.08)	Observed significantly < expected
Bell's Palsy overall[d]	1658	10827.12	42	20.2	0.15 (0.15 - 0.16)	Observed significantly < expected
Bell's Palsy (including unknown TTO)[d]	2301	10827.12	42	20.2	0.21 (0.2 - 0.22)	Observed significantly < expected
Acute disseminated encephalomyelitis	46	26.8	14	0.15	1.72 (1.26 - 2.29)	Observed significantly > expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Acute disseminated encephalomyelitis (including unknown TTO)	67	26.8	14	0.15	2.5 (1.94 - 3.17)	Observed significantly > expected
Acute disseminated encephalomyelitis	55	57.43	30	0.15	0.96 (0.72 - 1.25)	Observed < expected
Acute disseminated encephalomyelitis including unknown TTO)	76	57.43	30	0.15	1.32 (1.04 - 1.66)	Observed significantly > expected
Acute disseminated encephalomyelitis	57	80.4	42	0.15	0.71 (0.54 - 0.92)	Observed significantly < expected
Acute disseminated encephalomyelitis including unknown TTO)	78	80.4	42	0.15	0.97 (0.77 - 1.21)	Observed < expected
GBS Overall [e]	466	807.57	14	4.52	0.58 (0.53 - 0.63)	Observed significantly < expected
GBS Overall [e] (including unknown TTO)	992	807.57	14	4.52	1.23 (1.15 - 1.31)	Observed significantly > expected
GBS Overall [e]	916	1730.5	30	4.52	0.53 (0.5 - 0.56)	Observed significantly < expected
GBS Overall [e] (including unknown TTO)	1442	1730.5	30	4.52	0.83 (0.79 - 0.88)	Observed significantly < expected
GBS Overall [e]	983	2422.7	42	4.52	0.41 (0.38 - 0.43)	Observed significantly < expected
GBS Overall [e] (including unknown TTO)	1509	2422.7	42	4.52	0.62 (0.59 - 0.66)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Multiple sclerosis - Multiple sclerosis relapse	196	5895.96	42	11	0.03 (0.03 - 0.04)	Observed significantly < expected
Multiple sclerosis - Multiple sclerosis relapse (including unknown TTO)	310	5895.96	42	11	0.05 (0.05 - 0.06)	Observed significantly < expected
Multiple sclerosis - Multiple sclerosis relapse	213	25268.39	180	11	0.01 (0.01 - 0.01)	Observed significantly < expected
Multiple sclerosis - Multiple sclerosis relapse (including unknown TTO)	327	25268.39	180	11	0.01 (0.01 - 0.01)	Observed significantly < expected
Multiple sclerosis Multiple sclerosis relapse (Extended RW)	215	33129.67	236	11	0.01 (0.01 - 0.01)	Observed significantly < expected
Multiple sclerosis Multiple sclerosis relapse (Extended RW+ Unk TTO)	329	33129.67	236	11	0.01 (0.01 - 0.01)	Observed significantly < expected
Myelitis transverse [f]	214	519.92	42	0.97	0.41 (0.36 - 0.47)	Observed significantly < expected
Myelitis transverse [f] (including unknown TTO)	339	519.92	42	0.97	0.65 (0.58 - 0.73)	Observed significantly < expected
Neuropathy	3666	41271.7	42	77	0.09 (0.09 - 0.09)	Observed significantly < expected
Neuropathy (including unknown TTO)	5140	41271.7	42	77	0.12 (0.12 - 0.13)	Observed significantly < expected
Optic neuritis	135	1983.19	42	3.7	0.07 (0.06 - 0.08)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Optic neuritis (including unknown TTO)	199	1983.19	42	3.7	0.1 (0.09 - 0.12)	Observed significantly < expected
Myasthenia gravis	45	943.35	42	1.76	0.05 (0.03 - 0.06)	Observed significantly < expected
Myasthenia gravis (including unknown TTO)	77	943.35	42	1.76	0.08 (0.06 - 0.1)	Observed significantly < expected
Myasthenia gravis	62	4042.94	180	1.76	0.02 (0.01 - 0.02)	Observed significantly < expected
Myasthenia gravis (including unknown TTO)	94	4042.94	180	1.76	0.02 (0.02 - 0.03)	Observed significantly < expected
Myasthenia gravis (Extended RW)	62	5300.75	236	1.76	0.01 (0.01 - 0.01)	Observed significantly < expected
Myasthenia gravis (Extended RW+Unk TTO)	94	5300.75	236	1.76	0.02 (0.01 - 0.02)	Observed significantly < expected
Myocardial infarction[g]	169	66820.85	28	187	0 (0 - 0)	Observed significantly < expected
Myocardial infarction[g] (including unknown TTO)	355	66820.85	28	187	0.01 (0 - 0.01)	Observed significantly < expected
Myocarditis All cases all ages	115	859.38	7	9.62	0.13 (0.11 - 0.16)	Observed significantly < expected
Myocarditis All cases all ages	166	1718.76	14	9.62	0.1 (0.08 - 0.11)	Observed significantly < expected
Myocarditis All cases all ages	196	2578.14	21	9.62	0.08 (0.07 - 0.09)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Myocarditis All cases all ages	274	5156.28	42	9.62	0.05 (0.05 - 0.06)	Observed significantly < expected
Myocarditis All cases all ages (RW 7+Unk TTO)	512	859.38	7	9.62	0.6 (0.55 - 0.65)	Observed significantly < expected
Myocarditis All cases all ages (RW 14+Unk TTO)	563	1718.76	14	9.62	0.33 (0.3 - 0.36)	Observed significantly < expected
Myocarditis All cases all ages (RW 21+Unk TTO)	593	2578.14	21	9.62	0.23 (0.21 - 0.25)	Observed significantly < expected
Myocarditis All cases all ages (RW 42+Unk TTO)	671	5156.28	42	9.62	0.13 (0.12 - 0.14)	Observed significantly < expected
Pericarditis All cases all ages	112	2356.6	7	26.38	0.05 (0.04 - 0.06)	Observed significantly < expected
Pericarditis All cases all ages	201	4713.19	14	26.38	0.04 (0.04 - 0.05)	Observed significantly < expected
Pericarditis All cases all ages	249	7069.79	21	26.38	0.04 (0.03 - 0.04)	Observed significantly < expected
Pericarditis All cases all ages	343	14139.58	42	26.38	0.02 (0.02 - 0.03)	Observed significantly < expected
Pericarditis All cases all ages (RW 7+Unk TTO)	336	2356.6	7	26.38	0.14 (0.13 - 0.16)	Observed significantly < expected
Pericarditis All cases all ages (RW 14+Unk TTO)	425	4713.19	14	26.38	0.09 (0.08 - 0.1)	Observed significantly < expected
Pericarditis All cases all ages (RW 21+Unk TTO)	473	7069.79	21	26.38	0.07 (0.06 - 0.07)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Pericarditis All cases all ages (RW 42+Unk TTO)	567	14139.58	42	26.38	0.04 (0.04 - 0.04)	Observed significantly < expected
Narcolepsy	23	1238.15	42	2.31	0.02 (0.01 - 0.03)	Observed significantly < expected
Narcolepsy (including unknown TTO)	38	1238.15	42	2.31	0.03 (0.02 - 0.04)	Observed significantly < expected
POTS	31	3215.98	42	6	0.01 (0.01 - 0.01)	Observed significantly < expected
POTS (including unknown TTO)	71	3215.98	42	6	0.02 (0.02 - 0.03)	Observed significantly < expected
Pregnancy outcome – Maternal						
Gestational diabetes	10	6778207.2	60	8852.2	0 (0 - 0)	Observed significantly < expected
Gestational diabetes (including unknown TTO)	19	6778207.2	60	8852.2	0 (0 - 0)	Observed significantly < expected
Gestational diabetes (Extended RW)	18	13104533.91	116	8852.2	0 (0 - 0)	Observed significantly < expected
Gestational diabetes (Extended RW+Unk TTO)	27	13104533.91	116	8852.2	0 (0 - 0)	Observed significantly < expected
Rhabdomyolysis	59	31623.77	42	59	0 (0 - 0)	Observed significantly < expected
Rhabdomyolysis (including unknown TTO	94	31623.77	42	59	0 (0 - 0)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Generalised convulsions	2587	18223.87	14	102	0.14 (0.14 - 0.15)	Observed significantly < expected
Generalised convulsions (including unknown TTO)	3803	18223.87	14	102	0.21 (0.2 - 0.22)	Observed significantly < expected
Stress Cardiomyopathy	14	2149.34	42	4.01	0.01 (0 - 0.01)	Observed significantly < expected
Stress Cardiomyopathy (including unknown TTO)	21	2149.34	42	4.01	0.01 (0.01 - 0.01)	Observed significantly < expected
Sudden Death [h] (cases within RW of 07 days)	118	5250.98	7	58.78	0.02 (0.02 - 0.03)	Observed significantly < expected
Sudden Death [h] (including cases with unknown TTO)	320	5250.98	7	58.78	0.06 (0.05 - 0.07)	Observed significantly < expected
Thrombocytopenia [i]	1426	24086.22	21	89.87	0.06 (0.06 - 0.06)	Observed significantly < expected
Thrombocytopenia [i] (with unknown TTO)	2327	24086.22	21	89.87	0.1 (0.09 - 0.1)	Observed significantly < expected
Thrombocytopenia [i]	1759	48172.45	42	89.87	0.04 (0.03 - 0.04)	Observed significantly < expected
Thrombocytopenia [i] (with unknown TTO)	2660	48172.45	42	89.87	0.06 (0.05 - 0.06)	Observed significantly < expected
Embolic and thrombotic events (Thrombosis)	11189	265811.2	14	1487.76	0.04 (0.04 - 0.04)	Observed significantly < expected
Embolic and thrombotic events (Thrombosis) (including unknown TTO)	18797	265811.2	14	1487.76	0.07 (0.07 - 0.07)	Observed significantly < expected

Table 1 Observed versus expected analyses for AESI and Safety Concerns in the COVID-19 VACCINE ASTRAZENECA RMP – cumulative to 28 December 2022 (Global Cases)

Medical Concept	Observed cases [a]	Expected cases	Risk Window (days)	Background rate/100,000 person years	Rate ratio (CI 95%)	
Embolic and thrombotic events (Thrombosis)	14778	531622.4	28	1487.76	0.03 (0.03 - 0.03)	Observed significantly < expected
Embolic and thrombotic events (Thrombosis) (including unknown TTO)	22386	531622.4	28	1487.76	0.04 (0.04 - 0.04)	Observed significantly < expected
Embolic and thrombotic events (Thrombosis)	16584	797433.6	42	1487.76	0.02 (0.02 - 0.02)	Observed significantly < expected
Embolic and thrombotic events (Thrombosis) (including unknown TTO)	24192	797433.6	42	1487.76	0.03 (0.03 - 0.03)	Observed significantly < expected
VTE [j]	5150	160688.07	28	449.69	0.03 (0.03 - 0.03)	Observed significantly < expected
VTE (including unknown TTO)	7413	160688.07	28	449.69	0.05 (0.05 - 0.05)	Observed significantly < expected
Type III hypersensitivity	76	8404.42	42	15.68	0.01 (0.01 - 0.01)	Observed significantly < expected
Type III hypersensitivity (including unknown TTO)	102	8404.42	42	15.68	0.01 (0.01 - 0.01)	Observed significantly < expected

Overall global exposure: 466115644

[a] PTs from suppressed and in-valid reports were excluded. All cases irrespective of risk windows were included in the analysis unless stated otherwise.

[b] PTs included are from MedDRA SMQ Anaphylactic reaction-narrow

[c] PTs included are from MedDRA SMQ- Angioedema-narrow and PT of Hypersensitivity

[d] PTs included Bell's palsy, Facial paralysis, Facial paresis

[e] PTs included from the MedDRA SMQ- Guillain-Barré syndrome-Narrow

[f] PTs included are Demyelination, Myelitis, Myelitis transverse, Myelopathy

[g] Most of the PTs from Myocardial infarction SMQ are included under AESI of Embolic and Thrombotic events

[h] PTs included Sudden death, Sudden cardiac death; events occurring within risk window of 0-7 days were included

[i] PTs included are from MedDRA HLT of "Thrombocytopenias" and SMQ of "Hematopoietic Thrombocytopenia-Narrow, Source: Willame et al 2021 CPRD (UK;2019) = 20.12; ARS (Italy; 2019) = 29.86; BIFAP PC/HOSP (Spain, 2018) = 63.07

[j] PTs included: Deep vein thrombosis; Pulmonary embolism; Pulmonary infarction; Pulmonary microemboli; Pulmonary thrombosis; Pulmonary venous thrombosis.

AESI Adverse Event of Special Interest; ARDS Acute respiratory distress syndrome; CI Confidence Interval; COVID 19 Coronavirus Disease of 2019; GBS Guillain-Barre syndrome; POTS Postural orthostatic tachycardia syndrome; RMP Risk Management Plan; RW Risk Window; TTO Time To Onset; SMQ Standardised MedDRA Query; VTE Venous Thromboembolism.

2 REFERENCES

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Willame C et al 2021
Willame C, Dodd C, van der Aa L, Picelli G, Emborg HD, Kahlert J et al. Incidence Rates of Autoimmune Diseases in European Healthcare Databases: A Contribution of the ADVANCE Project. Drug Saf. 2021;44(3):383-395.

PBRER – Appendix 9 Observed versus Expected Analyses Supporting Information	
Medicinal Product	VAXZEVRIA (ChAdOx1-S [recombinant])
Period covered	29 June 2022 to 28 December 2022
Date	17 February 2023

Appendix 9

Observed versus Expected Analyses Supporting Information

LIST OF TABLES

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Observed versus Expectedness (O/E) analytical period is up to 28 December 2022. For O/E analysis in this report the actual exposure data is based on the most recent data on administered doses shared by respective healthy authority

- UK until 12 September 2022
- EU/EEA until 11 December 2022 (except Germany 30 November 2022)
- Australia until 21 December 2022
- Philippines until 30 November 2022
- Taiwan until 29 December 2022
- Malaysia and Argentina until 28 December 2022
- Colombia until 27 December 2022
- Thailand until 25 November 2022
- New Zealand until 06 December 2022
- Brazil until 25 December 2022
- Canada until 04 December 2022
- Mexico until 01 October 2022.

The exposure data, totals 48925906 (UK), 68798587 (EU/EEA) and 348391153 collectively for Brazil, New Zealand, Canada, Australia, Philippines, Mexico, Taiwan, Malaysia, Argentina, Colombia and Thailand doses administered. The total exposure data used for O/E analysis was 466115644.

Risk period/window (days), background incidence rates considered (100,000 person-years) for each concepts and sensitivity analyses are provided below. The sensitivity analyses and figures were prepared based on the algorithm proposed by Mahaux et al 2015.

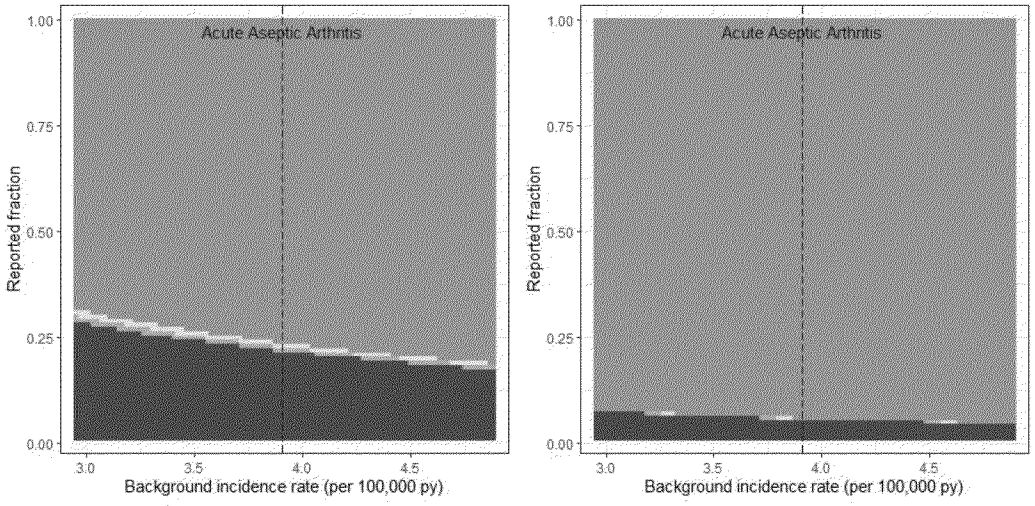
Description of literature background incidence rates is provided in Appendix A.

Table 1 Observed Versus Expected analysis for Acute aseptic arthritis

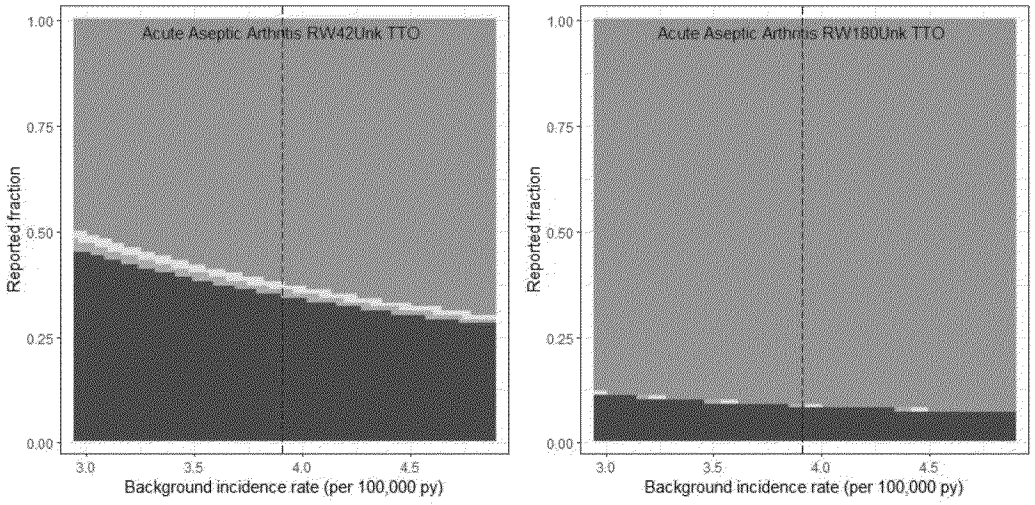
Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Acute Aseptic Arthritis	476	2095.74	42	3.91	466115644	0.23 (0.21 - 0.25)	Observed significantly < expected
Acute Aseptic Arthritis	522	8981.76	180	3.91	466115644	0.06 (0.05 - 0.06)	Observed significantly < expected
Acute Aseptic Arthritis (RW42+Unk TTO)	764	2095.74	42	3.91	466115644	0.36 (0.34 - 0.39)	Observed significantly < expected
Acute Aseptic Arthritis (RW180+Unk TTO)	810	8981.76	180	3.91	466115644	0.09 (0.08 - 0.1)	Observed significantly < expected
Acute Aseptic Arthritis	476	61639.56	42	115	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis	522	264169.53	180	115	466115644	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis (RW42+Unk TTO)	764	61639.56	42	115	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis (RW180+Unk TTO)	810	264169.53	180	115	466115644	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis	476	13399.9	42	25	466115644	0.04 (0.03 - 0.04)	Observed significantly < expected
Acute Aseptic Arthritis	522	57428.16	180	25	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis (RW42+Unk TTO)	764	13399.9	42	25	466115644	0.06 (0.05 - 0.06)	Observed significantly < expected
Acute Aseptic Arthritis (RW180+Unk TTO)	810	57428.16	180	25	466115644	0.01 (0.01 - 0.02)	Observed significantly < expected

Table 1 Observed Versus Expected analysis for Acute aseptic arthritis

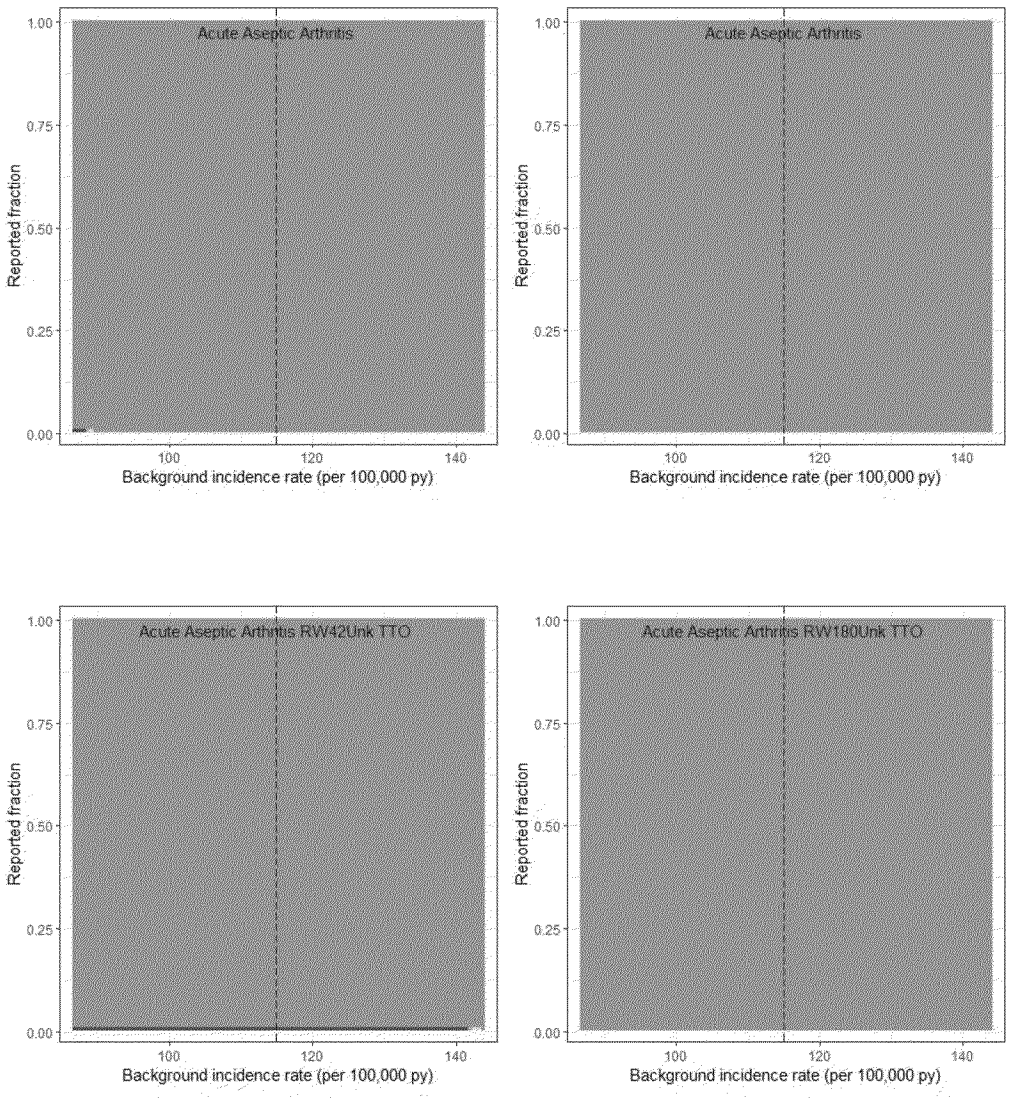
Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Acute Aseptic Arthritis (Extended RW)	533	11776.09	236	3.91	466115644	0.05 (0.04 - 0.05)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW+Unk TTO)	821	11776.09	236	3.91	466115644	0.07 (0.07 - 0.07)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW)	533	346355.6	236	115	466115644	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW+Unk TTO)	821	346355.6	236	115	466115644	0 (0 - 0)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW)	533	75294.7	236	25	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute Aseptic Arthritis (Extended RW+Unk TTO)	821	75294.7	236	25	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected

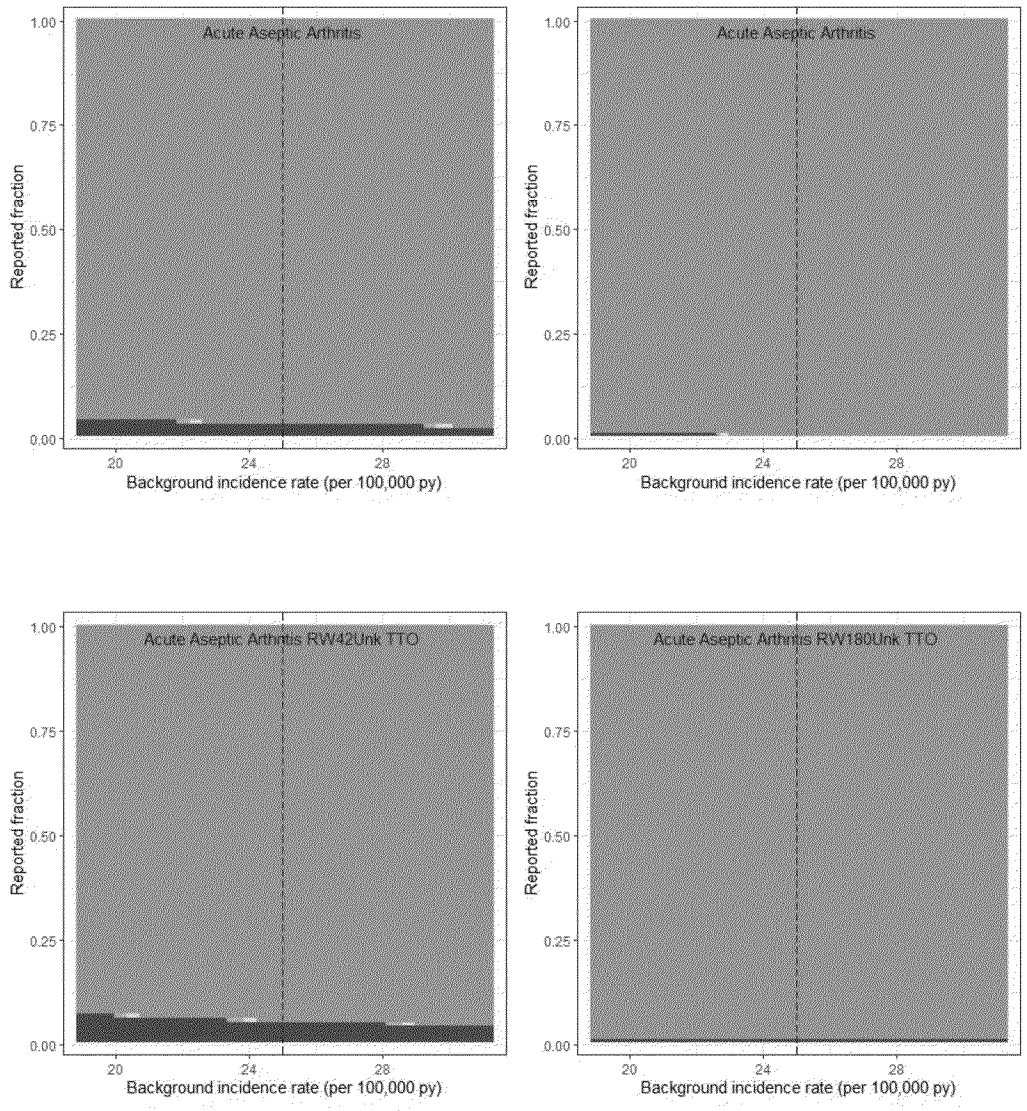

Acute Aseptic Arthritis
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)

Acute Aseptic Arthritis
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)


Acute Aseptic Arthritis RW42Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)

Acute Aseptic Arthritis RW180Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)


Acute Aseptic Arthritis
Acute Aseptic Arthritis
Acute Aseptic Arthritis RW42Unk TTO
Acute Aseptic Arthritis RW180Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
100
120
140
Background incidence rate (per 100,000 py)


Acute Aseptic Arthritis
Acute Aseptic Arthritis
Acute Aseptic Arthritis RW42Unk TTO
Acute Aseptic Arthritis RW180Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
24
28
Background incidence rate (per 100,000 py)

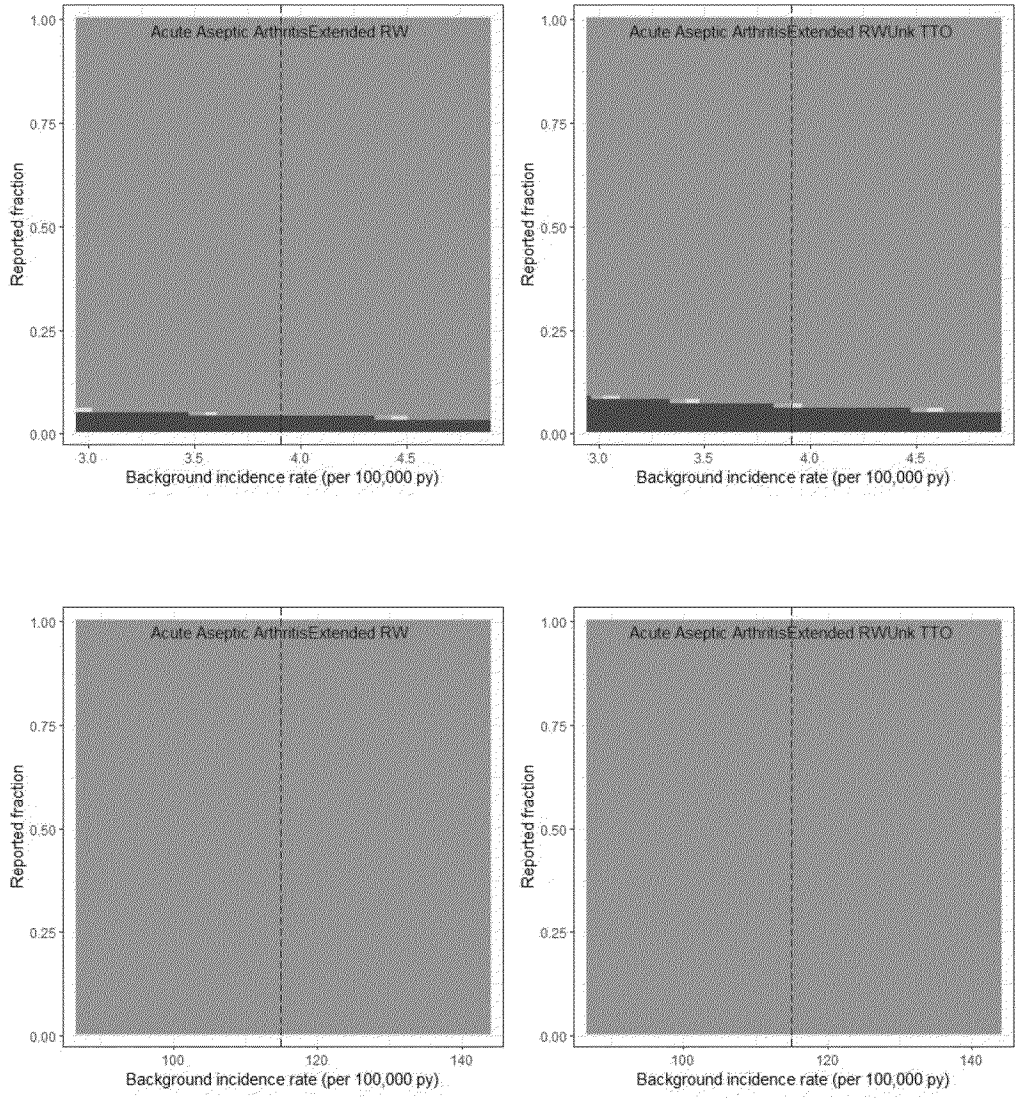
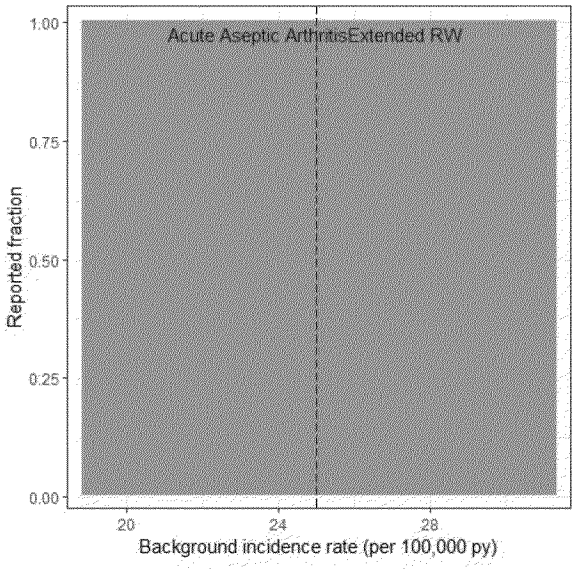
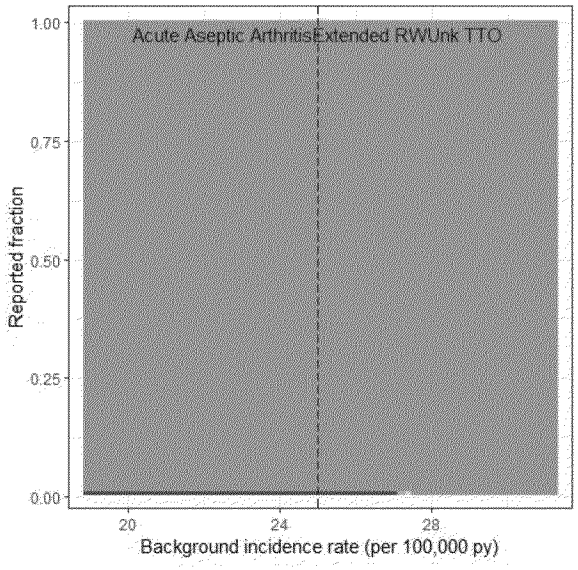

Acute Aseptic ArthritisExtended RW
Acute Aseptic ArthritisExtended RWUnk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
100
120
140
Background incidence rate (per 100,000 py)

Table 1 Observed Versus Expected analysis for Acute aseptic arthritis

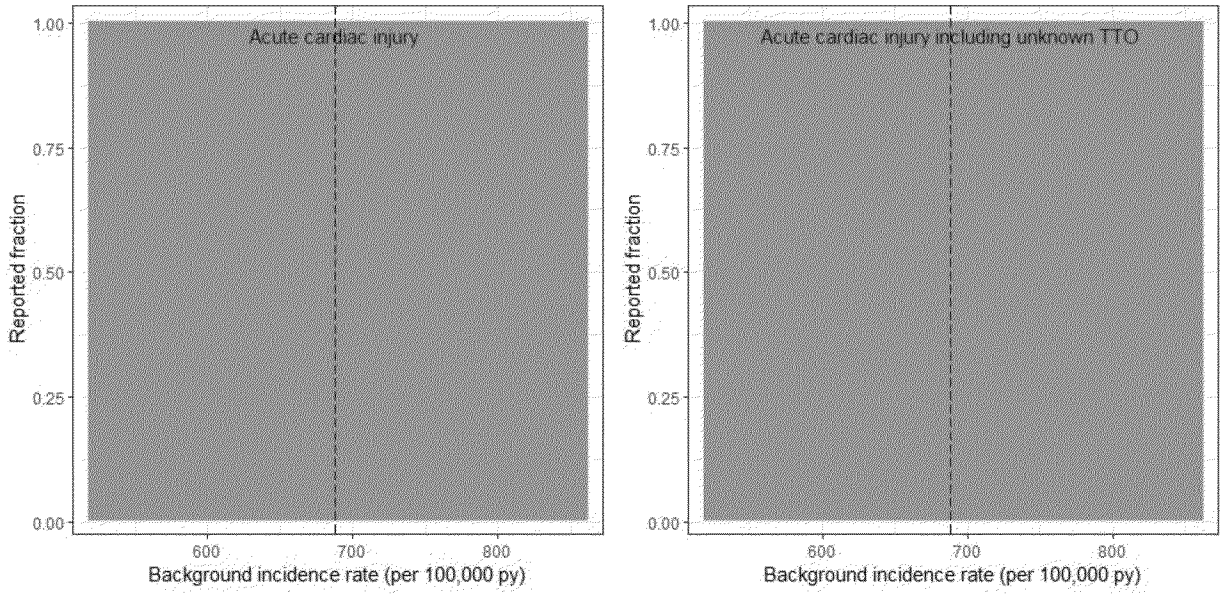
Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							
							

[a] Incidence rate (IR): Source: IR=115 (Söderlin et al 2002), IR=25 (Hazes and Luime 2011) and IR=3.91 (Willame et al 2021 [A]) (Meta-analysis IR from 2017-2019 – Acute aseptic arthritis (Narrow))

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed; RW Risk Window; TTO Time to onset; Unk Unknown

Table 2 Observed Versus Expected analysis for Acute cardiac injury

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Acute cardiac injury	332	354871.34	42	688.38	0 (0 - 0)	Observed significantly < expected
Acute cardiac injury (including unknown TTO)	671	368969.02	42	688.38	0 (0 - 0)	Observed significantly < expected



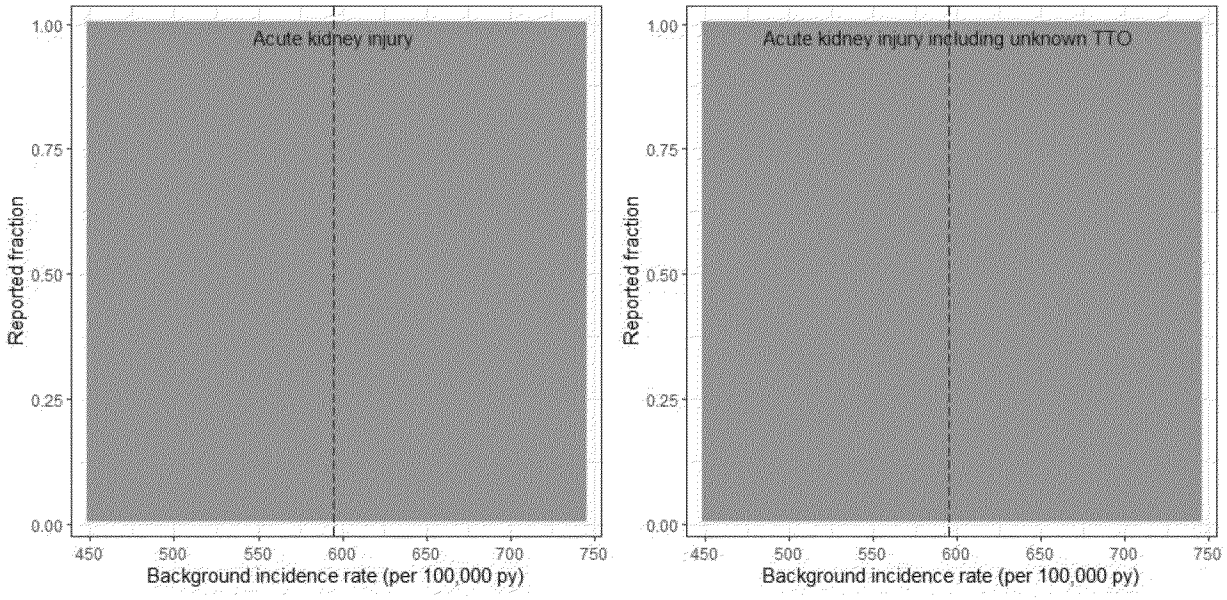
[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Heart Failure (Narrow)).

CI Confidence Interval: E Expected; IR Incidence Rate; O Observed, TTO Time to onset; Unk Unknown

466115644-Postmarketing exposure

Table 3 Observed Versus Expected analysis for Acute kidney injury

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Acute kidney injury	225	106327.34	14	595.12	0 (0 - 0)	Observed significantly < expected
Acute kidney injury (including unknown TTO)	506	106327.34	14	595.12	0 (0 - 0.01)	Observed significantly < expected

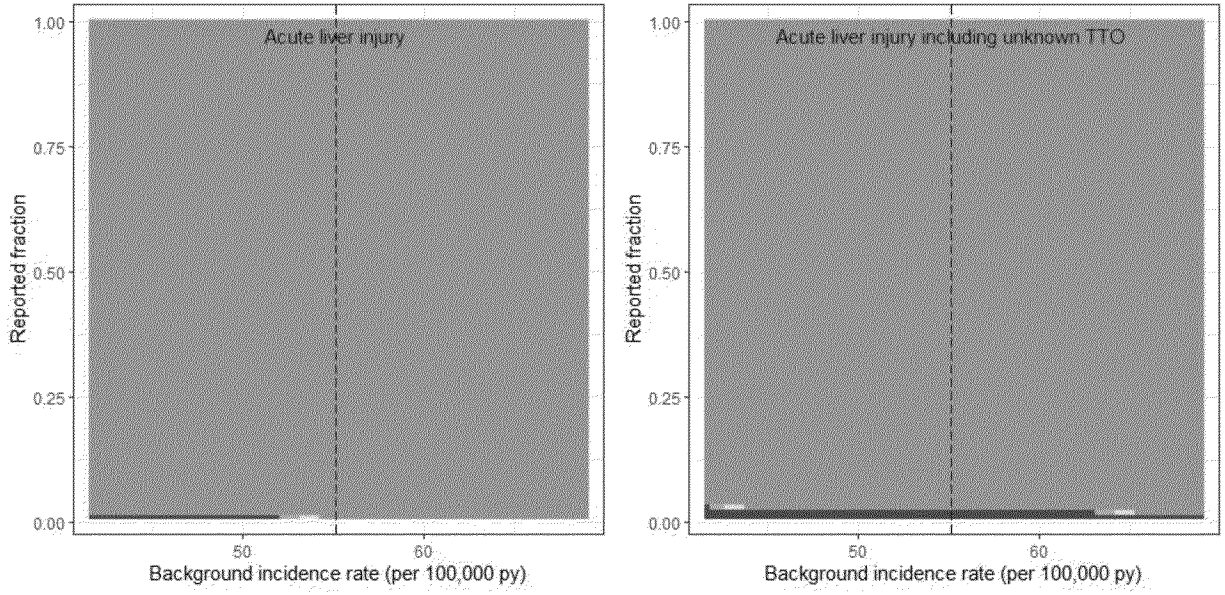


[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Acute kidney injury (Narrow)).

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset; Unk Unknown

Table 4 Observed Versus Expected analysis for Acute liver injury

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Acute liver injury	95	9853.4	14	55.15	0.01 (0.01 - 0.01)	Observed significantly < expected
Acute liver injury (including unknown TTO)	229	9853.4	14	55.15	0.02 (0.02 - 0.03)	Observed significantly < expected

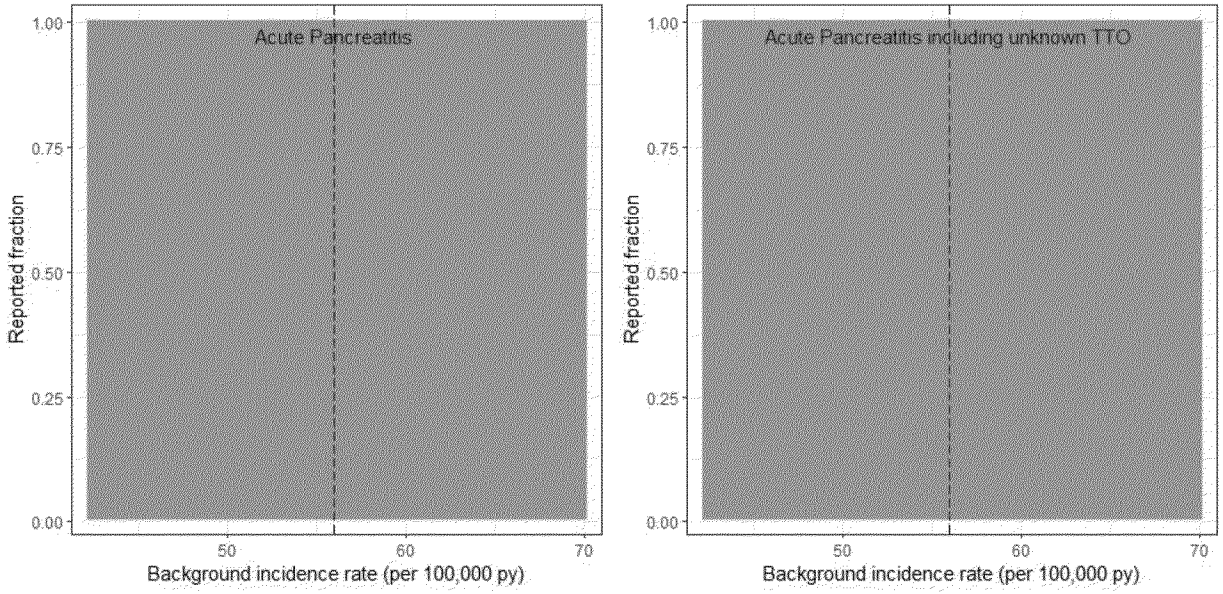


[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Acute Liver Injury (Narrow)).

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset; Unk Unknown

Table 5 Observed Versus Expected analysis for Acute Pancreatitis

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Acute Pancreatitis	109	30015.78	42	56	0 (0 - 0)	Observed significantly < expected
Acute Pancreatitis (including unknown TTO)	163	30015.78	42	56	0.01 (0 - 0.01)	Observed significantly < expected



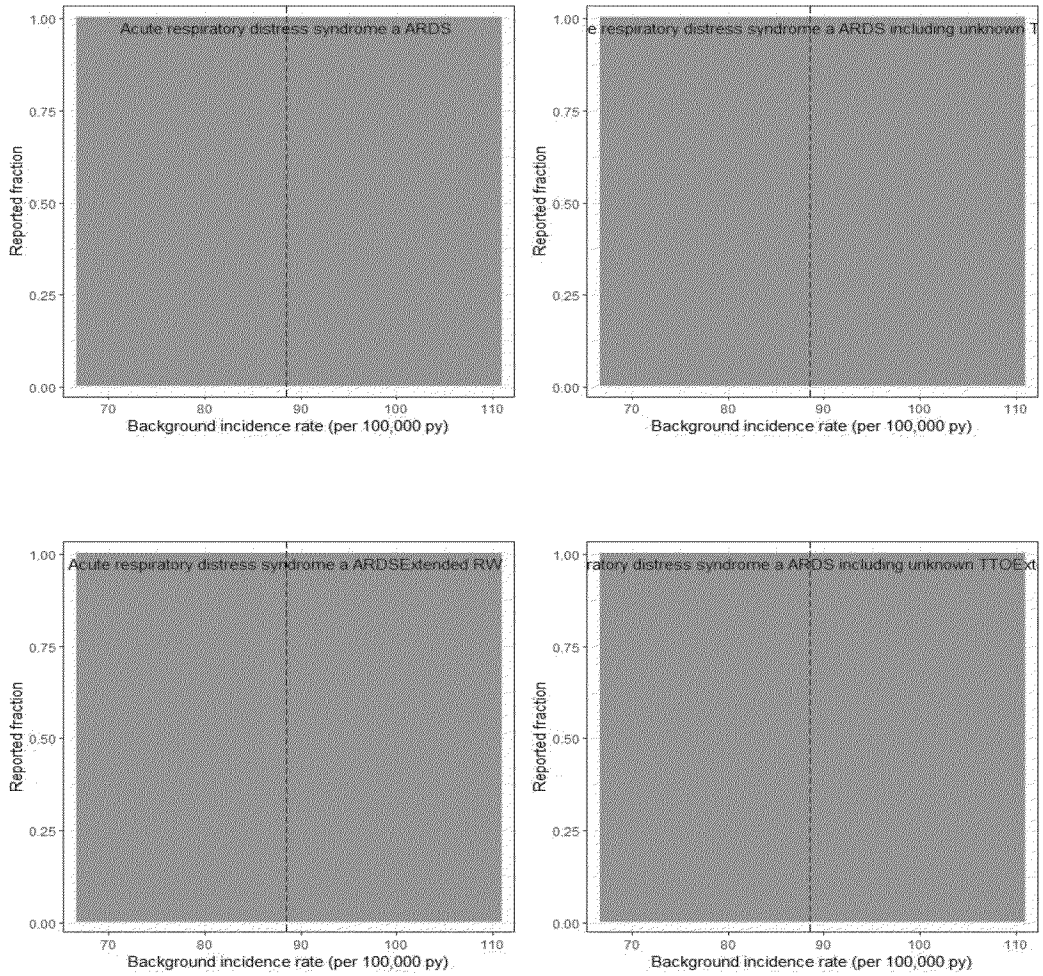
[a] IR: NICE guideline Pancreatitis

CI Confidence Interval; E Expected; O Observed, TTO Time to onset; Unk Unknown

Table 6 Observed Versus Expected analysis for Acute respiratory distress syndrome – ARDS

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Acute respiratory distress syndrome	177	412564.52	365	88.57	0 (0 - 0)	Observed significantly < expected
Acute respiratory distress syndrome (including unknown TTO)	215	412564.52	365	88.57	0 (0 - 0)	Observed significantly < expected
Acute respiratory distress syndrome (Extended RW)	177	475862.1	421	88.57	0 (0 - 0)	Observed significantly < expected
Acute respiratory distress syndrome (Extended RW+ Unk TTO)	215	475862.1	421	88.57	0 (0 - 0)	Observed significantly < expected

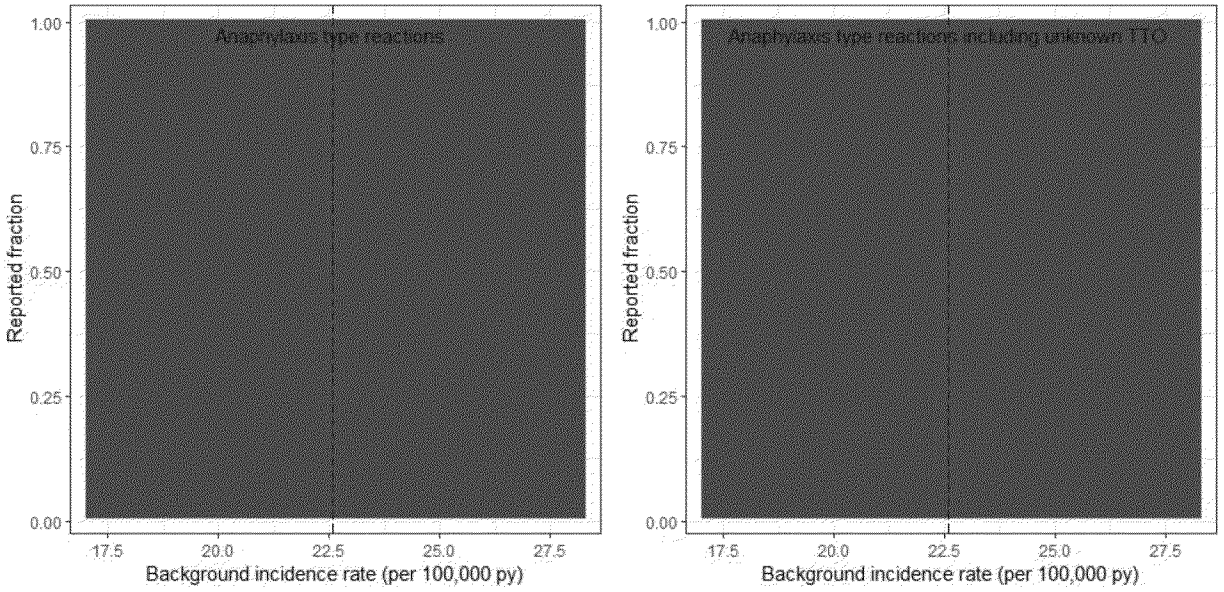
Table 6 Observed Versus Expected analysis for Acute respiratory distress syndrome – ARDS



[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Acute respiratory distress syndrome (Narrow)).
CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, RW Risk Window; TTO Time to onset; Unk Unknown

Table 7 Observed Versus Expected analysis for Anaphylaxis type reactions

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Anaphylaxis type reactions	1478	576.83	2	22.6	2.56 (2.43 - 2.7)	Observed significantly > expected
Anaphylaxis type reactions including unknown TTO	2280	576.83	2	22.6	3.95 (3.79 - 4.12)	Observed significantly > expected

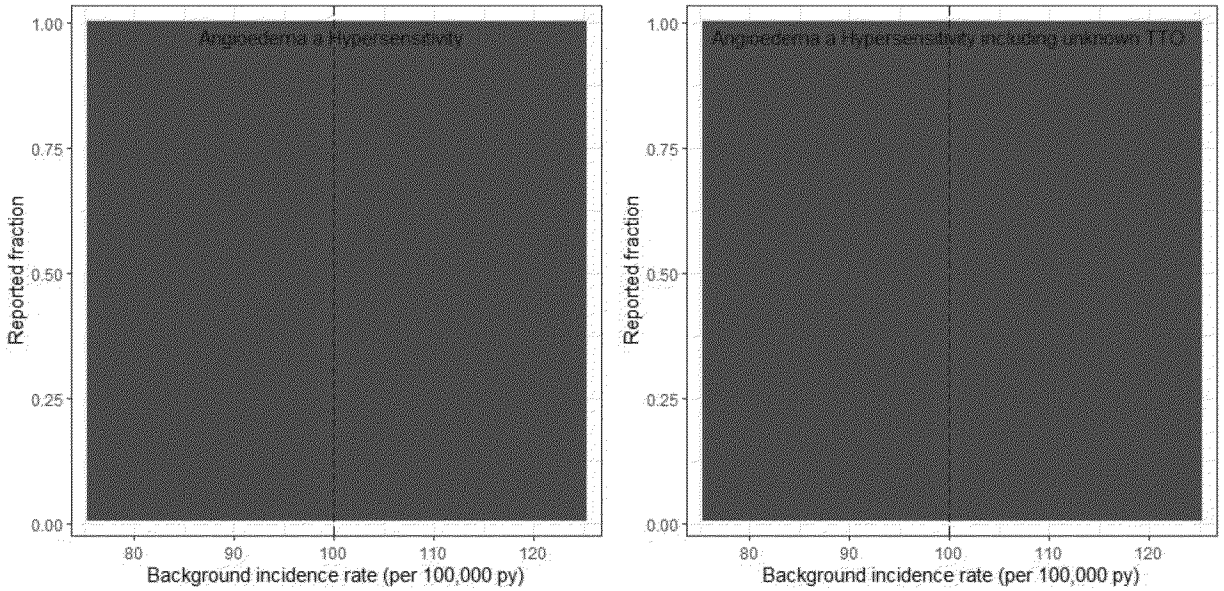


[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Anaphylaxis (Narrow)).

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, RW risk window, TTO Time to onset.

Table 8 Observed Versus Expected analysis for Angioedema - Hypersensitivity

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Angioedema Hypersensitivity	10545	2552.36	2	100	4.13 (4.05 - 4.21)	Observed significantly > expected
Angioedema Hypersensitivity (including unknown TTO)	15589	2552.36	2	100	6.11 (6.01 - 6.2)	Observed significantly > expected

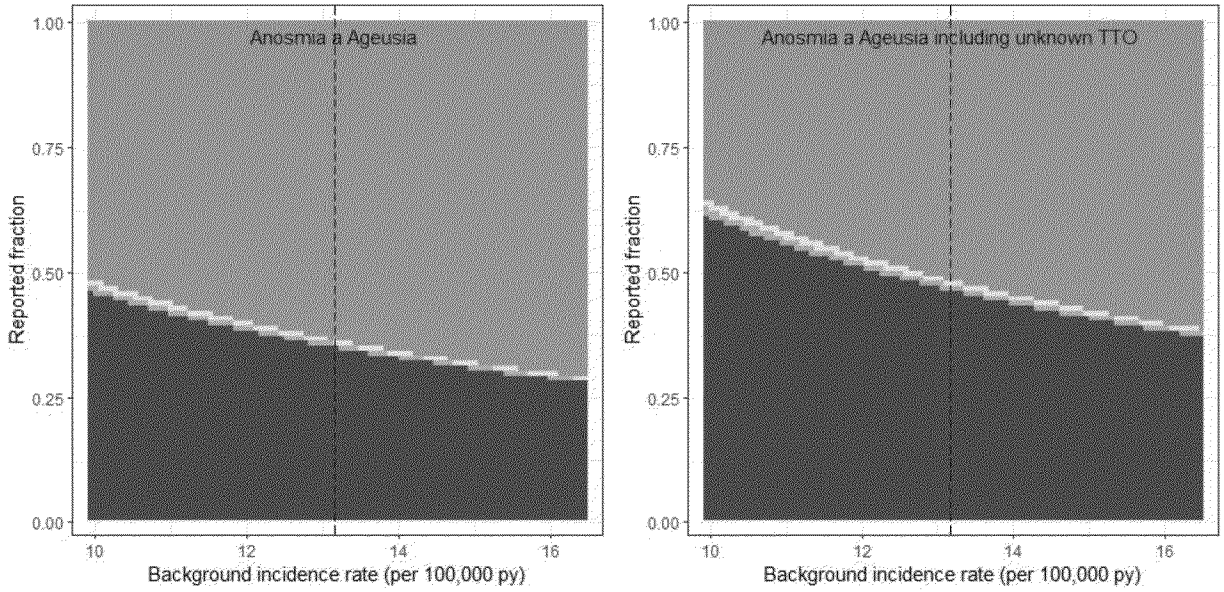


[a] Incidence rate (IR): Source: NICE guideline CG183

CI Confidence Interval; E Expected; O Observed, RW risk window, TTO Time to onset;

Table 9 Observed Versus Expected analysis for Anosmia - Ageusia

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Anosmia Ageusia	2530	7059.07	42	13.17	0.36 (0.34 - 0.37)	Observed significantly < expected
Anosmia Ageusia (including unknown TTO)	3358	7059.07	42	13.17	0.48 (0.46 - 0.49)	Observed significantly < expected

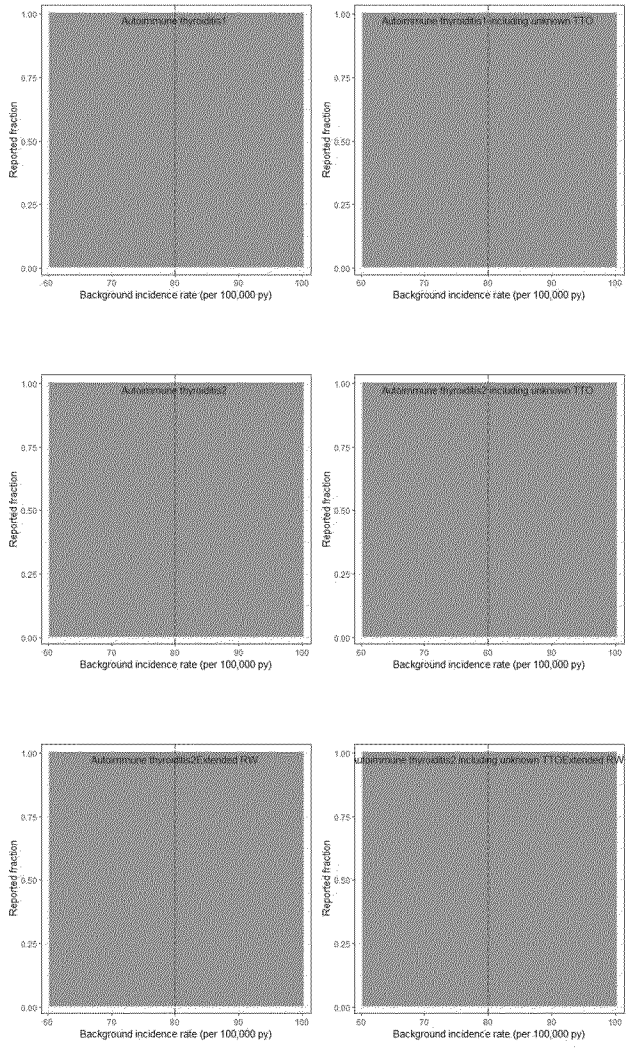


[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - anosmia/ageusia (Narrow)).

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, RW risk window, TTO Time to onset

Table 10 Observed Versus Expected analysis for Autoimmune thyroiditis

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Autoimmune thyroiditis	117	42879.69	42	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (including unknown TTO)	175	42879.69	42	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis	137	183770.11	180	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (including unknown TTO)	195	183770.11	180	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (Extended RW)	140	240943.03	236	80	0 (0 - 0)	Observed significantly < expected
Autoimmune thyroiditis (Extended RW+Unk TTO)	198	240943.03	236	80	0 (0 - 0)	Observed significantly < expected

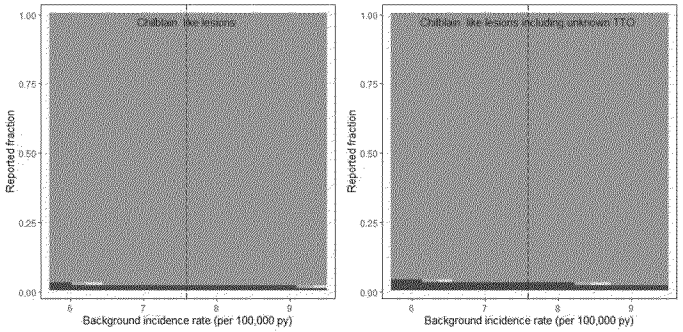


[a] Incidence rate (IR) Source: McGrogan et al 2008

CI Confidence Interval; E Expected; O Observed, RW Risk Window, TTO Time to onset, Unk Unknown.

Table 11 Observed Versus Expected analysis for Chilblain - like lesions

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Chilblain like lesions	100	4068.21	42	7.59	0.02 (0.02 - 0.03)	Observed significantly < expected
Chilblain like lesions (including unknown TTO)	136	4068.21	42	7.59	0.03 (0.03 - 0.04)	Observed significantly < expected



[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Chilblain like lesions (Narrow)).

CI Confidence Interval; E Expected; O Observed; RW risk window; TTO; Time to onset.

Table 12 Observed Versus Expected analysis for Chronic fatigue syndrome

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Chronic fatigue syndrome	157	7932.74	42	14.8	0.02 (0.02 - 0.02)	Observed significantly < expected
Chronic fatigue syndrome (including unknown TTO)	272	7932.74	42	14.8	0.03 (0.03 - 0.04)	Observed significantly < expected
Chronic fatigue syndrome	167	33997.47	180	14.8	0 (0 - 0.01)	Observed significantly < expected
Chronic fatigue syndrome (including unknown TTO)	282	33997.47	180	14.8	0.01 (0.01 - 0.01)	Observed significantly < expected
Chronic fatigue syndrome (Extended RW)	168	44574.46	236	14.8	0 (0 - 0)	Observed significantly < expected
Chronic fatigue syndrome (Extended RW+Unk TTO)	283	44574.46	236	14.8	0.01 (0.01 - 0.01)	Observed significantly < expected

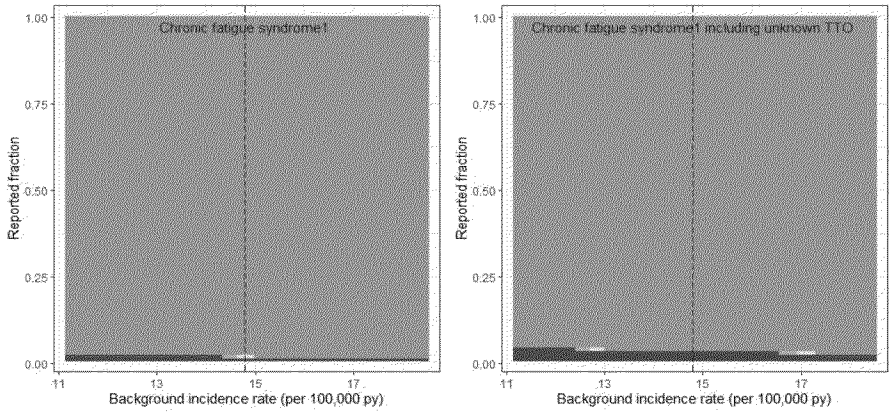
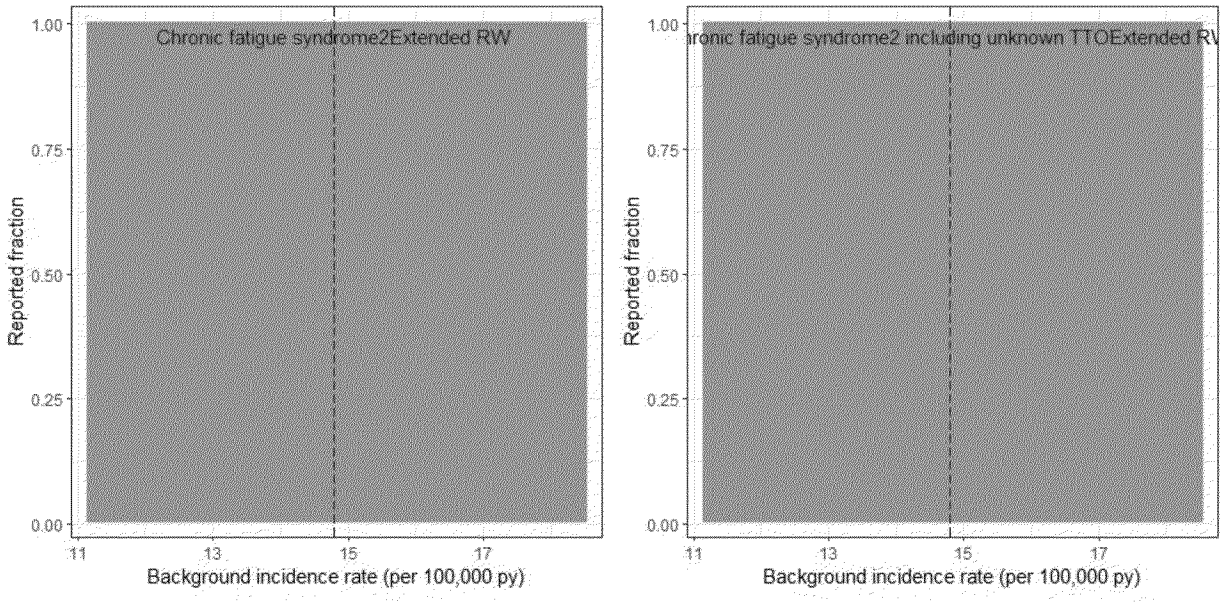

Chronic fatigue syndrome1
Chronic fatigue syndrome1 including unknown TTO
Chronic fatigue syndrome2
Chronic fatigue syndrome2 including unknown TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
11
13
15
17
Background incidence rate (per 100,000 py)

Table 12 Observed Versus Expected analysis for Chronic fatigue syndrome

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
						

[a] IR Source: Collin et al 2017.

CI Confidence Interval; E Expected; O Observed, RW risk window; TTO Time to onset; Unk Unknown

Table 13 Observed Versus Expected analysis for Post viral fatigue syndrome

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Post viral fatigue syndrome	139	6539.15	42	12.2	0.02 (0.02 - 0.03)	Observed significantly < expected
Post viral fatigue syndrome (including unknown TTO)	217	6539.15	42	12.2	0.03 (0.03 - 0.04)	Observed significantly < expected
Post viral fatigue syndrome	151	28024.94	180	12.2	0.01 (0 - 0.01)	Observed significantly < expected
Post viral fatigue syndrome (including unknown TTO)	229	28024.94	180	12.2	0.01 (0.01 - 0.01)	Observed significantly < expected
Post viral fatigue syndrome (Extended RW)	152	36743.81	236	12.2	0 (0 - 0)	Observed significantly < expected
Post viral fatigue syndrome (Extended RW+Unk TTO)	230	36743.81	236	12.2	0.01 (0.01 - 0.01)	Observed significantly < expected

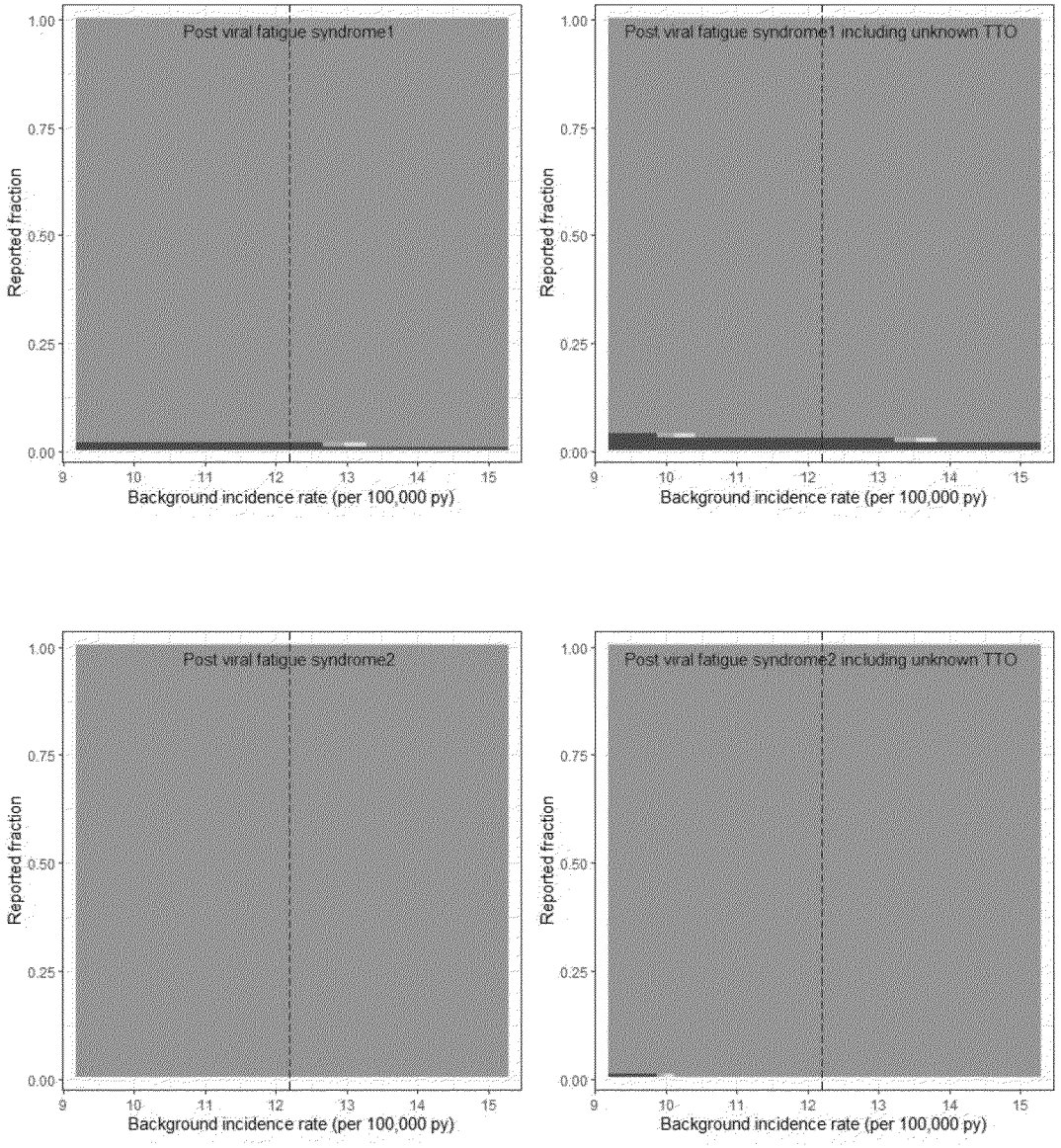
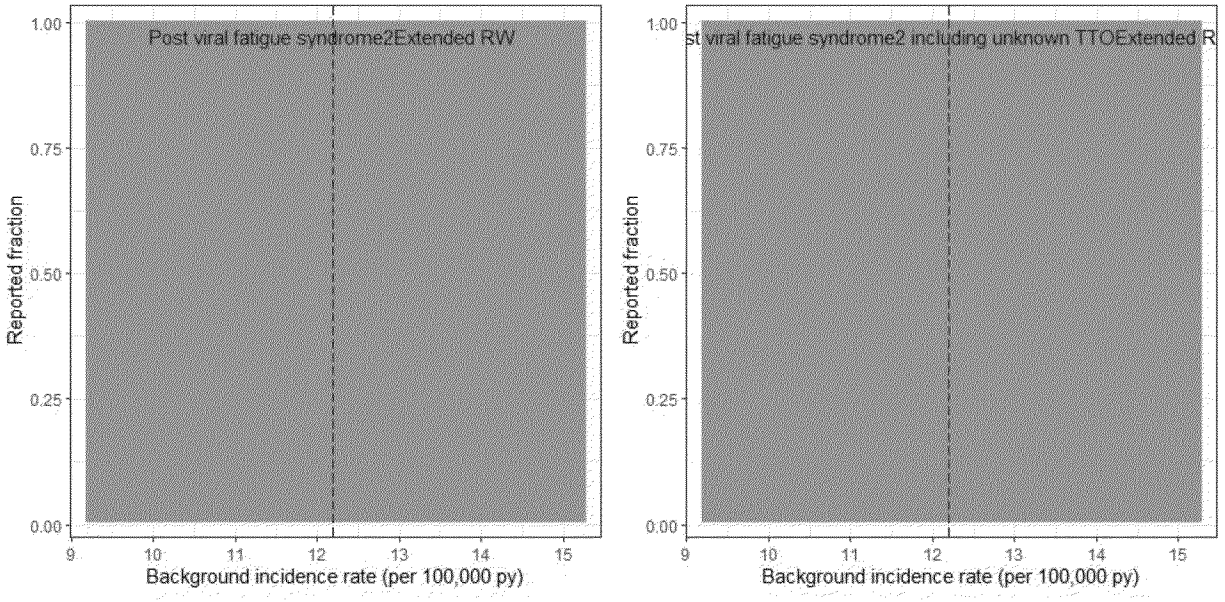

Post viral fatigue syndrome1
Post viral fatigue syndrome1 including unknown TTO
Post viral fatigue syndrome2
Post viral fatigue syndrome2 including unknown TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
14
15
Background incidence rate (per 100,000 py)

Table 13 Observed Versus Expected analysis for Post viral fatigue syndrome

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	

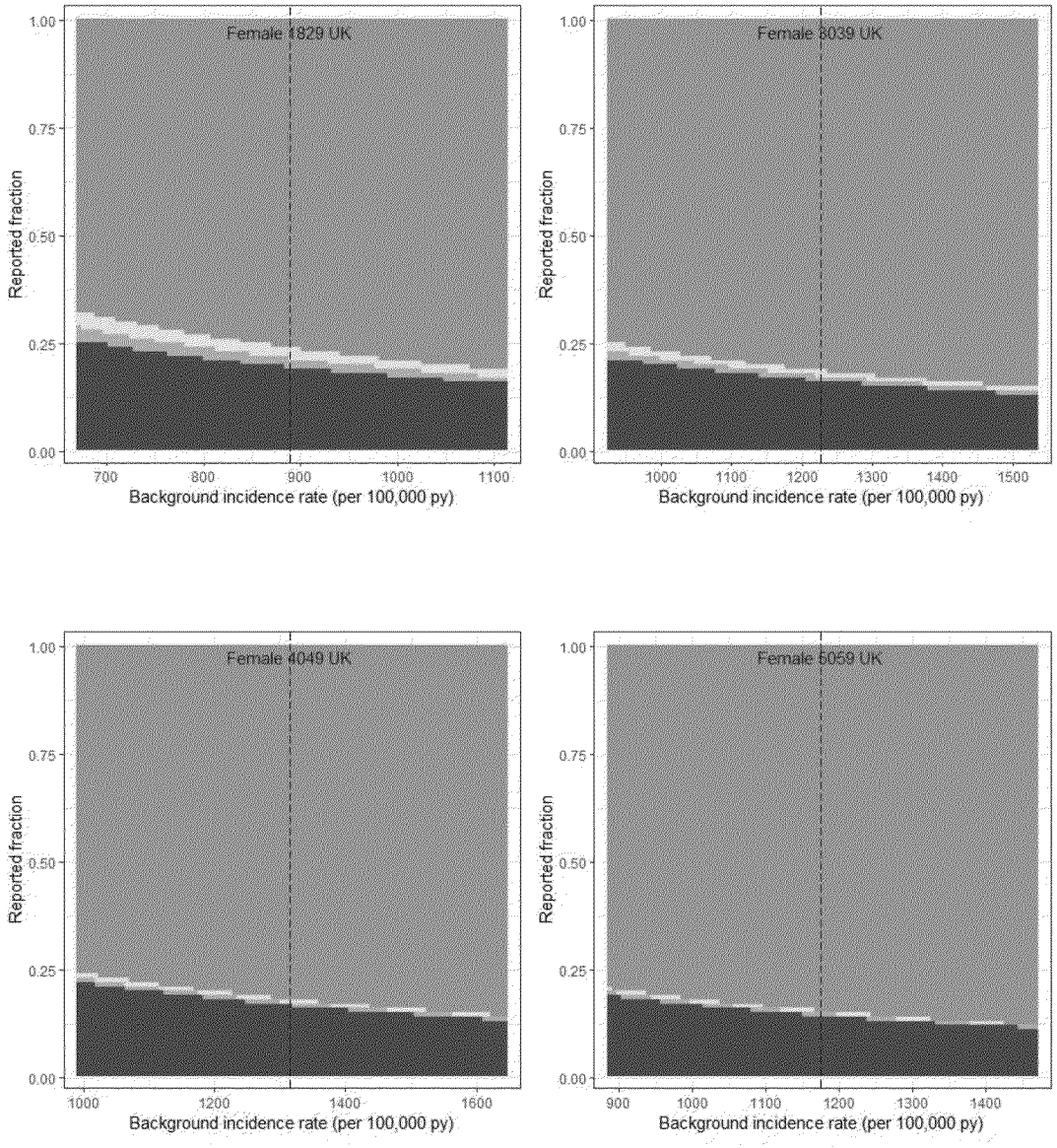


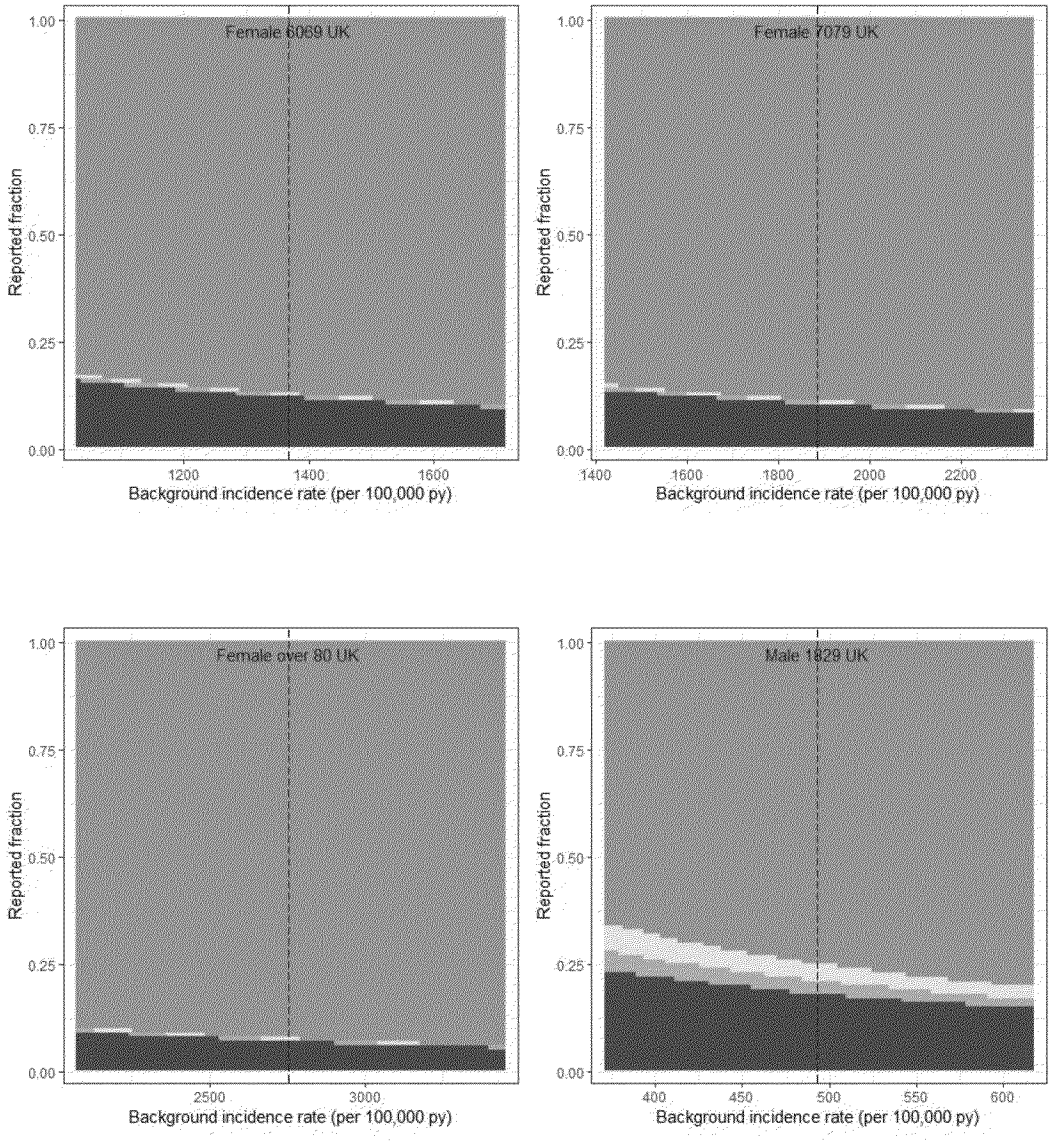
[a] IR Source: Collin et al 2017.

CI Confidence Interval; E Expected; O Observed, RW Risk Window; TTO Time to onset; Unk Unknown.

Table 14 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
Female 18-29	83	378.1	14	889.0	1109488	0.22 (0.17 - 0.27)	Observed significantly < expected
Female 30-39	159	889.6	14	1226.1	1892968	0.18 (0.15 - 0.21)	Observed significantly < expected
Female 40-49	396	2224.4	14	1315.3	4412245	0.18 (0.16 - 0.2)	Observed significantly < expected
Female 50-59	408	2674.9	14	1173.9	5944683	0.15 (0.14 - 0.17)	Observed significantly < expected
Female 60-69	318	2508.4	14	1368.1	4783416	0.13 (0.11 - 0.14)	Observed significantly < expected
Female 70-79	277	2510.1	14	1884.0	3475875	0.11 (0.1 - 0.12)	Observed significantly < expected
Female over 80	133	1721.3	14	2754.4	1630324	0.08 (0.06 - 0.09)	Observed significantly < expected
Male 18-29	33	152.8	14	492.7	808938	0.22 (0.15 - 0.3)	Observed significantly < expected
Male 30-39	77	566.0	14	1043.6	1415003	0.14 (0.11 - 0.17)	Observed significantly < expected
Male 40-49	247	2358.7	14	1354.8	4542157	0.1 (0.09 - 0.12)	Observed significantly < expected
Male 50-59	454	3905.5	14	1564.9	6510960	0.12 (0.11 - 0.13)	Observed significantly < expected
Male 60-69	364	3237.6	14	1711.6	4934728	0.11 (0.1 - 0.12)	Observed significantly < expected
Male 70-79	265	2591.1	14	2154.7	3137304	0.1 (0.09 - 0.12)	Observed significantly < expected
Male over 80	78	1153.0	14	2934.6	1025046	0.07 (0.05 - 0.08)	Observed significantly < expected


Female 1829 UK
Female 3039 UK
Female 4049 UK
Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
700
800
900
1000
1100
1200
1300
1400
1500
1600


Female 6069 UK
Female 7079 UK
Female over 80 UK
Male 1829 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1200
1400
1600
1800
2000
2200
2500
3000
400
450
500
550
600
Background incidence rate (per 100,000 py)

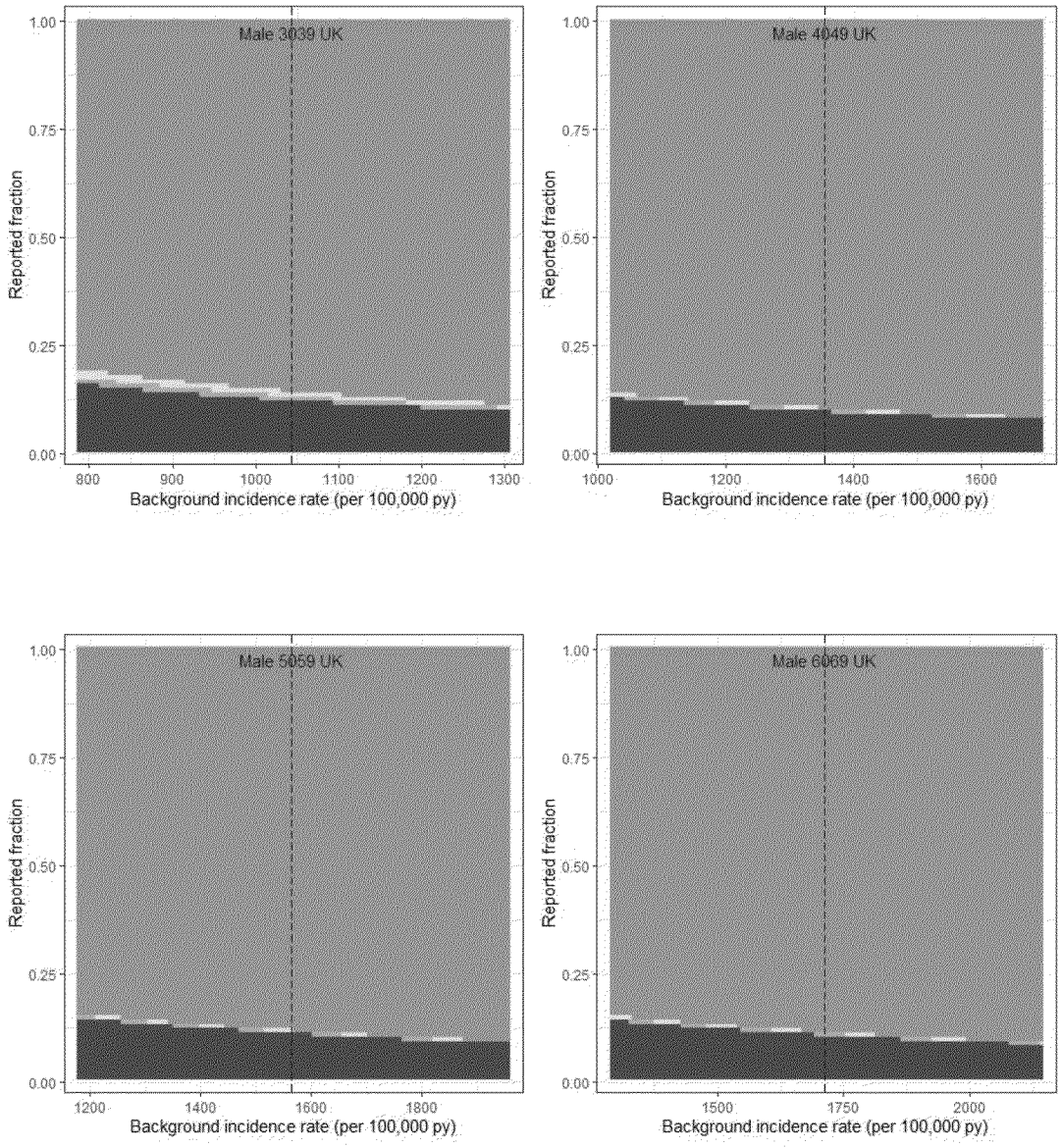

Male 3039 UK
Male 4049 UK
Male 5059 UK
Male 6069 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
800
900
1000
1100
1200
1300
1400
1500
1600
1750
1800
2000

Table 14 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK

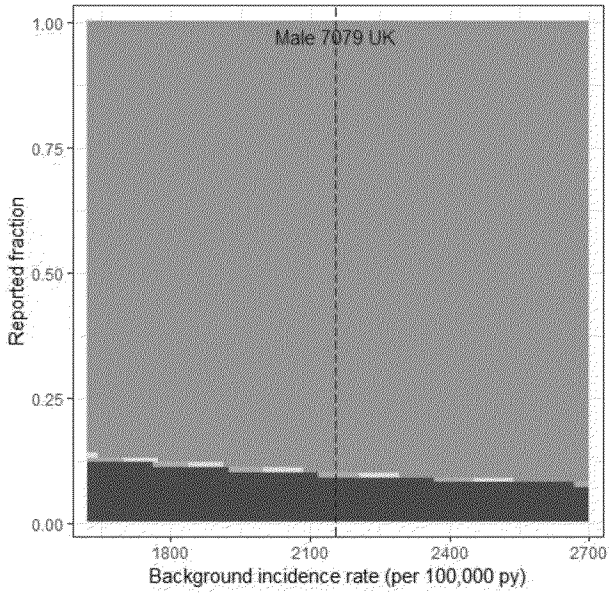
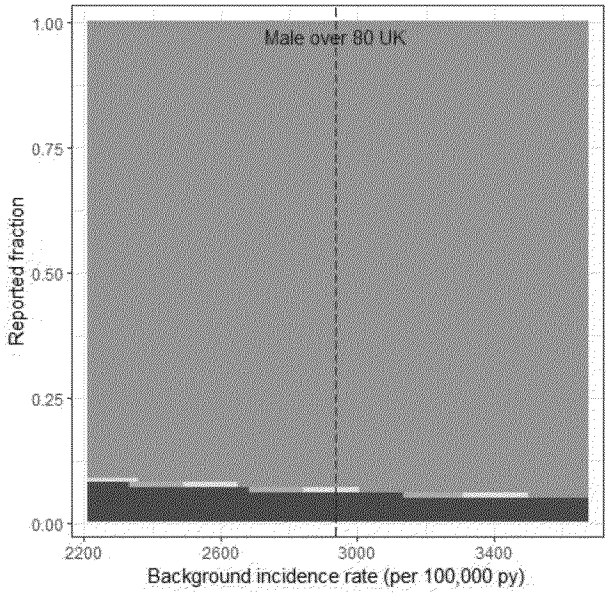
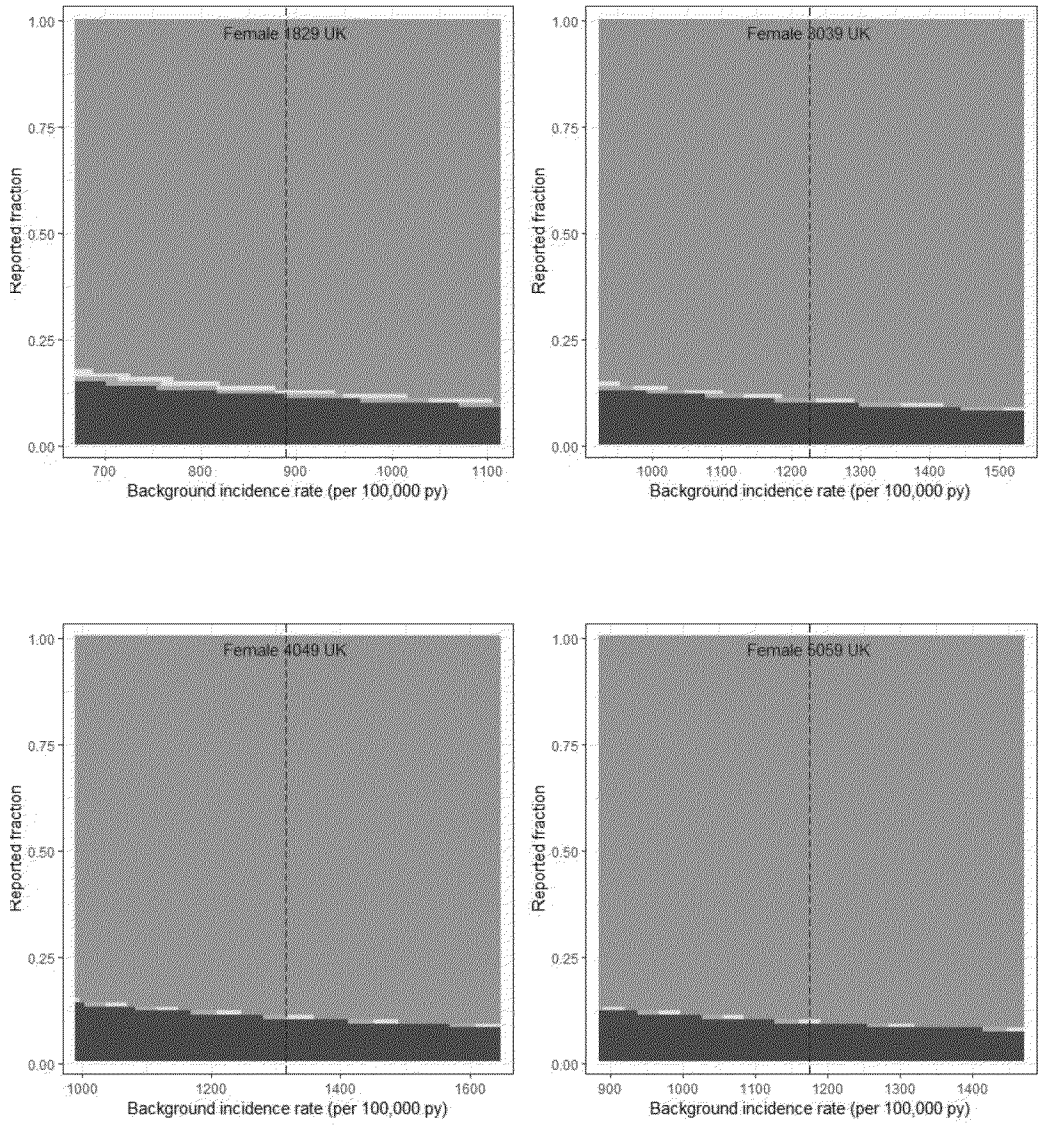
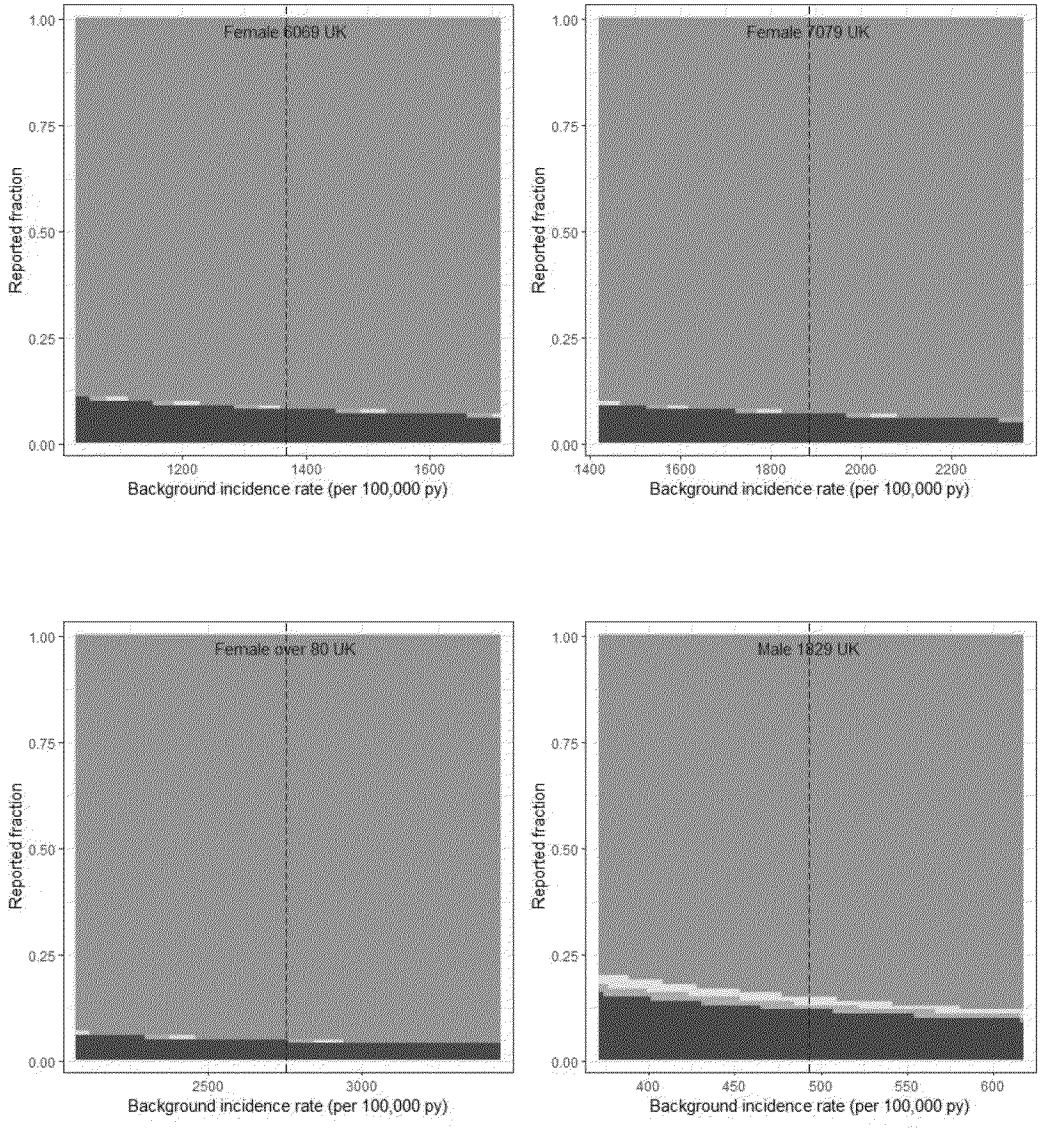
Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
 							
Female 18-29	97	756.2	28	889.03	1109488	0.13 (0.1 - 0.16)	Observed significantly < expected
Female 30-39	197	1779.2	28	1226.05	1892968	0.11 (0.1 - 0.13)	Observed significantly < expected
Female 40-49	490	4448.9	28	1315.26	4412245	0.11 (0.1 - 0.12)	Observed significantly < expected
Female 50-59	527	5349.8	28	1173.9	5944683	0.1 (0.09 - 0.11)	Observed significantly < expected
Female 60-69	436	5016.8	28	1368.08	4783416	0.09 (0.08 - 0.1)	Observed significantly < expected

Table 14 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
Female 70-79	377	5020.2	28	1883.99	3475875	0.08 (0.07 - 0.08)	Observed significantly < expected
Female over 80	178	3442.5	28	2754.4	1630324	0.05 (0.04 - 0.06)	Observed significantly < expected
Male 18-29	42	305.6	28	492.71	808938	0.14 (0.1 - 0.19)	Observed significantly < expected
Male 30-39	106	1132.0	28	1043.58	1415003	0.09 (0.08 - 0.11)	Observed significantly < expected
Male 40-49	331	4717.5	28	1354.79	4542157	0.07 (0.06 - 0.08)	Observed significantly < expected
Male 50-59	600	7810.9	28	1564.88	6510960	0.08 (0.07 - 0.08)	Observed significantly < expected
Male 60-69	493	6475.2	28	1711.63	4934728	0.08 (0.07 - 0.08)	Observed significantly < expected
Male 70-79	364	5182.2	28	2154.68	3137304	0.07 (0.06 - 0.08)	Observed significantly < expected
Male over 80	100	2306.1	28	2934.62	1025046	0.04 (0.04 - 0.05)	Observed significantly < expected


Female 1829 UK
Female 3039 UK
Female 4049 UK
Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
700
800
900
1000
1100
1200
1300
1400
1500
1600


Female 6069 UK
Female 7079 UK
Female over 80 UK
Male 1829 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1200
1400
1600
1800
2000
2200
2500
3000
400
450
500
550
600
Background incidence rate (per 100,000 py)

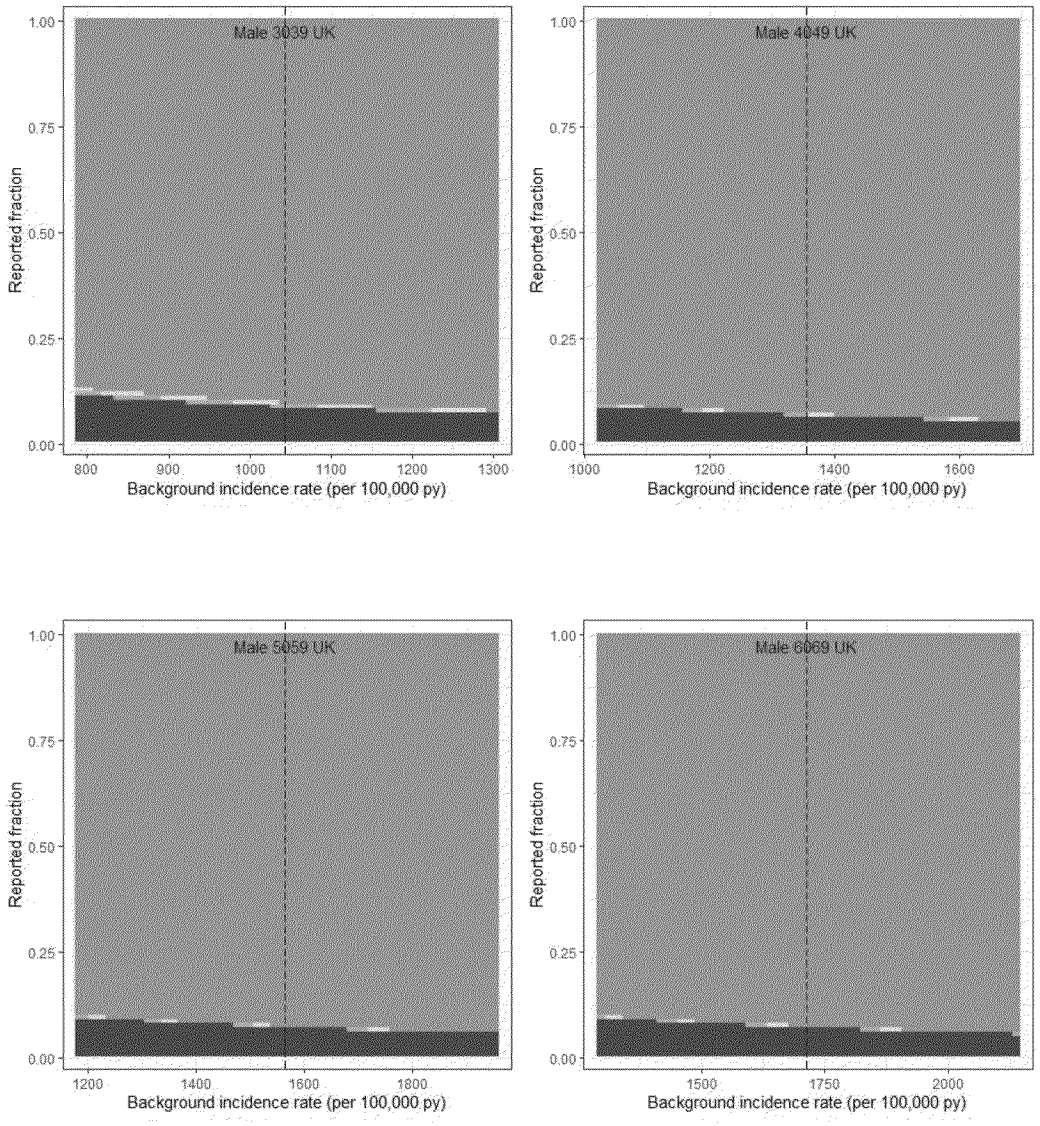

Male 3039 UK
Male 4049 UK
Male 5059 UK
Male 6069 UK
Reported fraction
Background incidence rate (per 100,000 py)

Table 14 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
Female 18-29	110	1134.3	42	889.03	1109488	0.1 (0.08 - 0.12)	Observed significantly < expected
Female 30-39	219	2668.8	42	1226.05	1892968	0.08 (0.07 - 0.09)	Observed significantly < expected
Female 40-49	540	6673.3	42	1315.26	4412245	0.08 (0.07 - 0.09)	Observed significantly < expected
Female 50-59	581	8024.7	42	1173.9	5944683	0.07 (0.07 - 0.08)	Observed significantly < expected
Female 60-69	483	7525.2	42	1368.08	4783416	0.06 (0.06 - 0.07)	Observed significantly < expected
Female 70-79	436	7530.3	42	1883.99	3475875	0.06 (0.05 - 0.06)	Observed significantly < expected

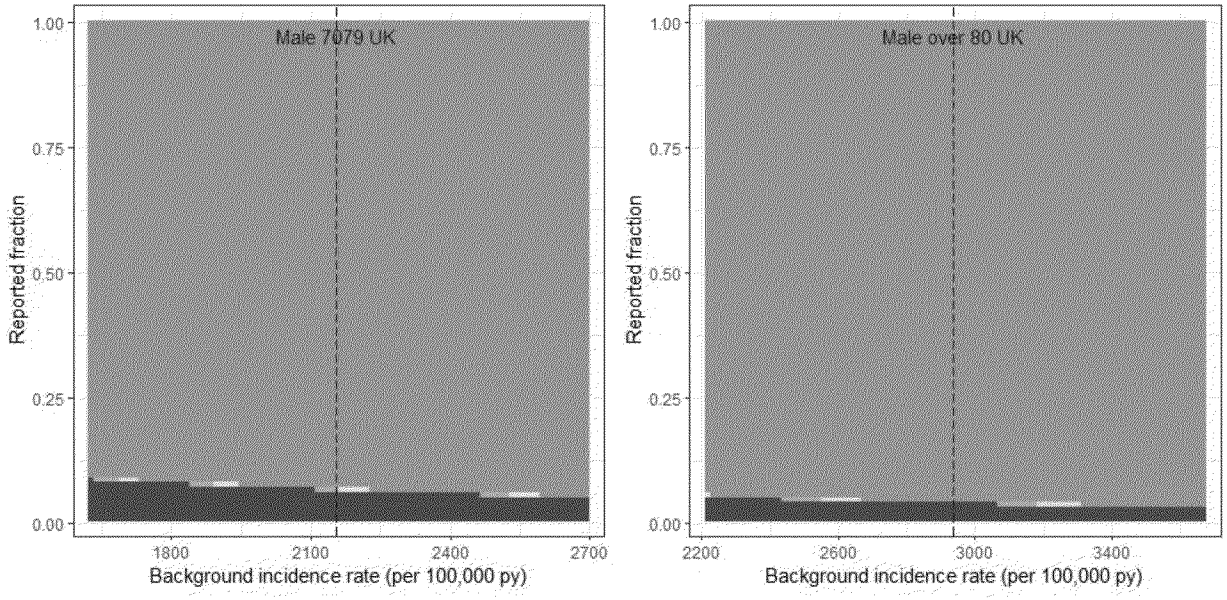
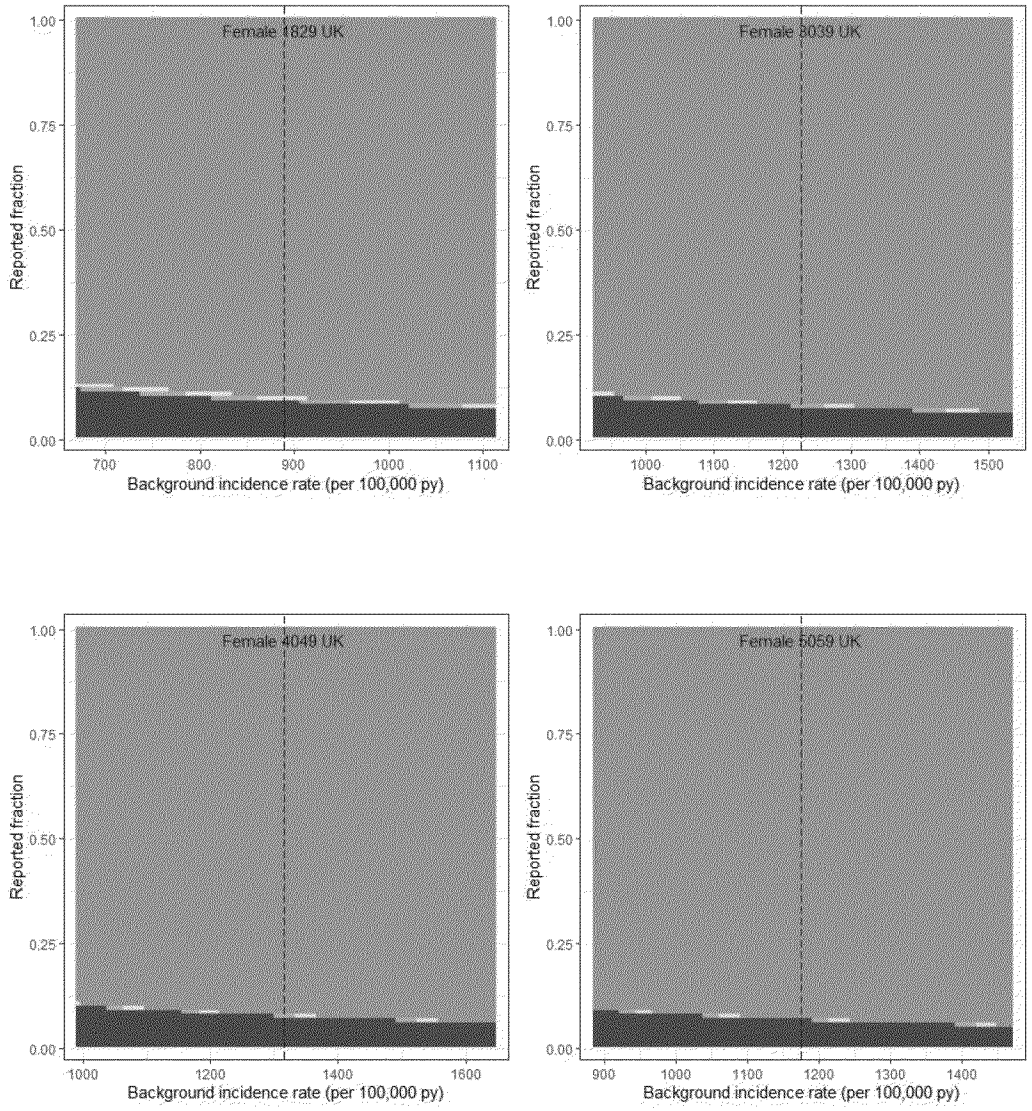
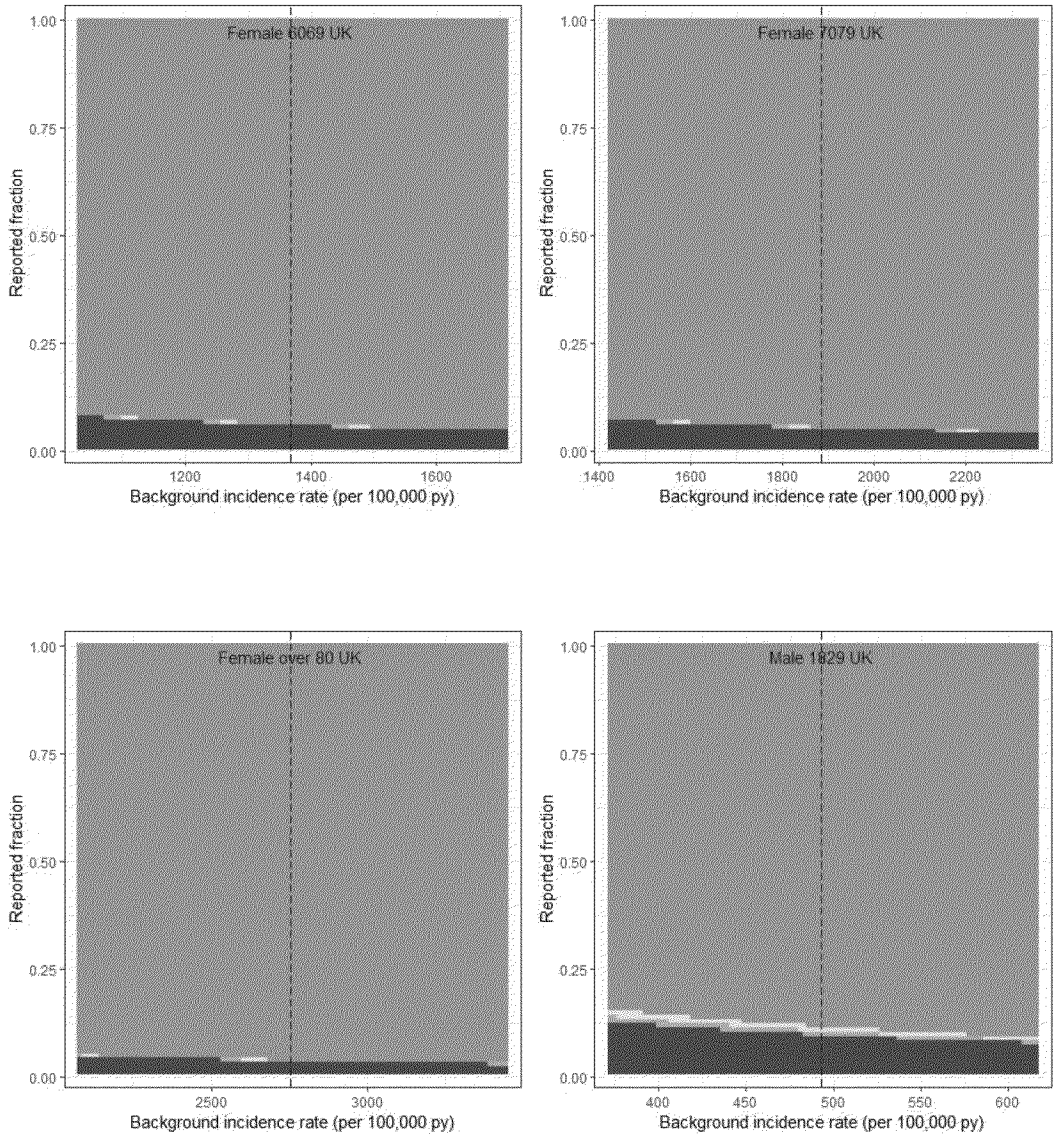


Table 14 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
Female over 80	195	5163.8	42	2754.4	1630324	0.04 (0.03 - 0.04)	Observed significantly < expected
Male 18-29	49	458.3	42	492.71	808938	0.11 (0.08 - 0.14)	Observed significantly < expected
Male 30-39	124	1698.1	42	1043.58	1415003	0.07 (0.06 - 0.09)	Observed significantly < expected
Male 40-49	396	7076.2	42	1354.79	4542157	0.06 (0.05 - 0.06)	Observed significantly < expected
Male 50-59	680	11716.4	42	1564.88	6510960	0.06 (0.05 - 0.06)	Observed significantly < expected
Male 60-69	573	9712.7	42	1711.63	4934728	0.06 (0.05 - 0.06)	Observed significantly < expected
Male 70-79	424	7773.3	42	2154.68	3137304	0.05 (0.05 - 0.06)	Observed significantly < expected
Male over 80	112	3459.1	42	2934.62	1025046	0.03 (0.03 - 0.04)	Observed significantly < expected


Female 1829 UK
Female 3039 UK
Female 4049 UK
Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)


Female 6069 UK
Female 7079 UK
Female over 80 UK
Male 1829 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1200
1400
1600
1800
2000
2200
2500
3000
400
450
500
550
600
Background incidence rate (per 100,000 py)

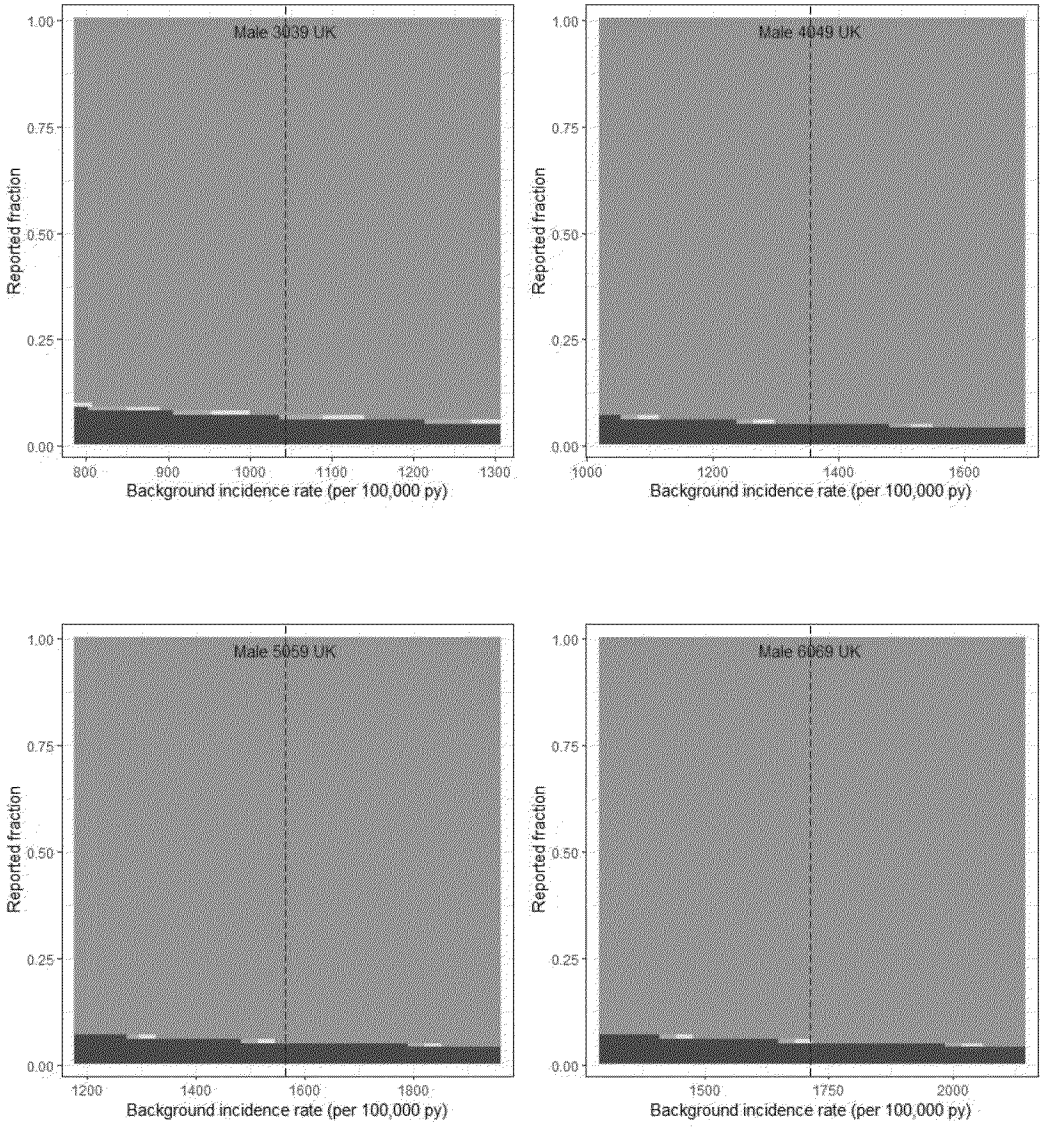
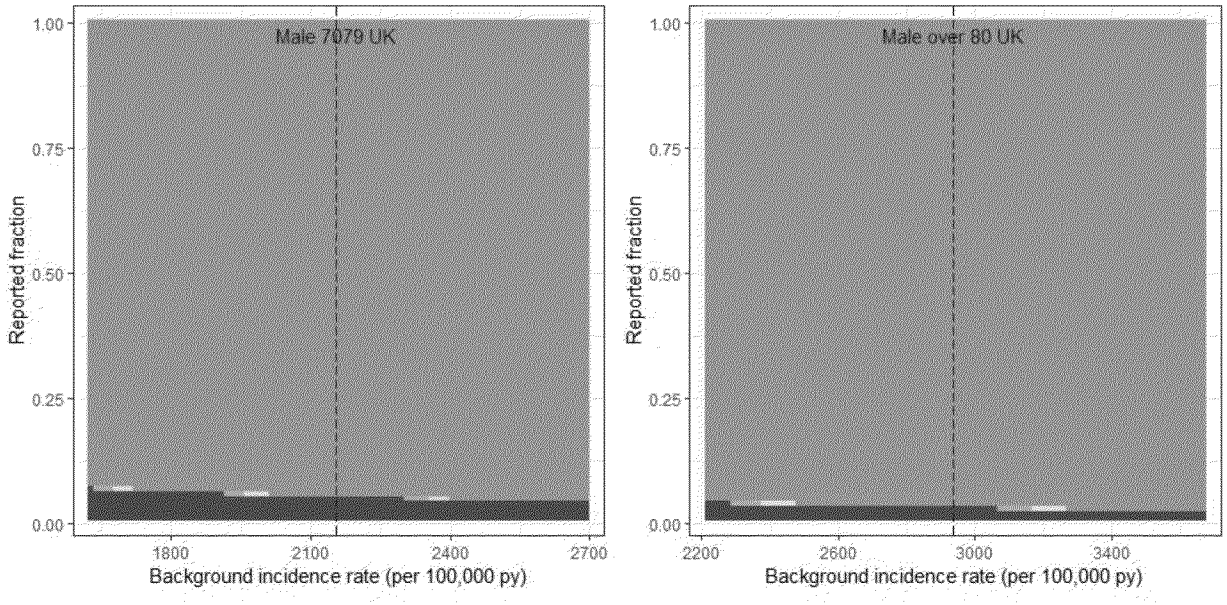

Male 3039 UK
Male 4049 UK
Male 5059 UK
Male 6069 UK
Reported fraction
Background incidence rate (per 100,000 py)

Table 14 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	

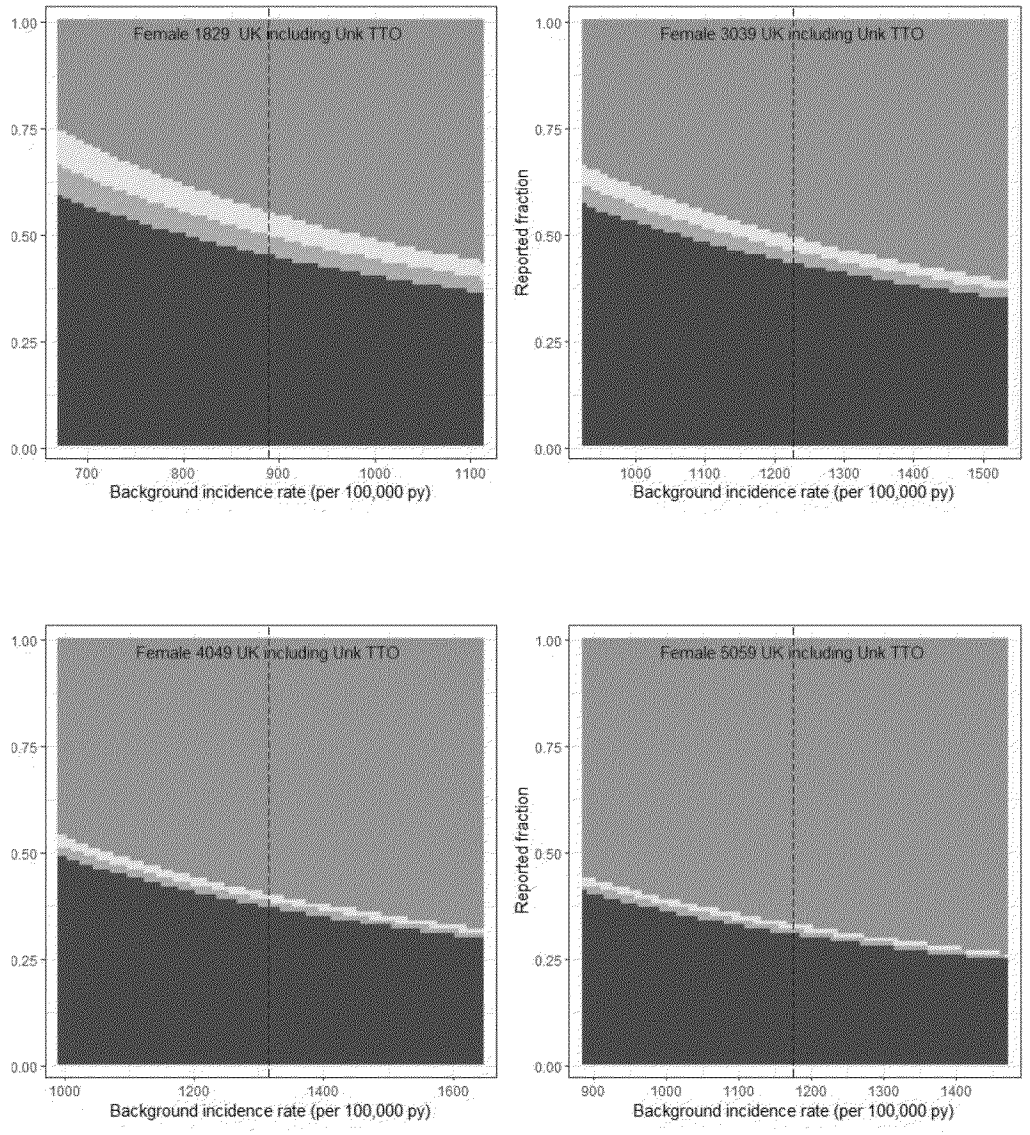


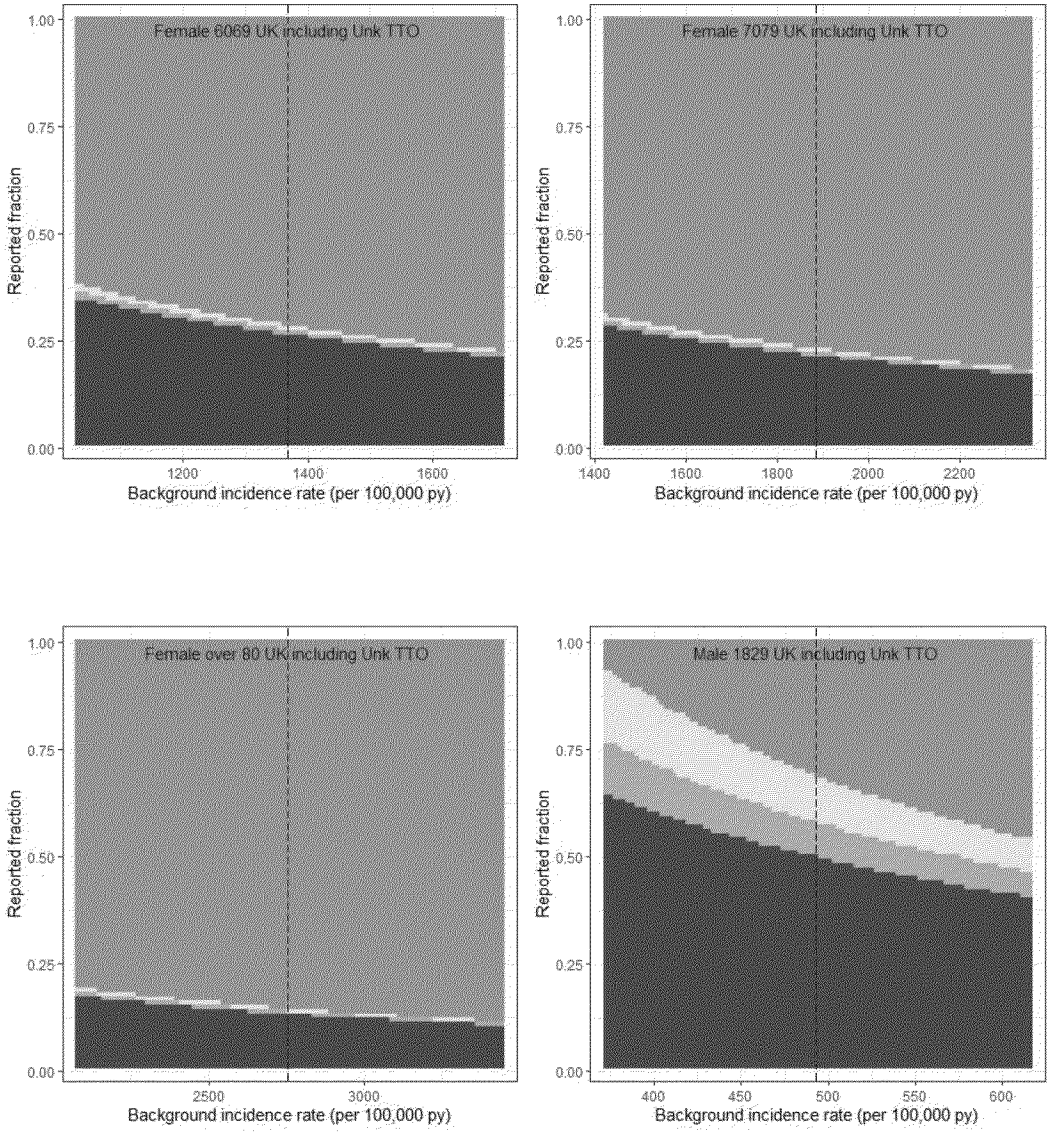
[a] Incidence rate (TR): Source: (Willame et al 2021 [A]) ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: Coagulation disorders-Narrow (Median IR from 2017-2019 and excluding IR from BIPS/GePaRD)

CI Confidence Interval; E Expected; O Observed UK United Kingdom.

Table 15 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK with unknown TTO

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Female 18-29	189	378.1	14	889.03	0.5 (0.43 - 0.58)	Observed significantly < expected
Female 30-39	413	889.6	14	1226.05	0.46 (0.42 - 0.51)	Observed significantly < expected
Female 40-49	870	2224.4	14	1315.26	0.39 (0.37 - 0.42)	Observed significantly < expected
Female 50-59	867	2674.9	14	1173.9	0.32 (0.3 - 0.35)	Observed significantly < expected
Female 60-69	692	2508.4	14	1368.08	0.28 (0.26 - 0.3)	Observed significantly < expected
Female 70-79	564	2510.1	14	1883.99	0.22 (0.21 - 0.24)	Observed significantly < expected
Female over 80	241	1721.3	14	2754.4	0.14 (0.12 - 0.16)	Observed significantly < expected
Male 18-29	89	152.8	14	492.71	0.58 (0.47 - 0.72)	Observed significantly < expected
Male 30-39	161	566.0	14	1043.58	0.28 (0.24 - 0.33)	Observed significantly < expected
Male 40-49	533	2358.7	14	1354.79	0.23 (0.21 - 0.25)	Observed significantly < expected
Male 50-59	915	3905.5	14	1564.88	0.23 (0.22 - 0.25)	Observed significantly < expected
Male 60-69	701	3237.6	14	1711.63	0.22 (0.2 - 0.23)	Observed significantly < expected
Male 70-79	503	2591.1	14	2154.68	0.19 (0.18 - 0.21)	Observed significantly < expected
Male over 80	162	1153.0	14	2934.62	0.14 (0.12 - 0.16)	Observed significantly < expected


Female 1829 UK including Unk TTO
Female 3039 UK including Unk TTO
Female 4049 UK including Unk TTO
Female 5059 UK including Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
700
800
900
1000
1100
1200
1300
1400
1500
1600
Background incidence rate (per 100,000 py)


Female 6069 UK including Unk TTO
Female 7079 UK including Unk TTO
Female over 80 UK including Unk TTO
Male 1829 UK including Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1200
1400
1600
1800
2000
2200
2500
3000
400
450
500
550
600
Background incidence rate (per 100,000 py)

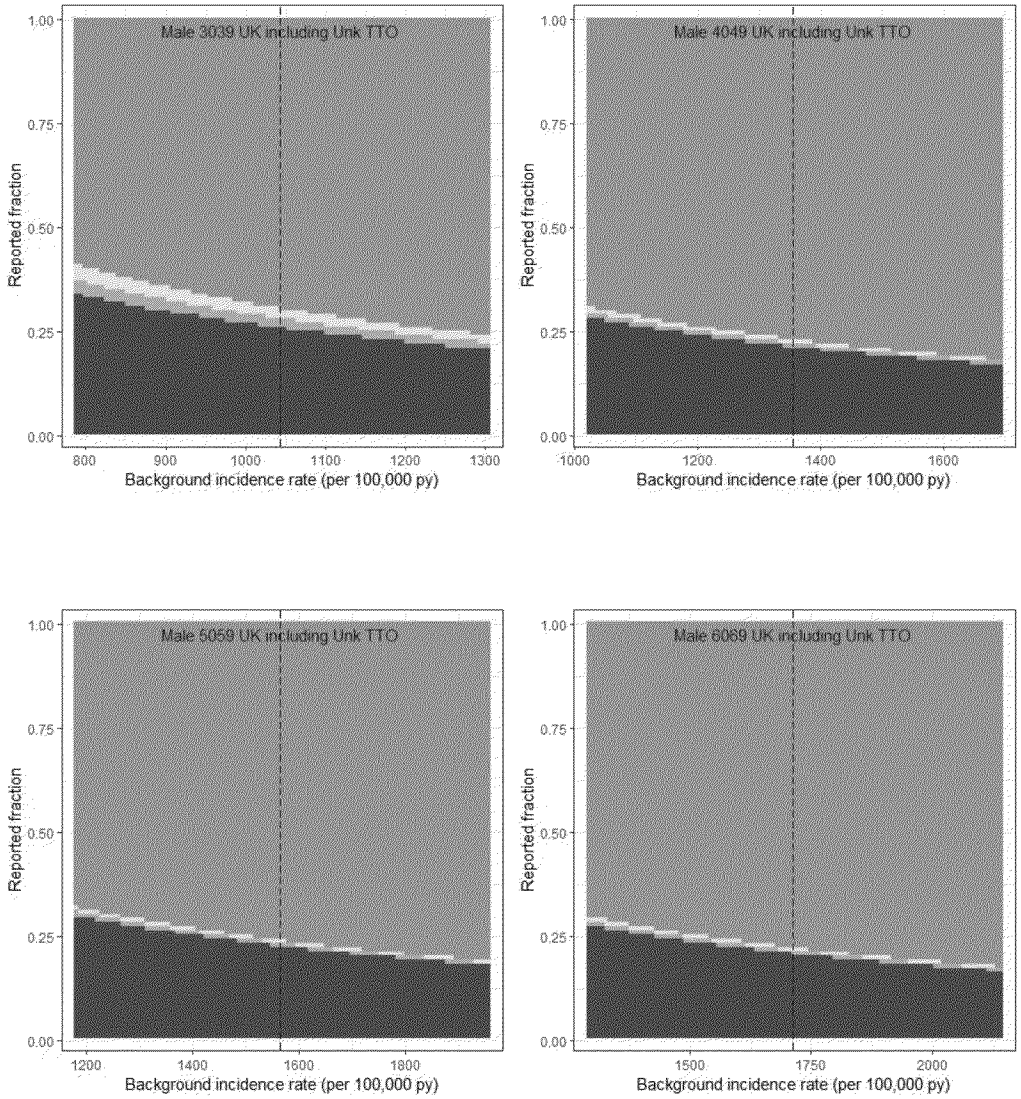

Male 3039 UK including Unk TTO
Male 4049 UK including Unk TTO
Male 5059 UK including Unk TTO
Male 6069 UK including Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
800
900
1000
1100
1200
1300
1000
1200
1400
1600
1800
1500
1750
2000
Background incidence rate (per 100,000 py)

Table 15 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK with unknown TTO

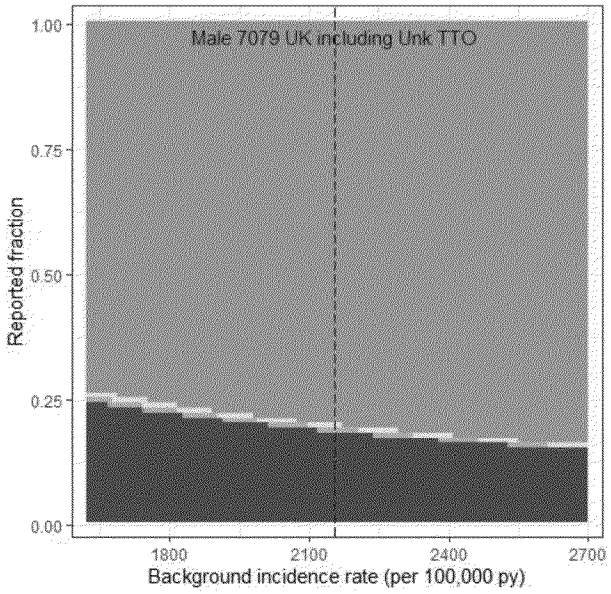
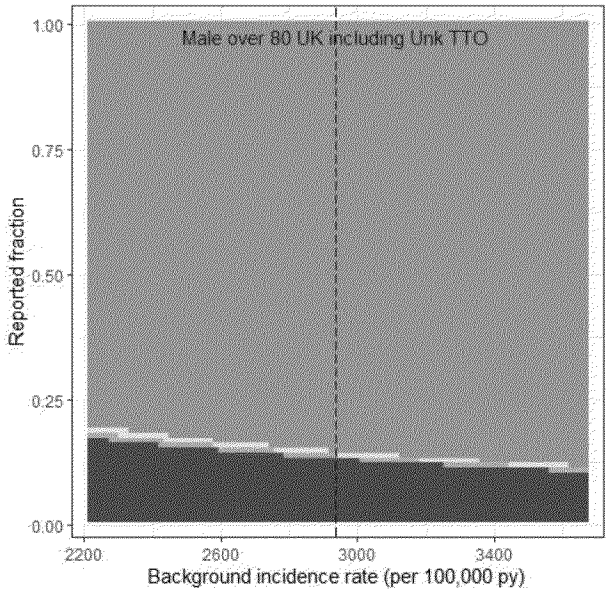
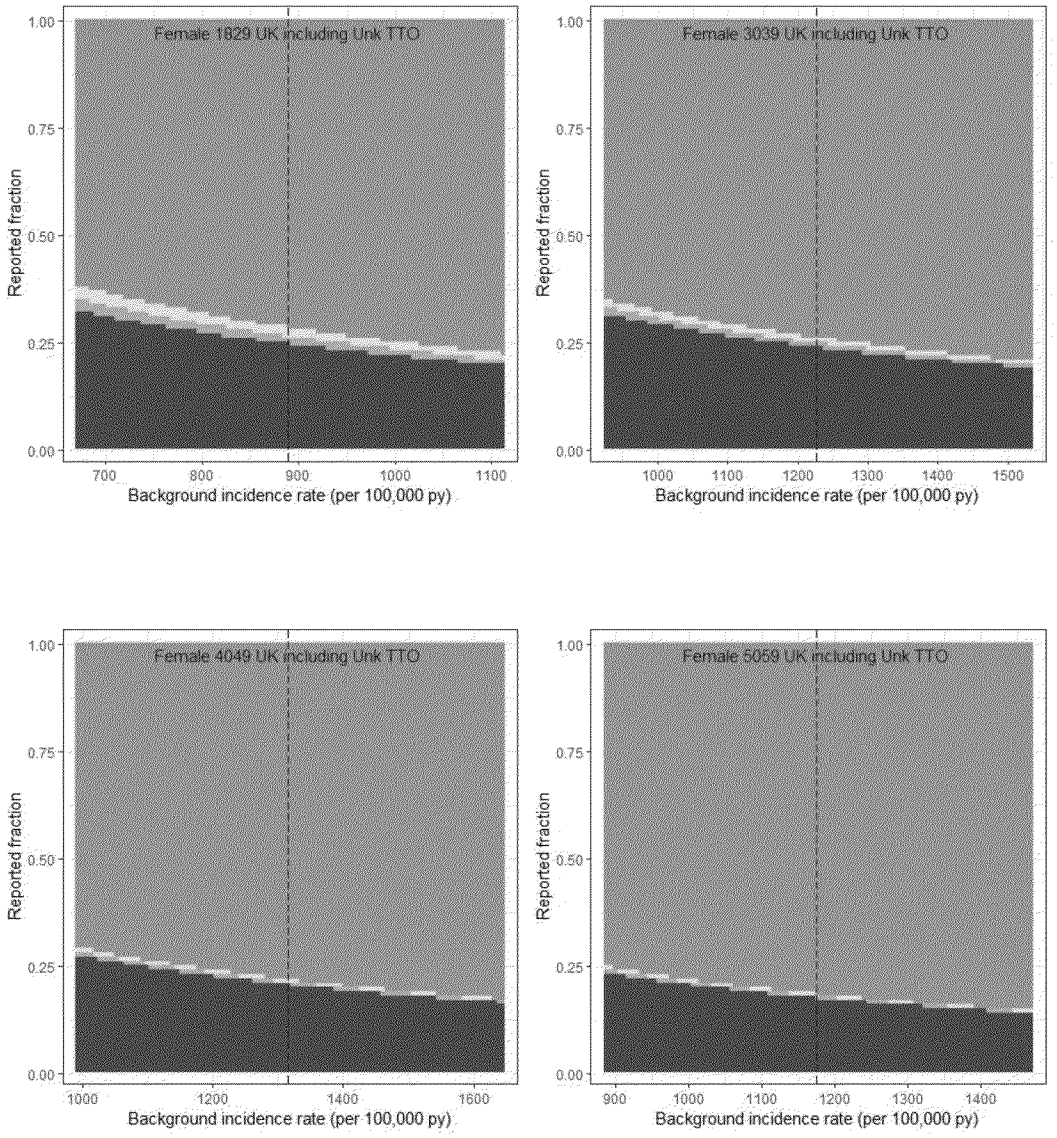
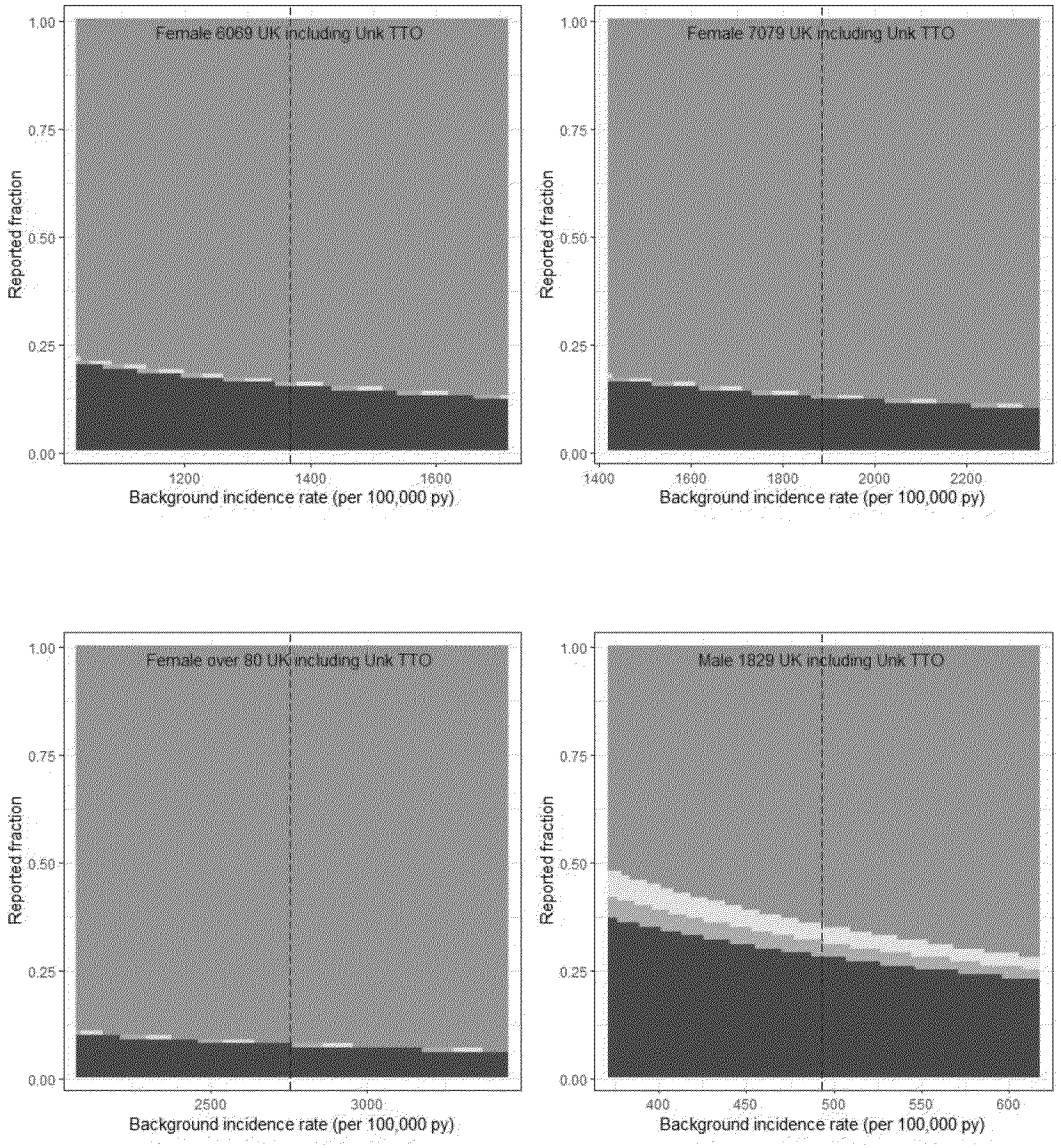
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
						
						
Female 18-29	203	756.2	28	889.03	0.27 (0.23 - 0.31)	Observed significantly < expected
Female 30-39	451	1779.2	28	1226.05	0.25 (0.23 - 0.28)	Observed significantly < expected
Female 40-49	964	4448.9	28	1315.26	0.22 (0.2 - 0.23)	Observed significantly < expected
Female 50-59	986	5349.8	28	1173.9	0.18 (0.17 - 0.2)	Observed significantly < expected
Female 60-69	810	5016.8	28	1368.08	0.16 (0.15 - 0.17)	Observed significantly < expected
Female 70-79	664	5020.2	28	1883.99	0.13 (0.12 - 0.14)	Observed significantly < expected
Female over 80	286	3442.5	28	2754.4	0.08 (0.07 - 0.09)	Observed significantly < expected

Table 15 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK with unknown TTO

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Male 18-29	98	305.6	28	492.71	0.32 (0.26 - 0.39)	Observed significantly < expected
Male 30-39	190	1132.0	28	1043.58	0.17 (0.14 - 0.19)	Observed significantly < expected
Male 40-49	617	4717.5	28	1354.79	0.13 (0.12 - 0.14)	Observed significantly < expected
Male 50-59	1061	7810.9	28	1564.88	0.14 (0.13 - 0.14)	Observed significantly < expected
Male 60-69	830	6475.2	28	1711.63	0.13 (0.12 - 0.14)	Observed significantly < expected
Male 70-79	602	5182.2	28	2154.68	0.12 (0.11 - 0.13)	Observed significantly < expected
Male over 80	184	2306.1	28	2934.62	0.08 (0.07 - 0.09)	Observed significantly < expected


Female 1829 UK including Unk TTO
Female 3039 UK including Unk TTO
Female 4049 UK including Unk TTO
Female 5059 UK including Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
700
800
900
1000
1100
1200
1300
1400
1500
1600


Female 6069 UK including Unk TTO
Female 7079 UK including Unk TTO
Female over 80 UK including Unk TTO
Male 1829 UK including Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1200
1400
1600
1800
2000
2200
2500
3000
400
450
500
550
600
Background incidence rate (per 100,000 py)

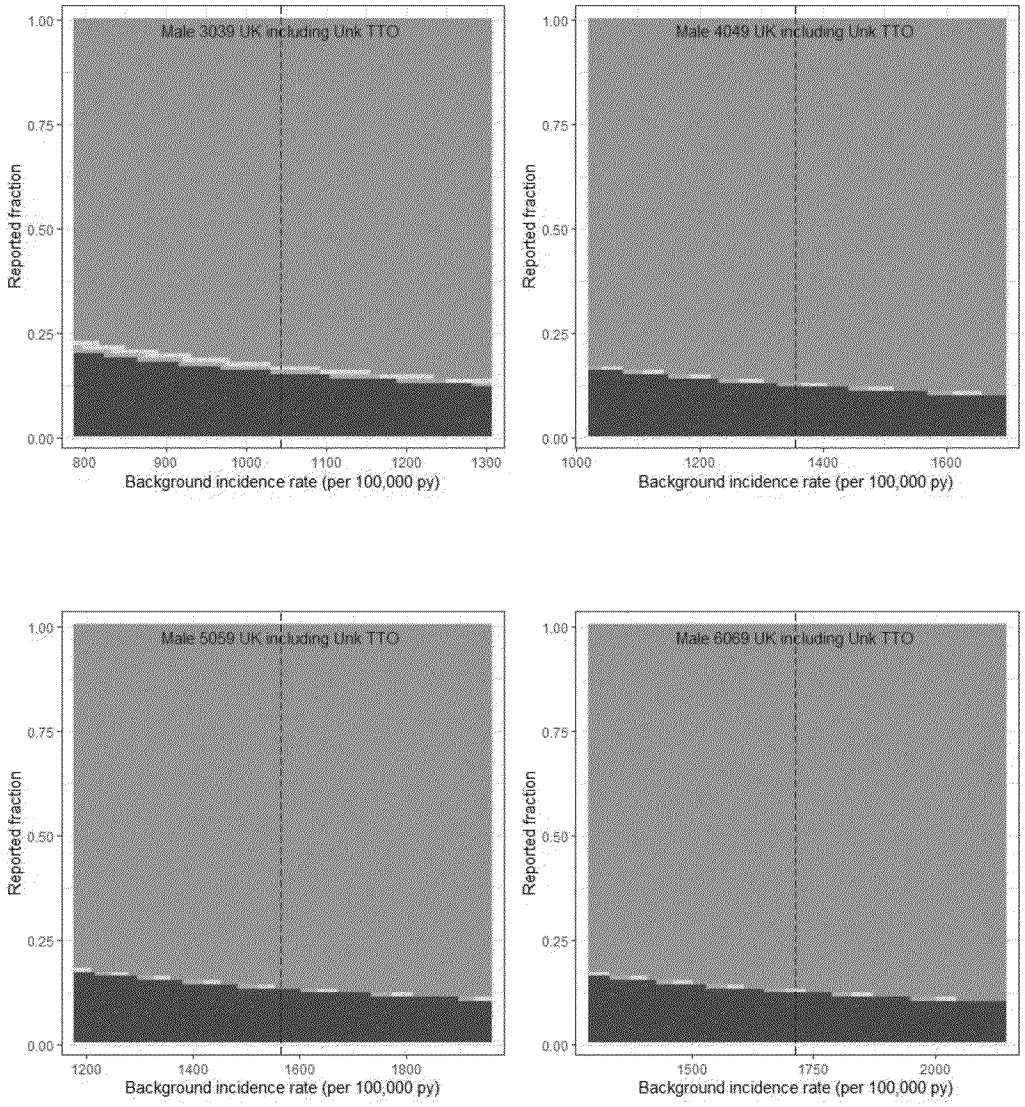

Male 3039 UK including Unk TTO
Male 4049 UK including Unk TTO
Male 5059 UK including Unk TTO
Male 6069 UK including Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
800
900
1000
1100
1200
1300
1400
1500
1600
1750
1800
2000

Table 15 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK with unknown TTO

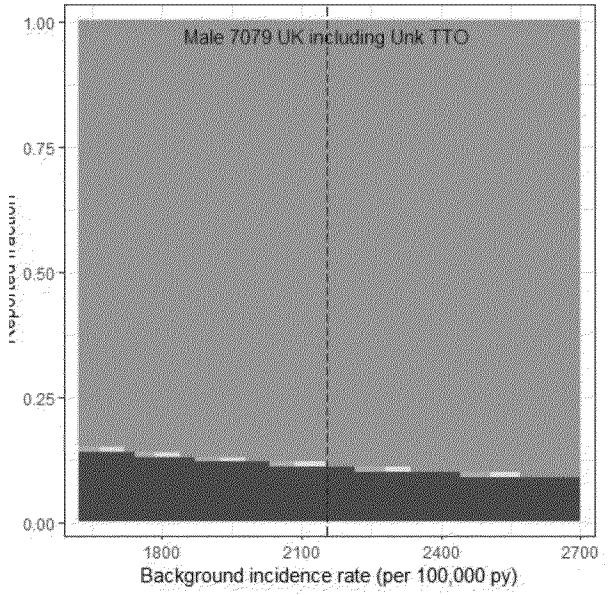
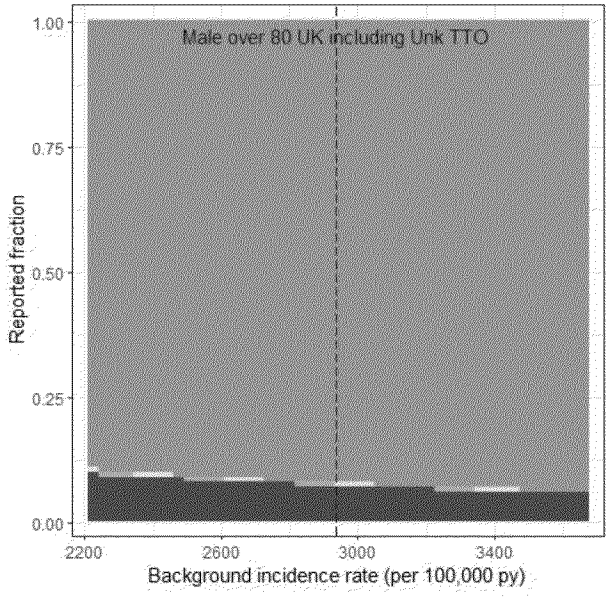
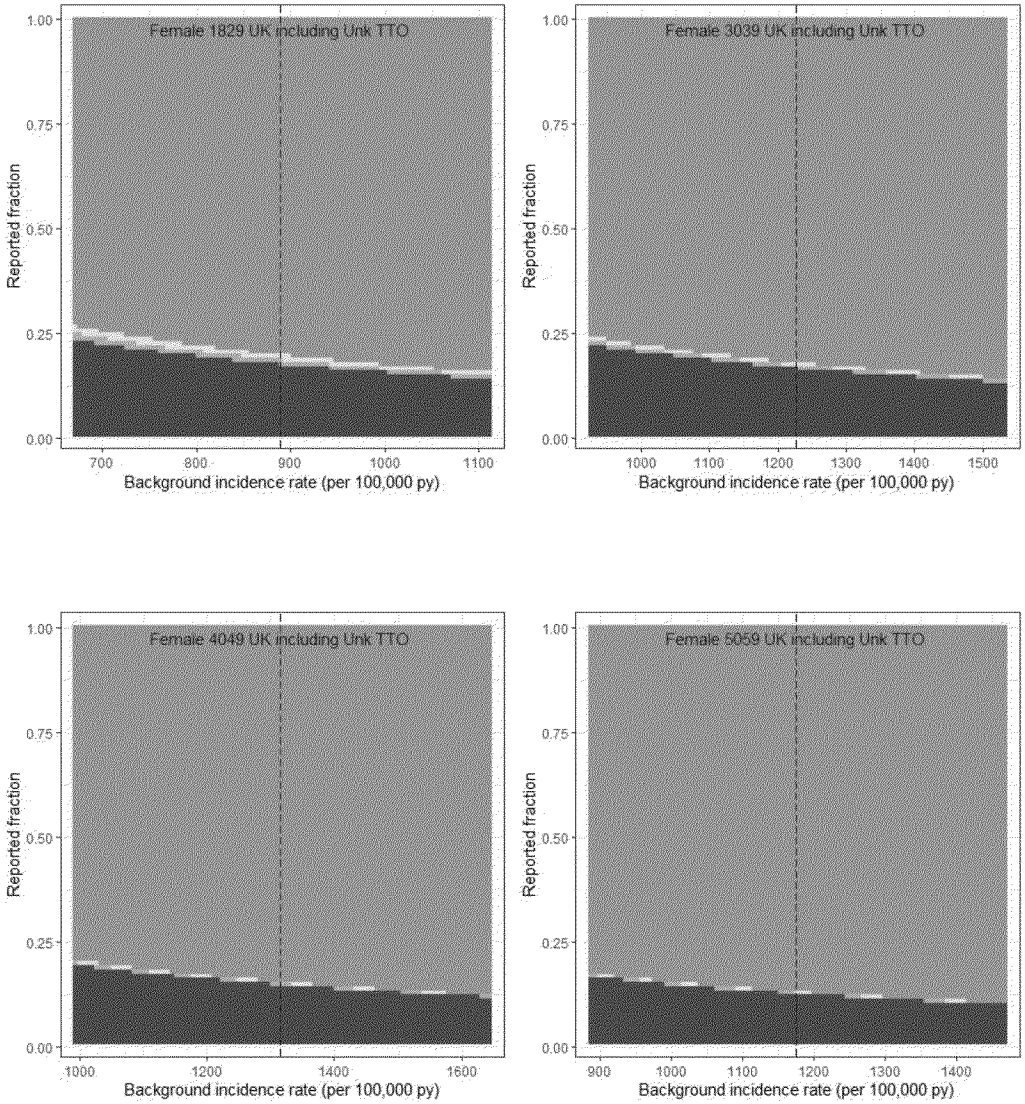
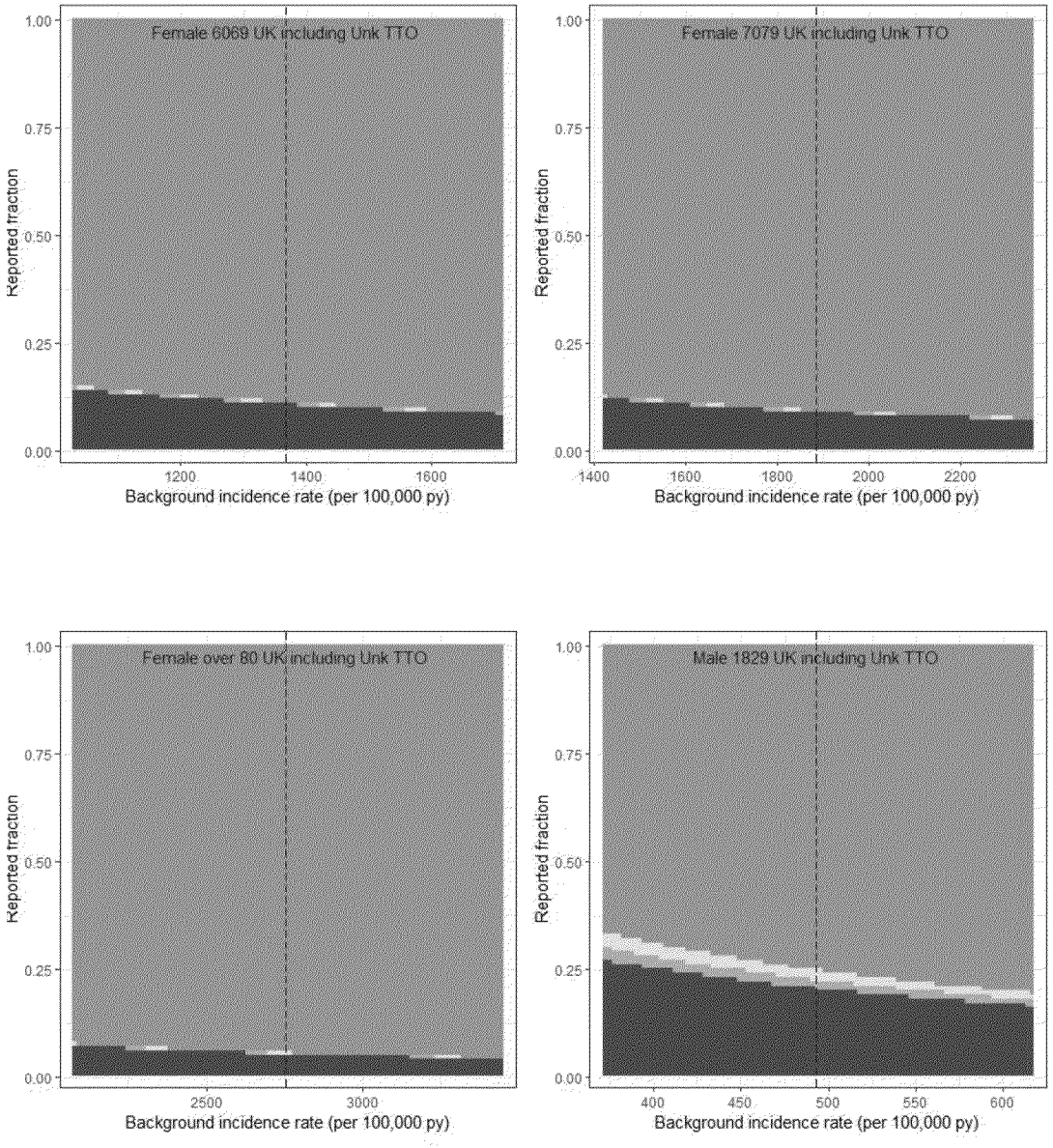
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
 						
Female 18-29	216	1134.3	42	889.03	0.19 (0.17 - 0.22)	Observed significantly < expected
Female 30-39	473	2668.8	42	1226.05	0.18 (0.16 - 0.19)	Observed significantly < expected
Female 40-49	1014	6673.3	42	1315.26	0.15 (0.14 - 0.16)	Observed significantly < expected
Female 50-59	1040	8024.7	42	1173.9	0.13 (0.12 - 0.14)	Observed significantly < expected
Female 60-69	857	7525.2	42	1368.08	0.11 (0.11 - 0.12)	Observed significantly < expected
Female 70-79	723	7530.3	42	1883.99	0.1 (0.09 - 0.1)	Observed significantly < expected
Female over 80	303	5163.8	42	2754.4	0.06 (0.05 - 0.07)	Observed significantly < expected

Table 15 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK with unknown TTO

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Male 18-29	105	458.3	42	492.71	0.23 (0.19 - 0.28)	Observed significantly < expected
Male 30-39	208	1698.1	42	1043.58	0.12 (0.11 - 0.14)	Observed significantly < expected
Male 40-49	682	7076.2	42	1354.79	0.1 (0.09 - 0.1)	Observed significantly < expected
Male 50-59	1141	11716.4	42	1564.88	0.1 (0.09 - 0.1)	Observed significantly < expected
Male 60-69	910	9712.7	42	1711.63	0.09 (0.09 - 0.1)	Observed significantly < expected
Male 70-79	662	7773.3	42	2154.68	0.09 (0.08 - 0.09)	Observed significantly < expected
Male over 80	196	3459.1	42	2934.62	0.06 (0.05 - 0.07)	Observed significantly < expected


Female 1829 UK including Unk TTO
Female 3039 UK including Unk TTO
Female 4049 UK including Unk TTO
Female 5059 UK including Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
700
800
900
1000
1100
1200
1300
1400
1500
1600


Female 6069 UK including Unk TTO
Female 7079 UK including Unk TTO
Female over 80 UK including Unk TTO
Male 1829 UK including Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1200
1400
1600
1800
2000
2200
2500
3000
400
450
500
550
600
Background incidence rate (per 100,000 py)

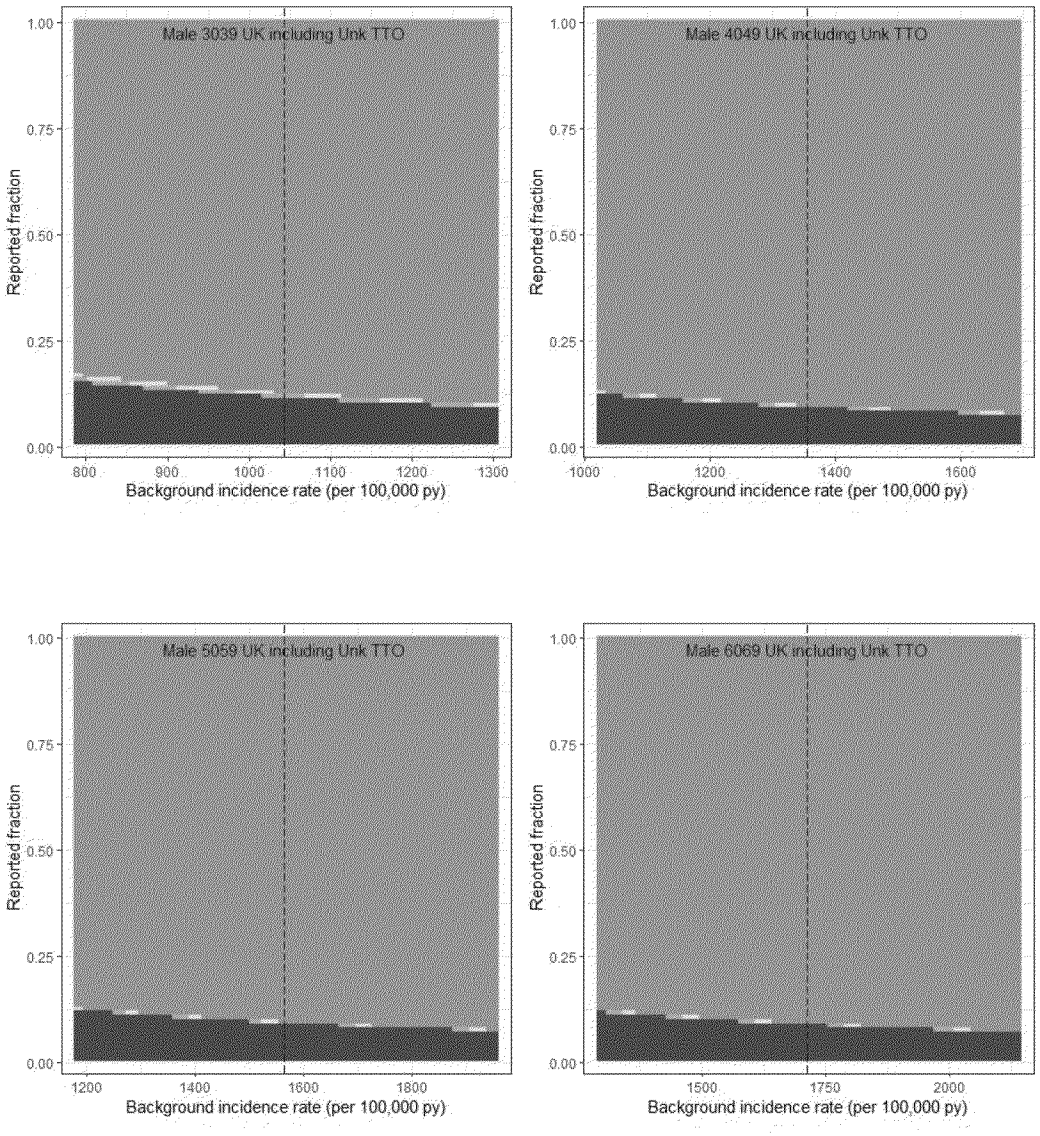
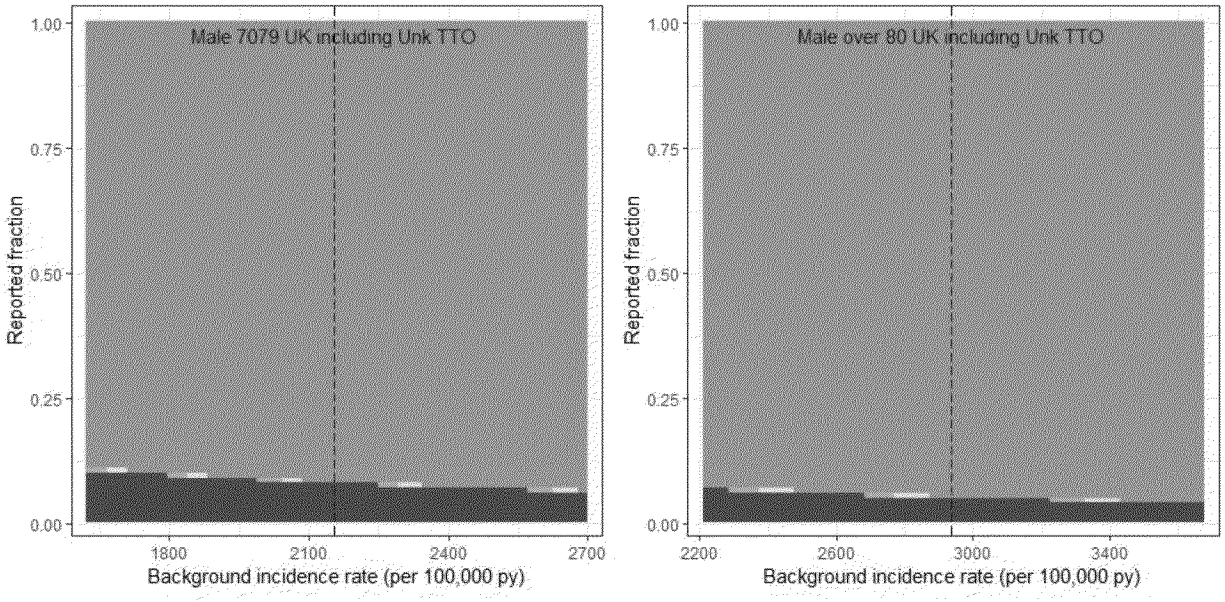

Male 3039 UK including Unk TTO
Male 4049 UK including Unk TTO
Male 5059 UK including Unk TTO
Male 6069 UK including Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
800
900
1000
1100
1200
1300
1400
1500
1600
1750
1800
2000

Table 15 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) by age and gender from UK with unknown TTO

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	

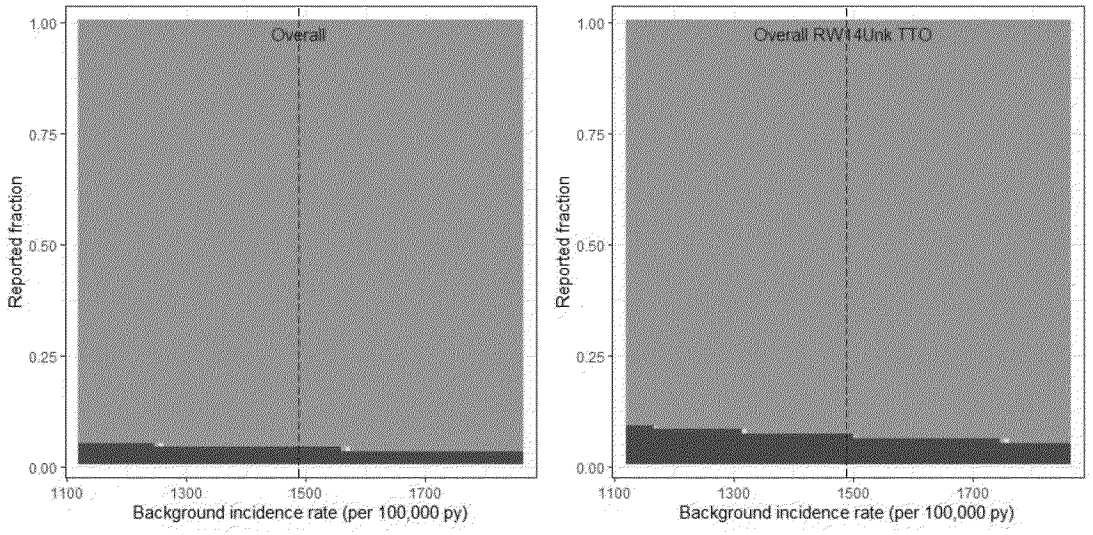


[a] Incidence rate (IR): Willame et al 2021 [A] ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: Coagulation disorders-Narrow (Median IR from 2017-2019 and excluding IR from BIPS/GePaRD).

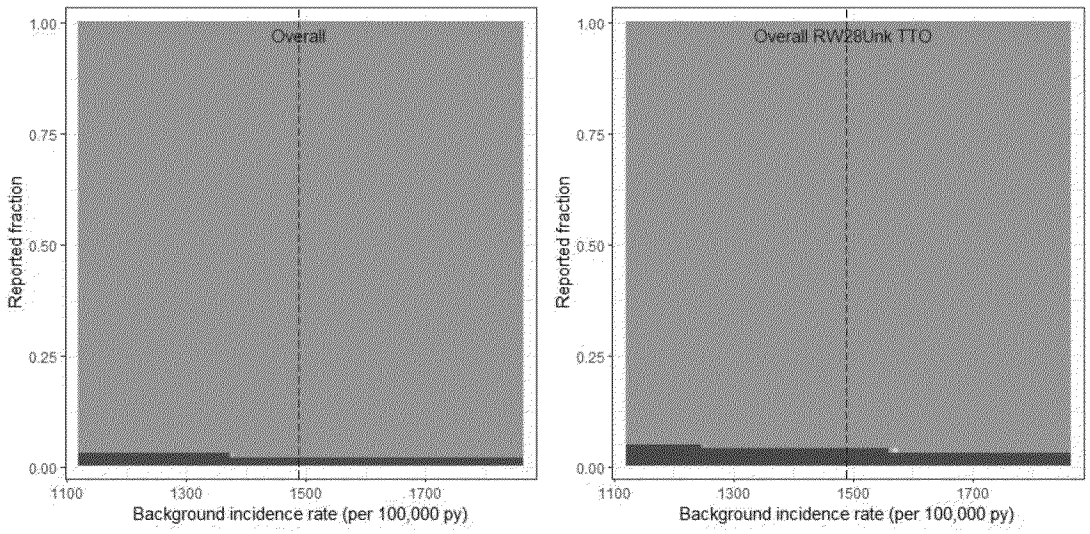
CI Confidence Interval; E Expected; IR Incidence Rate; O Observed TTO: Time to onset; UK United Kingdom

Table 16 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) Overall

Description	Observed Cases	Expected number of cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Overall	11189	265811.2	14	1487.76	0.04 (0.04 - 0.04)	Observed significantly < expected
Overall (RW14 + Unk TTO)	18797	265811.2	14	1487.76	0.07 (0.07 - 0.07)	Observed significantly < expected
Overall	14778	531622.4	28	1487.76	0.03 (0.03 - 0.03)	Observed significantly < expected
Overall (RW28 + Unk TTO)	22386	531622.4	28	1487.76	0.04 (0.04 - 0.04)	Observed significantly < expected
Overall	16584	797433.6	42	1487.76	0.02 (0.02 - 0.02)	Observed significantly < expected
Overall (RW42 + Unk TTO)	24192	797433.6	42	1487.76	0.03 (0.03 - 0.03)	Observed significantly < expected

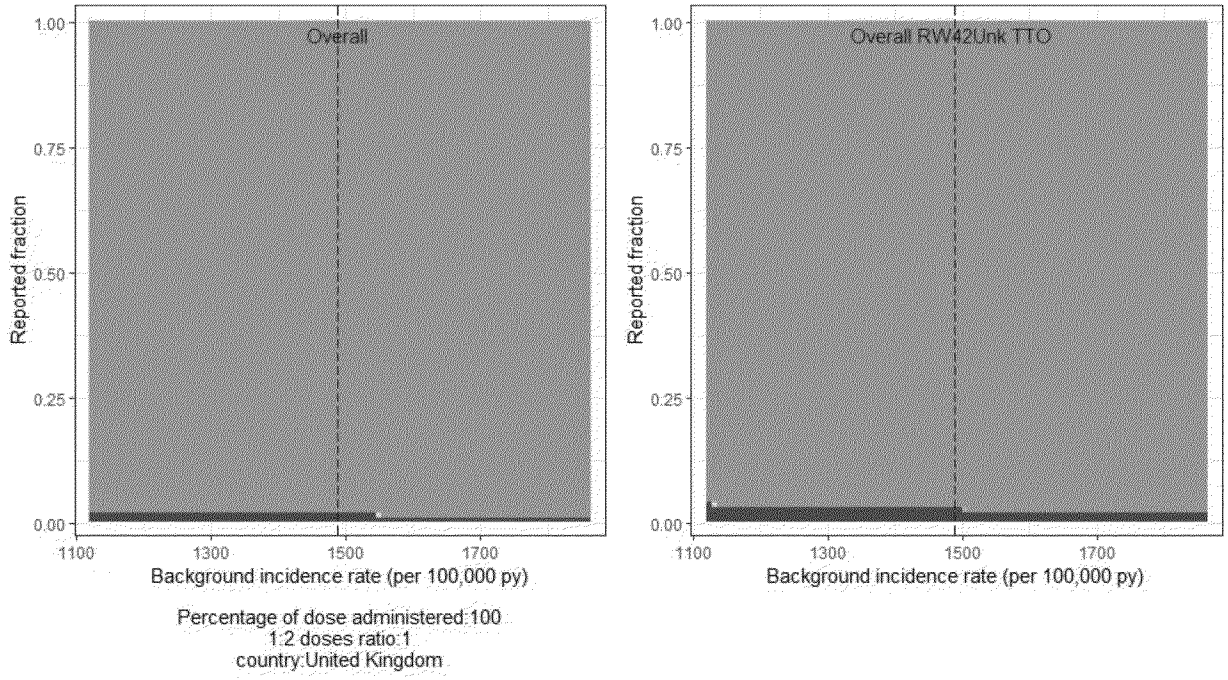

Overall
Reported fraction
1.00
0.75
0.50
0.25
0.00
1100
1300
1500
1700
Background incidence rate (per 100,000 py)

Overall RW14Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1100
1300
1500
1700
Background incidence rate (per 100,000 py)


Overall
Reported fraction
1.00
0.75
0.50
0.25
0.00
1100
1300
1500
1700
Background incidence rate (per 100,000 py)

Overall RW28Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1100
1300
1500
1700
Background incidence rate (per 100,000 py)

Table 16 Observed Versus Expected analysis for Embolic and thrombotic events (Thrombosis) Overall

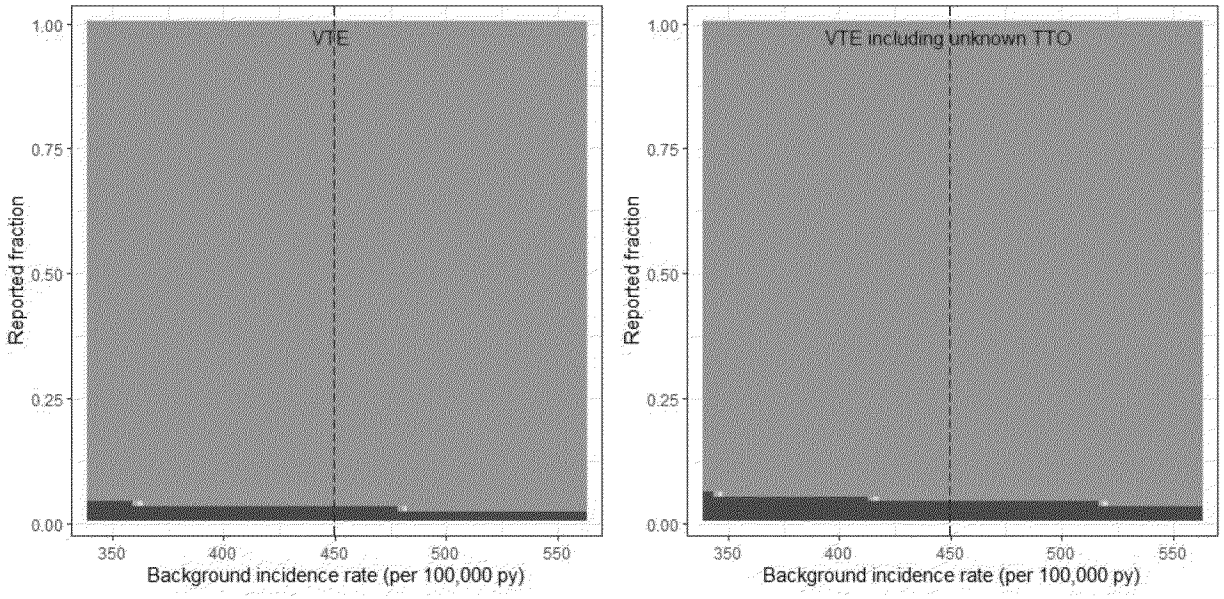
Description	Observed Cases	Expected number of cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
						

[a] Incidence Rate (IR) (Willame et al 2021 [A]) ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: Coagulation disorders-Narrow (Median IR from 2017-2019 and excluding IR from BIPS/GePaRD).

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed; RW risk window; TTO: Time to onset; Unk Unknown

Table 17 Observed Versus Expected analysis for Venous Thromboembolism[b] (VTE)

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
VTE	5150	160688.07	28	449.69	0.03 (0.03 - 0.03)	Observed significantly < expected
VTE (including unknown TTO)	7413	160688.07	28	449.69	0.05 (0.05 - 0.05)	Observed significantly < expected



[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Venous thromboembolism (Narrow))

[b] Preferred Terms included: Deep vein thrombosis; Pulmonary embolism; Pulmonary infarction; Pulmonary microemboli; Pulmonary thrombosis; Pulmonary venous thrombosis

CI Confidence Interval; E Expected; O Observed, TTO Time to onset.

Table 18 Observed Versus Expected analysis for Fibromyalgia

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Fibromyalgia	226	17848.67	42	33.3	0.01 (0.01 - 0.01)	Observed significantly < expected
Fibromyalgia (including unknown TTO)	478	17848.67	42	33.3	0.03 (0.02 - 0.03)	Observed significantly < expected
Fibromyalgia	233	76494.31	180	33.3	0 (0 - 0)	Observed significantly < expected
Fibromyalgia (including unknown TTO)	485	76494.31	180	33.3	0.01 (0.01 - 0.01)	Observed significantly < expected
Fibromyalgia (Extended RW)	235	100292.54	236	33.3	0 (0 - 0)	Observed significantly < expected
Fibromyalgia (Extended RW+Unk TTO)	487	100292.54	236	33.3	0 (0 - 0.01)	Observed significantly < expected

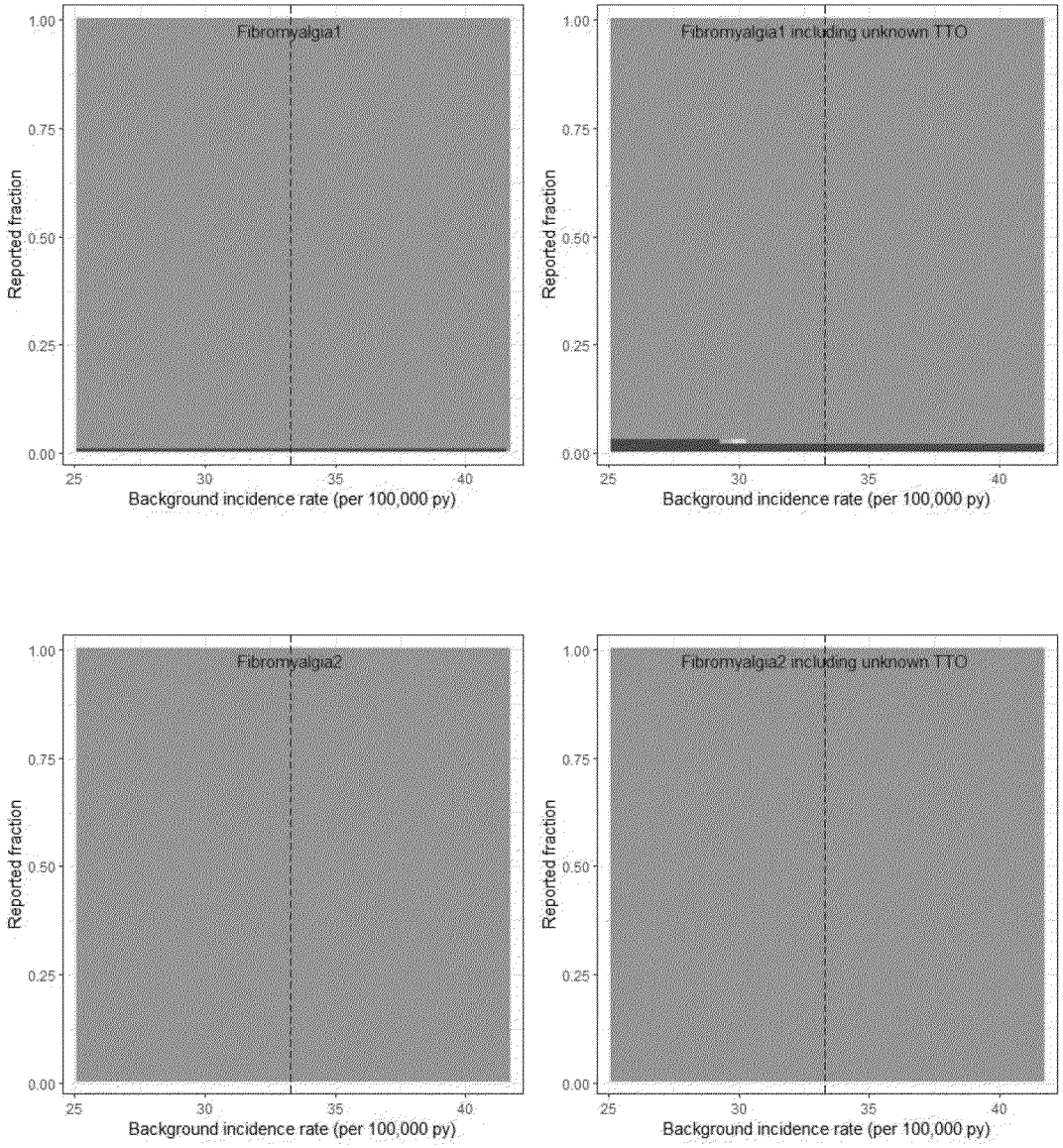
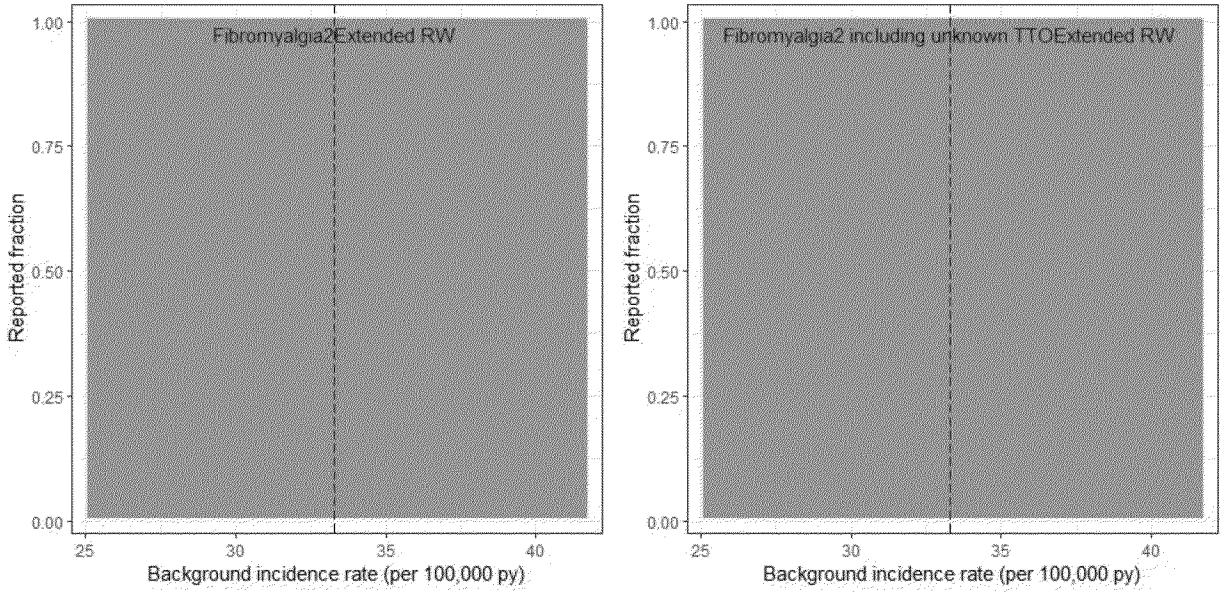

Fibromyalgia1
Fibromyalgia1 including unknown TTO
Fibromyalgia2
Fibromyalgia2 including unknown TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
25
30
35
40
Background incidence rate (per 100,000 py)

Table 18 Observed Versus Expected analysis for Fibromyalgia

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
						

[a] IR Source: Collin et al 2017

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, RW Risk window; TTO Time to onset; Unk Unknown.

Table 19 Observed Versus Expected analysis for Acute disseminated encephalomyelitis (ADEM) all reports (Global)

Adverse Events	Observed Cases [b]	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	
Overall-Access Incidence rates	46	26.8	14	0.15	466115644	1.72 (1.26 - 2.29)	Observed significantly > expected
Overall-Access Incidence rates	55	57.43	30	0.15	466115644	0.96 (0.72 - 1.25)	Observed < expected
Overall- Access Incidence Rate	57	80.4	42	0.15	466115644	0.71 (0.54 - 0.92)	Observed significantly < expected
Overall (RW14+ Unk TTO)	67	26.8	14	0.15	466115644	2.5 (1.94 - 3.17)	Observed significantly > expected
Overall (RW30 + Unk TTO)	76	57.43	30	0.15	466115644	1.32 (1.04 - 1.66)	Observed significantly > expected
Overall (RW42 + Unk TTO)	78	80.4	42	0.15	466115644	0.97 (0.77 - 1.21)	Observed < expected

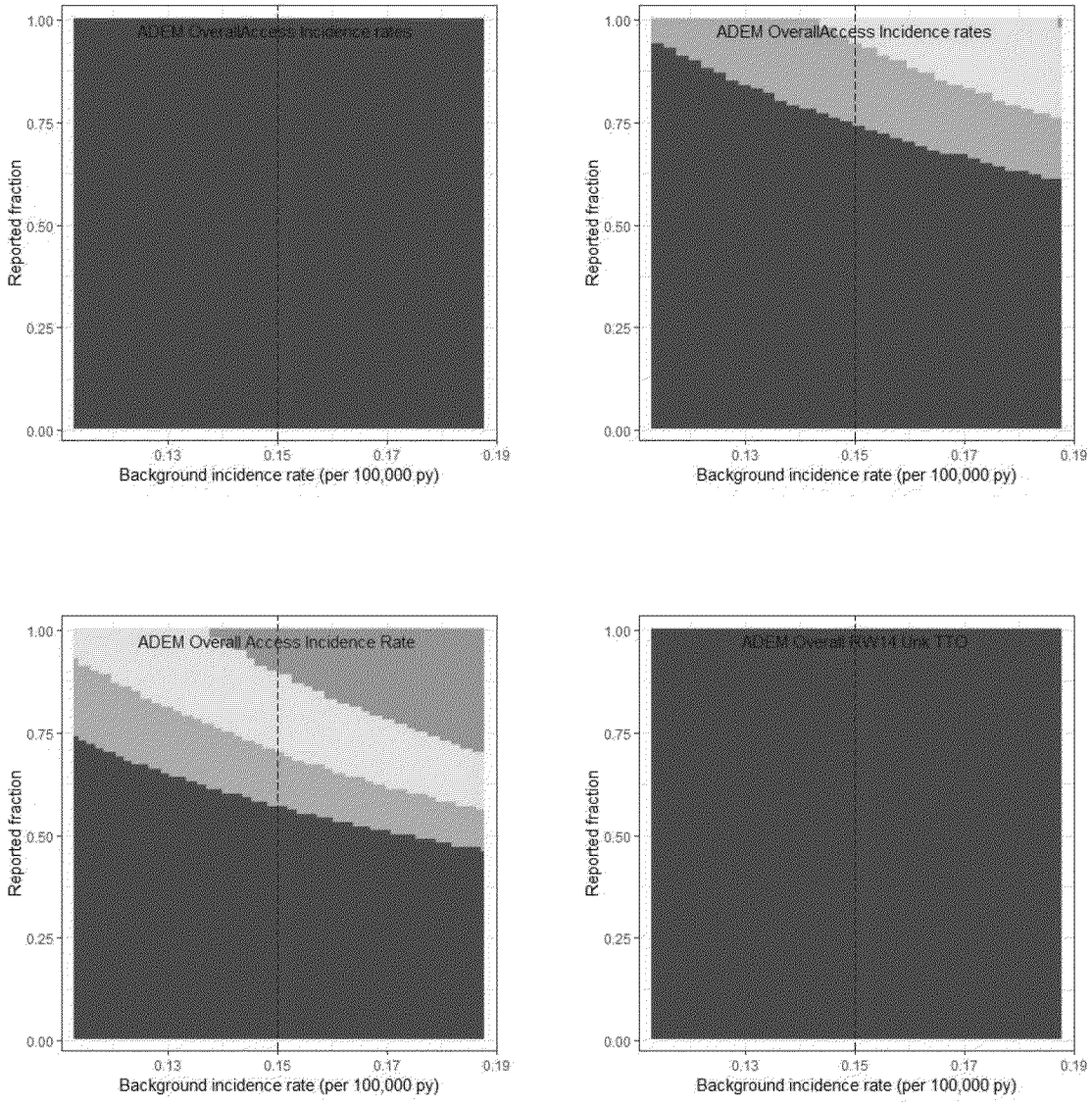
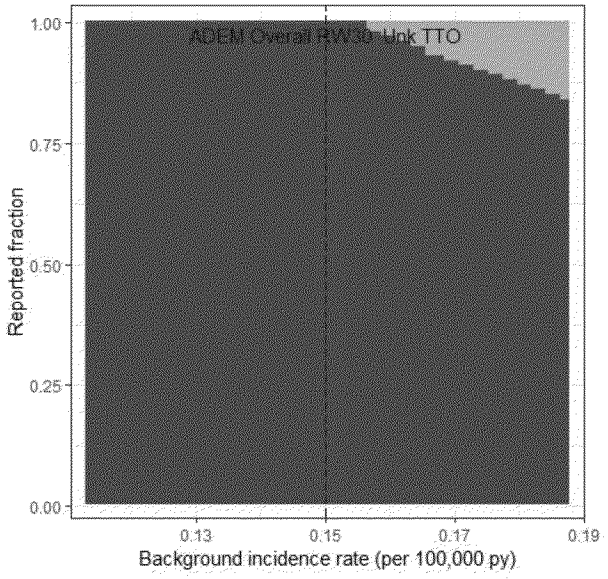
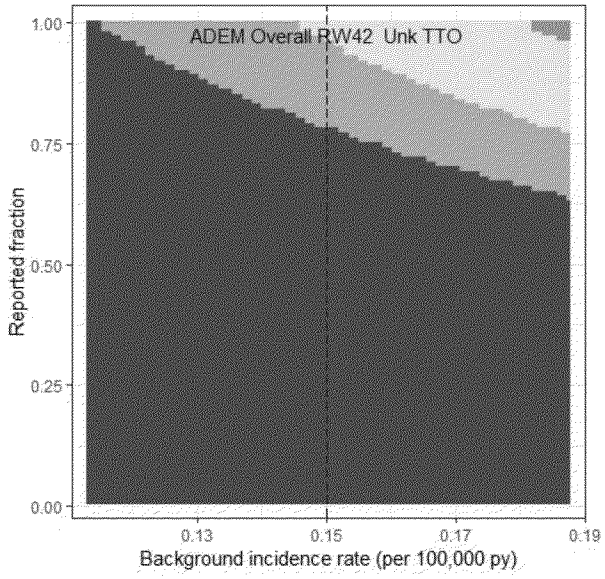

ADEM OverallAccess Incidence rates
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.13
0.15
0.17
0.19
Background incidence rate (per 100,000 py)
ADEM OverallAccess Incidence rates
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.13
0.15
0.17
0.19
Background incidence rate (per 100,000 py)
ADEM Overall Access Incidence Rate
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.13
0.15
0.17
0.19
Background incidence rate (per 100,000 py)
ADEM Overall RW14 Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.13
0.15
0.17
0.19
Background incidence rate (per 100,000 py)

Table 19 Observed Versus Expected analysis for Acute disseminated encephalomyelitis (ADEM) all reports (Global)

Adverse Events	Observed Cases [b]	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	





[a]Source: Willame et al 2021 [A] (Meta-analysis IRs from ADEM Narrow 2017-2019).
ADEM Acute disseminated encephalomyelitis, CI Confidence Interval, E Expected, O Observed, RW Risk window, TTO Time To Onset, Unk Unknown.

Table 20 Observed Versus Expected analysis for ADEM Acute disseminated encephalomyelitis (ADEM) cases meeting the Brighton collaboration criteria (BCC) Level 1, 2 or 3 (Global reports)

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	
Overall -Access Incidence rates	24	26.8	14	0.15	466115644	0.9 (0.57 - 1.33)	Observed < expected
Overall-Access Incidence rates	30	57.43	30	0.15	466115644	0.52 (0.35 - 0.75)	Observed significantly < expected
Overall-Access Incidence rates	31	80.4	42	0.15	466115644	0.39 (0.26 - 0.55)	Observed significantly < expected
Overall-ACCESS Incidence Rate (RW14 + Unk TTO)	28	26.8	14	0.15	466115644	1.04 (0.69 - 1.51)	Observed > expected
Overall-ACCESS Incidence Rate (RW30 + Unk TTO)	34	57.43	30	0.15	466115644	0.59 (0.41 - 0.83)	Observed significantly < expected
Overall-ACCESS Incidence Rate (RW42 + Unk TTO)	35	80.4	42	0.15	466115644	0.44 (0.3 - 0.61)	Observed significantly < expected

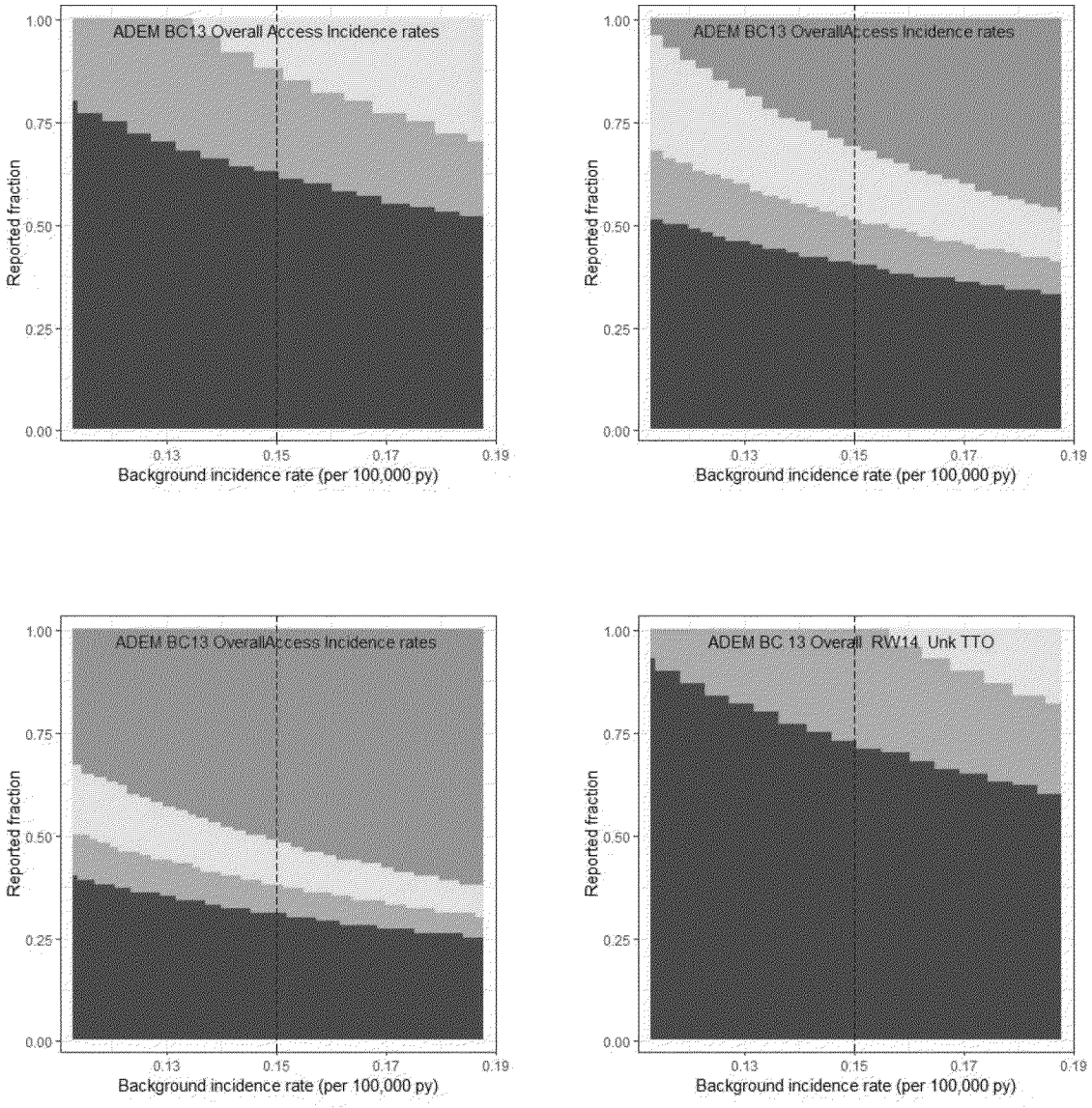
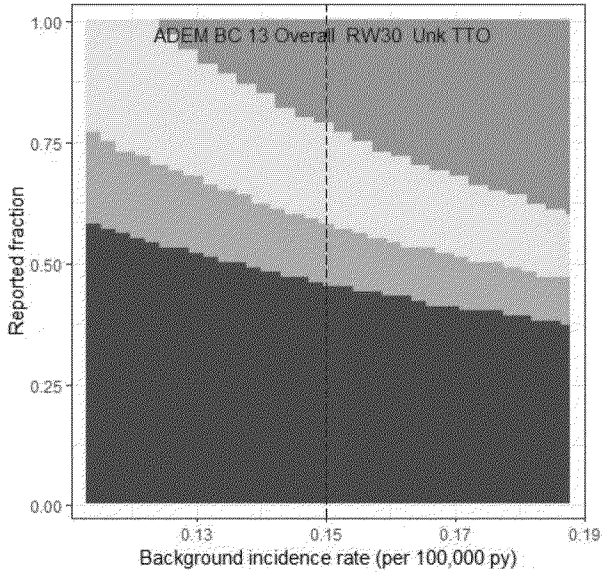
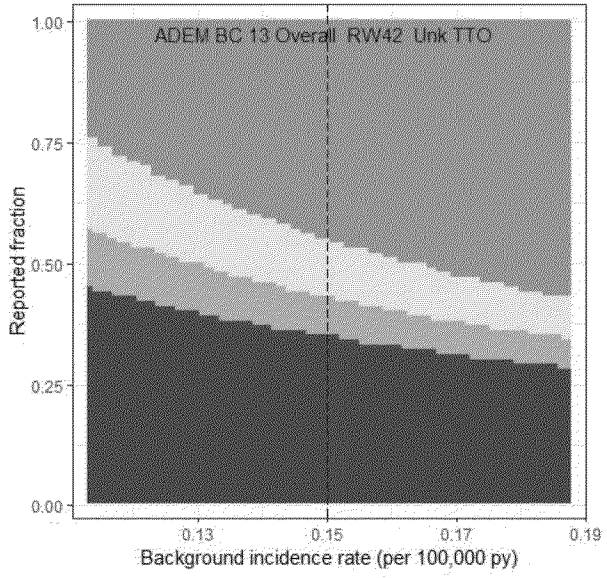

ADEM BC13 Overall Access Incidence rates
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.13
0.15
0.17
0.19
Background incidence rate (per 100,000 py)
ADEM BC13 OverallAccess Incidence rates
Reported fraction
Background incidence rate (per 100,000 py)
ADEM BC13 OverallAccess Incidence rates
Reported fraction
Background incidence rate (per 100,000 py)
ADEM BC 13 Overall RW14 Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)

Table 20 Observed Versus Expected analysis for ADEM Acute disseminated encephalomyelitis (ADEM) cases meeting the Brighton collaboration criteria (BCC) Level 1, 2 or 3 (Global reports)

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	



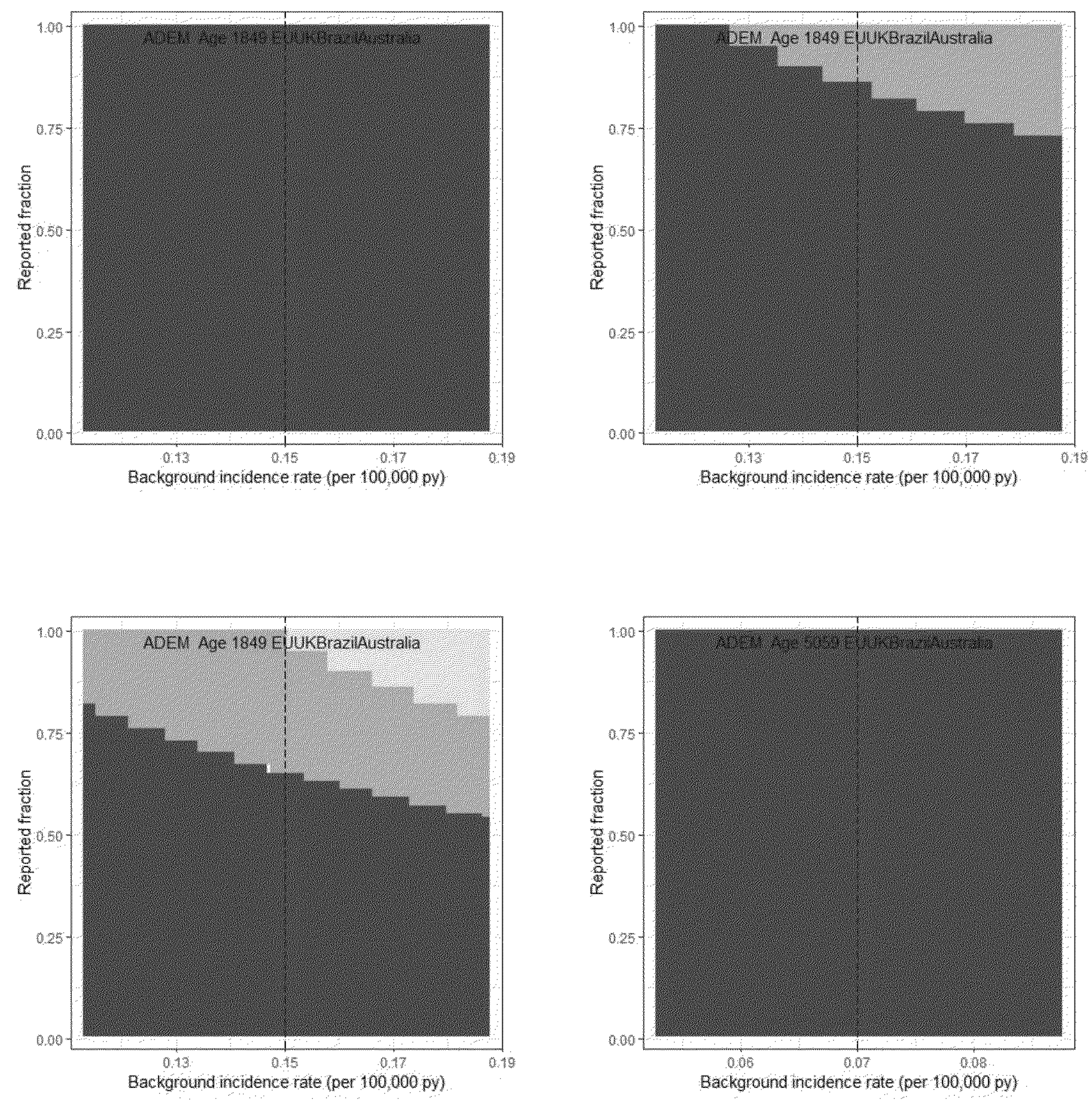


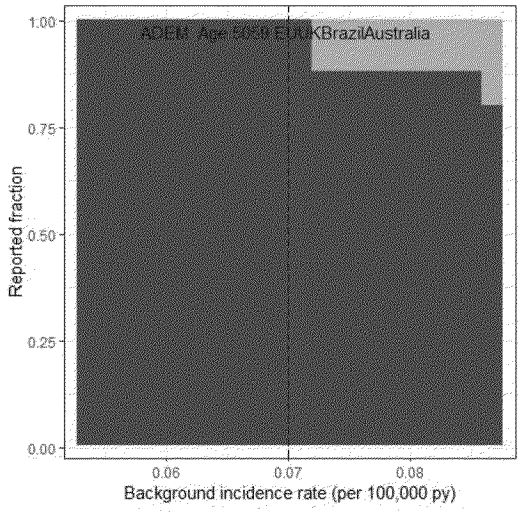
[a] Incidence rate (IR) = 0.15/100,000 person years. Source: Willame et al 2021 [A] (Meta-analysis IR from 2017-2019 ADEM-Narrow).

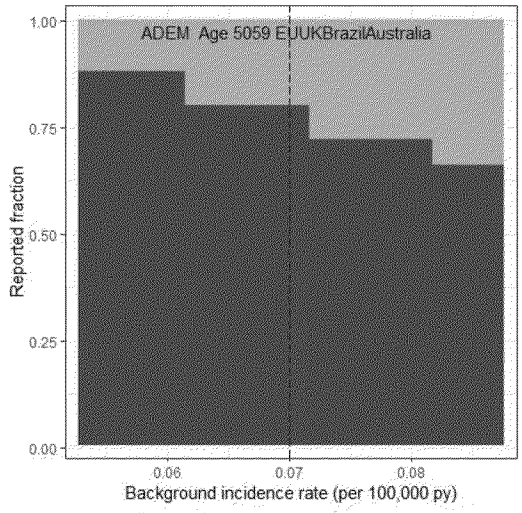
ADEM Acute disseminated encephalomyelitis, BCC Brighton collaboration criteria, CI Confidence Interval, E Expected, O Observed, RW risk window, TTO Time to onset, Unk Unknown.

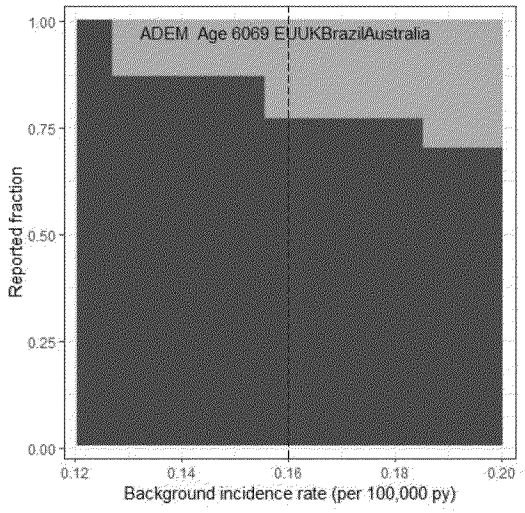
Table 21 Observed Versus Expected analysis for ADEM cases stratified by age for EU+UK+Brazil+Australia regions

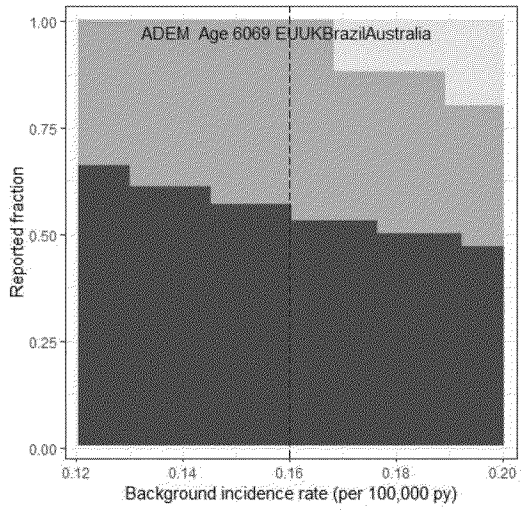
Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY	Exposure [a]	O over E ratio (95% CI)	
18-49	18	6.33	14	0.15	110094983	2.84 (1.69 - 4.49)	Observed significantly > expected
18-49	19	13.56	30	0.15	110094983	1.4 (0.84 - 2.19)	Observed > expected
18-49	19	18.99	42	0.15	110094983	1 (0.6 - 1.56)	Observed > expected
50-59	7	1.57	14	0.07	58336094	4.46 (1.79 - 9.19)	Observed significantly > expected
50-59	8	3.35	30	0.07	58336094	2.39 (1.03 - 4.71)	Observed significantly > expected
50-59	8	4.7	42	0.07	58336094	1.7 (0.73 - 3.35)	Observed > expected
60-69	7	3.55	14	0.16	57960860	1.97 (0.79 - 4.06)	Observed > expected
60-69	8	7.62	30	0.16	57960860	1.05 (0.45 - 2.07)	Observed > expected
60-69	8	10.66	42	0.16	57960860	0.75 (0.32 - 1.48)	Observed < expected
Over 70	3	0.99	14	0.08	32376365	3.03 (0.62 - 8.86)	Observed > expected
Over 70	4	2.13	30	0.08	32376365	1.88 (0.51 - 4.81)	Observed > expected
Over 70	5	2.98	42	0.08	32376365	1.68 (0.54 - 3.92)	Observed > expected

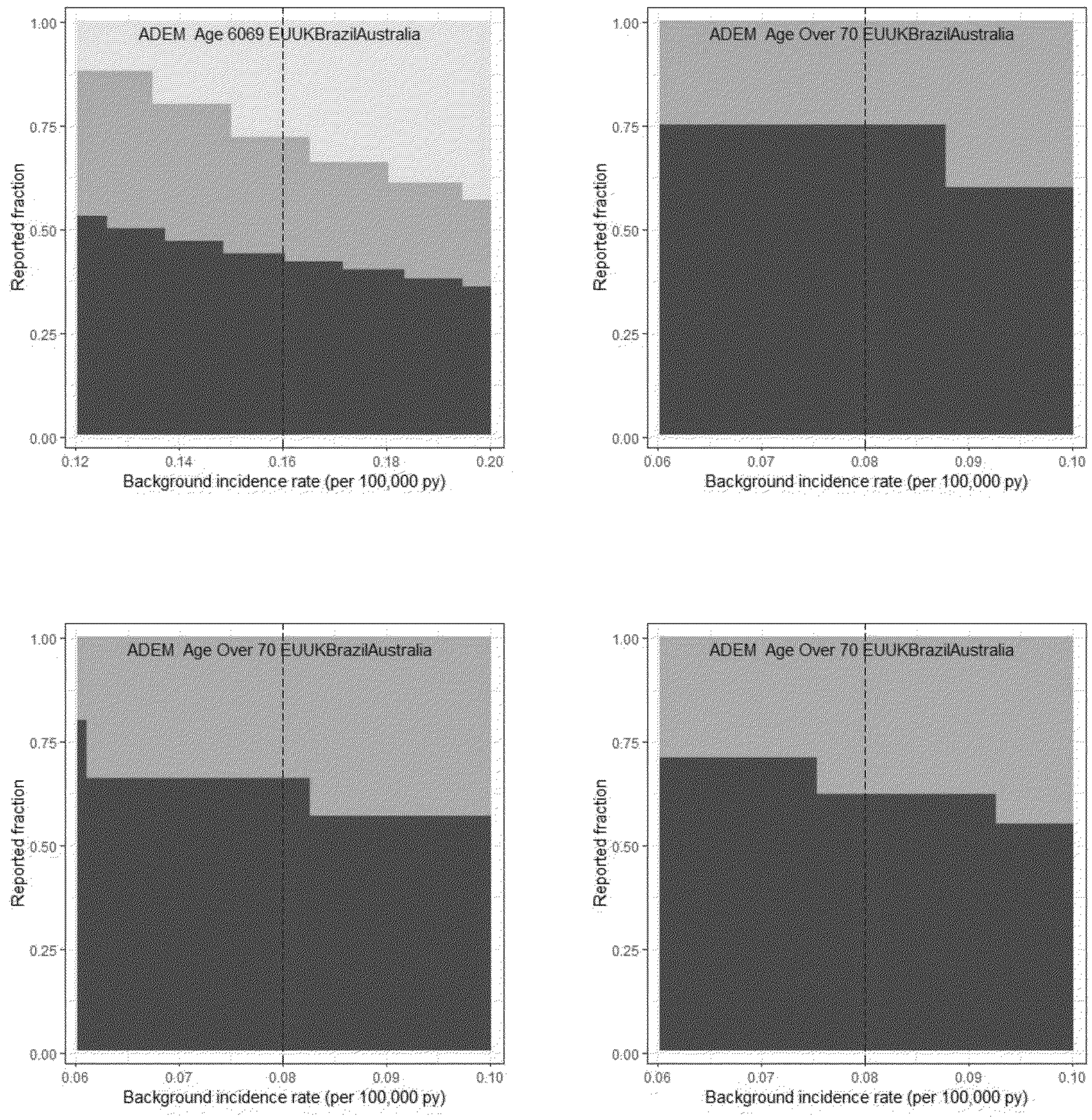

ADEM Age 1849 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.13
0.15
0.17
0.19
Background incidence rate (per 100,000 py)
ADEM Age 1849 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
ADEM Age 1849 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
ADEM Age 5059 EUUKBrazilAustralia
Reported fraction
0.06
0.07
0.08
Background incidence rate (per 100,000 py)


ADEM Age 5059 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)


ADEM Age 5059 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)


ADEM Age 6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
0.18
0.20
Background incidence rate (per 100,000 py)


ADEM Age 6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
0.18
0.20
Background incidence rate (per 100,000 py)


ADEM Age 6069 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
ADEM Age Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
ADEM Age Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
ADEM Age Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

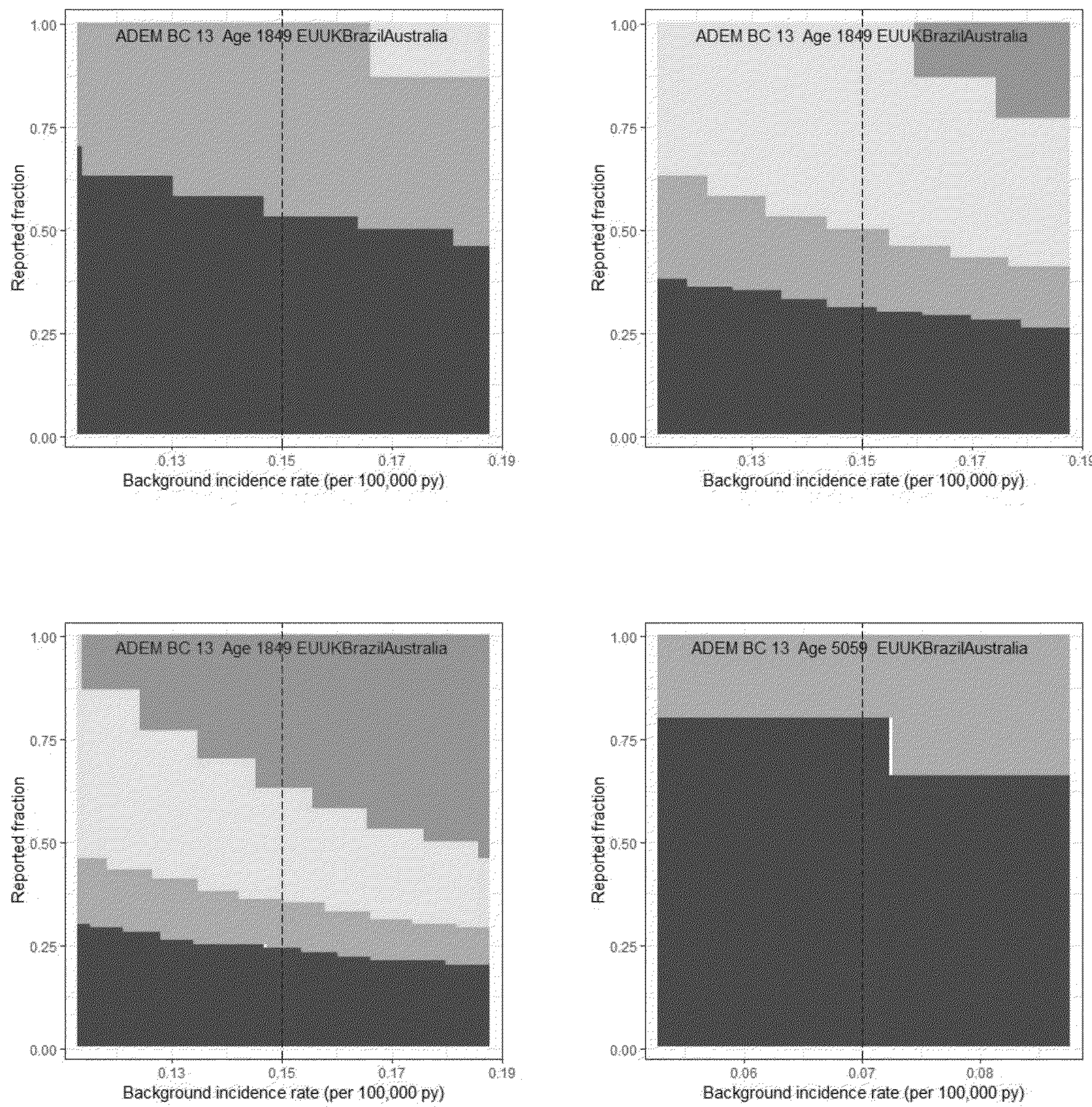
[a] Exposure until 28 December 2022 for EU+UK+Brazil+Australia.

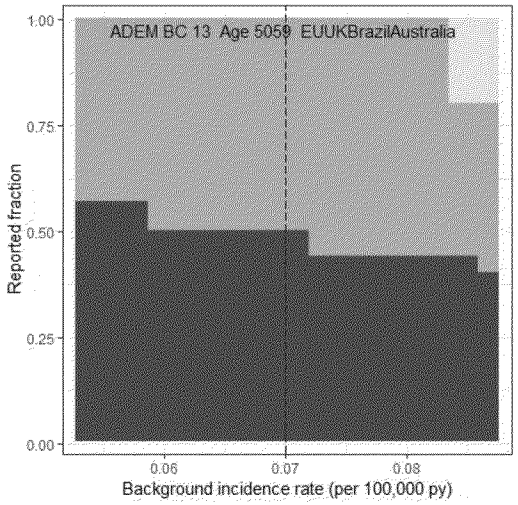
Source: Willame et al 2021 [A] (Meta-analysis IRs from ADEM Narrow 2017-2019).

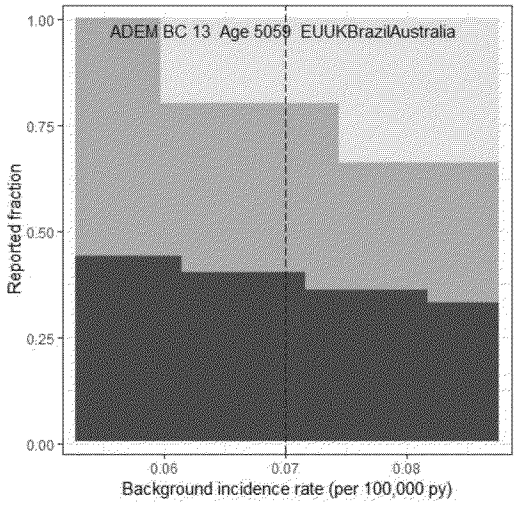
ADEM Acute Disseminated Encephalomyelitis, CI Confidence Interval; E Expected; EU European Union; IR: Incident Ratio, O Observed; UK United Kingdom.

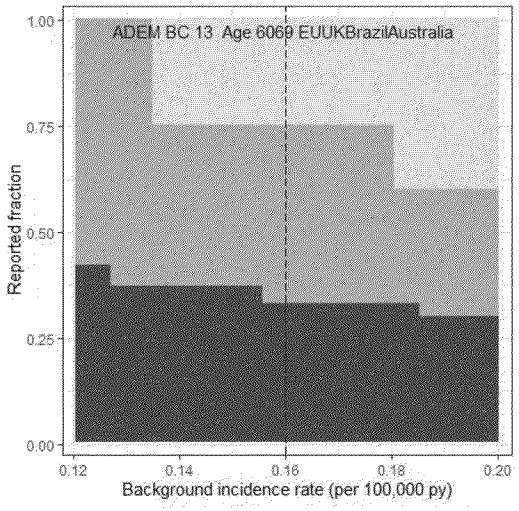
Table 22 Observed Versus Expected analysis for ADEM cases meeting the Brighton collaboration criteria Level 1, 2 or 3 and stratified by age for EU+UK+Brazil+Australia regions

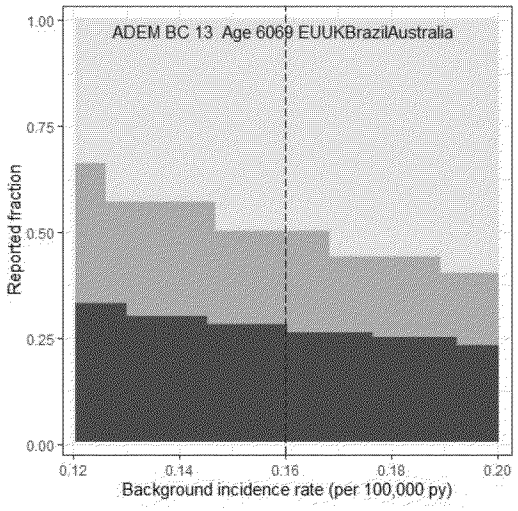
Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY	Exposure [a]	O over E ratio (95% CI)	
18-49	7	6.33	14	0.15	110094983	1.11 (0.44 - 2.28)	Observed > expected
18-49	7	13.56	30	0.15	110094983	0.52 (0.21 - 1.06)	Observed < expected
18-49	7	18.99	42	0.15	110094983	0.37 (0.15 - 0.76)	Observed significantly < expected
50-59	4	1.57	14	0.07	58336094	2.55 (0.69 - 6.52)	Observed > expected
50-59	4	3.35	30	0.07	58336094	1.19 (0.33 - 3.06)	Observed > expected
50-59	4	4.7	42	0.07	58336094	0.85 (0.23 - 2.18)	Observed < expected
60-69	3	3.55	14	0.16	57960860	0.85 (0.17 - 2.47)	Observed < expected
60-69	4	7.62	30	0.16	57960860	0.52 (0.14 - 1.34)	Observed < expected
60-69	4	10.66	42	0.16	57960860	0.38 (0.1 - 0.96)	Observed significantly < expected
Over 70	0	0.99	14	0.08	32376365	0 (0 - 3.73)	Observed < expected
Over 70	0	2.13	30	0.08	32376365	0 (0 - 1.73)	Observed < expected
Over 70	0	2.98	42	0.08	32376365	0 (0 - 1.24)	Observed < expected

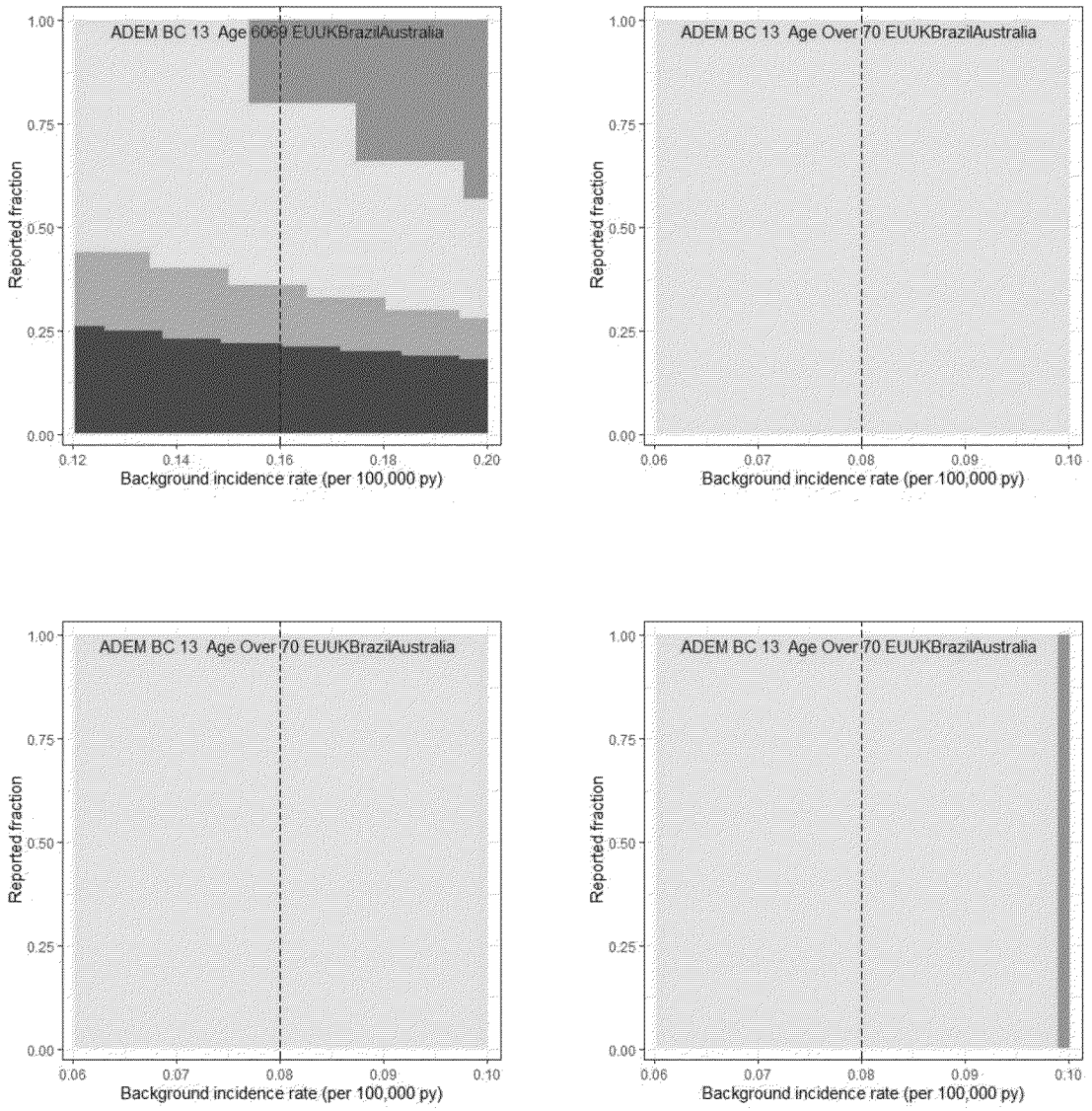

ADEM BC 13 Age 1849 EUUKBrazilAustralia
ADEM BC 13 Age 1849 EUUKBrazilAustralia
ADEM BC 13 Age 1849 EUUKBrazilAustralia
ADEM BC 13 Age 5059 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.13
0.15
0.17
0.19
0.06
0.07
0.08


ADEM BC 13 Age 5059 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 5059 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
0.18
0.20
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
0.18
0.20
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
0.18
0.20
Background incidence rate (per 100,000 py)
ADEM BC 13 Age Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
0.09
0.10
Background incidence rate (per 100,000 py)
ADEM BC 13 Age Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
0.09
0.10
Background incidence rate (per 100,000 py)
ADEM BC 13 Age Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
0.09
0.10
Background incidence rate (per 100,000 py)

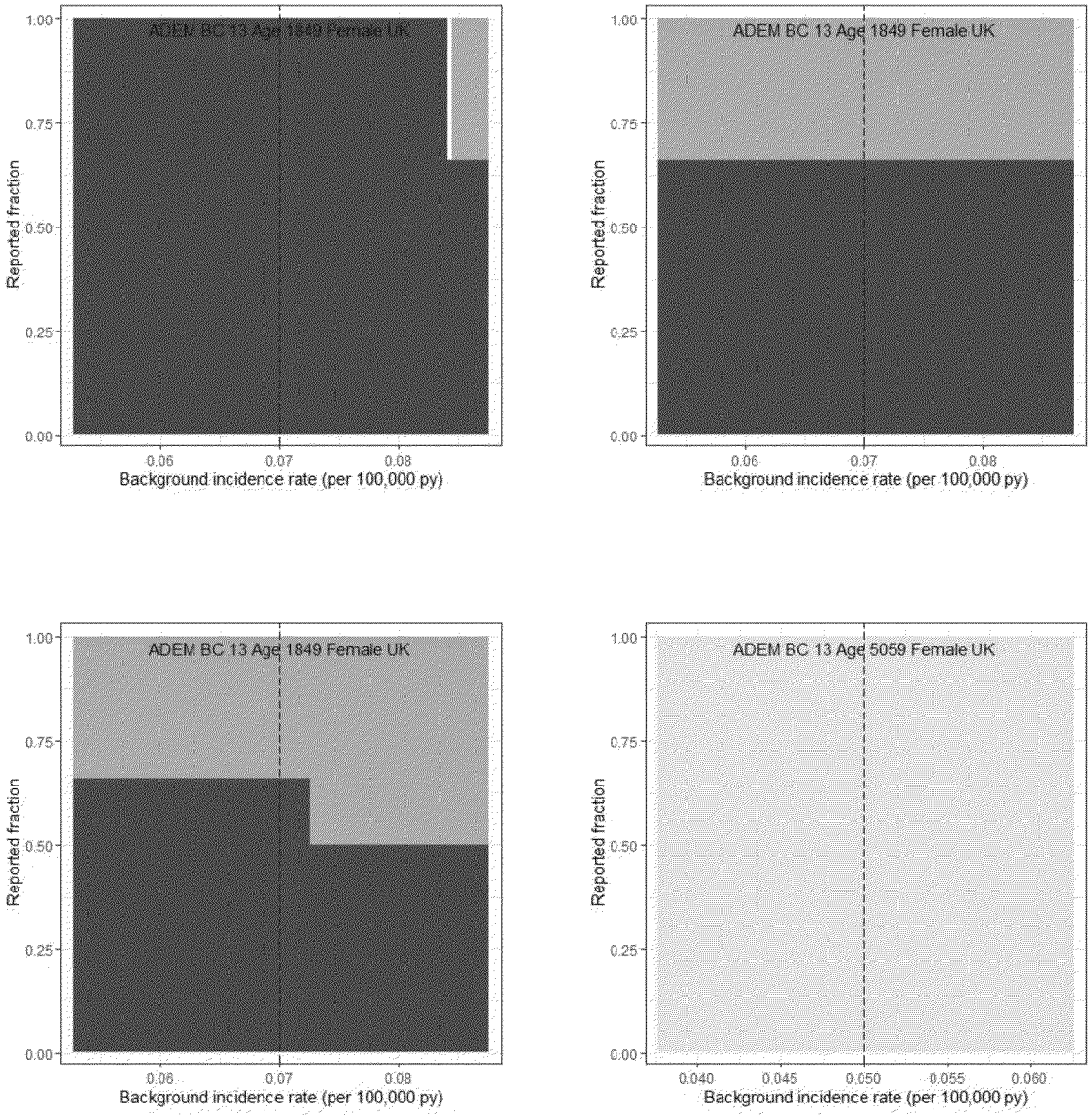
[a] Exposure until 28 December 2022 for EU+UK+Brazil+Australia.

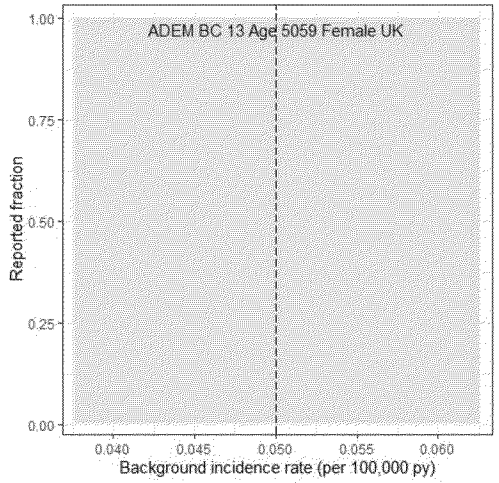
Source: Willame et al 2021 [A] (Meta-analysis IRs from ADEM Narrow 2017-2019).

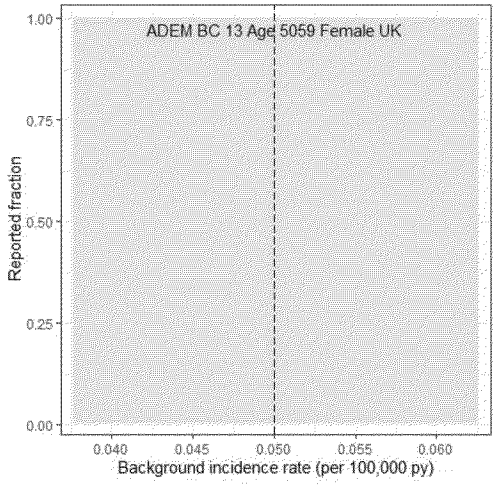
ADEM: Acute Disseminated Encephalomyelitis, BCC: Brighton collaboration criteria, CI Confidence Interval; E Expected; EU European Union; O Observed; PY person years; TTO Time to onset; UK United Kingdom.

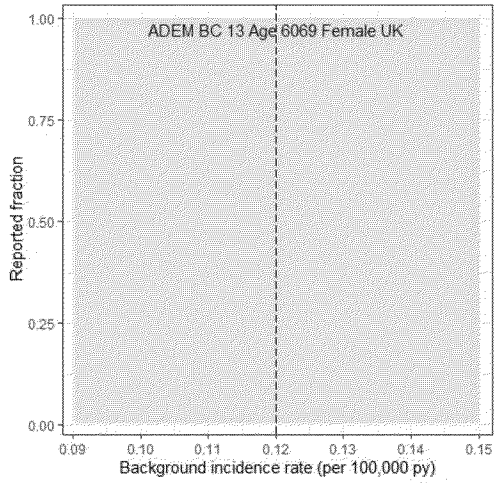
Table 23 Observed Versus Expected analysis for ADEM cases meeting the Brighton collaboration criteria Level 1, 2 or 3 and stratified by age and for UK region

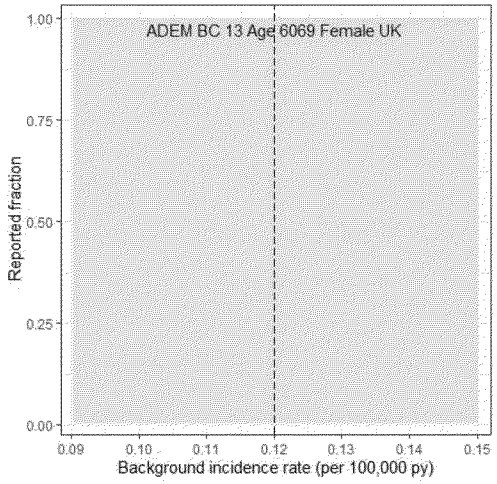
Age Group	Observed Cases	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	
18-49 Female UK	2	0.2	14	0.07	7414701	10 (1.21 - 36.12)	Observed significantly > expected
18-49 Female UK	2	0.43	30	0.07	7414701	4.65 (0.56 - 16.8)	Observed > expected
18-49 Female UK	2	0.6	42	0.07	7414701	3.33 (0.4 - 12.04)	Observed > expected
50-59 Female UK	0	0.11	14	0.05	5944683	0 (0 - 33.54)	Observed < expected
50-59 Female UK	0	0.24	30	0.05	5944683	0 (0 - 15.37)	Observed < expected
50-59 Female UK	0	0.34	42	0.05	5944683	0 (0 - 10.85)	Observed < expected
60-69 Female UK	0	0.22	14	0.12	4783416	0 (0 - 16.77)	Observed < expected
60-69 Female UK	0	0.47	30	0.12	4783416	0 (0 - 7.85)	Observed < expected
60-69 Female UK	0	0.66	42	0.12	4783416	0 (0 - 5.59)	Observed < expected
70-79 Female UK	0	0.12	14	0.09	3475875	0 (0 - 30.74)	Observed < expected
70-79 Female UK	0	0.26	30	0.09	3475875	0 (0 - 14.19)	Observed < expected
70-79 Female UK	0	0.36	42	0.09	3475875	0 (0 - 10.25)	Observed < expected
Over 80 Female UK	0	0.01	14	0.02	1630324	0 (0 - 368.89)	Observed < expected
Over 80 Female UK	0	0.03	30	0.02	1630324	0 (0 - 122.96)	Observed < expected
Over 80 Female UK	0	0.04	42	0.02	1630324	0 (0 - 92.22)	Observed < expected


ADEM BC 13 Age 1849 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)
ADEM BC 13 Age 1849 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)
ADEM BC 13 Age 1849 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)
ADEM BC 13 Age 5059 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.040
0.045
0.050
0.055
0.060
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 5059 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.040
0.045
0.050
0.055
0.060
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 5059 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.040
0.045
0.050
0.055
0.060
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 6069 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.09
0.10
0.11
0.12
0.13
0.14
0.15
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 6069 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.09
0.10
0.11
0.12
0.13
0.14
0.15
Background incidence rate (per 100,000 py)

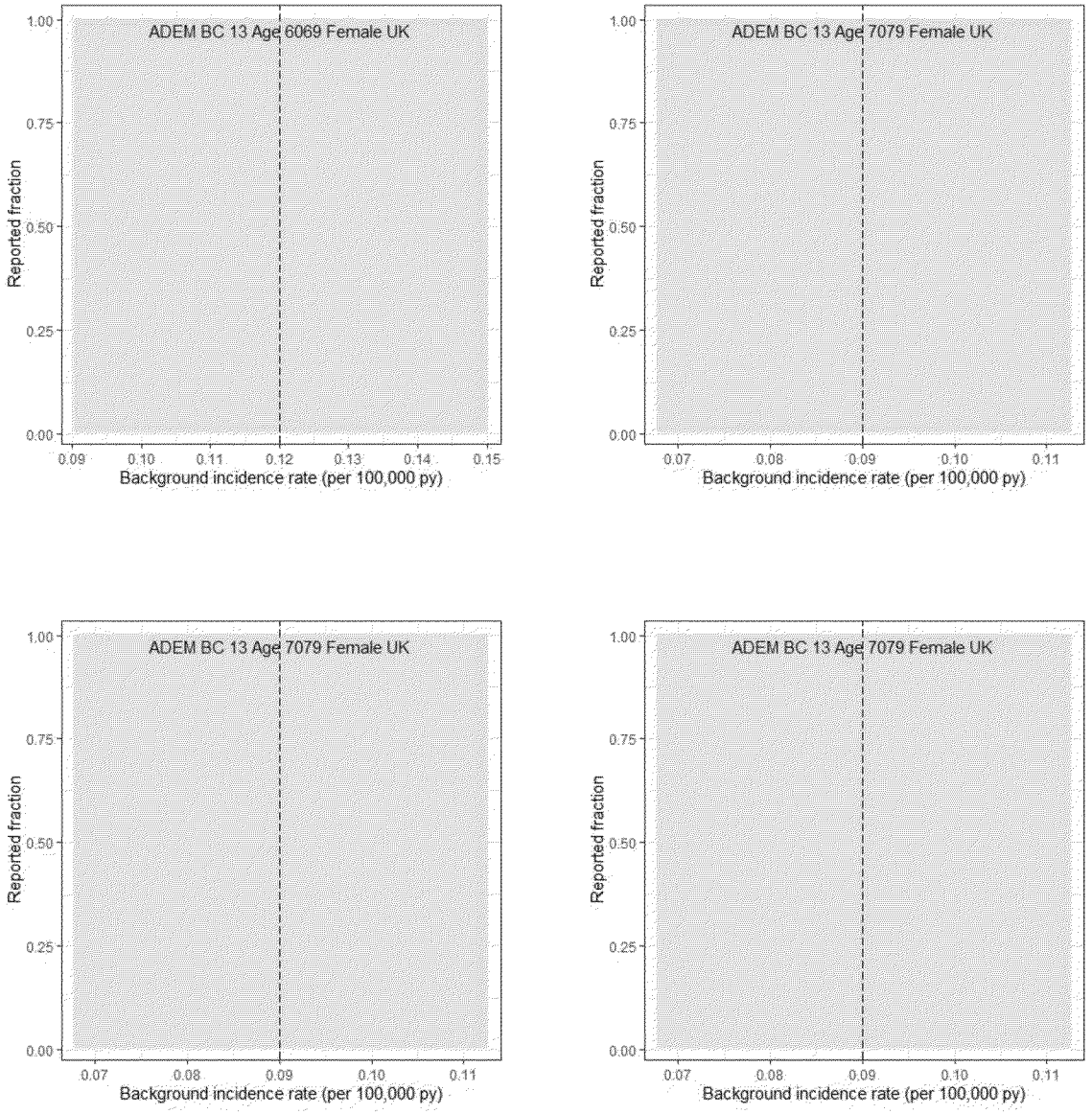
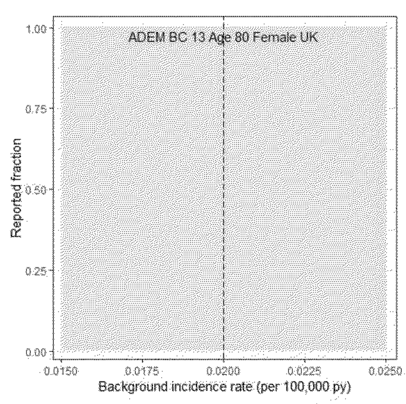
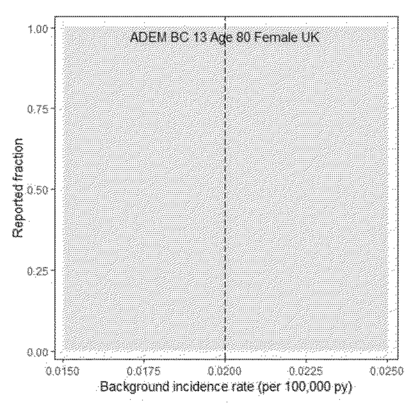
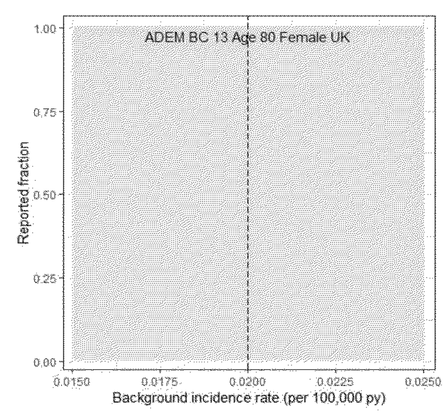

ADEM BC 13 Age 6069 Female UK
ADEM BC 13 Age 7079 Female UK
ADEM BC 13 Age 7079 Female UK
ADEM BC 13 Age 7079 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.09
0.10
0.11
0.12
0.13
0.14
0.15
0.07
0.08
0.09
0.10
0.11
Background incidence rate (per 100,000 py)

Table 23 Observed Versus Expected analysis for ADEM cases meeting the Brighton collaboration criteria Level 1, 2 or 3 and stratified by age and for UK region

Age Group	Observed Cases	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	
  							

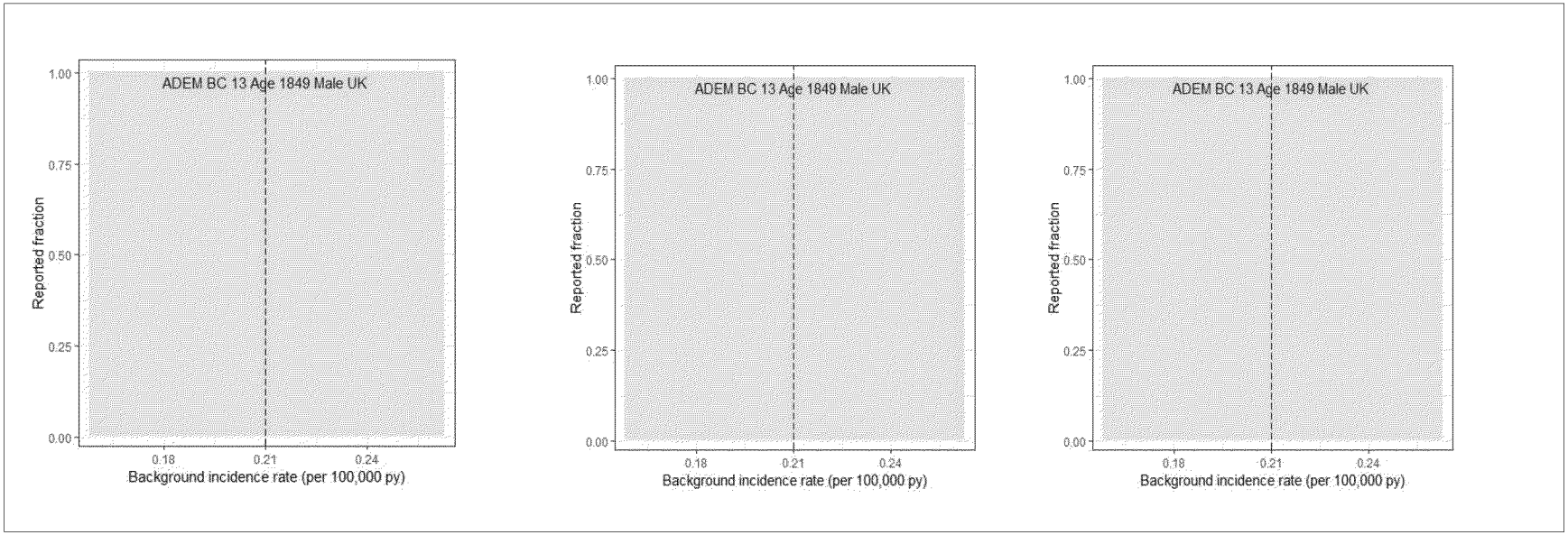
[a] Exposure until 28 December 2022 for UK.

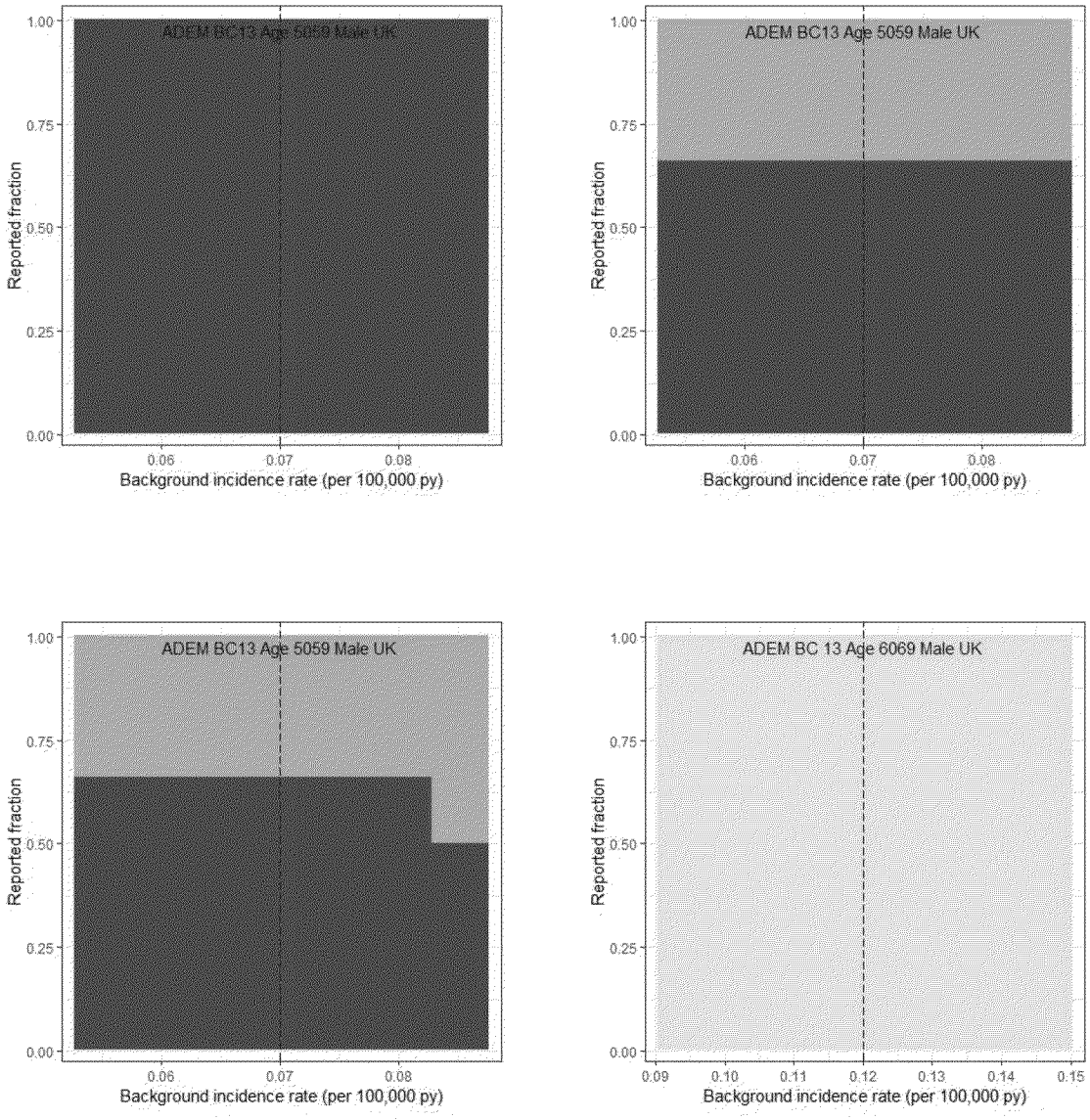
Source: Willame et al 2021 [A] (Meta-analysis IRs from ADEM Narrow 2017-2019).

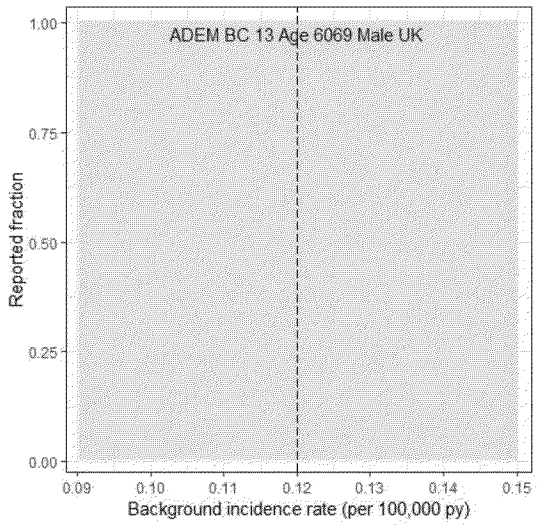
ADEM: Acute Disseminated Encephalomyelitis, BCC: Brighton collaboration criteria, CI Confidence Interval; E Expected; O Observed; PY person years;; UK United Kingdom.

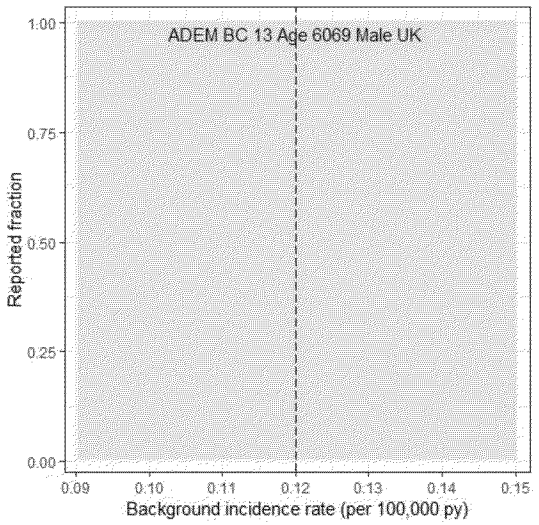
Table 24 Observed Versus Expected analysis for ADEM cases meeting the Brighton collaboration criteria Level 1, 2 or 3 and stratified by age for UK region

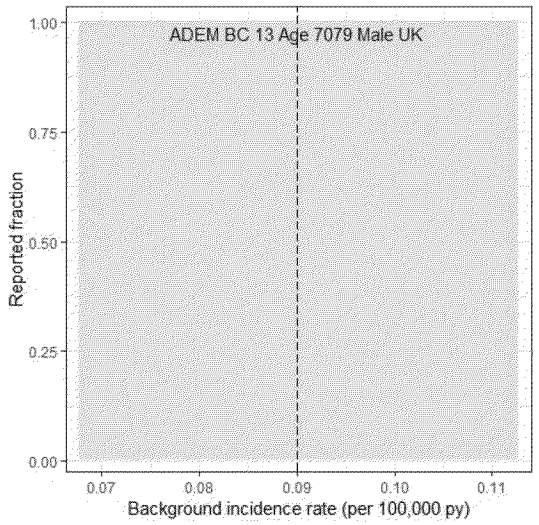
Age Group	Observed Cases	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	
18-49 Male UK	0	0.54	14	0.21	6766098	0 (0 - 6.83)	Observed < expected
18-49 Male UK	0	1.17	30	0.21	6766098	0 (0 - 3.15)	Observed < expected
18-49 Male UK	0	1.63	42	0.21	6766098	0 (0 - 2.26)	Observed < expected
50-59 Male UK	2	0.17	14	0.07	6510960	11.76 (1.42 - 42.5)	Observed significantly > expected
50-59 Male UK	2	0.37	30	0.07	6510960	5.41 (0.65 - 19.53)	Observed > expected
50-59 Male UK	2	0.52	42	0.07	6510960	3.85 (0.47 - 13.89)	Observed > expected
60-69 Male UK	0	0.23	14	0.12	4934728	0 (0 - 16.04)	Observed < expected
60-69 Male UK	0	0.49	30	0.12	4934728	0 (0 - 7.53)	Observed < expected
60-69 Male UK	0	0.68	42	0.12	4934728	0 (0 - 5.42)	Observed < expected
70-79 Male UK	0	0.11	14	0.09	3137304	0 (0 - 33.54)	Observed < expected
70-79 Male UK	0	0.23	30	0.09	3137304	0 (0 - 16.04)	Observed < expected
70-79 Male UK	0	0.32	42	0.09	3137304	0 (0 - 11.53)	Observed < expected


ADEM BC 13 Age 1849 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.18
0.21
0.24
Background incidence rate (per 100,000 py)
ADEM BC 13 Age 1849 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.18
0.21
0.24
Background incidence rate (per 100,000 py)
ADEM BC 13 Age 1849 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.18
0.21
0.24
Background incidence rate (per 100,000 py)


ADEM BC13 Age 5059 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)
ADEM BC13 Age 5059 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)
ADEM BC13 Age 5059 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.06
0.07
0.08
Background incidence rate (per 100,000 py)
ADEM BC 13 Age 6069 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.09
0.10
0.11
0.12
0.13
0.14
0.15
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 6069 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.09
0.10
0.11
0.12
0.13
0.14
0.15
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 6069 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.09
0.10
0.11
0.12
0.13
0.14
0.15
Background incidence rate (per 100,000 py)


ADEM BC 13 Age 7079 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.07
0.08
0.09
0.10
0.11
Background incidence rate (per 100,000 py)

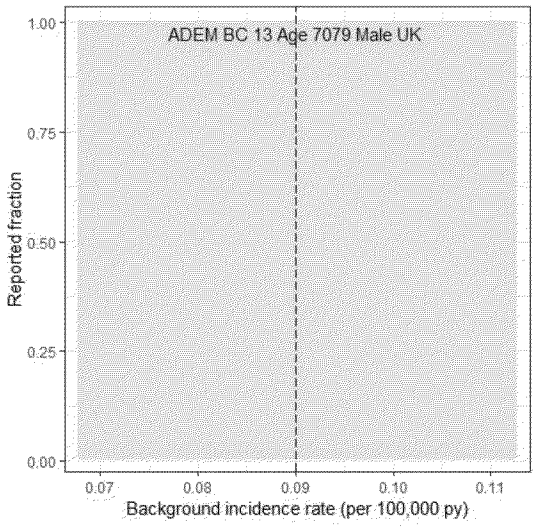
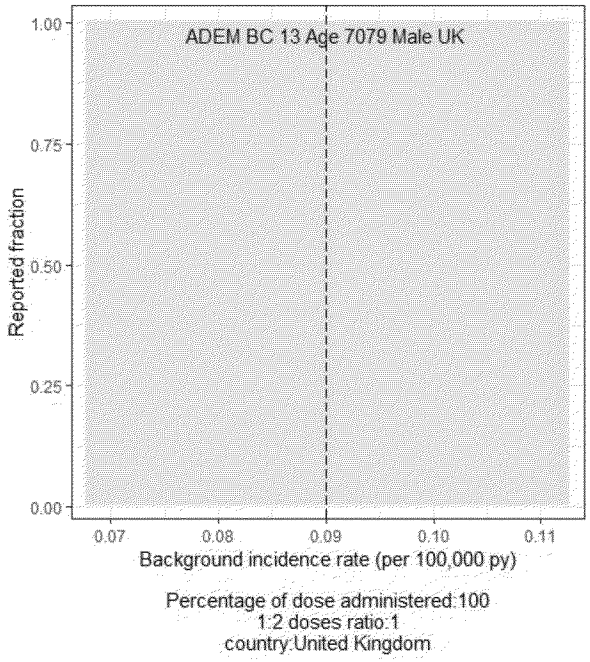

ADEM BC 13 Age 7079 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.07
0.08
0.09
0.10
0.11
Background incidence rate (per 100,000 py)

Table 24 Observed Versus Expected analysis for ADEM cases meeting the Brighton collaboration criteria Level 1, 2 or 3 and stratified by age for UK region

Age Group	Observed Cases	Expected cases	Risk window	Incidence Rate	Exposure [a]	O over E ratio (95% CI)	
							

[a] Exposure until 28 December 2022 for UK

Source: Willame et al 2021 [A] (Meta-analysis IRs from ADEM Narrow 2017-2019).

ADEM: Acute Disseminated Encephalomyelitis, BCC: Brighton collaboration criteria, CI Confidence Interval; E Expected; O Observed; PY person years; UK United Kingdom.

Table 25 Observed Versus Expected analysis for all cases reporting encephalitis (Global reports)

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
Encephalitis Overall	146	1625.85	14	9.1	466115644	0.09 (0.08 - 0.11)	Observed significantly < expected
Encephalitis Overall	181	3483.97	30	9.1	466115644	0.05 (0.04 - 0.06)	Observed significantly < expected
Encephalitis Overall	214	4877.56	42	9.1	466115644	0.04 (0.04 - 0.05)	Observed significantly < expected
Encephalitis Overall (Including Unk TTO)	278	1625.85	14	9.1	466115644	0.17 (0.15 - 0.19)	Observed significantly < expected
Encephalitis Overall (Including Unk TTO)	313	3483.97	30	9.1	466115644	0.09 (0.08 - 0.1)	Observed significantly < expected
Encephalitis Overall (Including Unk TTO)	346	4877.56	42	9.1	466115644	0.07 (0.06 - 0.08)	Observed significantly < expected

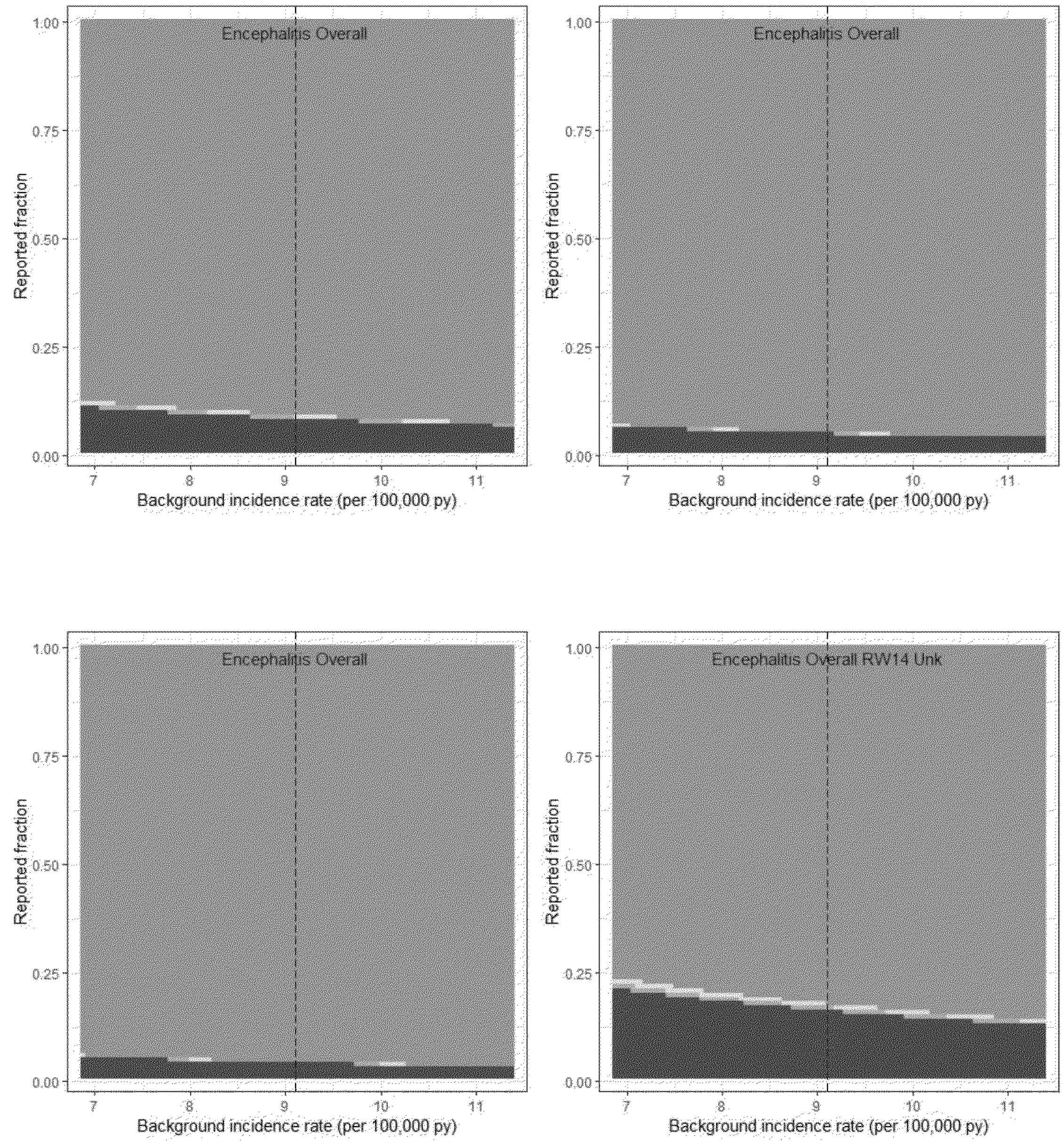
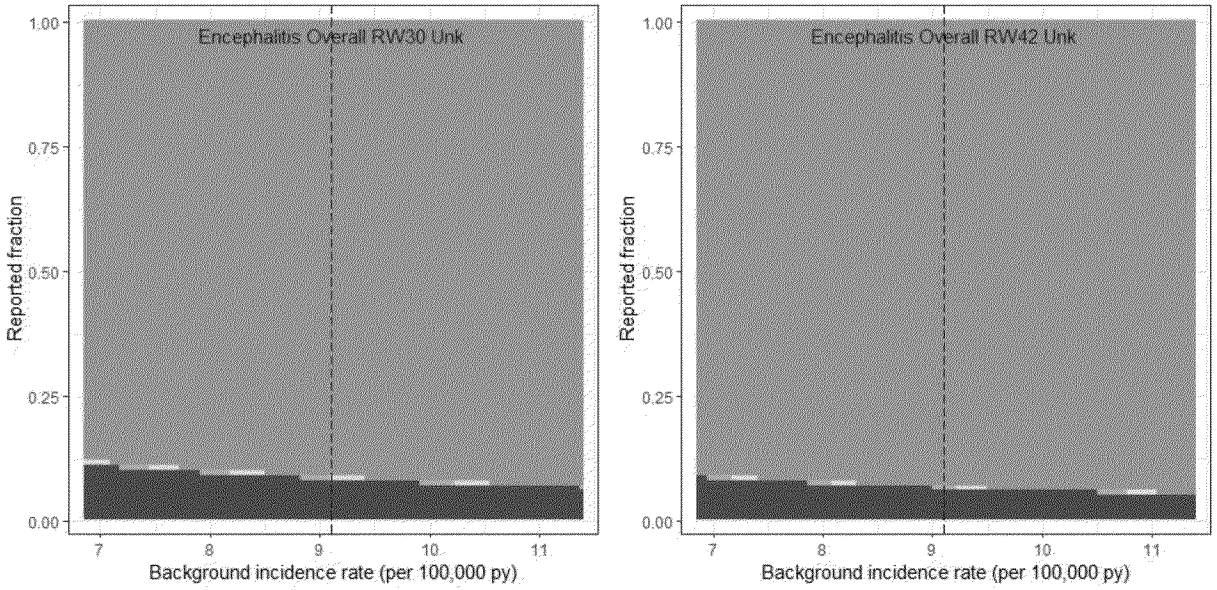

Encephalitis Overall
Reported fraction
Background incidence rate (per 100,000 py)
Encephalitis Overall
Reported fraction
Background incidence rate (per 100,000 py)
Encephalitis Overall
Reported fraction
Background incidence rate (per 100,000 py)
Encephalitis Overall RW14 Unk
Reported fraction
Background incidence rate (per 100,000 py)

Table 25 Observed Versus Expected analysis for all cases reporting encephalitis (Global reports)

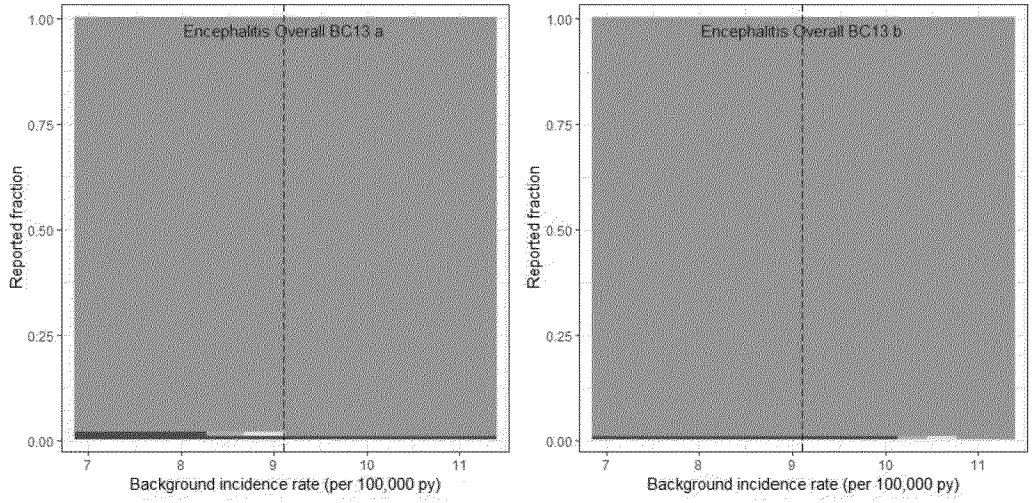
Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) ACCESS Rates. Willame et al 2021 [A] (Meta-analysis IRs from Meningoencephalitis Narrow 2010-2013 and 2017-2019)

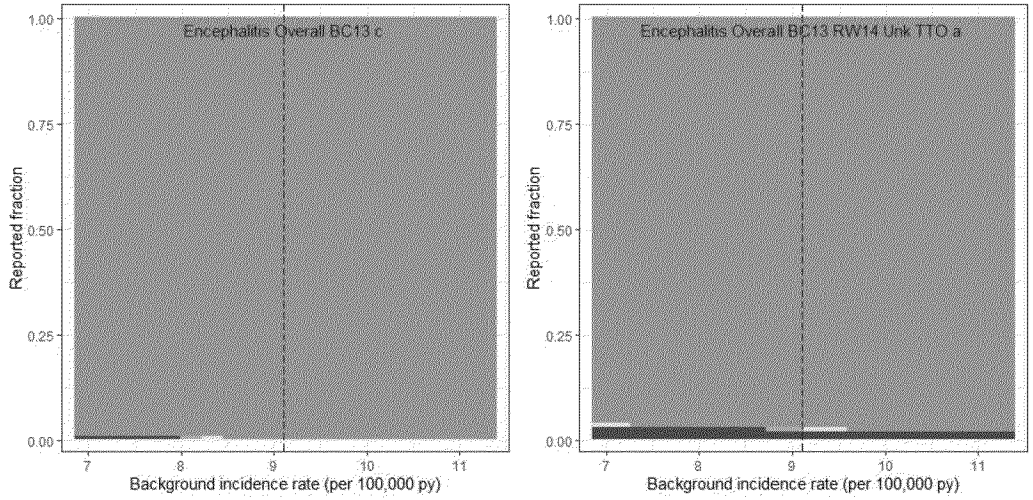
CI confidence Interval; O observed; E Expected; TTO Time to onset, Unk Unknown.

Table 26 Observed Versus Expected analysis for all cases reporting encephalitis (Global reports) stratified by Brighton Collaboration Criteria (BCC) 1,2,3

Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
Encephalitis Overall	31	1625.85	14	9.1	466115644	0.02 (0.01 - 0.03)	Observed significantly < expected
Encephalitis Overall	40	3483.97	30	9.1	466115644	0.01 (0.01 - 0.02)	Observed significantly < expected
Encephalitis Overall	44	4877.56	42	9.1	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Encephalitis Overall (Including Unk TTO)	49	1625.85	14	9.1	466115644	0.03 (0.02 - 0.04)	Observed significantly < expected
Encephalitis Overall (Including Unk TTO)	58	3483.97	30	9.1	466115644	0.02 (0.01 - 0.02)	Observed significantly < expected
Encephalitis Overall (Including Unk TTO)	62	4877.56	42	9.1	466115644	0.01 (0.01 - 0.02)	Observed significantly < expected

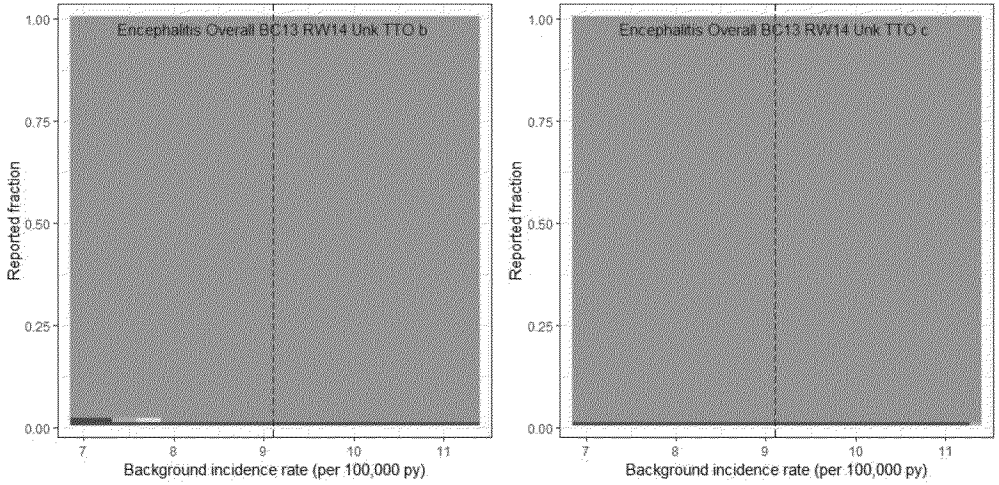

Encephalitis Overall BC13 a
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
11
Background incidence rate (per 100,000 py)

Encephalitis Overall BC13 b
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
11
Background incidence rate (per 100,000 py)


Encephalitis Overall BC13 c
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
11
Background incidence rate (per 100,000 py)

Encephalitis Overall BC13 RW14 Unk TTO a
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
11
Background incidence rate (per 100,000 py)

Table 26 Observed Versus Expected analysis for all cases reporting encephalitis (Global reports) stratified by Brighton Collaboration Criteria (BCC) 1,2,3

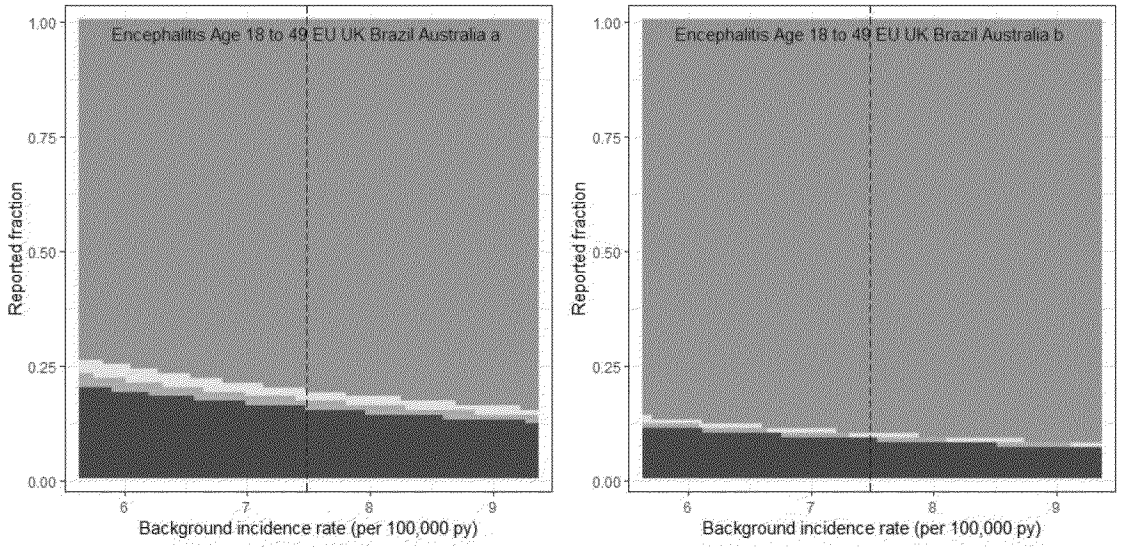
Adverse Events	Observed Cases	Expected cases	Risk window	Incidence Rate [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR): ACCESS Rates. Willame et al 2021 [A] (Meta-analysis IRs from Meningoencephalitis Narrow 2010-2013 and 2017-2019)

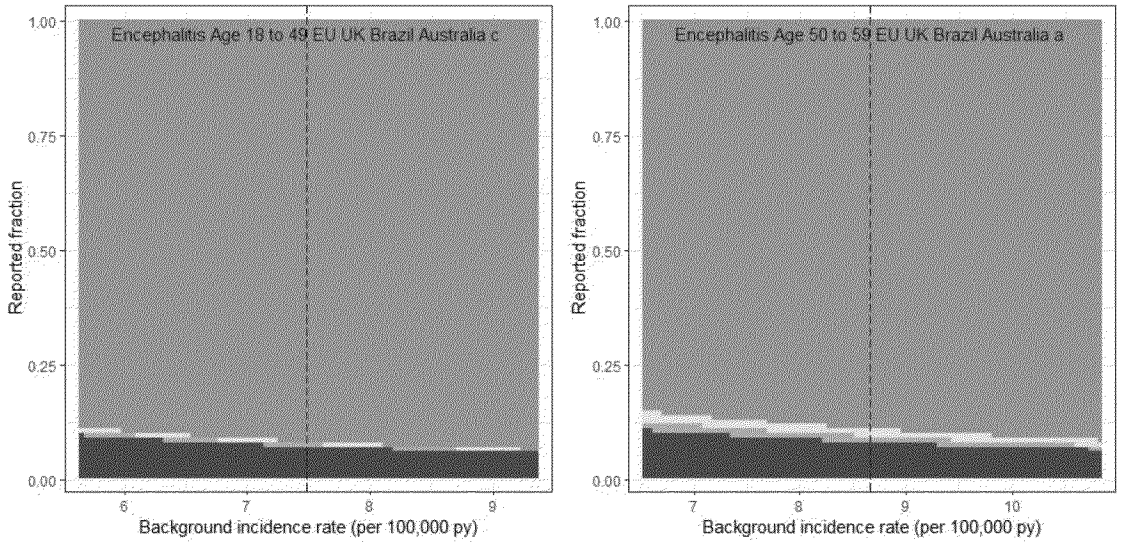
BCC Brighton Collaboration Criteria, CI confidence Interval; O observed; E Expected; TTO Time to onset, Unk Unknown.

Table 27 Observed Versus Expected analysis for Encephalitis cases stratified by age for EU+UK+Brazil+Australia regions

Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY [a]	Exposure	O over E ratio (95% CI)	
Age 18-49	56	315.66	14	7.48	110094983	0.18 (0.13 - 0.23)	Observed significantly < expected
Age 18-49	66	676.41	30	7.48	110094983	0.1 (0.08 - 0.12)	Observed significantly < expected
Age 18-49	77	946.97	42	7.48	110094983	0.08 (0.06 - 0.1)	Observed significantly < expected
Age 50-59	19	193.64	14	8.66	58336094	0.1 (0.06 - 0.15)	Observed significantly < expected
Age 50-59	27	414.95	30	8.66	58336094	0.07 (0.04 - 0.09)	Observed significantly < expected
Age 50-59	34	580.93	42	8.66	58336094	0.06 (0.04 - 0.08)	Observed significantly < expected
Age 60-69	33	219.28	14	9.87	57960860	0.15 (0.1 - 0.21)	Observed significantly < expected
Age 60-69	44	469.89	30	9.87	57960860	0.09 (0.07 - 0.13)	Observed significantly < expected
Age 60-69	50	657.84	42	9.87	57960860	0.08 (0.06 - 0.1)	Observed significantly < expected
Age 70+	20	132.91	14	10.71	32376365	0.15 (0.09 - 0.23)	Observed significantly < expected
Age 70+	21	284.81	30	10.71	32376365	0.07 (0.05 - 0.11)	Observed significantly < expected
Age 70+	25	398.74	42	10.71	32376365	0.06 (0.04 - 0.09)	Observed significantly < expected


Encephalitis Age 18 to 49 EU UK Brazil Australia a
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
9
Background incidence rate (per 100,000 py)

Encephalitis Age 18 to 49 EU UK Brazil Australia b
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
9
Background incidence rate (per 100,000 py)


Encephalitis Age 18 to 49 EU UK Brazil Australia c
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
9
Background incidence rate (per 100,000 py)

Encephalitis Age 50 to 59 EU UK Brazil Australia a
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
Background incidence rate (per 100,000 py)

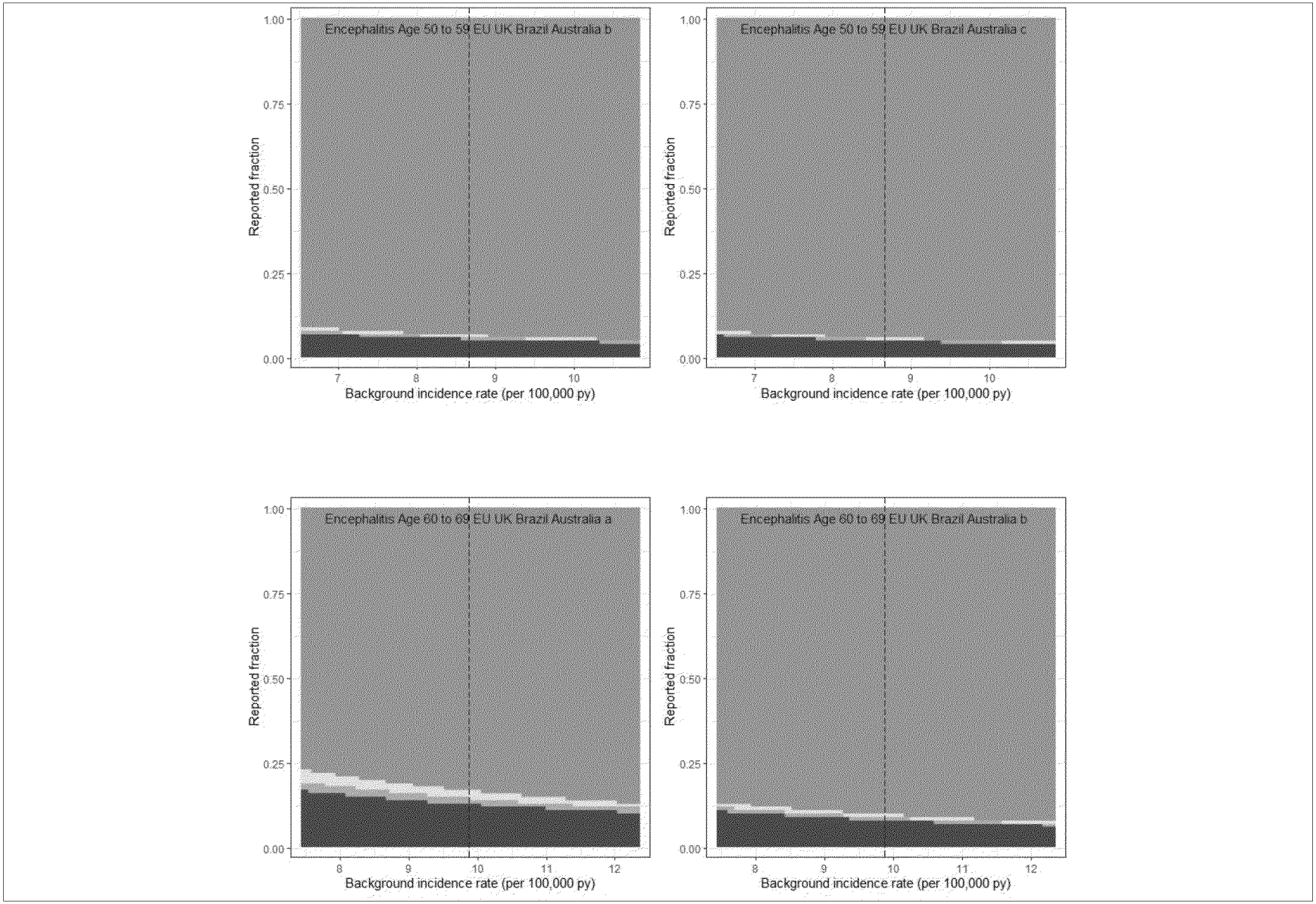
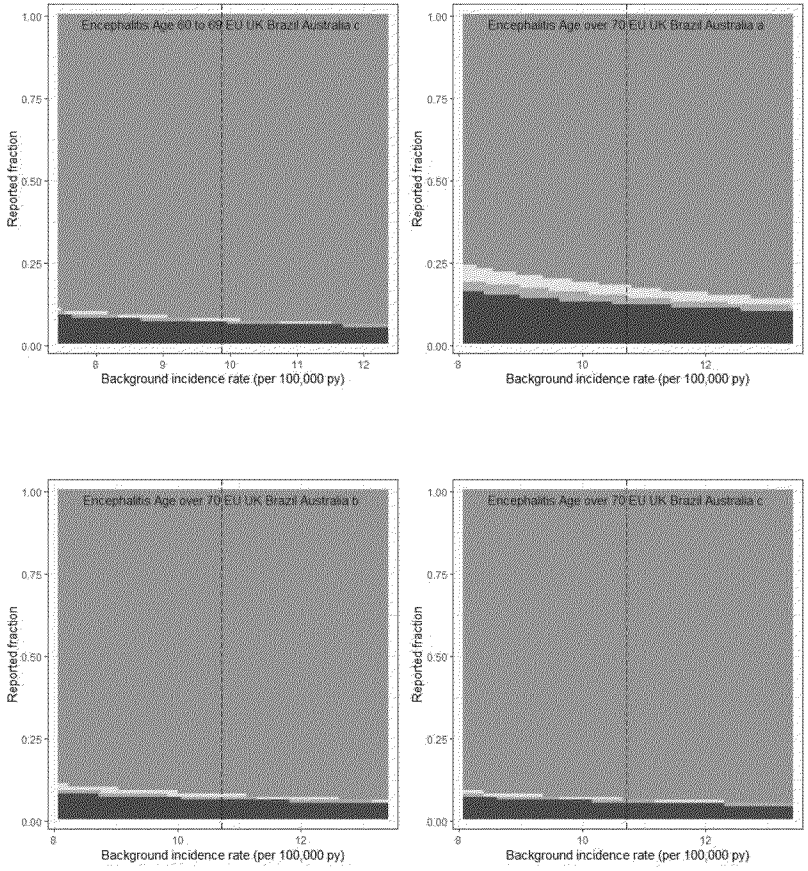

Encephalitis Age 50 to 59 EU UK Brazil Australia b
Encephalitis Age 50 to 59 EU UK Brazil Australia c
Encephalitis Age 60 to 69 EU UK Brazil Australia a
Encephalitis Age 60 to 69 EU UK Brazil Australia b
Reported fraction
Background incidence rate (per 100,000 py)

Table 27 Observed Versus Expected analysis for Encephalitis cases stratified by age for EU+UK+Brazil+Australia regions

Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY [a]	Exposure	O over E ratio (95% CI)

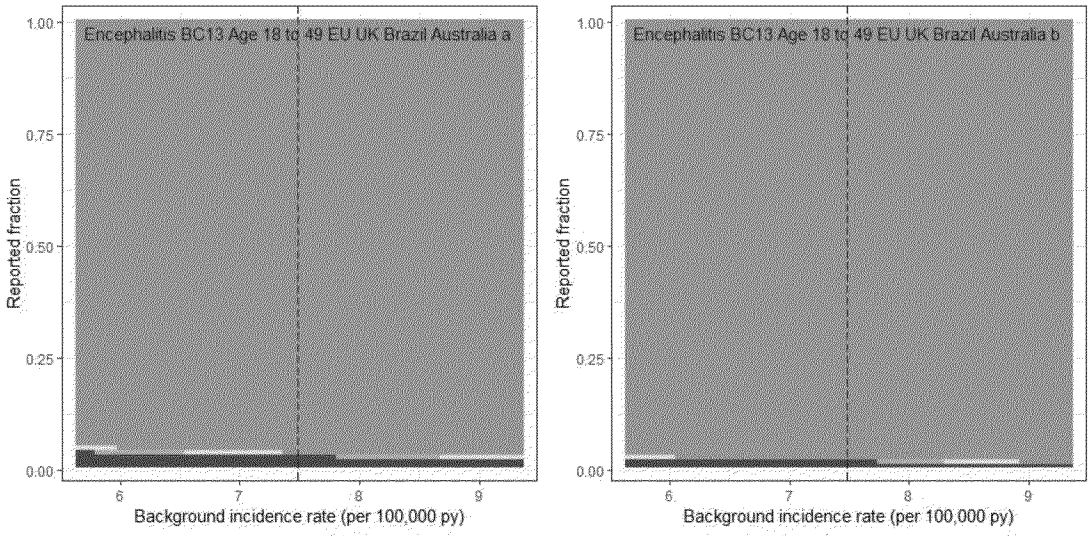


[a] Incidence rate (IR): ACCESS Rates. Willame et al 2021 [A] (Meta-analysis IRs from Meningoencephalitis Narrow 2010-2013 and 2017-2019)

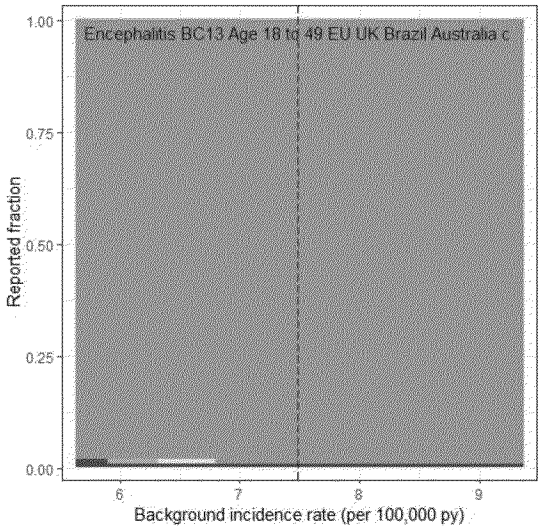
CI Confidence Interval; CPRD Clinical Practice Research Database; E Expected; EU European Union; O Observed; PY Person years; TTO Time to onset; UK United Kingdom; Unk Unknown.

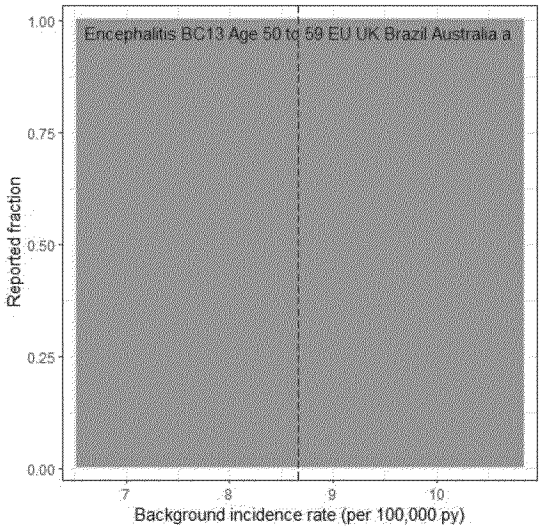
Table 28 Observed Versus Expected analysis for encephalitis cases meeting the Brighton collaboration criteria (BCC) Level 1, 2 or 3 and stratified by age for EU+UK+Brazil+Australia regions

Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY[b]	Exposure [a]	O over E ratio (95% CI)	
Age 18-49	11	315.66	14	7.48	110094983	0.03 (0.02 - 0.06)	Observed significantly < expected
Age 18-49	15	676.41	30	7.48	110094983	0.02 (0.01 - 0.04)	Observed significantly < expected
Age 18-49	16	946.97	42	7.48	110094983	0.02 (0.01 - 0.03)	Observed significantly < expected
Age 50-59	1	193.64	14	8.66	58336094	0.01 (0 - 0.03)	Observed significantly < expected
Age 50-59	1	414.95	30	8.66	58336094	0 (0 - 0.01)	Observed significantly < expected
Age 50-59	3	580.93	42	8.66	58336094	0.01 (0 - 0.02)	Observed significantly < expected
Age 60-69	5	219.28	14	9.87	57960860	0.02 (0.01 - 0.05)	Observed significantly < expected
Age 60-69	7	469.89	30	9.87	57960860	0.01 (0.01 - 0.03)	Observed significantly < expected
Age 60-69	7	657.84	42	9.87	57960860	0.01 (0 - 0.02)	Observed significantly < expected
Age 70+	5	132.91	14	10.71	32376365	0.04 (0.01 - 0.09)	Observed significantly < expected
Age 70+	5	284.81	30	10.71	32376365	0.02 (0.01 - 0.04)	Observed significantly < expected
Age 70+	5	398.74	42	10.71	32376365	0.01 (0 - 0.03)	Observed significantly < expected


Encephalitis BC13 Age 18 to 49 EU UK Brazil Australia a
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
9
Background incidence rate (per 100,000 py)

Encephalitis BC13 Age 18 to 49 EU UK Brazil Australia b
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
9
Background incidence rate (per 100,000 py)


Encephalitis BC13 Age 18 to 49 EU UK Brazil Australia c
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
9
Background incidence rate (per 100,000 py)


Encephalitis BC13 Age 50 to 59 EU UK Brazil Australia a
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
Background incidence rate (per 100,000 py)

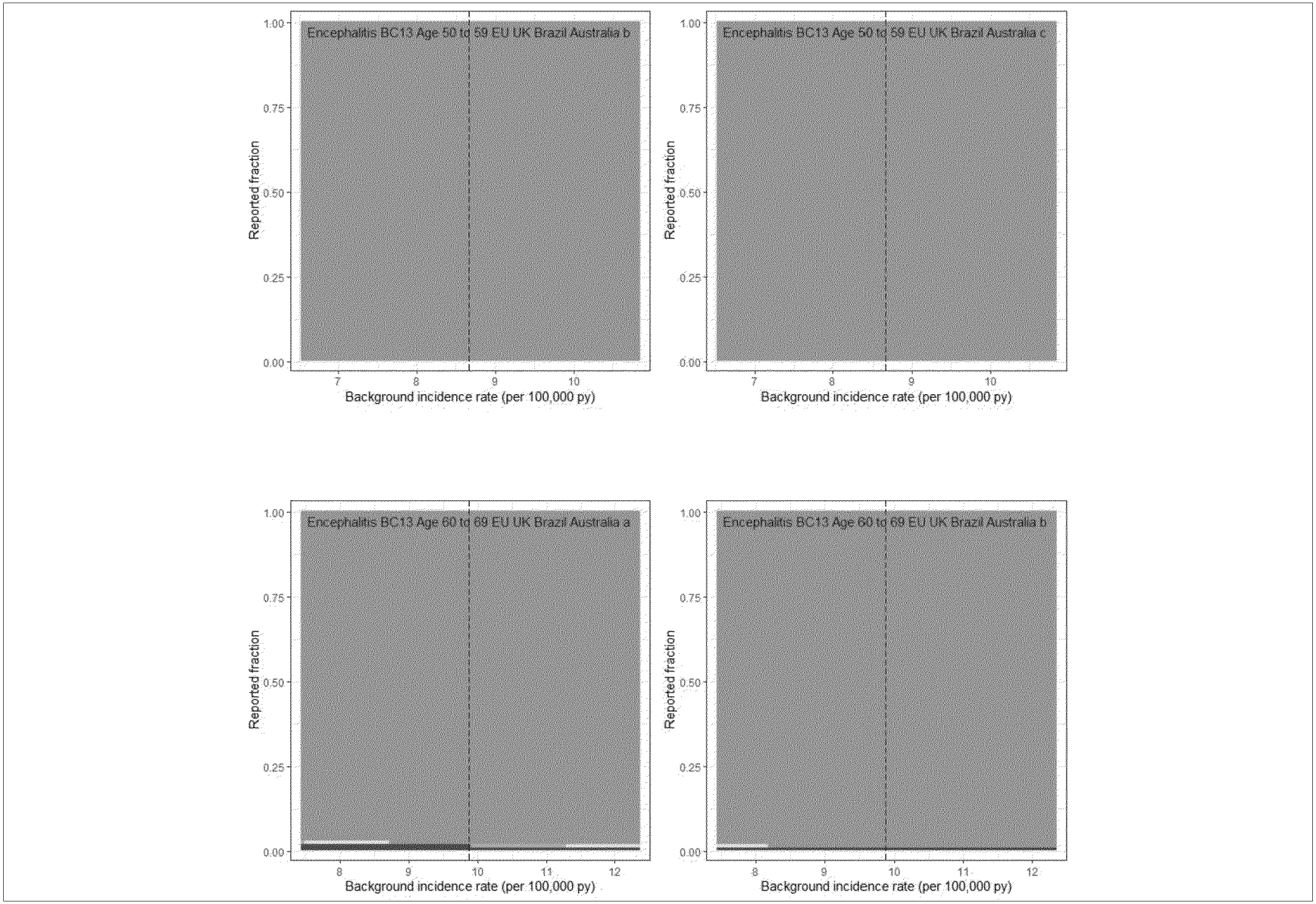
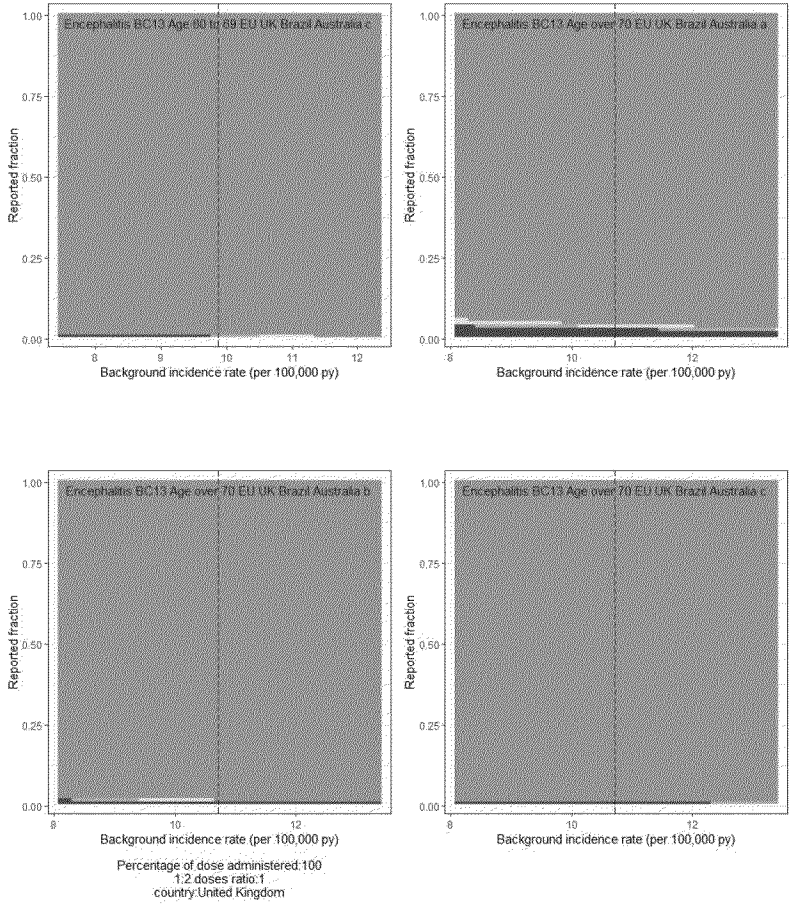

Encephalitis BC13 Age 50 to 59 EU UK Brazil Australia b
Encephalitis BC13 Age 50 to 59 EU UK Brazil Australia c
Encephalitis BC13 Age 60 to 69 EU UK Brazil Australia a
Encephalitis BC13 Age 60 to 69 EU UK Brazil Australia b
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
11
12

Table 28 Observed Versus Expected analysis for encephalitis cases meeting the Brighton collaboration criteria (BCC) Level 1, 2 or 3 and stratified by age for EU+UK+Brazil+Australia regions

Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY[b]	Exposure [a]	O over E ratio (95% CI)
						

[a] Exposure until 28 December 2022 for EU+UK+Brazil+Australia

[b] Incidence rate (IR): ACCESS Rates. Willame et al 2021 [A] (Meta-analysis IRs from Meningoencephalitis Narrow 2010-2013 and 2017-2019)

BCC Brighton Collaboration Criteria, CI Confidence Interval; E Expected; EU European Union; O Observed; PY Person years; TTO Time to onset; UK United Kingdom.

Table 29 Observed Versus Expected analysis for GBS cases Overall

Description	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	
GBS	466	807.57	14	4.52	466115644	0.58 (0.53 - 0.63)	Observed significantly < expected
GBS	916	1730.5	30	4.52	466115644	0.53 (0.5 - 0.56)	Observed significantly < expected
GBS	983	2422.7	42	4.52	466115644	0.41 (0.38 - 0.43)	Observed significantly < expected
GBS (Including unk TTO)	992	807.57	14	4.52	466115644	1.23 (1.15 - 1.31)	Observed significantly > expected
GBS (Including unk TTO)	1442	1730.5	30	4.52	466115644	0.83 (0.79 - 0.88)	Observed significantly < expected
GBS (Including unk TTO)	1509	2422.7	42	4.52	466115644	0.62 (0.59 - 0.66)	Observed significantly < expected

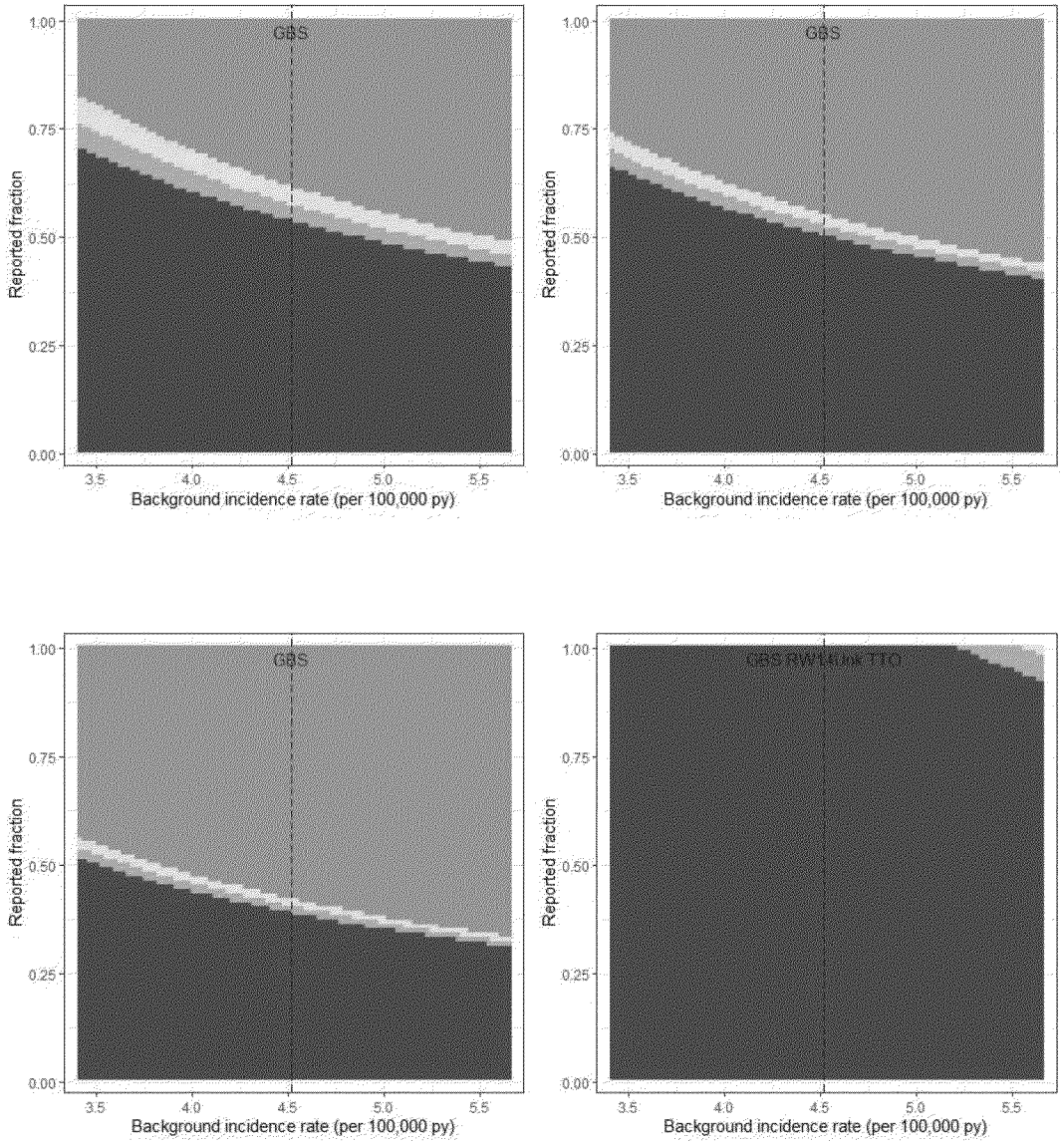
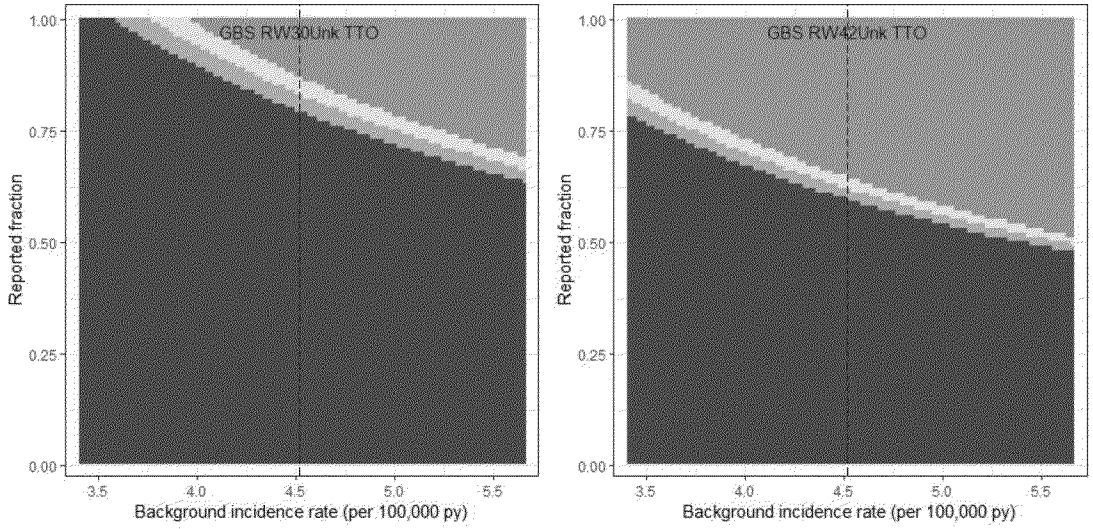

GBS
GBS
GBS
GBS RW14/nx TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.5
4.0
4.5
5.0
5.5
Background incidence rate (per 100,000 py)

Table 29 Observed Versus Expected analysis for GBS cases Overall

Description	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	



[a] Exposure until 28 December 2022

[b] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Guillain-Barré Syndrome (Narrow).

CI Confidence Interval; E Expected; GBS Guillain Barre Syndrome; O observed; TTO Time to onset; Unk Unknown

Table 30 Observed Versus Expected analysis for GBS cases meeting the Brighton Collaboration Criteria (BCC) Level 1, 2 or 3 (Overall)

Adverse Events	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	
GBS BCC 1-3	164	807.57	14	4.52	466115644	0.2 (0.17 - 0.24)	Observed significantly < expected
GBS BCC 1-3	309	1730.5	30	4.52	466115644	0.18 (0.16 - 0.2)	Observed significantly < expected
GBS BCC 1-3	329	2422.7	42	4.52	466115644	0.14 (0.12 - 0.15)	Observed significantly < expected
GBS BCC 1-3 all cases (Including unk TTO)	257	807.57	14	4.52	466115644	0.32 (0.28 - 0.36)	Observed significantly < expected
GBS BCC 1-3 all cases (Including unk TTO)	402	1730.5	30	4.52	466115644	0.23 (0.21 - 0.26)	Observed significantly < expected
GBS BCC 1-3 all cases (Including unk TTO)	422	2422.7	42	4.52	466115644	0.17 (0.16 - 0.19)	Observed significantly < expected

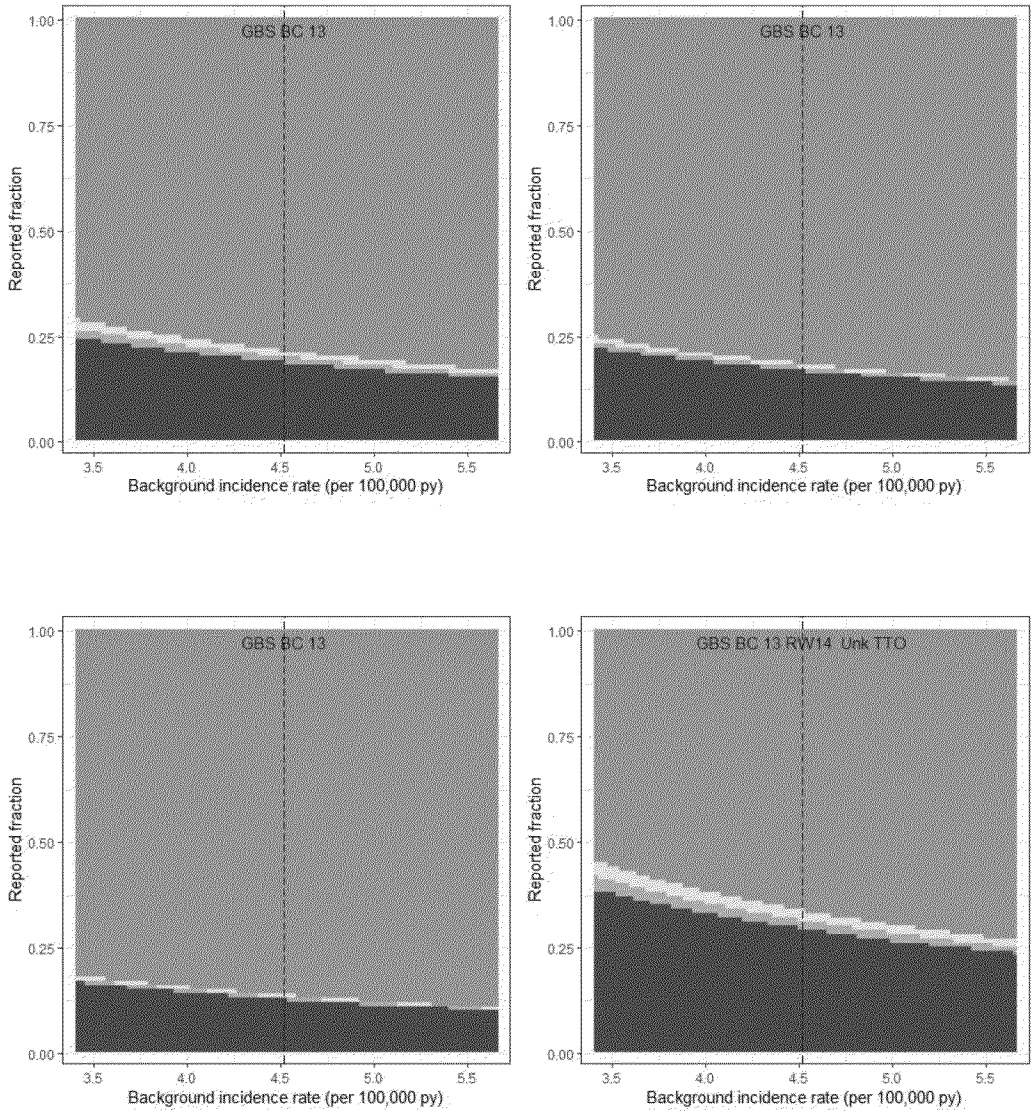
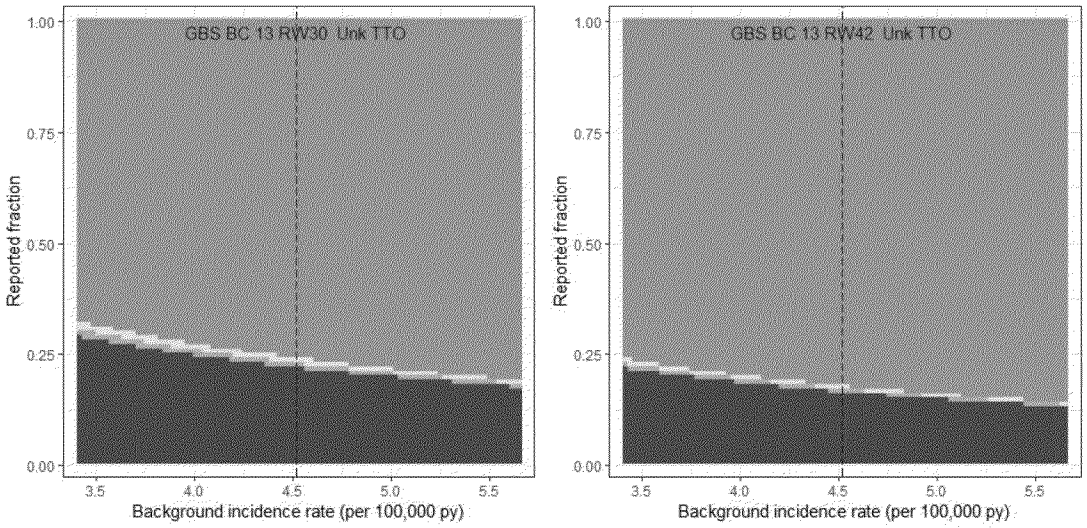

GBS BC 13
GBS BC 13
GBS BC 13
GBS BC 13 RW14 Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
3.5
4.0
4.5
5.0
5.5

Table 30 Observed Versus Expected analysis for GBS cases meeting the Brighton Collaboration Criteria (BCC) Level 1, 2 or 3 (Overall)

Adverse Events	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	
							

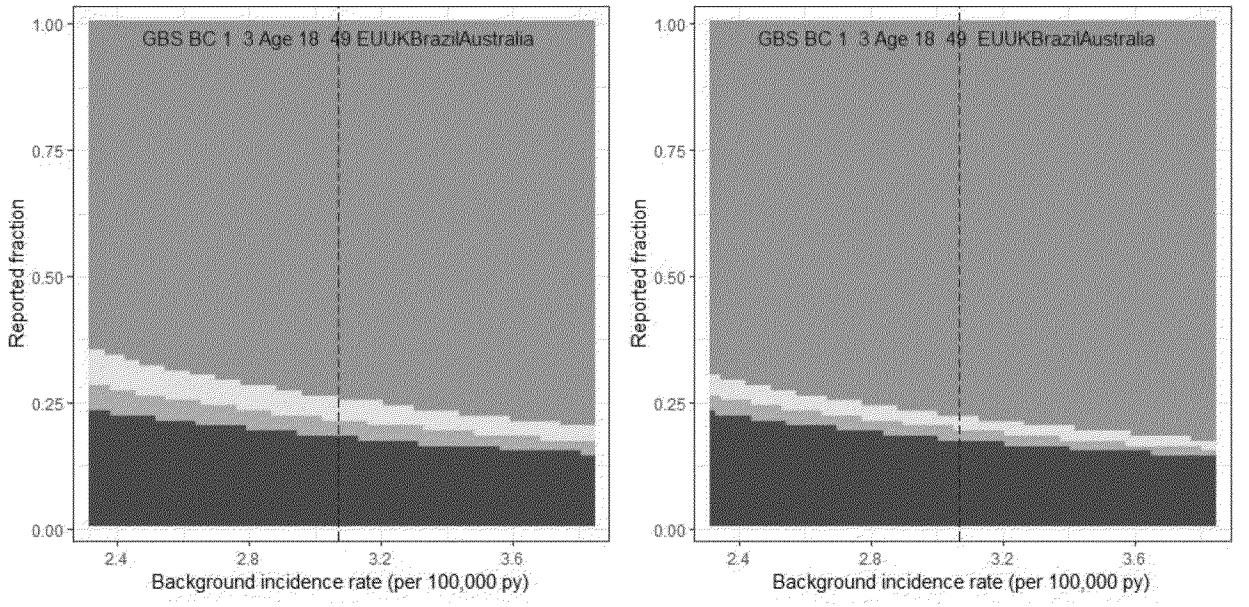
[a] Exposure until 28 December 2022

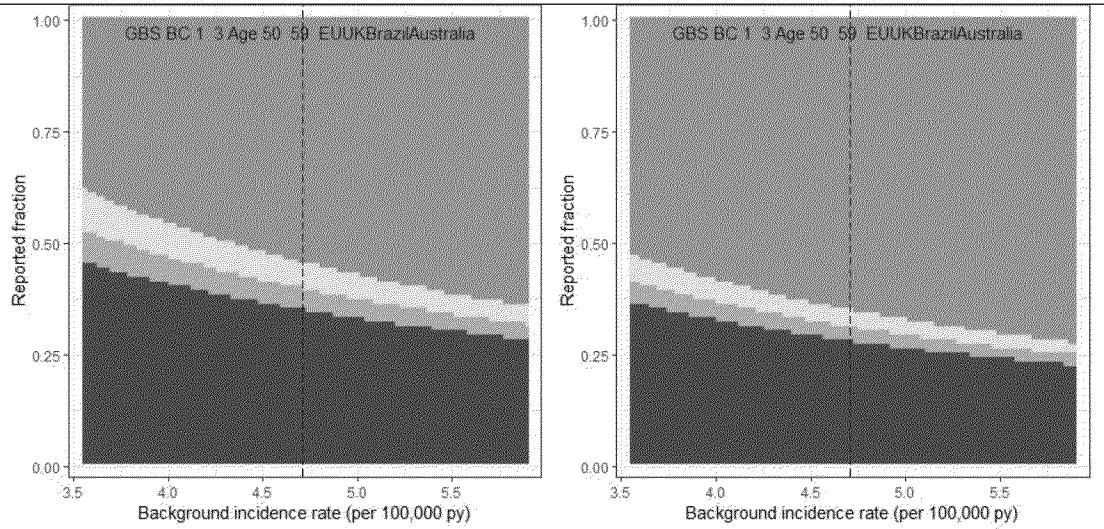
[b] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Guillain-Barré Syndrome (Narrow).

BCC Brighton Collaboration Criteria; CI Confidence Interval; E Expected; GBS Guillain-Barré syndrome, IR Incidence Rate; O Observed; RW Risk Window; TTO Time to onset; Unk Unknown.

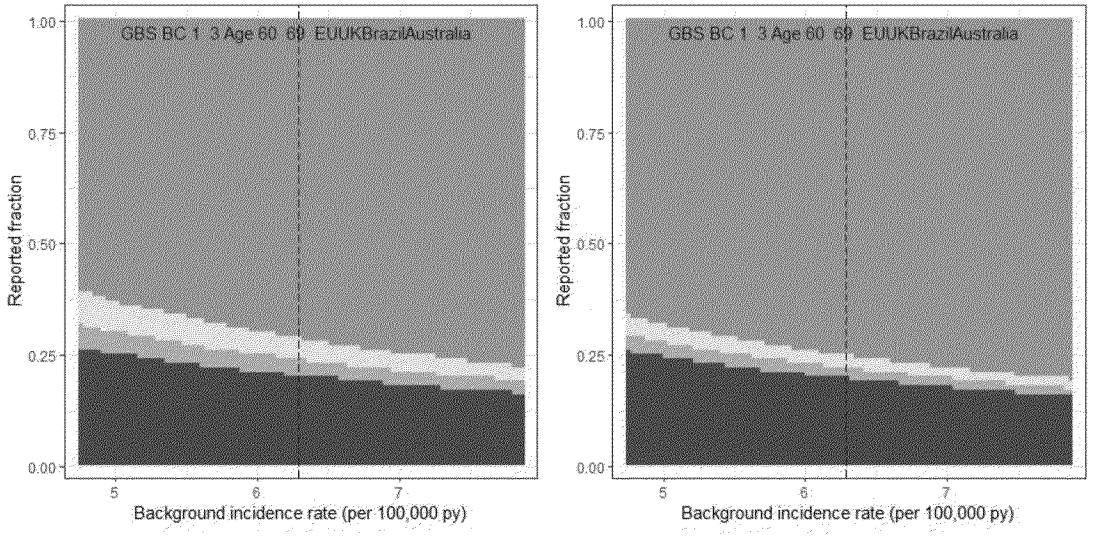
Table 31 Observed Versus Expected analysis for GBS cases meeting the Brighton Collaboration Criteria (BCC) Level 1, 2 or 3 and stratified by age for EU+UK+Brazil+Australia regions

Adverse Events	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	
GBS BCC 1-3 Age 18-49	28	129.55	14	3.07	110094983	0.22 (0.14 - 0.31)	Observed significantly < expected
GBS BCC 1-3 Age 18-49	55	277.62	30	3.07	110094983	0.2 (0.15 - 0.26)	Observed significantly < expected
GBS BCC 1-3 Age 18-49	60	388.66	42	3.07	110094983	0.15 (0.12 - 0.2)	Observed significantly < expected
GBS BCC 1-3 Age 50-59	48	105.32	14	4.71	58336094	0.46 (0.34 - 0.6)	Observed significantly < expected
GBS BCC 1-3 Age 50-59	90	225.68	30	4.71	58336094	0.4 (0.32 - 0.49)	Observed significantly < expected
GBS BCC 1-3 Age 50-59	99	315.96	42	4.71	58336094	0.31 (0.25 - 0.38)	Observed significantly < expected
GBS BCC 1-3 Age 60-69	34	139.74	14	6.29	57960860	0.24 (0.17 - 0.34)	Observed significantly < expected
GBS BCC 1-3 Age 60-69	67	299.45	30	6.29	57960860	0.22 (0.17 - 0.28)	Observed significantly < expected
GBS BCC 1-3 Age 60-69	68	419.23	42	6.29	57960860	0.16 (0.13 - 0.21)	Observed significantly < expected
GBS BCC 1-3 Over 70	18	73.96	14	5.96	32376365	0.24 (0.14 - 0.38)	Observed significantly < expected
GBS BCC 1-3 Over 70	35	158.49	30	5.96	32376365	0.22 (0.15 - 0.31)	Observed significantly < expected
GBS BCC 1-3 Over 70	38	221.89	42	5.96	32376365	0.17 (0.12 - 0.24)	Observed significantly < expected

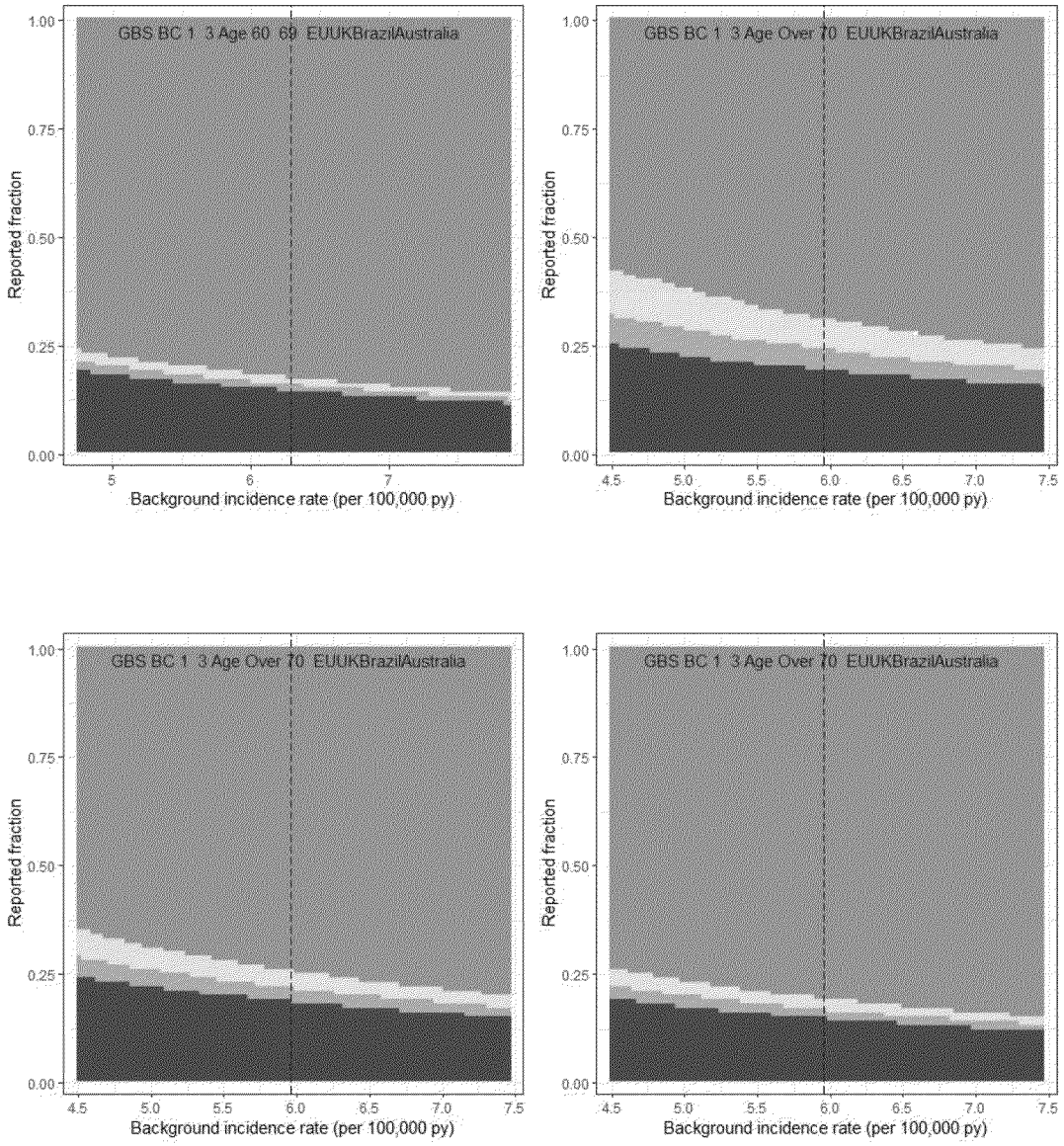

GBS BC 1 3 Age 18 49 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.4
2.8
3.2
3.6
Background incidence rate (per 100,000 py)
GBS BC 1 3 Age 18 49 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.4
2.8
3.2
3.6
Background incidence rate (per 100,000 py)


GBS BC 1 3 Age 50 59 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.5
4.0
4.5
5.0
5.5
Background incidence rate (per 100,000 py)

GBS BC 1 3 Age 50 59 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.5
4.0
4.5
5.0
5.5
Background incidence rate (per 100,000 py)


GBS BC 1 3 Age 60 69 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)

GBS BC 1 3 Age 60 69 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)


GBS BC 1 3 Age 60 69 EUUKBrazilAustralia
GBS BC 1 3 Age Over 70 EUUKBrazilAustralia
GBS BC 1 3 Age Over 70 EUUKBrazilAustralia
GBS BC 1 3 Age Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

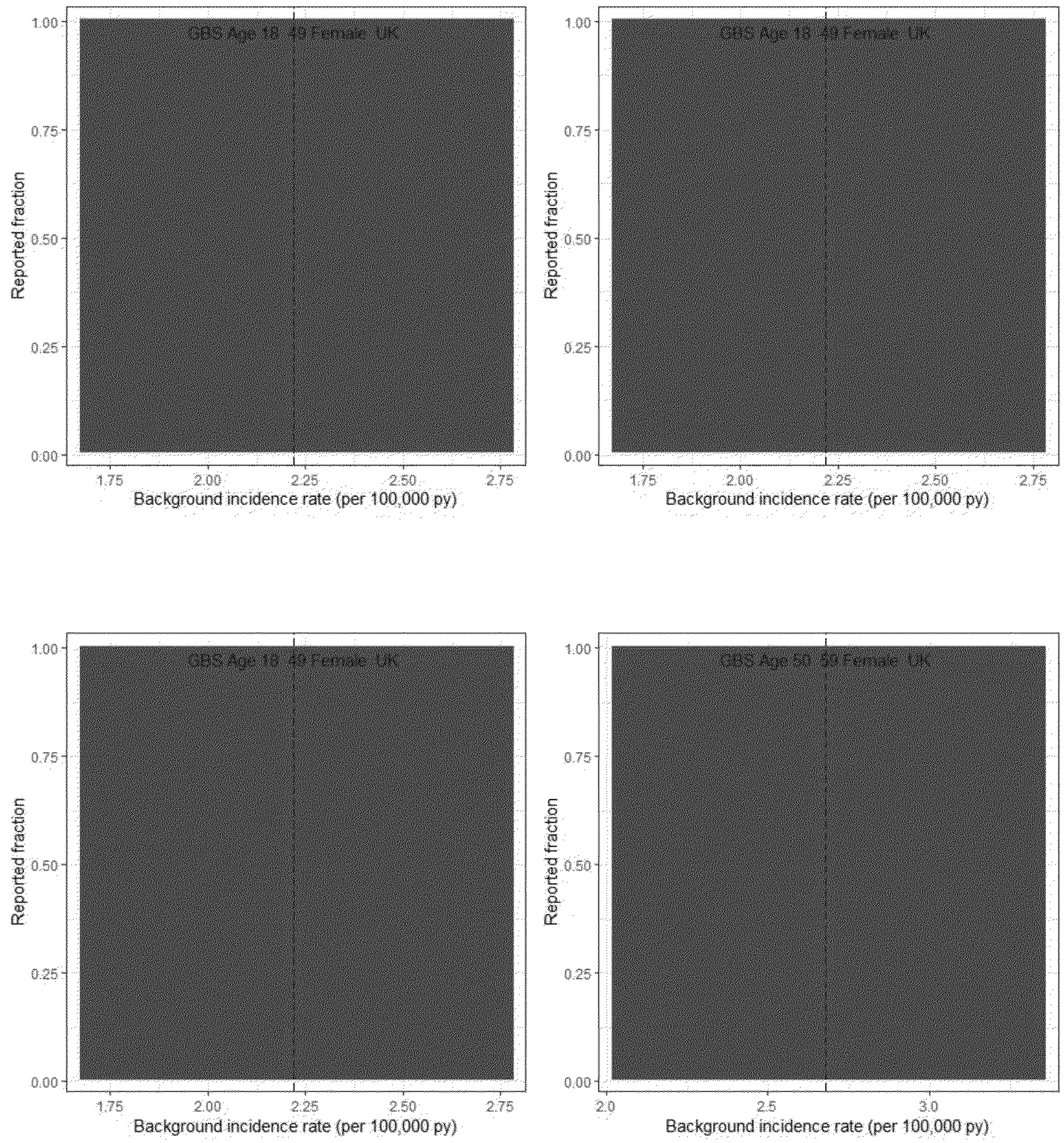
[a] Exposure until 28 December 2022

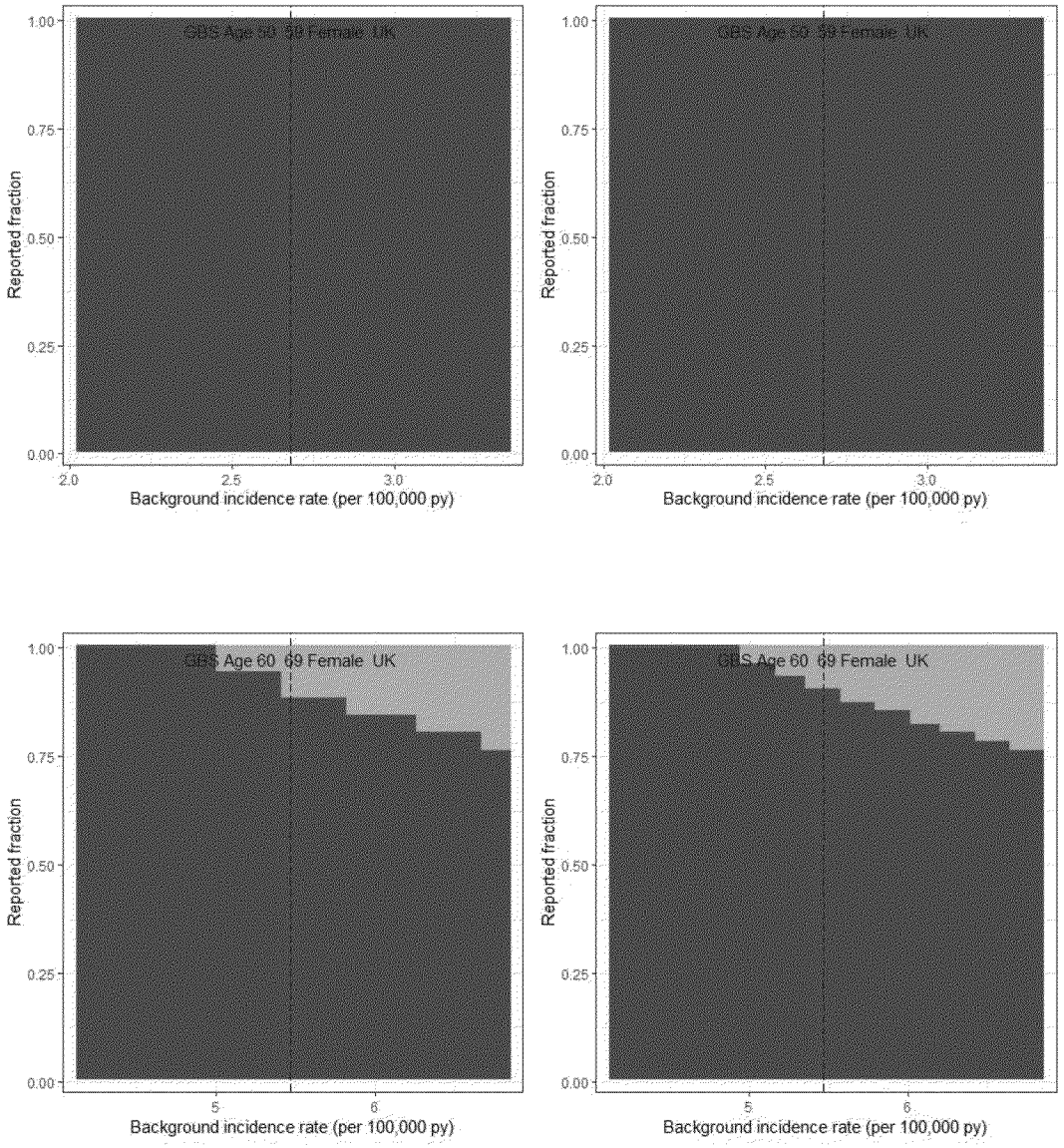
[b] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Guillain-Barré Syndrome (Narrow)).

BCC Brighton Collaboration Criteria; CI Confidence Interval; E Expected; EU European Union; GBS Guillain-Barré syndrome, IR Incidence Rate; O Observed; RW Risk Window; TTO Time to onset; Unk Unknown.; UK United Kingdom.

Table 32 Observed Versus Expected analysis for GBS cases stratified by age and gender for UK only

Description	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	
Age 18 – 49 Female	17	6.31	14	2.22	7414701	2.69 (1.57 - 4.31)	Observed significantly > expected
Age 18 – 49 Female	34	13.52	30	2.22	7414701	2.51 (1.74 - 3.51)	Observed significantly > expected
Age 18 – 49 Female	37	18.93	42	2.22	7414701	1.95 (1.38 - 2.69)	Observed significantly > expected
Age 50 – 59 Female	15	6.11	14	2.68	5944683	2.45 (1.37 - 4.05)	Observed significantly > expected
Age 50 – 59 Female	31	13.09	30	2.68	5944683	2.37 (1.61 - 3.36)	Observed significantly > expected
Age 50 – 59 Female	35	18.32	42	2.68	5944683	1.91 (1.33 - 2.66)	Observed significantly > expected
Age 60 – 69 Female	16	10.03	14	5.47	4783416	1.6 (0.91 - 2.59)	Observed > expected
Age 60 – 69 Female	29	21.49	30	5.47	4783416	1.35 (0.9 - 1.94)	Observed > expected
Age 60 – 69 Female	29	30.09	42	5.47	4783416	0.96 (0.65 - 1.38)	Observed < expected
Age 70 – 79 Female	11	7.26	14	5.45	3475875	1.52 (0.76 - 2.71)	Observed > expected
Age 70 – 79 Female	18	15.56	30	5.45	3475875	1.16 (0.69 - 1.83)	Observed > expected
Age 70 – 79 Female	19	21.78	42	5.45	3475875	0.87 (0.53 - 1.36)	Observed < expected
Age 80+ Female	1	1.44	14	2.3	1630324	0.69 (0.02 - 3.87)	Observed < expected
Age 80+ Female	1	3.08	30	2.3	1630324	0.32 (0.01 - 1.81)	Observed < expected
Age 80+ Female	2	4.31	42	2.3	1630324	0.46 (0.06 - 1.68)	Observed < expected


GBS Age 18 49 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)
GBS Age 18 49 Female UK
Reported fraction
Background incidence rate (per 100,000 py)
GBS Age 18 49 Female UK
Reported fraction
Background incidence rate (per 100,000 py)
GBS Age 50 59 Female UK
Reported fraction
2.0
2.5
3.0
Background incidence rate (per 100,000 py)


GBS Age 50 59 Female UK
GBS Age 50 59 Female UK
GBS Age 60 69 Female UK
GBS Age 60 69 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.5
3.0
5
6
Background incidence rate (per 100,000 py)

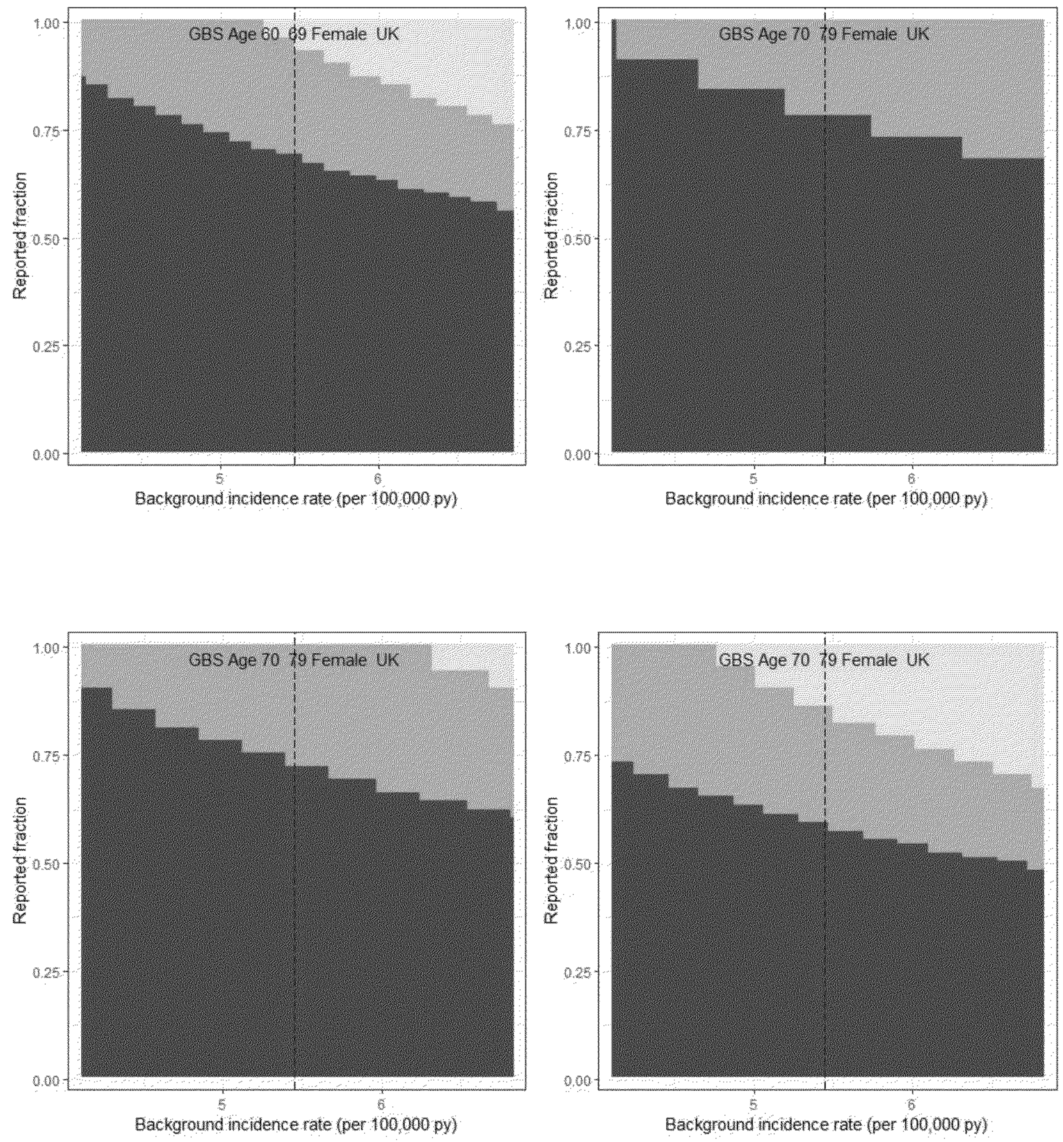
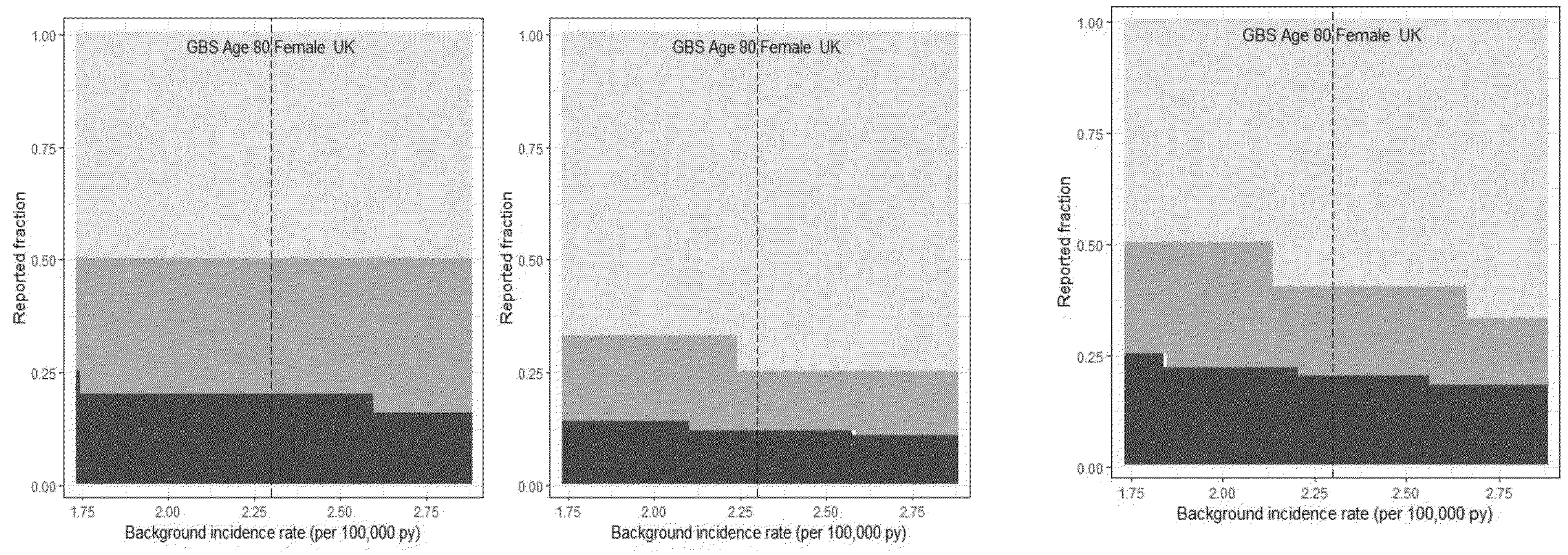

GBS Age 60 69 Female UK
GBS Age 70 79 Female UK
GBS Age 70 79 Female UK
GBS Age 70 79 Female UK
Reported fraction
Background incidence rate (per 100,000 py)

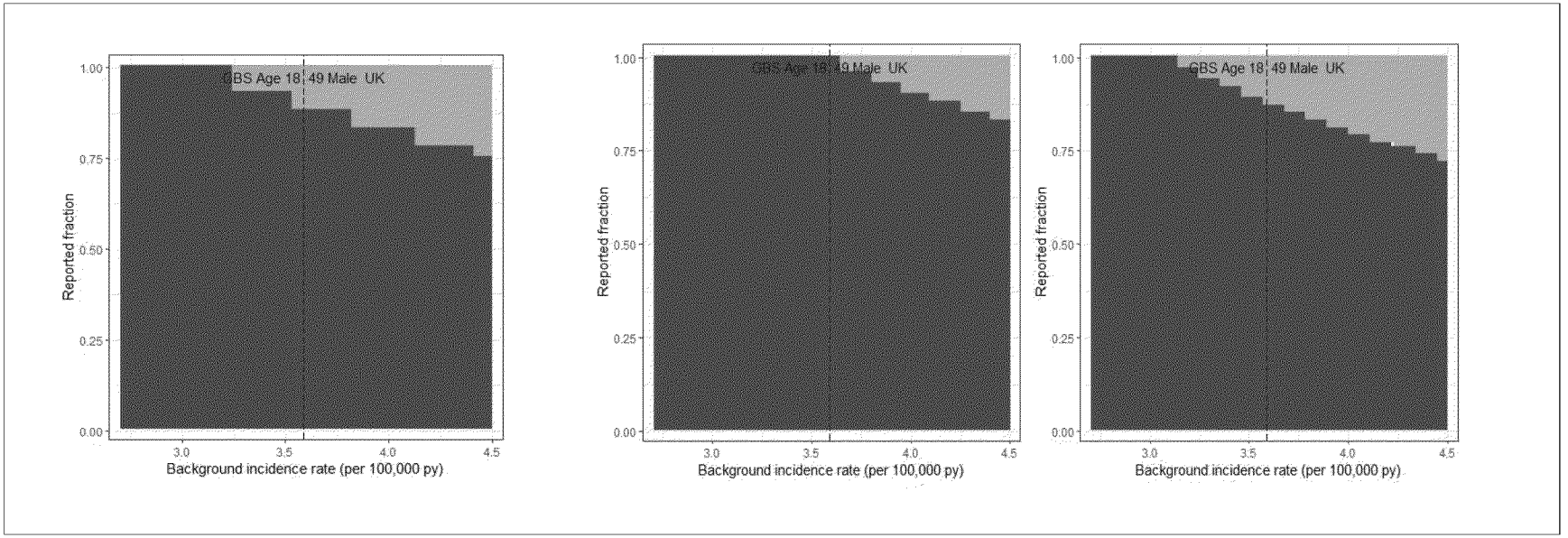
Table 32 Observed Versus Expected analysis for GBS cases stratified by age and gender for UK only

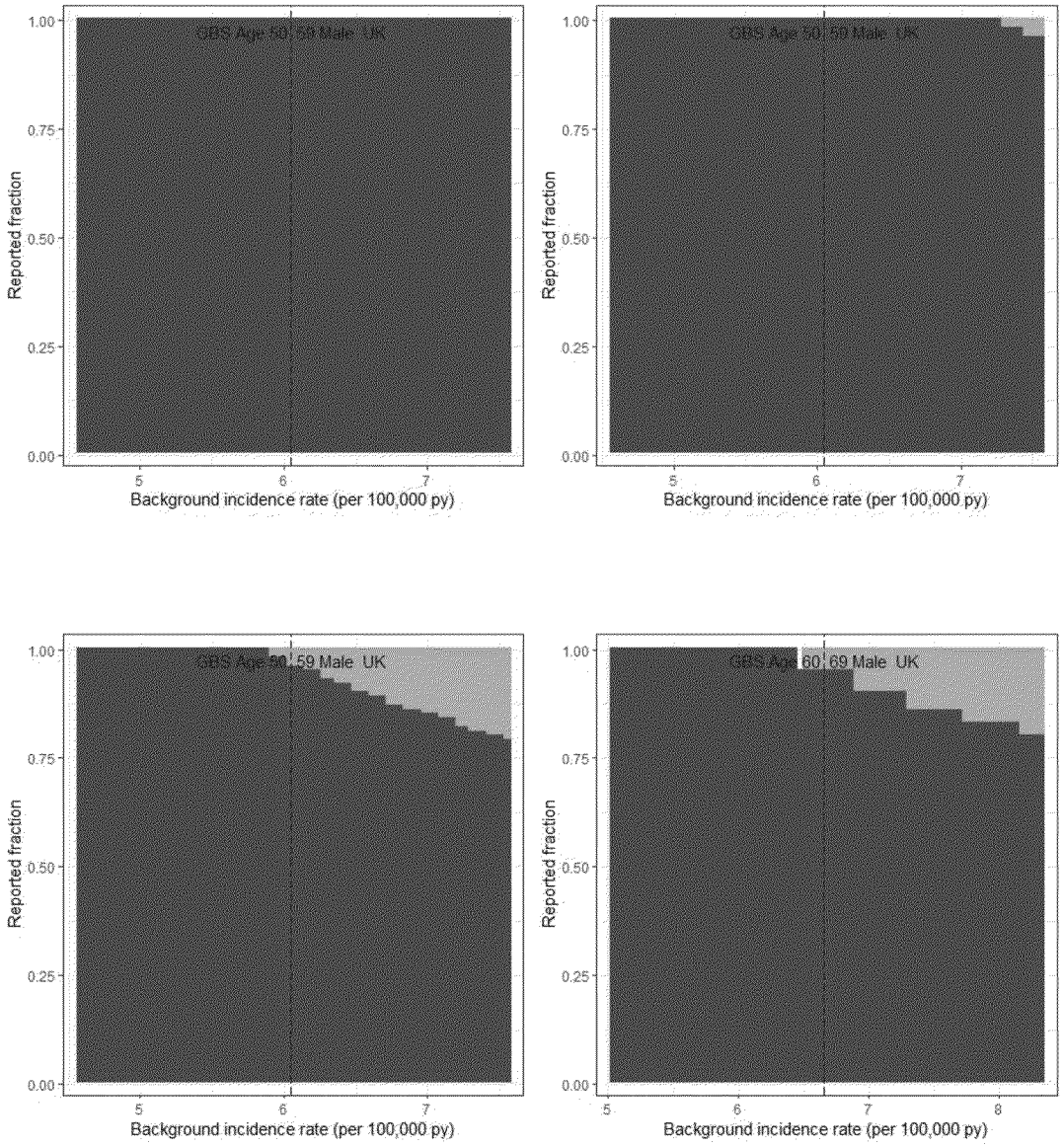


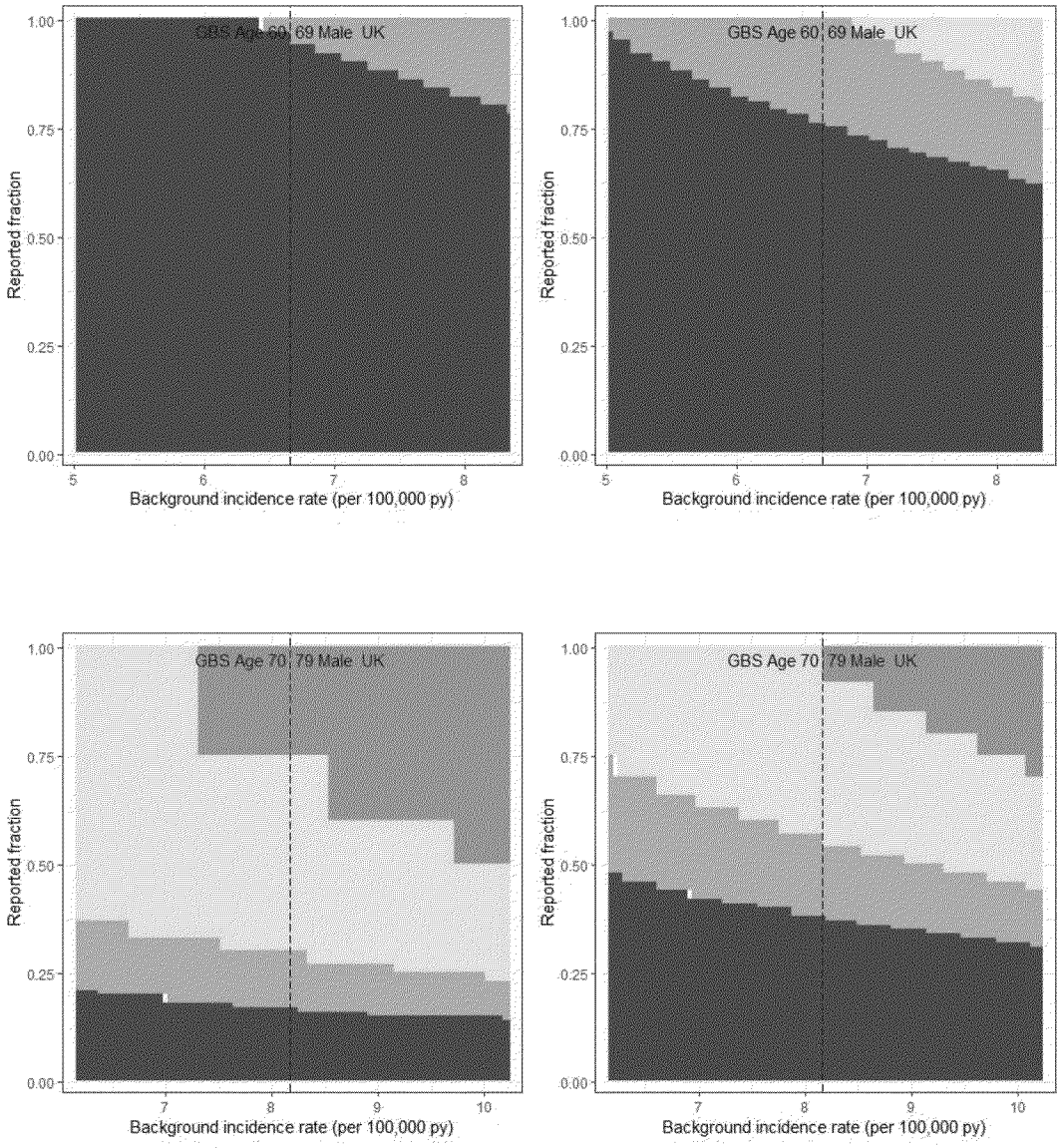
Description	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	
Age 18 - 49 Male	15	9.31	14	3.59	6766098	1.61 (0.9 - 2.66)	Observed > expected
Age 18 - 49 Male	30	19.95	30	3.59	6766098	1.5 (1.01 - 2.15)	Observed significantly > expected
Age 18 - 49 Male	35	27.93	42	3.59	6766098	1.25 (0.87 - 1.74)	Observed > expected
Age 50 - 59 Male	31	15.1	14	6.05	6510960	2.05 (1.39 - 2.91)	Observed significantly > expected
Age 50 - 59 Male	52	32.35	30	6.05	6510960	1.61 (1.2 - 2.11)	Observed significantly > expected
Age 50 - 59 Male	58	45.3	42	6.05	6510960	1.28 (0.97 - 1.66)	Observed > expected
Age 60 - 69 Male	20	12.6	14	6.66	4934728	1.59 (0.97 - 2.45)	Observed > expected
Age 60 - 69 Male	37	26.99	30	6.66	4934728	1.37 (0.97 - 1.89)	Observed > expected

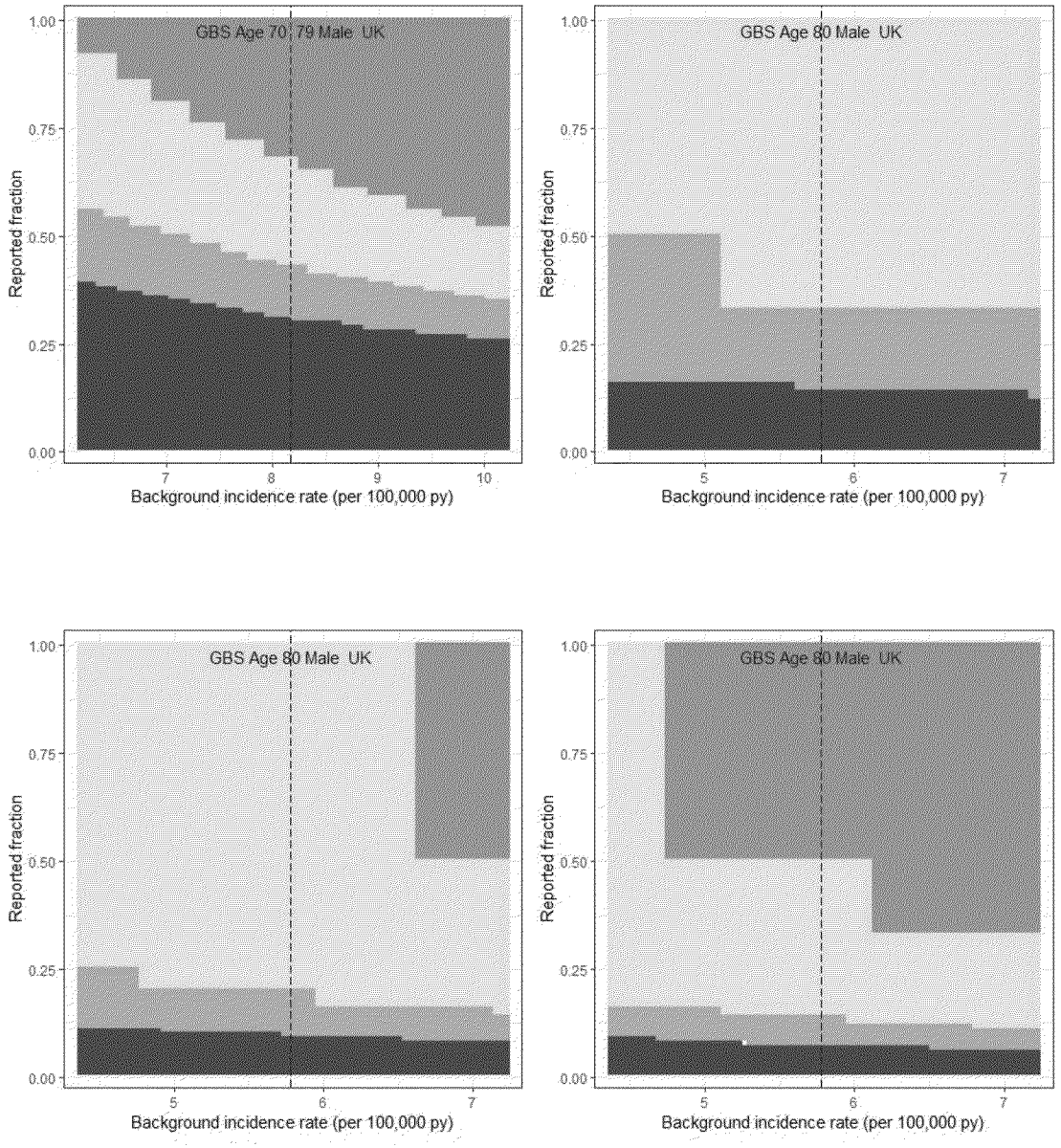
Table 32 Observed Versus Expected analysis for GBS cases stratified by age and gender for UK only

Description	Observed Cases	Expected Cases	Risk window	Incidence Rate [b]	Exposure [a]	O over E ratio (95% CI)	
Age 60 - 69 Male	39	37.79	42	6.66	4934728	1.03 (0.73 - 1.41)	Observed > expected
Age 70 - 79 Male	3	9.82	14	8.17	3137304	0.31 (0.06 - 0.89)	Observed significantly < expected
Age 70 - 79 Male	12	21.05	30	8.17	3137304	0.57 (0.29 - 1)	Observed significantly < expected
Age 70 - 79 Male	13	29.47	42	8.17	3137304	0.44 (0.23 - 0.75)	Observed significantly < expected
Age 80+ Male	1	2.27	14	5.78	1025046	0.44 (0.01 - 2.45)	Observed < expected
Age 80+ Male	1	4.87	30	5.78	1025046	0.21 (0.01 - 1.14)	Observed < expected
Age 80+ Male	1	6.81	42	5.78	1025046	0.15 (0 - 0.82)	Observed significantly < expected


GBS Age 18 49 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)
GBS Age 18 49 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)
GBS Age 18 49 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)


GBS Age 50 59 Male UK
GBS Age 50 59 Male UK
GBS Age 50 59 Male UK
GBS Age 60 69 Male UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
5
6
7
8


GBS Age 60_69 Male UK
Reported fraction
Background incidence rate (per 100,000 py)
GBS Age 60_69 Male UK
Reported fraction
Background incidence rate (per 100,000 py)
GBS Age 70_79 Male UK
Reported fraction
Background incidence rate (per 100,000 py)
GBS Age 70_79 Male UK
Reported fraction
Background incidence rate (per 100,000 py)


GBS Age 70 79 Male UK
GBS Age 80 Male UK
GBS Age 80 Male UK
GBS Age 80 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
5
6
7
Background incidence rate (per 100,000 py)

[a] Exposure until 28 December 2022.

[b] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Guillain-Barré Syndrome (Narrow)).

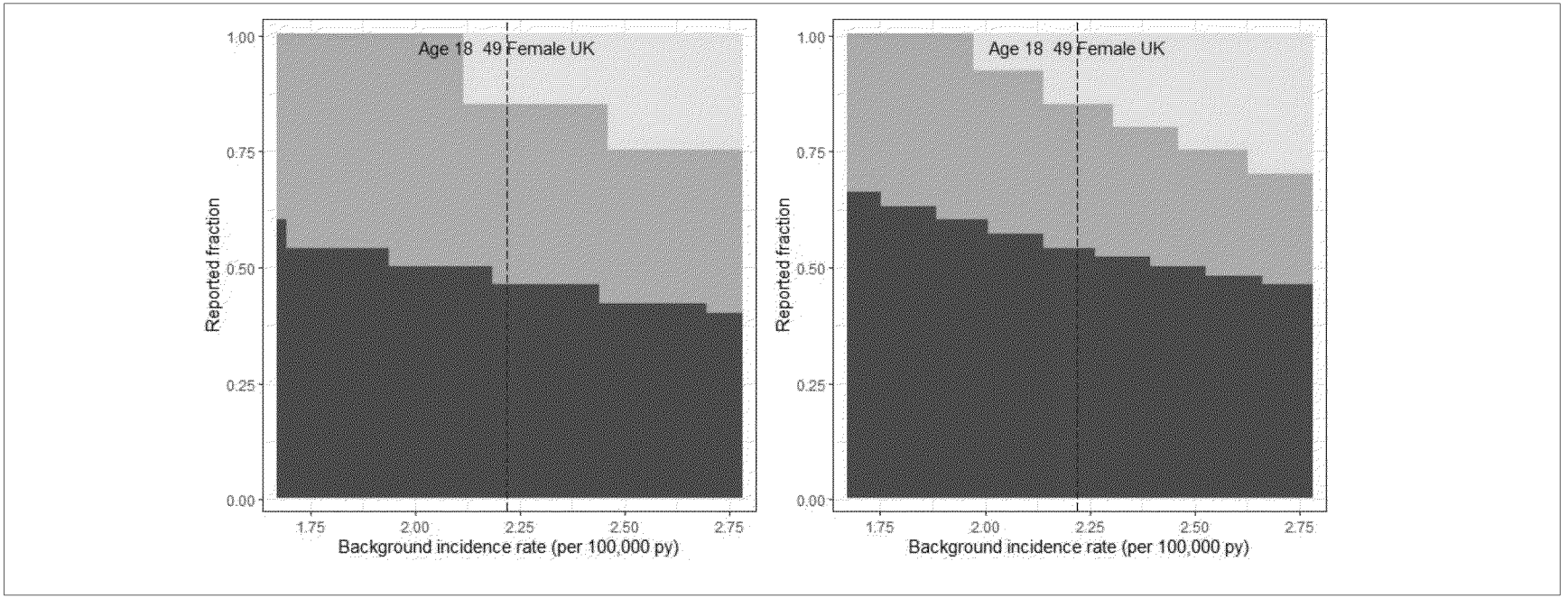
BCC Brighton Collaboration Criteria; CI Confidence Interval; E Expected; GBS Guillain-Barré syndrome, IR Incidence Rate; O Observed; UK United Kingdom.

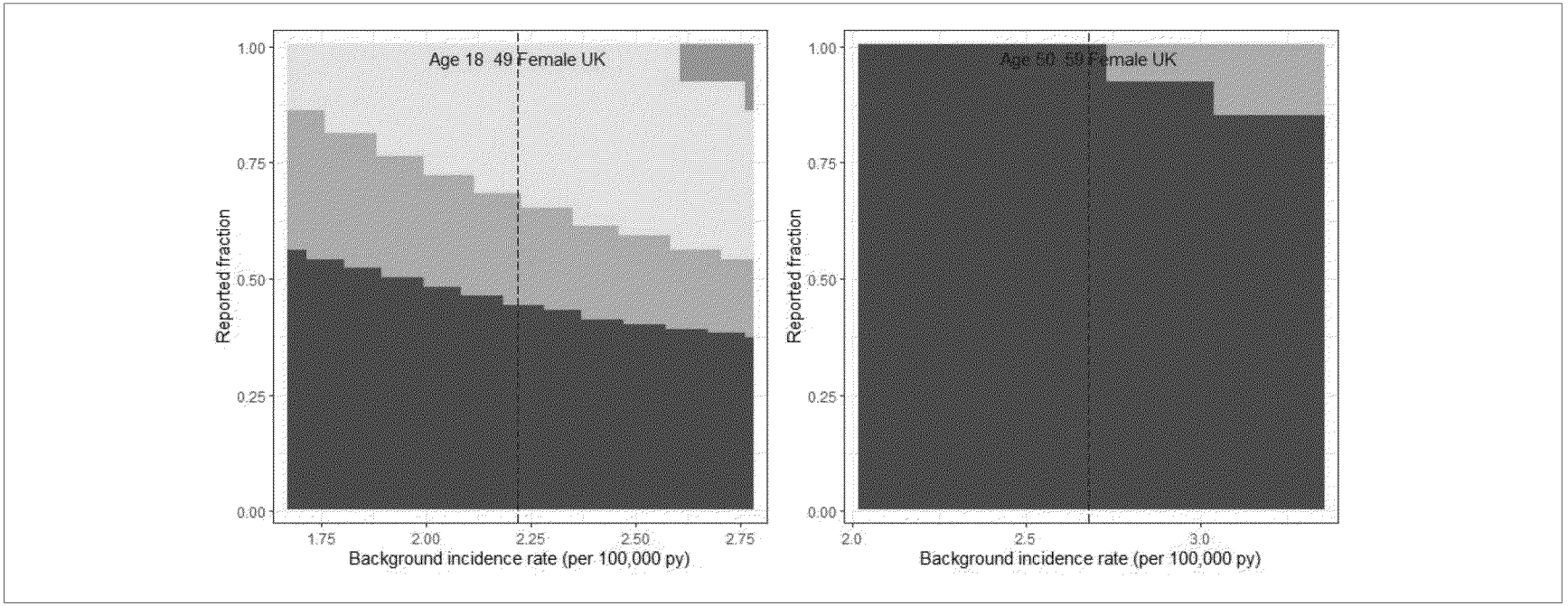
Table 33 Observed Versus Expected analysis for GBS cases meeting the Brighton Criteria (BC) Level 1, 2 or 3 and stratified by age and gender for UK only

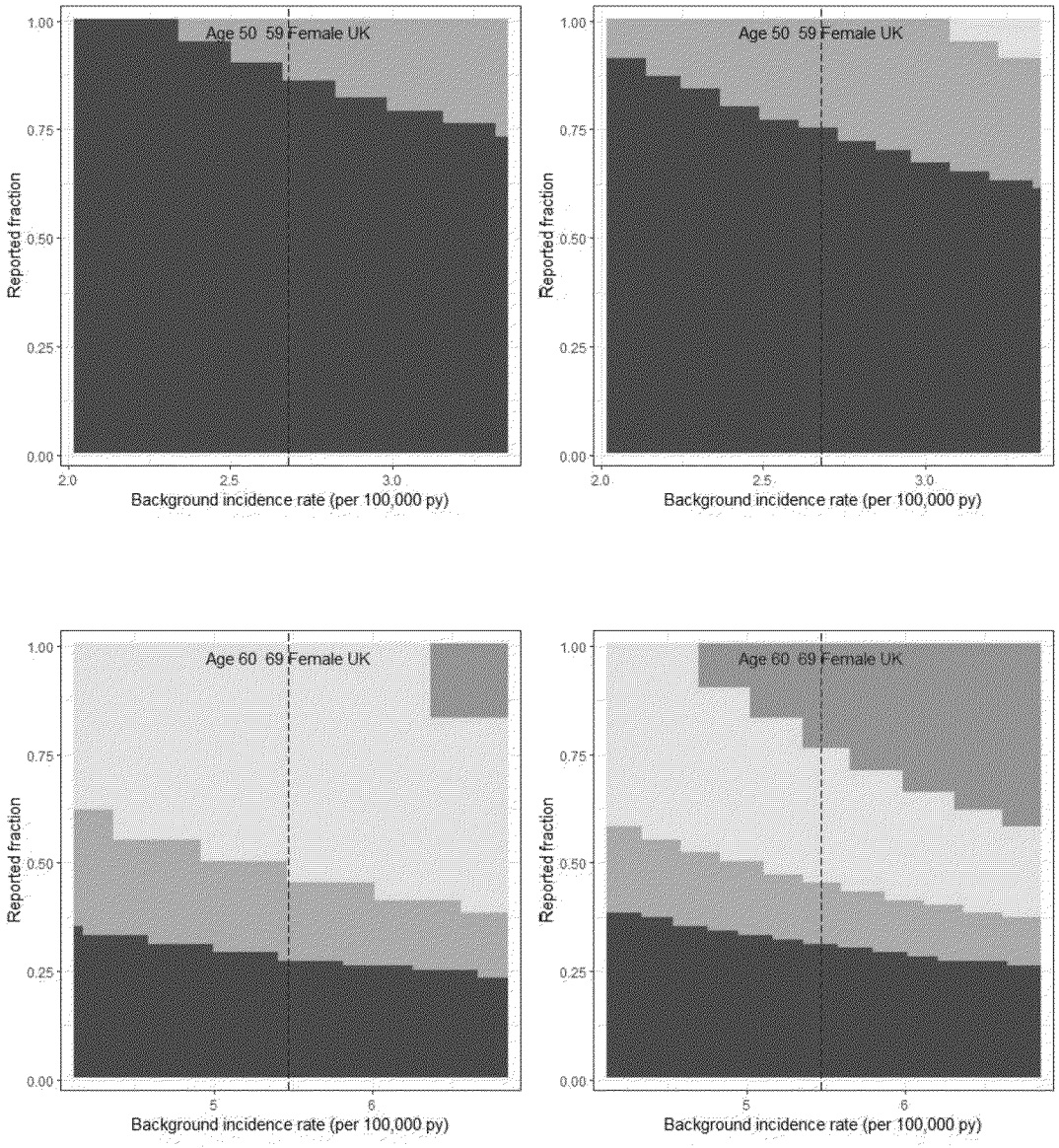
Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY [b]	Exposure [a]	O over E ratio (95% CI)	
Age 18 - 49 Female	6	6.31	14	2.22	7414701	0.95 (0.35 - 2.07)	Observed < expected
Age 18 - 49 Female	12	13.52	30	2.22	7414701	0.89 (0.46 - 1.55)	Observed < expected
Age 18 - 49 Female	13	18.93	42	2.22	7414701	0.69 (0.37 - 1.17)	Observed < expected
Age 50 - 59 Female	12	6.11	14	2.68	5944683	1.96 (1.01 - 3.43)	Observed significantly > expected
Age 50 - 59 Female	19	13.09	30	2.68	5944683	1.45 (0.87 - 2.27)	Observed > expected
Age 50 - 59 Female	21	18.32	42	2.68	5944683	1.15 (0.71 - 1.75)	Observed > expected
Age 60 - 69 Female	5	10.03	14	5.47	4783416	0.5 (0.16 - 1.16)	Observed < expected
Age 60 - 69 Female	10	21.49	30	5.47	4783416	0.47 (0.22 - 0.86)	Observed significantly < expected
Age 60 - 69 Female	10	30.09	42	5.47	4783416	0.33 (0.16 - 0.61)	Observed significantly < expected
Age 70 - 79 Female	7	7.26	14	5.45	3475875	0.96 (0.39 - 1.99)	Observed < expected
Age 70 - 79 Female	9	15.56	30	5.45	3475875	0.58 (0.26 - 1.1)	Observed < expected
Age 70 - 79 Female	9	21.78	42	5.45	3475875	0.41 (0.19 - 0.78)	Observed significantly < expected
Age 80+ Female	1	1.44	14	2.3	1630324	0.69 (0.02 - 3.87)	Observed < expected
Age 80+ Female	1	3.08	30	2.3	1630324	0.32 (0.01 - 1.81)	Observed < expected
Age 80+ Female	2	4.31	42	2.3	1630324	0.46 (0.06 - 1.68)	Observed < expected
Age 18 - 49 Male	6	9.31	14	3.59	6766098	0.64 (0.24 - 1.4)	Observed < expected
Age 18 - 49 Male	12	19.95	30	3.59	6766098	0.6 (0.31 - 1.05)	Observed < expected
Age 18 - 49 Male	14	27.93	42	3.59	6766098	0.5 (0.27 - 0.84)	Observed significantly < expected
Age 50 - 59 Male	14	15.1	14	6.05	6510960	0.93 (0.51 - 1.56)	Observed < expected
Age 50 - 59 Male	24	32.35	30	6.05	6510960	0.74 (0.48 - 1.1)	Observed < expected
Age 50 - 59 Male	28	45.3	42	6.05	6510960	0.62 (0.41 - 0.89)	Observed significantly < expected
Age 60 - 69 Male	8	12.6	14	6.66	4934728	0.63 (0.27 - 1.25)	Observed < expected

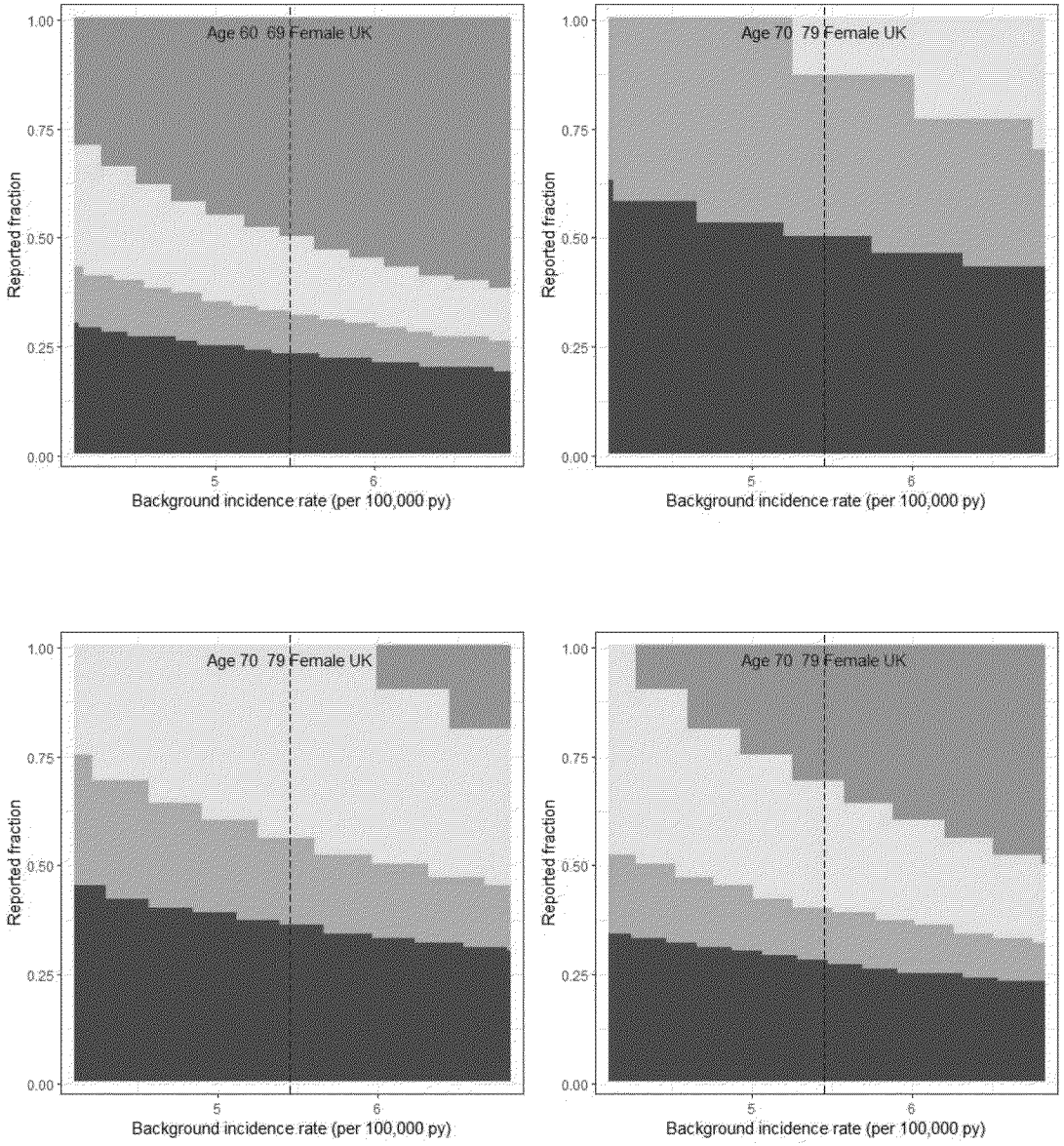
Table 33 Observed Versus Expected analysis for GBS cases meeting the Brighton Criteria (BC) Level 1, 2 or 3 and stratified by age and gender for UK only

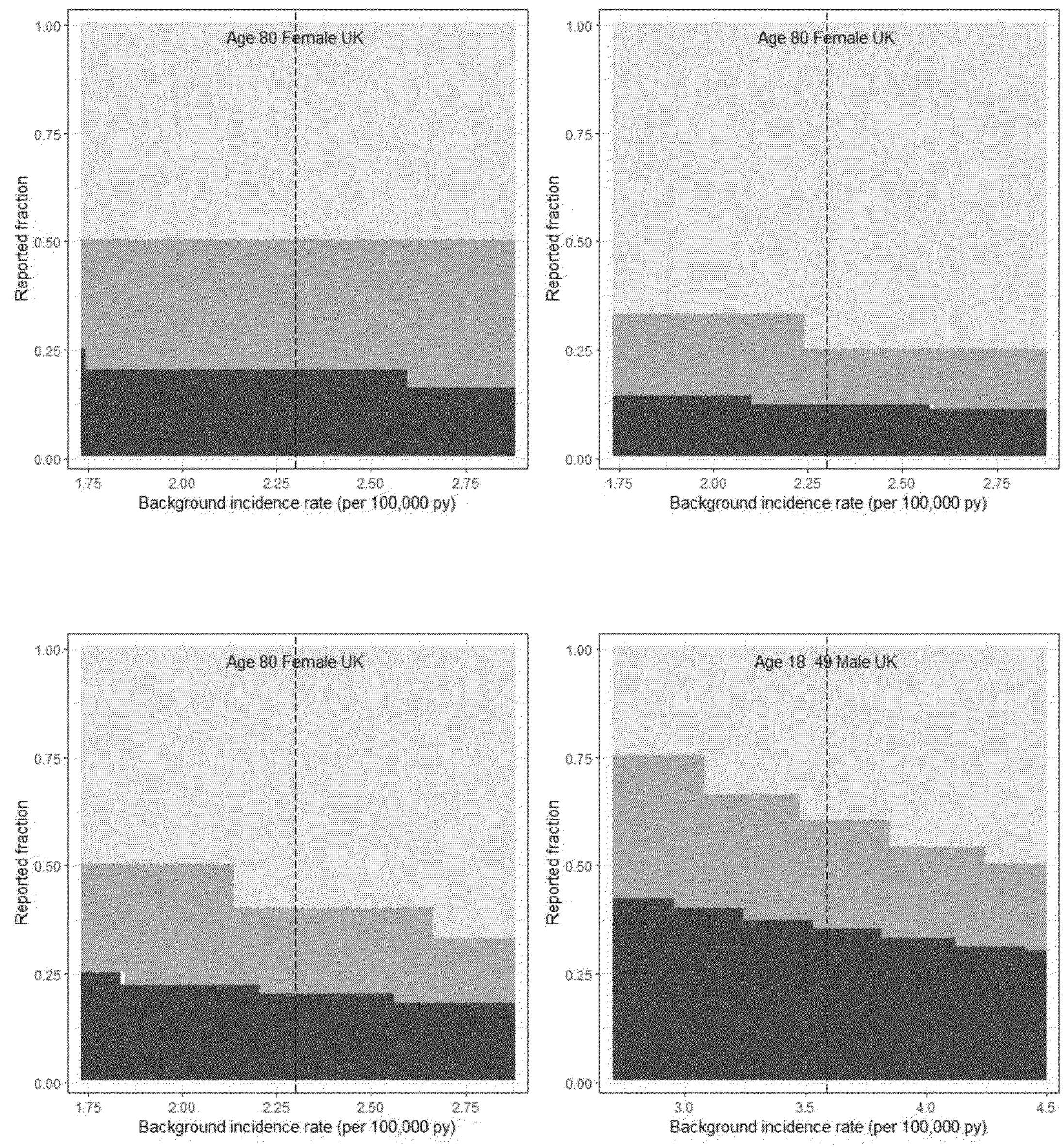
Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY [b]	Exposure [a]	O over E ratio (95% CI)	
Age 60 - 69 Male	20	26.99	30	6.66	4934728	0.74 (0.45 - 1.14)	Observed < expected
Age 60 - 69 Male	20	37.79	42	6.66	4934728	0.53 (0.32 - 0.82)	Observed significantly < expected
Age 70 - 79 Male	3	9.82	14	8.17	3137304	0.31 (0.06 - 0.89)	Observed significantly < expected
Age 70 - 79 Male	6	21.05	30	8.17	3137304	0.29 (0.1 - 0.62)	Observed significantly < expected
Age 70 - 79 Male	7	29.47	42	8.17	3137304	0.24 (0.1 - 0.49)	Observed significantly < expected
Age 80+ Male	0	2.27	14	5.78	1025046	0 (0 - 1.63)	Observed < expected
Age 80+ Male	0	4.87	30	5.78	1025046	0 (0 - 0.76)	Observed significantly < expected
Age 80+ Male	0	6.81	42	5.78	1025046	0 (0 - 0.54)	Observed significantly < expected

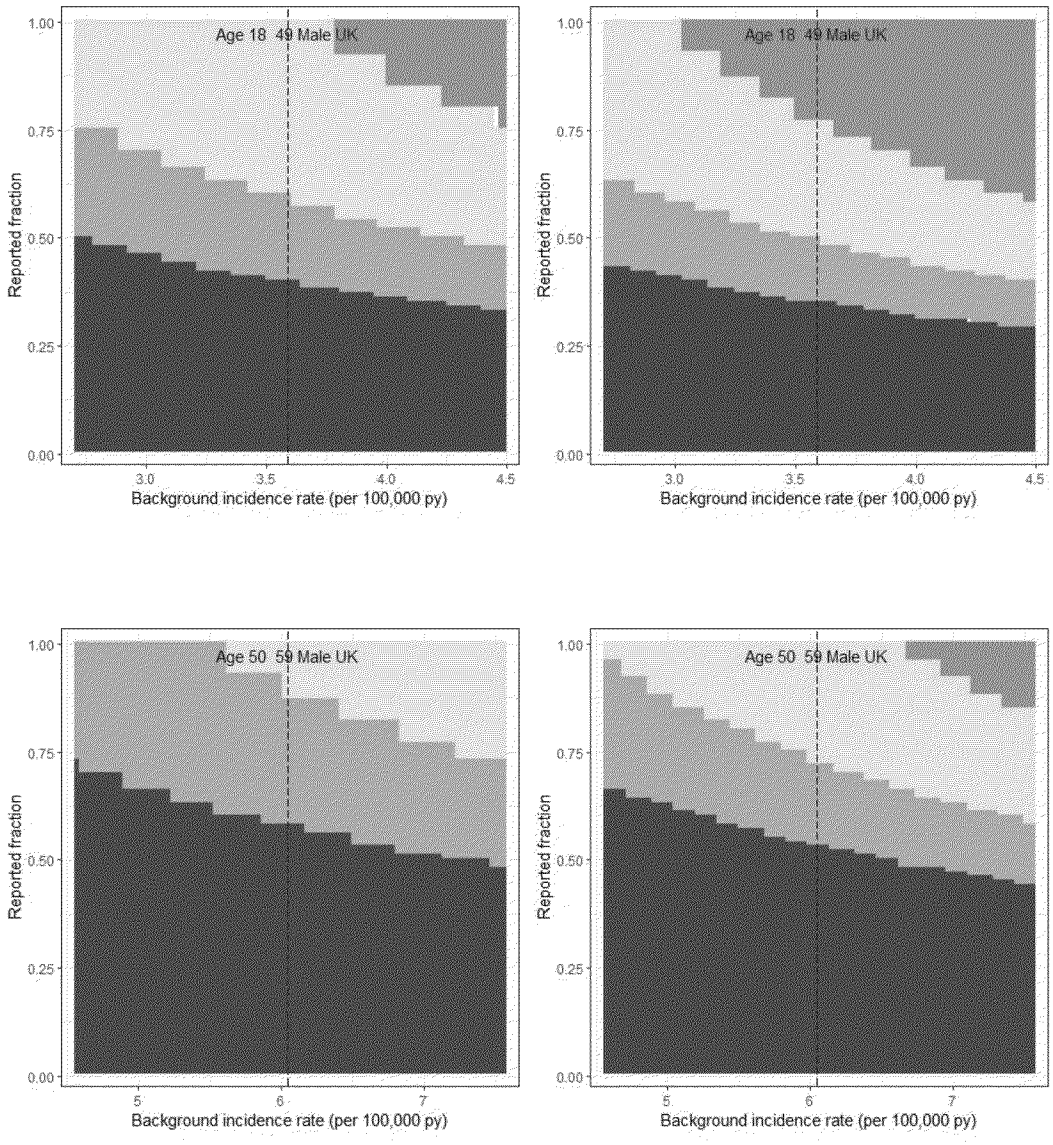

Age 18 49 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)
Age 18 49 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)

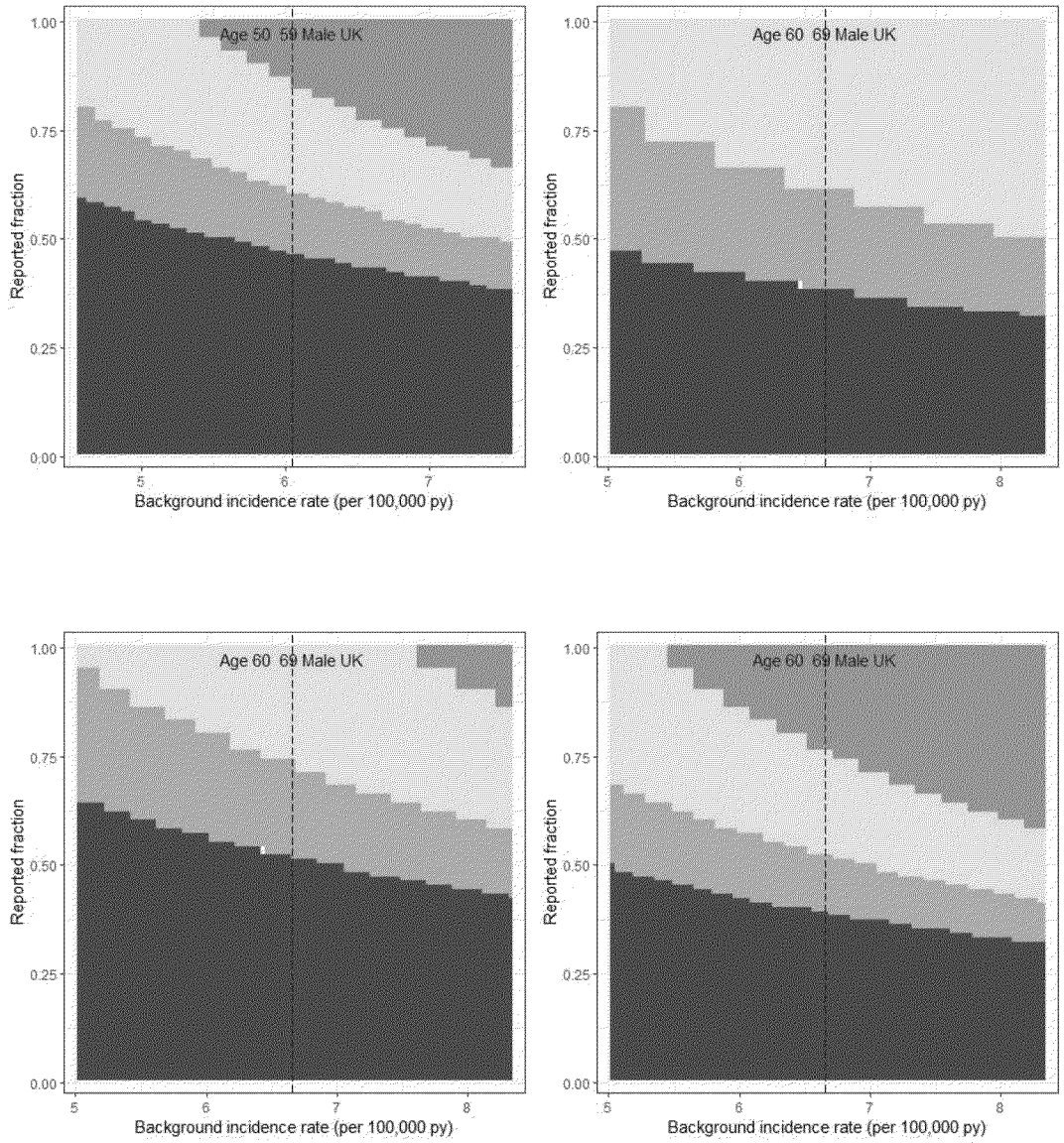

Age 18 49 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)
Age 50 59 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.5
3.0
Background incidence rate (per 100,000 py)


Age 50 59 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.5
3.0
Background incidence rate (per 100,000 py)
Age 50 59 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.5
3.0
Background incidence rate (per 100,000 py)
Age 60 69 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
Background incidence rate (per 100,000 py)
Age 60 69 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
Background incidence rate (per 100,000 py)


Age 60 69 Female UK
Age 70 79 Female UK
Age 70 79 Female UK
Age 70 79 Female UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
Background incidence rate (per 100,000 py)


Age 80 Female UK
Age 80 Female UK
Age 80 Female UK
Age 18 49 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)


Age 18 49 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)
Age 18 49 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)
Age 50 59 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)
Age 50 59 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)


Age 50 59 Male UK
Age 60 69 Male UK
Age 60 69 Male UK
Age 60 69 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
8
Background incidence rate (per 100,000 py)

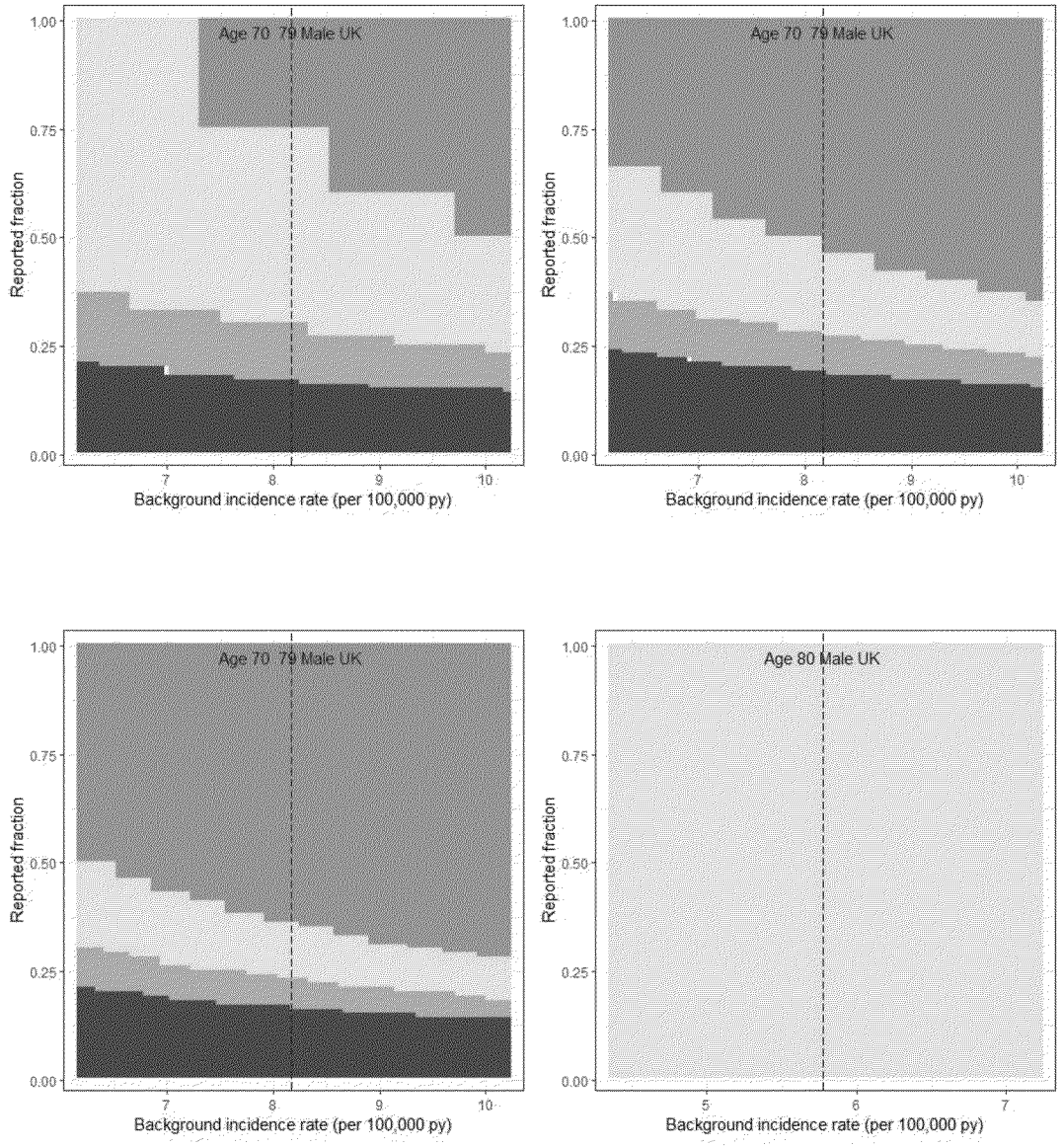
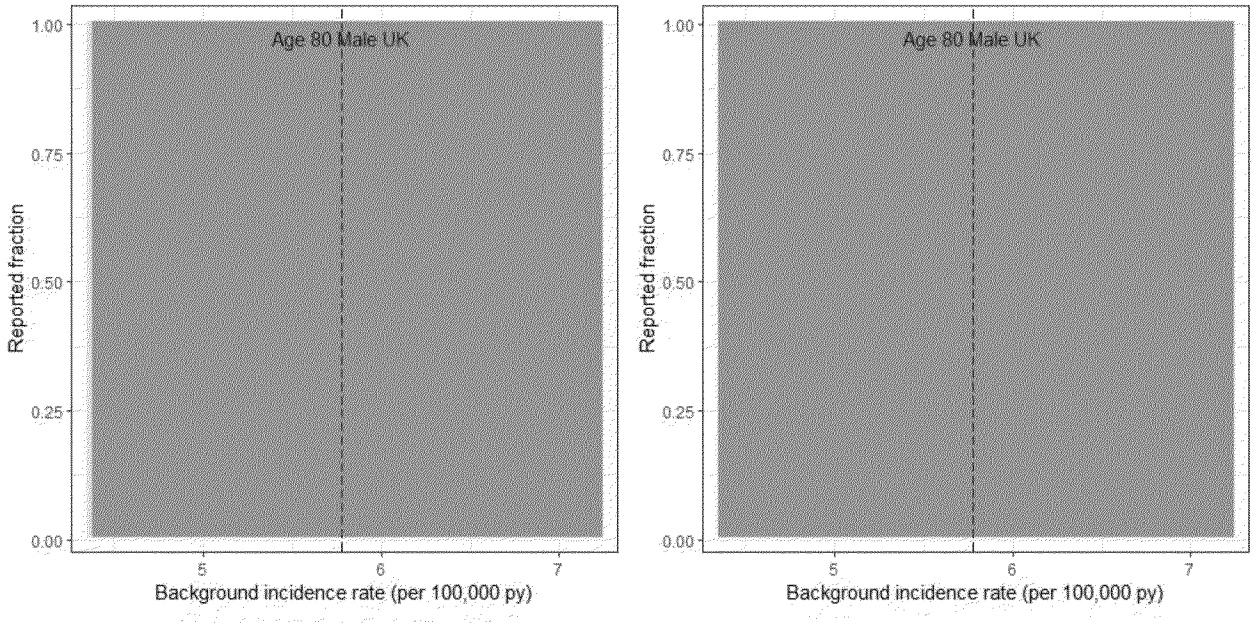

Age 70 79 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
Background incidence rate (per 100,000 py)
Age 70 79 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
Background incidence rate (per 100,000 py)
Age 70 79 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
Background incidence rate (per 100,000 py)
Age 80 Male UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)

Table 33 Observed Versus Expected analysis for GBS cases meeting the Brighton Criteria (BC) Level 1, 2 or 3 and stratified by age and gender for UK only

Age group	Observed Cases	Expected cases	Risk window	Incidence rate /100,000 PY [b]	Exposure [a]	O over E ratio (95% CI)	
							

[a] Exposure until 28 December 2022 for UK.

[b] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Guillain-Barré Syndrome (Narrow))

CI Confidence Interval; E Expected; GBS Guillain-Barré syndrome IR Incidence Rate; O Observed; PY Person Years; UK United Kingdom.

Table 34 Observed Versus Expected analysis for Multiple sclerosis - Multiple sclerosis relapse

Description	Observed Cases	Expected cases	Risk Window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Multiple sclerosis - Multiple sclerosis relapse	196	5895.96	42	11	466115644	0.03 (0.03 - 0.04)	Observed significantly < expected
Multiple sclerosis-Multiple sclerosis relapse (including unknown TTO)	310	5895.96	42	11	466115644	0.05 (0.05 - 0.06)	Observed significantly < expected
Multiple sclerosis - Multiple sclerosis relapse	213	25268.39	180	11	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Multiple sclerosis - Multiple sclerosis relapse (including unknown TTO)	327	25268.39	180	11	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Multiple sclerosis -Multiple sclerosis relapse (Extended RW)	215	33129.67	236	11	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Multiple sclerosis-Multiple sclerosis relapse (Extended RW+Unk TTO)	329	33129.67	236	11	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected

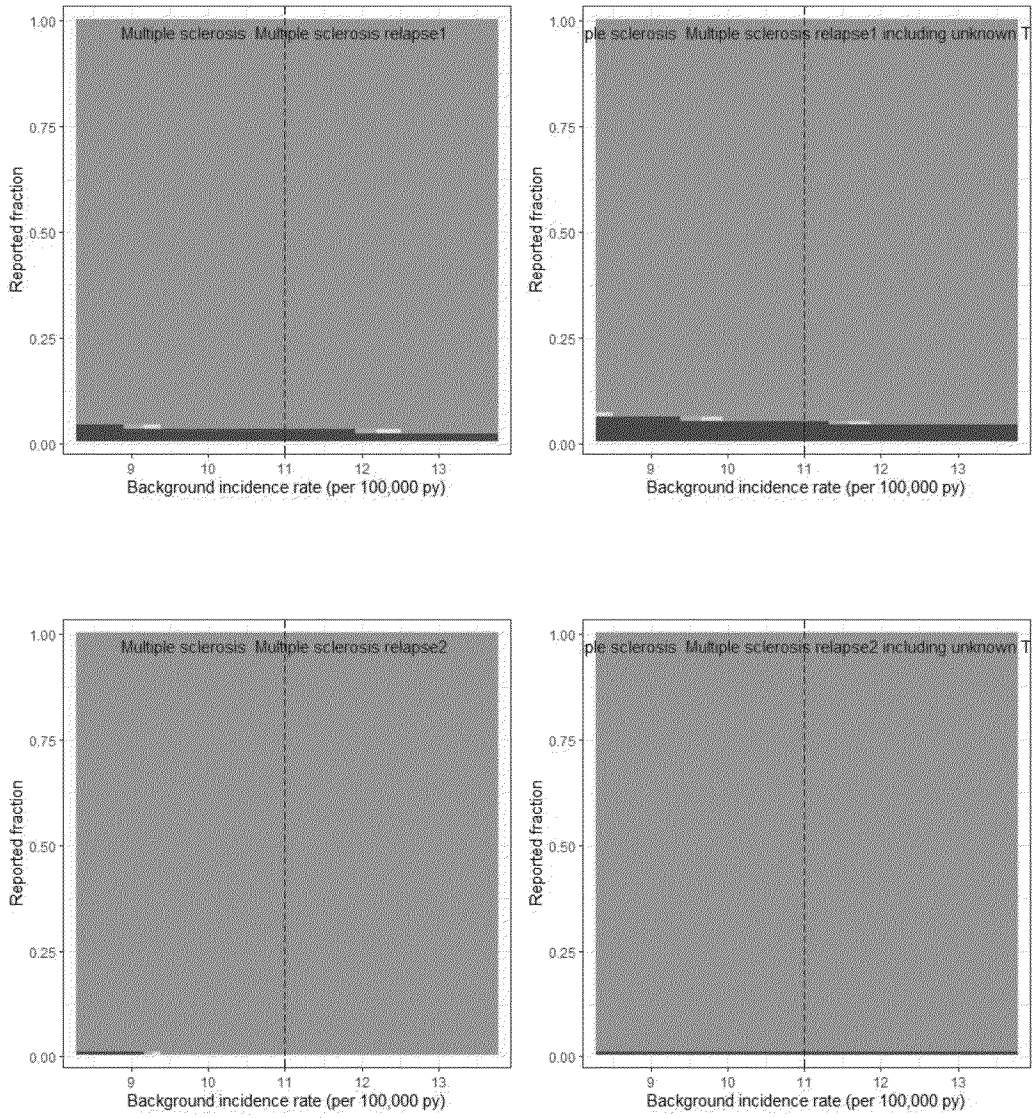
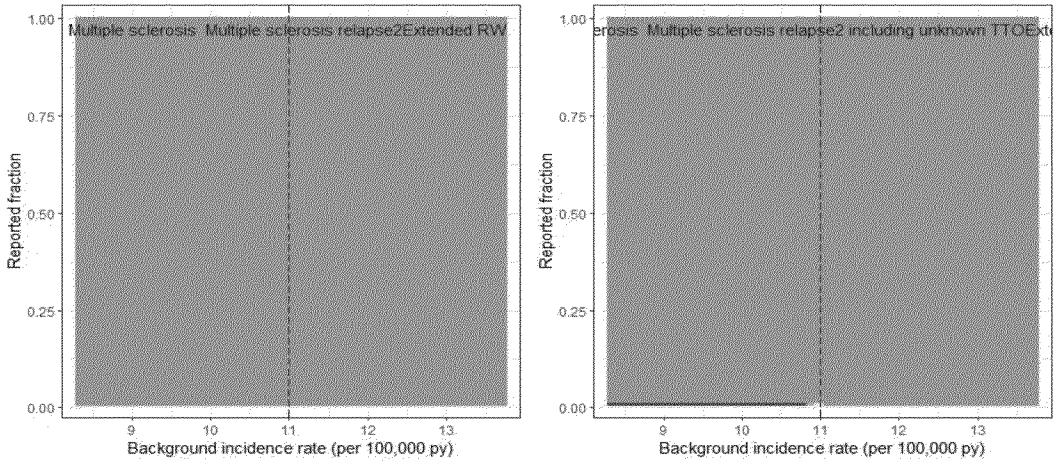

Multiple sclerosis Multiple sclerosis relapse1
ple sclerosis Multiple sclerosis relapse1 including unknown T
Multiple sclerosis Multiple sclerosis relapse2
ple sclerosis Multiple sclerosis relapse2 including unknown T
Reported fraction
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
Background incidence rate (per 100,000 py)

Table 34 Observed Versus Expected analysis for Multiple sclerosis - Multiple sclerosis relapse

Description	Observed Cases	Expected cases	Risk Window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Multiple sclerosis - Multiple sclerosis relapse	196	5895.96	42	11	466115644	0.03 (0.03 - 0.04)	Observed significantly < expected
Multiple sclerosis-Multiple sclerosis relapse (including unknown TTO)	310	5895.96	42	11	466115644	0.05 (0.05 - 0.06)	Observed significantly < expected
Multiple sclerosis - Multiple sclerosis relapse	213	25268.39	180	11	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected

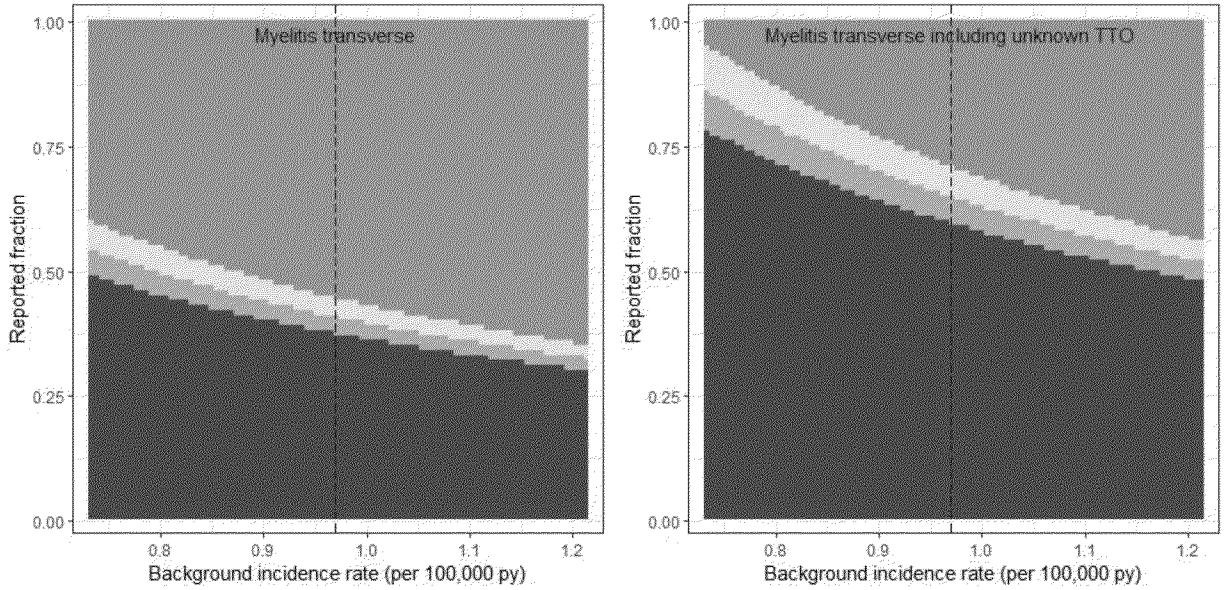


[a] Incidence Rate (IR): source: Multiple sclerosis UK guidance 2020

CI Confidence Interval; E expected; O Observed; RW Risk Window; TTO Time to onset; Unk Unknown.

Table 35 Observed Versus Expected analysis for Myelitis transverse

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Myelitis transverse	214	519.92	42	0.97	0.41 (0.36 - 0.47)	Observed significantly < expected
Myelitis transverse (including unknown TTO)	339	519.92	42	0.97	0.65 (0.58 - 0.73)	Observed significantly < expected



[a] Incidence rate (IR) Source: Willame et al 2021 [B]

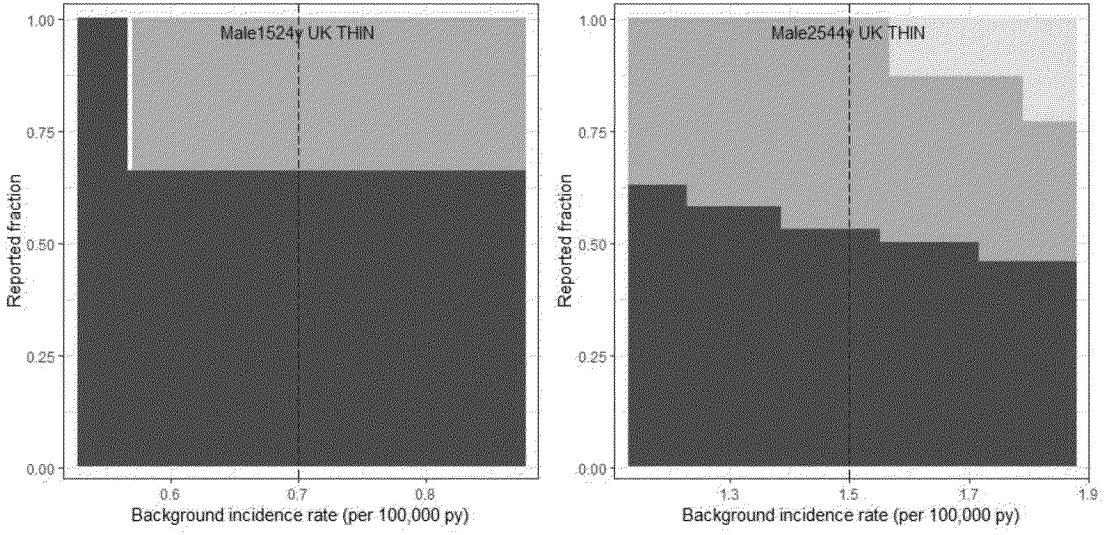
CI Confidence Interval; E expected; O Observed; TTO: Time to onset.

Table 36 Observed Versus Expected analysis for Myelitis transverse cases stratified by age and gender from UK

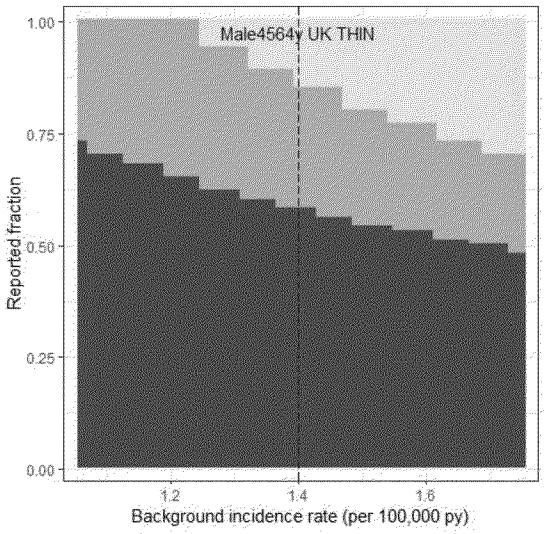
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male-15-24y UK THIN	2	0.3	42	0.7	368837	6.67 (0.81 - 24.08)	Observed > expected
Male-25-44y UK THIN	7	6.71	42	1.5	3890126	1.04 (0.42 - 2.15)	Observed > expected
Male-45-64y UK THIN	17	19.11	42	1.4	11873029	0.89 (0.52 - 1.42)	Observed < expected
Male-65y+ UK THIN	14	6.45	42	0.9	6228335	2.17 (1.19 - 3.64)	Observed significantly > expected
Male-Overall UK THIN	40	28.31	42	1.1	22377923	1.41 (1.01 - 1.92)	Observed significantly > expected
Female-15-24y UK THIN	1	0.69	42	1.2	501314	1.45 (0.04 - 8.07)	Observed > expected
Female-25-44y UK THIN	18	13.58	42	2.6	4541193	1.33 (0.79 - 2.09)	Observed > expected
Female-45-64y UK THIN	15	24	42	1.9	10983490	0.62 (0.35 - 1.03)	Observed < expected
Female-65y+ UK THIN	18	6.61	42	0.8	7188495	2.72 (1.61 - 4.3)	Observed significantly > expected
Female-Overall UK THIN	52	42.78	42	1.6	23252503	1.22 (0.91 - 1.59)	Observed > expected
15-24y UK ADV	3	0.64	42	0.64	871148	4.69 (0.97 - 13.7)	Observed > expected
25-44y UK ADV	25	13.2	42	1.36	8438999	1.89 (1.23 - 2.8)	Observed significantly > expected
45-64y UK ADV	32	32.36	42	1.23	22877522	0.99 (0.68 - 1.4)	Observed < expected
65y+ UK ADV	33	11.75	42	0.76	13443624	2.81 (1.93 - 3.94)	Observed significantly > expected
Overall UK ADV	93	54.57	42	0.97	48925906	1.7 (1.38 - 2.09)	Observed significantly > expected
Male-15-24y UK THIN (Including unk TTO)	2	0.3	42	0.7	368837	6.67 (0.81 - 24.08)	Observed > expected

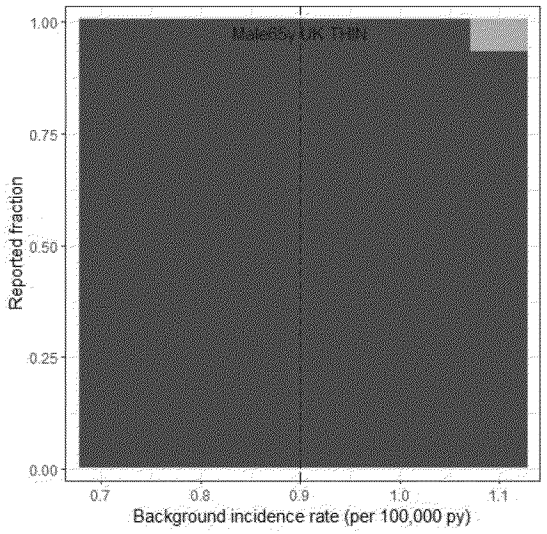
Table 36 Observed Versus Expected analysis for Myelitis transverse cases stratified by age and gender from UK

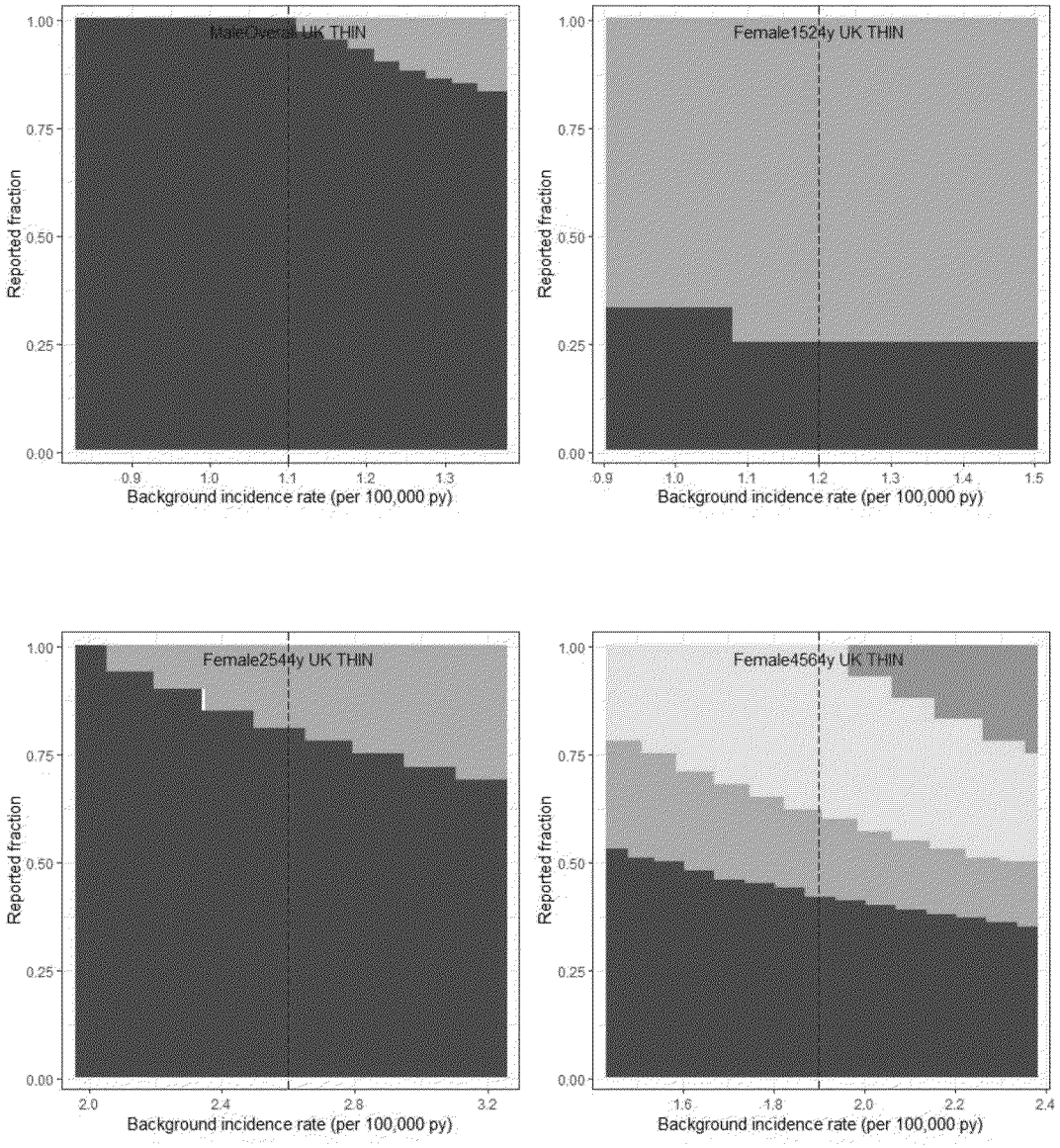
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male-25-44y UK THIN (Including unk TTO)	8	6.71	42	1.5	3890126	1.19 (0.51 - 2.35)	Observed > expected
Male-45-64y UK THIN (Including unk TTO)	30	19.11	42	1.4	11873029	1.57 (1.06 - 2.24)	Observed significantly > expected
Male-65y+ UK THIN (Including unk TTO)	25	6.45	42	0.9	6228335	3.88 (2.51 - 5.72)	Observed significantly > expected
Male-Overall UK THIN (Including unk TTO)	65	28.31	42	1.1	22377923	2.3 (1.77 - 2.93)	Observed significantly > expected
Female-15-24y UK THIN (Including unk TTO)	2	0.69	42	1.2	501314	2.9 (0.35 - 10.47)	Observed > expected
Female-25-44y UK THIN (Including unk TTO)	27	13.58	42	2.6	4541193	1.99 (1.31 - 2.89)	Observed significantly > expected
Female-45-64y UK THIN (Including unk TTO)	25	24	42	1.9	10983490	1.04 (0.67 - 1.54)	Observed > expected
Female-65y+ UK THIN (Including unk TTO)	26	6.61	42	0.8	7188495	3.93 (2.57 - 5.76)	Observed significantly > expected
Female-Overall UK THIN (Including unk TTO)	80	42.78	42	1.6	23252503	1.87 (1.48 - 2.33)	Observed significantly > expected

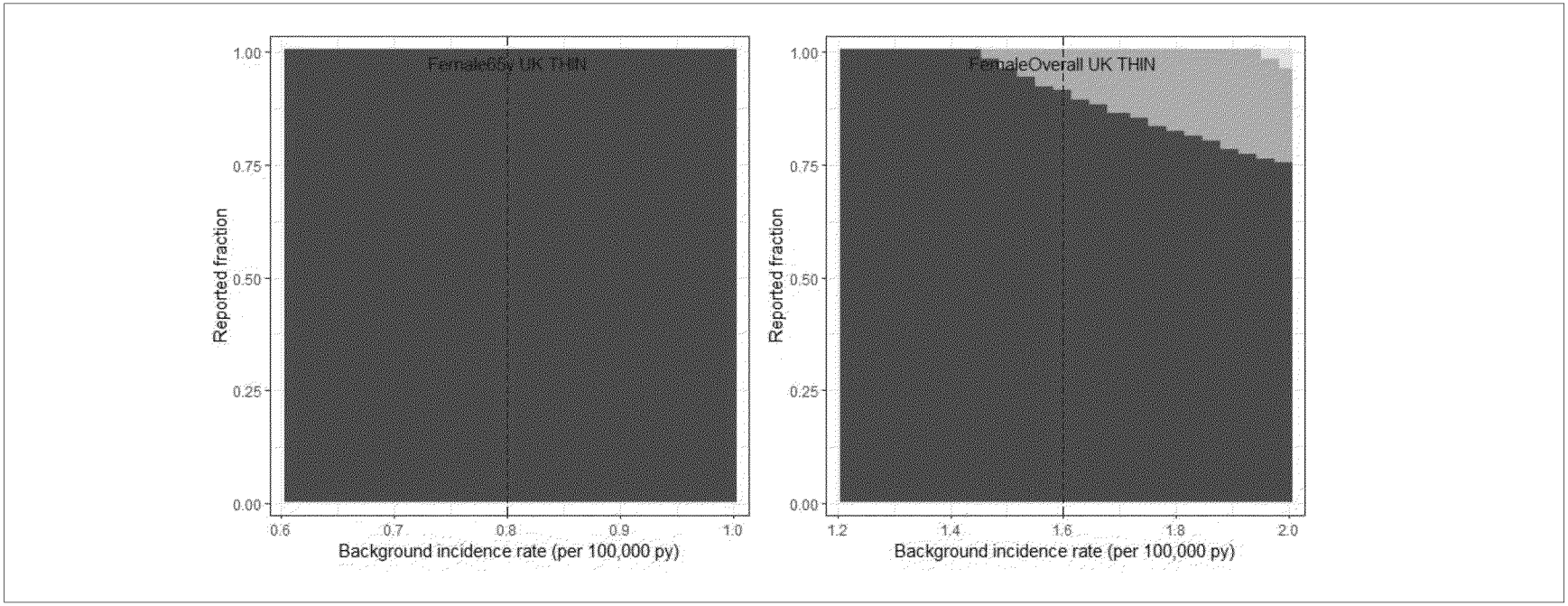

Male1524y UK THIN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)

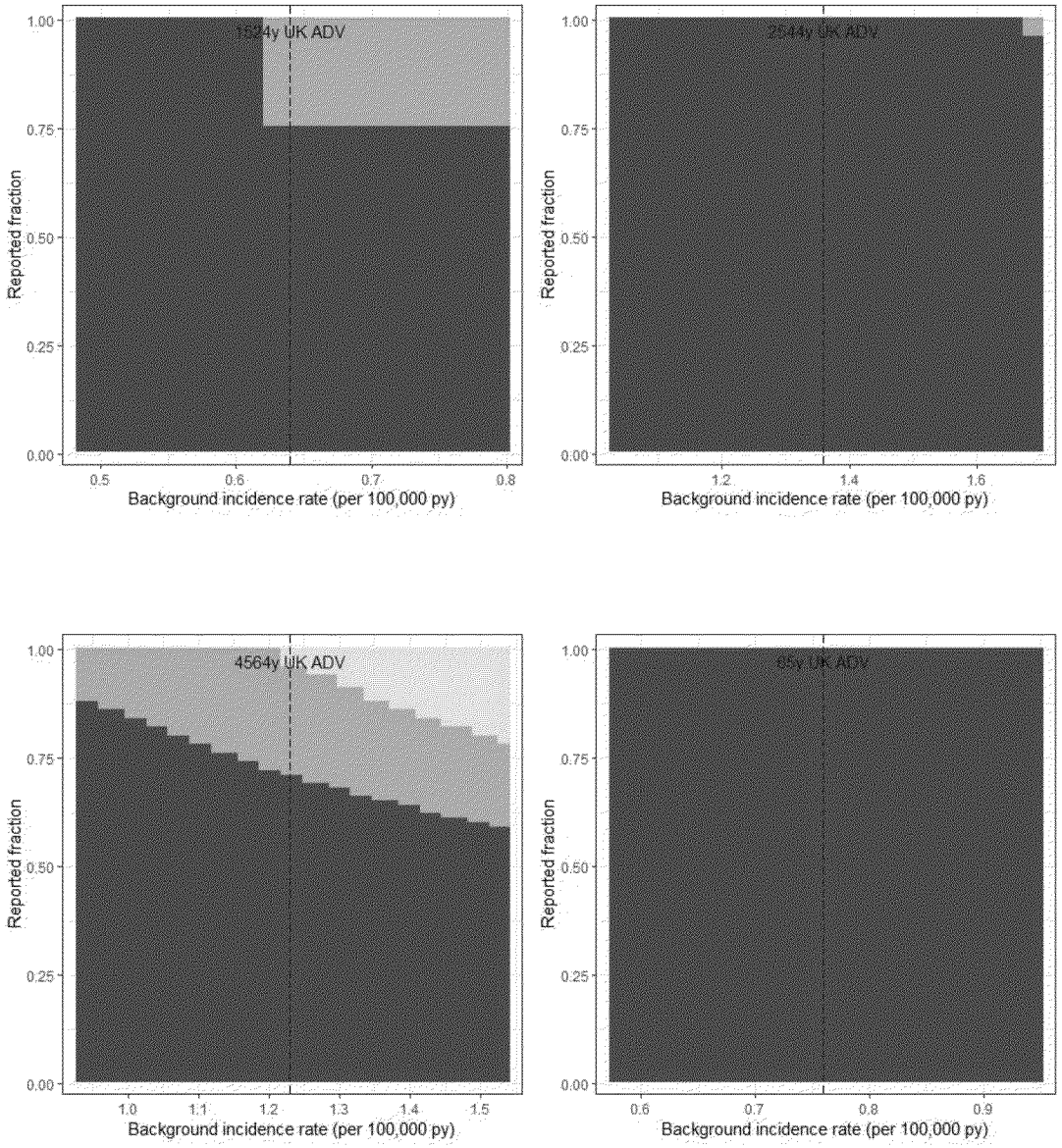
Male2544y UK THIN
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.3
1.5
1.7
1.9
Background incidence rate (per 100,000 py)

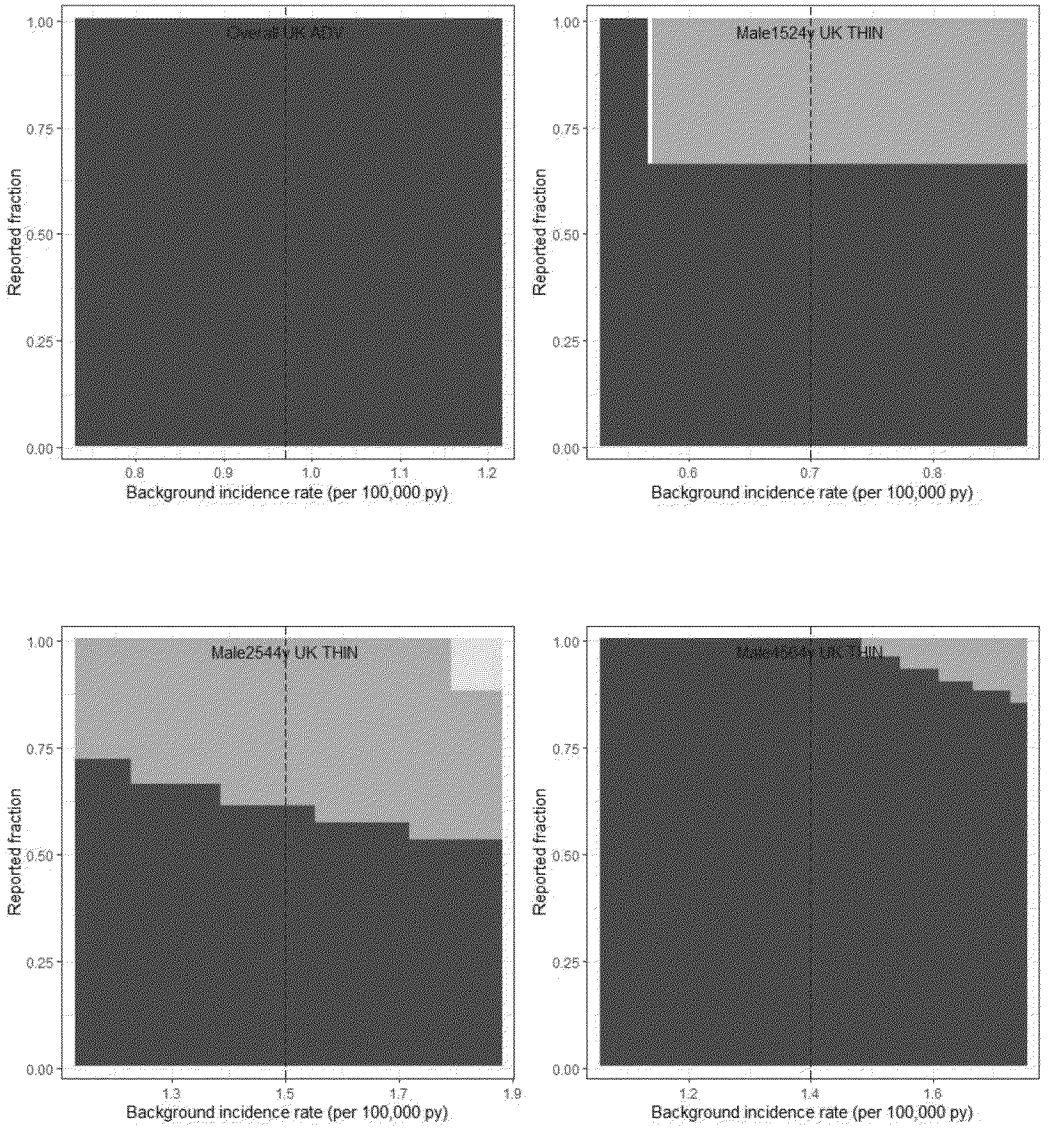

Male4564y UK THIN
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
Background incidence rate (per 100,000 py)


Male65y UK THIN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)


Male≥65y UK THIN
Female1524y UK THIN
Female2544y UK THIN
Female4564y UK THIN
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.9
1.0
1.1
1.2
1.3
1.4
1.5
2.0
2.4
2.8
3.2
1.6
1.8
2.2
2.4


Female65y UK THIN
FemaleOverall UK THIN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
1.0
1.2
1.4
1.6
1.8
2.0
Background incidence rate (per 100,000 py)


1824y UK ADV
2544y UK ADV
4564y UK ADV
65y UK ADV
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.5
0.6
0.7
0.8
1.2
1.4
1.6
1.0
1.1
1.2
1.3
1.4
1.5
0.6
0.7
0.8
0.9


Overall UK ADV
Male1524y UK THIN
Male2544y UK THIN
Male4564y UK THIN
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.8
0.9
1.0
1.1
1.2
0.6
0.7
1.3
1.5
1.7
1.9
1.4
1.6

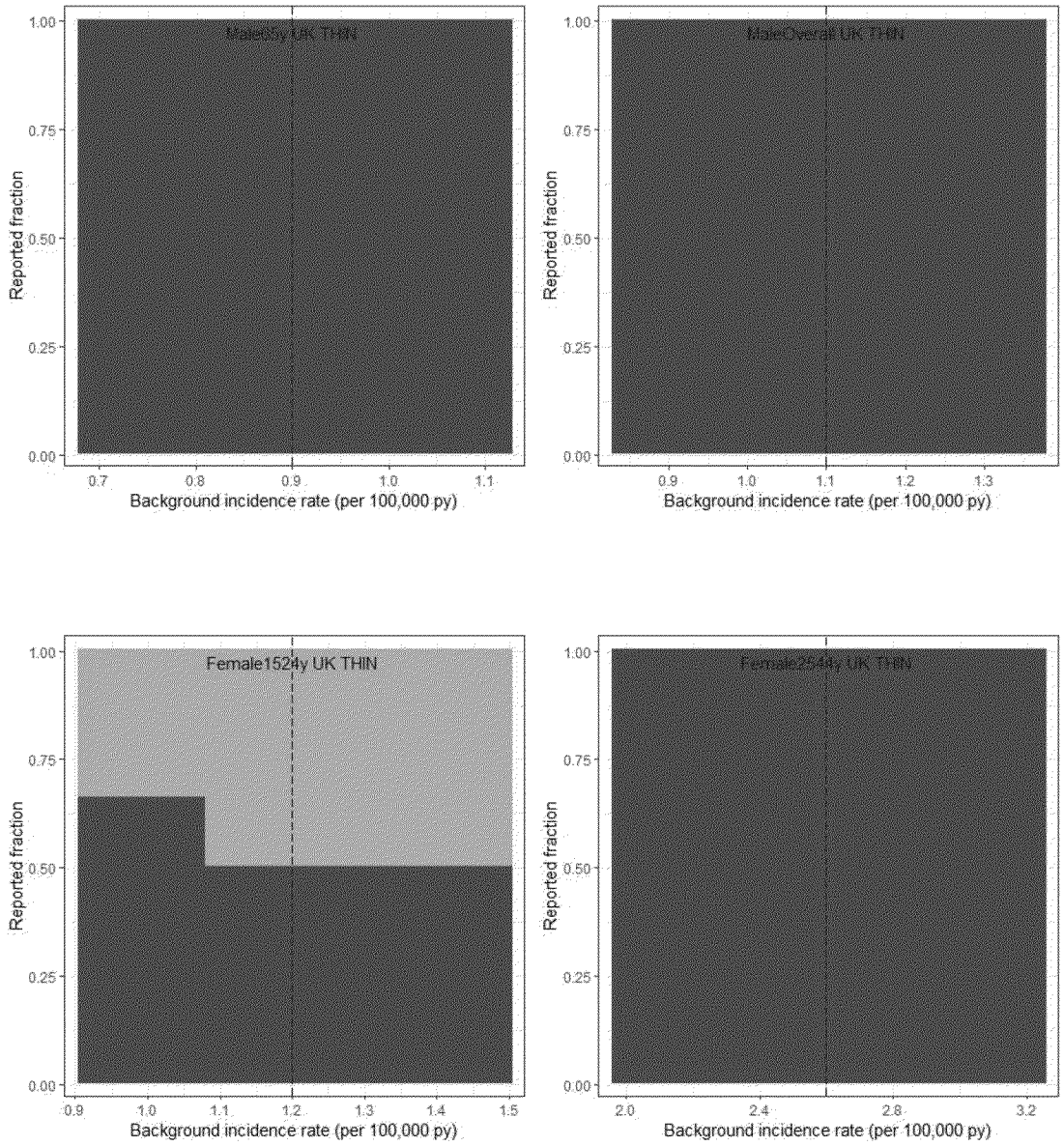
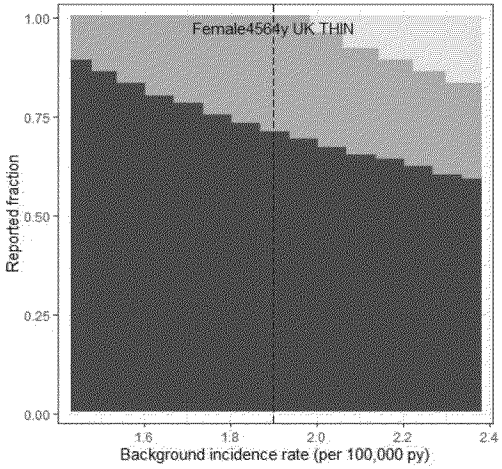
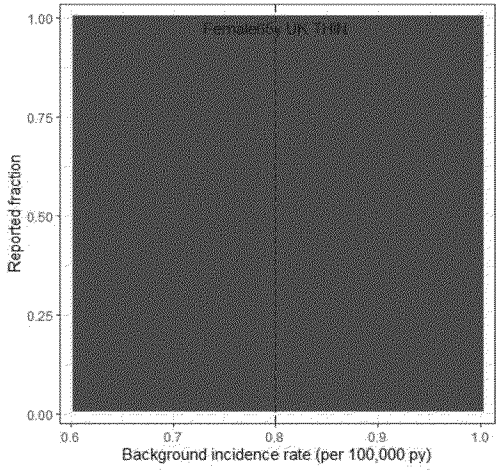
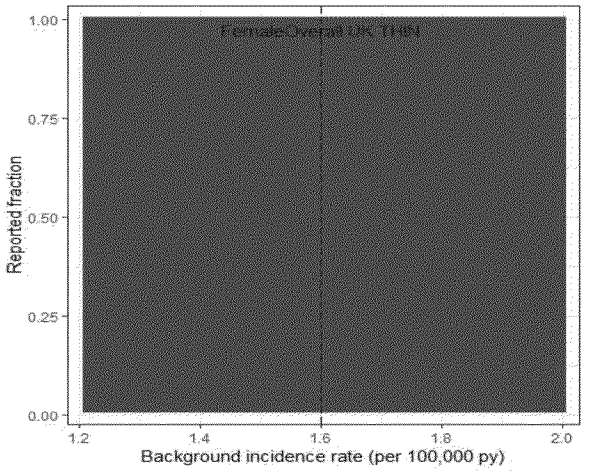

Male65y UK THIN
MaleOverall UK THIN
Female1524y UK THIN
Female2544y UK THIN
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
2.0
2.4
2.8
3.2

Table 36 Observed Versus Expected analysis for Myelitis transverse cases stratified by age and gender from UK

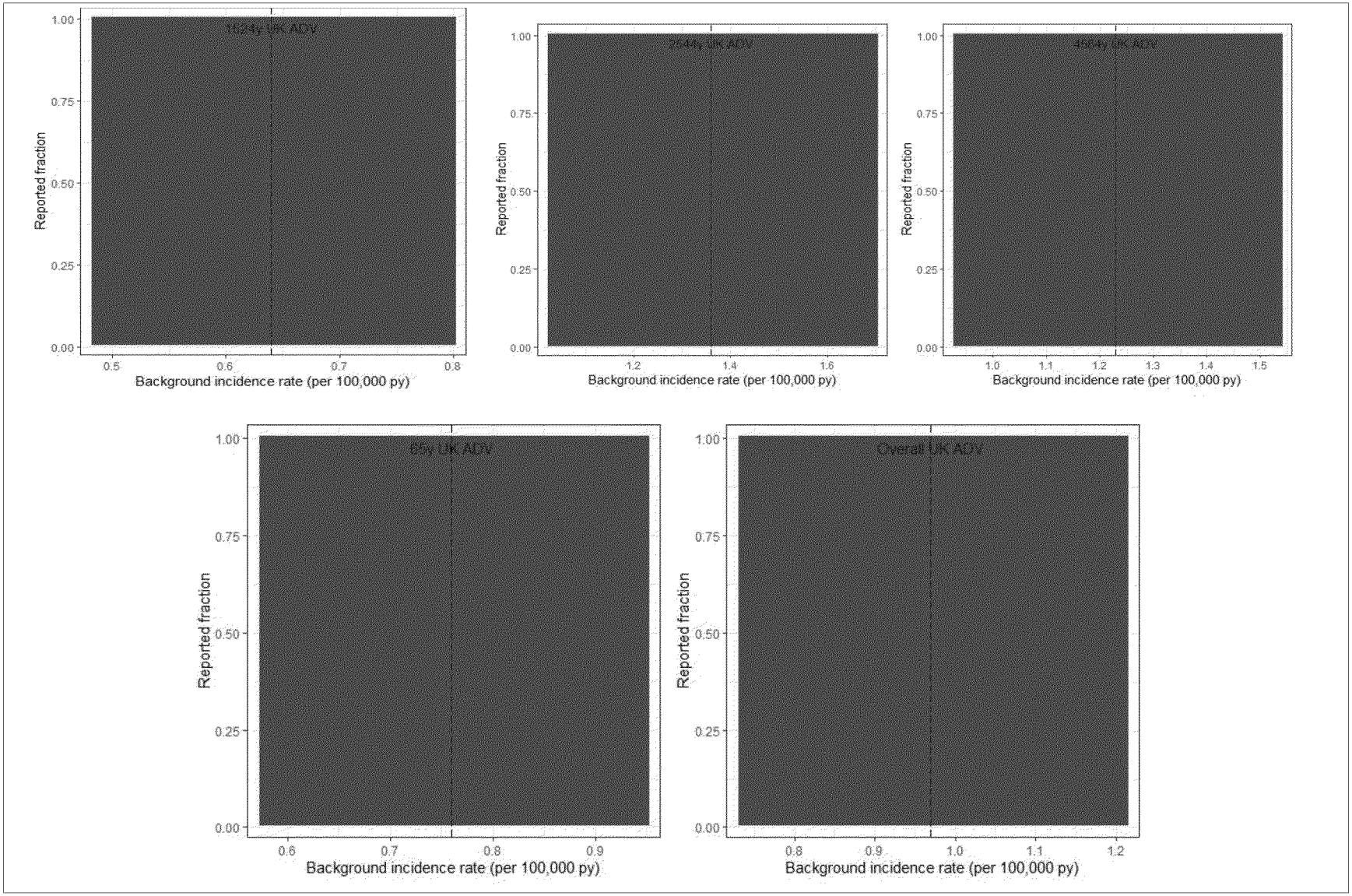
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							
							
							

[b] Incidence rate (IR) Source: Willame et al 2021 [B]

CI Confidence Interval; E expected; O Observed; THIN The Health Improvement Network, TTO: Time to onset, UK United Kingdom, Unk Unknown

Table 37 Observed Versus Expected analysis for Myelitis transverse cases stratified by age from UK including unknown TTO

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
15-24 UK ADV (Including unk TTO)	4	0.64	42	0.64	871148	6.25 (1.7 - 16)	Observed significantly > expected
25-44 UK ADV (Including unk TTO)	36	13.2	42	1.36	8438999	2.73 (1.91 - 3.78)	Observed significantly > expected
45-64 UK ADV (Including unk TTO)	55	32.36	42	1.23	22877522	1.7 (1.28 - 2.21)	Observed significantly > expected
65 UK ADV (Including unk TTO)	53	11.75	42	0.76	13443624	4.51 (3.38 - 5.9)	Observed significantly > expected
Overall UK ADV (Including unk TTO)	148	54.57	42	0.97	48925906	2.71 (2.29 - 3.19)	Observed significantly > expected
Willame et al 2021 [B], **ADVANCE EUROPE rates - stratified by Dose 1 vs Dose 2 - EU/UK/Australia/Canada/Argentina/Malaysia/New Zealand/Colombia/Taiwan/Brazil/Thailand**							
Dose 1	101	195.25	42	0.97	175045647	0.52 (0.42 - 0.63)	Observed significantly < expected
Dose 1 - incl cases with Unk TTO	142	195.25	42	0.97	175045647	0.73 (0.61 - 0.86)	Observed significantly < expected
Dose 2	23	188.89	42	0.97	169346503	0.12 (0.08 - 0.18)	Observed significantly < expected
Dose 2 - incl cases with unk TTO	33	188.89	42	0.97	169346503	0.17 (0.12 - 0.25)	Observed significantly < expected
Overall (Global)	218	519.92	42	0.97	466115644	0.42 (0.37 - 0.48)	Observed significantly < expected
Overall (Global) (Including unk TTO)	339	519.92	42	0.97	466115644	0.65 (0.58 - 0.73)	Observed significantly < expected


1524y UK ADV
2544y UK ADV
4564y UK ADV
65y UK ADV
Overall UK ADV
Reported fraction
Background incidence rate (per 100,000 py)

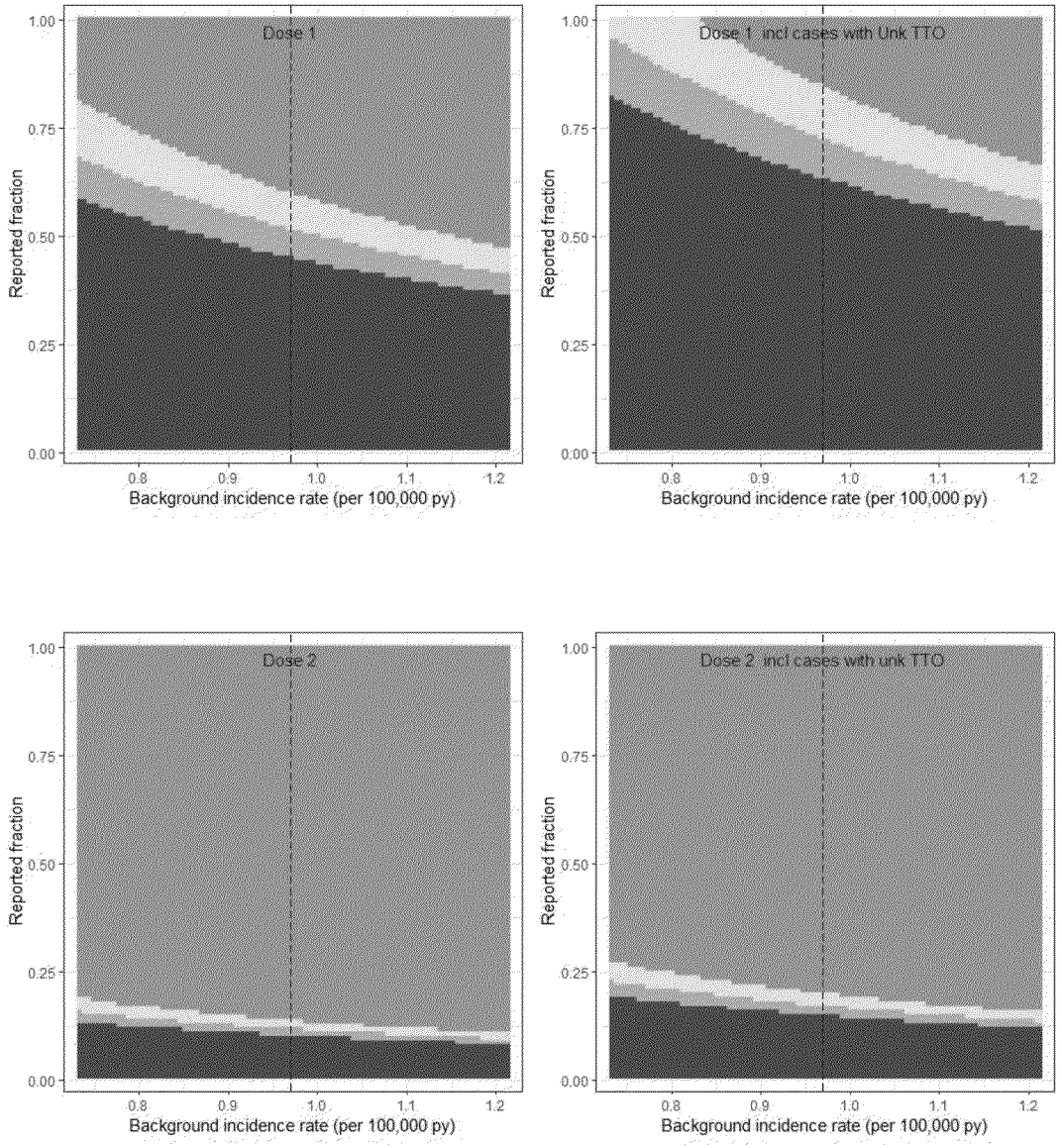
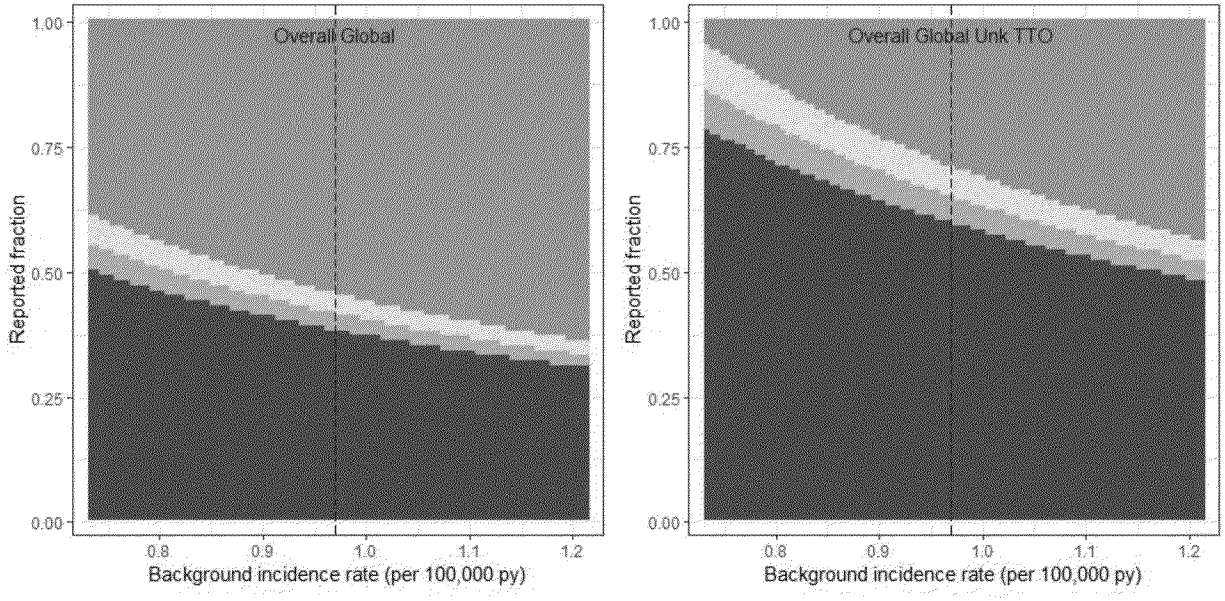

Dose 1
Dose 1 incl cases with Unk TTO
Dose 2
Dose 2 incl cases with unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.8
0.9
1.0
1.1
1.2
Background incidence rate (per 100,000 py)

Table 37 Observed Versus Expected analysis for Myelitis transverse cases stratified by age from UK including unknown TTO

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) Source: Willame et al 2021 [B]

ADV Advance, CI Confidence Interval; E expected; EEA European Economic Area; O Observed; TTO: Time to onset, UK United Kingdom, Unk Unknown

Table 38 Observed Versus Expected analysis for Myelitis transverse cases stratified by dose age and gender from UK

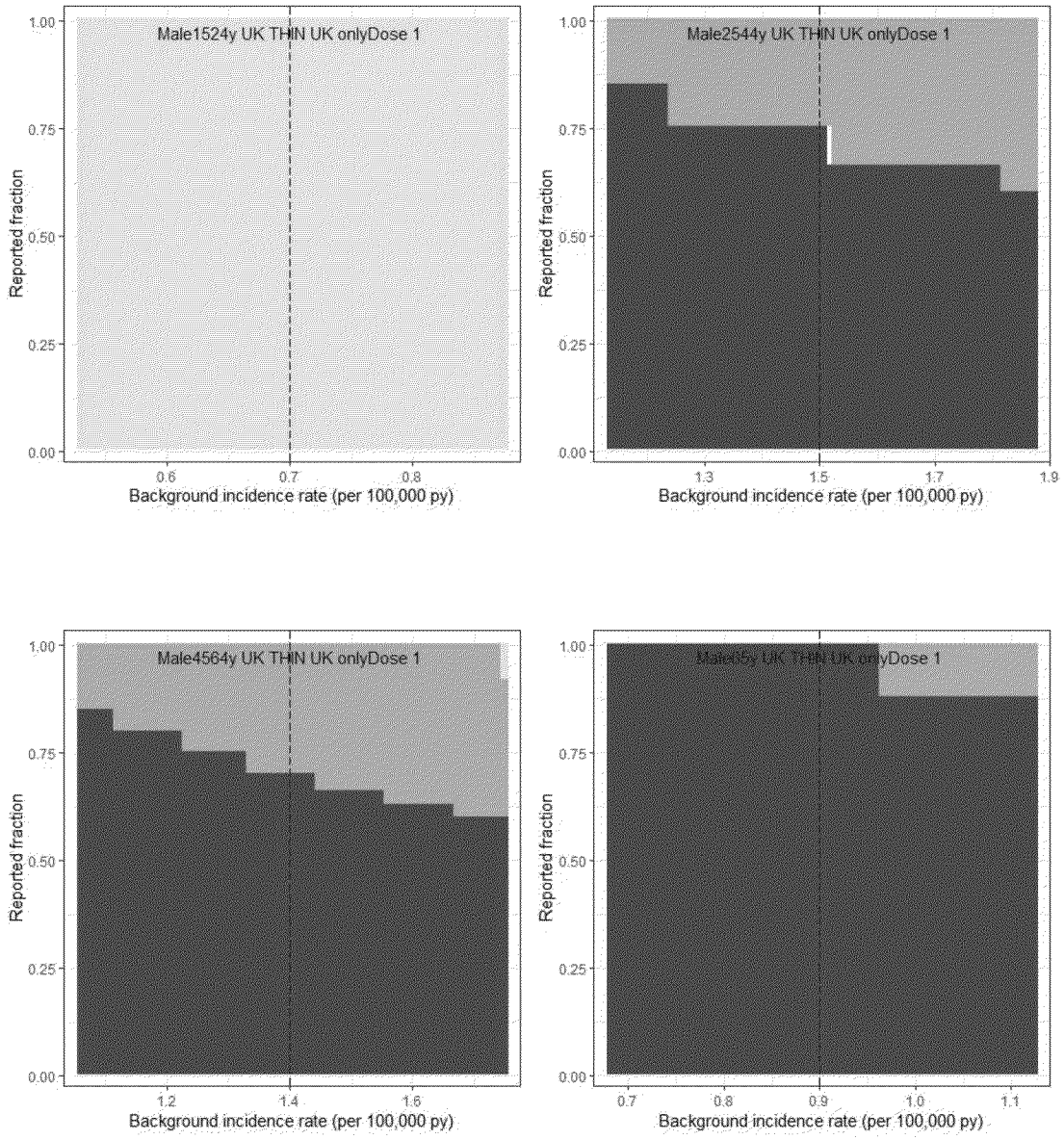
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 15-24 UK THIN Dose 1	0	0.15	42	0.7	188508	0 (0 - 24.59)	Observed < expected
Male 25 to 44 UK THIN Dose 1	6	3.42	42	1.5	1980408	1.75 (0.64 - 3.82)	Observed > expected
Male 45 to 64y UK THIN Dose 1	12	9.64	42	1.4	5990807	1.24 (0.64 - 2.17)	Observed > expected
Male 65 plus UK THIN Dose 1	8	3.24	42	0.9	3126893	2.47 (1.07 - 4.87)	Observed significantly > expected
Male Overall UK THIN Dose 1	26	14.28	42	1.1	11286808	1.82 (1.19 - 2.67)	Observed significantly > expected
Female 15 to 24 UK THIN Dose 1	1	0.35	42	1.2	255760	2.86 (0.07 - 15.92)	Observed > expected
Female 25 to 44 UK THIN Dose 1	12	6.91	42	2.6	2310305	1.74 (0.9 - 3.03)	Observed > expected
Female 45 to 64 UK THIN Dose 1	9	12.1	42	1.9	5537396	0.74 (0.34 - 1.41)	Observed < expected
Female 65 plus UK THIN Dose 1	10	3.32	42	0.8	3610734	3.01 (1.44 - 5.54)	Observed significantly > expected
Female Overall UK THIN Dose 1	32	21.55	42	1.6	11714377	1.48 (1.02 - 2.1)	Observed significantly > expected
Male 15 to 24 UK THIN Dose 2	0	0.15	42	0.7	180329	0 (0 - 24.59)	Observed < expected

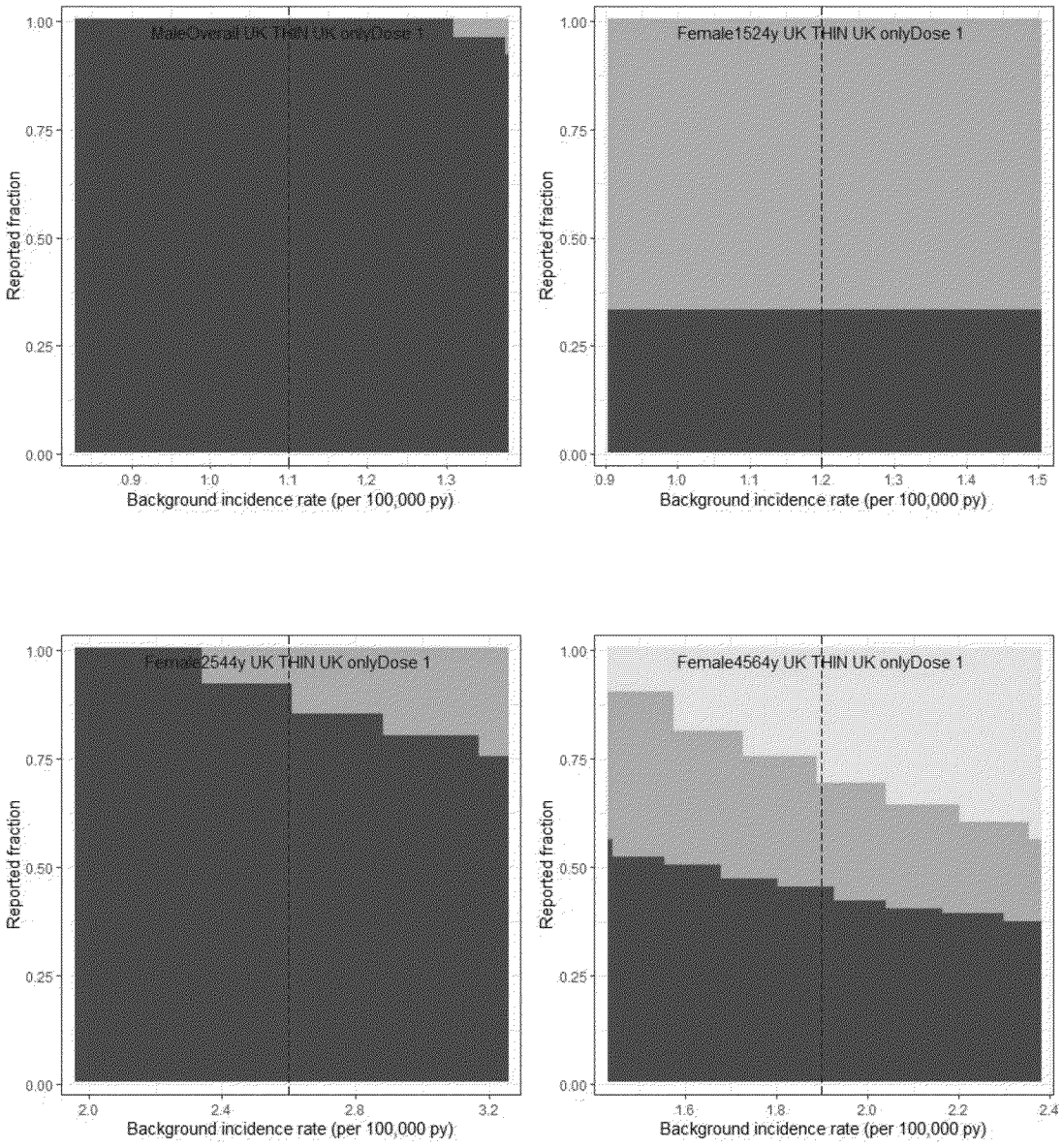
Table 38 Observed Versus Expected analysis for Myelitis transverse cases stratified by dose age and gender from UK

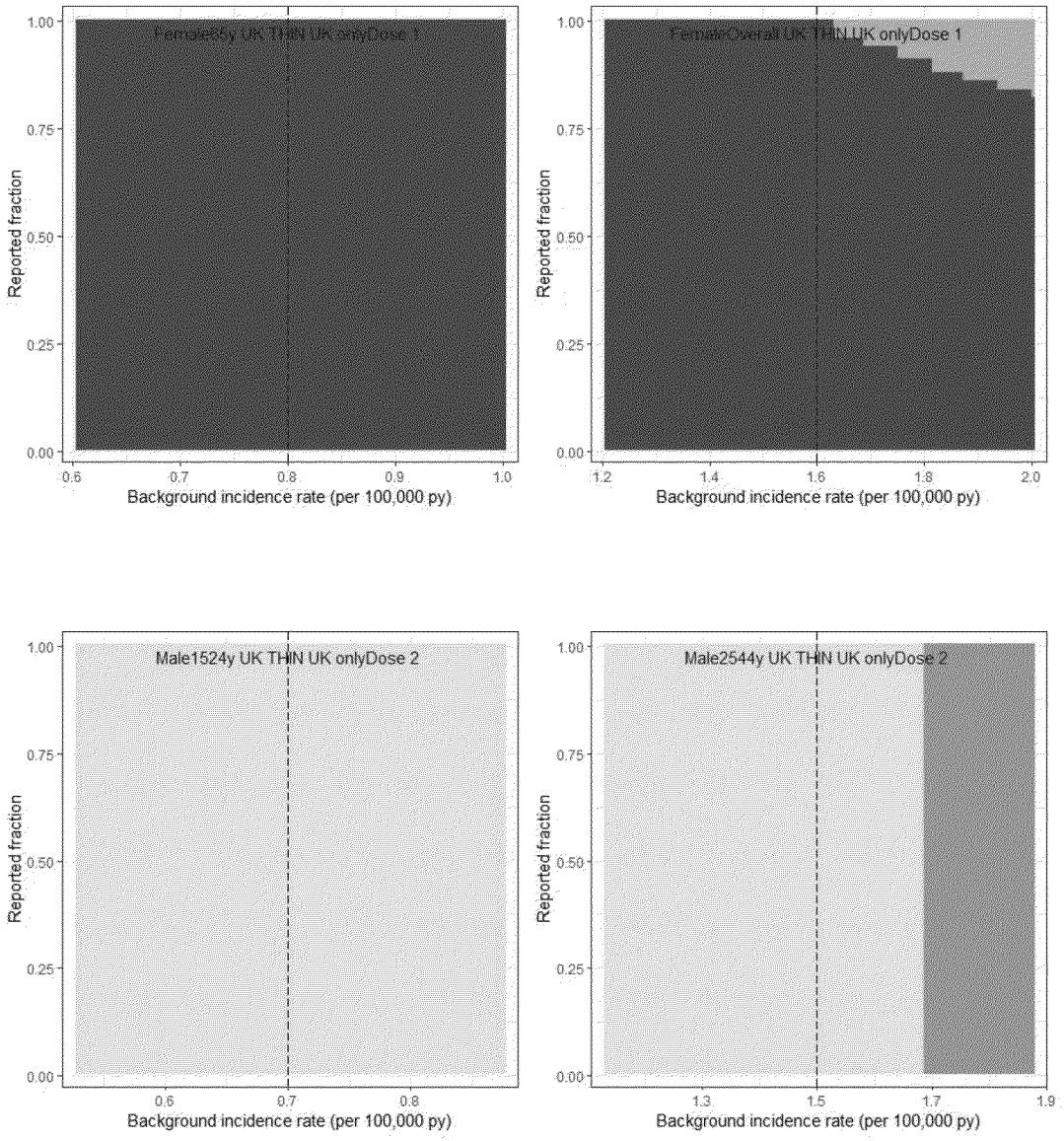
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 25 to 44 UK THIN Dose 2	0	3.29	42	1.5	1909718	0 (0 - 1.12)	Observed < expected
Male 45 to 64 UK THIN Dose 2	4	9.47	42	1.4	5882222	0.42 (0.12 - 1.08)	Observed < expected
Male 65 plus UK THIN Dose 2	3	3.21	42	0.9	3101442	0.93 (0.19 - 2.73)	Observed < expected
Male Overall UK THIN Dose 2	7	14.01	42	1.1	11073845	0.5 (0.2 - 1.03)	Observed < expected
Female 15 to 24 UK THIN Dose 2	0	0.34	42	1.2	245554	0 (0 - 10.85)	Observed < expected
Female 25 to 44 UK THIN Dose 2	2	6.67	42	2.6	2230888	0.3 (0.04 - 1.08)	Observed < expected
Female 45 to 64 UK THIN Dose 2	3	11.9	42	1.9	5446094	0.25 (0.05 - 0.74)	Observed significantly < expected
Female 65 plus UK THIN Dose 2	1	3.29	42	0.8	3577761	0.3 (0.01 - 1.69)	Observed < expected
Female Overall UK THIN Dose 2	6	21.16	42	1.6	11500418	0.28 (0.1 - 0.62)	Observed significantly < expected
15 to 24 UK ADV Dose 1	1	0.33	42	0.64	444378	3.03 (0.08 - 16.88)	Observed > expected
25 to 44y UK ADV Dose 1	18	6.71	42	1.36	4291068	2.68 (1.59 - 4.24)	Observed significantly > expected

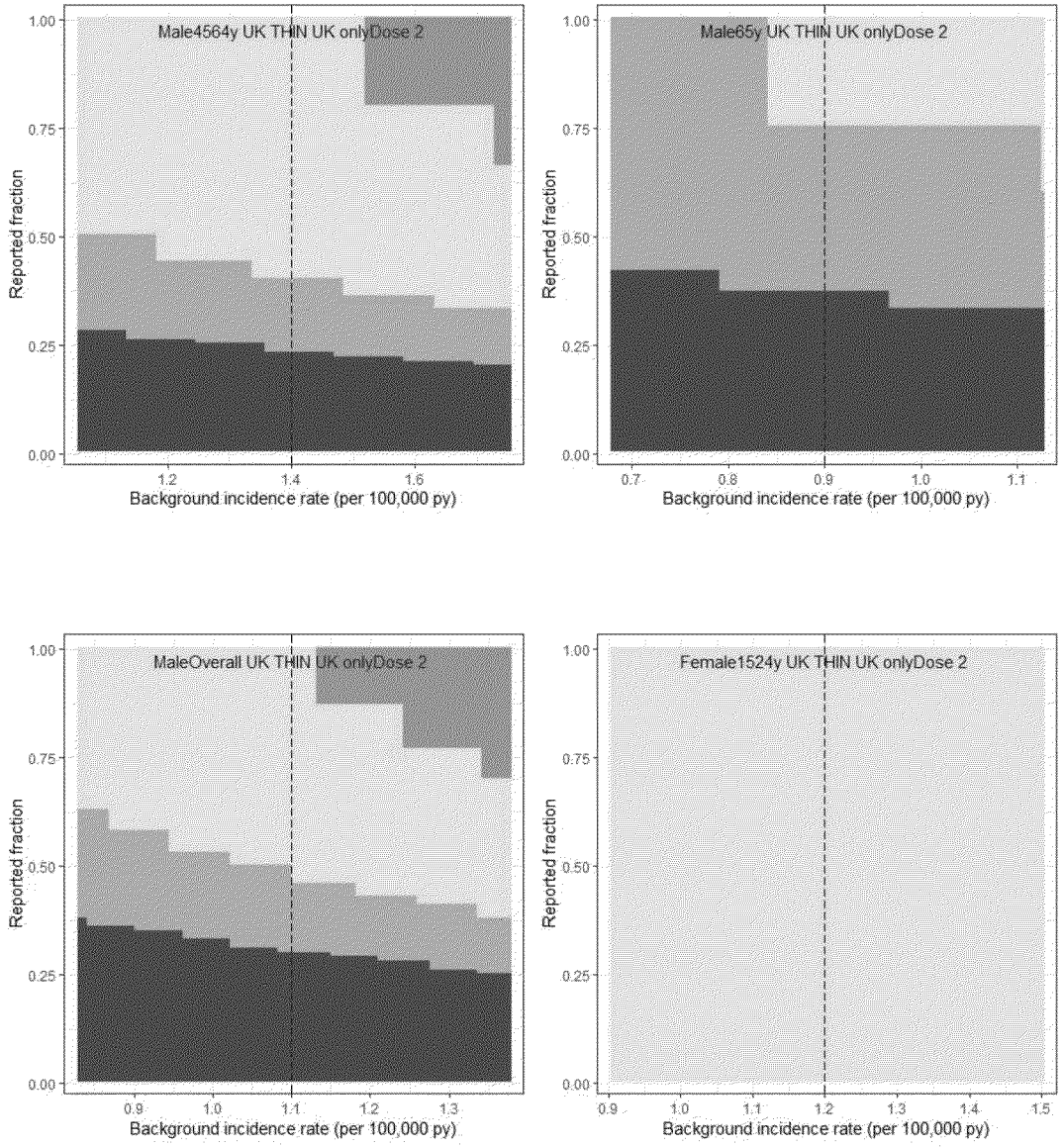
Table 38 Observed Versus Expected analysis for Myelitis transverse cases stratified by dose age and gender from UK

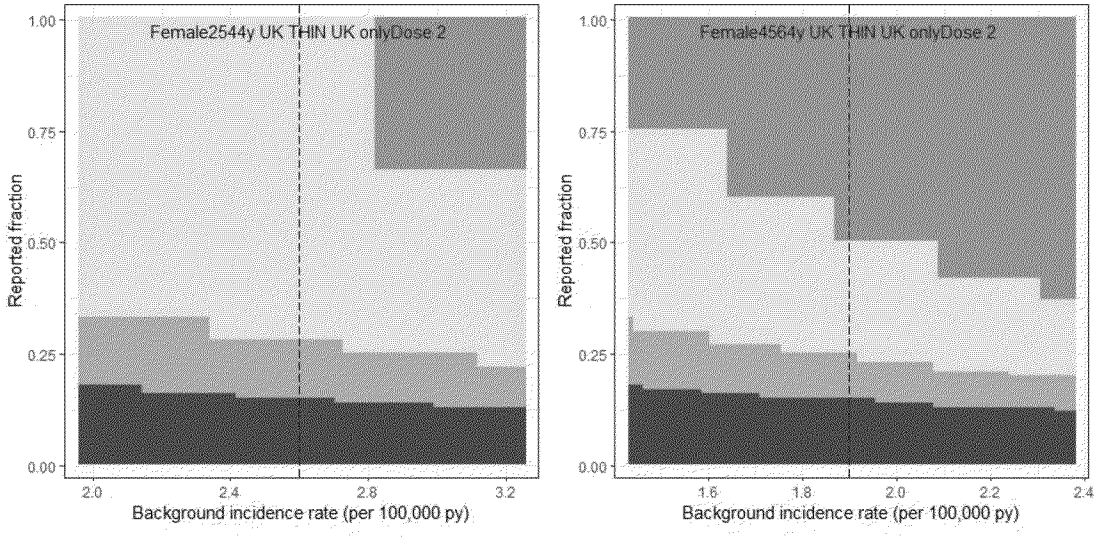
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
45 to 64 UK ADV Dose 1	21	16.31	42	1.23	11528448	1.29 (0.8 - 1.97)	Observed > expected
65y plus UK ADV Dose 1	19	2.73	42	0.76	3126893	6.96 (4.19 - 10.87)	Observed significantly > expected
Overall UK ADV Dose 1	59	27.58	42	0.97	24725401	2.14 (1.63 - 2.76)	Observed significantly > expected
15 to 24 UK ADV Dose 2	0	0.31	42	0.64	425986	0 (0 - 11.9)	Observed < expected
25 to 44 UK ADV Dose 2	2	6.48	42	1.36	4140925	0.31 (0.04 - 1.11)	Observed < expected
45 to 64 UK ADV Dose 2	7	16.02	42	1.23	11328542	0.44 (0.18 - 0.9)	Observed significantly < expected
65 plus UK ADV Dose 2	4	5.84	42	0.76	6679268	0.68 (0.19 - 1.75)	Observed < expected
Overall UK ADV Dose 2	13	26.93	42	0.97	24141350	0.48 (0.26 - 0.83)	Observed significantly < expected


Male1524y UK THIN UK onlyDose 1
Male2544y UK THIN UK onlyDose 1
Male4564y UK THIN UK onlyDose 1
Male65y UK THIN UK onlyDose 1
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
1.3
1.5
1.7
1.9
1.2
1.4
1.6
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)

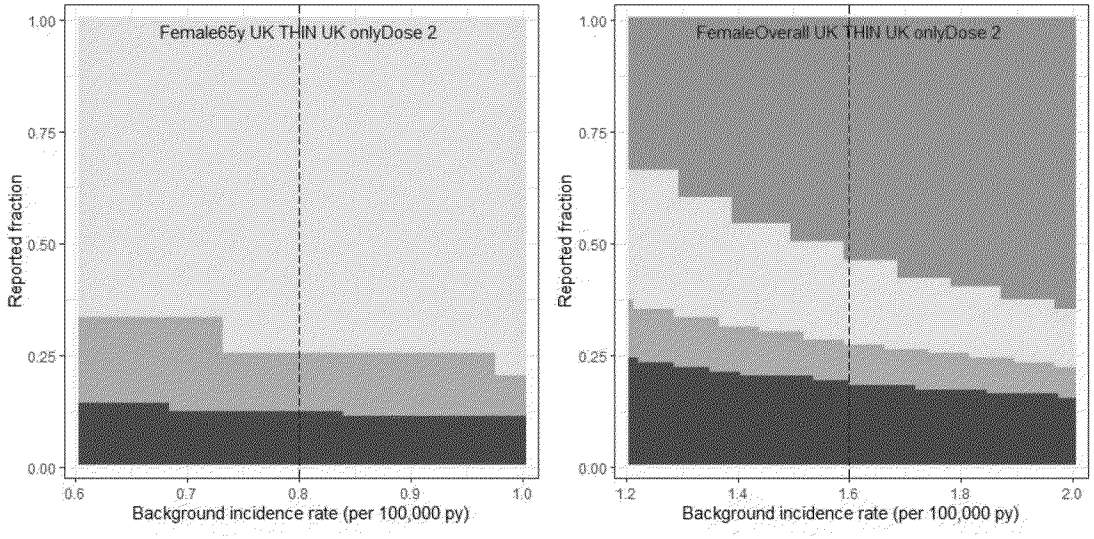

MaleOverall UK THIN UK onlyDose 1
Female1524y UK THIN UK onlyDose 1
Female2544y UK THIN UK onlyDose 1
Female4564y UK THIN UK onlyDose 1
Reported fraction
Background incidence rate (per 100,000 py)


Female65y UK THIN UK onlyDose 1
FemaleOverall UK THIN UK onlyDose 1
Male1524y UK THIN UK onlyDose 2
Male2544y UK THIN UK onlyDose 2
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.6
0.7
0.8
0.9
1.0
1.2
1.4
1.6
1.8
2.0
1.3
1.5
1.7
1.9

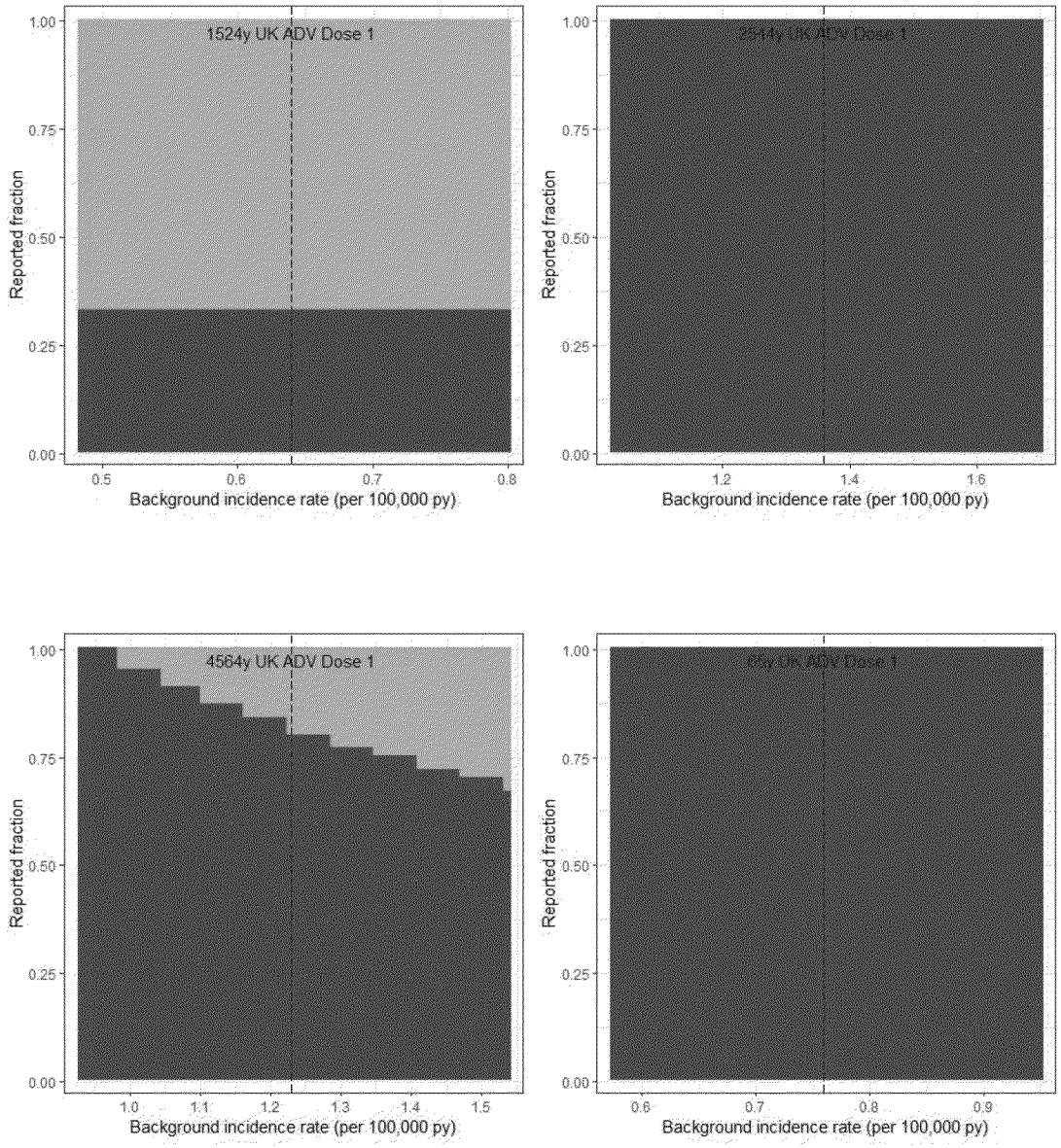

Male4564y UK THIN UK onlyDose 2
Male65y UK THIN UK onlyDose 2
MaleOverall UK THIN UK onlyDose 2
Female1524y UK THIN UK onlyDose 2
Reported fraction
Background incidence rate (per 100,000 py)


Female2544y UK THIN UK onlyDose 2
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.4
2.8
3.2
Background incidence rate (per 100,000 py)

Female4564y UK THIN UK onlyDose 2
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.6
1.8
2.0
2.2
2.4
Background incidence rate (per 100,000 py)


Female65y UK THIN UK onlyDose 2
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)

FemaleOverall UK THIN UK onlyDose 2
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
1.8
2.0
Background incidence rate (per 100,000 py)


1524y UK ADV Dose 1
2544y UK ADV Dose 1
4564y UK ADV Dose 1
65y UK ADV Dose 1
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.5
0.6
0.7
0.8
1.2
1.4
1.6
1.0
1.1
1.2
1.3
1.4
1.5
0.6
0.7
0.8
0.9

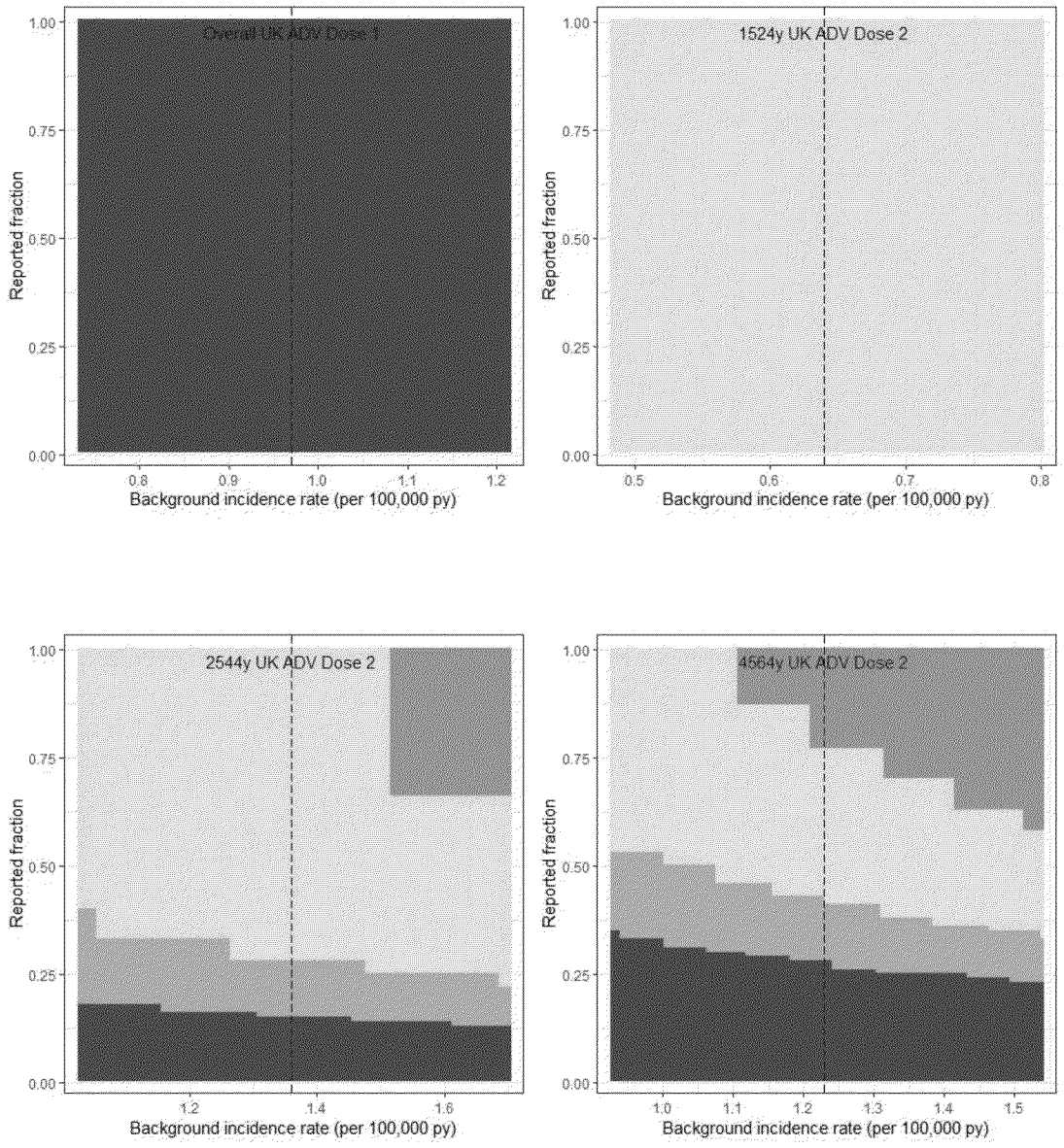
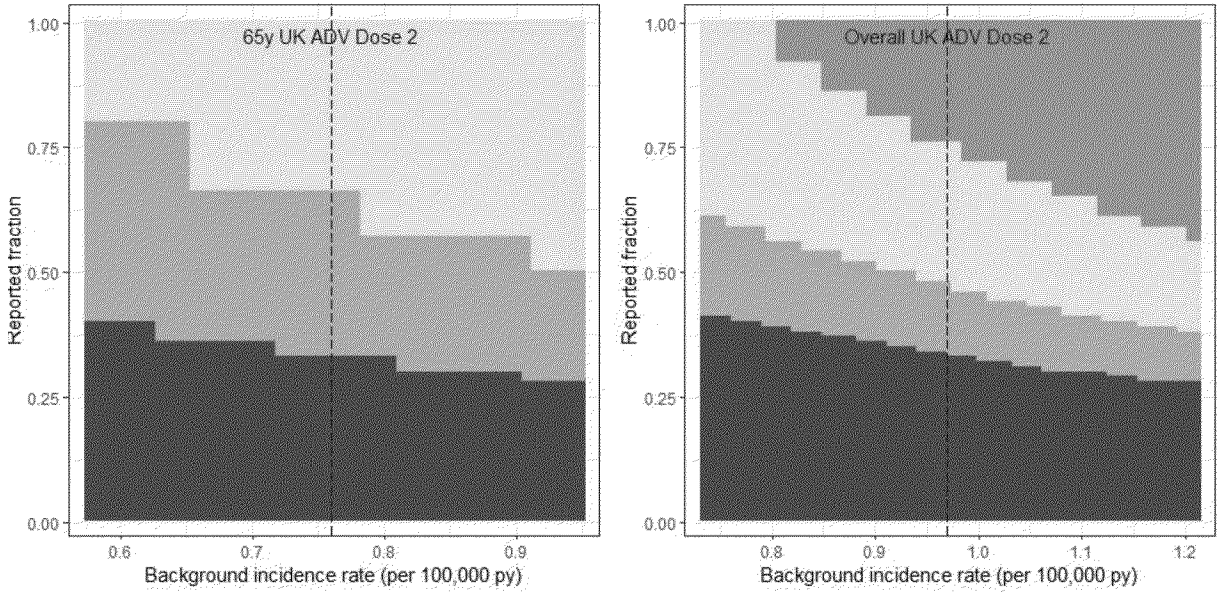

Overall UK ADV Dose 1
1524y UK ADV Dose 2
2544y UK ADV Dose 2
4564y UK ADV Dose 2
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.8
0.9
1.0
1.1
1.2
0.5
0.6
0.7
1.2
1.4
1.6
1.0
1.1
1.2
1.3
1.4
1.5

Table 38 Observed Versus Expected analysis for Myelitis transverse cases stratified by dose age and gender from UK

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) Source: Willame et al 2021 [B]

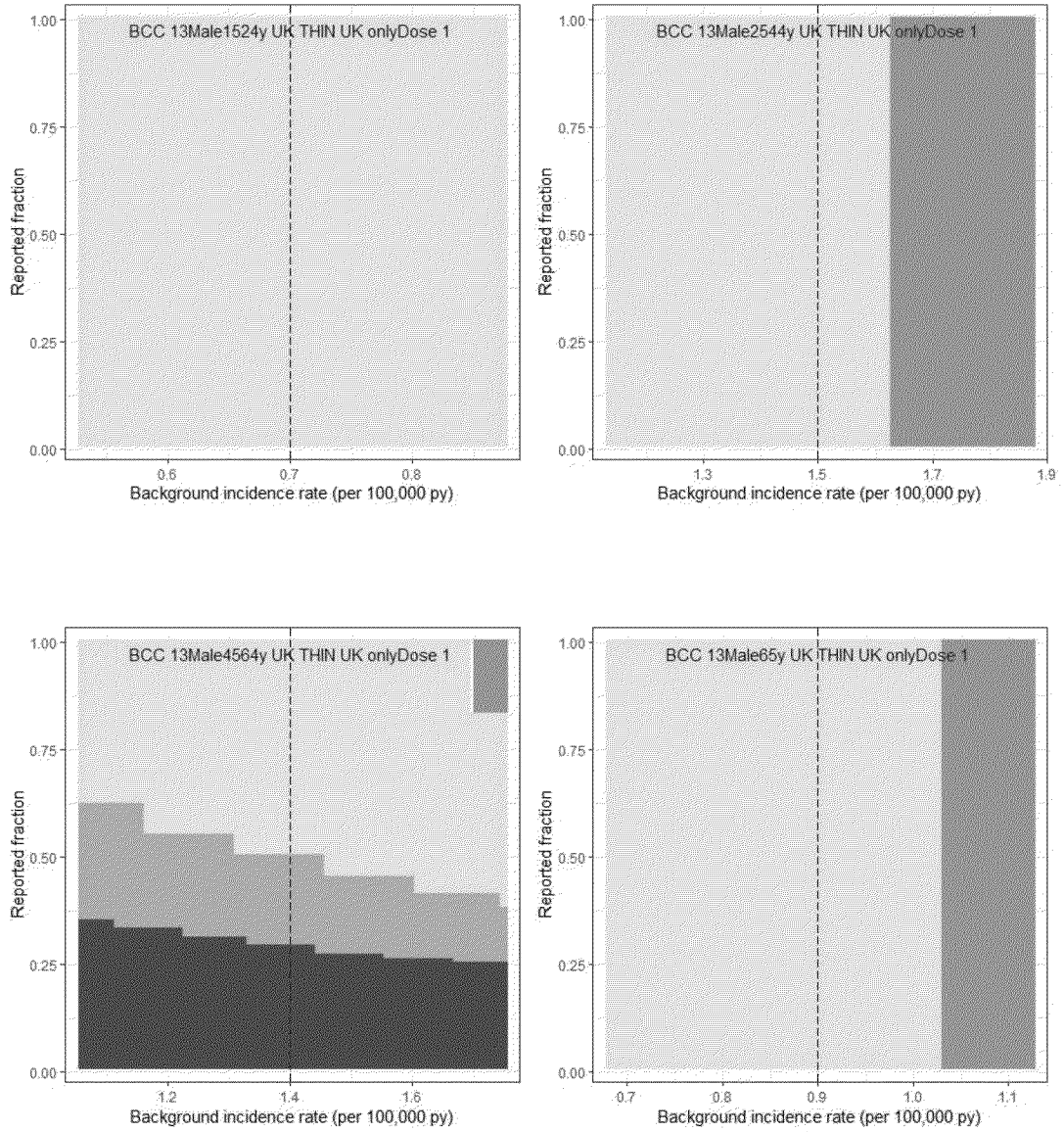
ADV Advance, CI Confidence Interval; E expected; O Observed; THIN The Health Improvement Network, TTO: Time to onset, UK United Kingdom, Unk Unknown

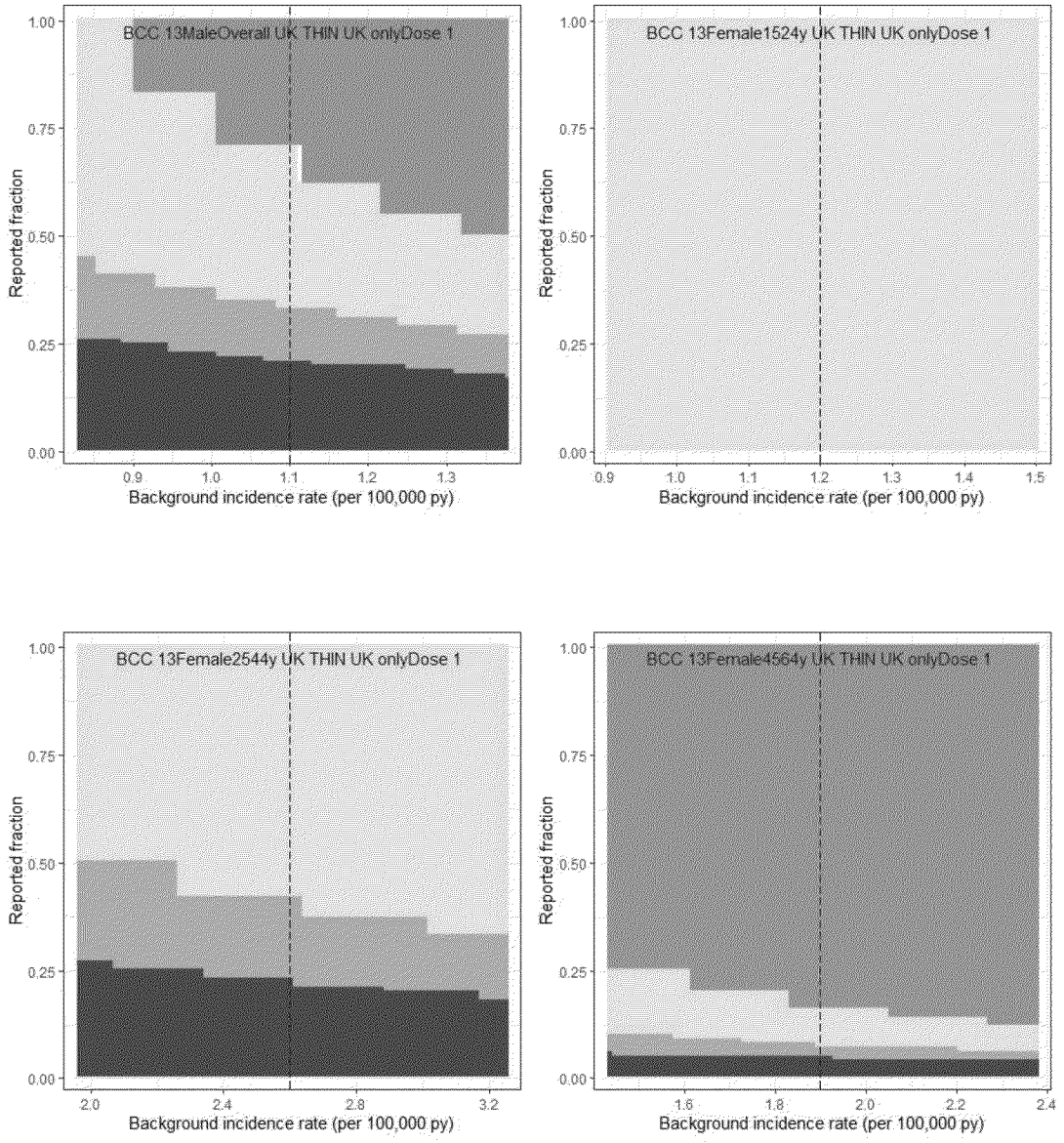
Table 39 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria level 1, 2 or 3 and stratified by dose, age and gender from UK only

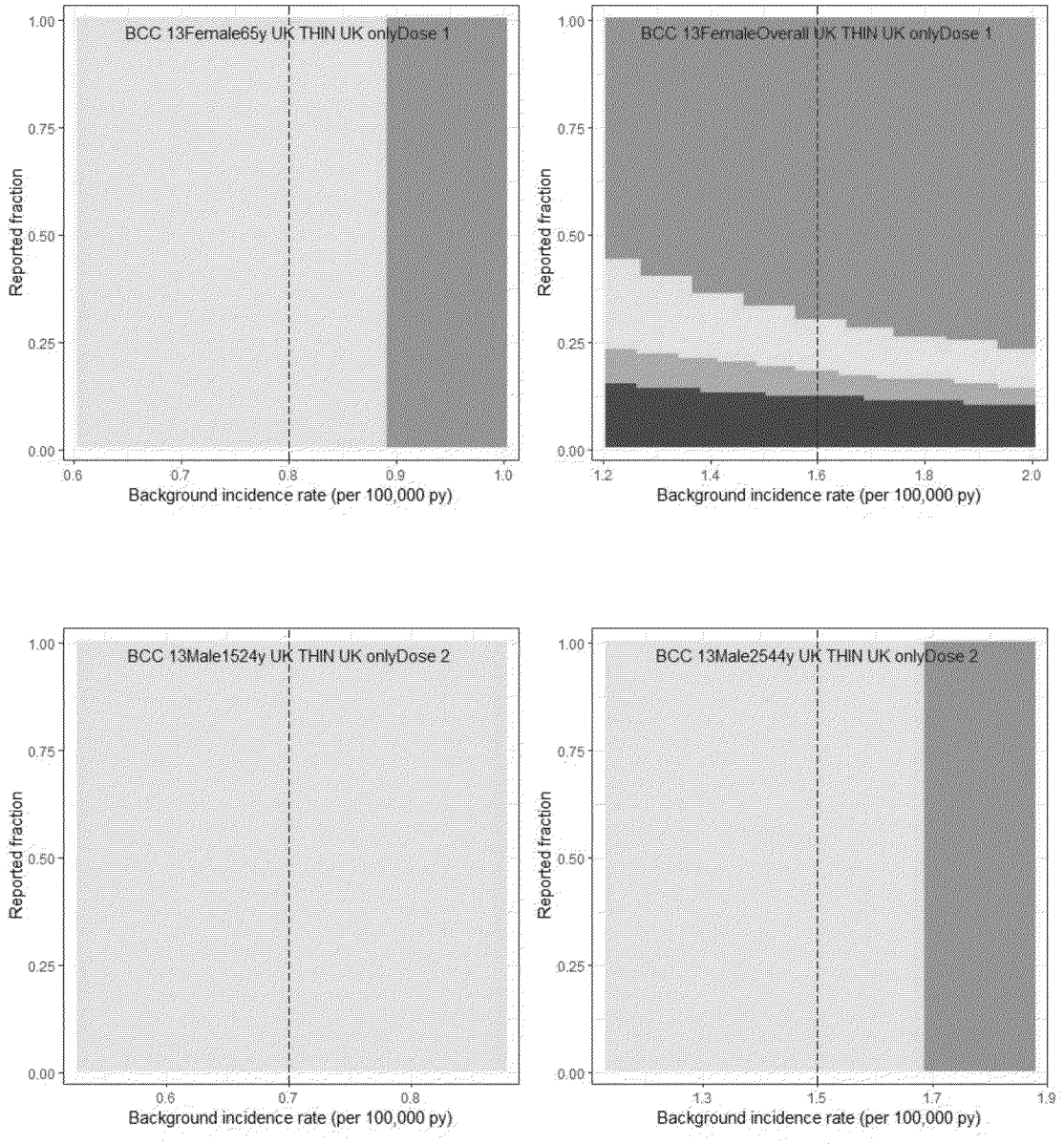
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 15 to 24 UK THIN UK Dose 1	0	0.15	42	0.7	188508	0 (0 - 24.59)	Observed < expected
Male 25 to 44 UK THIN UK Dose 1	0	3.42	42	1.5	1980408	0 (0 - 1.08)	Observed < expected
Male 45 to 64 UK THIN UK Dose 1	5	9.64	42	1.4	5990807	0.52 (0.17 - 1.21)	Observed < expected
Male 65 plus UK THIN UK Dose 1	0	3.24	42	0.9	3126893	0 (0 - 1.14)	Observed < expected
Male Overall UK THIN UK Dose 1	5	14.28	42	1.1	11286808	0.35 (0.11 - 0.82)	Observed significantly < expected
Female 15 to 24 UK THIN UK Dose 1	0	0.35	42	1.2	255760	0 (0 - 10.54)	Observed < expected
Female 25 to 44 UK THIN UK Dose 1	3	6.91	42	2.6	2310305	0.43 (0.09 - 1.27)	Observed < expected
Female 45 to 64 UK THIN UK Dose 1	1	12.1	42	1.9	5537396	0.08 (0 - 0.46)	Observed significantly < expected
Female 65 plus UK THIN UK Dose 1	0	3.32	42	0.8	3610734	0 (0 - 1.11)	Observed < expected
Female Overall UK THIN UK Dose 1	4	21.55	42	1.6	11714377	0.19 (0.05 - 0.48)	Observed significantly < expected
Male 15 to 24 UK THIN UK Dose 2	0	0.15	42	0.7	180329	0 (0 - 24.59)	Observed < expected
Male 25 to 44 UK THIN UK Dose 2	0	3.29	42	1.5	1909718	0 (0 - 1.12)	Observed < expected

Table 39 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria level 1, 2 or 3 and stratified by dose, age and gender from UK only

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 45 to 64 UK THIN UK Dose 2	1	9.47	42	1.4	5882222	0.11 (0 - 0.59)	Observed significantly < expected
Male 65 plus UK THIN UK Dose 2	1	3.21	42	0.9	3101442	0.31 (0.01 - 1.74)	Observed < expected
Male Overall UK THIN UK Dose 2	2	14.01	42	1.1	11073845	0.14 (0.02 - 0.52)	Observed significantly < expected
Female 15 to 24 UK THIN UK Dose 2	0	0.34	42	1.2	245554	0 (0 - 10.85)	Observed < expected
Female 25 to 44 UK THIN UK Dose 2	1	6.67	42	2.6	2230888	0.15 (0 - 0.84)	Observed significantly < expected
Female 45 to 64 UK THIN UK Dose 2	0	11.9	42	1.9	5446094	0 (0 - 0.31)	Observed significantly < expected
Female 65 plus UK THIN UK Dose 2	0	3.29	42	0.8	3577761	0 (0 - 1.12)	Observed < expected
Female Overall UK THIN UK Dose 2	1	21.16	42	1.6	11500418	0.05 (0 - 0.26)	Observed significantly < expected


BCC 13Male1524y UK THIN UK onlyDose 1
BCC 13Male2544y UK THIN UK onlyDose 1
BCC 13Male4564y UK THIN UK onlyDose 1
BCC 13Male65y UK THIN UK onlyDose 1
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.6
0.7
0.8
1.3
1.5
1.7
1.9
1.2
1.4
1.6
0.7
0.8
0.9
1.0
1.1


BCC 13MaleOverall UK THIN UK onlyDose 1
BCC 13Female1524y UK THIN UK onlyDose 1
BCC 13Female2544y UK THIN UK onlyDose 1
BCC 13Female4564y UK THIN UK onlyDose 1
Reported fraction
Background incidence rate (per 100,000 py)


BCC 13Female65y UK THIN UK onlyDose 1
BCC 13FemaleOverall UK THIN UK onlyDose 1
BCC 13Male1524y UK THIN UK onlyDose 2
BCC 13Male2544y UK THIN UK onlyDose 2
Reported fraction
Background incidence rate (per 100,000 py)

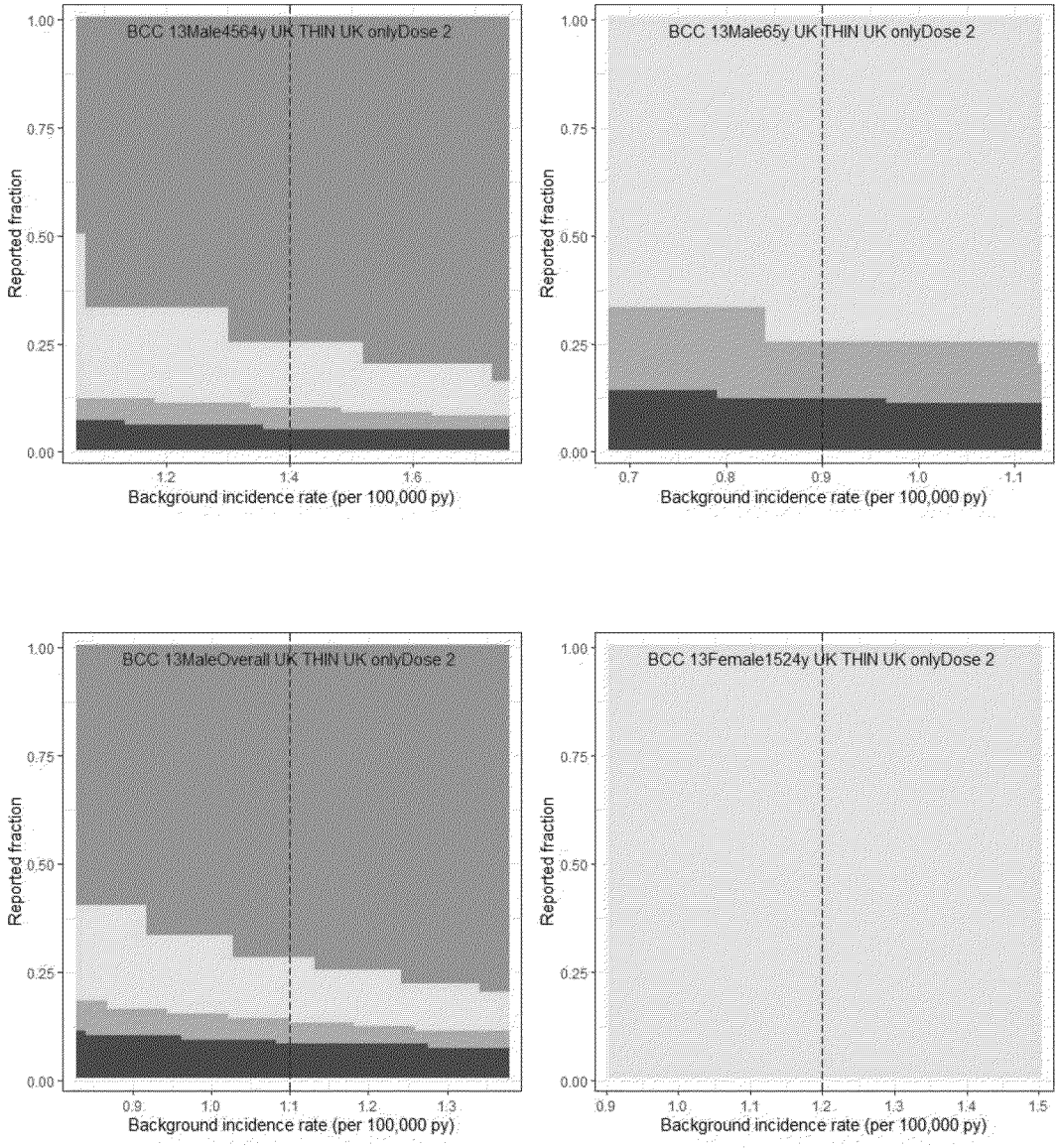
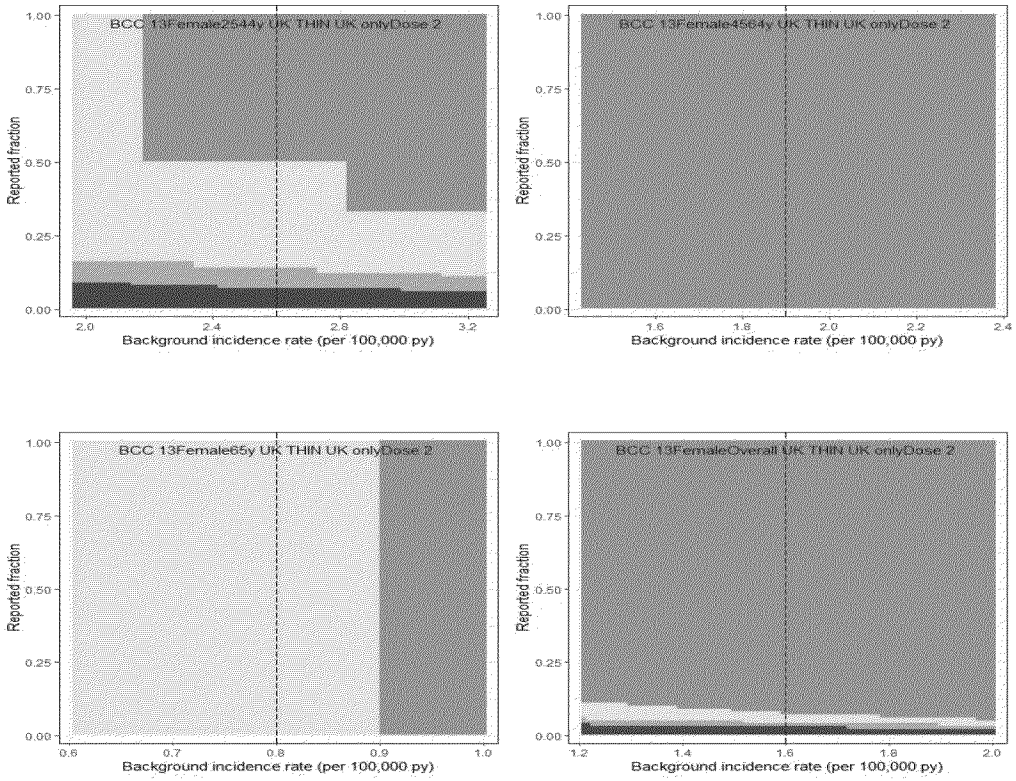

BCC 13Male4564y UK THIN UK onlyDose 2
BCC 13Male65y UK THIN UK onlyDose 2
BCC 13MaleOverall UK THIN UK onlyDose 2
BCC 13Female1524y UK THIN UK onlyDose 2
Reported fraction
Background incidence rate (per 100,000 py)

Table 39 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria level 1, 2 or 3 and stratified by dose, age and gender from UK only

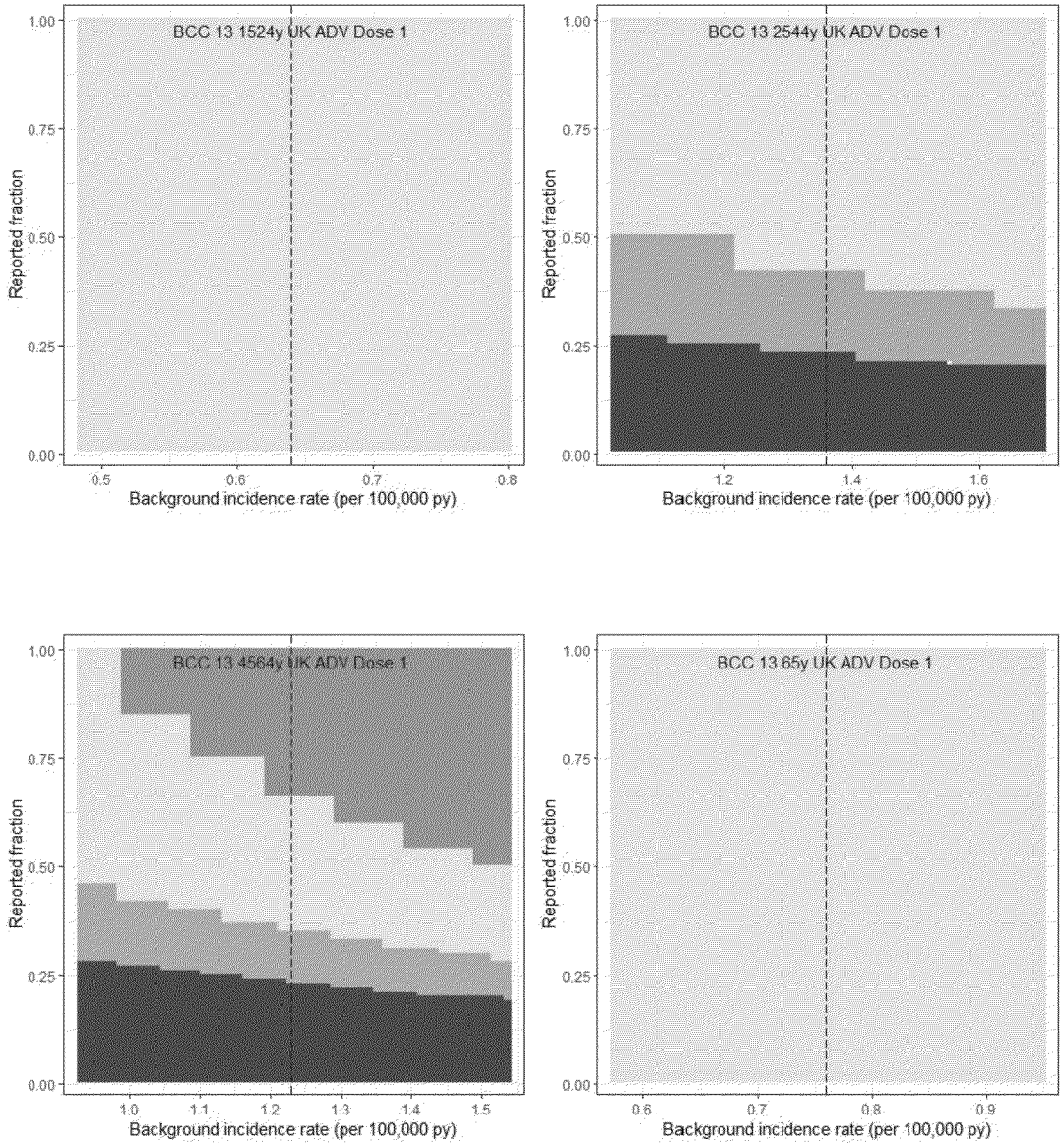
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) Source: Willame et al 2021 [B]

ADV Advance, CI Confidence Interval, E expected, EEA European Economic Area, O Observed, THIN The Health Improvement Network, TTO, Time to onset, UK United Kingdom, Unk Unknown

Table 40 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria level 1, 2 or 3 and stratified by dose and age from UK

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
15-24y ADV Dose 1	0	0.33	42	0.64	444378	0 (0 - 11.18)	Observed < expected
25-44y ADV Dose 1	3	6.71	42	1.36	4291068	0.45 (0.09 - 1.31)	Observed < expected
45-64y ADV Dose 1	6	16.31	42	1.23	11528448	0.37 (0.14 - 0.8)	Observed significantly < expected
65y+ ADV Dose 1	0	2.73	42	0.76	3126893	0 (0 - 1.35)	Observed < expected
Overall ADV Dose 1	9	27.58	42	0.97	24725401	0.33 (0.15 - 0.62)	Observed significantly < expected
15-24y ADV Dose 2	0	0.31	42	0.64	425986	0 (0 - 11.9)	Observed < expected
25-44y ADV Dose 2	1	6.48	42	1.36	4140925	0.15 (0 - 0.86)	Observed significantly < expected
45-64y ADV Dose 2	1	16.02	42	1.23	11328542	0.06 (0 - 0.35)	Observed significantly < expected
65y+ ADV Dose 2	1	5.84	42	0.76	6679268	0.17 (0 - 0.95)	Observed significantly < expected
Overall ADV Dose 2	3	26.93	42	0.97	24141350	0.11 (0.02 - 0.33)	Observed significantly < expected


BCC 13 1524y UK ADV Dose 1
BCC 13 2544y UK ADV Dose 1
BCC 13 4564y UK ADV Dose 1
BCC 13 65y UK ADV Dose 1
Reported fraction
Background incidence rate (per 100,000 py)

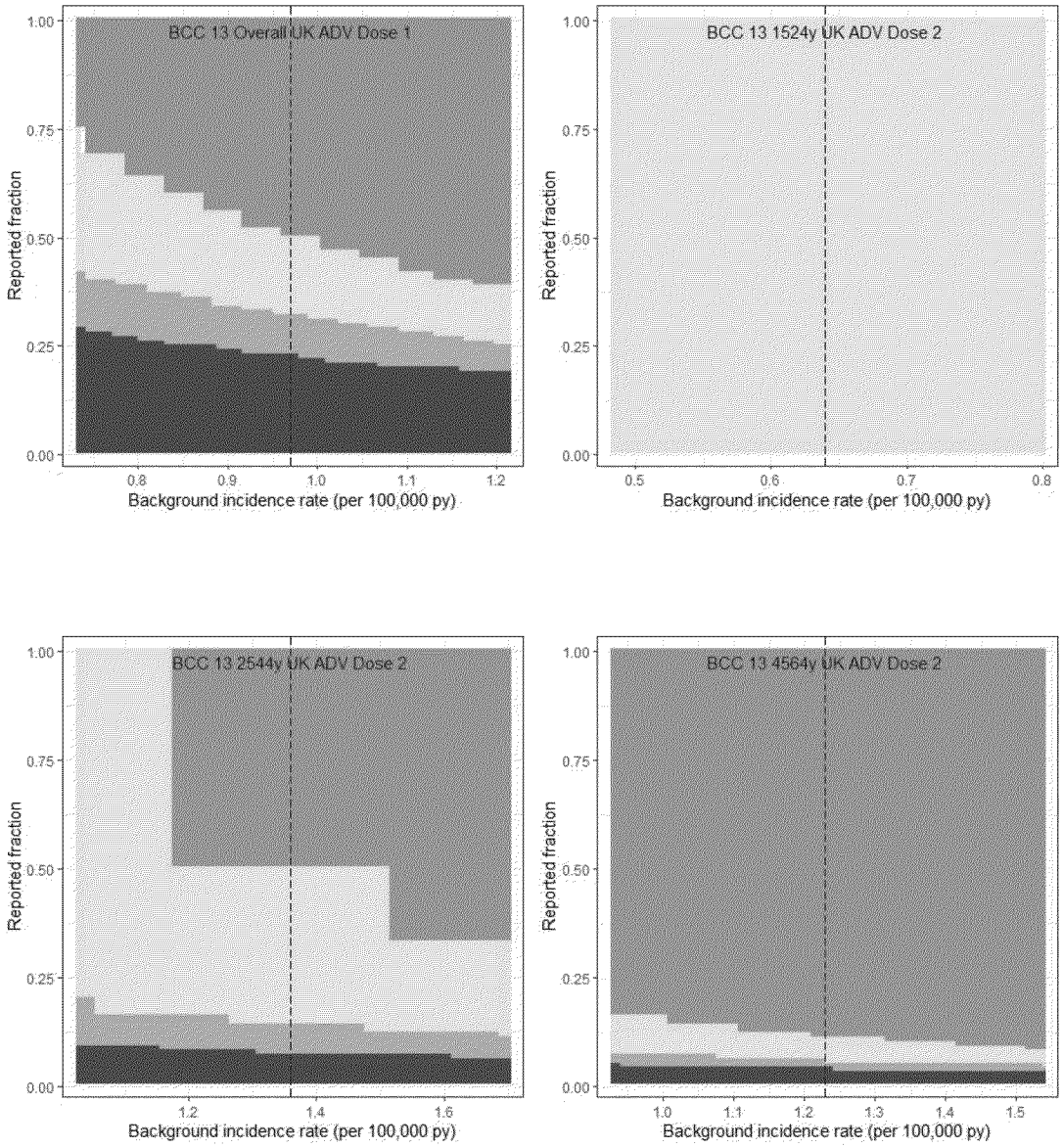
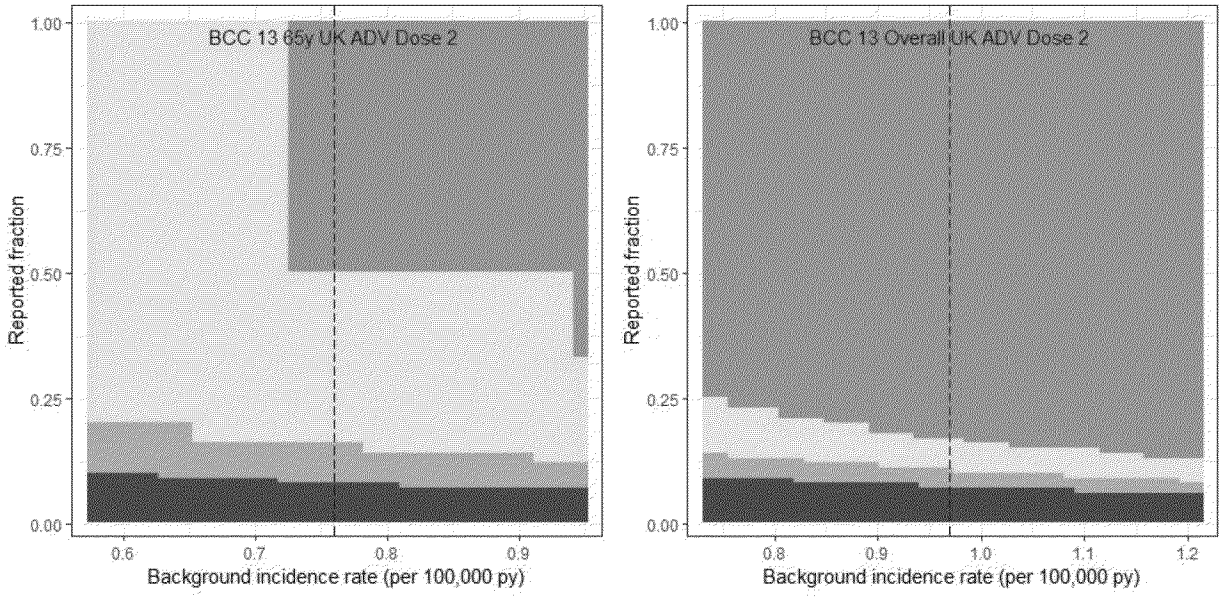

BCC 13 Overall UK ADV Dose 1
BCC 13 1524y UK ADV Dose 2
BCC 13 2544y UK ADV Dose 2
BCC 13 4564y UK ADV Dose 2
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.8
0.9
1.0
1.1
1.2
0.5
0.6
0.7
0.8
1.2
1.4
1.6
1.0
1.1
1.2
1.3
1.4
1.5

Table 40 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria level 1, 2 or 3 and stratified by dose and age from UK

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	



[a] Incidence rate (IR) Source: Willame et al 2021 [B]

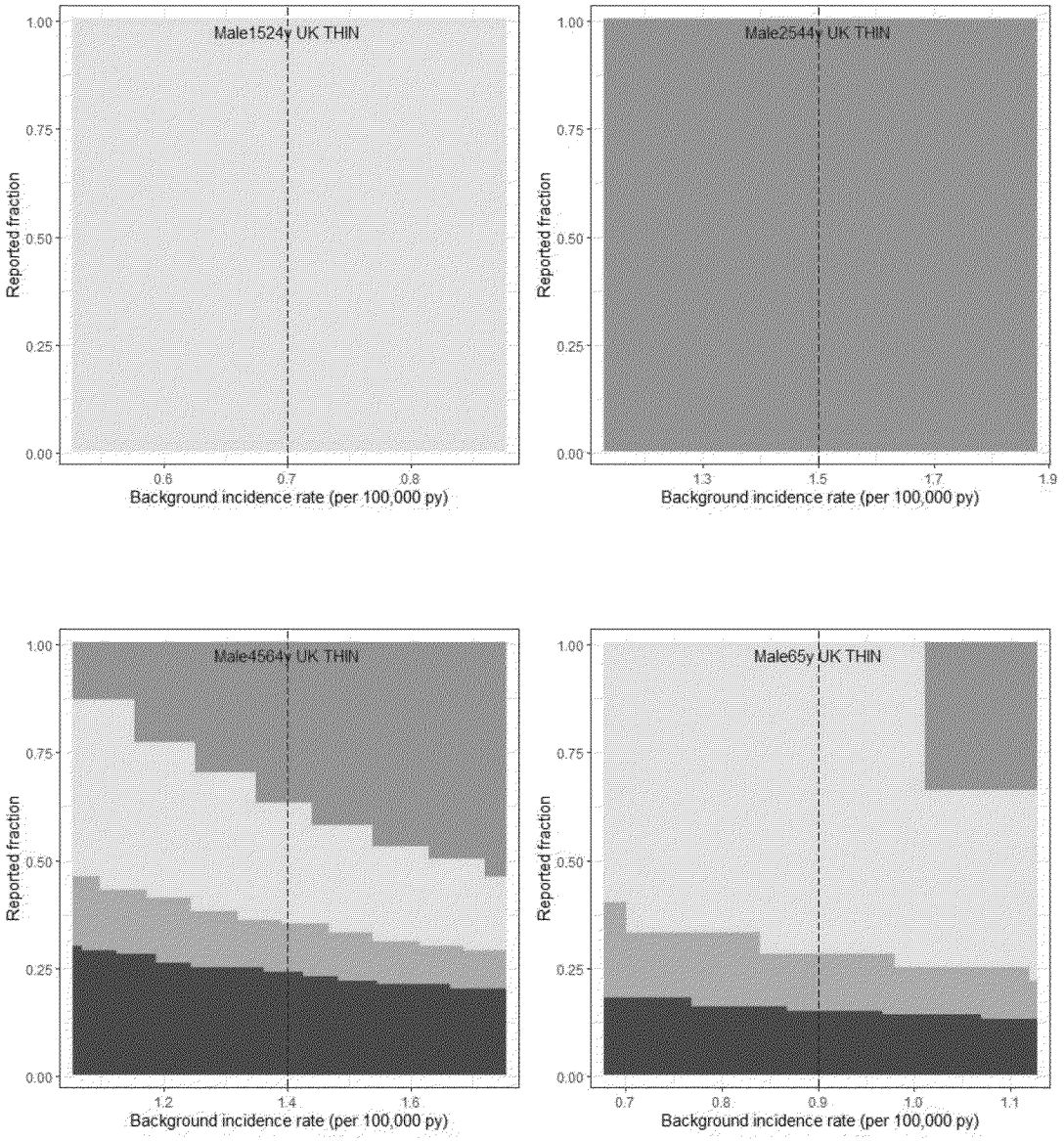
CI ADV Advance, CI Confidence Interval, E expected, O Observed, THIN The Health Improvement Network, TTO, Time to onset, UK United Kingdom, Unk Unknown.

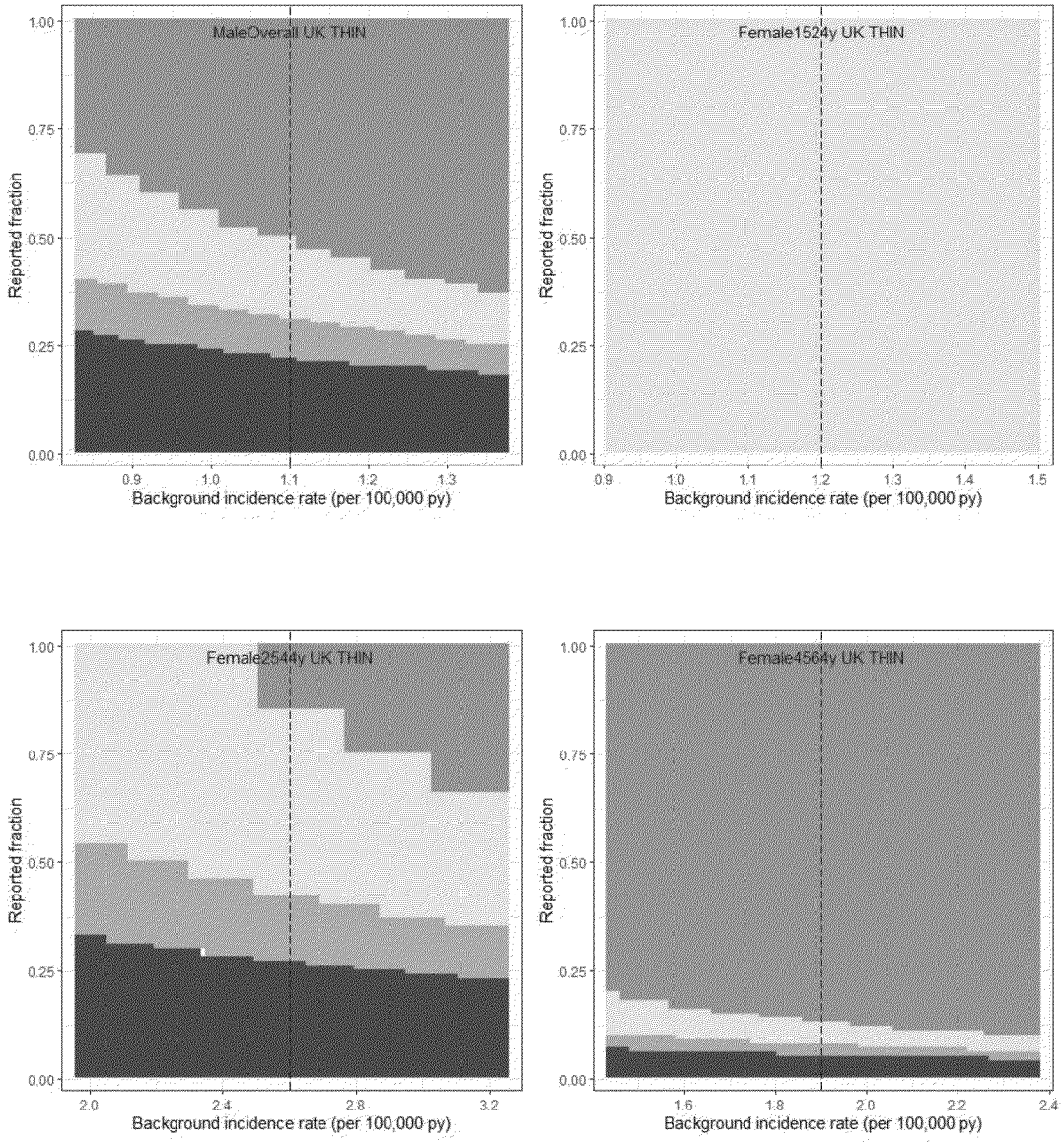
Table 41 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria (BCC 1-3) stratified by age and gender from UK including unknown TTO

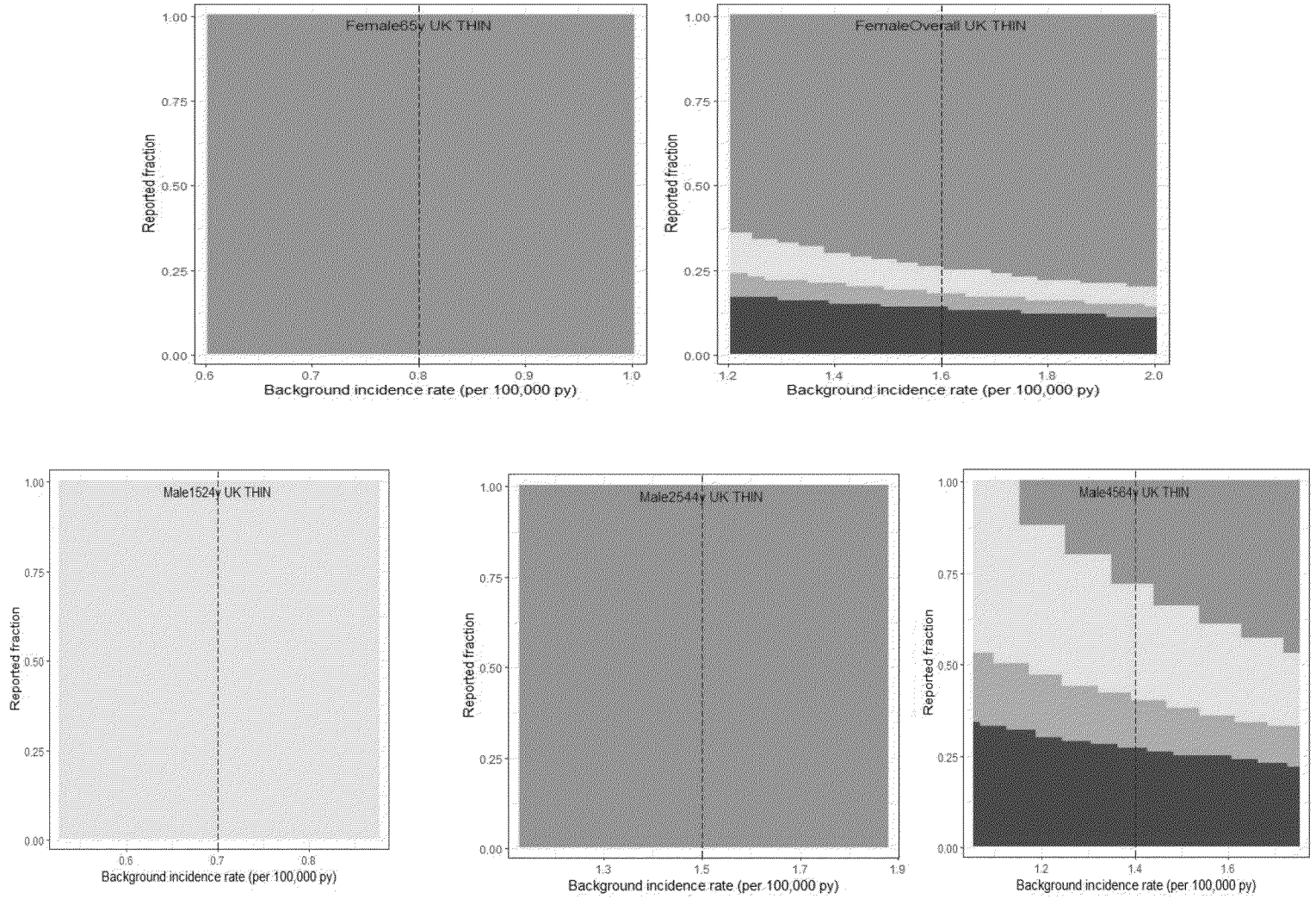
Description	Observed Cases	Expected number of cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male-15-24y UK THIN	0	0.3	42	0.7	368837	0 (0 - 12.3)	Observed < expected
Male-25-44y UK THIN	0	6.71	42	1.5	3890126	0 (0 - 0.55)	Observed significantly < expected
Male-45-64y UK THIN	7	19.11	42	1.4	11873029	0.37 (0.15 - 0.75)	Observed significantly < expected
Male-65y+ UK THIN	2	6.45	42	0.9	6228335	0.31 (0.04 - 1.12)	Observed < expected
Male-Overall UK THIN	9	28.31	42	1.1	22377923	0.32 (0.15 - 0.6)	Observed significantly < expected
Female-15-24y UK THIN	0	0.69	42	1.2	501314	0 (0 - 5.35)	Observed < expected
Female-25-44y UK THIN	6	13.58	42	2.6	4541193	0.44 (0.16 - 0.96)	Observed significantly < expected
Female-45-64y UK THIN	2	24	42	1.9	10983490	0.08 (0.01 - 0.3)	Observed significantly < expected
Female-65y+ UK THIN	0	6.61	42	0.8	7188495	0 (0 - 0.56)	Observed significantly < expected
Female-Overall UK THIN	8	42.78	42	1.6	23252503	0.19 (0.08 - 0.37)	Observed significantly < expected
Male-15-24y UK THIN (Including unk TTO)	0	0.3	42	0.7	368837	0 (0 - 12.3)	Observed < expected
Male-25-44y UK THIN (Including unk TTO)	0	6.71	42	1.5	3890126	0 (0 - 0.55)	Observed significantly < expected
Male-45-64y UK THIN (Including unk TTO)	8	19.11	42	1.4	11873029	0.42 (0.18 - 0.82)	Observed significantly < expected
Male-65y+ UK THIN (Including unk TTO)	3	6.45	42	0.9	6228335	0.47 (0.1 - 1.36)	Observed < expected
Male-Overall UK THIN (Including unk TTO)	11	28.31	42	1.1	22377923	0.39 (0.19 - 0.7)	Observed significantly < expected
Female-15-24y UK THIN (Including unk TTO)	0	0.69	42	1.2	501314	0 (0 - 5.35)	Observed < expected

Table 41 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria (BCC 1-3) stratified by age and gender from UK including unknown TTO

Description	Observed Cases	Expected number of cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Female-25-44y UK THIN (Including unk TTO)	8	13.58	42	2.6	4541193	0.59 (0.25 - 1.16)	Observed < expected
Female-45-64y UK THIN (Including unk TTO)	3	24	42	1.9	10983490	0.12 (0.03 - 0.37)	Observed significantly < expected
Female-65y+ UK THIN (Including unk TTO)	1	6.61	42	0.8	7188495	0.15 (0 - 0.84)	Observed significantly < expected
Female-Overall UK THIN (Including unk TTO)	12	42.78	42	1.6	23252503	0.28 (0.14 - 0.49)	Observed significantly < expected


Male1524y UK THIN
Male2544y UK THIN
Male4564y UK THIN
Male65y UK THIN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
1.3
1.5
1.7
1.9
1.2
1.4
1.6
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)


MaleOverall UK THIN
Female1524y UK THIN
Female2544y UK THIN
Female4564y UK THIN
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.8
2.0
2.2
2.4
2.8
3.2


Female65y UK THIN
FemaleOverall UK THIN
Male1524y UK THIN
Male2544y UK THIN
Male4564y UK THIN
Reported fraction
Background incidence rate (per 100,000 py)

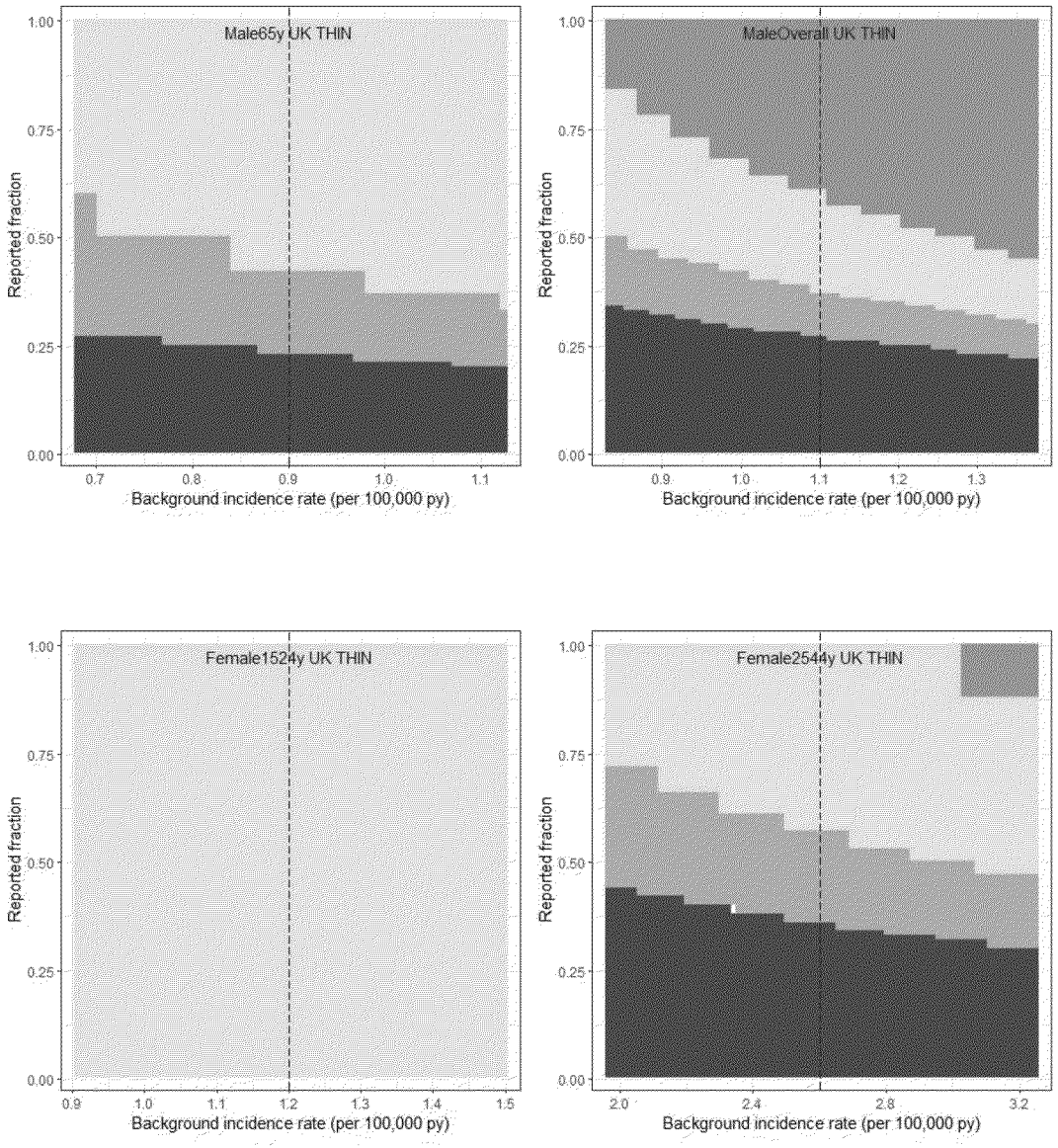
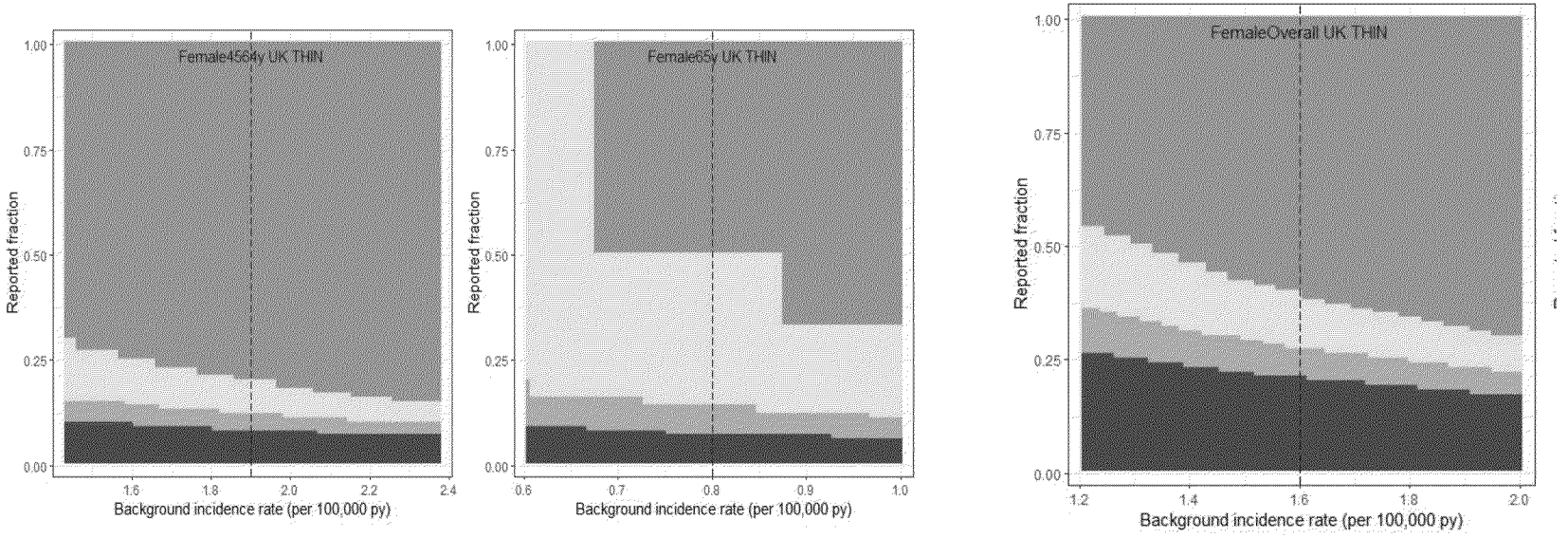

Male65y UK THIN
MaleOverall UK THIN
Female1524y UK THIN
Female2544y UK THIN
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
2.0
2.4
2.8
3.2

Table 41 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria (BCC 1-3) stratified by age and gender from UK including unknown TTO

Description	Observed Cases	Expected number of cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	

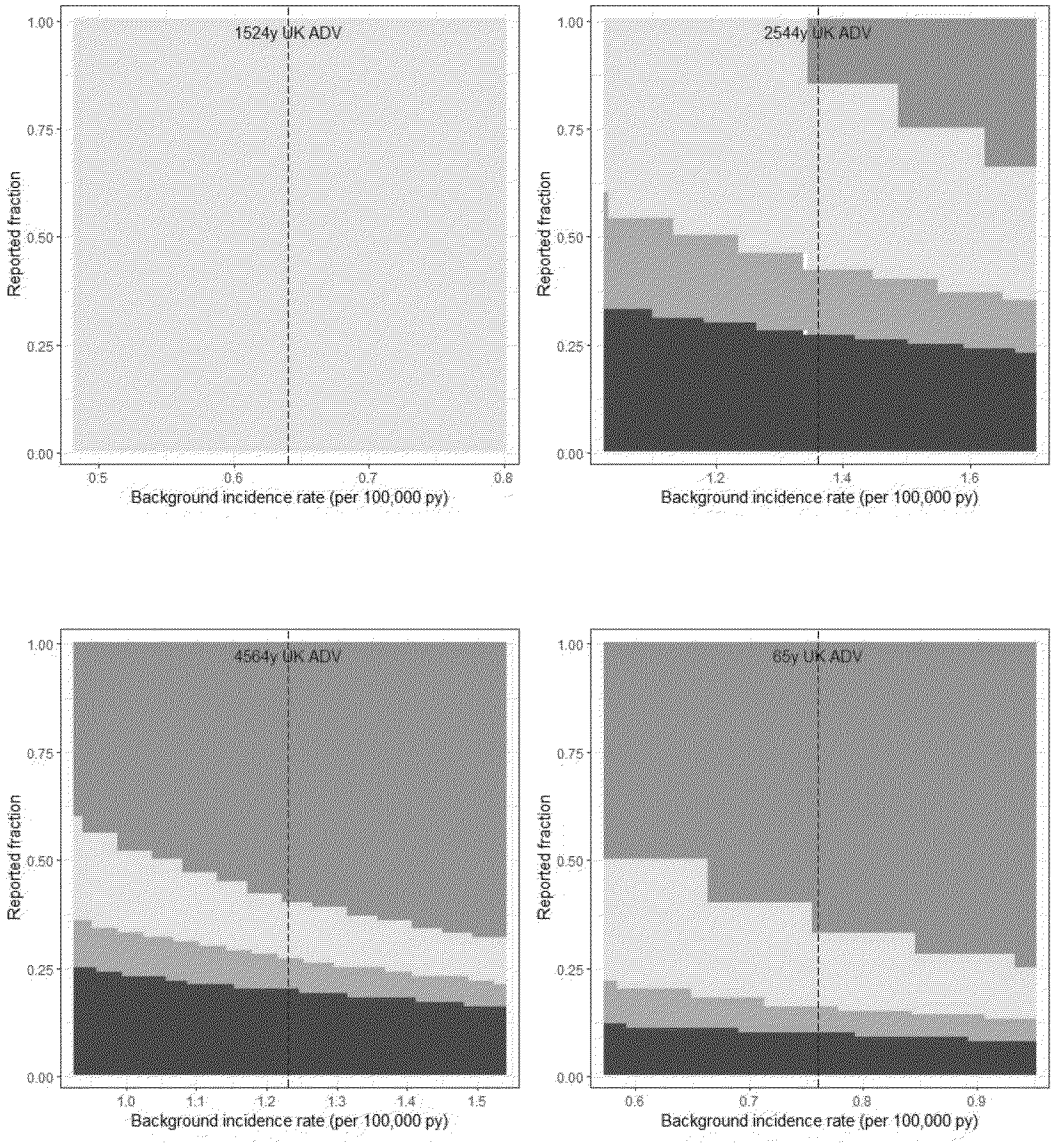


[a] Incidence rate (IR) Source: Willame et al 2021 [B]

BCC Brighton collaboration criteria; CI Confidence Interval; E expected; O Observed; THIN The Health Improvement Network, TTO Time to onset, UK United Kingdom, Unk Unknown

Table 42 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria (BCC 1-3) stratified by age from rates UK only including unknown TTO

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
15-24 UK ADV	0	0.64	42	0.64	871148	0 (0 - 5.76)	Observed < expected
25-44 UK ADV	6	13.2	42	1.36	8438999	0.45 (0.17 - 0.99)	Observed significantly < expected
45-64 UK ADV	9	32.36	42	1.23	22877522	0.28 (0.13 - 0.53)	Observed significantly < expected
65 plus UK ADV	2	11.75	42	0.76	13443624	0.17 (0.02 - 0.61)	Observed significantly < expected
Overall UK ADV	17	54.57	42	0.97	48925906	0.31 (0.18 - 0.5)	Observed significantly < expected
15-24 UK ADV (Including Unk TTO)	0	0.64	42	0.64	871148	0 (0 - 5.76)	Observed < expected
25-44 UK ADV (Including Unk TTO)	8	13.2	42	1.36	8438999	0.61 (0.26 - 1.19)	Observed < expected
45-64 UK ADV (Including Unk TTO)	11	32.36	42	1.23	22877522	0.34 (0.17 - 0.61)	Observed significantly < expected
65 plus UK ADV (Including Unk TTO)	4	11.75	42	0.76	13443624	0.34 (0.09 - 0.87)	Observed significantly < expected
Overall UK ADV (Including Unk TTO)	23	54.57	42	0.97	48925906	0.42 (0.27 - 0.63)	Observed significantly < expected


1524y UK ADV
2544y UK ADV
4564y UK ADV
65y UK ADV
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.5
0.6
0.7
0.8
1.2
1.4
1.6
1.0
1.1
1.3
1.5
0.9

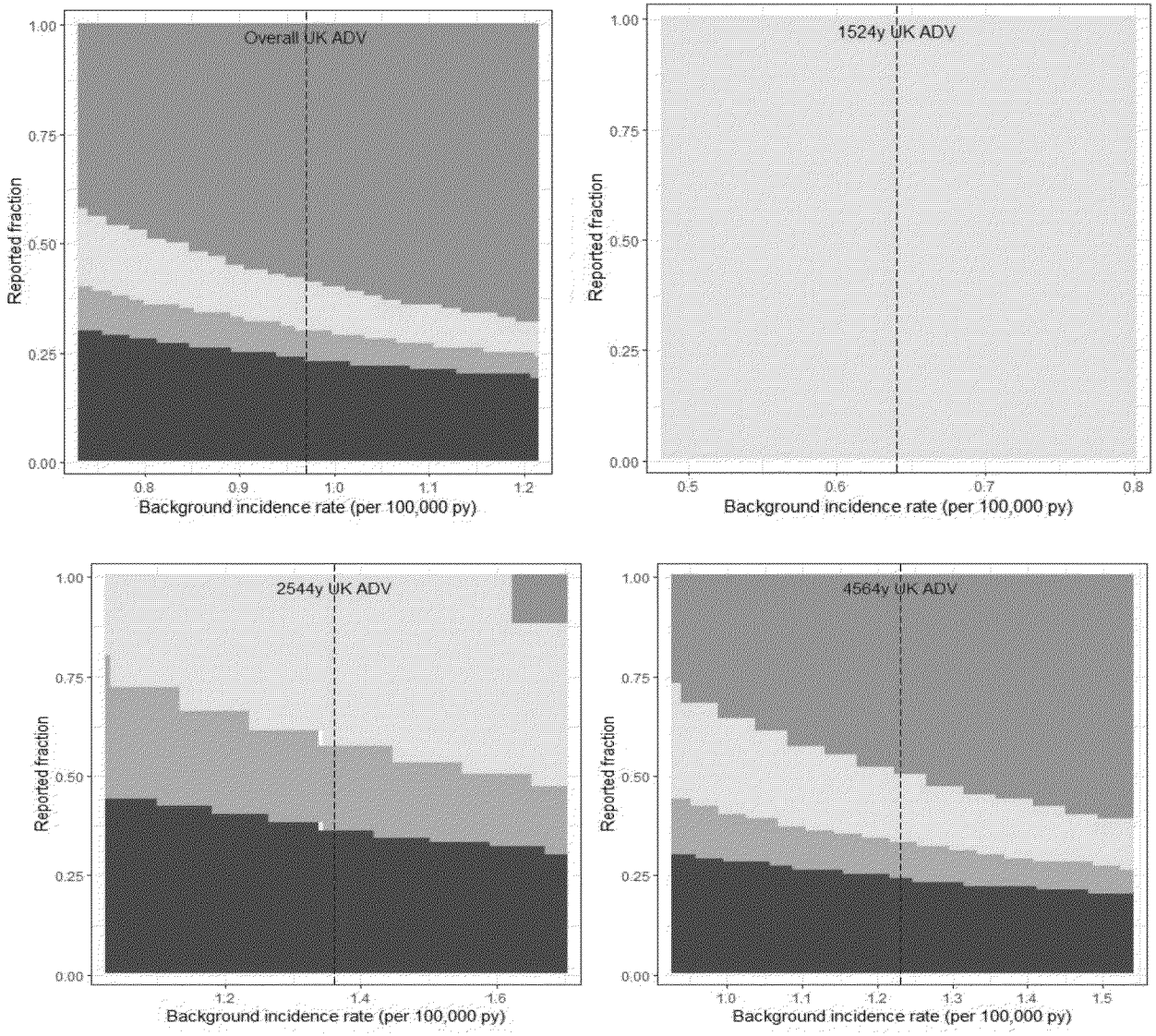
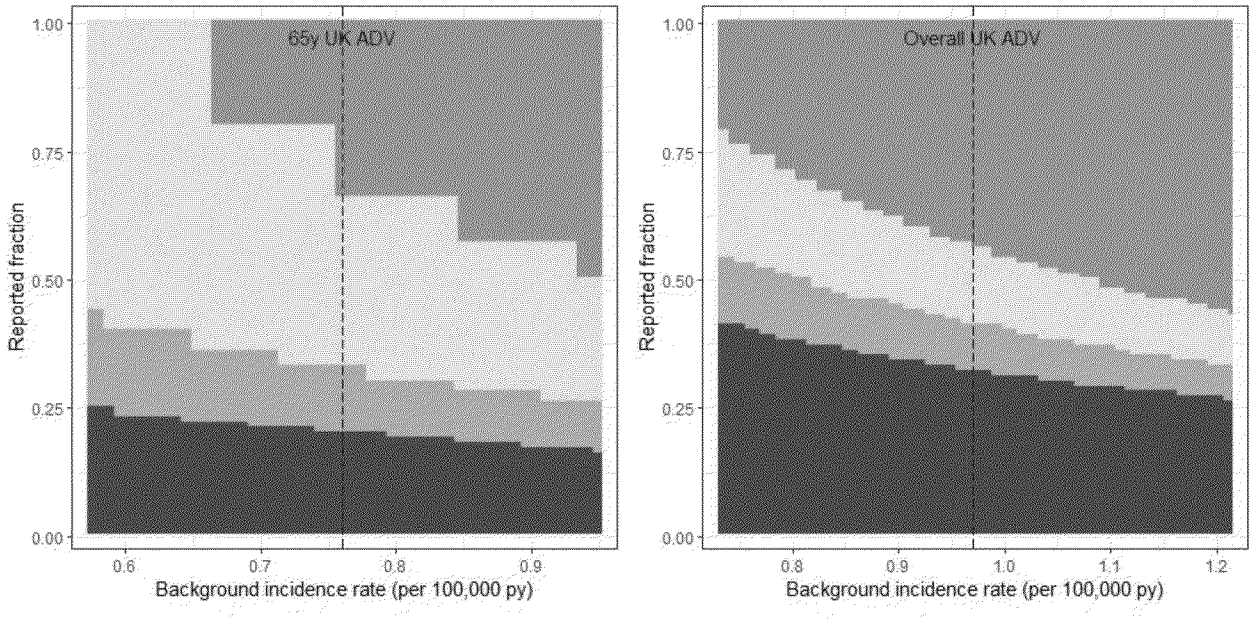

Overall UK ADV
1524y UK ADV
2544y UK ADV
4564y UK ADV
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.8
0.9
1.0
1.1
1.2
0.5
0.6
0.7
0.8
1.2
1.4
1.6
1.0
1.1
1.2
1.3
1.4
1.5

Table 42 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria (BCC 1-3) stratified by age from rates UK only including unknown TTO

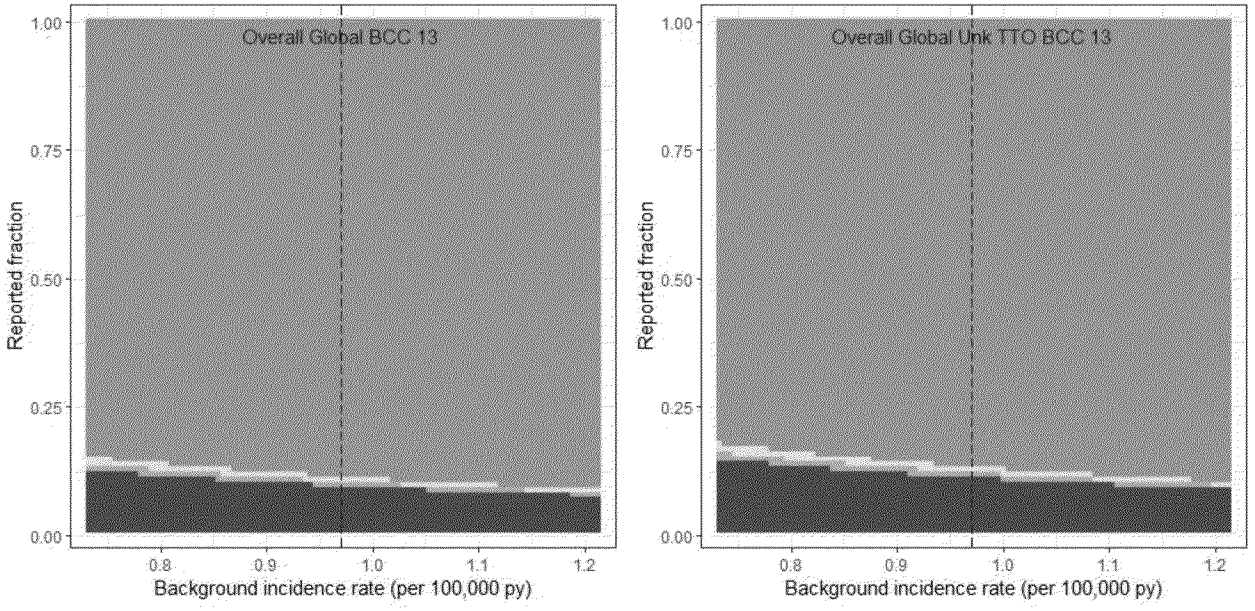
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) Source: Willame et al 2021 [B]

ADV Advance; BCC Brighton collaboration criteria; CI Confidence Interval; E expected; O Observed; TTO; Time to onset; UK United Kingdom; Unk Unknown

Table 43 Observed Versus Expected analysis for Myelitis transverse cases meeting Brighton collaboration criteria (BCC 1-3) EU

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Overall Global	55	519.92	42	0.97	466115644	0.11 (0.08 - 0.14)	Observed significantly < expected
Overall Global (including unknown TTO)	64	519.92	42	0.97	466115644	0.12 (0.09 - 0.16)	Observed significantly < expected

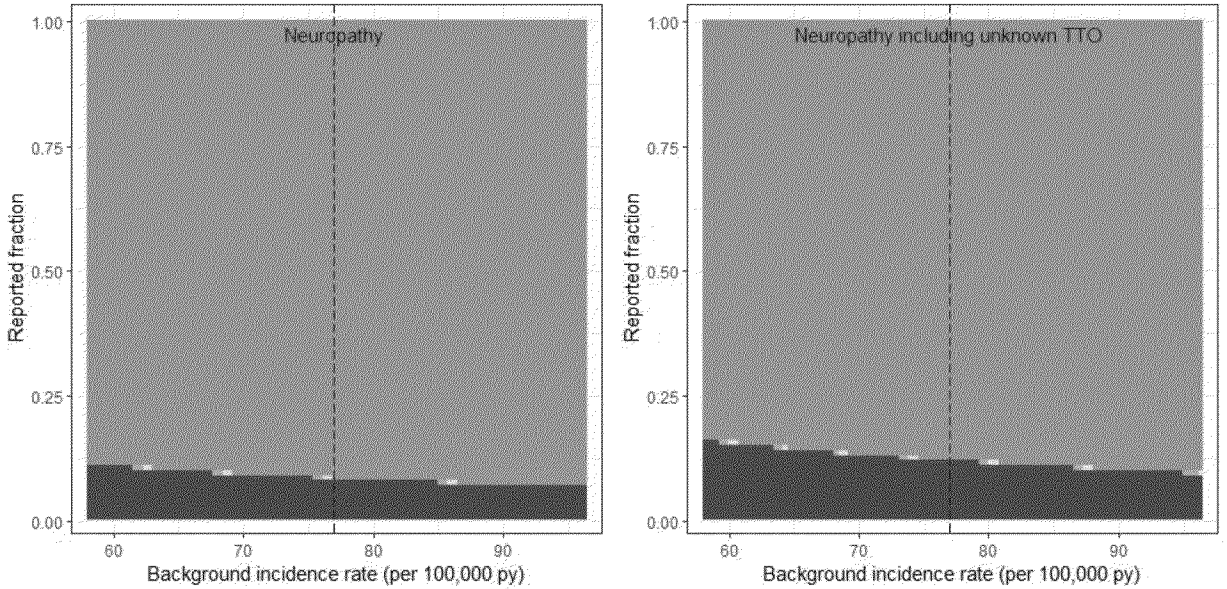


[a] Incidence rate (IR) Source: Willame et al 2021 [B]

CI Confidence Interval; E expected; EU European Union; O Observed; TTO: Time to onset; Unk Unknown.

Table 44 Observed Versus Expected analysis for Neuropathy

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Neuropathy	3666	41271.7	42	77	0.09 (0.09 - 0.09)	Observed significantly < expected
Neuropathy (including unknown TTO)	5140	41271.7	42	77	0.12 (0.12 - 0.13)	Observed significantly < expected

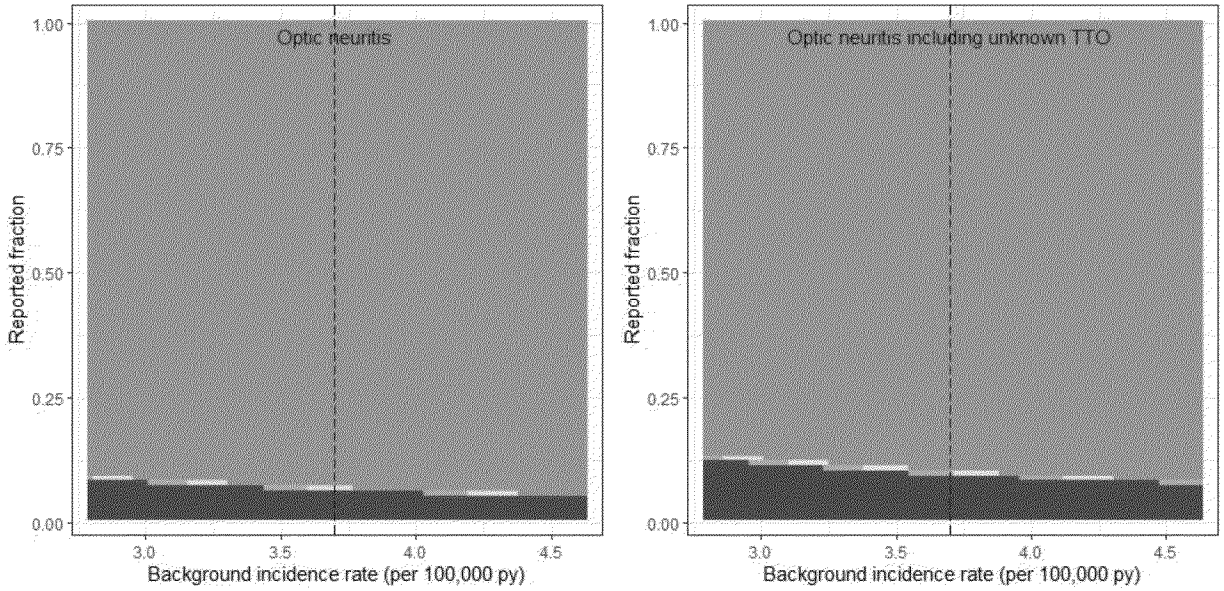


[a] Incidence rate (IR): Source: Lehmann et al 2020

CI Confidence Interval; E expected; O Observed; TTO: Time to onset.

Table 45 Observed Versus Expected analysis for Optic Neuritis

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Optic Overall global cases	135	1983.19	42	3.7	0.07 (0.06 - 0.08)	Observed significantly < expected
Optic Overall global cases (including unknown TTO)	199	1983.19	42	3.7	0.1 (0.09 - 0.12)	Observed significantly < expected



[a] Incidence Rate (IR): Braithwaite et al 2020

CI Confidence Interval; E expected; O Observed; TTO: Time to onset, Unk Unknown

Table 46 Observed Versus Expected analysis for Myasthenia gravis

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Myasthenia gravis	45	943.35	42	1.76	466115644	0.05 (0.03 - 0.06)	Observed significantly < expected
Myasthenia gravis (including unknown TTO)	77	943.35	42	1.76	466115644	0.08 (0.06 - 0.1)	Observed significantly < expected
Myasthenia gravis	62	4042.94	180	1.76	466115644	0.02 (0.01 - 0.02)	Observed significantly < expected
Myasthenia gravis (including unknown TTO)	94	4042.94	180	1.76	466115644	0.02 (0.02 - 0.03)	Observed significantly < expected
Myasthenia gravis (Extended RW)	62	5300.75	236	1.76	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
Myasthenia gravis (Extended RW+Unk TTO)	94	5300.75	236	1.76	466115644	0.02 (0.01 - 0.02)	Observed significantly < expected

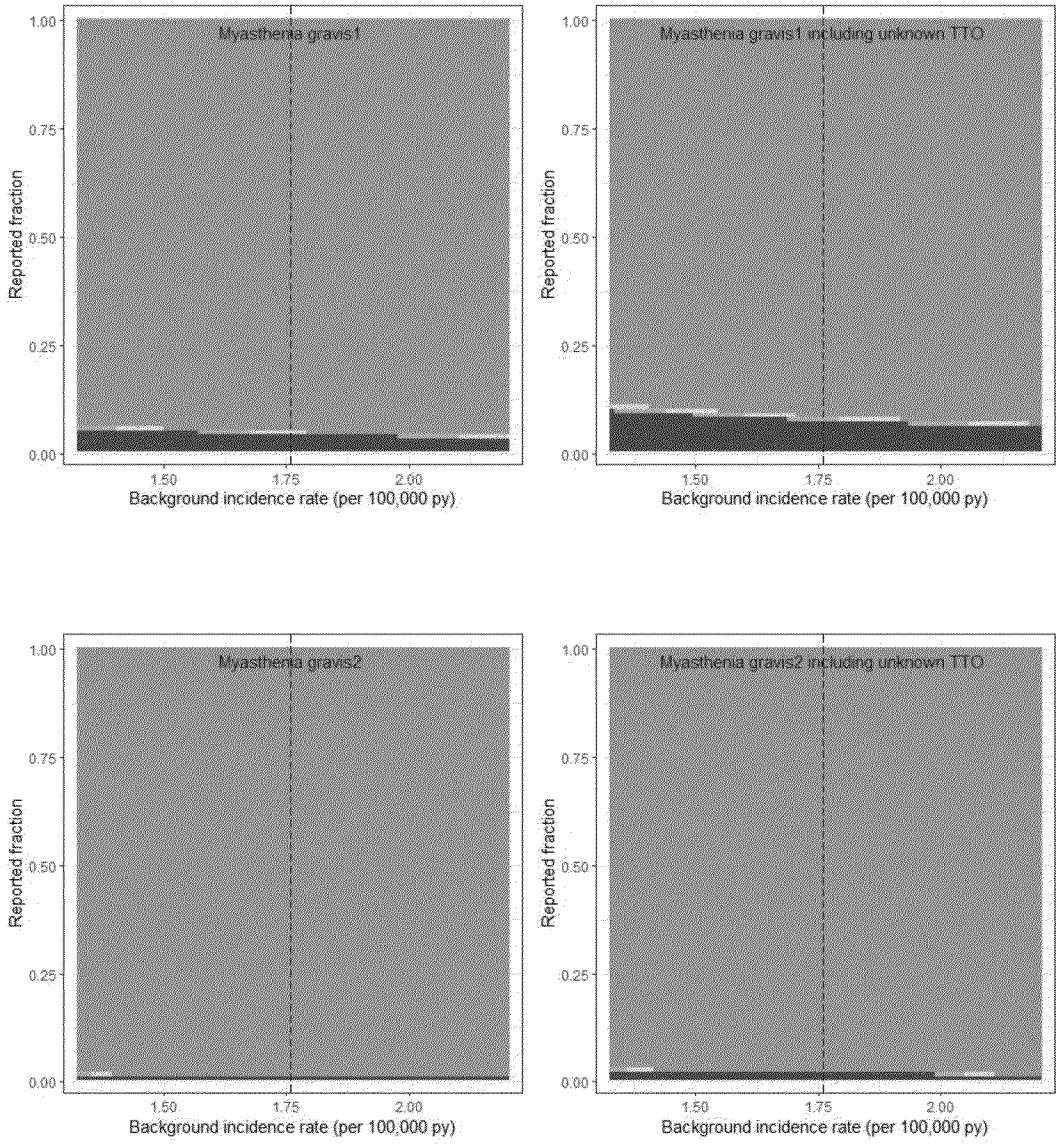
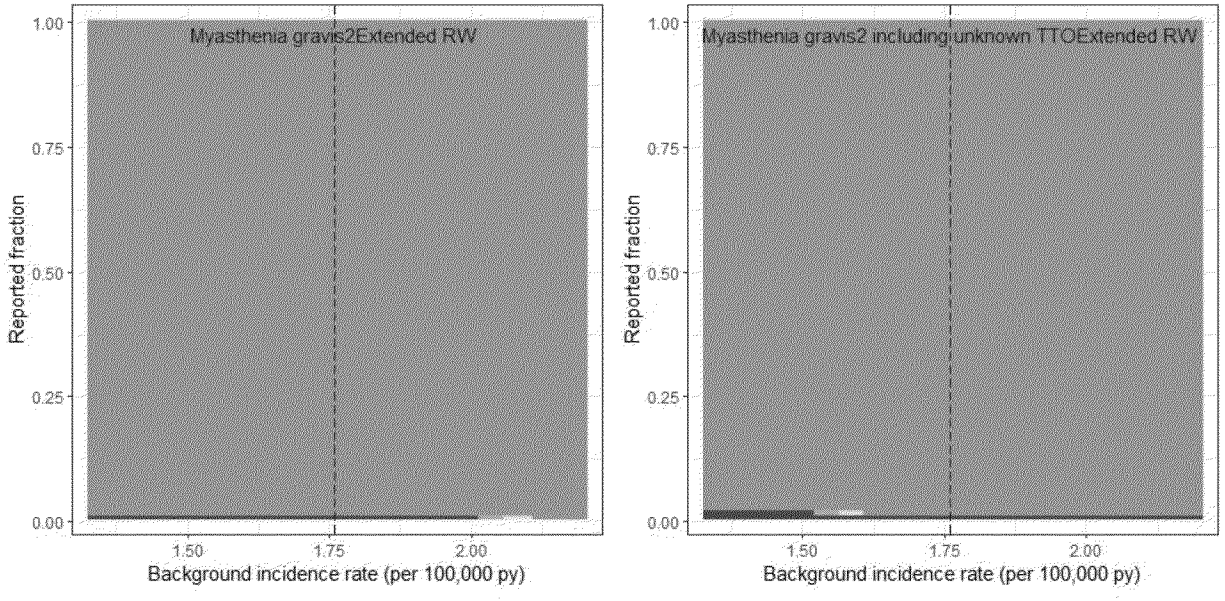

Myasthenia gravis1
Myasthenia gravis1 including unknown TTO
Myasthenia gravis2
Myasthenia gravis2 including unknown TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.50
1.75
2.00
Background incidence rate (per 100,000 py)

Table 46 Observed Versus Expected analysis for Myasthenia gravis

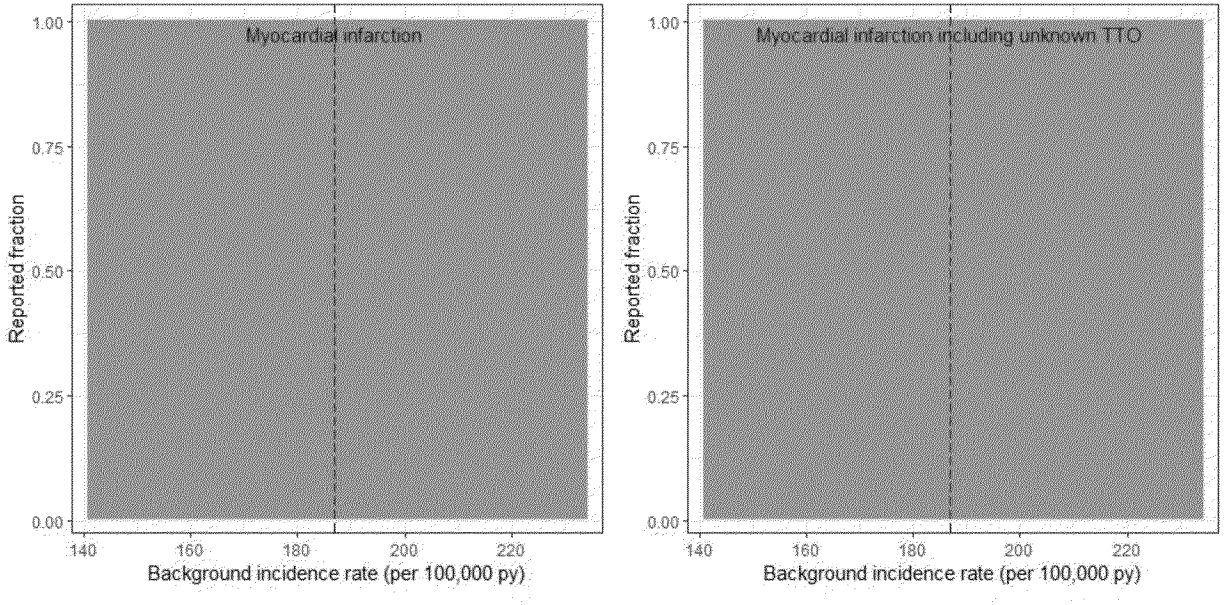
Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence Rate (IR): Source: Maddison Et al 2019

CI Confidence Interval; E expected; O Observed; RW Risk Window, TTO: Time to onset, Unk Unknown.

Table 47 Observed Versus Expected analysis for Myocardial infarction

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Myocardial infarction	169	66820.85	28	187	0 (0 - 0)	Observed significantly < expected
Myocardial infarction (including unknown TTO)	355	66820.85	28	187	0.01 (0 - 0.01)	Observed significantly < expected

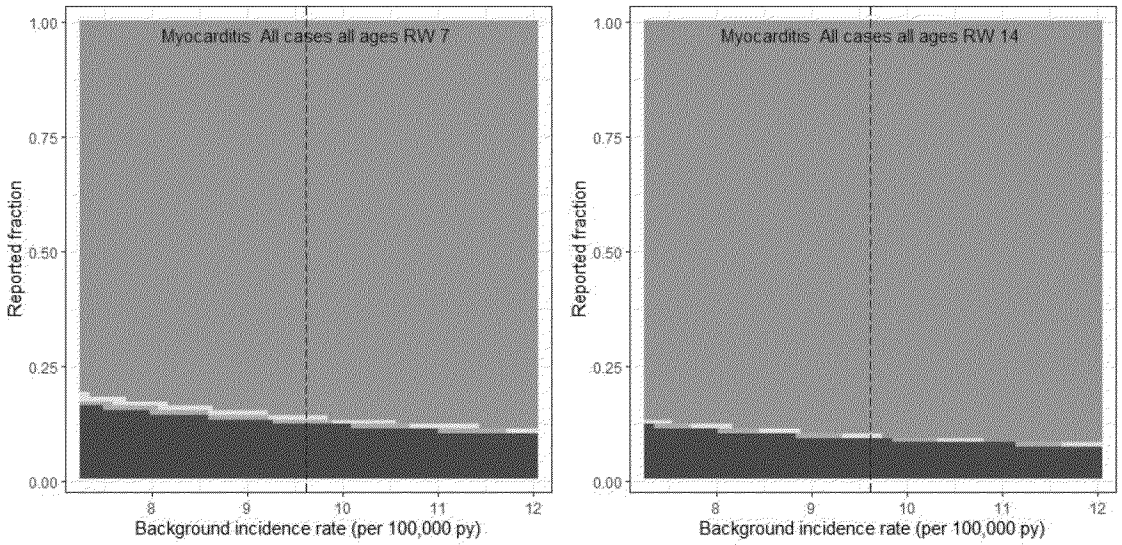


[a] Incidence Rate (IR): Source: Herrett et al 2013

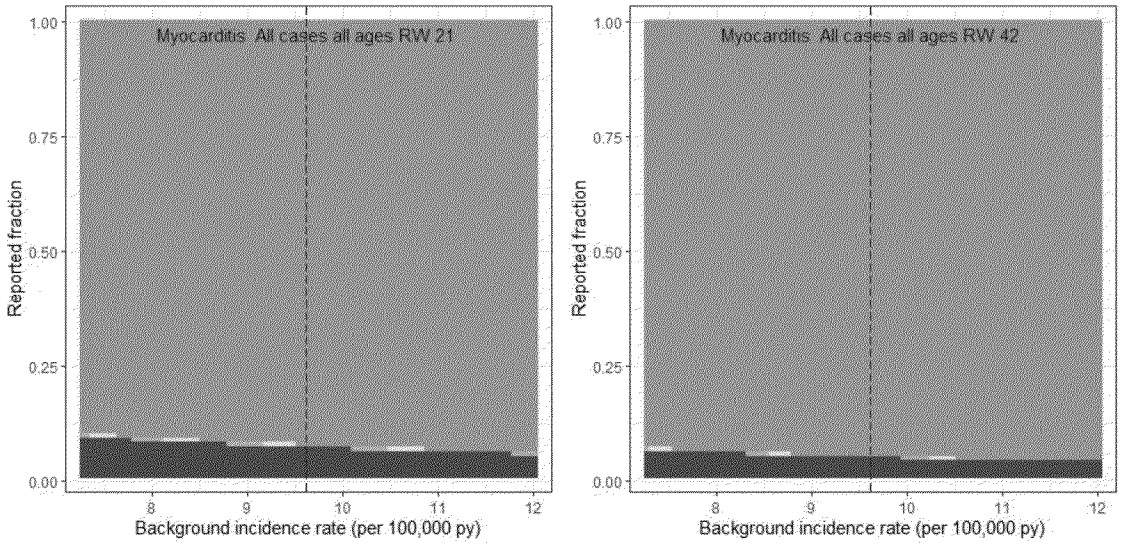
CI Confidence Interval; E expected; O Observed; TTO: Time to onset.

Table 48 Observed Versus Expected analysis for Myocarditis

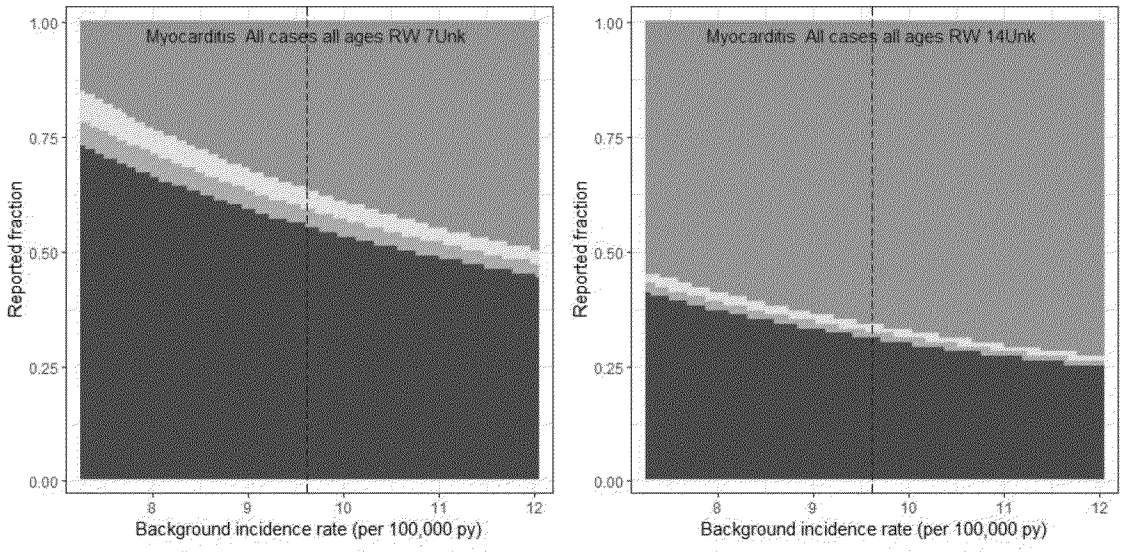
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
All Cases (Medically Confirmed and Non-Confirmed)							
All cases, all ages	115	859.38	7	9.62	466115644	0.13 (0.11 - 0.16)	Observed significantly < expected
All cases, all ages	166	1718.76	14	9.62	466115644	0.1 (0.08 - 0.11)	Observed significantly < expected
All cases, all ages	196	2578.14	21	9.62	466115644	0.08 (0.07 - 0.09)	Observed significantly < expected
All cases, all ages	274	5156.28	42	9.62	466115644	0.05 (0.05 - 0.06)	Observed significantly < expected
All cases, all ages (RW 7+Unk TTO)	512	859.38	7	9.62	466115644	0.6 (0.55 - 0.65)	Observed significantly < expected
All cases, all ages (RW 14+Unk TTO)	563	1718.76	14	9.62	466115644	0.33 (0.3 - 0.36)	Observed significantly < expected
All cases, all ages (RW 21+Unk TTO)	593	2578.14	21	9.62	466115644	0.23 (0.21 - 0.25)	Observed significantly < expected
All cases, all ages (RW 42+Unk TTO)	671	5156.28	42	9.62	466115644	0.13 (0.12 - 0.14)	Observed significantly < expected


Myocarditis All cases all ages RW 7
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

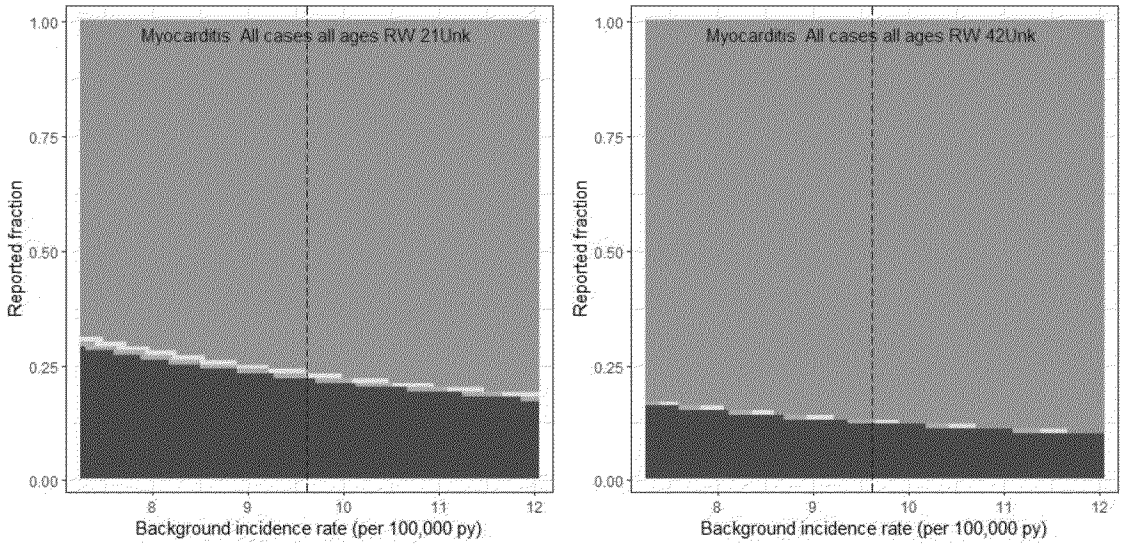
Myocarditis All cases all ages RW 14
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Myocarditis All cases all ages RW 21
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

Myocarditis All cases all ages RW 42
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Myocarditis All cases all ages RW 7Unk
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

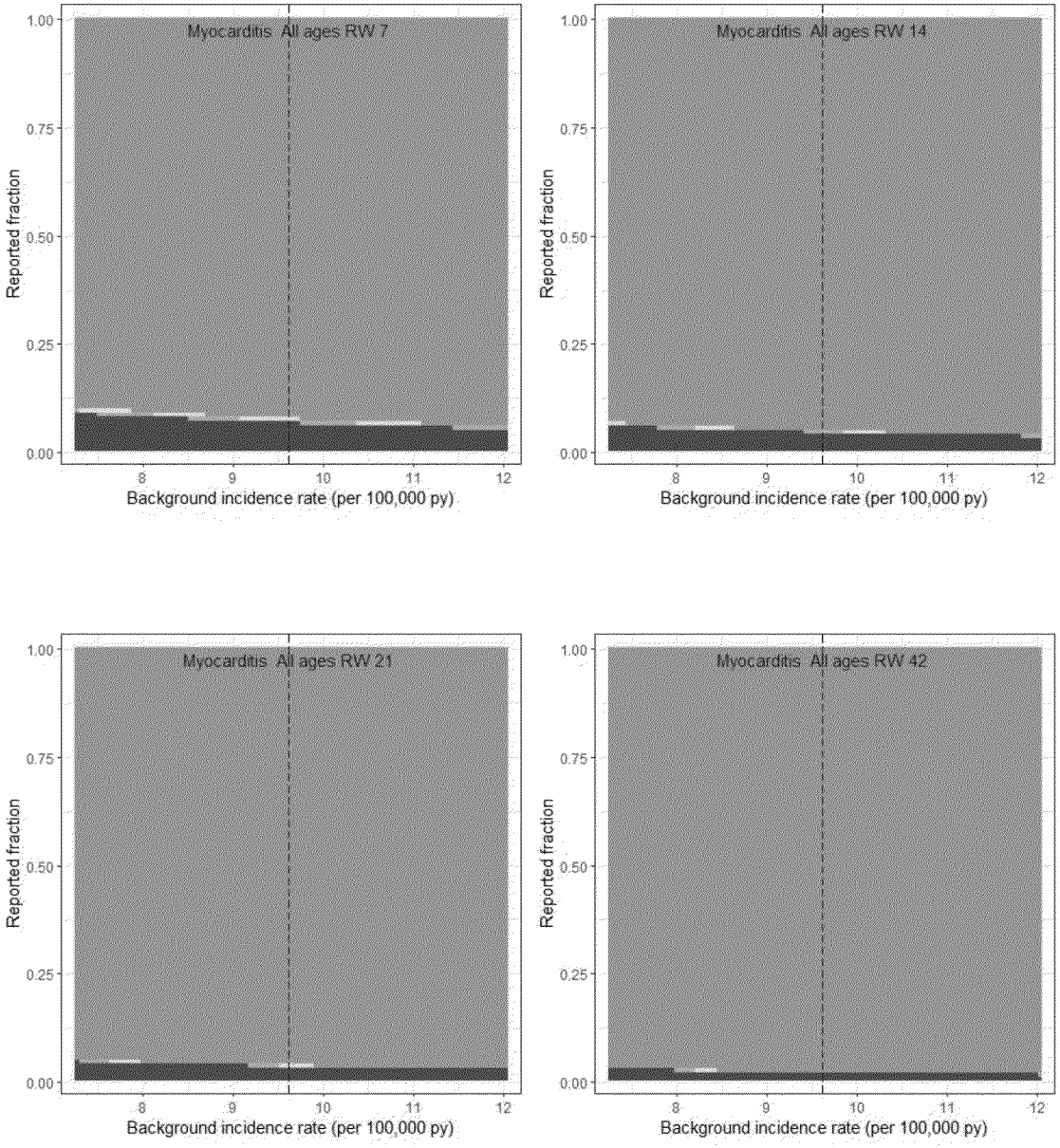
Myocarditis All cases all ages RW 14Unk
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Myocarditis All cases all ages RW 21Unk
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

Myocarditis All cases all ages RW 42Unk
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

Table 48 Observed Versus Expected analysis for Myocarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Medically Confirmed Cases							
All ages	65	859.38	7	9.62	466115644	0.08 (0.06 - 0.1)	Observed significantly < expected
All ages	88	1718.76	14	9.62	466115644	0.05 (0.04 - 0.06)	Observed significantly < expected
All ages	102	2578.14	21	9.62	466115644	0.04 (0.03 - 0.05)	Observed significantly < expected
All ages	132	5156.28	42	9.62	466115644	0.03 (0.02 - 0.03)	Observed significantly < expected
All ages (RW 7+Unk TTO)	129	859.38	7	9.62	466115644	0.15 (0.13 - 0.18)	Observed significantly < expected
All ages (RW 14+Unk TTO)	152	1718.76	14	9.62	466115644	0.09 (0.07 - 0.1)	Observed significantly < expected
All ages (RW 21+Unk TTO)	166	2578.14	21	9.62	466115644	0.06 (0.05 - 0.07)	Observed significantly < expected
All ages (RW 42+Unk TTO)	196	5156.28	42	9.62	466115644	0.04 (0.03 - 0.04)	Observed significantly < expected


Myocarditis All ages RW 7
Myocarditis All ages RW 14
Myocarditis All ages RW 21
Myocarditis All ages RW 42
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

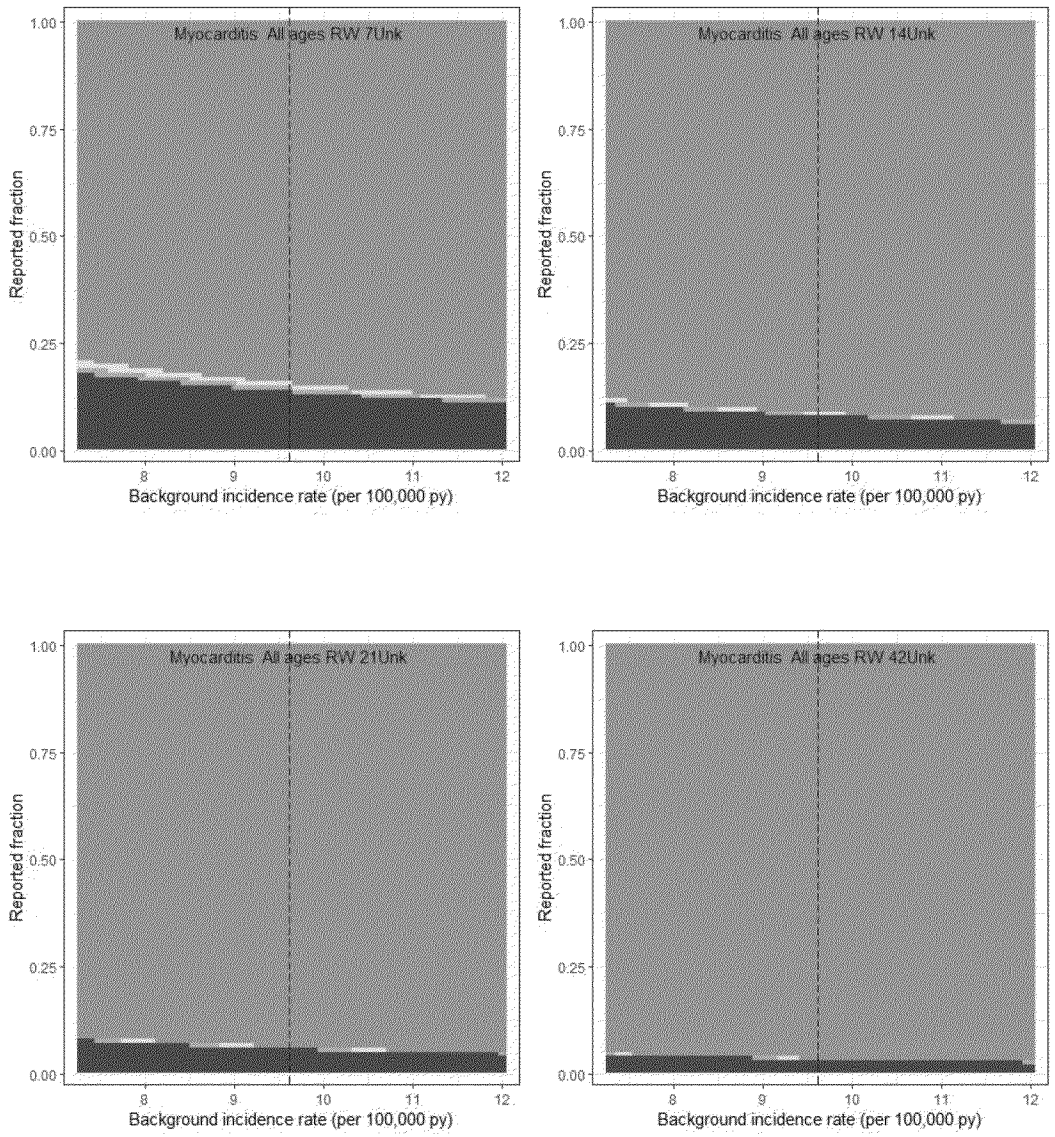
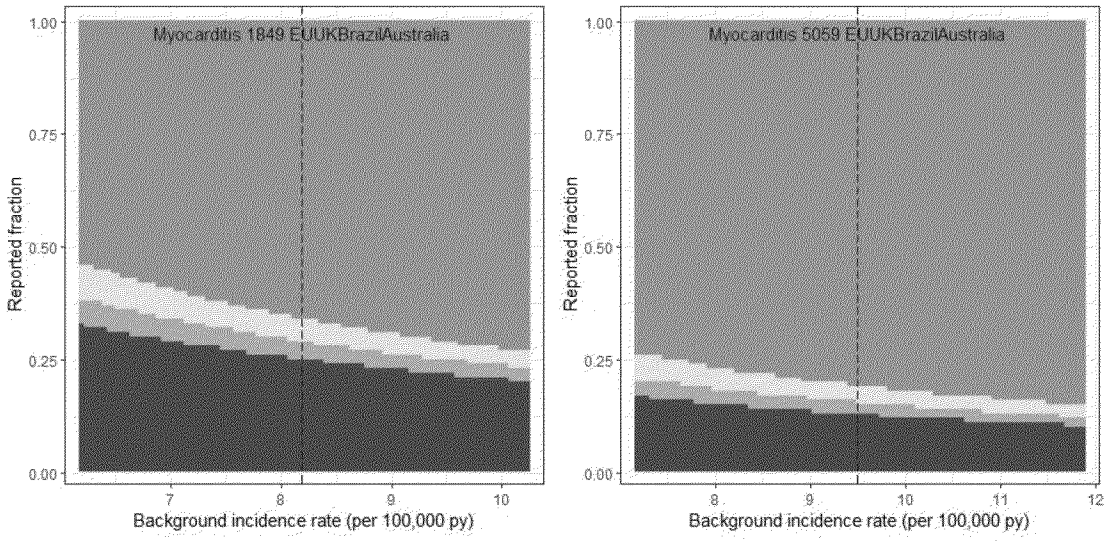

Myocarditis All ages RW 7Unk
Myocarditis All ages RW 14Unk
Myocarditis All ages RW 21Unk
Myocarditis All ages RW 42Unk
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

Table 48 Observed Versus Expected analysis for Myocarditis

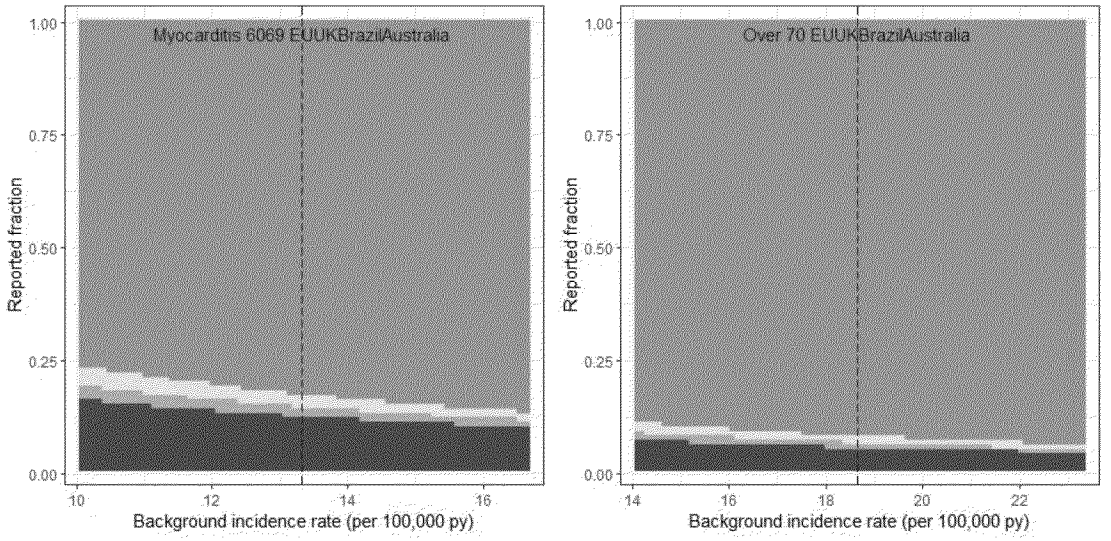
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
18-49 (EU/UK/BR/AU) (RW 7)	51	172.81	7	8.19	110094983	0.3 (0.22 - 0.39)	Observed significantly < expected
50-59 (EU/UK/BR/AU) (RW 7)	17	106.21	7	9.5	58336094	0.16 (0.09 - 0.26)	Observed significantly < expected
60-69 (EU/UK/BR/AU) (RW 7)	22	148.07	7	13.33	57960860	0.15 (0.09 - 0.22)	Observed significantly < expected
Over 70 (EU/UK/BR/AU) (RW 7)	8	115.79	7	18.66	32376365	0.07 (0.03 - 0.14)	Observed significantly < expected
18-49 (EU/UK/BR/AU) (RW 14)	71	345.62	14	8.19	110094983	0.21 (0.16 - 0.26)	Observed significantly < expected
50-59 (EU/UK/BR/AU) (RW 14)	27	212.43	14	9.5	58336094	0.13 (0.08 - 0.18)	Observed significantly < expected
60-69 (EU/UK/BR/AU) (RW 14)	30	296.15	14	13.33	57960860	0.1 (0.07 - 0.14)	Observed significantly < expected
Over 70 (EU/UK/BR/AU) (RW 14)	12	231.57	14	18.66	32376365	0.05 (0.03 - 0.09)	Observed significantly < expected
18-49 (EU/UK/BR/AU) (RW 21)	84	518.43	21	8.19	110094983	0.16 (0.13 - 0.2)	Observed significantly < expected
50-59 (EU/UK/BR/AU) (RW 21)	29	318.64	21	9.5	58336094	0.09 (0.06 - 0.13)	Observed significantly < expected
60-69 (EU/UK/BR/AU) (RW 21)	36	444.22	21	13.33	57960860	0.08 (0.06 - 0.11)	Observed significantly < expected

Table 48 Observed Versus Expected analysis for Myocarditis

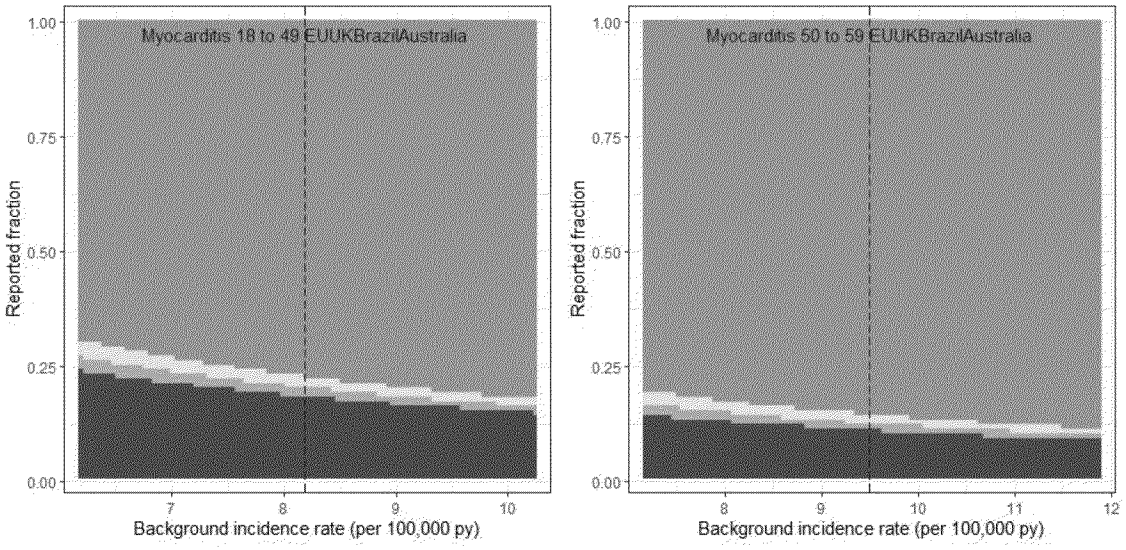
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Over 70 (EU/UK/BR/AU) (RW 21)	16	347.36	21	18.66	32376365	0.05 (0.03 - 0.07)	Observed significantly < expected
18-49 (EU/UK/BR/AU) (RW 42)	122	1036.86	42	8.19	110094983	0.12 (0.1 - 0.14)	Observed significantly < expected
50-59 (EU/UK/BR/AU) (RW 42)	45	637.28	42	9.5	58336094	0.07 (0.05 - 0.09)	Observed significantly < expected
60-69 (EU/UK/BR/AU) (RW 42)	49	888.45	42	13.33	57960860	0.06 (0.04 - 0.07)	Observed significantly < expected
Over 70 (EU/UK/BR/AU) (RW 42)	21	694.72	42	18.66	32376365	0.03 (0.02 - 0.05)	Observed significantly < expected


Myocarditis 1849 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
Background incidence rate (per 100,000 py)

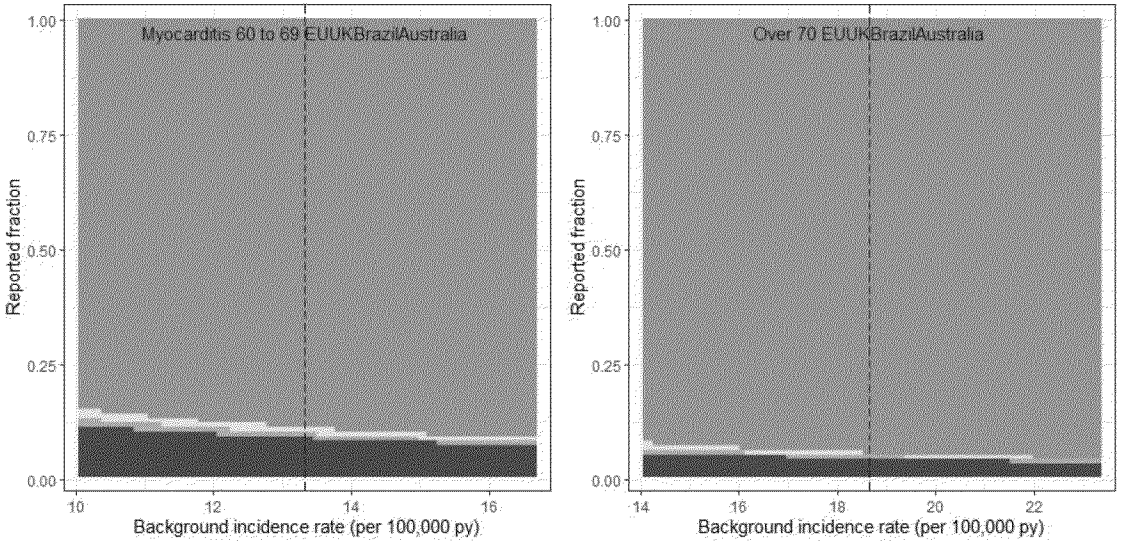
Myocarditis 5059 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Myocarditis 6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
10
12
14
16
Background incidence rate (per 100,000 py)

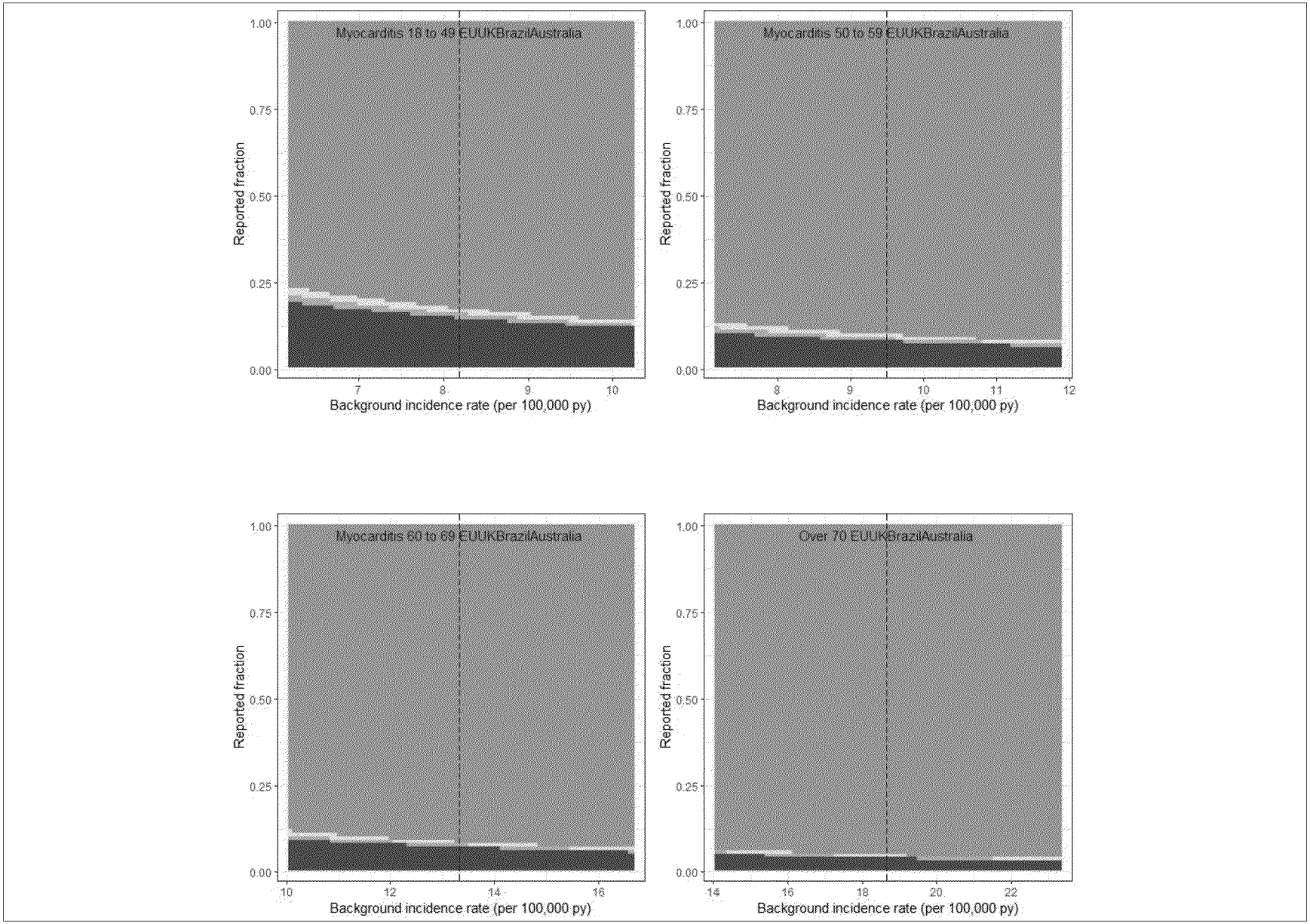
Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
14
16
18
20
22
Background incidence rate (per 100,000 py)


Myocarditis 18 to 49 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
Background incidence rate (per 100,000 py)

Myocarditis 50 to 59 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Myocarditis 60 to 69 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
10
12
14
16
Background incidence rate (per 100,000 py)

Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
14
16
18
20
22
Background incidence rate (per 100,000 py)


Myocarditis 18 to 49 EUUKBrazilAustralia
Myocarditis 50 to 59 EUUKBrazilAustralia
Myocarditis 60 to 69 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00

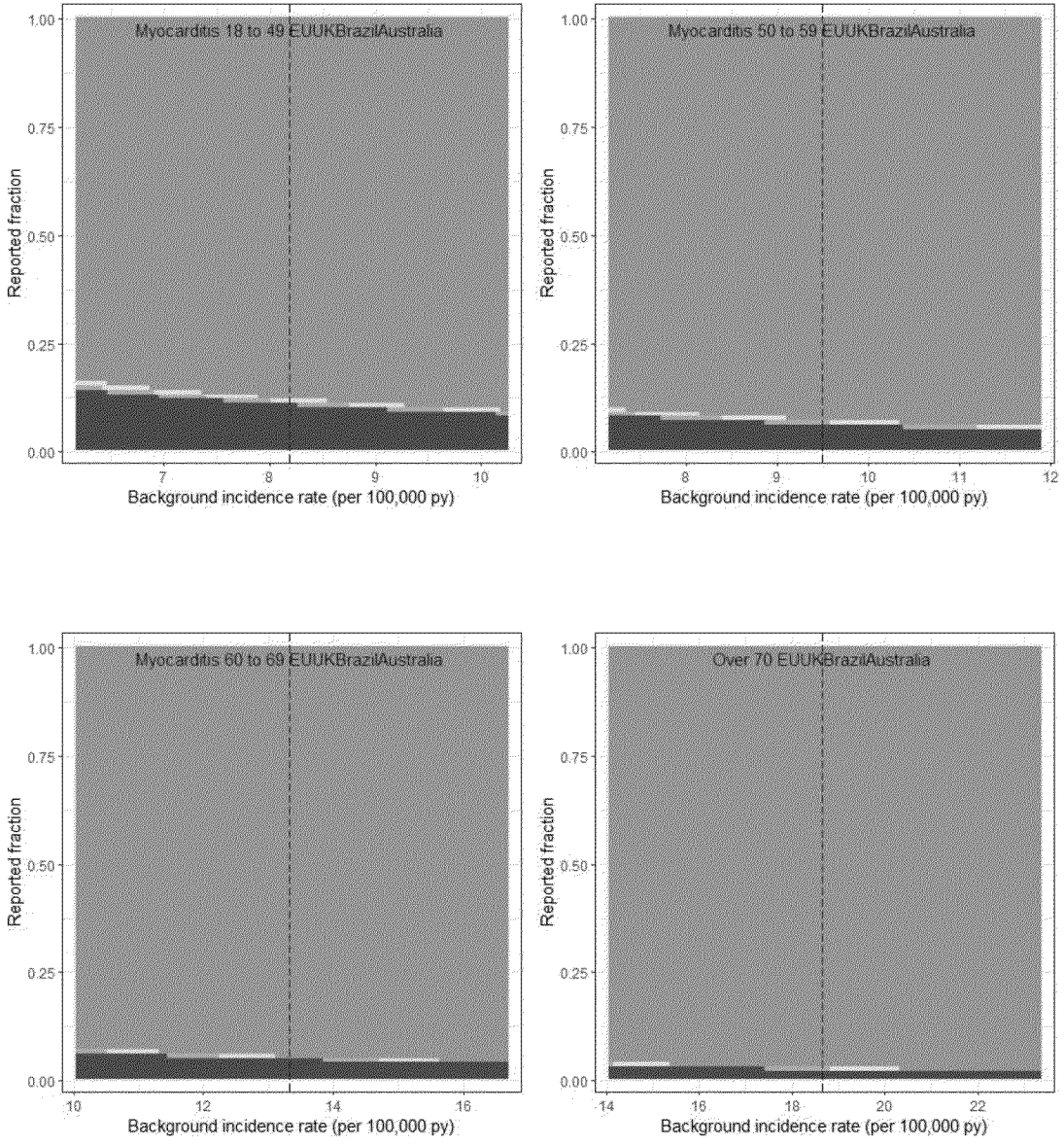
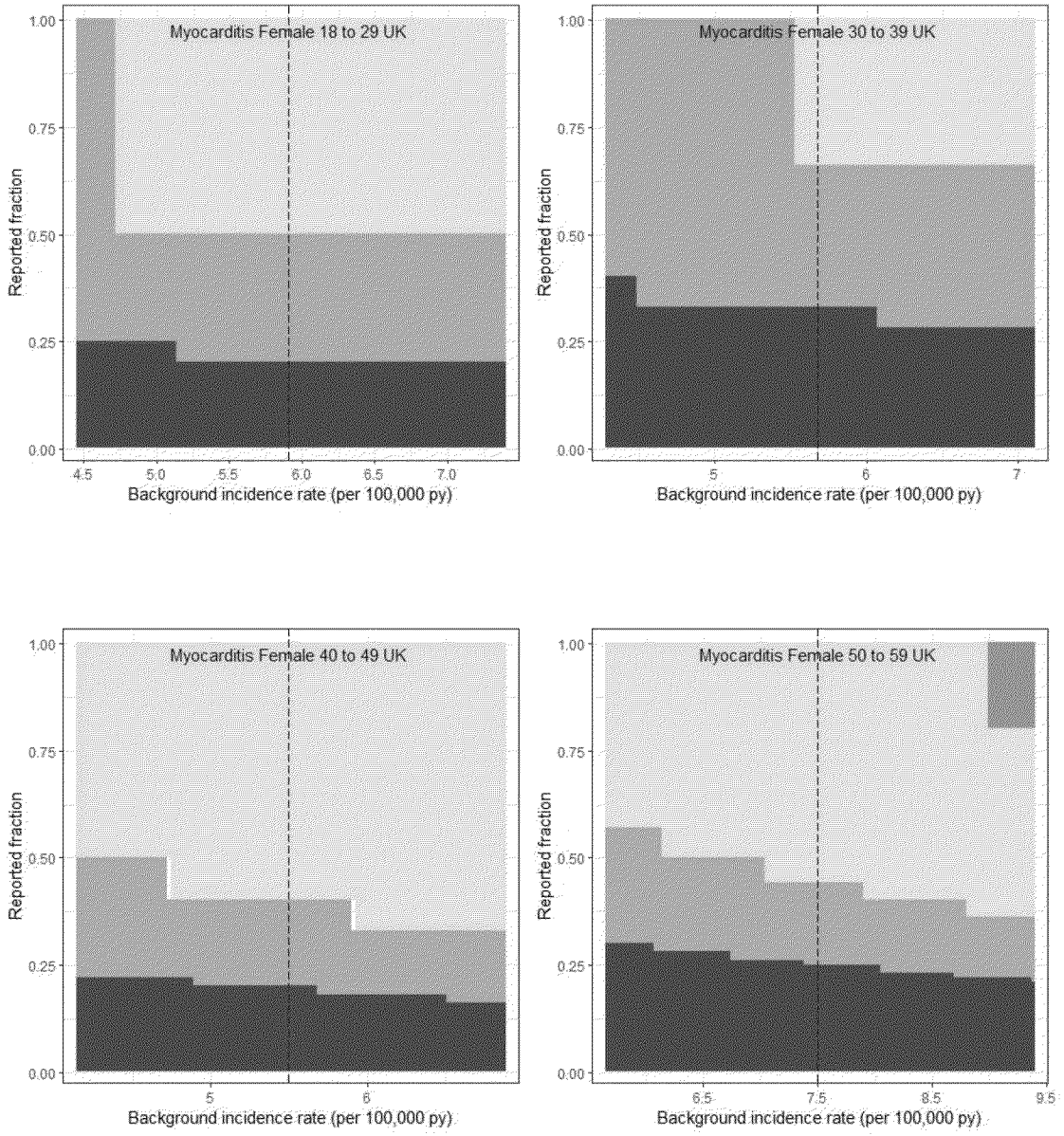
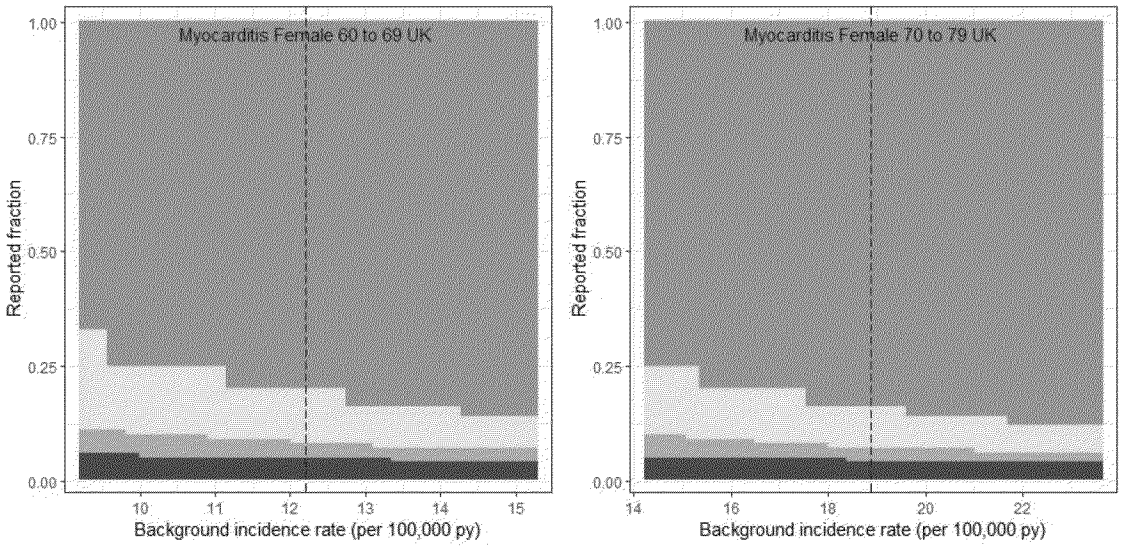

Myocarditis 18 to 49 EUUKBrazilAustralia
Myocarditis 50 to 59 EUUKBrazilAustralia
Myocarditis 60 to 69 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

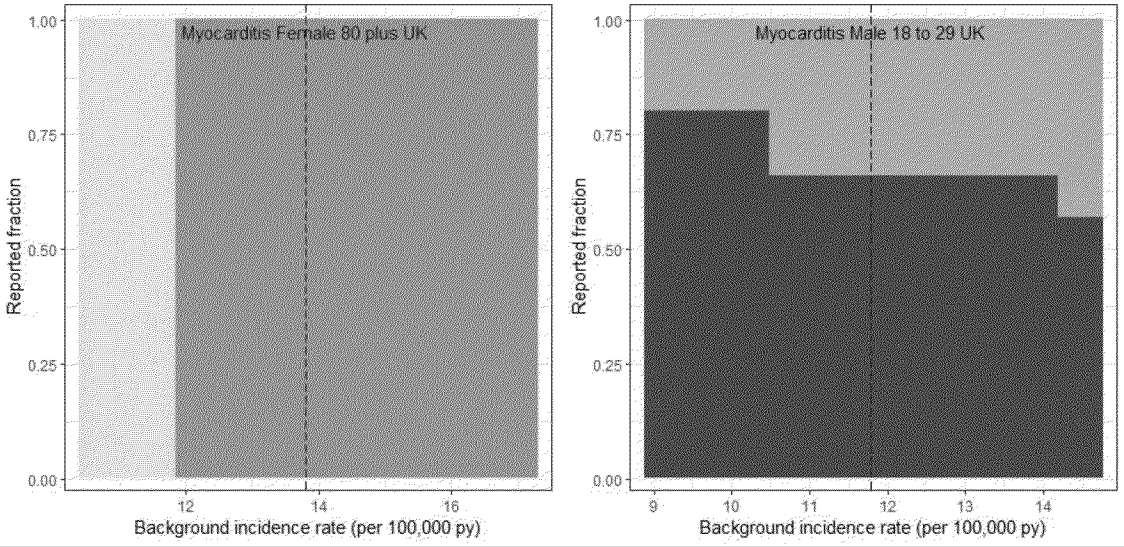
Table 48 Observed Versus Expected analysis for Myocarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Female 18-29 (UK)	1	1.26	7	5.91	1109488	0.79 (0.02 - 4.42)	Observed < expected
Female 30-39 (UK)	2	2.06	7	5.68	1892968	0.97 (0.12 - 3.51)	Observed < expected
Female 40-49 (UK)	2	4.65	7	5.5	4412245	0.43 (0.05 - 1.55)	Observed < expected
Female 50-59 (UK)	4	8.54	7	7.5	5944683	0.47 (0.13 - 1.2)	Observed < expected
Female 60-69 (UK)	1	11.19	7	12.21	4783416	0.09 (0 - 0.5)	Observed significantly < expected
Female 70-79 (UK)	1	12.58	7	18.88	3475875	0.08 (0 - 0.44)	Observed significantly < expected
Female ≥ 80 (UK)	0	4.32	7	13.81	1630324	0 (0 - 0.85)	Observed significantly < expected
Male 18-29 (UK)	4	1.83	7	11.79	808938	2.19 (0.6 - 5.6)	Observed > expected
Male 30-39 (UK)	2	2.89	7	10.67	1415003	0.69 (0.08 - 2.5)	Observed < expected
Male 40-49 (UK)	4	8.83	7	10.14	4542157	0.45 (0.12 - 1.16)	Observed < expected
Male 50-59 (UK)	5	14.64	7	11.73	6510960	0.34 (0.11 - 0.8)	Observed significantly < expected
Male 60-69 (UK)	1	13.78	7	14.57	4934728	0.07 (0 - 0.4)	Observed significantly < expected
Male 70-79 (UK)	1	12.86	7	21.39	3137304	0.08 (0 - 0.43)	Observed significantly < expected
Male ≥ 80 (UK)	0	2.57	7	13.09	1025046	0 (0 - 1.44)	Observed < expected

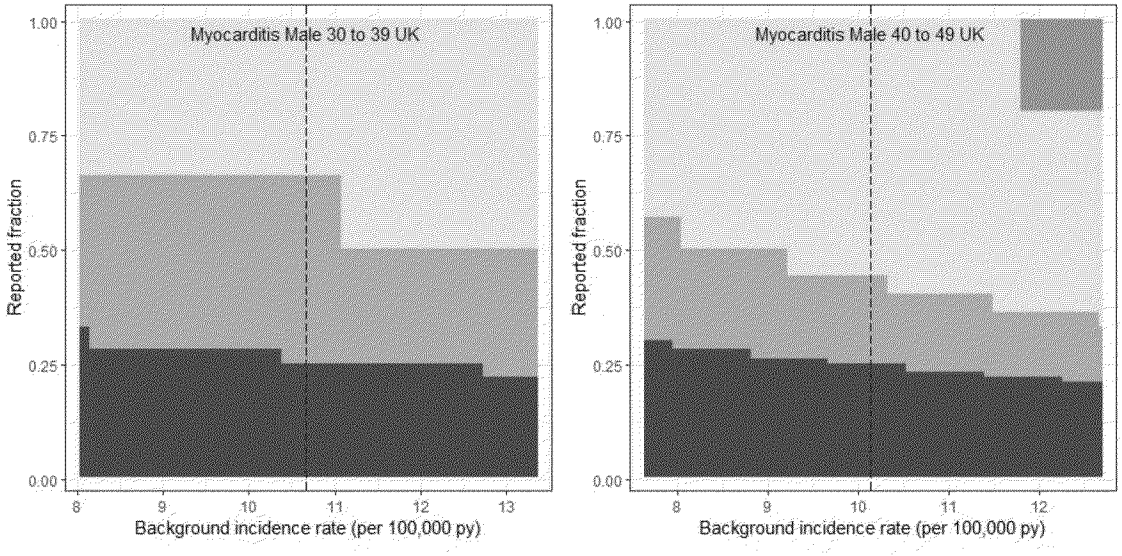

Myocarditis Female 18 to 29 UK
Myocarditis Female 30 to 39 UK
Myocarditis Female 40 to 49 UK
Myocarditis Female 50 to 59 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
4.5
5.0
5.5
6.0
6.5
7.0
5
6
7
6.5
7.5
8.5
9.5


Myocarditis Female 60 to 69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
10
11
12
13
14
15
Background incidence rate (per 100,000 py)

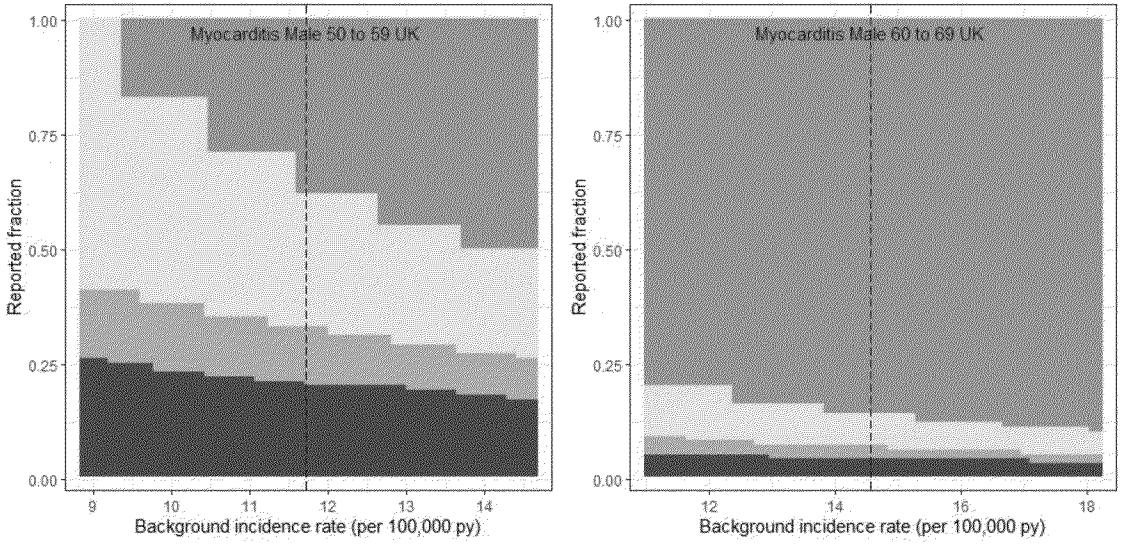
Myocarditis Female 70 to 79 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
14
16
18
20
22
Background incidence rate (per 100,000 py)


Myocarditis Female 80 plus UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
12
14
16
Background incidence rate (per 100,000 py)

Myocarditis Male 18 to 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
14
Background incidence rate (per 100,000 py)


Myocarditis Male 30 to 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
13
Background incidence rate (per 100,000 py)

Myocarditis Male 40 to 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Myocarditis Male 50 to 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
14
Background incidence rate (per 100,000 py)

Myocarditis Male 60 to 69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
12
14
16
18
Background incidence rate (per 100,000 py)

Table 48 Observed Versus Expected analysis for Myocarditis

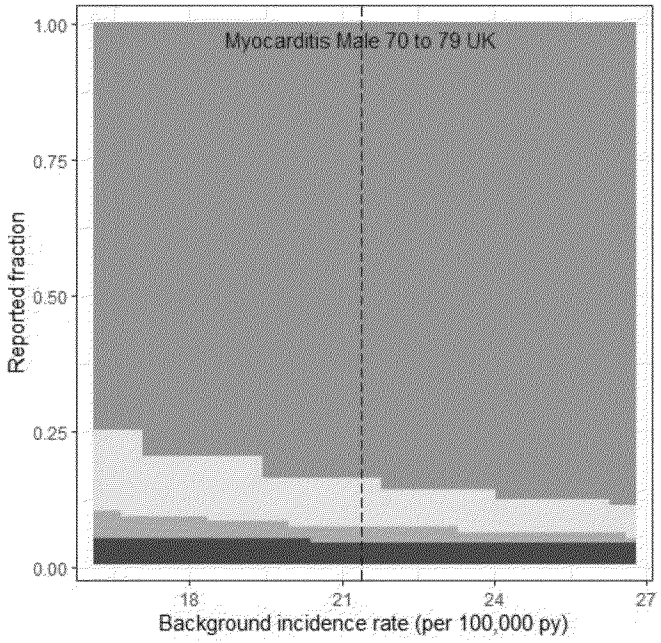
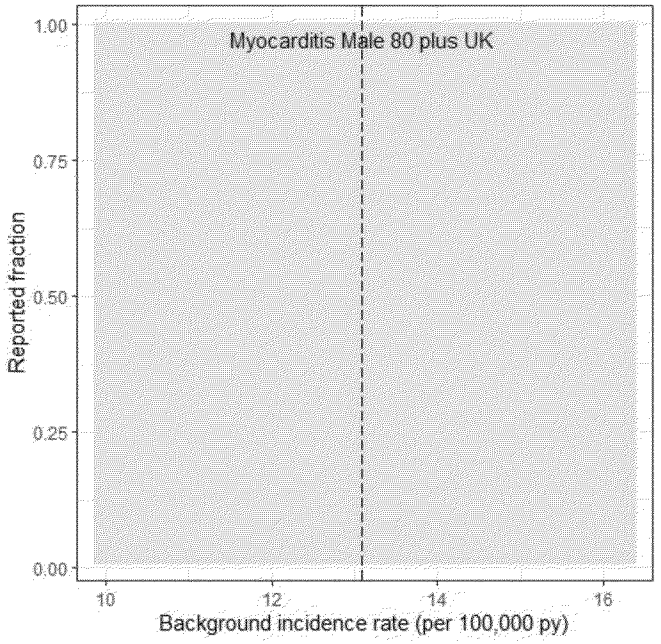
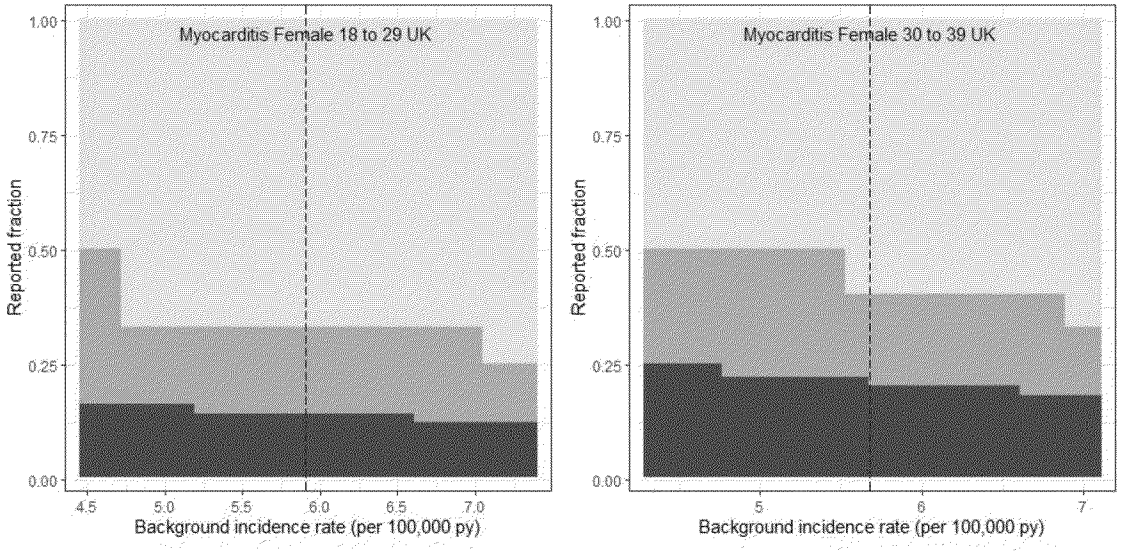
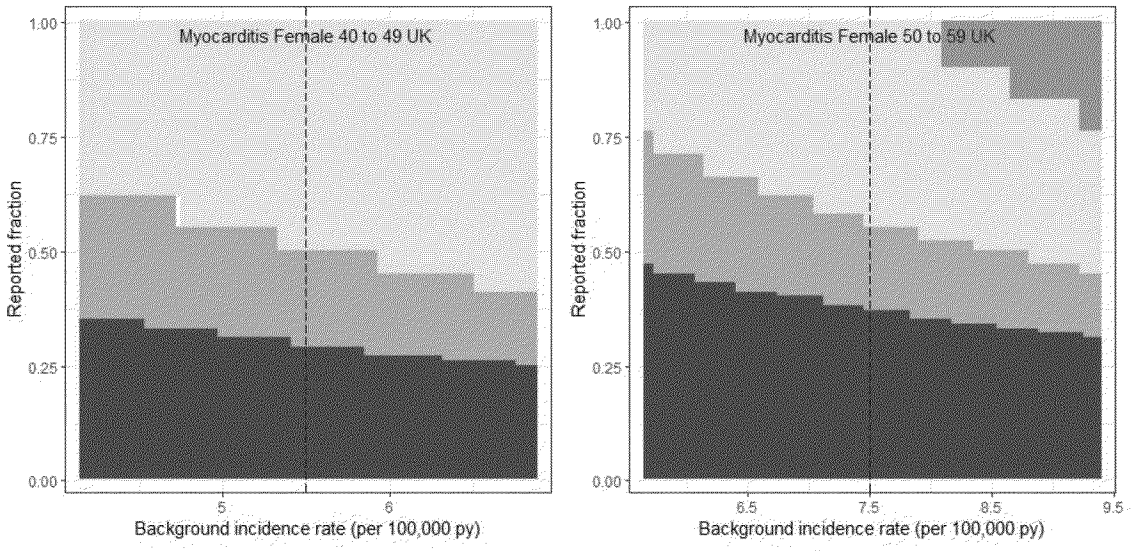
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							
							
Female 18-29 (UK)	1	2.51	14	5.91	1109488	0.4 (0.01 - 2.22)	Observed < expected
Female 30-39 (UK)	2	4.12	14	5.68	1892968	0.49 (0.06 - 1.75)	Observed < expected
Female 40-49 (UK)	5	9.3	14	5.5	4412245	0.54 (0.17 - 1.25)	Observed < expected
Female 50-59 (UK)	10	17.09	14	7.5	5944683	0.59 (0.28 - 1.08)	Observed < expected
Female 60-69 (UK)	4	22.39	14	12.21	4783416	0.18 (0.05 - 0.46)	Observed significantly < expected
Female 70-79 (UK)	1	25.15	14	18.88	3475875	0.04 (0 - 0.22)	Observed significantly < expected
Female ≥ 80 (UK)	0	8.63	14	13.81	1630324	0 (0 - 0.43)	Observed significantly < expected
Male 18-29 (UK)	5	3.66	14	11.79	808938	1.37 (0.44 - 3.19)	Observed > expected

Table 48 Observed Versus Expected analysis for Myocarditis

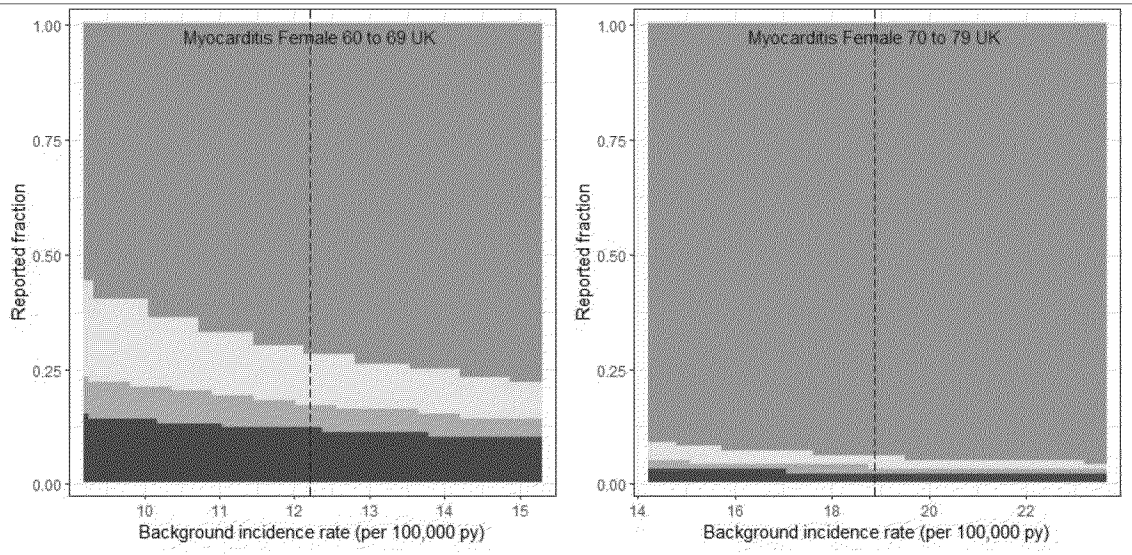
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Male 30-39 (UK)	2	5.79	14	10.67	1415003	0.35 (0.04 - 1.25)	Observed < expected
Male 40-49 (UK)	8	17.65	14	10.14	4542157	0.45 (0.2 - 0.89)	Observed significantly < expected
Male 50-59 (UK)	7	29.27	14	11.73	6510960	0.24 (0.1 - 0.49)	Observed significantly < expected
Male 60-69 (UK)	2	27.56	14	14.57	4934728	0.07 (0.01 - 0.26)	Observed significantly < expected
Male 70-79 (UK)	1	25.72	14	21.39	3137304	0.04 (0 - 0.22)	Observed significantly < expected
Male ≥ 80 (UK)	0	5.14	14	13.09	1025046	0 (0 - 0.72)	Observed significantly < expected


Myocarditis Female 18 to 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
4.5
5.0
5.5
6.0
6.5
7.0
Background incidence rate (per 100,000 py)

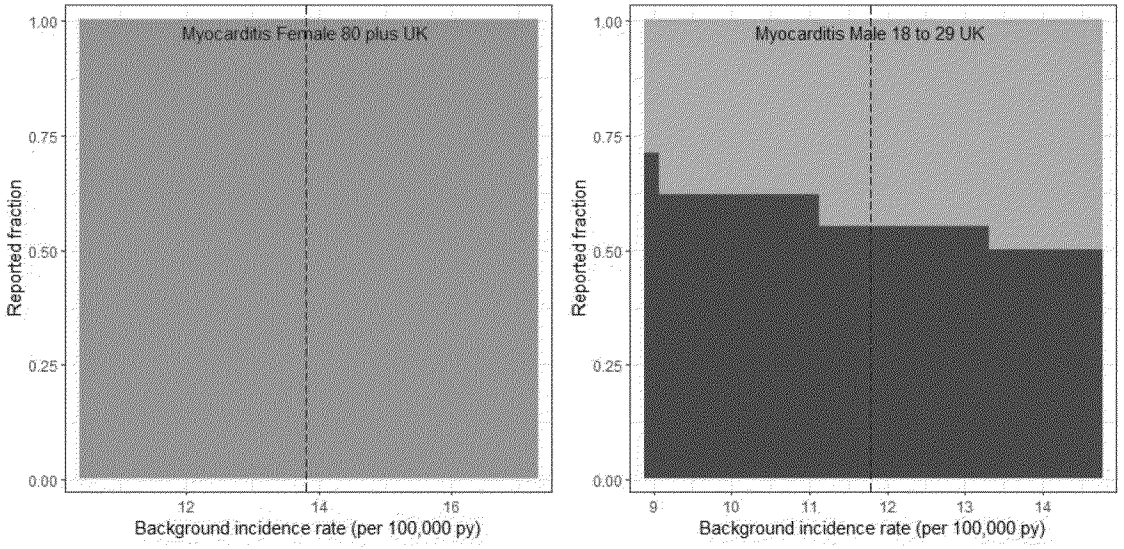
Myocarditis Female 30 to 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)


Myocarditis Female 40 to 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
Background incidence rate (per 100,000 py)

Myocarditis Female 50 to 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
6.5
7.5
8.5
9.5
Background incidence rate (per 100,000 py)


Myocarditis Female 60 to 69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
10
11
12
13
14
15
Background incidence rate (per 100,000 py)

Myocarditis Female 70 to 79 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
14
16
18
20
22
Background incidence rate (per 100,000 py)


Myocarditis Female 80 plus UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
12
14
16
Background incidence rate (per 100,000 py)

Myocarditis Male 18 to 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
14
Background incidence rate (per 100,000 py)

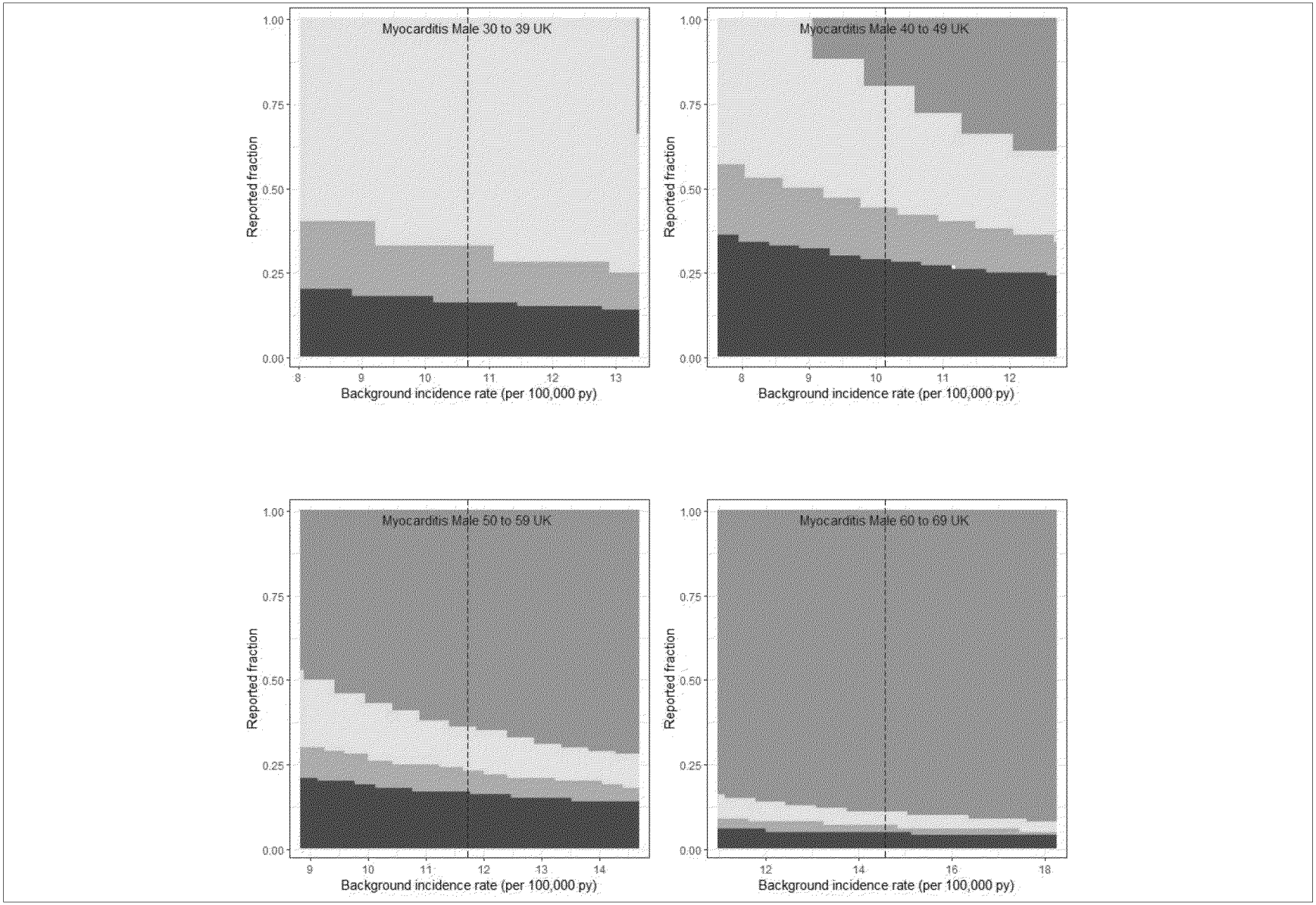

Myocarditis Male 30 to 39 UK
Myocarditis Male 40 to 49 UK
Myocarditis Male 50 to 59 UK
Myocarditis Male 60 to 69 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00

Table 48 Observed Versus Expected analysis for Myocarditis

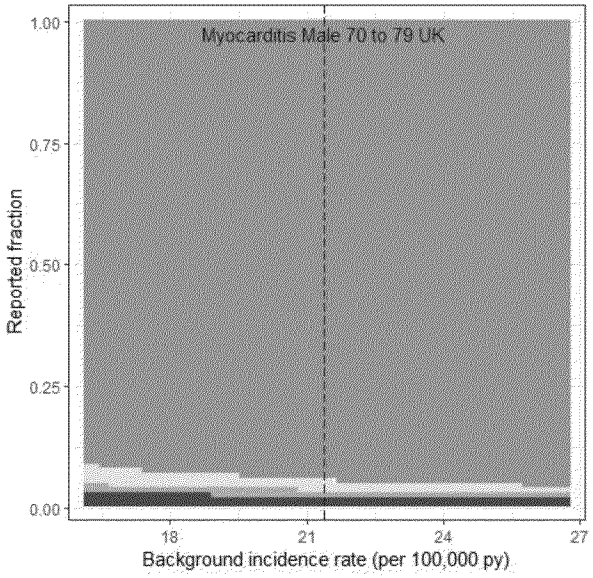
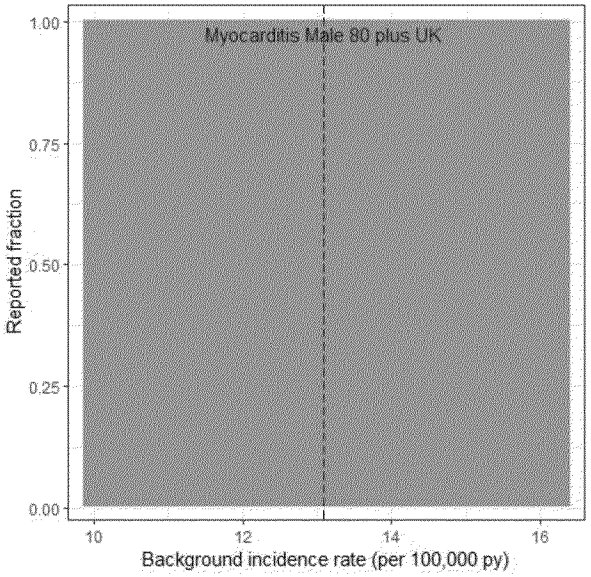
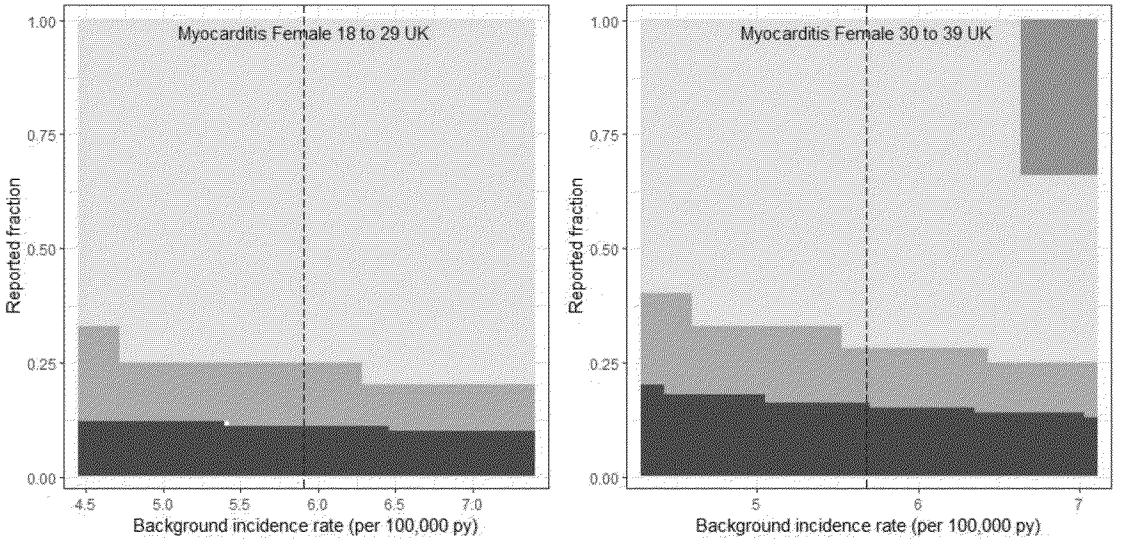
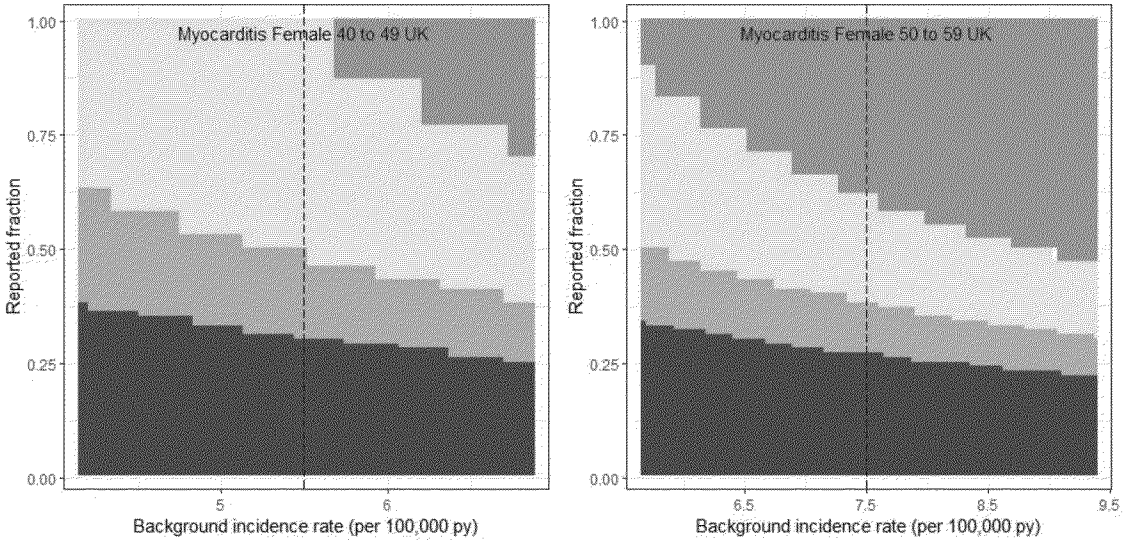
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							
							
Female 18-29 (UK)	1	3.77	21	5.91	1109488	0.27 (0.01 - 1.48)	Observed < expected
Female 30-39 (UK)	2	6.18	21	5.68	1892968	0.32 (0.04 - 1.17)	Observed < expected
Female 40-49 (UK)	7	13.95	21	5.5	4412245	0.5 (0.2 - 1.03)	Observed < expected
Female 50-59 (UK)	10	25.63	21	7.5	5944683	0.39 (0.19 - 0.72)	Observed significantly < expected
Female 60-69 (UK)	5	33.58	21	12.21	4783416	0.15 (0.05 - 0.35)	Observed significantly < expected
Female 70-79 (UK)	1	37.73	21	18.88	3475875	0.03 (0 - 0.15)	Observed significantly < expected
Female ≥ 80 (UK)	0	12.95	21	13.81	1630324	0 (0 - 0.28)	Observed significantly < expected
Male 18-29 (UK)	5	5.48	21	11.79	808938	0.91 (0.3 - 2.13)	Observed < expected
Male 30-39 (UK)	3	8.68	21	10.67	1415003	0.35 (0.07 - 1.01)	Observed < expected

Table 48 Observed Versus Expected analysis for Myocarditis

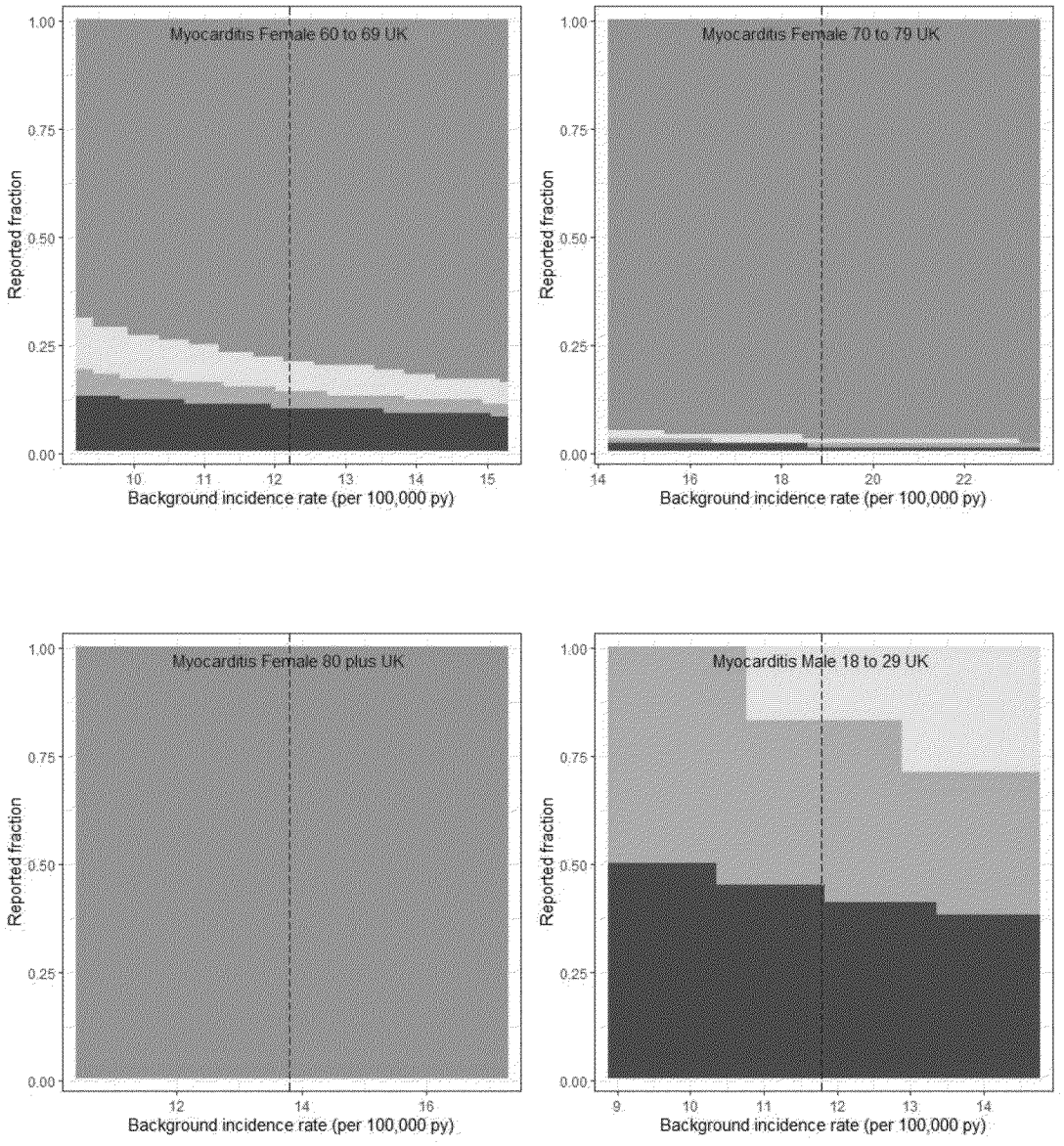
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Male 40-49 (UK)	8	26.48	21	10.14	4542157	0.3 (0.13 - 0.6)	Observed significantly < expected
Male 50-59 (UK)	7	43.91	21	11.73	6510960	0.16 (0.06 - 0.33)	Observed significantly < expected
Male 60-69 (UK)	2	41.34	21	14.57	4934728	0.05 (0.01 - 0.17)	Observed significantly < expected
Male 70-79 (UK)	1	38.58	21	21.39	3137304	0.03 (0 - 0.14)	Observed significantly < expected
Male ≥ 80 (UK)	0	7.71	21	13.09	1025046	0 (0 - 0.48)	Observed significantly < expected


Myocarditis Female 18 to 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
4.5
5.0
5.5
6.0
6.5
7.0
Background incidence rate (per 100,000 py)

Myocarditis Female 30 to 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)


Myocarditis Female 40 to 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
Background incidence rate (per 100,000 py)

Myocarditis Female 50 to 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
6.5
7.5
8.5
9.5
Background incidence rate (per 100,000 py)


Myocarditis Female 60 to 69 UK
Myocarditis Female 70 to 79 UK
Myocarditis Female 80 plus UK
Myocarditis Male 18 to 29 UK
Reported fraction
Background incidence rate (per 100,000 py)

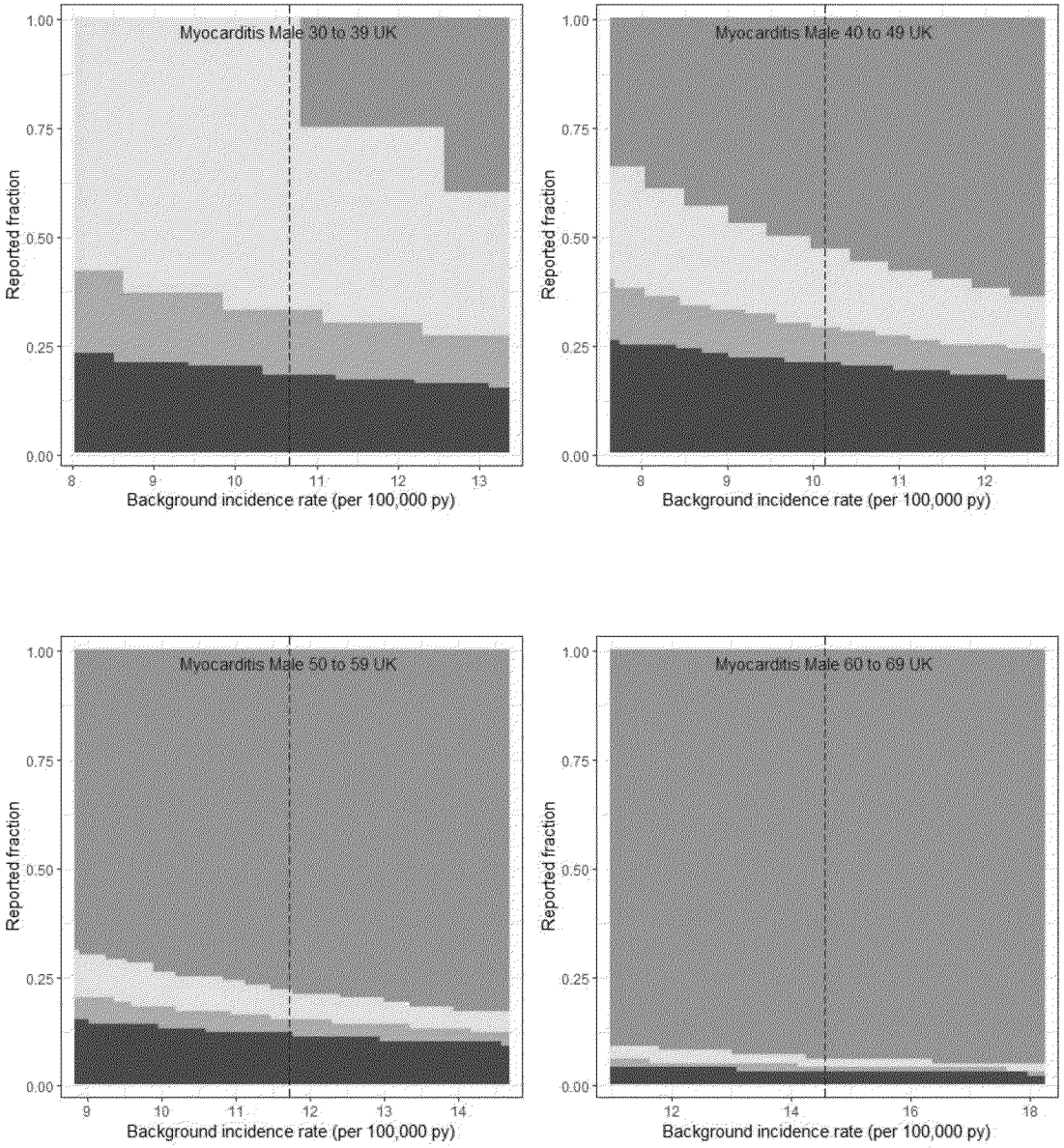

Myocarditis Male 30 to 39 UK
Myocarditis Male 40 to 49 UK
Myocarditis Male 50 to 59 UK
Myocarditis Male 60 to 69 UK
Reported fraction
Background incidence rate (per 100,000 py)

Table 48 Observed Versus Expected analysis for Myocarditis

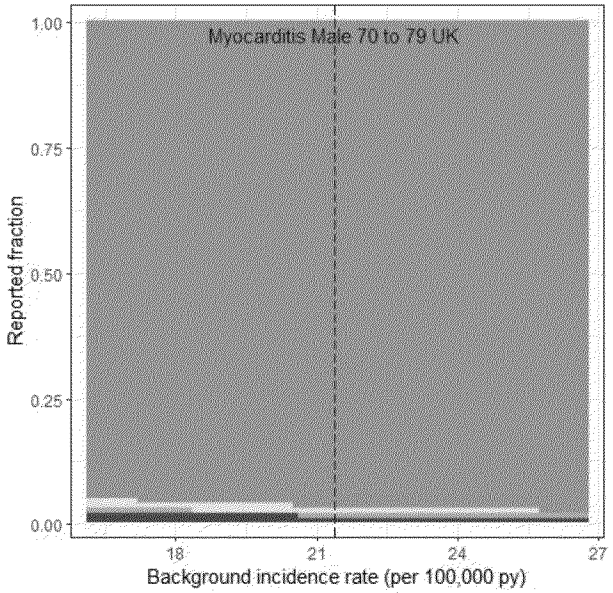
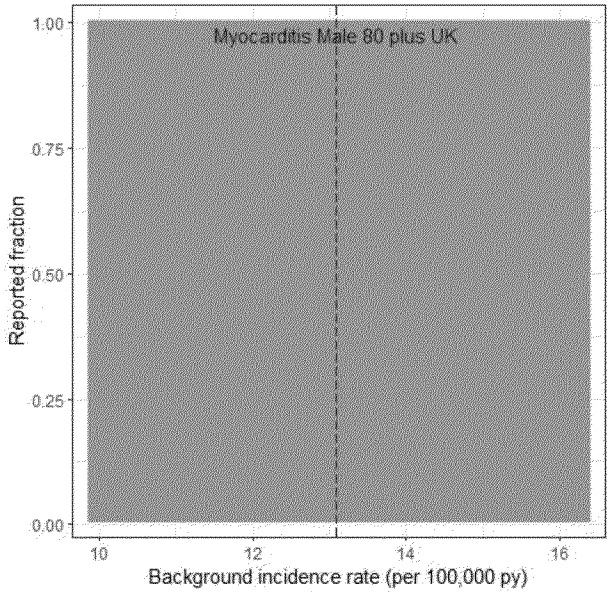
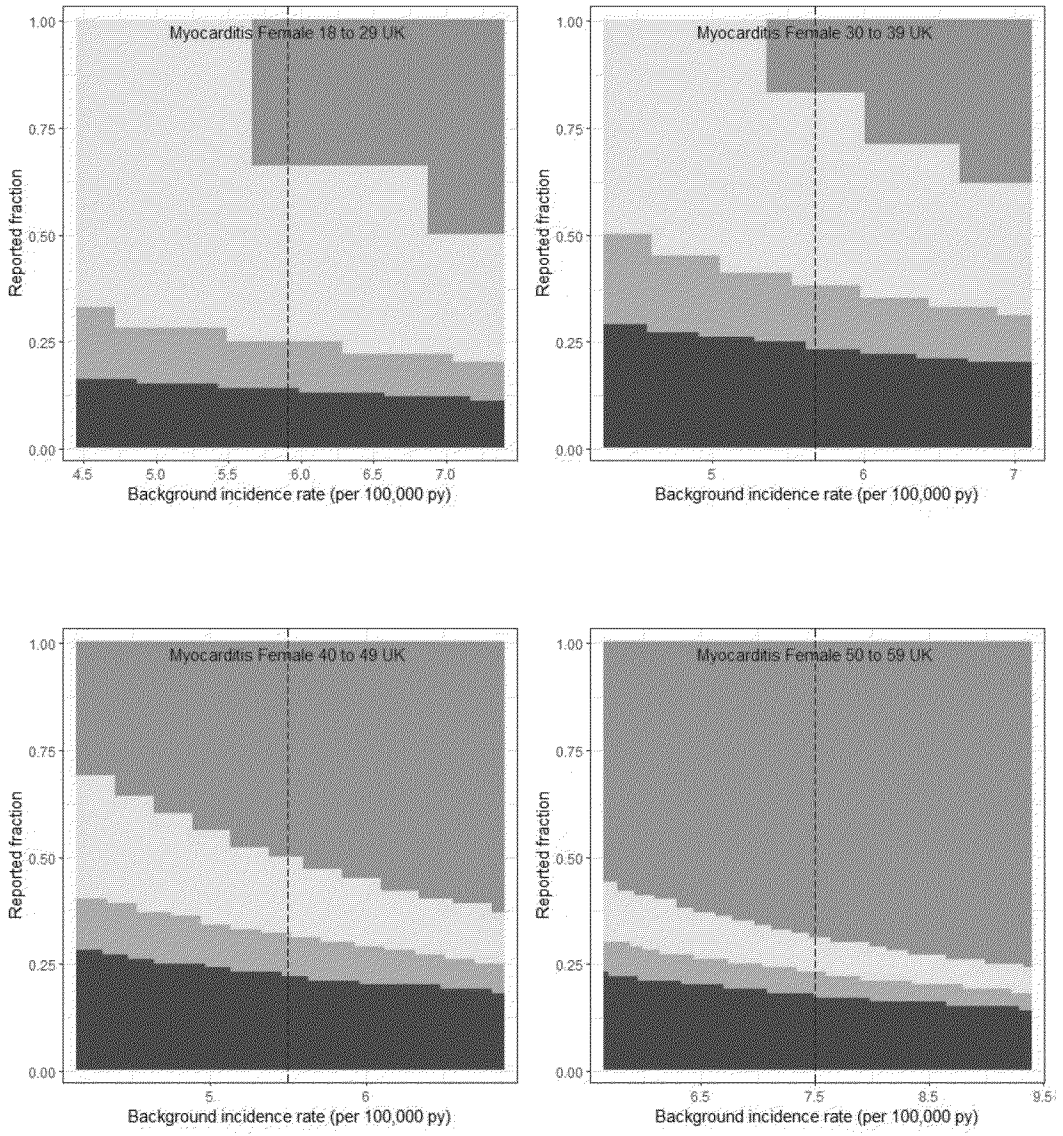
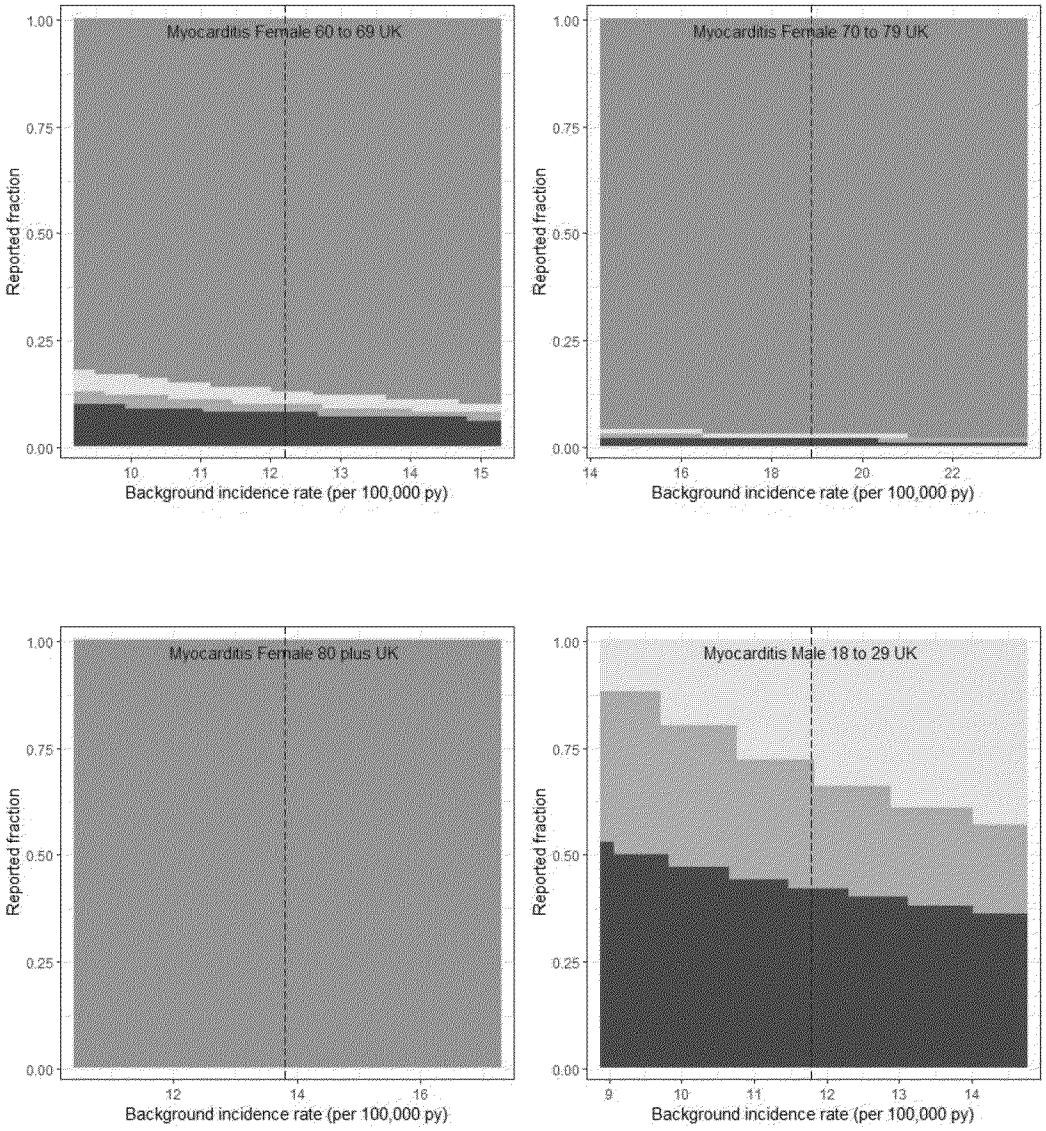
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							
							
Female 18-29 (UK)	2	7.54	42	5.91	1109488	0.27 (0.03 - 0.96)	Observed significantly < expected
Female 30-39 (UK)	5	12.36	42	5.68	1892968	0.4 (0.13 - 0.94)	Observed significantly < expected
Female 40-49 (UK)	9	27.91	42	5.5	4412245	0.32 (0.15 - 0.61)	Observed significantly < expected
Female 50-59 (UK)	12	51.27	42	7.5	5944683	0.23 (0.12 - 0.41)	Observed significantly < expected
Female 60-69 (UK)	7	67.16	42	12.21	4783416	0.1 (0.04 - 0.21)	Observed significantly < expected
Female 70-79 (UK)	2	75.46	42	18.88	3475875	0.03 (0 - 0.1)	Observed significantly < expected
Female ≥ 80 (UK)	0	25.89	42	13.81	1630324	0 (0 - 0.14)	Observed significantly < expected
Male 18-29 (UK)	8	10.97	42	11.79	808938	0.73 (0.31 - 1.44)	Observed < expected
Male 30-39 (UK)	5	17.36	42	10.67	1415003	0.29 (0.09 - 0.67)	Observed significantly < expected

Table 48 Observed Versus Expected analysis for Myocarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Male 40-49 (UK)	11	52.96	42	10.14	4542157	0.21 (0.1 - 0.37)	Observed significantly < expected
Male 50-59 (UK)	9	87.82	42	11.73	6510960	0.1 (0.05 - 0.19)	Observed significantly < expected
Male 60-69 (UK)	3	82.68	42	14.57	4934728	0.04 (0.01 - 0.11)	Observed significantly < expected
Male 70-79 (UK)	2	77.17	42	21.39	3137304	0.03 (0 - 0.09)	Observed significantly < expected
Male ≥ 80 (UK)	0	15.43	42	13.09	1025046	0 (0 - 0.24)	Observed significantly < expected


Myocarditis Female 18 to 29 UK
Myocarditis Female 30 to 39 UK
Myocarditis Female 40 to 49 UK
Myocarditis Female 50 to 59 UK
Reported fraction
Background incidence rate (per 100,000 py)


Myocarditis Female 60 to 69 UK
Myocarditis Female 70 to 79 UK
Myocarditis Female 80 plus UK
Myocarditis Male 18 to 29 UK
Reported fraction
Background incidence rate (per 100,000 py)

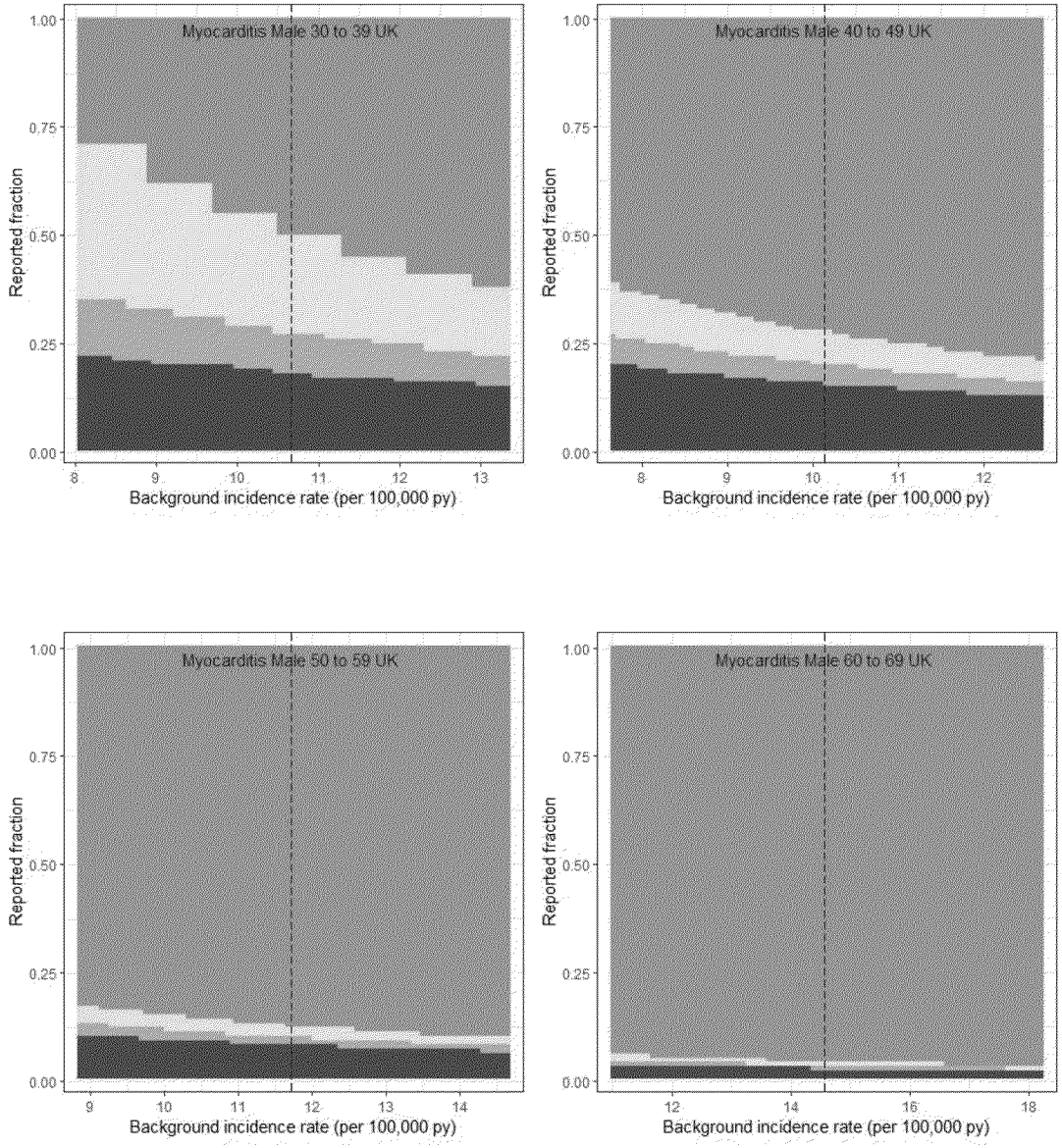
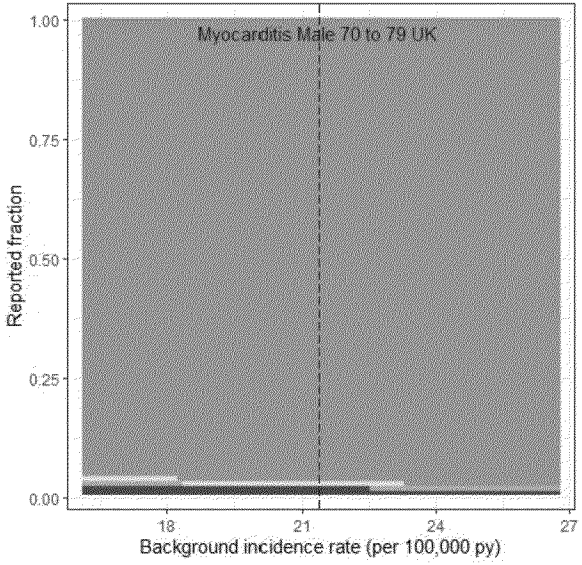
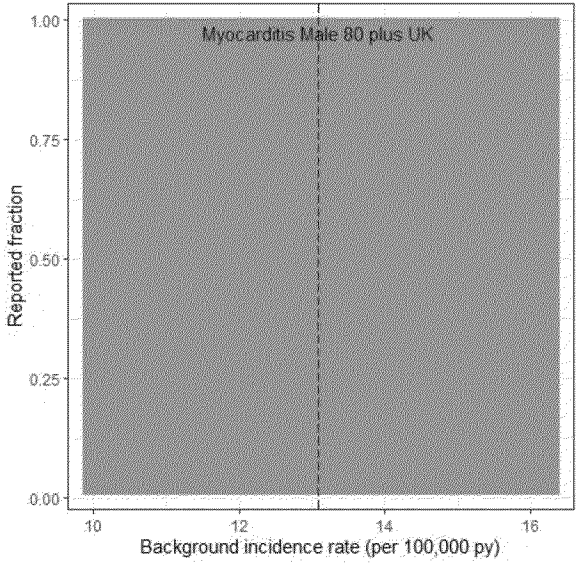

Myocarditis Male 30 to 39 UK
Myocarditis Male 40 to 49 UK
Myocarditis Male 50 to 59 UK
Myocarditis Male 60 to 69 UK
Reported fraction
Background incidence rate (per 100,000 py)

Table 48 Observed Versus Expected analysis for Myocarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							
							

[a] Incidence rate from Truven Marketscan.

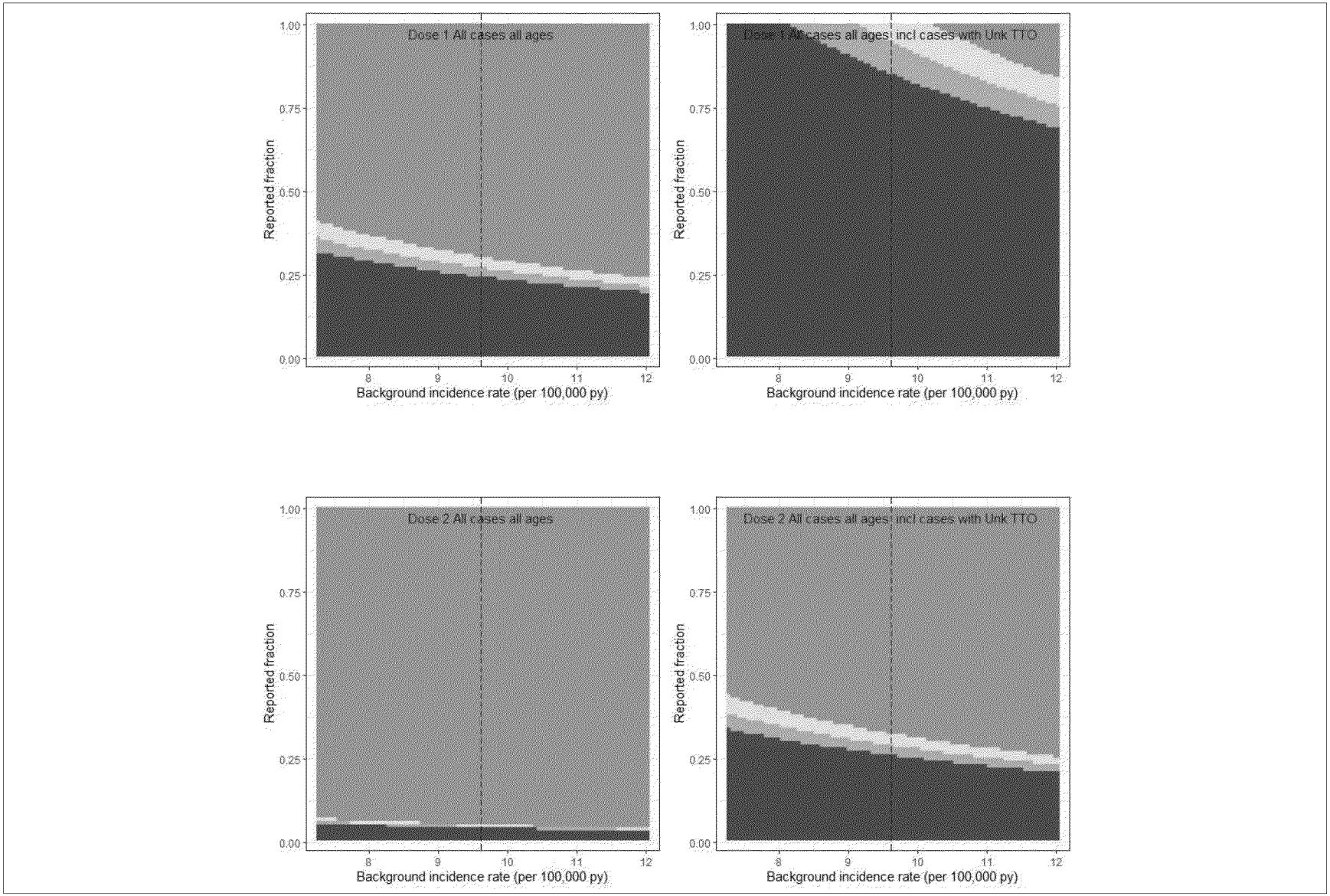
CI Confidence Interval; BR Brazil; AU Australia; E Expected; EU European Union; Observed; RW risk window; TTO Time to onset; UK United Kingdom

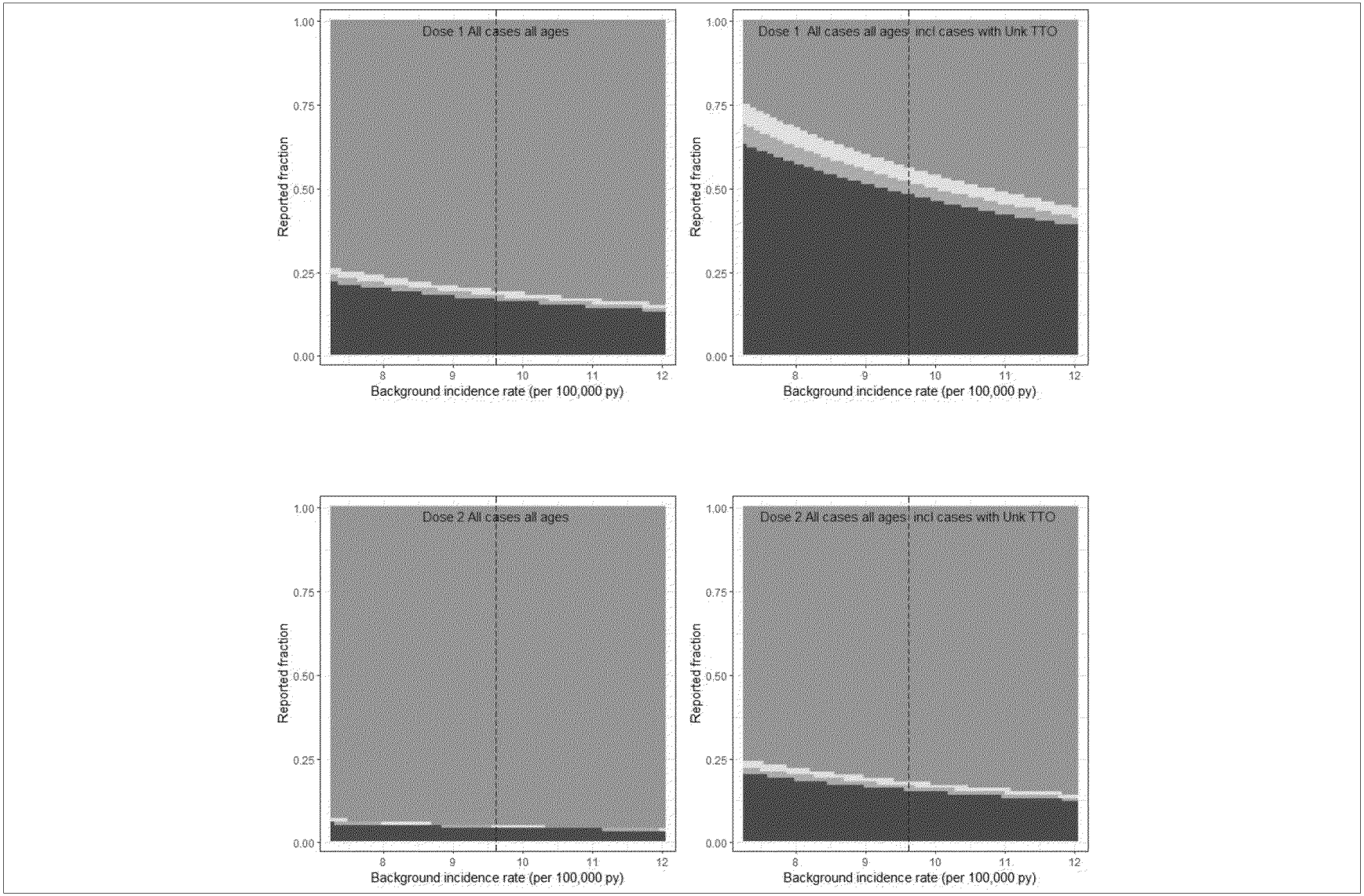
Table 49 Observed Versus Expected analysis for Myocarditis cases from EU/UK/Australia/Canada/Argentina/Malaysia/New Zealand/Colombia/Taiwan/Brazil/Thailand

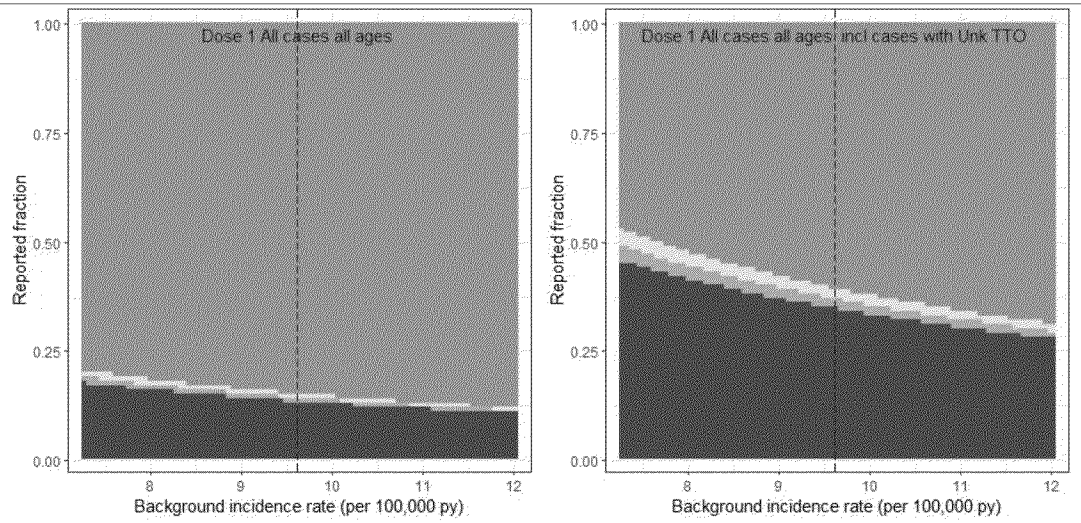
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Dose 1	88	322.73	7	9.62	175045647	0.27 (0.22 - 0.34)	Observed significantly < expected
Dose 1 (Including Unk TTO)	307	322.73	7	9.62	175045647	0.95 (0.85 - 1.06)	Observed < expected
Dose 2	15	312.23	7	9.62	169346503	0.05 (0.03 - 0.08)	Observed significantly < expected
Dose 2 (Including Unk TTO)	91	312.23	7	9.62	169346503	0.29 (0.23 - 0.36)	Observed significantly < expected
Dose 1	118	645.47	14	9.62	175045647	0.18 (0.15 - 0.22)	Observed significantly < expected
Dose 1 (Including Unk TTO)	337	645.47	14	9.62	175045647	0.52 (0.47 - 0.58)	Observed significantly < expected
Dose 2	31	624.45	14	9.62	169346503	0.05 (0.03 - 0.07)	Observed significantly < expected
Dose 2 (Including Unk TTO)	107	624.45	14	9.62	169346503	0.17 (0.14 - 0.21)	Observed significantly < expected
Dose 1	142	968.2	21	9.62	175045647	0.15 (0.12 - 0.17)	Observed significantly < expected
Dose 1 (Including Unk TTO)	361	968.2	21	9.62	175045647	0.37 (0.34 - 0.41)	Observed significantly < expected
Dose 2	35	936.68	21	9.62	169346503	0.04 (0.03 - 0.05)	Observed significantly < expected
Dose 2 (Including Unk TTO)	111	936.68	21	9.62	169346503	0.12 (0.1 - 0.14)	Observed significantly < expected
Dose 1	190	1936.4	42	9.62	175045647	0.1 (0.08 - 0.11)	Observed significantly < expected
Dose 1 (Including Unk TTO)	409	1936.4	42	9.62	175045647	0.21 (0.19 - 0.23)	Observed significantly < expected
Dose 2	63	1873.35	42	9.62	169346503	0.03 (0.03 - 0.04)	Observed significantly < expected

Table 49 Observed Versus Expected analysis for Myocarditis cases from EU/UK/Australia/Canada/Argentina/Malaysia/New Zealand/Colombia/Taiwan/Brazil/Thailand

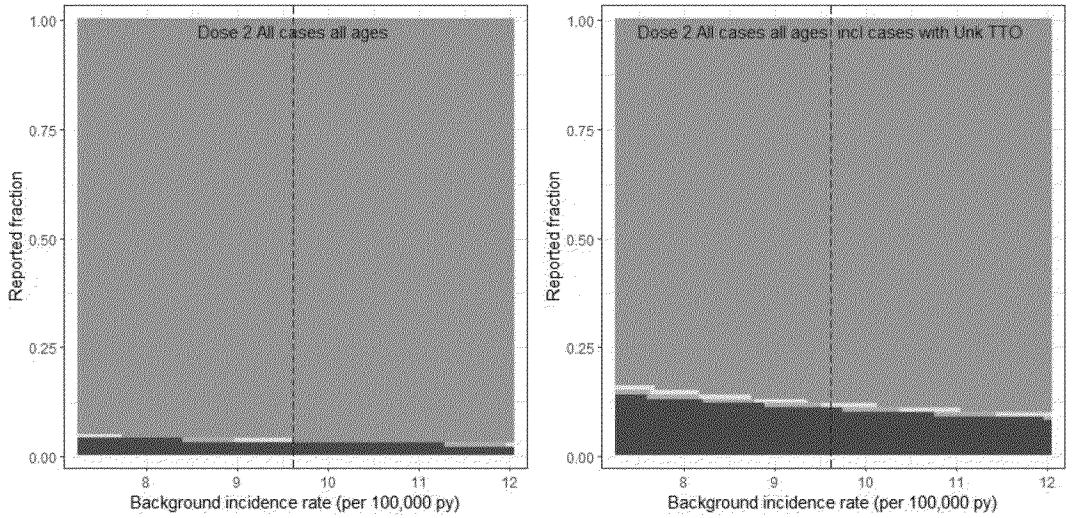
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Dose 2 (Including Unk TTO)	139	1873.35	42	9.62	169346503	0.07 (0.06 - 0.09)	Observed significantly < expected


Dose 1 All cases all ages
Dose 1 All cases all ages incl cases with Unk TTO
Dose 2 All cases all ages
Dose 2 All cases all ages incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Dose 1 All cases all ages
Dose 1 All cases all ages incl cases with Unk TTO
Dose 2 All cases all ages
Dose 2 All cases all ages incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

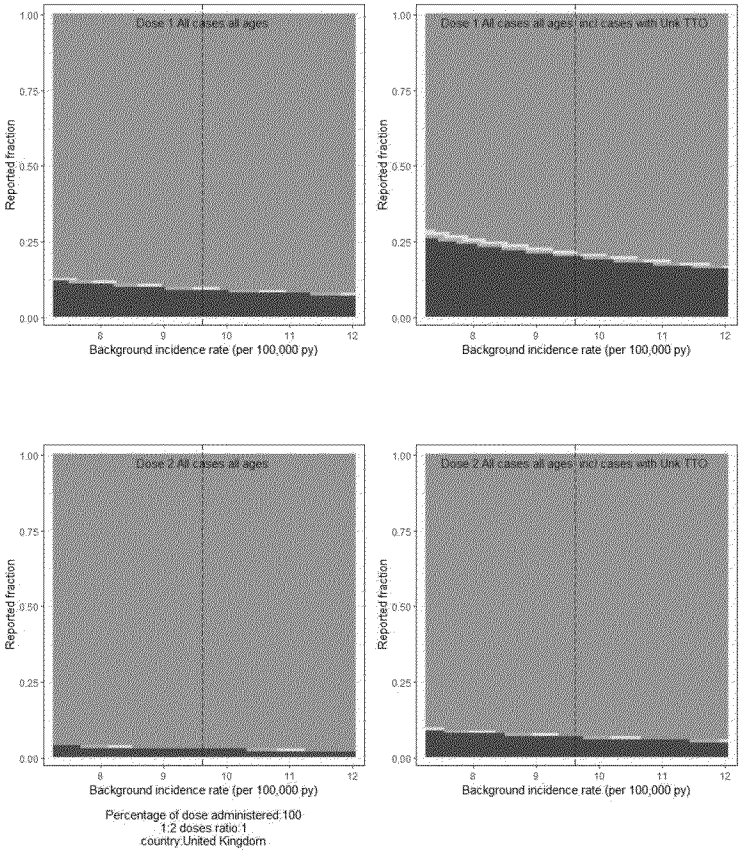

Dose 1 All cases all ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

Dose 1 All cases all ages; incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)


Dose 2 All cases all ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

Dose 2 All cases all ages; incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
8
9
10
11
12
Background incidence rate (per 100,000 py)

Table 49 Observed Versus Expected analysis for Myocarditis cases from EU/UK/Australia/Canada/Argentina/Malaysia/New Zealand/Colombia/Taiwan/Brazil/Thailand

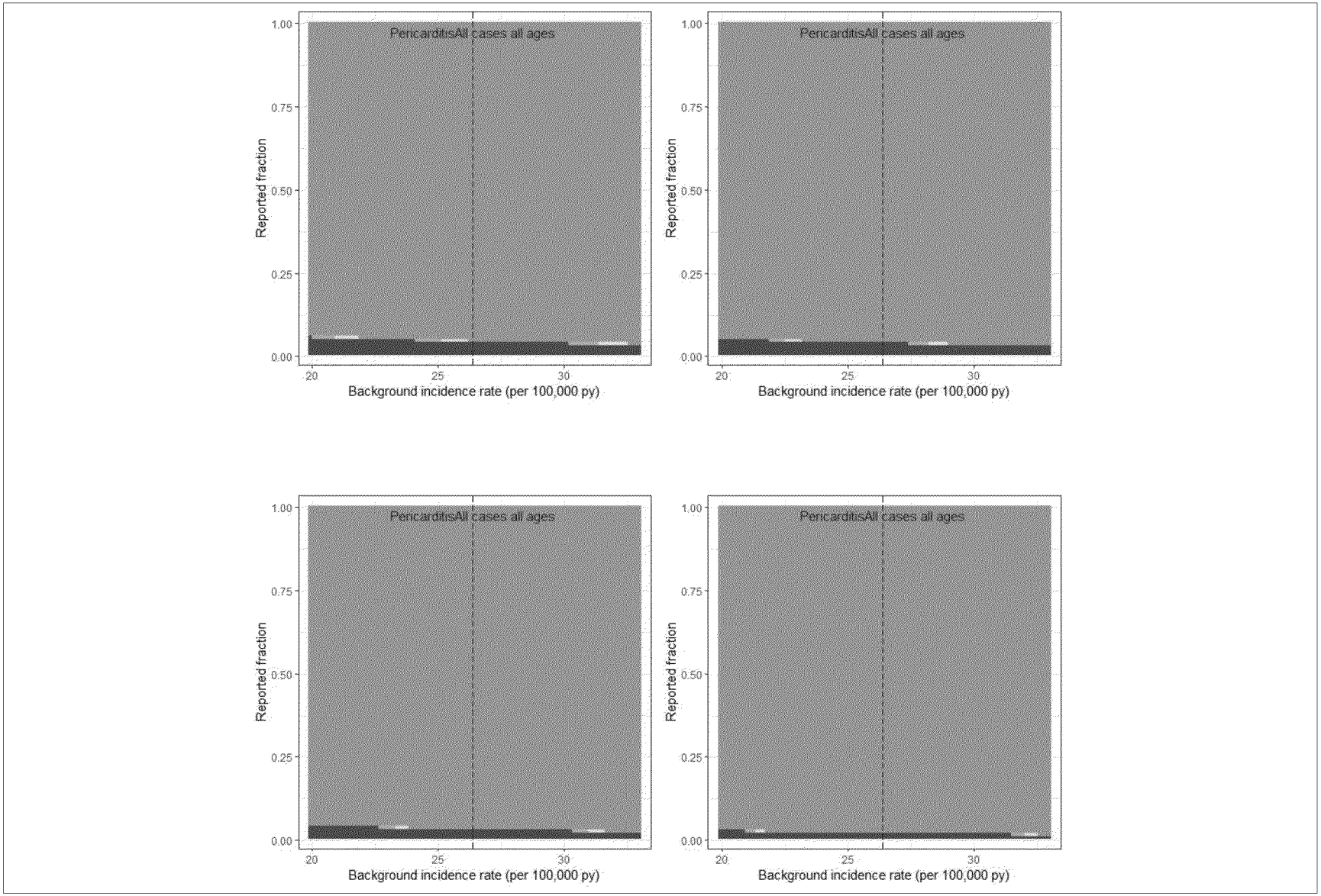
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

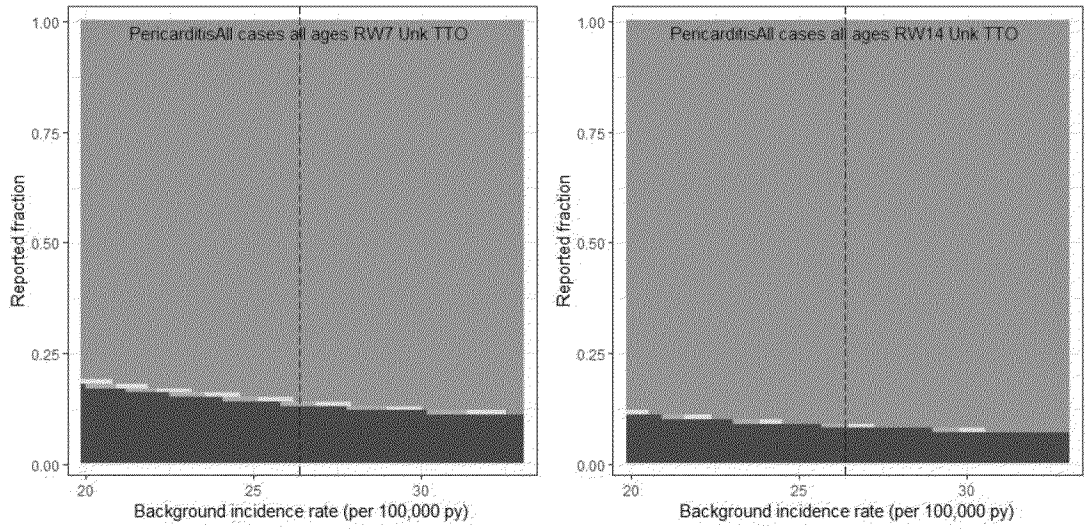
[a] Incidence rate from Truven Marketscan.

CI Confidence Interval; E Expected; EEA European Economic Area; O Observed; TTO Time to onset; UK United Kingdom; Unk Unknown

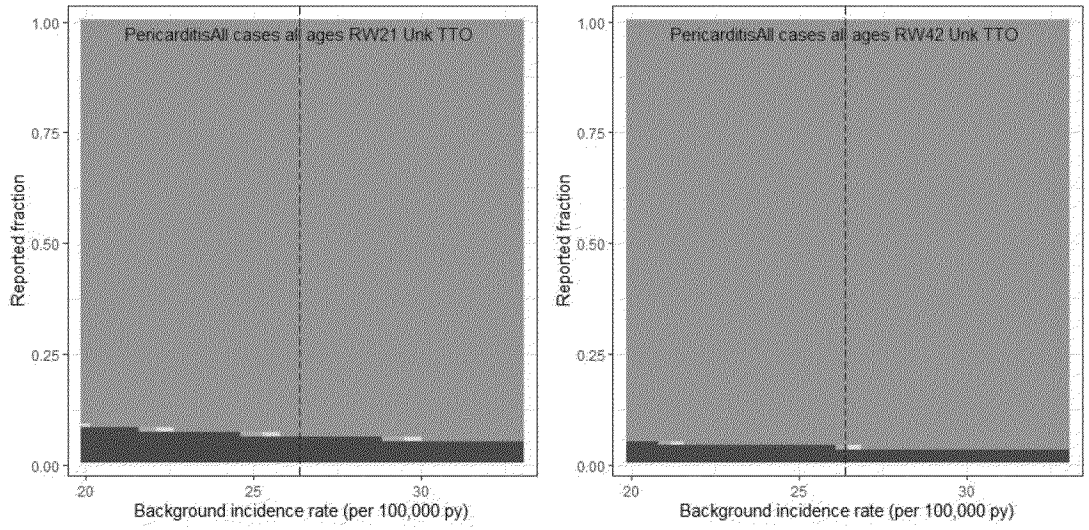
Table 50 Observed Versus Expected analysis for Pericarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
All Cases (Medically Confirmed and Non-Confirmed)							
All cases, all ages	112	2356.6	7	26.38	466115644	0.05 (0.04 - 0.06)	Observed significantly < expected
All cases, all ages	201	4713.19	14	26.38	466115644	0.04 (0.04 - 0.05)	Observed significantly < expected
All cases, all ages	249	7069.79	21	26.38	466115644	0.04 (0.03 - 0.04)	Observed significantly < expected
All cases, all ages	343	14139.58	42	26.38	466115644	0.02 (0.02 - 0.03)	Observed significantly < expected
All cases, all ages (RW 7+Unk TTO)	336	2356.6	7	26.38	466115644	0.14 (0.13 - 0.16)	Observed significantly < expected
All cases, all ages (RW 14+Unk TTO)	425	4713.19	14	26.38	466115644	0.09 (0.08 - 0.1)	Observed significantly < expected
All cases, all ages (RW 21+Unk TTO)	473	7069.79	21	26.38	466115644	0.07 (0.06 - 0.07)	Observed significantly < expected
All cases, all ages (RW 42+Unk TTO)	567	14139.58	42	26.38	466115644	0.04 (0.04 - 0.04)	Observed significantly < expected


PericarditisAll cases all ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)


PericarditisAll cases all ages RW7 Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

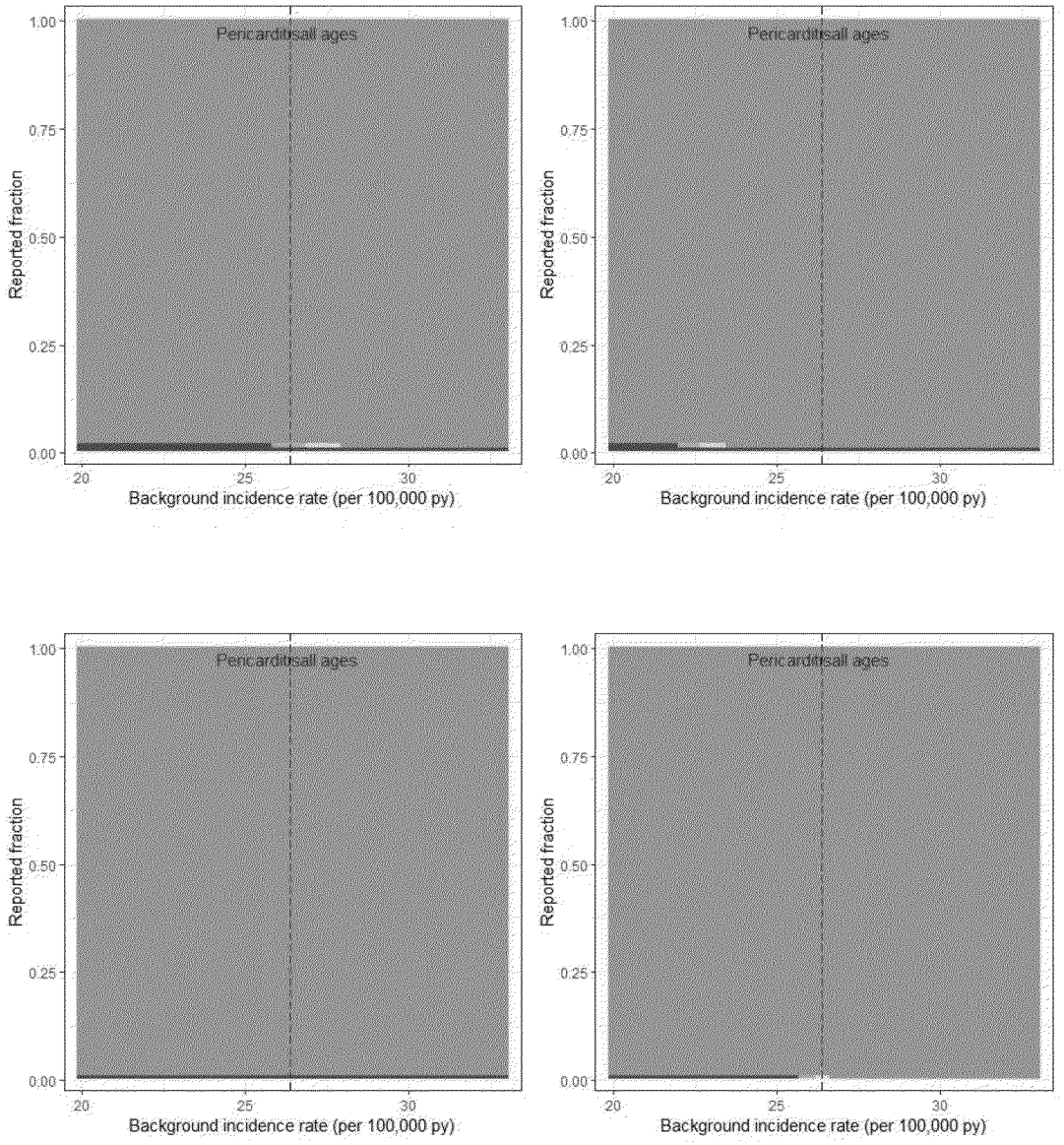
PericarditisAll cases all ages RW14 Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)


PericarditisAll cases all ages RW21 Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

PericarditisAll cases all ages RW42 Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

Table 50 Observed Versus Expected analysis for Pericarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Medically Confirmed Cases							
All ages	48	2356.6	7	26.38	466115644	0.02 (0.02 - 0.03)	Observed significantly < expected
All ages	81	4713.19	14	26.38	466115644	0.02 (0.01 - 0.02)	Observed significantly < expected
All ages	96	7069.79	21	26.38	466115644	0.01 (0.01 - 0.02)	Observed significantly < expected
All ages	140	14139.58	42	26.38	466115644	0.01 (0.01 - 0.01)	Observed significantly < expected
All ages (RW 7+Unk TTO)	122	2356.6	7	26.38	466115644	0.05 (0.04 - 0.06)	Observed significantly < expected
All ages (RW 14+Unk TTO)	155	4713.19	14	26.38	466115644	0.03 (0.03 - 0.04)	Observed significantly < expected
All ages (RW 21+Unk TTO)	170	7069.79	21	26.38	466115644	0.02 (0.02 - 0.03)	Observed significantly < expected
All ages (RW 42+Unk TTO)	214	14139.58	42	26.38	466115644	0.02 (0.01 - 0.02)	Observed significantly < expected


Pericarditisall ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

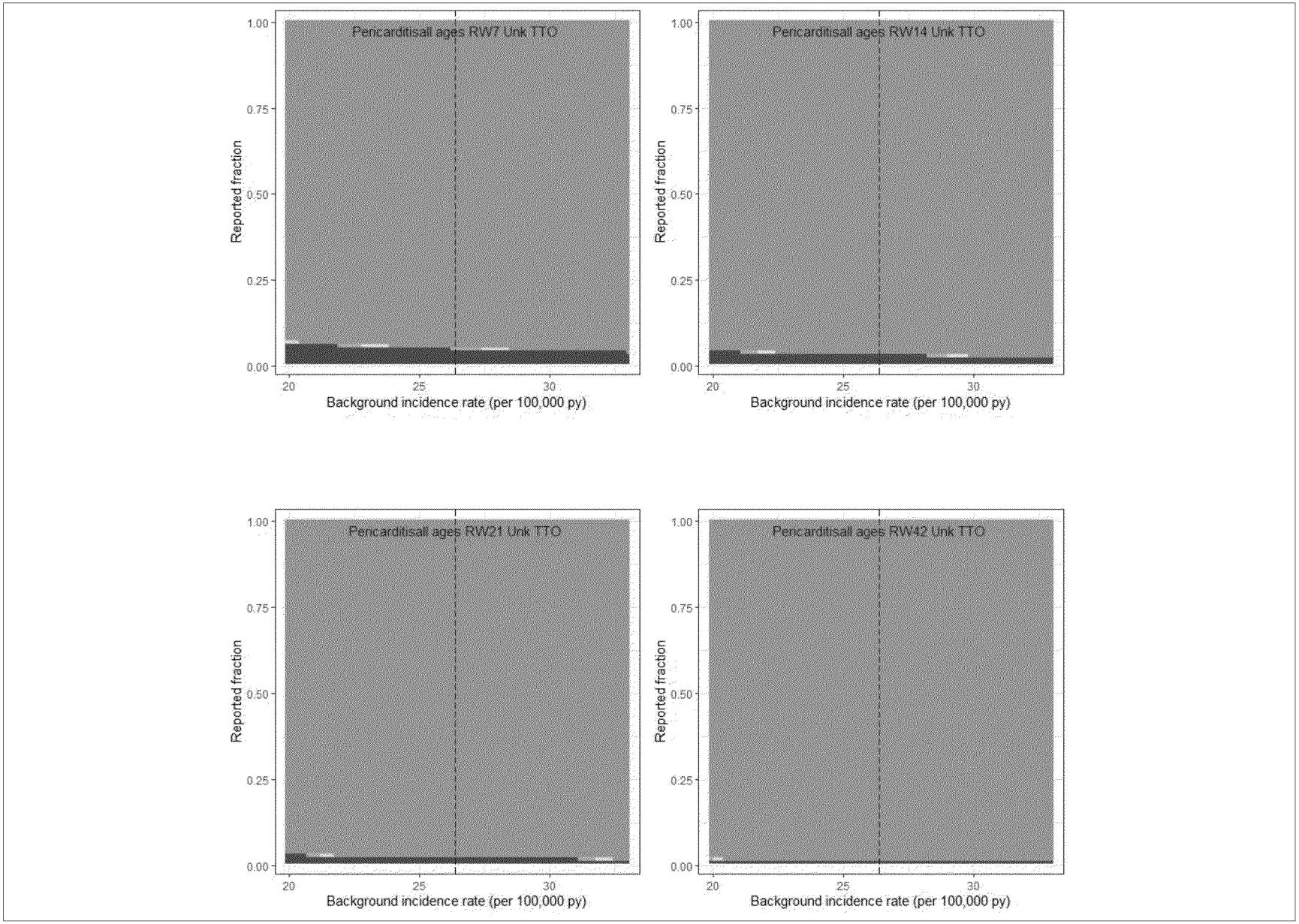
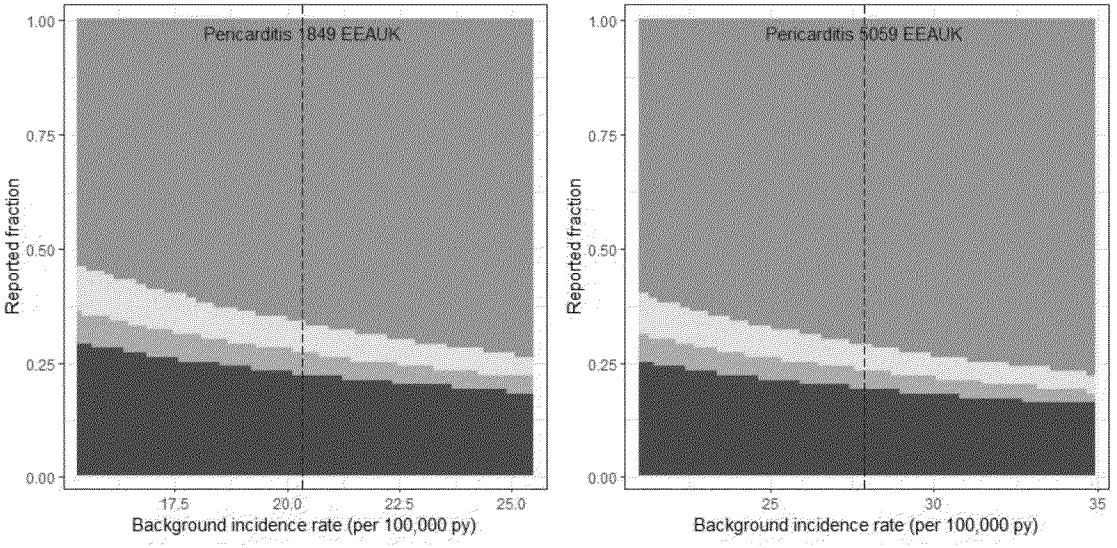

Pericarditisall ages RW7 Unk TTO
Pericarditisall ages RW14 Unk TTO
Pericarditisall ages RW21 Unk TTO
Pericarditisall ages RW42 Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

Table 50 Observed Versus Expected analysis for Pericarditis

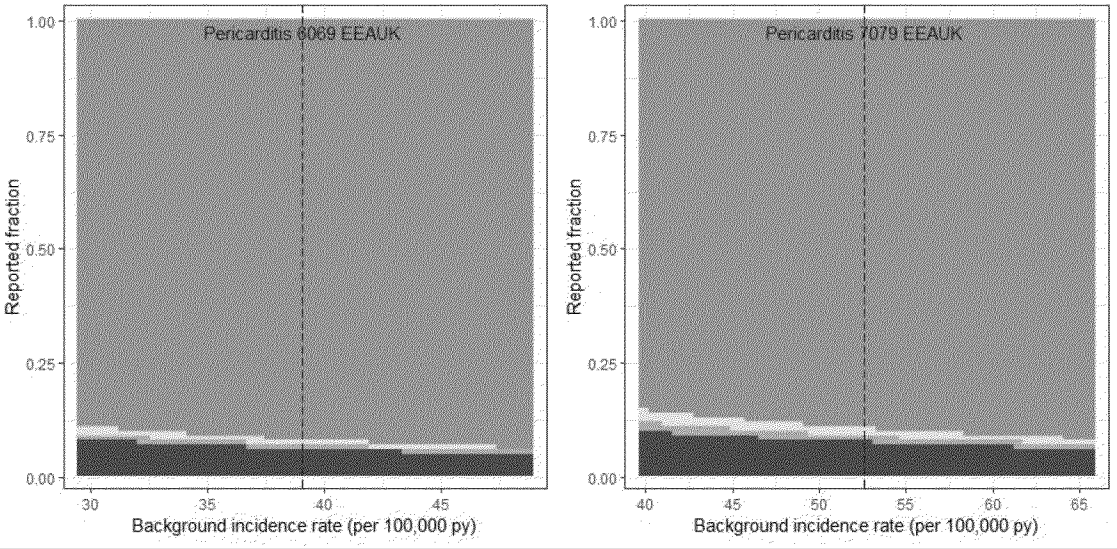
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
18-49 (EU/UK) (RW 7)	28	101.44	7	20.35	26009568	0.28 (0.18 - 0.4)	Observed significantly < expected
50-59 (EU/UK) (RW 7)	24	101.23	7	27.87	18951261	0.24 (0.15 - 0.35)	Observed significantly < expected
60-69 (EU/UK) (RW 7)	17	226.15	7	39.1	30179486	0.08 (0.04 - 0.12)	Observed significantly < expected
70-79 (EU/UK) (RW 7)	14	149.27	7	52.6	14806992	0.09 (0.05 - 0.16)	Observed significantly < expected
Over 80 (EU/UK) (RW 7)	0	49.52	7	67.63	3820736	0 (0 - 0.07)	Observed significantly < expected
18-49 (EU/UK) (RW 14)	54	202.88	14	20.35	26009568	0.27 (0.2 - 0.35)	Observed significantly < expected
50-59 (EU/UK) (RW 14)	38	202.45	14	27.87	18951261	0.19 (0.13 - 0.26)	Observed significantly < expected
60-69 (EU/UK) (RW 14)	29	452.31	14	39.1	30179486	0.06 (0.04 - 0.09)	Observed significantly < expected
70-79 (EU/UK) (RW 14)	19	298.54	14	52.6	14806992	0.06 (0.04 - 0.1)	Observed significantly < expected
Over 80 (EU/UK) (RW 14)	1	99.05	14	67.63	3820736	0.01 (0 - 0.06)	Observed significantly < expected
18-49 (EU/UK) (RW 21)	64	304.32	21	20.35	26009568	0.21 (0.16 - 0.27)	Observed significantly < expected
50-59 (EU/UK) (RW 21)	48	303.68	21	27.87	18951261	0.16 (0.12 - 0.21)	Observed significantly < expected
60-69 (EU/UK) (RW 21)	41	678.46	21	39.1	30179486	0.06 (0.04 - 0.08)	Observed significantly < expected
70-79 (EU/UK) (RW 21)	22	447.81	21	52.6	14806992	0.05 (0.03 - 0.07)	Observed significantly < expected
Over 80 (EU/UK) (RW 21)	1	148.57	21	67.63	3820736	0.01 (0 - 0.04)	Observed significantly < expected
18-49 (EU/UK) (RW 42)	87	608.65	42	20.35	26009568	0.14 (0.11 - 0.18)	Observed significantly < expected
50-59 (EU/UK) (RW 42)	64	607.36	42	27.87	18951261	0.11 (0.08 - 0.13)	Observed significantly < expected
60-69 (EU/UK) (RW 42)	58	1356.93	42	39.1	30179486	0.04 (0.03 - 0.06)	Observed significantly < expected
70-79 (EU/UK) (RW 42)	32	895.61	42	52.6	14806992	0.04 (0.02 - 0.05)	Observed significantly < expected

Table 50 Observed Versus Expected analysis for Pericarditis

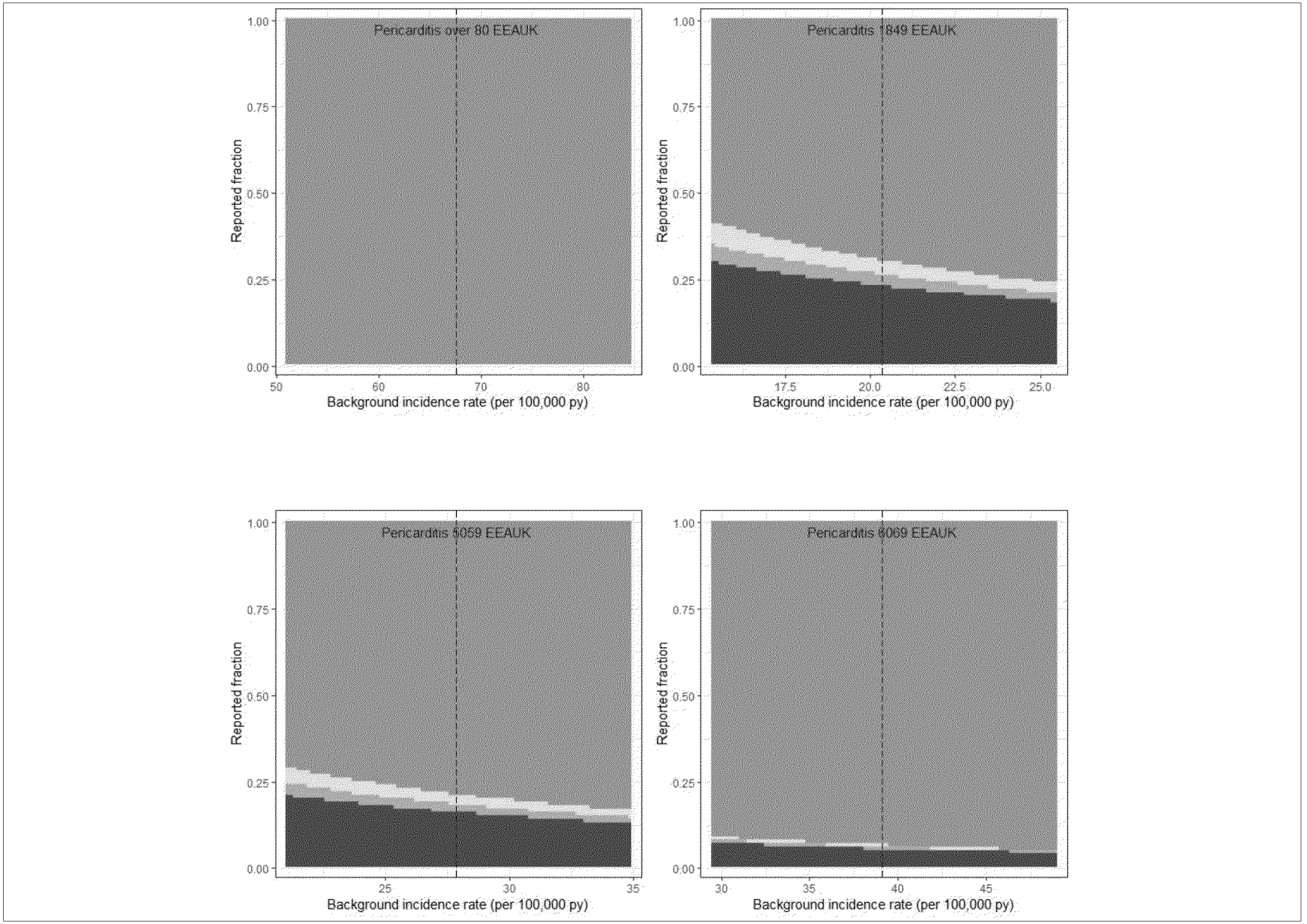
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Over 80 (EU/UK) (RW 42)	3	297.14	42	67.63	3820736	0.01 (0 - 0.03)	Observed significantly < expected

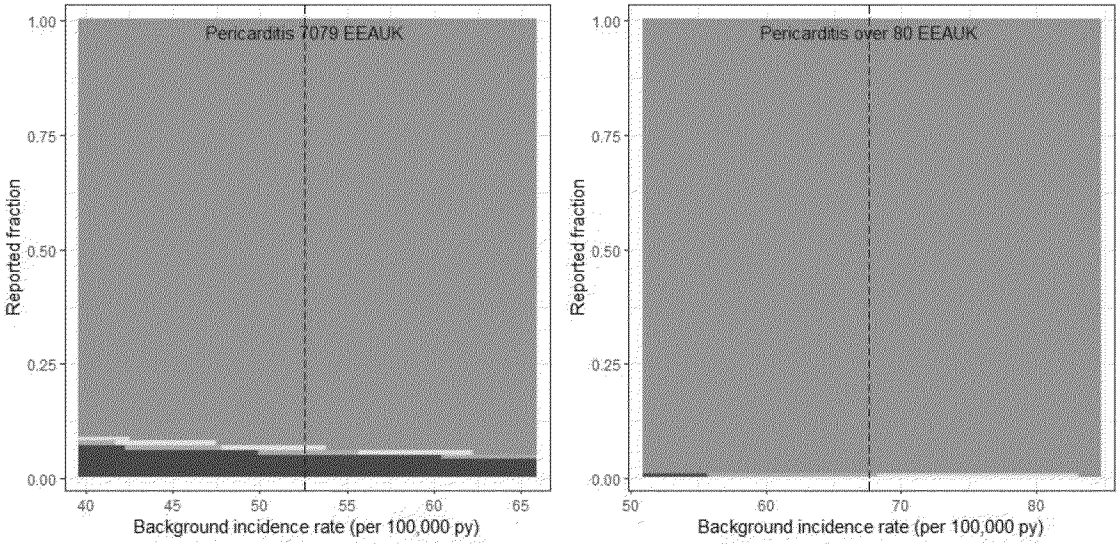

Pericarditis 1849 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
17.5
20.0
22.5
25.0
Background incidence rate (per 100,000 py)

Pericarditis 5059 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
25
30
35
Background incidence rate (per 100,000 py)

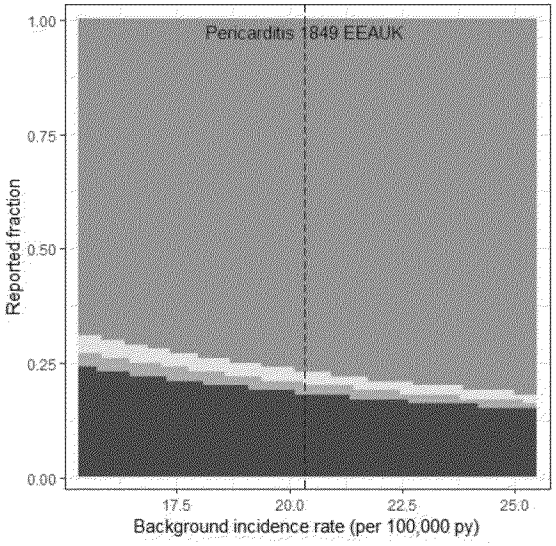

Pericarditis 6069 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
30
35
40
45
Background incidence rate (per 100,000 py)

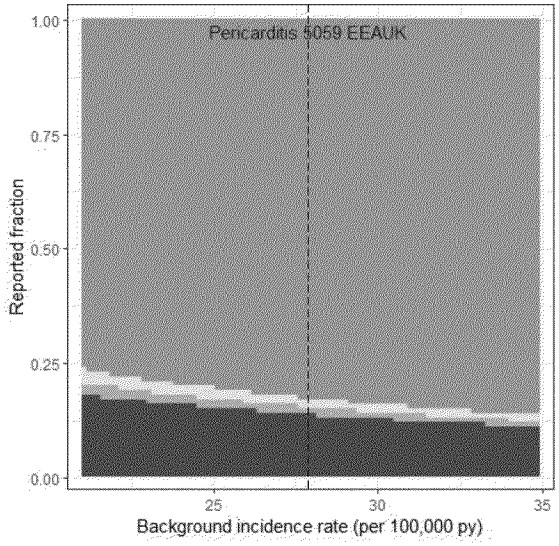
Pericarditis 7079 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
40
45
50
55
60
65
Background incidence rate (per 100,000 py)

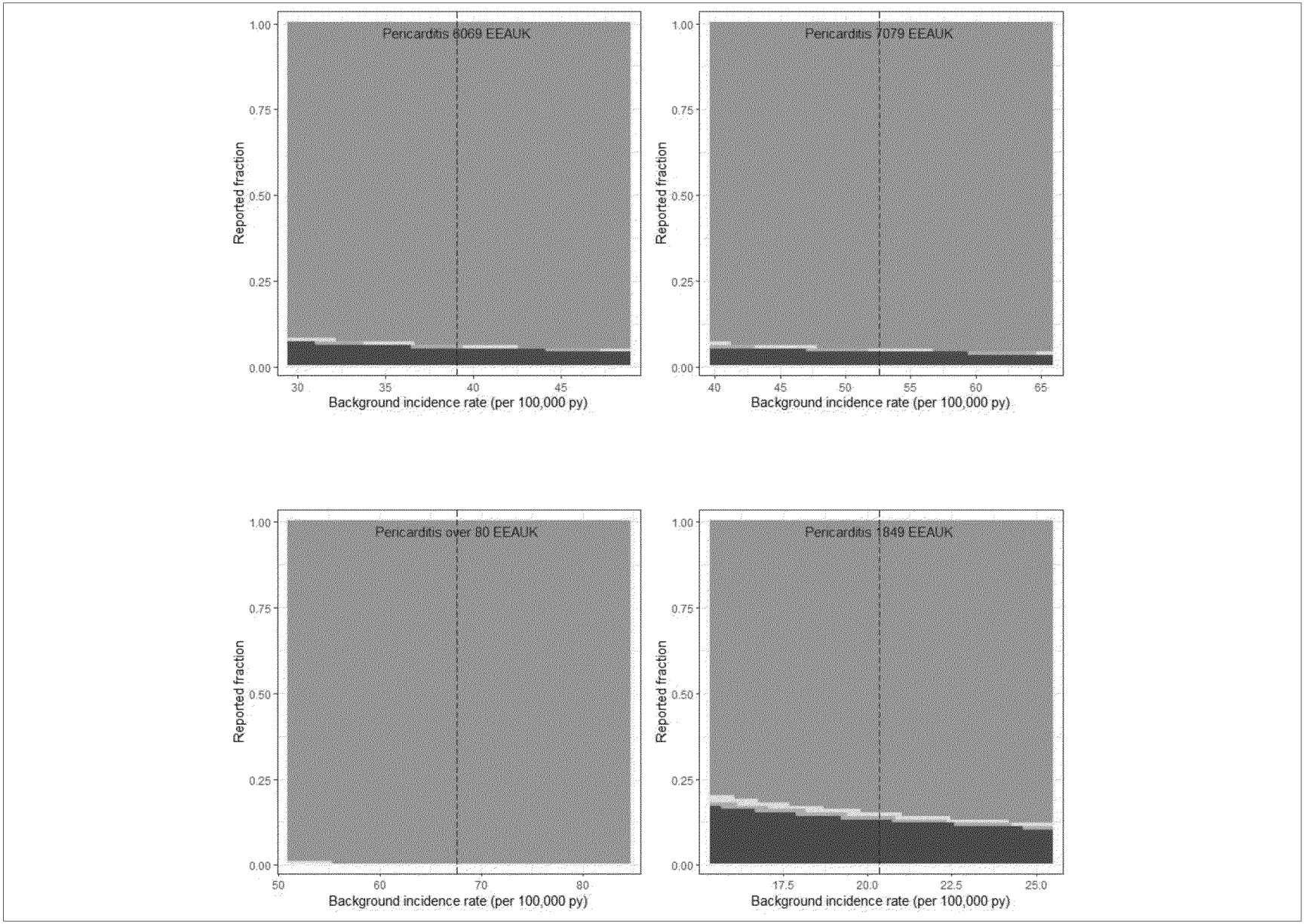

Pericarditis over 80 EEAUK
Pericarditis 1849 EEAUK
Pericarditis 5059 EEAUK
Pericarditis 6069 EEAUK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
50
60
70
80
17.5
20.0
22.5
25.0
25
30
35
40
45

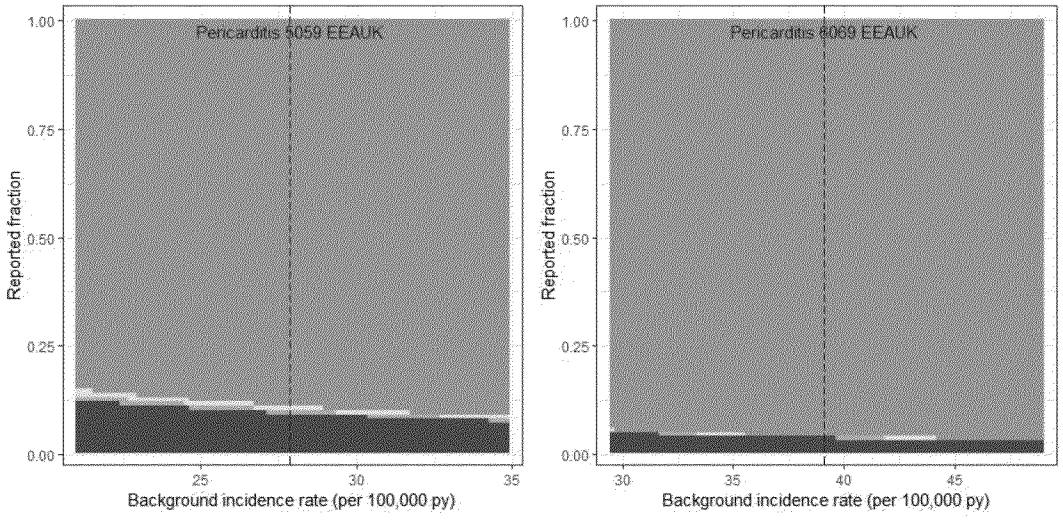

Pericarditis 7079 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
40
45
50
55
60
65
Background incidence rate (per 100,000 py)

Pericarditis over 80 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
50
60
70
80
Background incidence rate (per 100,000 py)

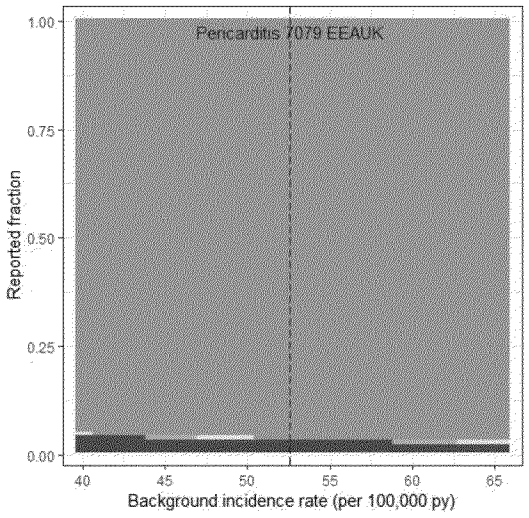

Pericarditis 1849 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
17.5
20.0
22.5
25.0
Background incidence rate (per 100,000 py)


Pericarditis 5059 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
25
30
35
Background incidence rate (per 100,000 py)


Pericarditis 6069 EEAUK
Pericarditis 7079 EEAUK
Pericarditis over 80 EEAUK
Pericarditis 1849 EEAUK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
30
35
40
45
50
55
60
65
70
80
17.5
20.0
22.5
25.0


Pericarditis 5059 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
25
30
35
Background incidence rate (per 100,000 py)

Pericarditis 6069 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
30
35
40
45
Background incidence rate (per 100,000 py)


Pericarditis 7079 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
40
45
50
55
60
65
Background incidence rate (per 100,000 py)

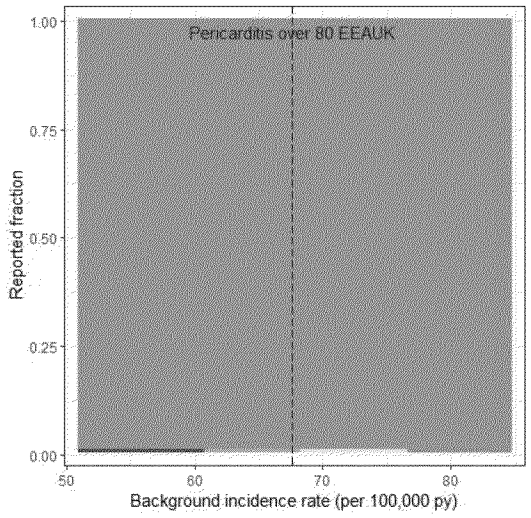
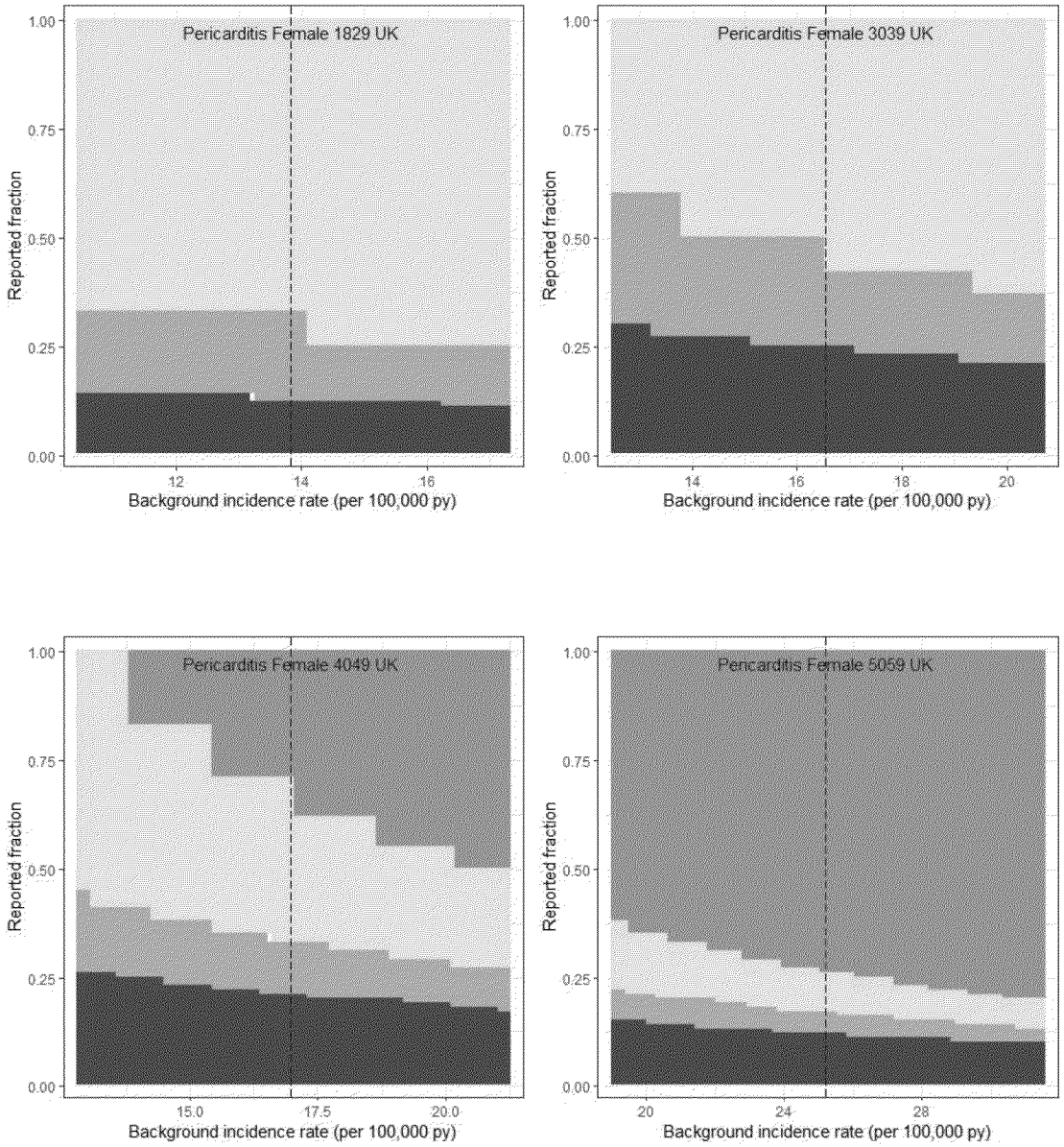
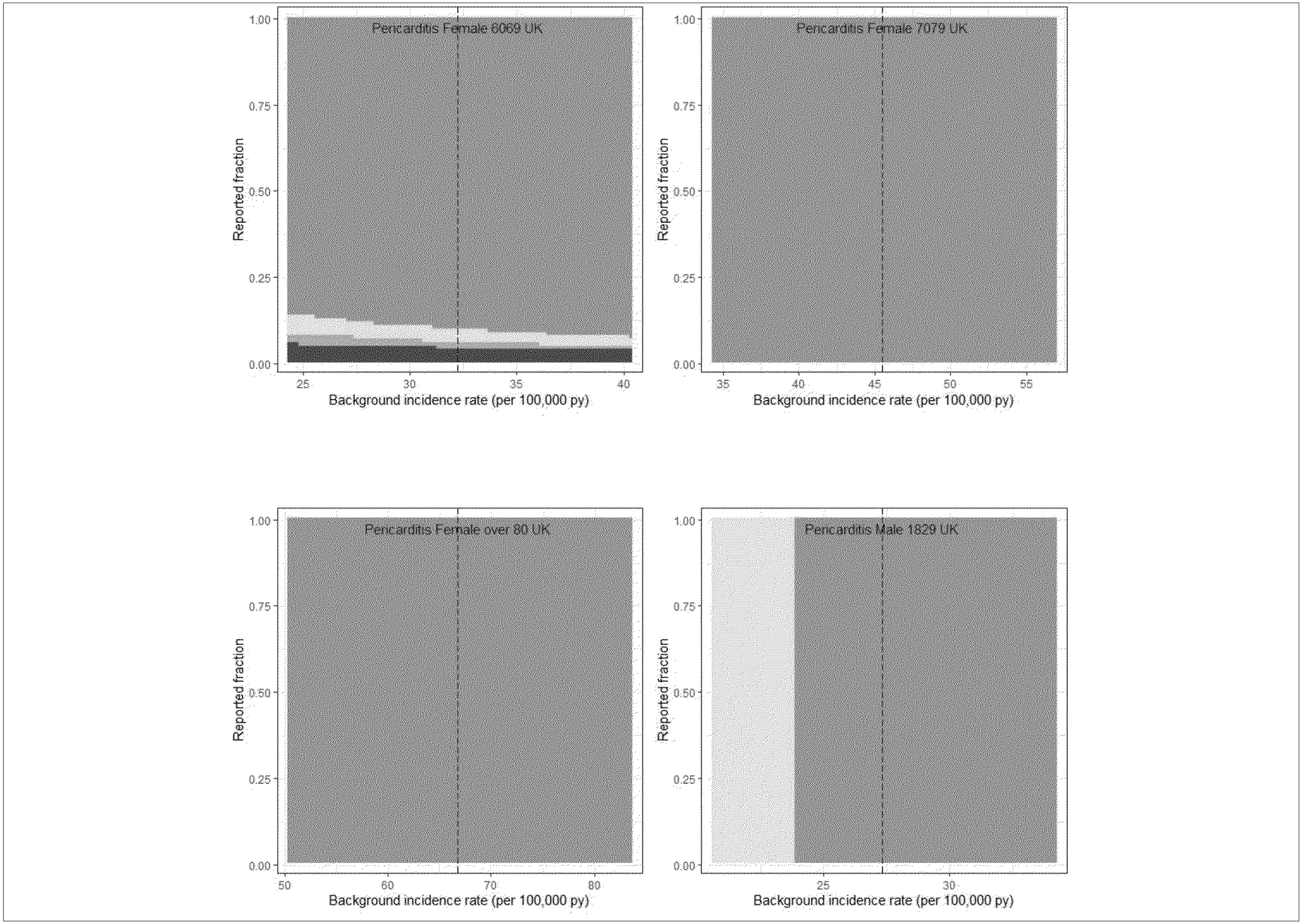
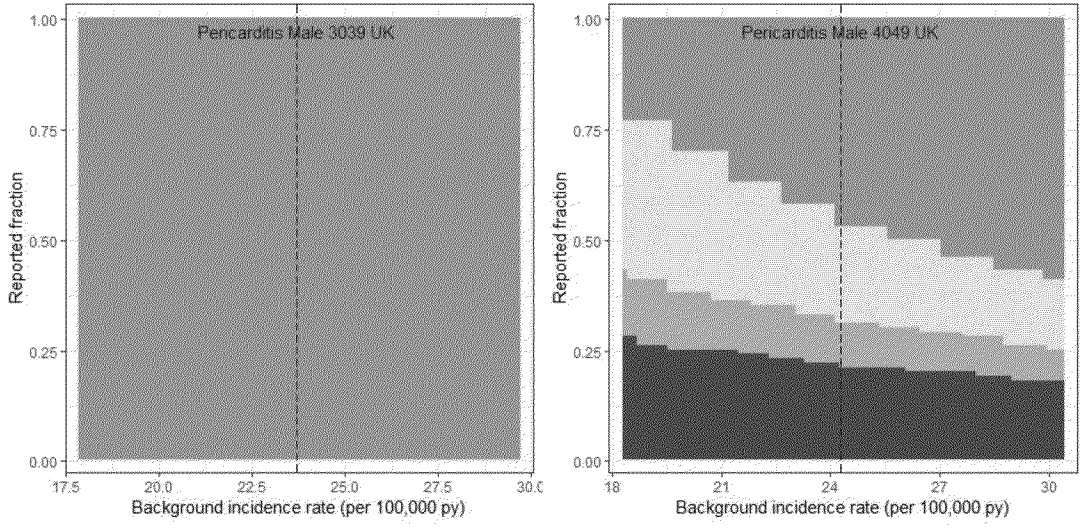

Pericarditis over 80 EEAUK
Reported fraction
1.00
0.75
0.50
0.25
0.00
50
60
70
80
Background incidence rate (per 100,000 py)

Table 50 Observed Versus Expected analysis for Pericarditis

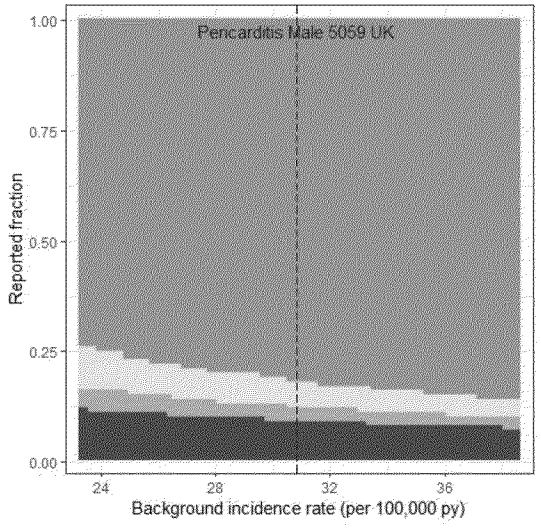
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Female 18-29 (UK)	1	2.94	7	13.84	1109488	0.34 (0.01 - 1.9)	Observed < expected
Female 30-39 (UK)	3	6	7	16.55	1892968	0.5 (0.1 - 1.46)	Observed < expected
Female 40-49 (UK)	5	14.36	7	16.98	4412245	0.35 (0.11 - 0.81)	Observed significantly < expected
Female 50-59 (UK)	5	28.71	7	25.2	5944683	0.17 (0.06 - 0.41)	Observed significantly < expected
Female 60-69 (UK)	2	29.57	7	32.25	4783416	0.07 (0.01 - 0.24)	Observed significantly < expected
Female 70-79 (UK)	0	30.32	7	45.51	3475875	0 (0 - 0.12)	Observed significantly < expected
Female ≥ 80 (UK)	0	20.87	7	66.8	1630324	0 (0 - 0.18)	Observed significantly < expected
Male 18-29 (UK)	0	4.24	7	27.33	808938	0 (0 - 0.87)	Observed significantly < expected
Male 30-39 (UK)	0	6.43	7	23.71	1415003	0 (0 - 0.57)	Observed significantly < expected
Male 40-49 (UK)	7	21.14	7	24.28	4542157	0.33 (0.13 - 0.68)	Observed significantly < expected
Male 50-59 (UK)	5	38.5	7	30.85	6510960	0.13 (0.04 - 0.3)	Observed significantly < expected
Male 60-69 (UK)	2	44.17	7	46.7	4934728	0.05 (0.01 - 0.16)	Observed significantly < expected
Male 70-79 (UK)	2	36.64	7	60.94	3137304	0.05 (0.01 - 0.2)	Observed significantly < expected
Male ≥ 80 (UK)	0	13.52	7	68.8	1025046	0 (0 - 0.27)	Observed significantly < expected


Pericarditis Female 1829 UK
Pericarditis Female 3039 UK
Pericarditis Female 4049 UK
Pericarditis Female 5059 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
12
14
16
14
16
18
20
15.0
17.5
20.0
20
24
28
Background incidence rate (per 100,000 py)


Pericarditis Female 6069 UK
Pericarditis Female 7079 UK
Pericarditis Female over 80 UK
Pericarditis Male 1829 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00


Pericarditis Male 3039 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
17.5
20.0
22.5
25.0
27.5
30.0
Background incidence rate (per 100,000 py)

Pericarditis Male 4049 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
18
21
24
27
30
Background incidence rate (per 100,000 py)


Pericarditis Male 5059 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
24
28
32
36
Background incidence rate (per 100,000 py)

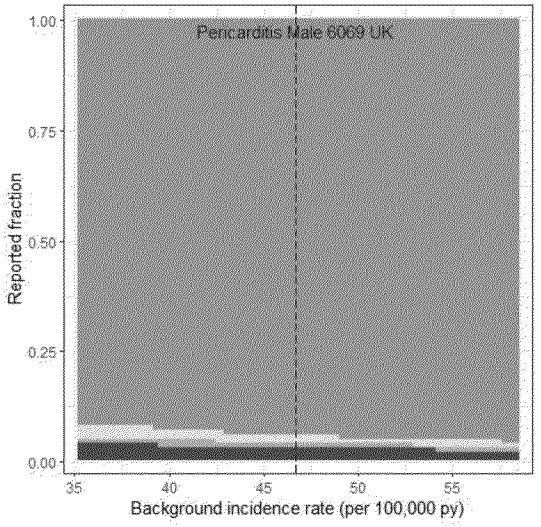

Pericarditis Male 6069 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
35
40
45
50
55
Background incidence rate (per 100,000 py)

Table 50 Observed Versus Expected analysis for Pericarditis

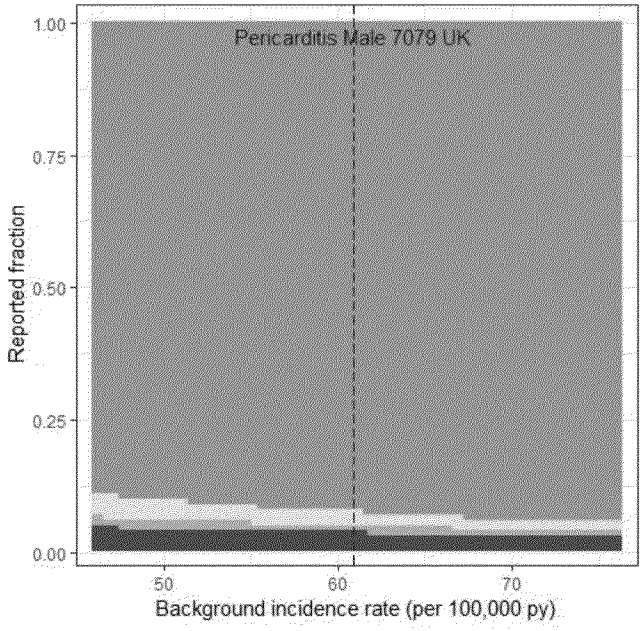
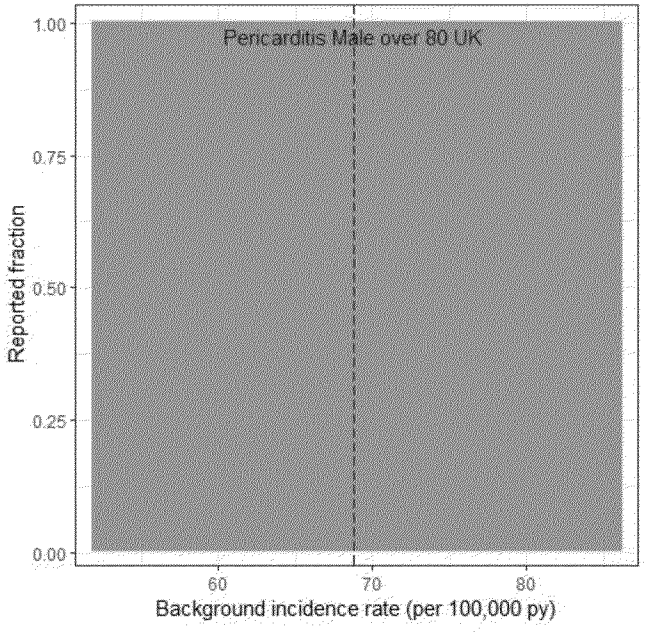
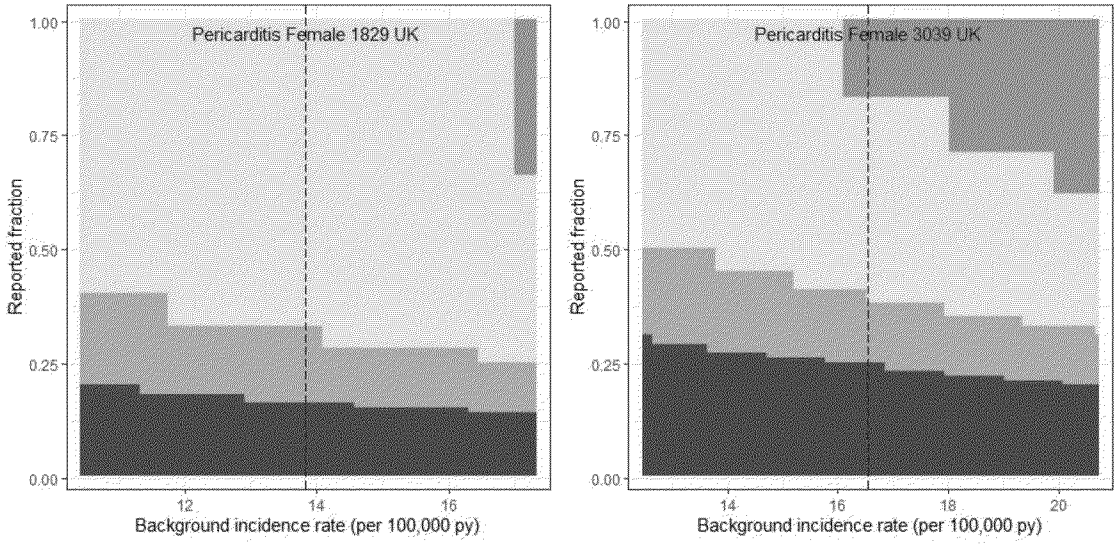
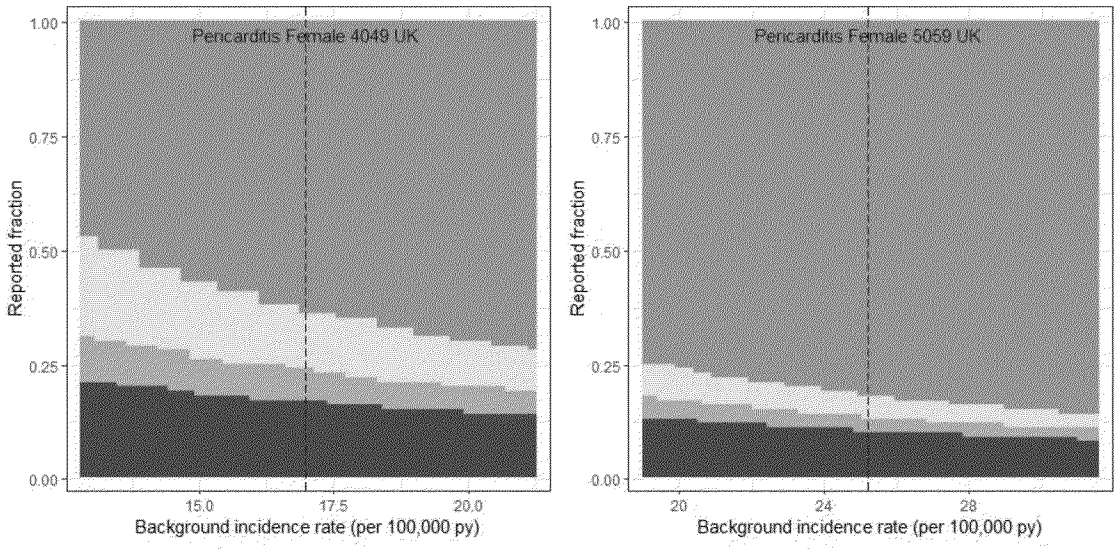
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							
							
Female 18-29 (UK)	2	5.89	14	13.84	1109488	0.34 (0.04 - 1.23)	Observed < expected
Female 30-39 (UK)	5	12.01	14	16.55	1892968	0.42 (0.14 - 0.97)	Observed significantly < expected
Female 40-49 (UK)	7	28.72	14	16.98	4412245	0.24 (0.1 - 0.5)	Observed significantly < expected
Female 50-59 (UK)	8	57.42	14	25.2	5944683	0.14 (0.06 - 0.27)	Observed significantly < expected
Female 60-69 (UK)	2	59.13	14	32.25	4783416	0.03 (0 - 0.12)	Observed significantly < expected
Female 70-79 (UK)	0	60.63	14	45.51	3475875	0 (0 - 0.06)	Observed significantly < expected
Female ≥ 80 (UK)	0	41.74	14	66.8	1630324	0 (0 - 0.09)	Observed significantly < expected
Male 18-29 (UK)	0	8.47	14	27.33	808938	0 (0 - 0.44)	Observed significantly < expected

Table 50 Observed Versus Expected analysis for Pericarditis

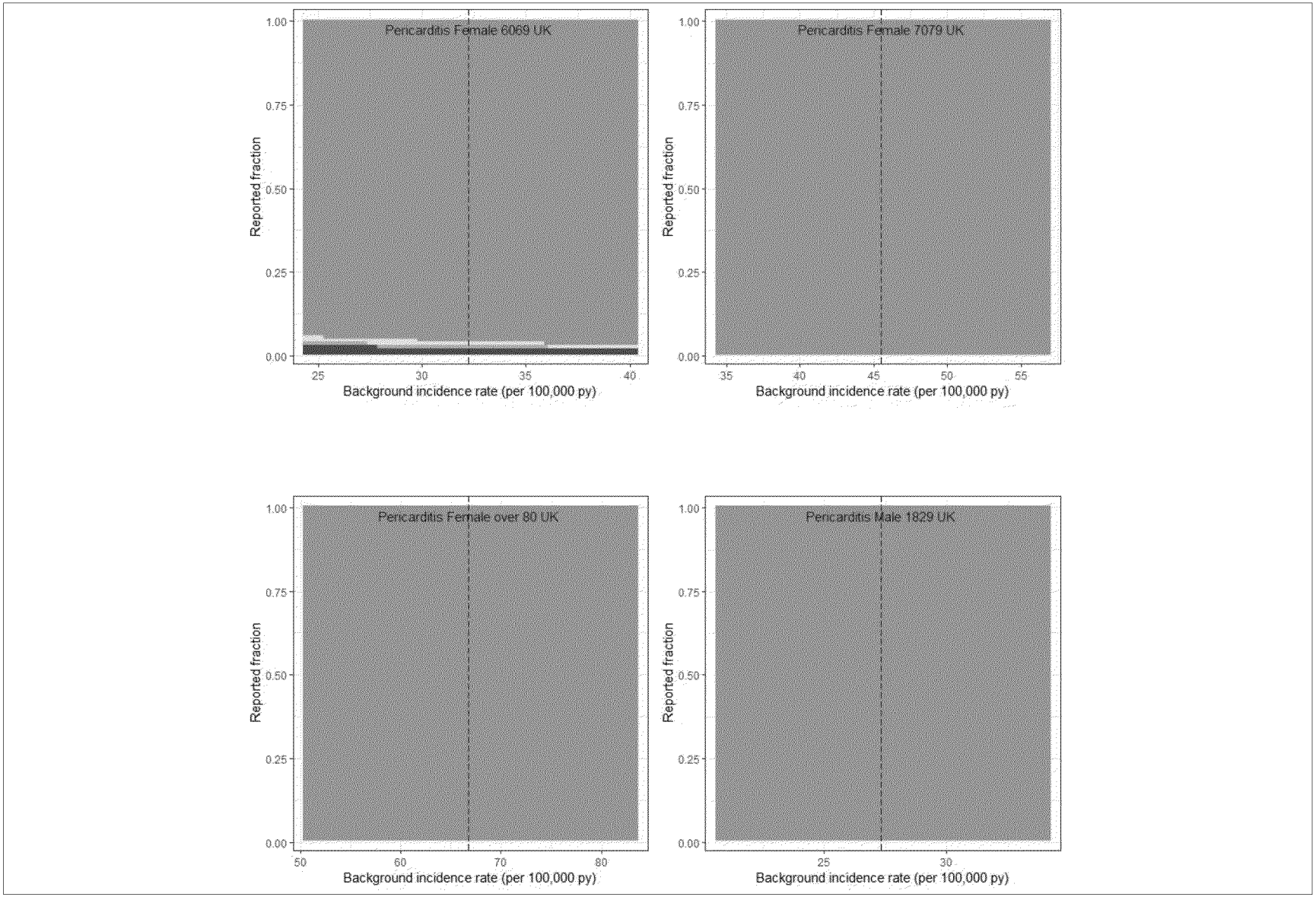
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Male 30-39 (UK)	0	12.86	14	23.71	1415003	0 (0 - 0.29)	Observed significantly < expected
Male 40-49 (UK)	14	42.27	14	24.28	4542157	0.33 (0.18 - 0.56)	Observed significantly < expected
Male 50-59 (UK)	8	76.99	14	30.85	6510960	0.1 (0.04 - 0.2)	Observed significantly < expected
Male 60-69 (UK)	3	88.33	14	46.7	4934728	0.03 (0.01 - 0.1)	Observed significantly < expected
Male 70-79 (UK)	4	73.28	14	60.94	3137304	0.05 (0.01 - 0.14)	Observed significantly < expected
Male ≥ 80 (UK)	1	27.03	14	68.8	1025046	0.04 (0 - 0.21)	Observed significantly < expected

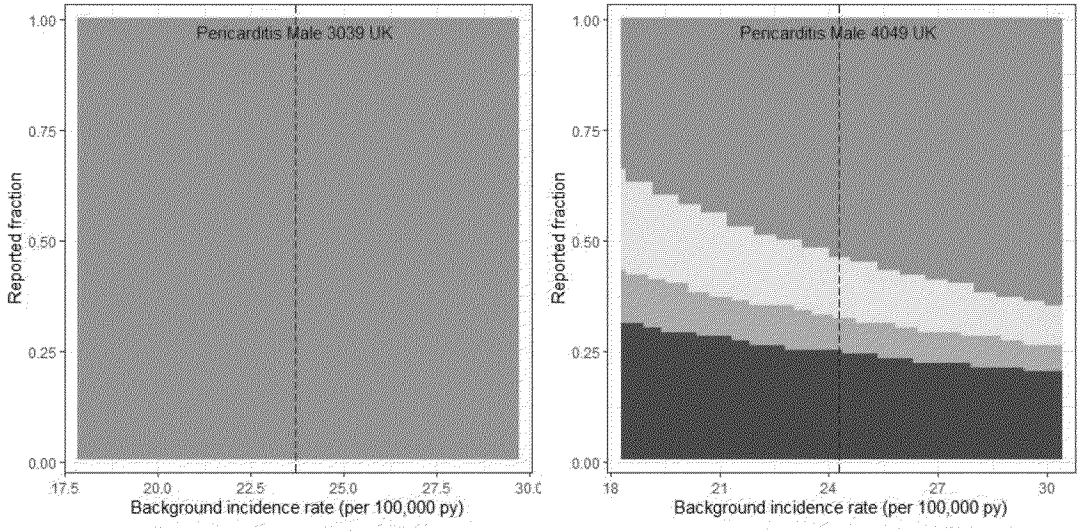

Pericarditis Female 1829 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
12
14
16
Background incidence rate (per 100,000 py)

Pericarditis Female 3039 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
14
16
18
20
Background incidence rate (per 100,000 py)

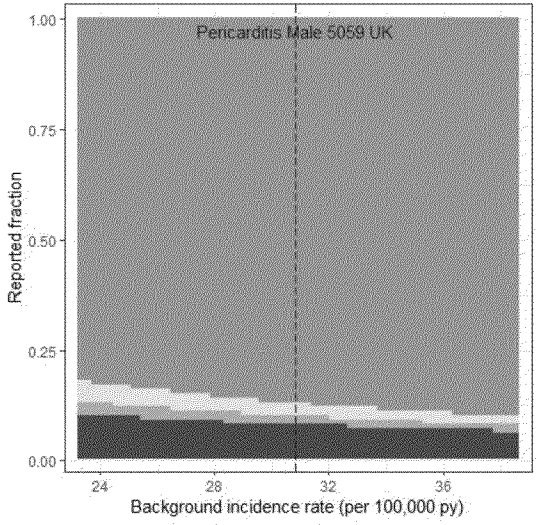

Pericarditis Female 4049 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
15.0
17.5
20.0
Background incidence rate (per 100,000 py)

Pericarditis Female 5059 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
24
28
Background incidence rate (per 100,000 py)


Pericarditis Female 6069 UK
Pericarditis Female 7079 UK
Pericarditis Female over 80 UK
Pericarditis Male 1829 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
25
30
35
40
45
50
55
60
70
80


Pericarditis Male 3039 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
17.5
20.0
22.5
25.0
27.5
Background incidence rate (per 100,000 py)

Pericarditis Male 4049 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
18
21
24
27
30
Background incidence rate (per 100,000 py)


Pericarditis Male 5059 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
24
28
32
36
Background incidence rate (per 100,000 py)

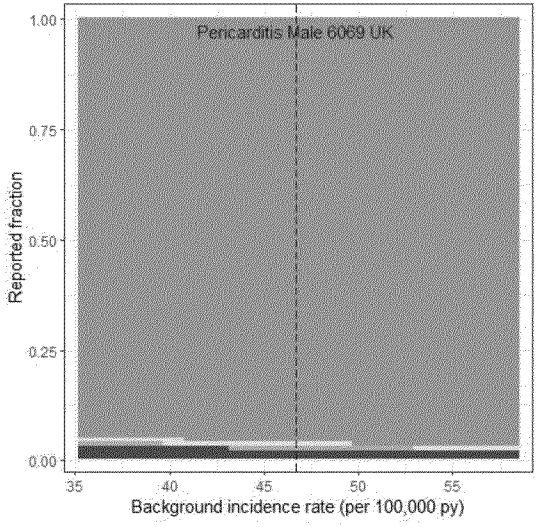

Pericarditis Male 6069 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
35
40
45
50
55
Background incidence rate (per 100,000 py)

Table 50 Observed Versus Expected analysis for Pericarditis

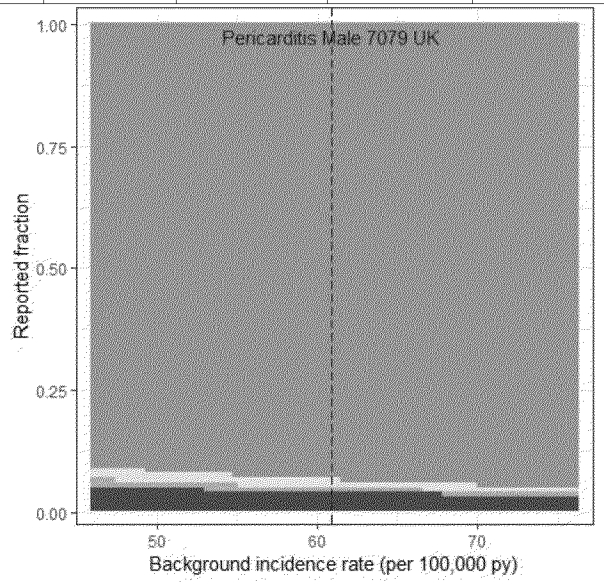
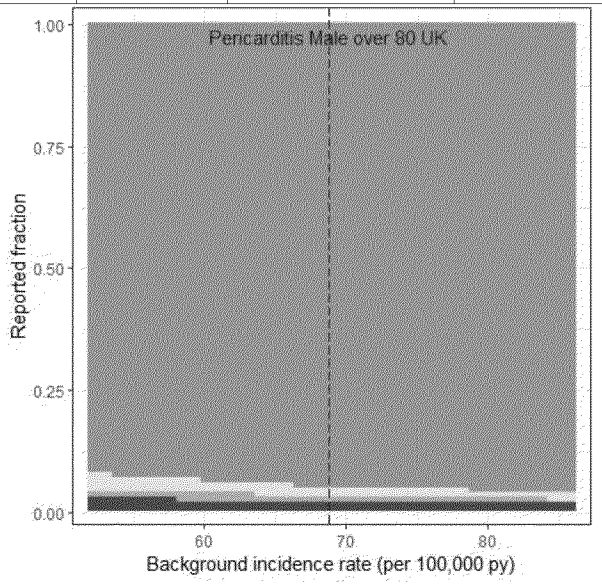
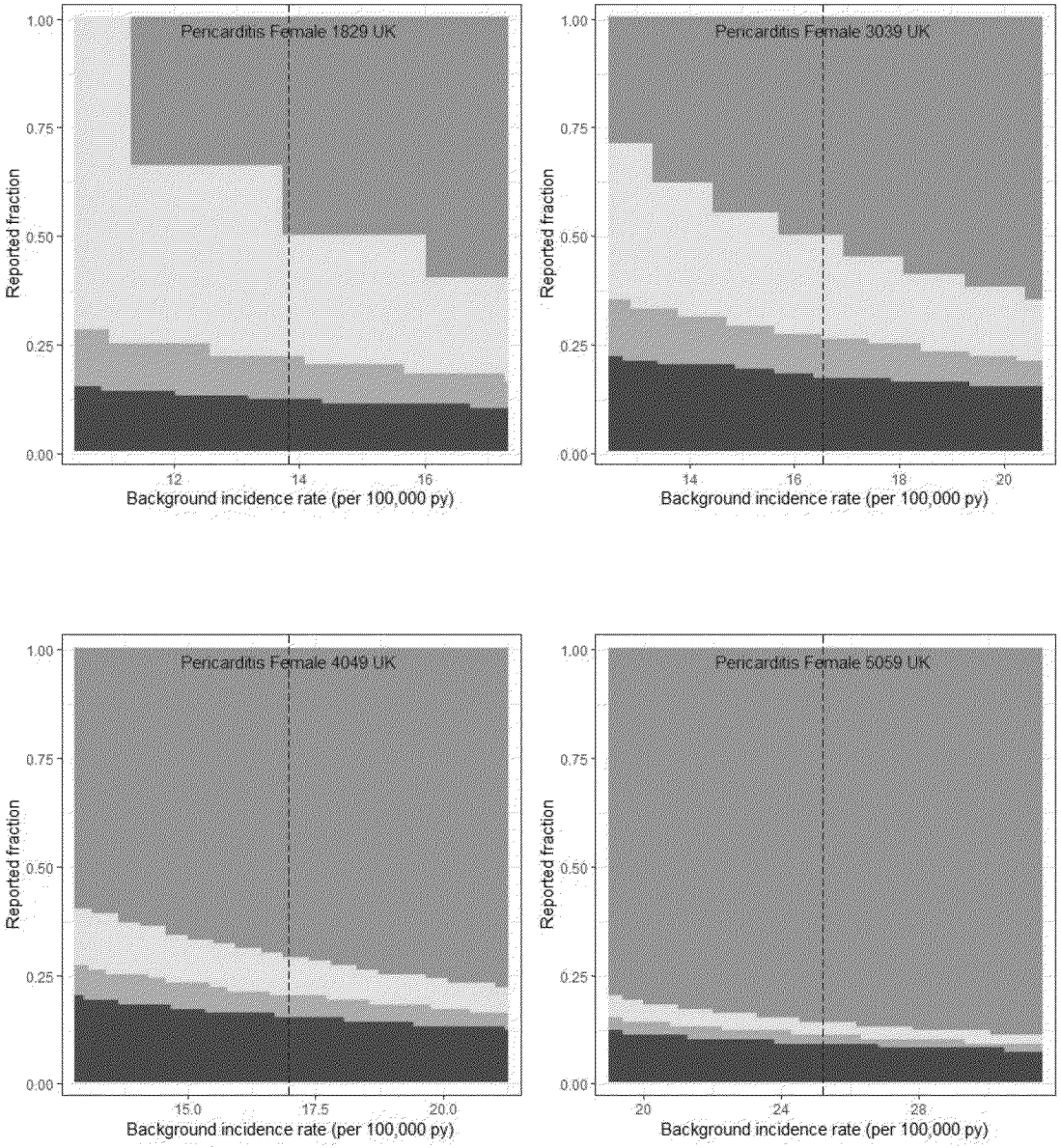
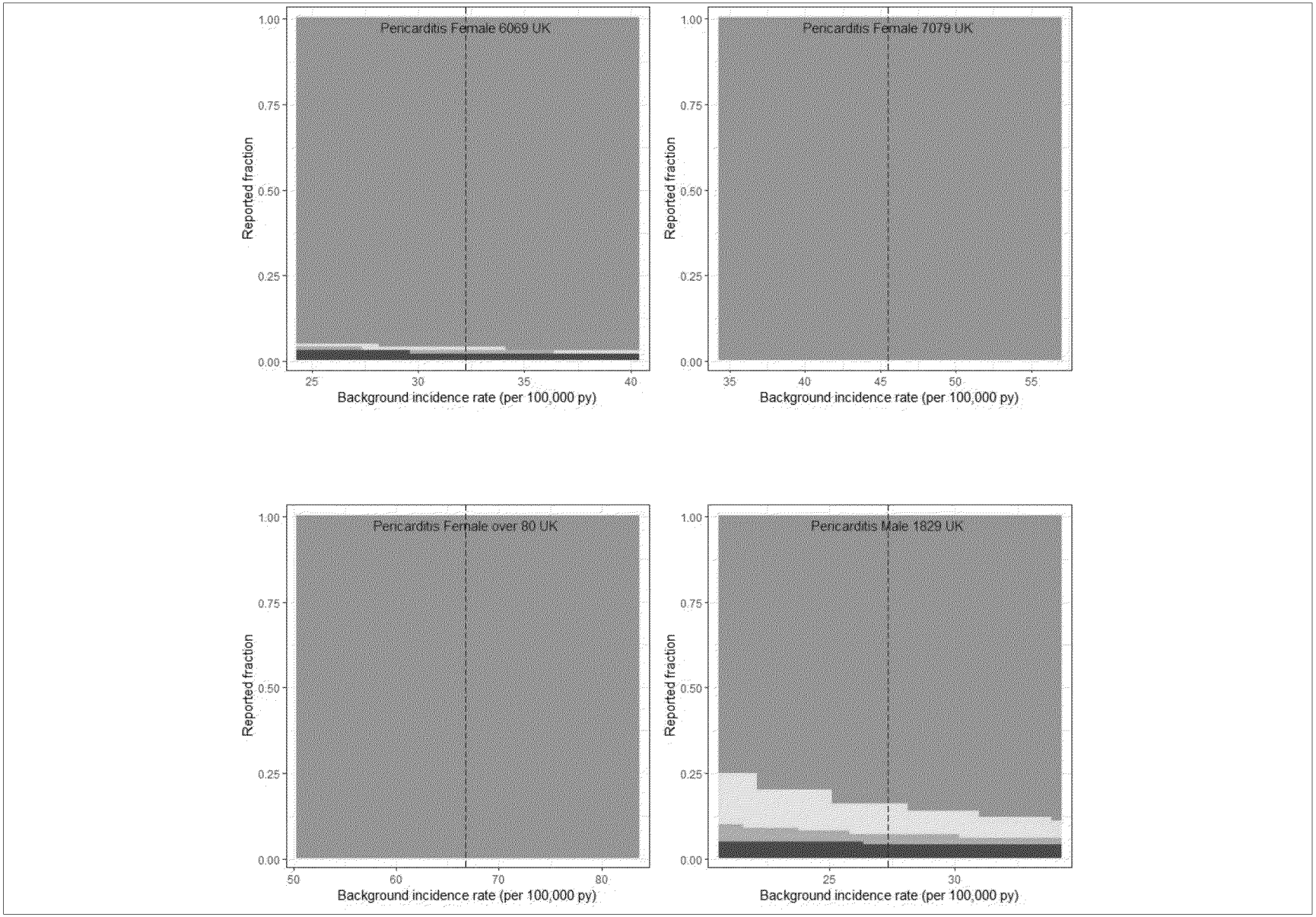
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							
							
Female 18-29 (UK)	2	8.83	21	13.84	1109488	0.23 (0.03 - 0.82)	Observed significantly < expected
Female 30-39 (UK)	5	18.01	21	16.55	1892968	0.28 (0.09 - 0.65)	Observed significantly < expected
Female 40-49 (UK)	9	43.08	21	16.98	4412245	0.21 (0.1 - 0.4)	Observed significantly < expected
Female 50-59 (UK)	10	86.13	21	25.2	5944683	0.12 (0.06 - 0.21)	Observed significantly < expected
Female 60-69 (UK)	3	88.7	21	32.25	4783416	0.03 (0.01 - 0.1)	Observed significantly < expected
Female 70-79 (UK)	0	90.95	21	45.51	3475875	0 (0 - 0.04)	Observed significantly < expected
Female ≥ 80 (UK)	0	62.62	21	66.8	1630324	0 (0 - 0.06)	Observed significantly < expected
Male 18-29 (UK)	1	12.71	21	27.33	808938	0.08 (0 - 0.44)	Observed significantly < expected
Male 30-39 (UK)	0	19.29	21	23.71	1415003	0 (0 - 0.19)	Observed significantly < expected

Table 50 Observed Versus Expected analysis for Pericarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Male 40-49 (UK)	18	63.41	21	24.28	4542157	0.28 (0.17 - 0.45)	Observed significantly < expected
Male 50-59 (UK)	12	115.49	21	30.85	6510960	0.1 (0.05 - 0.18)	Observed significantly < expected
Male 60-69 (UK)	7	132.5	21	46.7	4934728	0.05 (0.02 - 0.11)	Observed significantly < expected
Male 70-79 (UK)	4	109.93	21	60.94	3137304	0.04 (0.01 - 0.09)	Observed significantly < expected
Male ≥ 80 (UK)	1	40.55	21	68.8	1025046	0.02 (0 - 0.14)	Observed significantly < expected


Pericarditis Female 1829 UK
Pericarditis Female 3039 UK
Pericarditis Female 4049 UK
Pericarditis Female 5059 UK
Reported fraction
0.00
0.25
0.50
0.75
1.00
12
14
16
18
20
15.0
17.5
20.0
24
28
Background incidence rate (per 100,000 py)


Pericarditis Female 6069 UK
Pericarditis Female 7079 UK
Pericarditis Female over 80 UK
Pericarditis Male 1829 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
25
30
35
40
45
50
55
60
70
80

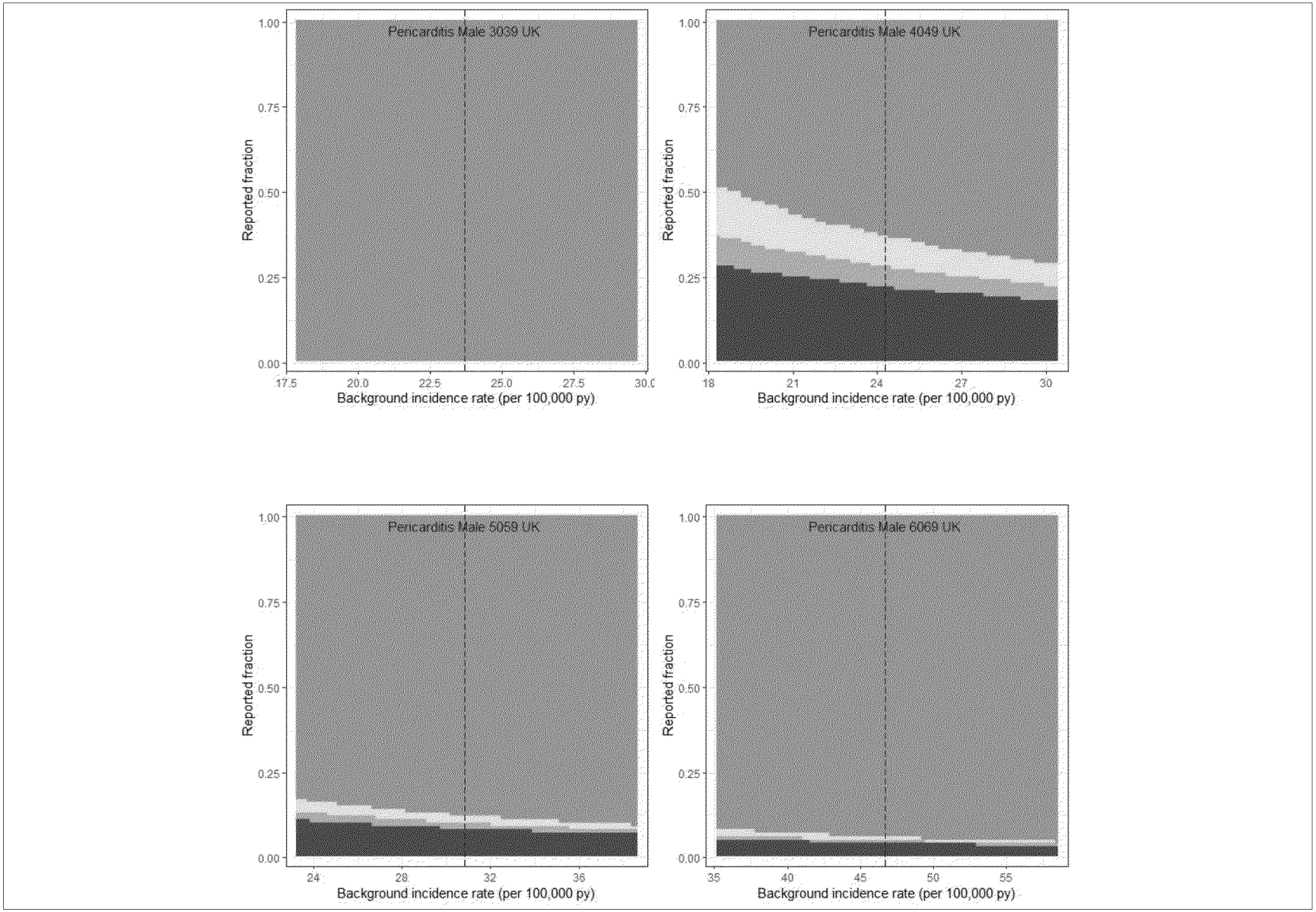

Pericarditis Male 3039 UK
Pericarditis Male 4049 UK
Pericarditis Male 5059 UK
Pericarditis Male 6069 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
17.5
20.0
22.5
25.0
27.5
18
21
24
27
30
28
32
36
35
40
45
50
55

Table 50 Observed Versus Expected analysis for Pericarditis

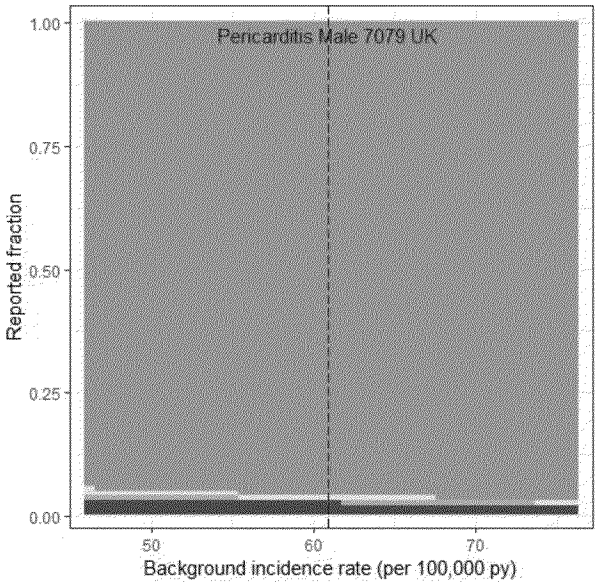
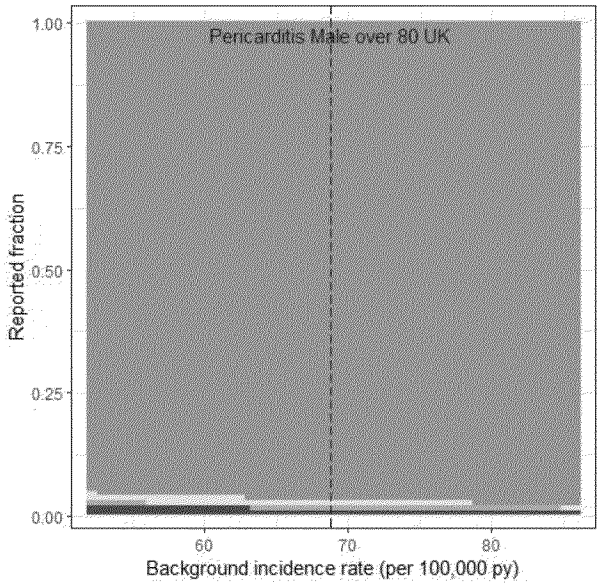
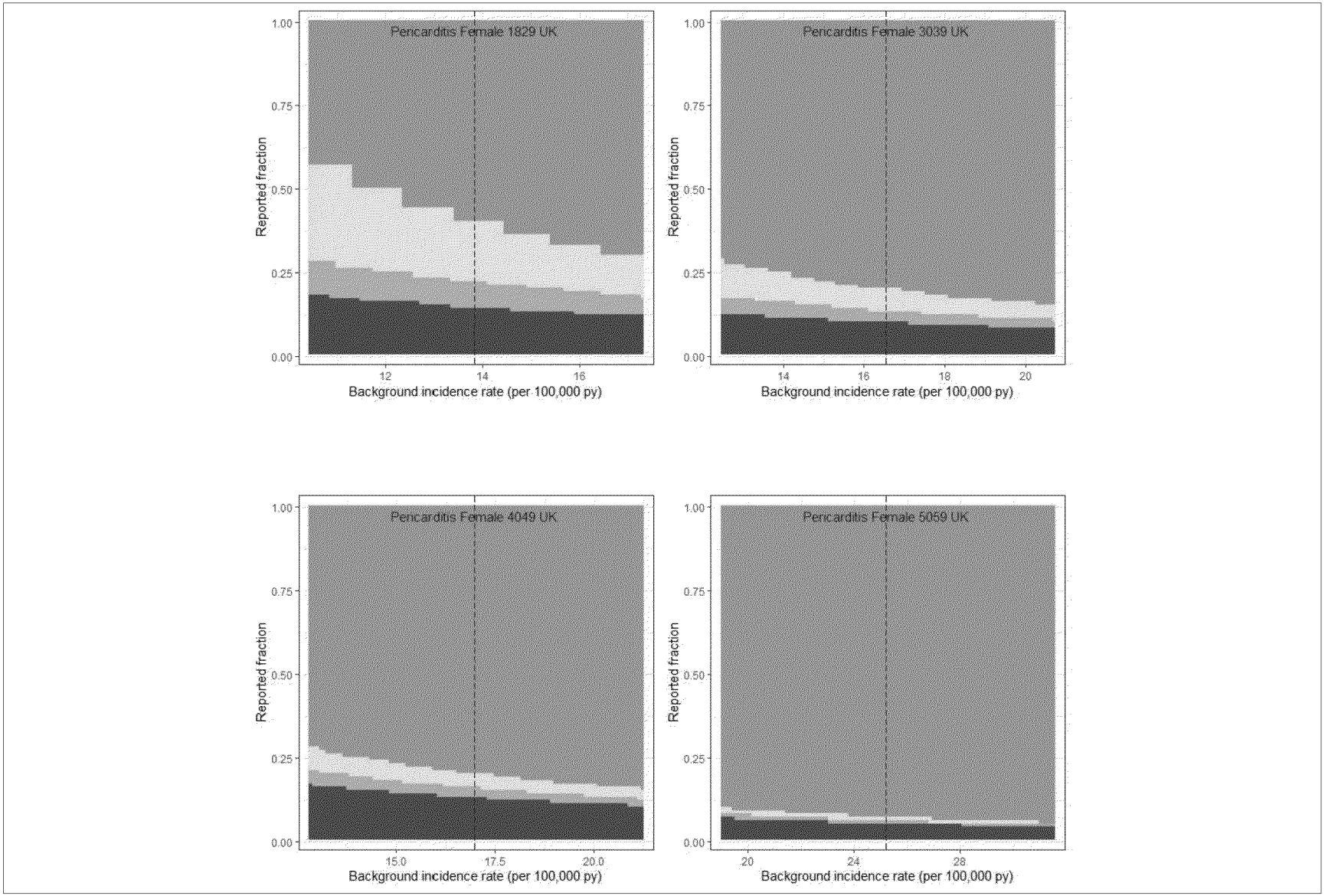
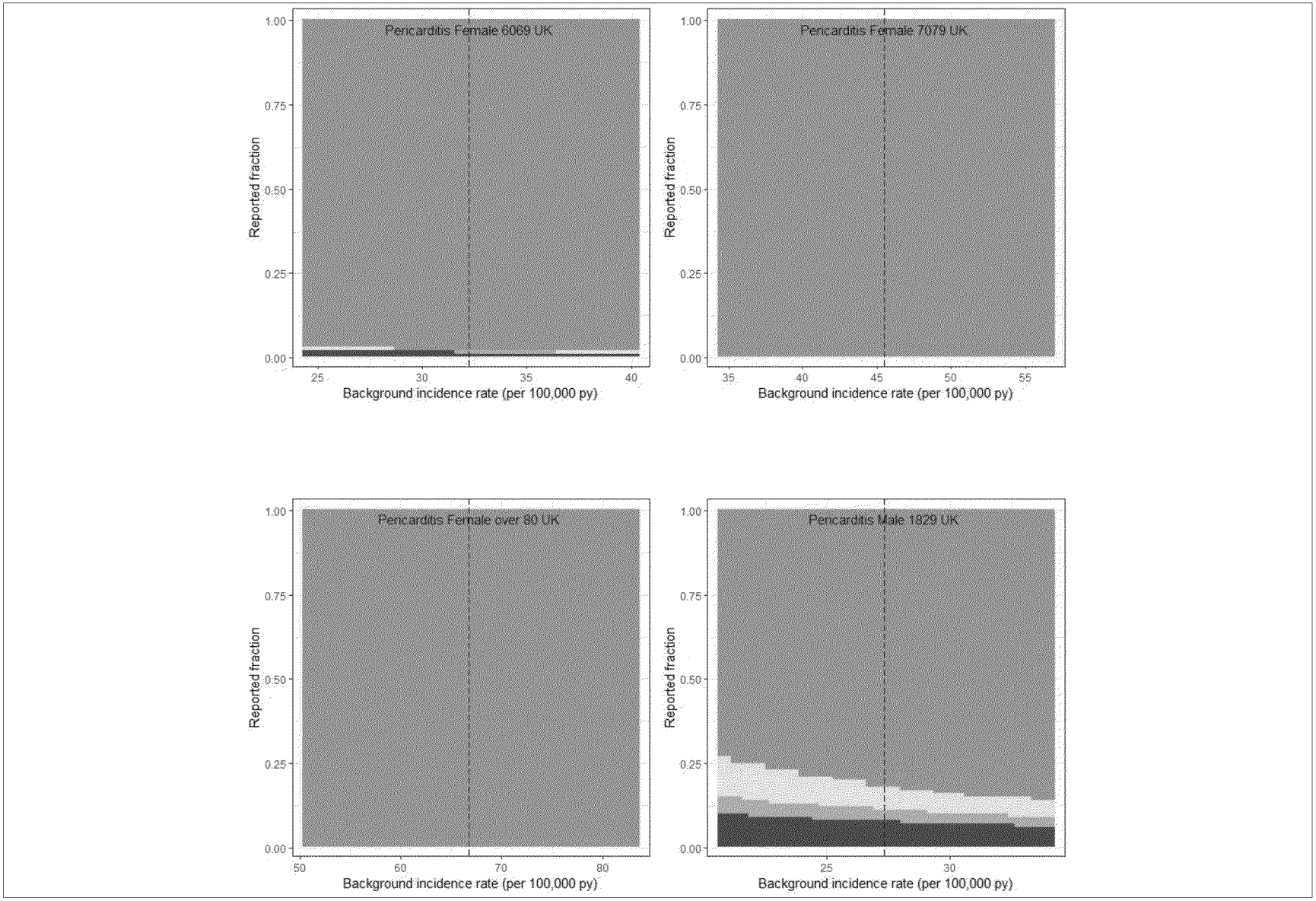
Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							
							
Female 18-29 (UK)	4	17.66	42	13.84	1109488	0.23 (0.06 - 0.58)	Observed significantly < expected
Female 30-39 (UK)	5	36.03	42	16.55	1892968	0.14 (0.05 - 0.32)	Observed significantly < expected
Female 40-49 (UK)	14	86.15	42	16.98	4412245	0.16 (0.09 - 0.27)	Observed significantly < expected
Female 50-59 (UK)	11	172.27	42	25.2	5944683	0.06 (0.03 - 0.11)	Observed significantly < expected
Female 60-69 (UK)	4	177.39	42	32.25	4783416	0.02 (0.01 - 0.06)	Observed significantly < expected
Female 70-79 (UK)	1	181.9	42	45.51	3475875	0.01 (0 - 0.03)	Observed significantly < expected
Female ≥ 80 (UK)	0	125.23	42	66.8	1630324	0 (0 - 0.03)	Observed significantly < expected
Male 18-29 (UK)	3	25.42	42	27.33	808938	0.12 (0.02 - 0.34)	Observed significantly < expected
Male 30-39 (UK)	0	38.58	42	23.71	1415003	0 (0 - 0.1)	Observed significantly < expected

Table 50 Observed Versus Expected analysis for Pericarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
Male 40-49 (UK)	21	126.82	42	24.28	4542157	0.17 (0.1 - 0.25)	Observed significantly < expected
Male 50-59 (UK)	15	230.98	42	30.85	6510960	0.06 (0.04 - 0.11)	Observed significantly < expected
Male 60-69 (UK)	7	265	42	46.7	4934728	0.03 (0.01 - 0.05)	Observed significantly < expected
Male 70-79 (UK)	5	219.85	42	60.94	3137304	0.02 (0.01 - 0.05)	Observed significantly < expected
Male ≥ 80 (UK)	1	81.1	42	68.8	1025046	0.01 (0 - 0.07)	Observed significantly < expected


Pericarditis Female 1829 UK
Pericarditis Female 3039 UK
Pericarditis Female 4049 UK
Pericarditis Female 5059 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
12
14
16
18
20
15.0
17.5
20.0
24
28
Background incidence rate (per 100,000 py)


Pericarditis Female 6069 UK
Pericarditis Female 7079 UK
Pericarditis Female over 80 UK
Pericarditis Male 1829 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
25
30
35
40
45
50
55
60
70
80

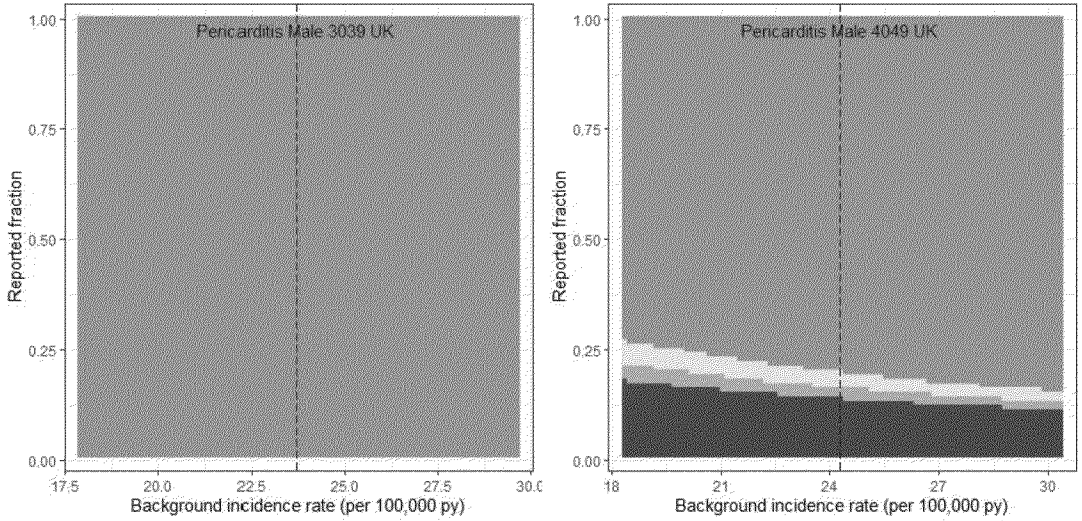
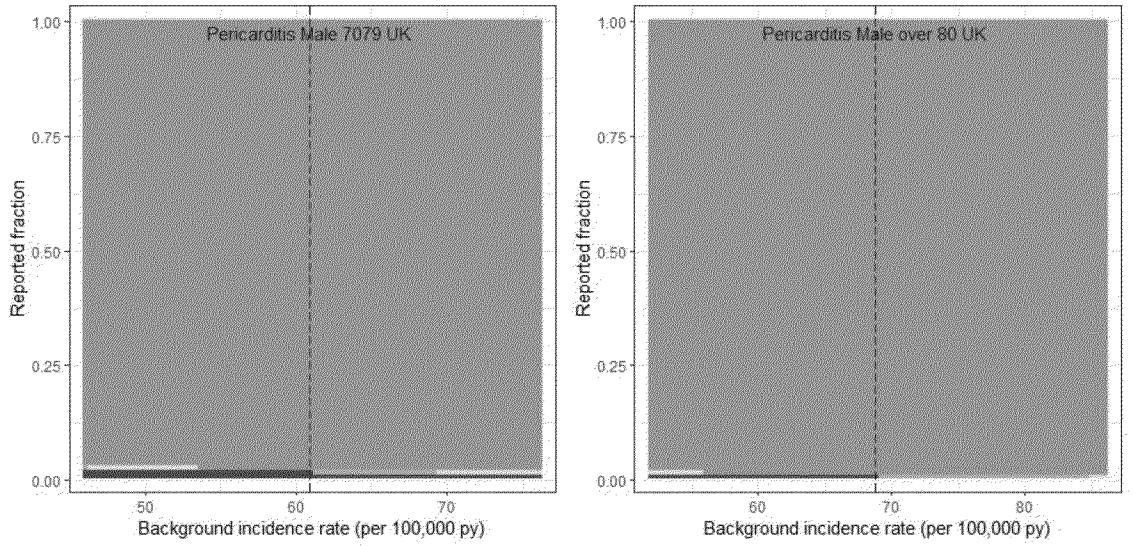

Pericarditis Male 3039 UK
Pericarditis Male 4049 UK
Pericarditis Male 5059 UK
Pericarditis Male 6069 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00

Table 50 Observed Versus Expected analysis for Pericarditis

Myocarditis by age groups (years) and gender	Observed Cases	Expected cases	Risk window (days)	Incidence rates (per 100,000) [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate from Truven Marketscan.

CI Confidence Interval; BR Brazil; AU Australia; E Expected; EU European Union; Observed; RW risk window; TTO Time to onset; UK United Kingdom;

Table 51 Observed Versus Expected analysis for Pericarditis cases from EU/UK/Australia/Canada/Argentina/Malaysia/New Zealand/Colombia/Taiwan/Brazil/Thailand

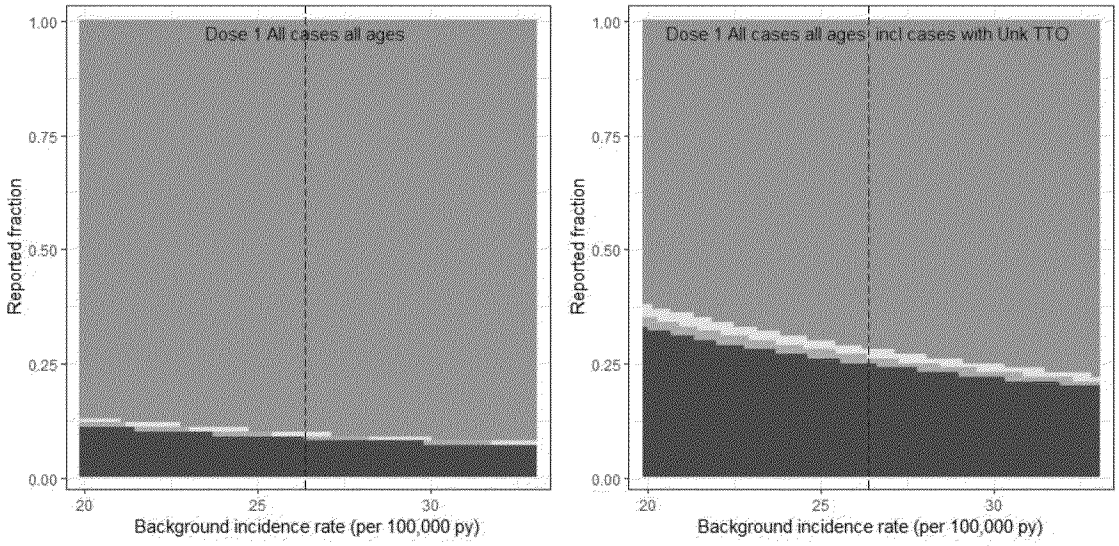
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Dose 1 All cases, all ages	85	885	7	26.38	175045647	0.1 (0.08 - 0.12)	Observed significantly < expected
Dose 1 -All cases, all ages including cases with Unk TTO	238	885	7	26.38	175045647	0.27 (0.24 - 0.31)	Observed significantly < expected
Dose 2 All cases, all ages	21	856.19	7	26.38	169346503	0.02 (0.02 - 0.04)	Observed significantly < expected
Dose 2 -All cases, all ages including cases with Unk TTO	44	856.19	7	26.38	169346503	0.05 (0.04 - 0.07)	Observed significantly < expected
Dose 1 All cases, all ages	162	1770	14	26.38	175045647	0.09 (0.08 - 0.11)	Observed significantly < expected
Dose 1 - All cases, all ages including cases with Unk TTO	315	1770	14	26.38	175045647	0.18 (0.16 - 0.2)	Observed significantly < expected
Dose 2 All cases, all ages	30	1712.37	14	26.38	169346503	0.02 (0.01 - 0.03)	Observed significantly < expected

Table 51 Observed Versus Expected analysis for Pericarditis cases from EU/UK/Australia/Canada/Argentina/Malaysia/New Zealand/Colombia/Taiwan/Brazil/Thailand

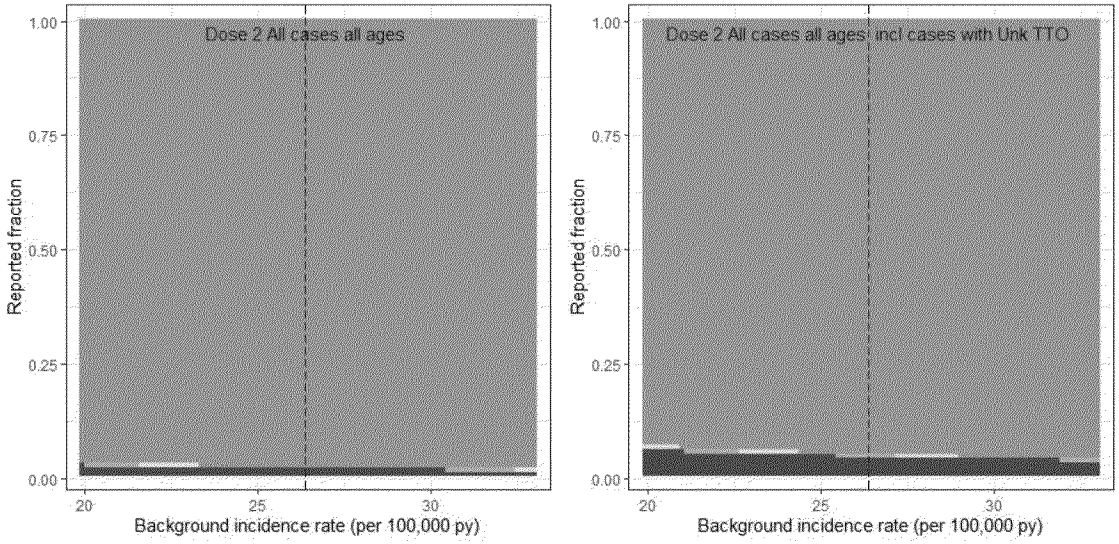
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Dose 2 -All cases, all ages including cases with Unk TTO	53	1712.37	14	26.38	169346503	0.03 (0.02 - 0.04)	Observed significantly < expected
Dose 1 All cases, all ages	199	2655	21	26.38	175045647	0.07 (0.06 - 0.09)	Observed significantly < expected
Dose 1 -All cases, all ages including cases with Unk TTO	352	2655	21	26.38	175045647	0.13 (0.12 - 0.15)	Observed significantly < expected
Dose 2 All cases, all ages	39	2568.56	21	26.38	169346503	0.02 (0.01 - 0.02)	Observed significantly < expected
Dose 2 -All cases, all ages including cases with Unk TTO	62	2568.56	21	26.38	169346503	0.02 (0.02 - 0.03)	Observed significantly < expected
Dose 1 All cases, all ages	266	5309.99	42	26.38	175045647	0.05 (0.04 - 0.06)	Observed significantly < expected
Dose 1 -All cases, all ages including cases with Unk TTO	419	5309.99	42	26.38	175045647	0.08 (0.07 - 0.09)	Observed significantly < expected

Table 51 Observed Versus Expected analysis for Pericarditis cases from EU/UK/Australia/Canada/Argentina/Malaysia/New Zealand/Colombia/Taiwan/Brazil/Thailand

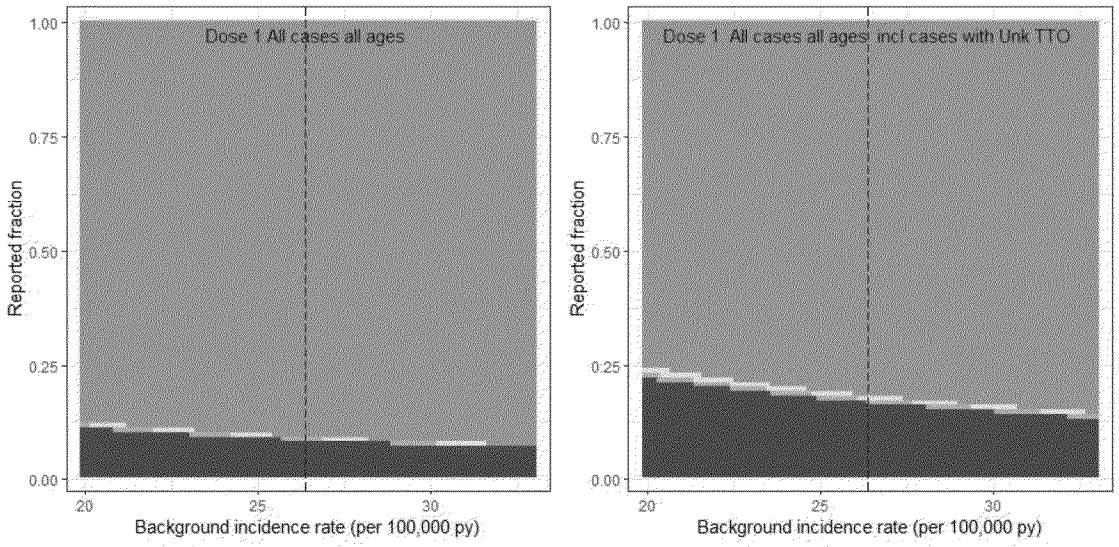
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Dose 2 All cases, all ages	64	5137.11	42	26.38	169346503	0.01 (0.01 - 0.02)	Observed significantly < expected
Dose 2 -All cases, all ages including cases with Unk TTO	87	5137.11	42	26.38	169346503	0.02 (0.01 - 0.02)	Observed significantly < expected


Dose 1 All cases all ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

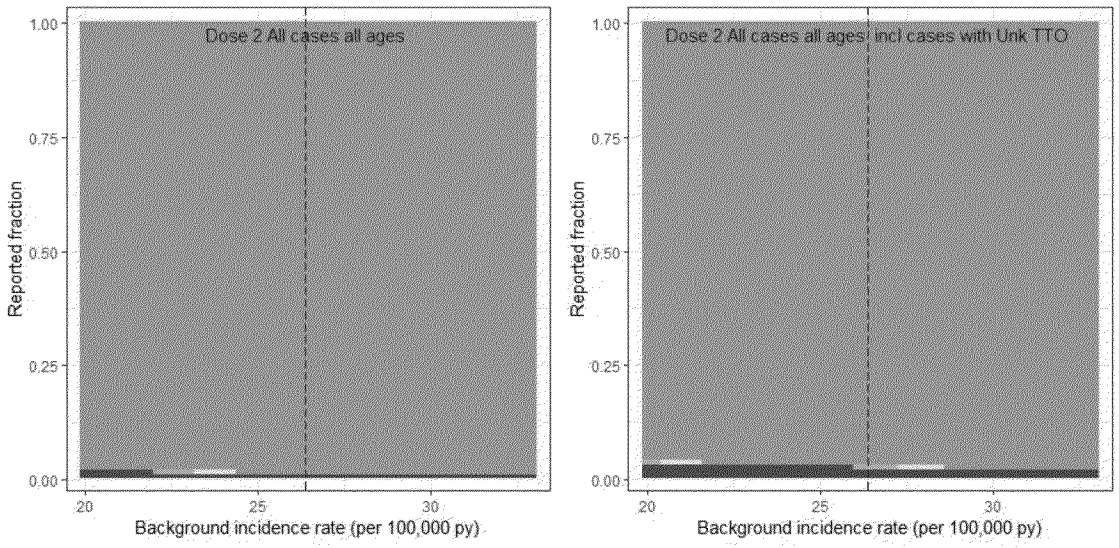
Dose 1 All cases all ages; incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)


Dose 2 All cases all ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

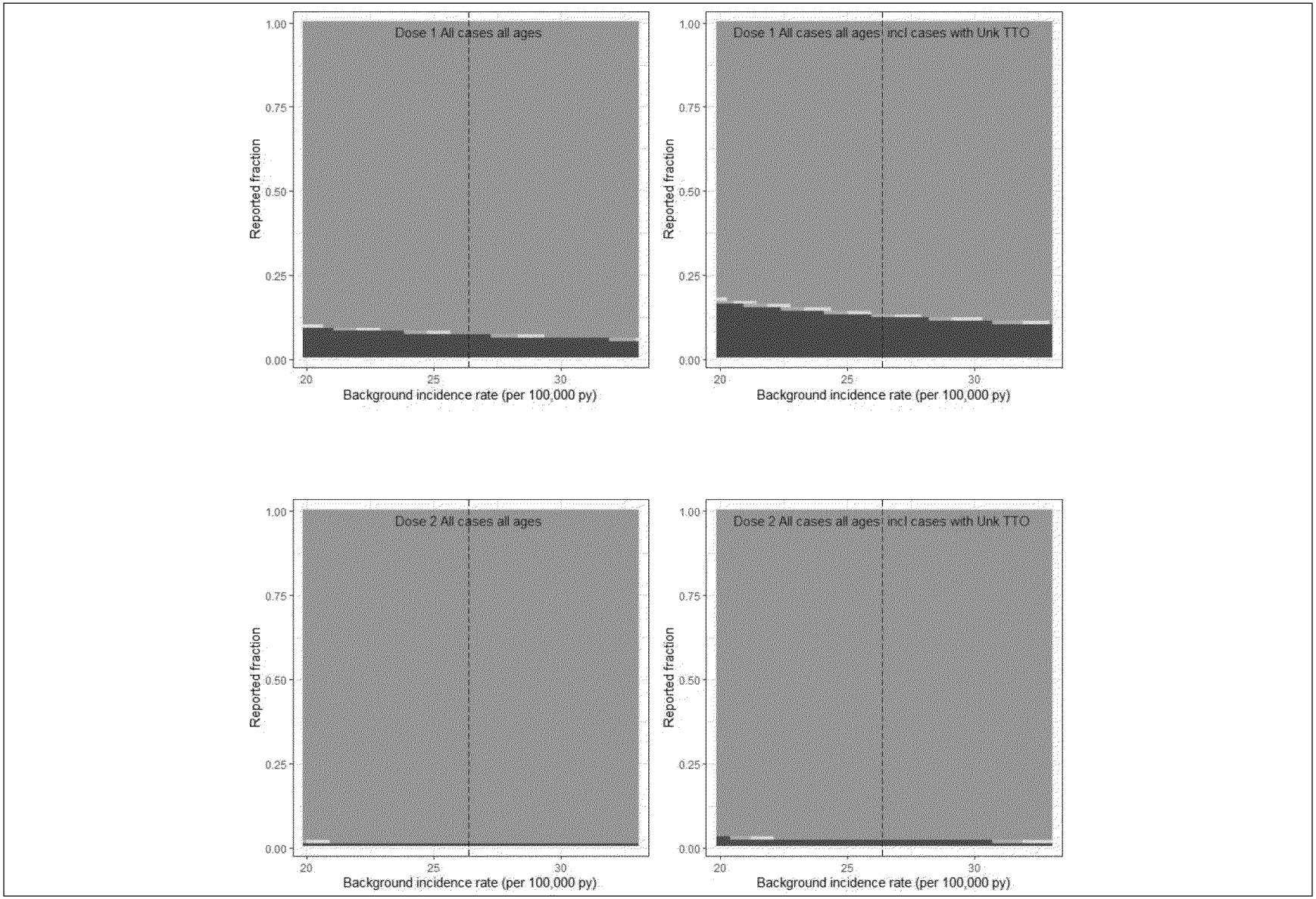
Dose 2 All cases all ages; incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

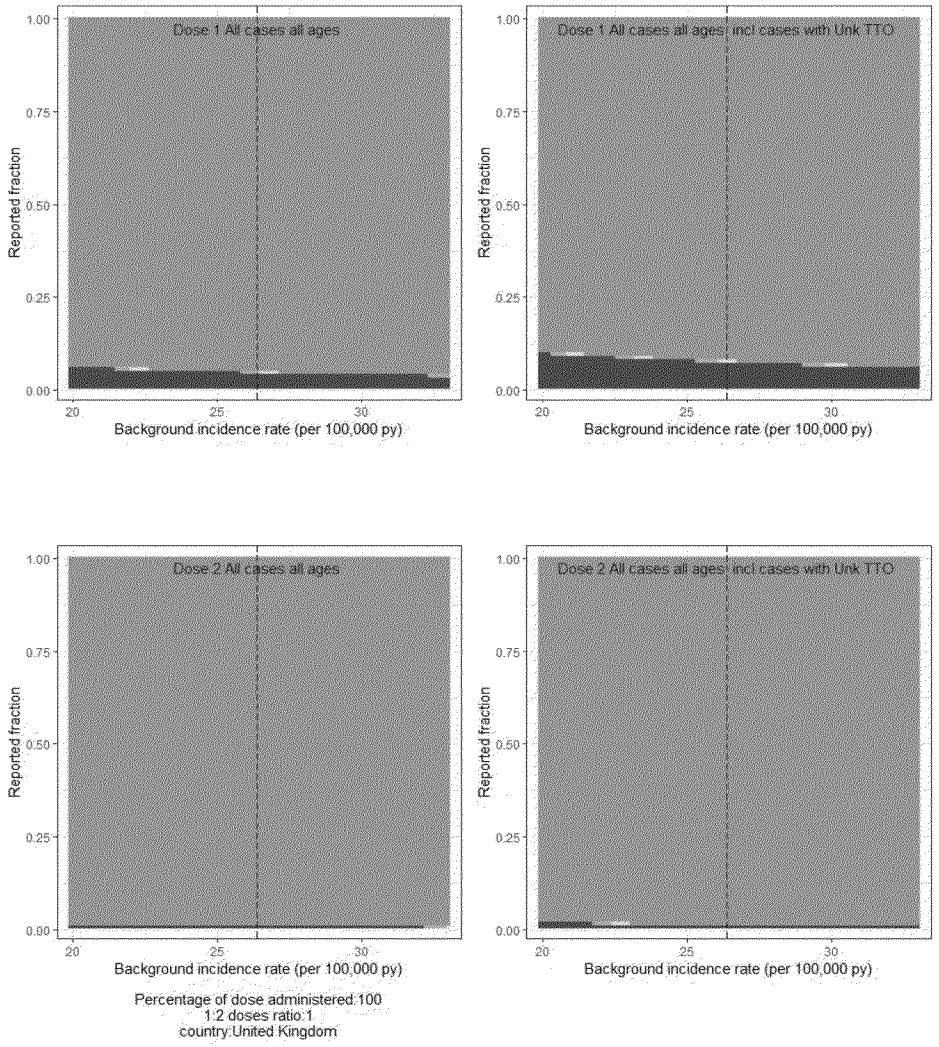

Dose 1 All cases all ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

Dose 1 All cases all ages incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)


Dose 2 All cases all ages
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

Dose 2 All cases all ages incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)


Dose 1 All cases all ages
Dose 1 All cases all ages incl cases with Unk TTO
Dose 2 All cases all ages
Dose 2 All cases all ages incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)

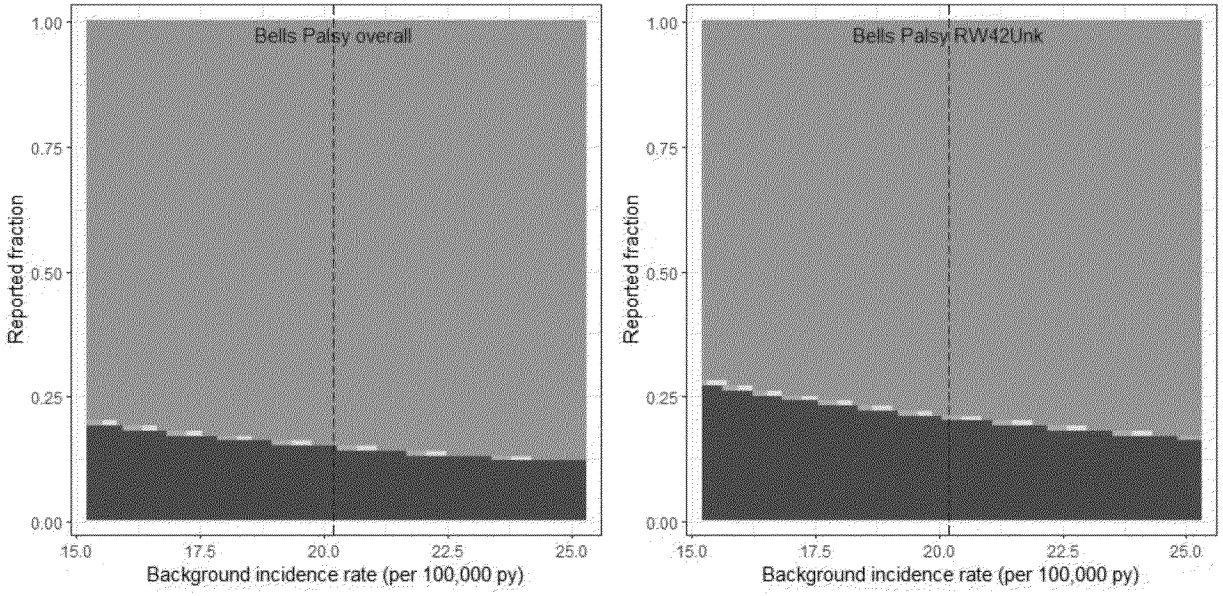

Dose 1 All cases all ages
Dose 1 All cases all ages incl cases with Unk TTO
Dose 2 All cases all ages
Dose 2 All cases all ages incl cases with Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
20
25
30
Background incidence rate (per 100,000 py)
Percentage of dose administered:100
1:2 doses ratio:1
country:United Kingdom

a Incidence Rate (IR) from Truven Marketscan

CI Confidence Interval; BR Brazil; AU Australia; E Expected; EU European Union; Observed; RW risk window; TTO Time to onset; UK United Kingdom

Table 52 Observed Versus Expected analysis for Bell's palsy

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Bell's Palsy overall	1658	10827.12	42	20.2	0.15 (0.15 - 0.16)	Observed significantly < expected
Bell's Palsy (RW42+Unk)	2301	10827.12	42	20.2	0.21 (0.2 - 0.22)	Observed significantly < expected

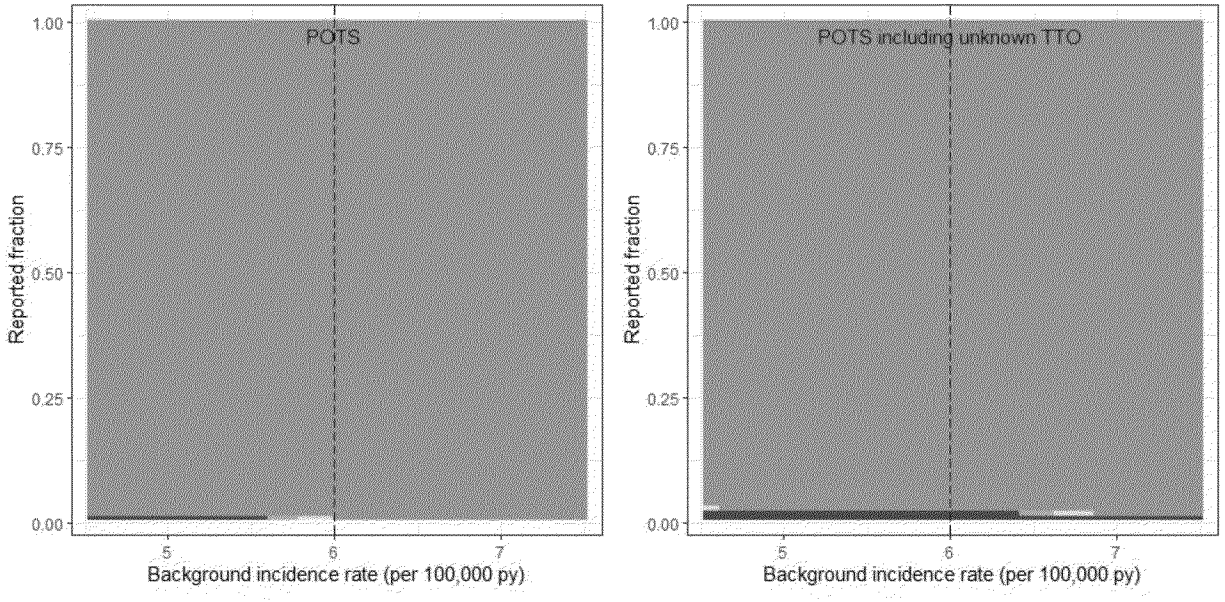


[a] Incidence rate (IR) Source: UK General Practice Research Database (GPRD)

CI Confidence Interval; E Expected; O observed, TTO Time to onset; RW risk window; Unk Unknown

Table 53 Observed Versus Expected analysis for Postural Orthostatic Tachycardia Syndrome (POTS)

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
POTS	31	3215.98	42	6	0.01 (0.01 - 0.01)	Observed significantly < expected
POTS (including unknown TTO)	71	3215.98	42	6	0.02 (0.02 - 0.03)	Observed significantly < expected

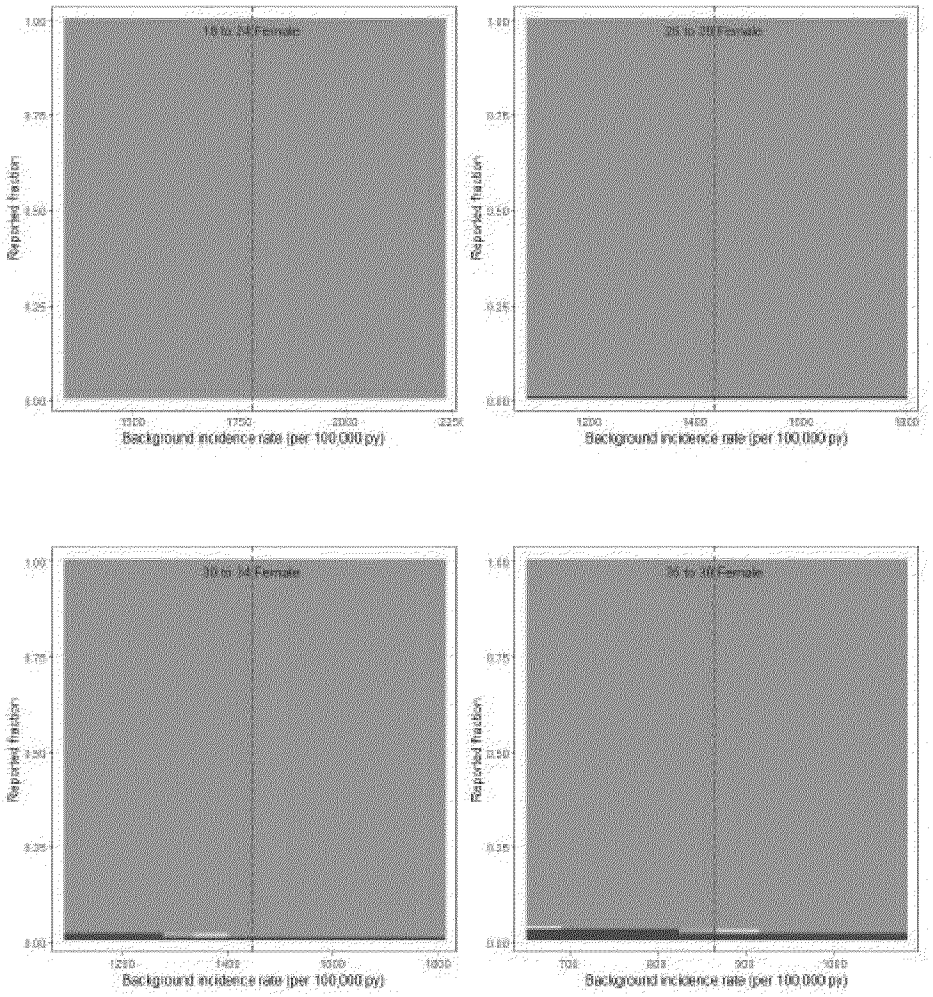


[a] Incidence Rate (IR): Source: AbdelRazek et al 2019

CI Confidence Interval; E Expected; O observed; POTS Postural Orthostatic Tachycardia Syndrome; TTO: Time to onset.

Table 54 Observed Versus Expected analysis for Pregnancy outcome – Maternal- Abortion spontaneous

Age Group	Observed Cases	Expected number of cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
18 to 24	3	1458.57	60	1780.8	498587	0 (0 - 0.01)
25 to 29	19	1442.61	60	1437.5	610901	0.01 (0.01 - 0.02)
30 to 34	37	2001.49	60	1447	842004	0.02 (0.01 - 0.03)
35 to 39	45	1492.7	60	864.6	1050964	0.03 (0.02 - 0.04)
40 to 44	28	749.05	60	223.3	2041971	0.04 (0.02 - 0.05)
18 to 24 (RW60 + Unk TTO)	9	1458.57	60	1780.8	498587	0.01 (0 - 0.01)
25 to 29 (RW60 + Unk TTO)	25	1442.61	60	1437.5	610901	0.02 (0.01 - 0.03)
30 to 34 (RW60 + Unk TTO)	62	2001.49	60	1447	842004	0.03 (0.02 - 0.04)
35 to 39 (RW60 + Unk TTO)	72	1492.7	60	864.6	1050964	0.05 (0.04 - 0.06)
40 to 44 (RW60 + Unk TTO)	39	749.05	60	223.3	2041971	0.05 (0.04 - 0.07)
All ages	150	12128.77	60	995.3	7418105	0.01 (0.01 - 0.01)
All ages (RW60 + Unk TTO)	251	12128.77	60	995.3	7418105	0.02 (0.02 - 0.02)


16 to 24 Female
25 to 29 Female
30 to 34 Female
35 to 39 Female
Reported fraction
Background incidence rate (per 100,000 py)

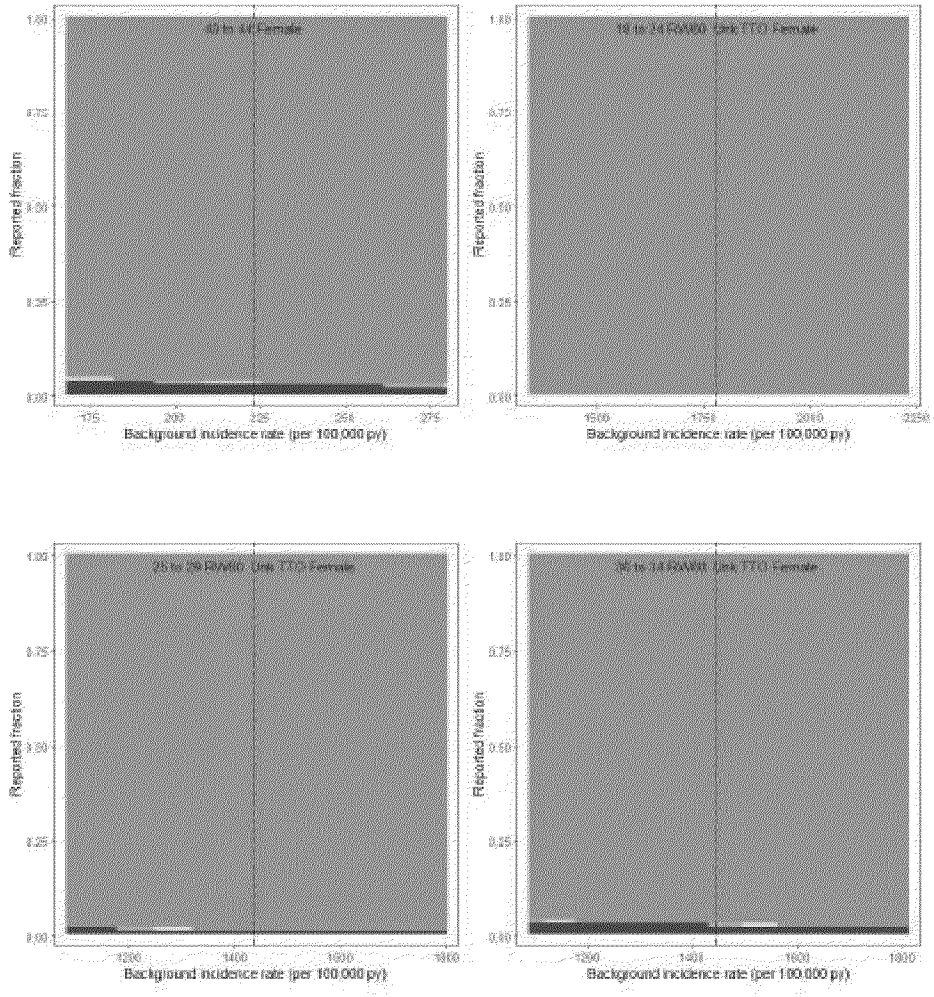
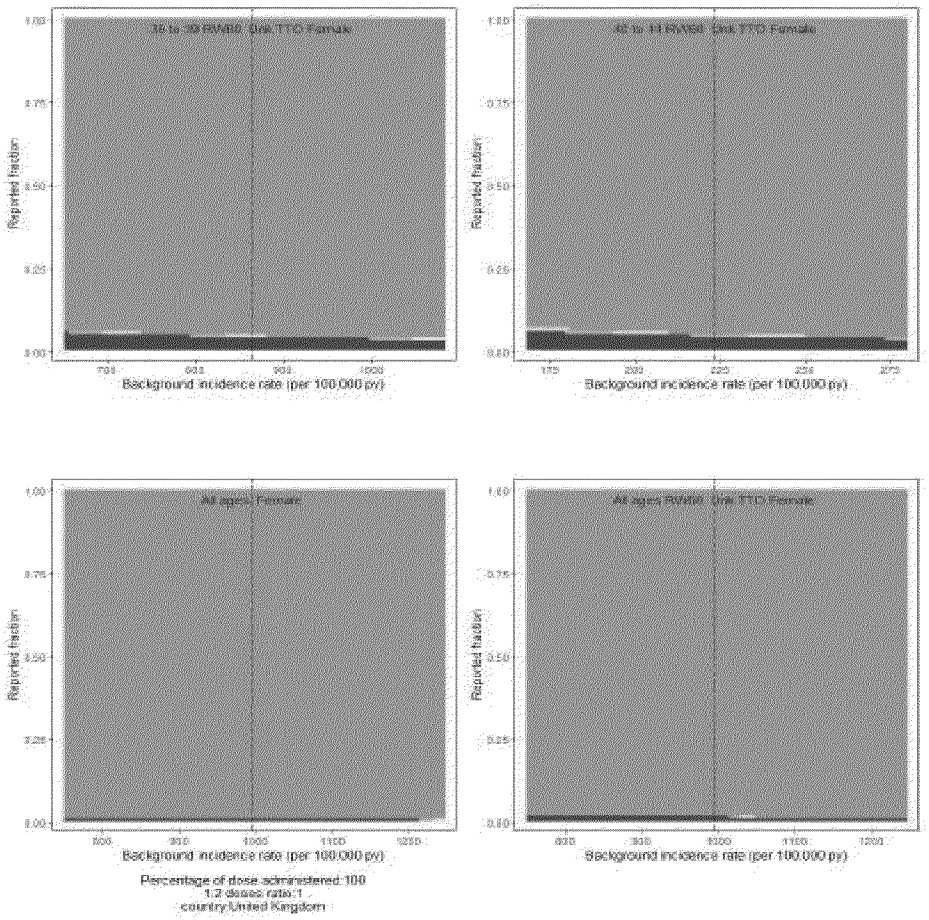

40 to 44 Female
18 to 24 RAM0 Unk TTO Female
25 to 29 RAM0 Unk TTO Female
30 to 34 RAM0 Unk TTO Female
Reported fraction
Background incidence rate (per 100,000 py)

Table 54 Observed Versus Expected analysis for Pregnancy outcome – Maternal- Abortion spontaneous

Age Group	Observed Cases	Expected number of cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
						

[a] US Claims: Truven Marketscan 2018.

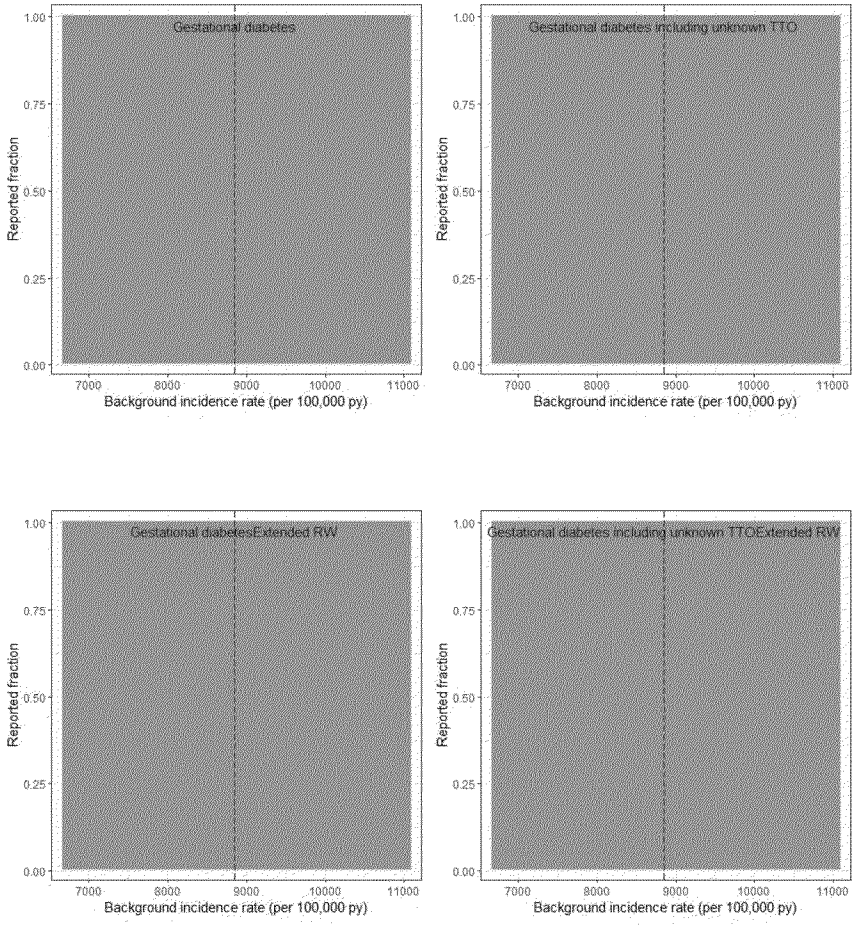
Exposure used for calculation until 28 December 2022 (female vaccinee, aged < 50 yrs from UK).

CI Confidence Interval; E Expected; O observed; RW Risk Window; TTO Time to onset; Unk Unknown

Table 55 Observed Versus Expected analysis for Pregnancy outcome – Maternal- Gestational diabetes [a]

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [b]	O over E ratio (95% CI)	
Gestational diabetes	10	6778207.2	60	8852.2	0 (0 - 0)	Observed significantly < expected
Gestational diabetes (including unknown TTO)	19	6778207.2	60	8852.2	0 (0 - 0)	Observed significantly < expected
Gestational diabetes	18	13104533.91	116	8852.2	0 (0 - 0)	Observed significantly < expected
Gestational diabetes (including unknown TTO)	27	13104533.91	116	8852.2	0 (0 - 0)	Observed significantly < expected

Table 55 Observed Versus Expected analysis for Pregnancy outcome – Maternal- Gestational diabetes [a]



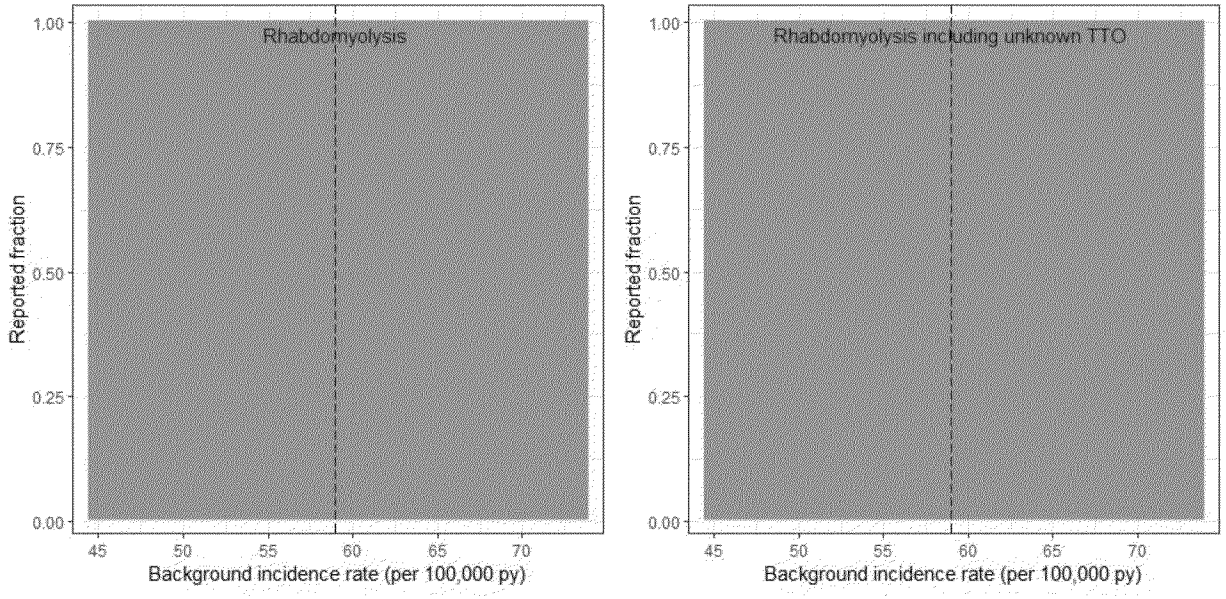
[a] US Claims: Truven Marketscan 2018.

[b] Exposure used for calculation until 28 December 2022 (female vaccinee, aged < 50 yrs from UK).

CI Confidence Interval; E Expected; O observed; TTO Time to onset.

Table 56 Observed Versus Expected analysis for Rhabdomyolysis

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Rhabdomyolysis	59	31623.77	42	59	0 (0 - 0)	Observed significantly < expected
Rhabdomyolysis including unknown TTO	94	31623.77	42	59	0 (0 - 0)	Observed significantly < expected

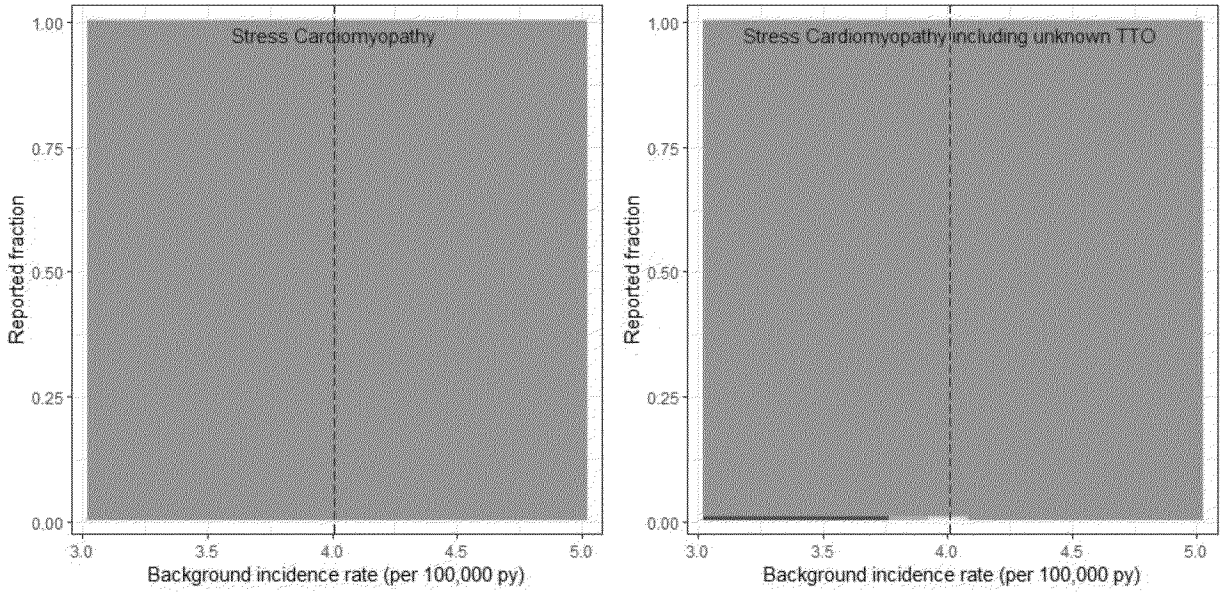


[a] Incidence rate: (IR): Torres et al 2015

CI Confidence Interval; E Expected; O observed; TTO Time to onset.

Table 57 Observed Versus Expected analysis for Stress cardiomyopathy

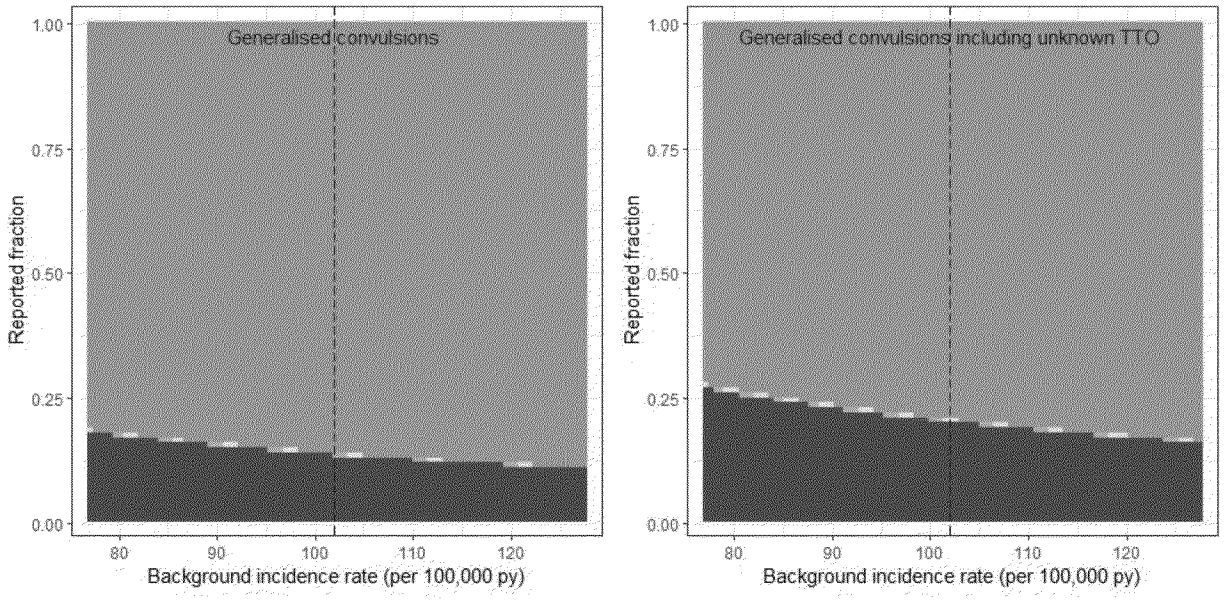
Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Stress Cardiomyopathy	14	2149.34	42	4.01	0.01 (0 - 0.01)	Observed significantly < expected
Stress Cardiomyopathy (including unknown TTO)	21	2149.34	42	4.01	0.01 (0.01 - 0.01)	Observed significantly < expected



[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2017-2019 - Stress cardiomyopathy (Narrow)).
CI Confidence Interval; E Expected; O observed; TTO Time to onset.

Table 58 Observed Versus Expected analysis for Generalised convulsions

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Generalised convulsions	2587	18223.87	14	102	0.14 (0.14 - 0.15)	Observed significantly < expected
Generalised convulsions (including unknown TTO)	3803	18223.87	14	102	0.21 (0.2 - 0.22)	Observed significantly < expected

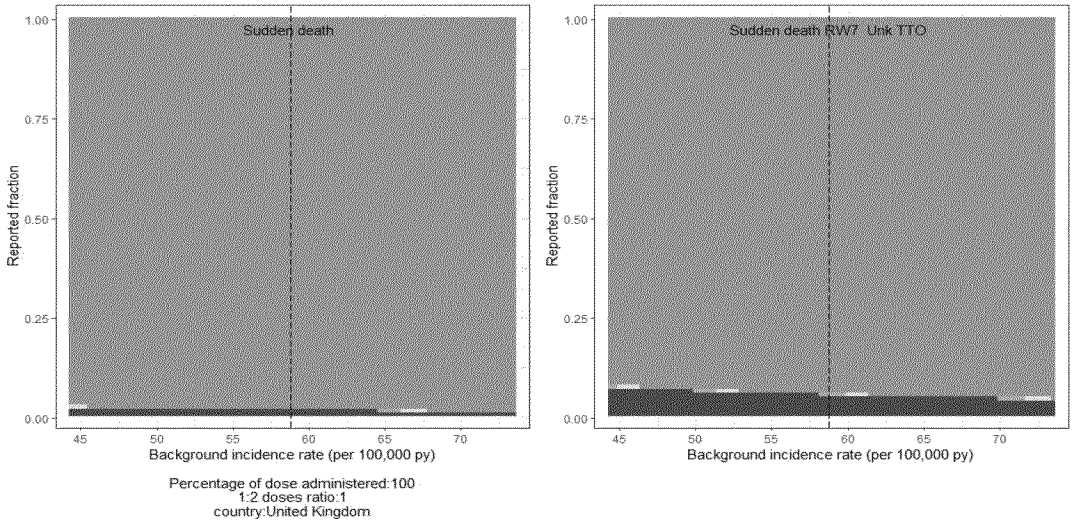


[a] Incidence rate: Maloney et al 2020

CI Confidence Interval; E Expected; O observed; TTO Time to onset.

Table 59 Observed Versus Expected analysis for Sudden death [b]

Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
118	5250.98	7	58.78	0.02 (0.02 - 0.03)	Observed significantly < expected
320	5250.98	7	58.78	0.06 (0.05 - 0.07)	Observed significantly < expected



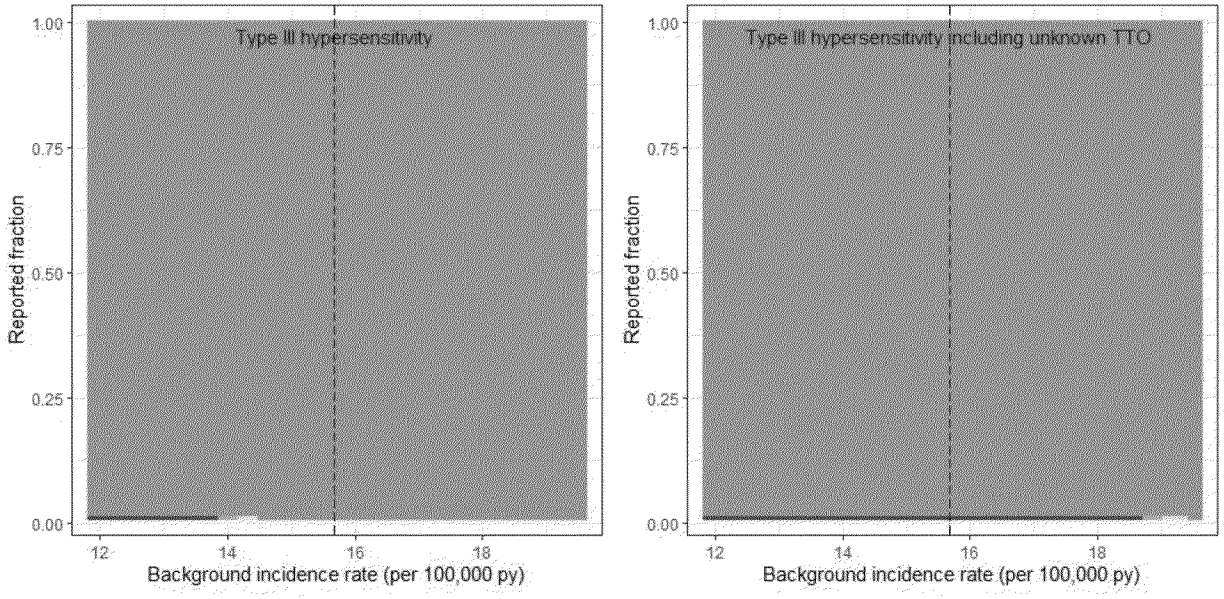
[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 - 2017-2019 – Sudden Death (Narrow)).

[b] Preferred Terms included Sudden death, Sudden cardiac death; events occurring within risk window of 0-7 days were included.

CI Confidence Interval; E Expected; O observed; TTO Time to onset.

Table 60 Observed Versus Expected analysis for Type III hypersensitivity

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	O over E ratio (95% CI)	
Type III hypersensitivity	76	8404.42	42	15.68	0.01 (0.01 - 0.01)	Observed significantly < expected
Type III hypersensitivity including unknown TTO	102	8404.42	42	15.68	0.01 (0.01 - 0.01)	Observed significantly < expected



[a] Incidence rate: source: (Willame et al 2021 [A]) ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: SOCV-Narrow (Median IR from 2017-2019 and excluding IR from BIPS/GePaRD).

CI Confidence Interval; E Expected; O observed; TTO: Time to onset.

Table 61 Observed Versus Expected analysis for Fatal reports[a] from EU+UK+Brazil+Australia

Age Group	Observed Cases [b]	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18-49	453	8337.91	42	65.86	110094983	0.05 (0.05 - 0.06)	Observed significantly < expected
50-59	428	12960.22	42	193.2	58336094	0.03 (0.03 - 0.04)	Observed significantly < expected
60-69	806	20982.88	42	314.82	57960860	0.04 (0.04 - 0.04)	Observed significantly < expected
Over 70	1256	37630.11	42	1010.74	32376365	0.03 (0.03 - 0.04)	Observed significantly < expected
18-49 (RW 42+Unk TTO)	673	8337.91	42	65.86	110094983	0.08 (0.07 - 0.09)	Observed significantly < expected
50-59 (RW 42+Unk TTO)	533	12960.22	42	193.2	58336094	0.04 (0.04 - 0.04)	Observed significantly < expected
60-69 (RW 42+Unk TTO)	973	20982.88	42	314.82	57960860	0.05 (0.04 - 0.05)	Observed significantly < expected
Over 70 (RW 42+Unk TTO)	1586	37630.11	42	1010.74	32376365	0.04 (0.04 - 0.04)	Observed significantly < expected

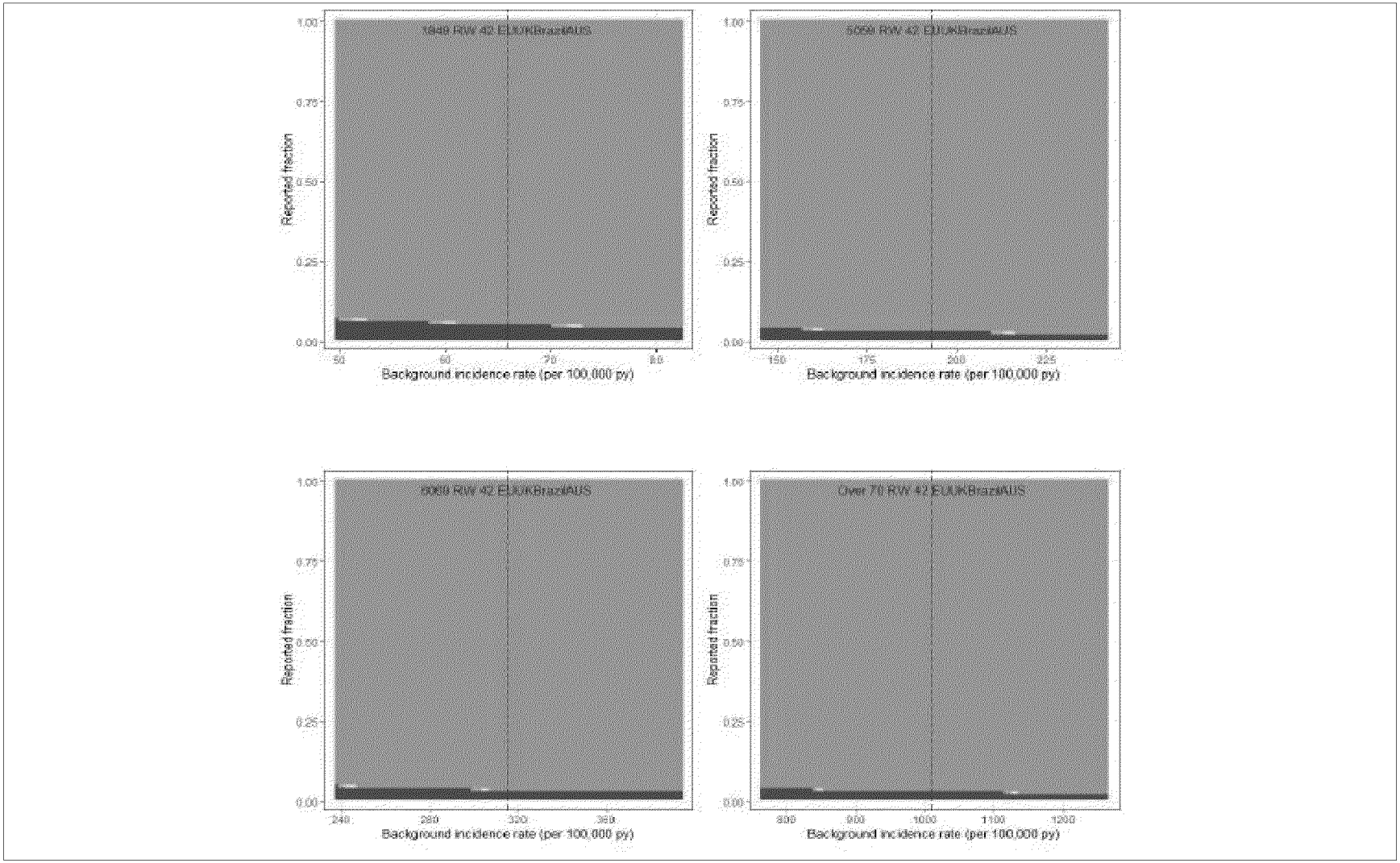
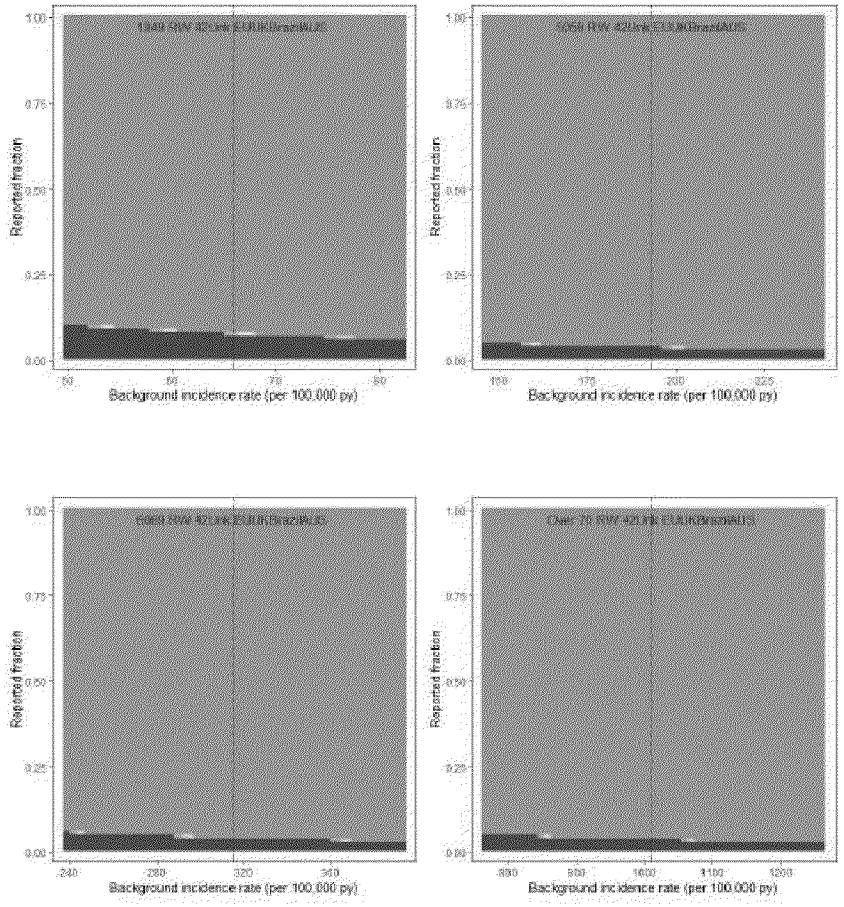

1849 RW 42 EUUKBrazilAUS
5059 RW 42 EUUKBrazilAUS
8069 RW 42 EUUKBrazilAUS
Over 70 RW 42 EUUKBrazilAUS
Reported fraction
Background incidence rate (per 100,000 py)

Table 61 Observed Versus Expected analysis for Fatal reports[a] from EU+UK+Brazil+Australia

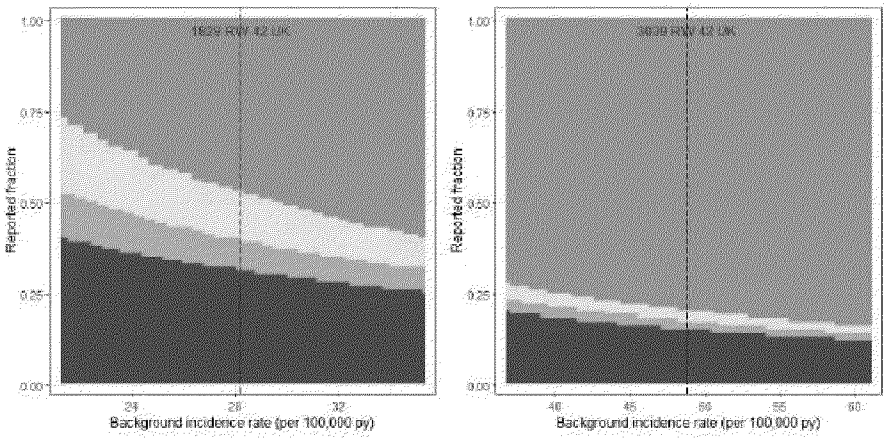
Age Group	Observed Cases [b]	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

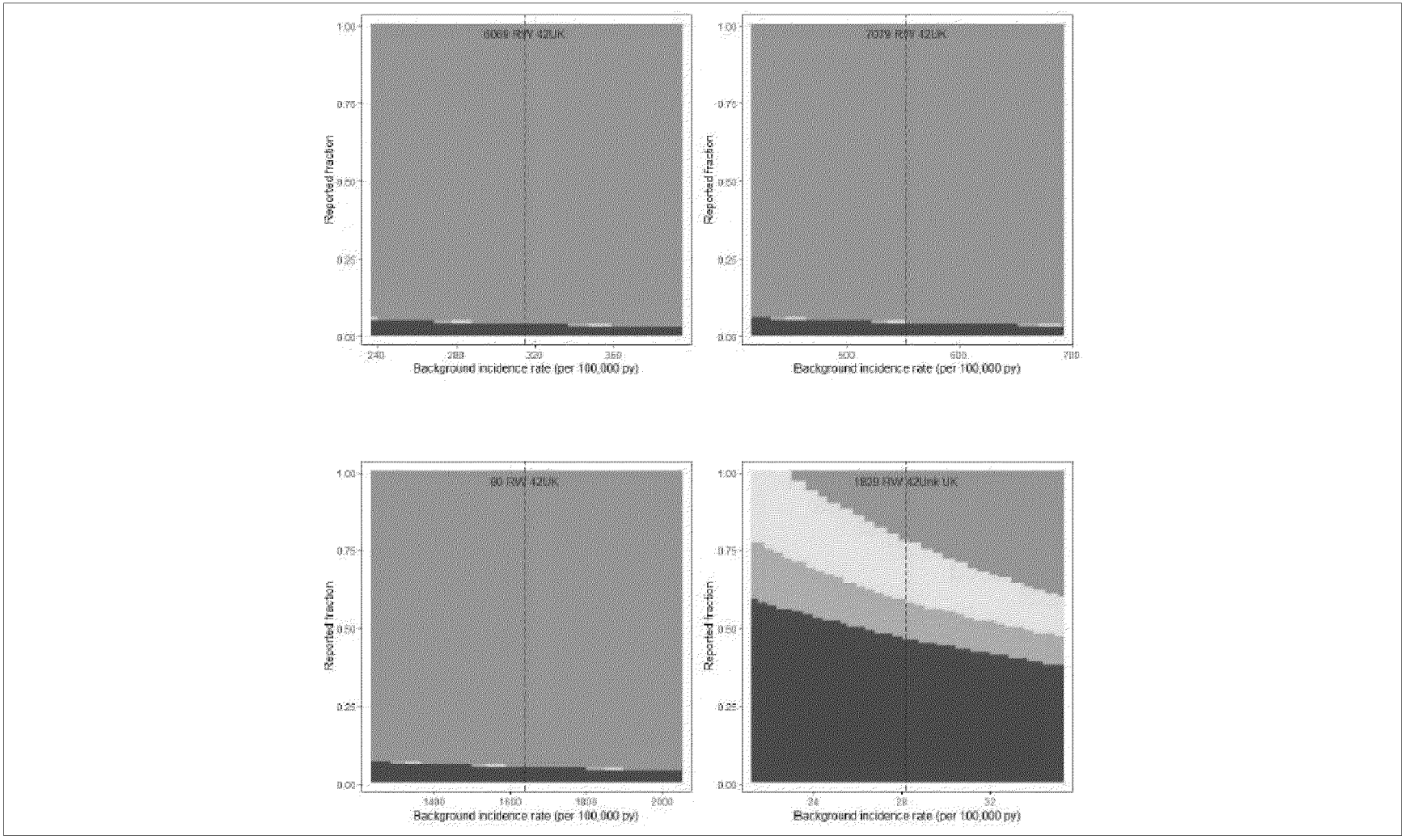
[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Death (Narrow))

CI Confidence Interval; EU European Union; E Expected; O observed, TTO Time to onset; UK United Kingdom

Table 62 Observed Versus Expected analysis for Fatal reports from UK

Age Group	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18-29	25	62.27	42	28.22	1918869	0.4 (0.26 - 0.59)	Observed significantly < expected
30-39	33	185.65	42	48.8	3308256	0.18 (0.12 - 0.25)	Observed significantly < expected
40-49	74	1038.58	42	100.86	8954709	0.07 (0.06 - 0.09)	Observed significantly < expected
50-59	134	2767.26	42	193.2	12455887	0.05 (0.04 - 0.06)	Observed significantly < expected
60-69	155	3518.19	42	314.82	9718273	0.04 (0.04 - 0.05)	Observed significantly < expected
70-79	204	4207.16	42	553.23	6613249	0.05 (0.04 - 0.06)	Observed significantly < expected
80+	282	5002.41	42	1638.26	2655389	0.06 (0.05 - 0.06)	Observed significantly < expected
18-29 (RW 42+Unk TTO)	37	62.27	42	28.22	1918869	0.59 (0.42 - 0.82)	Observed significantly < expected
30-39 (RW 42+Unk TTO)	57	185.65	42	48.8	3308256	0.31 (0.23 - 0.4)	Observed significantly < expected
40-49 (RW 42+Unk TTO)	105	1038.58	42	100.86	8954709	0.1 (0.08 - 0.12)	Observed significantly < expected
50-59 (RW 42+Unk TTO)	175	2767.26	42	193.2	12455887	0.06 (0.05 - 0.07)	Observed significantly < expected
60-69 (RW 42+Unk TTO)	202	3518.19	42	314.82	9718273	0.06 (0.05 - 0.07)	Observed significantly < expected
70-79 (RW 42+Unk TTO)	247	4207.16	42	553.23	6613249	0.06 (0.05 - 0.07)	Observed significantly < expected
80+ (RW 42+Unk TTO)	326	5002.41	42	1638.26	2655389	0.07 (0.06 - 0.07)	Observed significantly < expected


1829 RW 42 UK
3839 RW 42 UK
4849 RW 42 UK
5859 RW 42 UK
Reported fraction
Background incidence rate (per 100,000 py)


6069 RfV 42Unk
7079 RfV 42Unk
80 RfV 42Unk
1839 RfV 42Unk UK
Reported fraction
Background incidence rate (per 100,000 py)

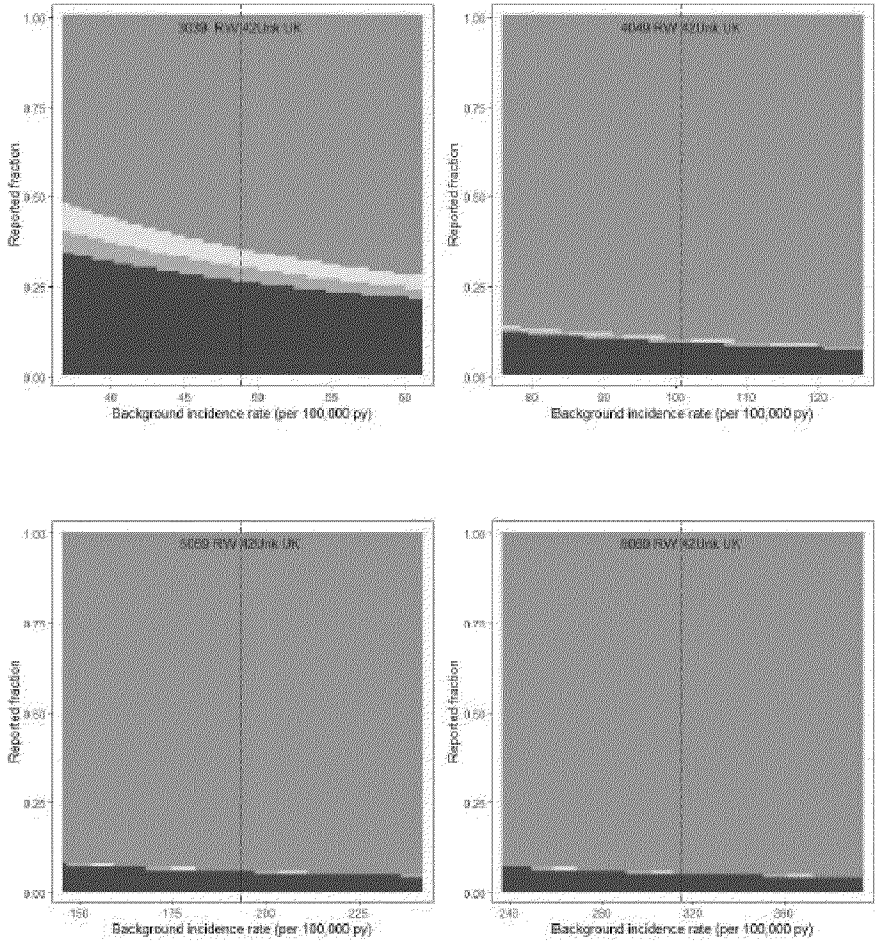
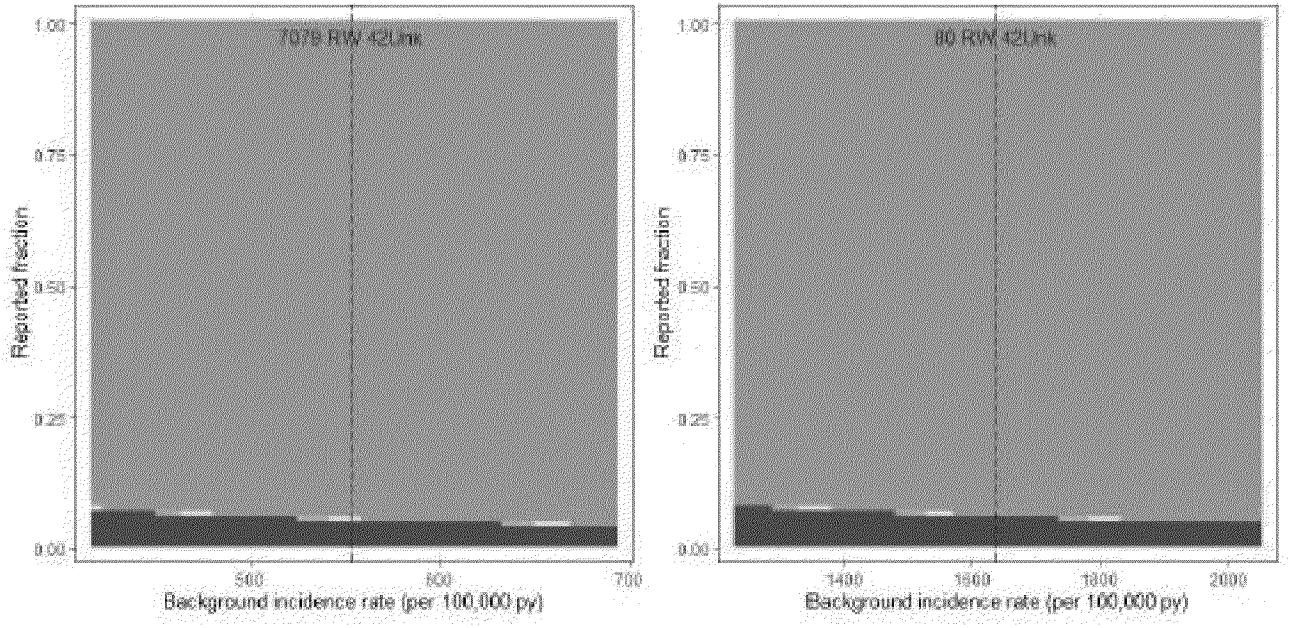

Reported fraction
Background incidence rate (per 100,000 py)

Table 62 Observed Versus Expected analysis for Fatal reports from UK

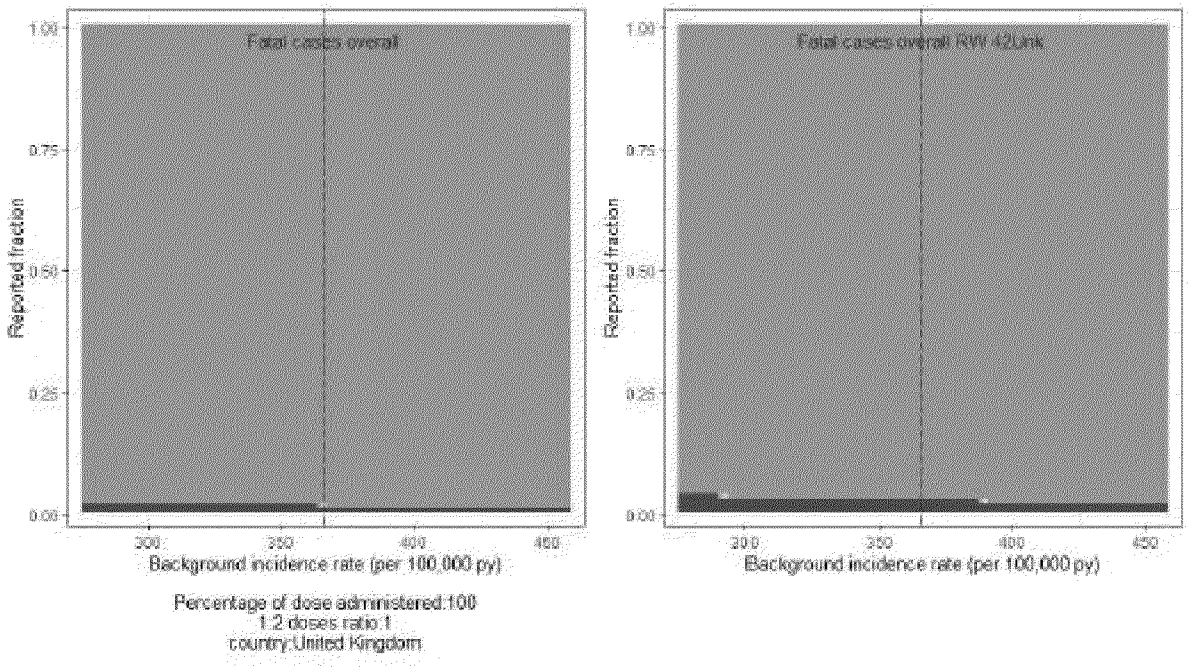
Age Group	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Death (Narrow))

CI Confidence Interval; E Expected; O observed; TTO; RW risk window; Time to onset; UK United Kingdom; Unk Unknown.

Table 63 Observed Versus Expected analysis for Fatal reports Overall

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000-person years[a]	Exposure	O over E ratio (95% CI)	
Fatal cases overall	3914	196040.59	42	365.75	466115644	0.02 (0.02 - 0.02)	Observed significantly < expected
Fatal cases overall (Including Unk TTO)	6259	196040.59	42	365.75	466115644	0.03 (0.03 - 0.03)	Observed significantly < expected

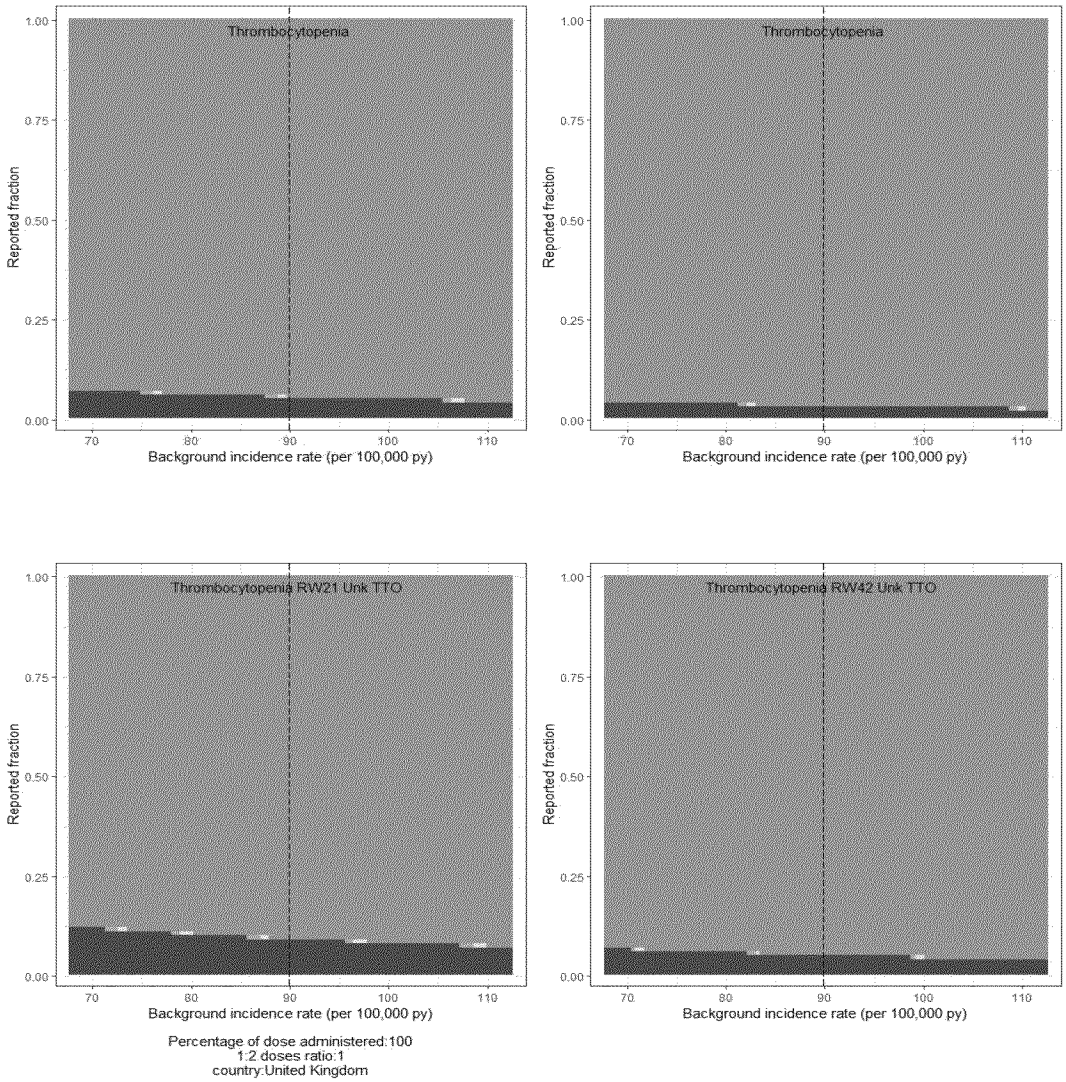


[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Death (Narrow)).

CI Confidence Interval; E Expected; O observed, TTO Time to onset, Unk Unknown.

Table 64 Observed Versus Expected analysis for Thrombocytopenia [a]

Description	Observed Cases	Expected Cases	Risk window	Background rates [b]	Exposure	O over E ratio (95% CI)	
Thrombocytopenia	1426	24086.22	21	89.87	466115644	0.06 (0.06 - 0.06)	Observed significantly < expected
Thrombocytopenia	1759	48172.45	42	89.87	466115644	0.04 (0.03 - 0.04)	Observed significantly < expected
Thrombocytopenia (RW21+ Unk TTO)	2327	24086.22	21	89.87	466115644	0.1 (0.09 - 0.1)	Observed significantly < expected
Thrombocytopenia (RW42+ Unk TTO)	2660	48172.45	42	89.87	466115644	0.06 (0.05 - 0.06)	Observed significantly < expected


Thrombocytopenia
Thrombocytopenia
Thrombocytopenia RW21 Unk TTO
Thrombocytopenia RW42 Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
70
80
90
100
110
Percentage of dose administered:100
1:2 doses ratio:1
country:United Kingdom

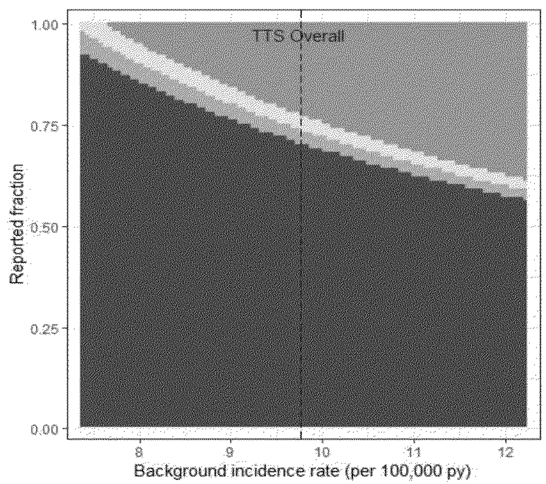
[a] Preferred Terms included are from MedDRA HLT of "Thrombocytopenias" and SMQ of "Hematopoietic Thrombocytopenia-Narrow, Cases only reported within Risk window were considered.

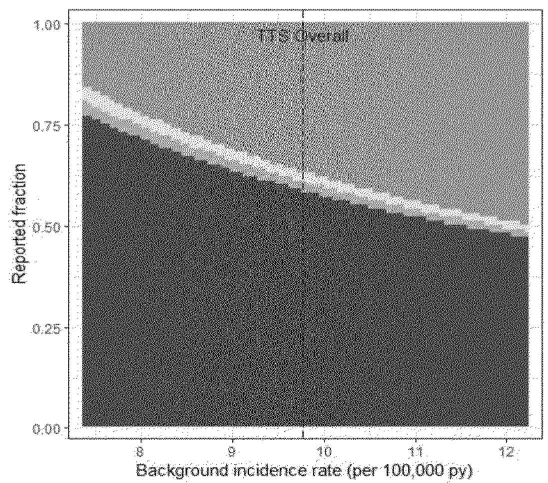
[b] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 – Thrombocytopenia (Narrow)).

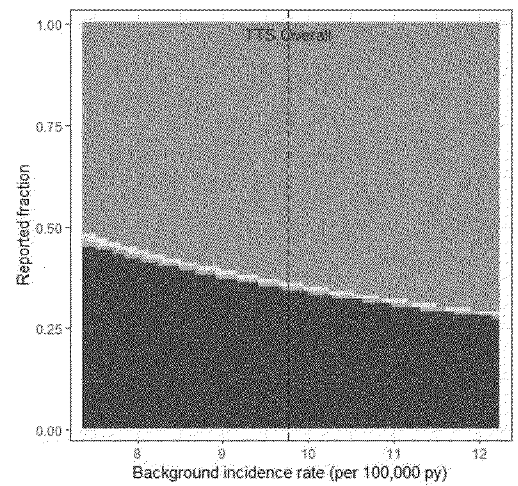
CI Confidence Interval; E Expected; O observed; TTO Time to onset, Unk Unknown.

Table 65 Observed Versus Expected analysis for Thrombosis with thrombocytopenia (TTS) (Overall)

Adverse Events	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS Overall	1292	1745.56	14	9.77	466115644	0.74 (0.7 - 0.78)	Observed significantly < expected
TTS Overall	1603	2618.34	21	9.77	466115644	0.61 (0.58 - 0.64)	Observed significantly < expected
TTS Overall	1866	5236.68	42	9.77	466115644	0.36 (0.34 - 0.37)	Observed significantly < expected







Adverse Events	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS Overall (RW14+Unk TTO)	1942	1745.56	14	9.77	466115644	1.11 (1.06 - 1.16)	Observed significantly > expected
TTS Overall (RW21+Unk TTO)	2253	2618.34	21	9.77	466115644	0.86 (0.83 - 0.9)	Observed significantly < expected
TTS Overall (RW42+Unk TTO)	2516	5236.68	42	9.77	466115644	0.48 (0.46 - 0.5)	Observed significantly < expected

Table 65 Observed Versus Expected analysis for Thrombosis with thrombocytopenia (TTS) (Overall)

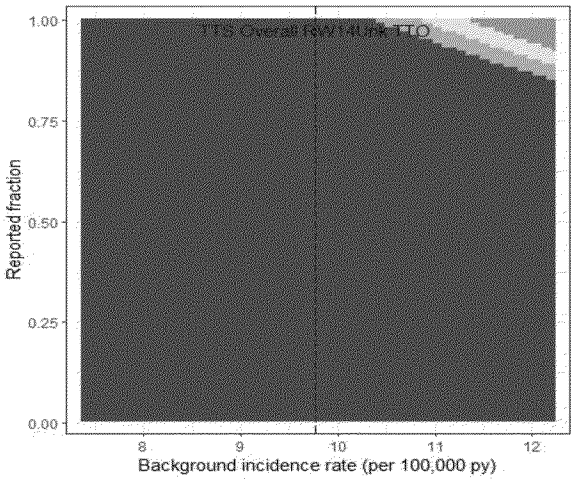
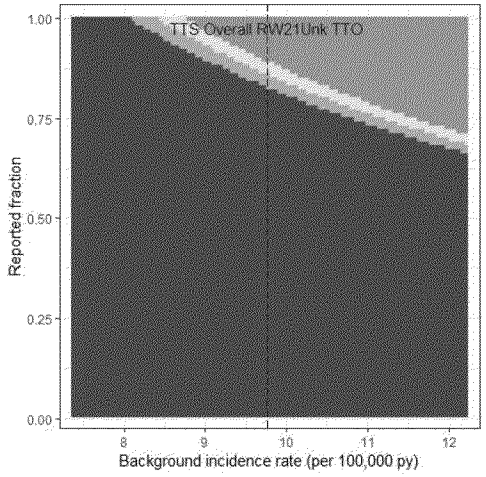
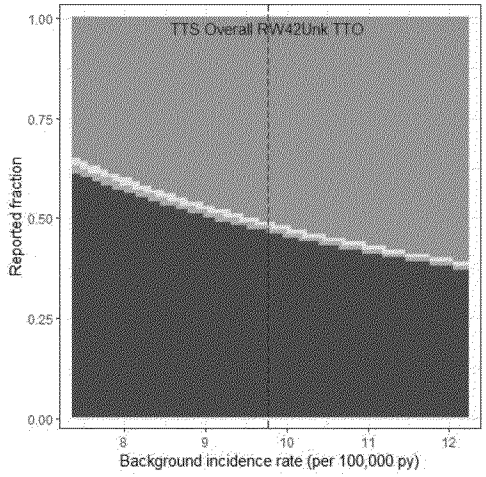
Adverse Events	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
							
							
							
TTS Overall	1292	1990.33	14	11.14	466115644	0.65 (0.61 - 0.69)	Observed significantly < expected
TTS Overall	1603	2985.5	21	11.14	466115644	0.54 (0.51 - 0.56)	Observed significantly < expected
TTS Overall	1866	5971	42	11.14	466115644	0.31 (0.3 - 0.33)	Observed significantly < expected

Table 65 Observed Versus Expected analysis for Thrombosis with thrombocytopenia (TTS) (Overall)

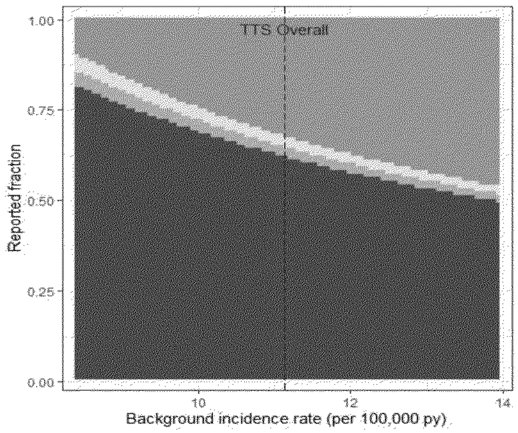
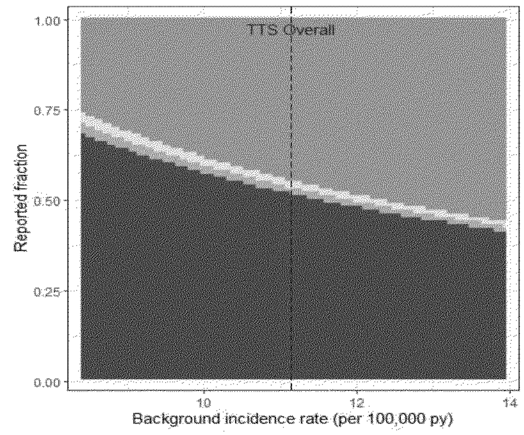
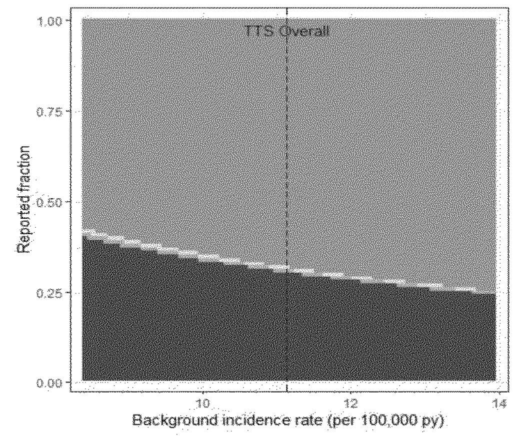
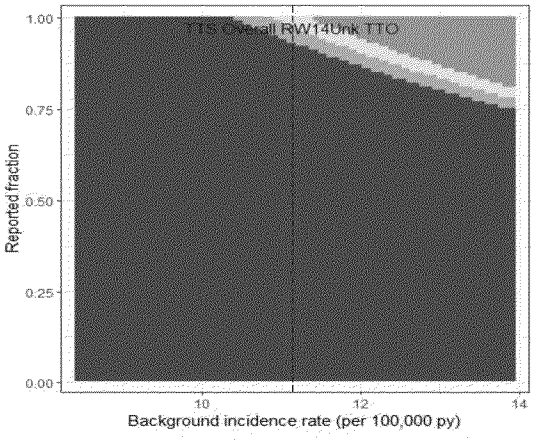
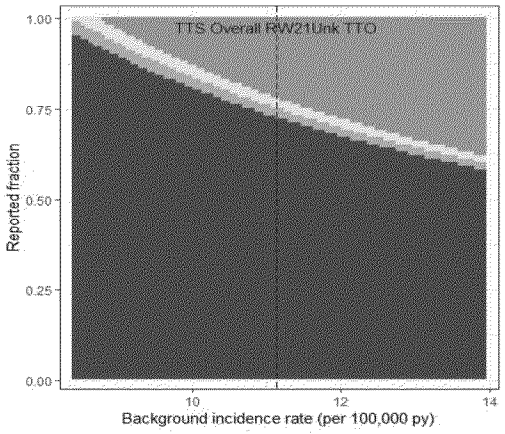
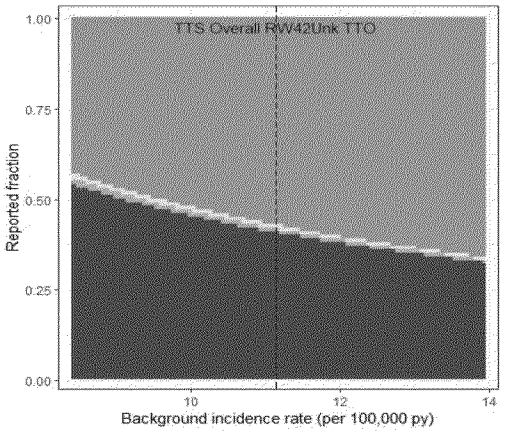
Adverse Events	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
  							
TTS Overall (RW14+Unk TTO)	1942	1914.29	14	11.14	448306152	0.89 (0.85 - 0.94)	Observed significantly < expected
TTS Overall (RW21+Unk TTO)	2253	2985.5	21	11.14	466115644	0.75 (0.72 - 0.79)	Observed significantly < expected
TTS Overall (RW42+Unk TTO)	2516	5971	42	11.14	466115644	0.42 (0.41 - 0.44)	Observed significantly < expected

Table 65 Observed Versus Expected analysis for Thrombosis with thrombocytopenia (TTS) (Overall)

Adverse Events	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
							 

[a] Only cases observed within 0-14, 0-21, and 0-42 days were included; Risk Window: 14, 21, and 42 days.

Incidence Rate 9.77/100,000 PY from Truven Market Scan (2019) aligned with the OHDSI TTS algorithm.

Incidence Rate 11.14/100,000 PY from Truven Market Scan database (2019) aligned with the OHDSI TTS algorithm, updated OHDSI-aligned codelists and washout periods.

CI Confidence interval; E Expected; O Observed; OHDSI Observational Health Data Science and Informatics; RW risk window; TCP Thrombocytopenia; TTS Thrombosis with thrombocytopenia syndrome; TTO Time to onset; Unk Unknown

Table 66 Observed versus Expected analysis for Thrombosis with thrombocytopenia by age group (EU+UK+Brazil+Australia)

Adverse Events	Observed cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
Incidence Rate from Truven Market Scan (2019) aligned with the OHDSI TTS algorithm							
TTS - 18-49	488	191.17	14	4.53	110094983	2.55 (2.33 - 2.79)	Observed significantly > expected
TTS - 50-59	220	232.55	14	10.4	58336094	0.95 (0.83 - 1.08)	Observed < expected
TTS - 60-69	244	426.34	14	19.19	57960860	0.57 (0.5 - 0.65)	Observed significantly < expected
TTS – Over 70	190	574.71	14	46.31	32376365	0.33 (0.29 - 0.38)	Observed significantly < expected

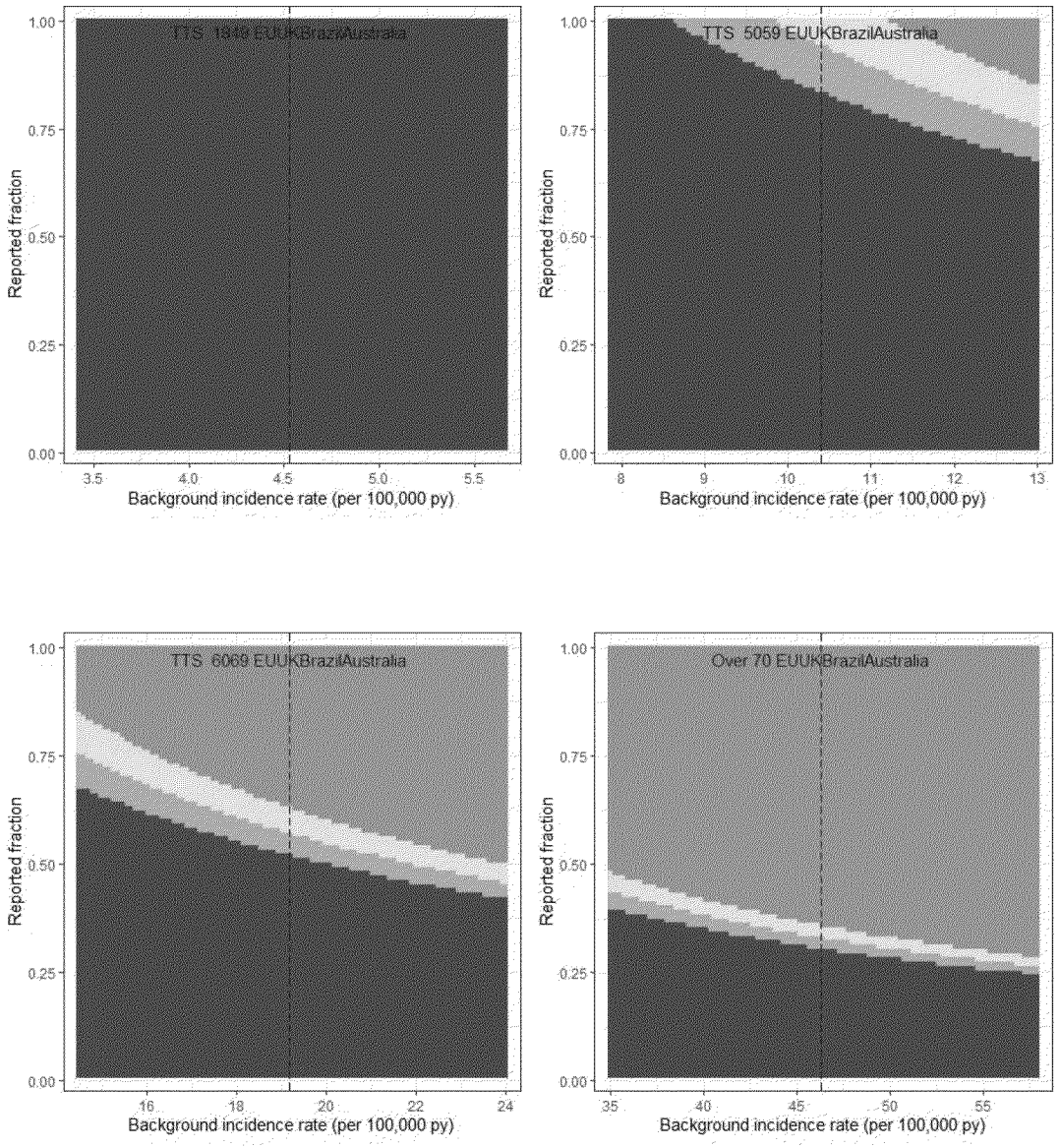

TTS 1849 EUUKBrazilAustralia
TTS 5059 EUUKBrazilAustralia
TTS 6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

Table 66 Observed versus Expected analysis for Thrombosis with thrombocytopenia by age group (EU+UK+Brazil+Australia)

Adverse Events	Observed cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - 18-49	567	286.75	21	4.53	110094983	1.98 (1.82 - 2.15)	Observed significantly > expected
TTS - 50-59	292	348.83	21	10.4	58336094	0.84 (0.74 - 0.94)	Observed significantly < expected
TTS - 60-69	315	639.51	21	19.19	57960860	0.49 (0.44 - 0.55)	Observed significantly < expected
TTS – Over 70	249	862.07	21	46.31	32376365	0.29 (0.25 - 0.33)	Observed significantly < expected

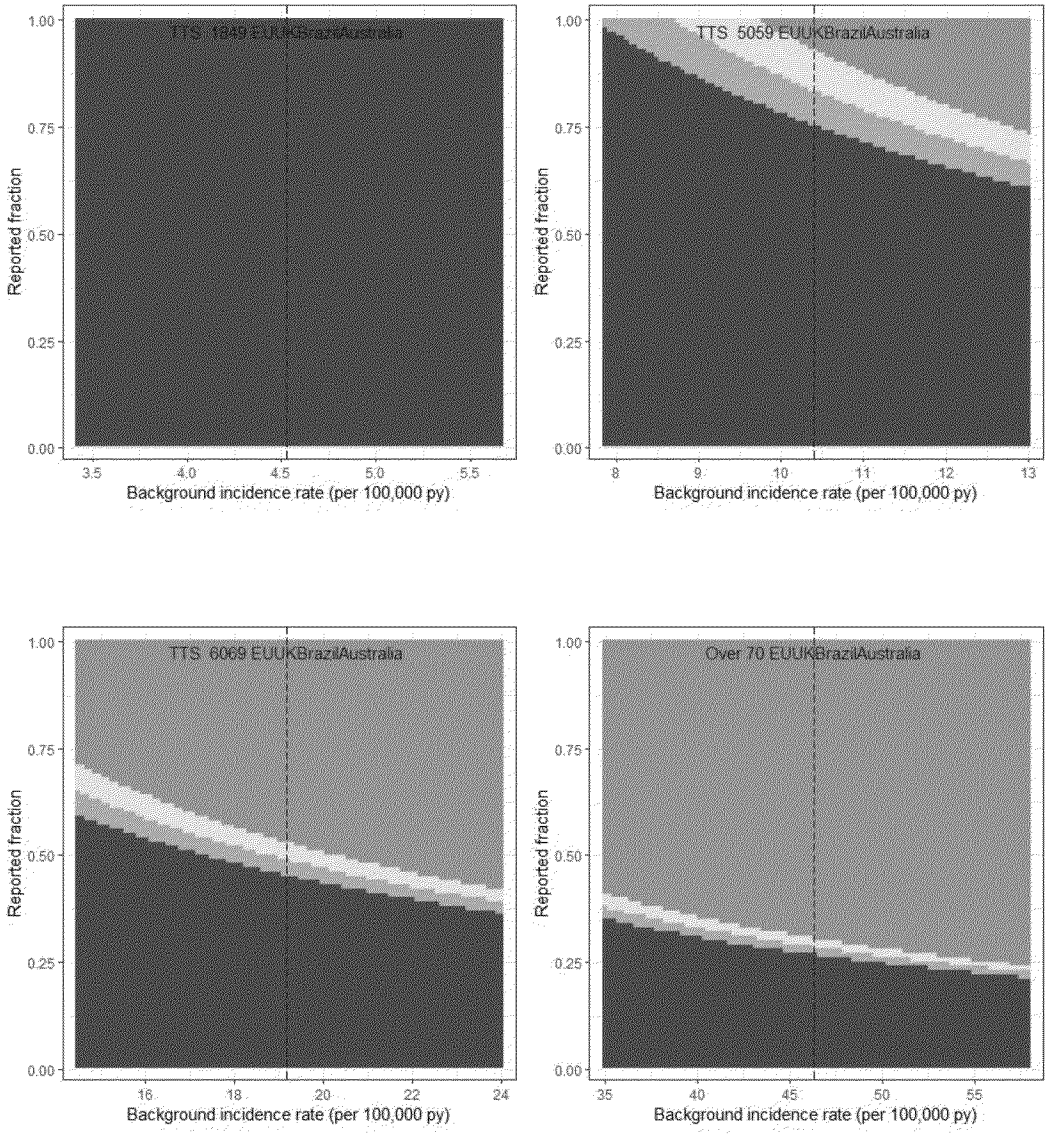

TTS 1849 EUUKBrazilAustralia
TTS 5059 EUUKBrazilAustralia
TTS 6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

Table 66 Observed versus Expected analysis for Thrombosis with thrombocytopenia by age group (EU+UK+Brazil+Australia)

Adverse Events	Observed cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - 18-49	624	573.5	42	4.53	110094983	1.09 (1 - 1.18)	Observed significantly > expected
TTS - 50-59	337	697.65	42	10.4	58336094	0.48 (0.43 - 0.54)	Observed significantly < expected
TTS - 60-69	379	1279.02	42	19.19	57960860	0.3 (0.27 - 0.33)	Observed significantly < expected
TTS – Over 70	322	1724.13	42	46.31	32376365	0.19 (0.17 - 0.21)	Observed significantly < expected
Incidence Rate from Truven Market Scan database (2019) aligned with the OHDSI TTS algorithm, updated OHDSI-aligned codelists and washout periods							
TTS - 18-49	488	210.58	14	4.99	110094983	2.32 (2.12 - 2.53)	Observed significantly > expected
TTS - 50-59	220	281.74	14	12.6	58336094	0.78 (0.68 - 0.89)	Observed significantly < expected
TTS - 60-69	244	496.1	14	22.33	57960860	0.49 (0.43 - 0.56)	Observed significantly < expected
TTS – Over 70	190	614.3	14	49.5	32376365	0.31 (0.27 - 0.36)	Observed significantly < expected

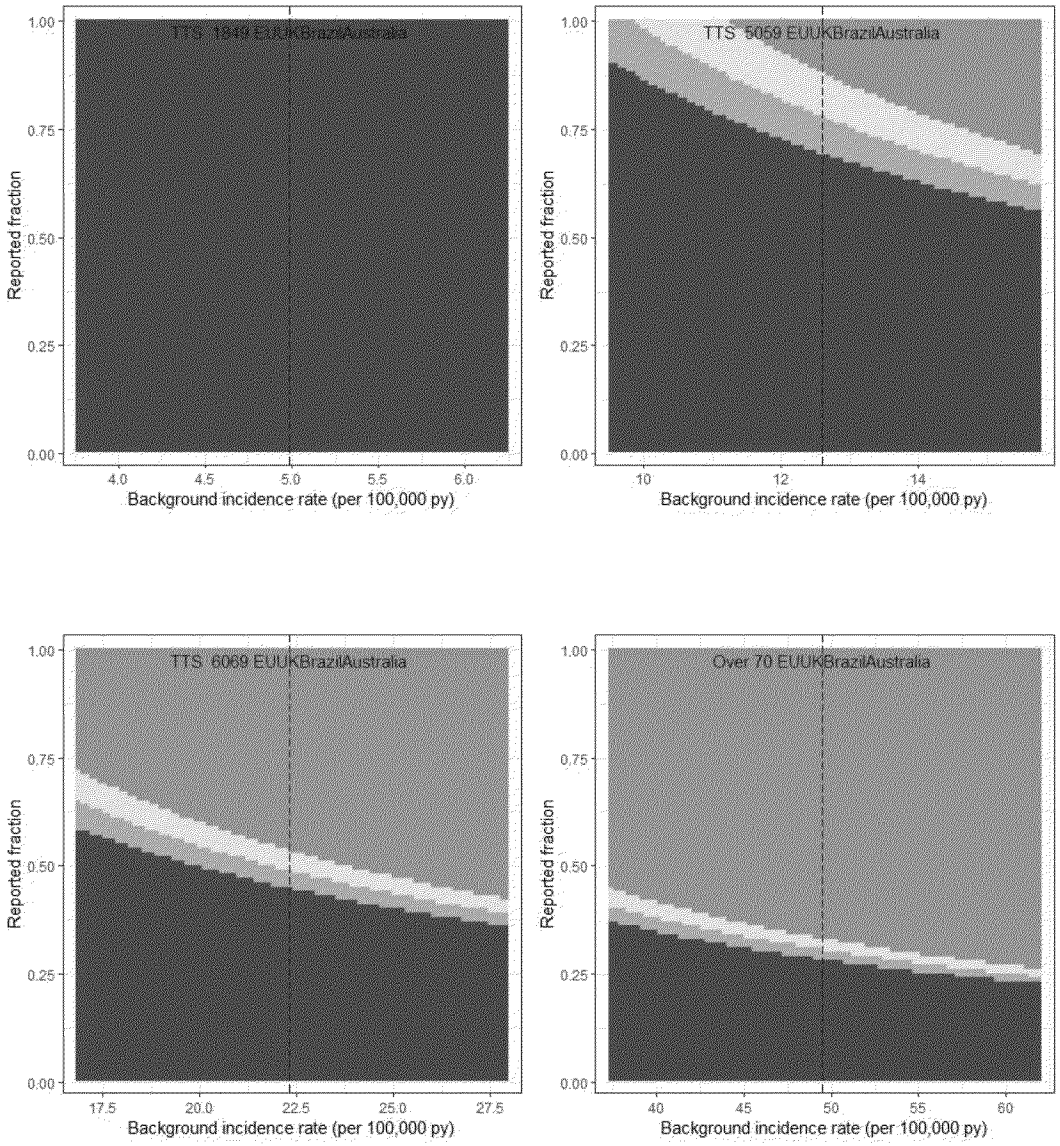

TTS 1849 EUUKBrazilAustralia
TTS 5059 EUUKBrazilAustralia
TTS 6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
4.0
4.5
5.0
5.5
6.0
10
12
14
17.5
20.0
22.5
25.0
27.5
40
45
50
55
60
Background incidence rate (per 100,000 py)

Table 66 Observed versus Expected analysis for Thrombosis with thrombocytopenia by age group (EU+UK+Brazil+Australia)

Adverse Events	Observed cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - 18-49	567	315.87	21	4.99	110094983	1.8 (1.65 - 1.95)	Observed significantly > expected
TTS - 50-59	292	422.62	21	12.6	58336094	0.69 (0.61 - 0.77)	Observed significantly < expected
TTS - 60-69	315	744.15	21	22.33	57960860	0.42 (0.38 - 0.47)	Observed significantly < expected
TTS – Over 70	249	921.45	21	49.5	32376365	0.27 (0.24 - 0.31)	Observed significantly < expected

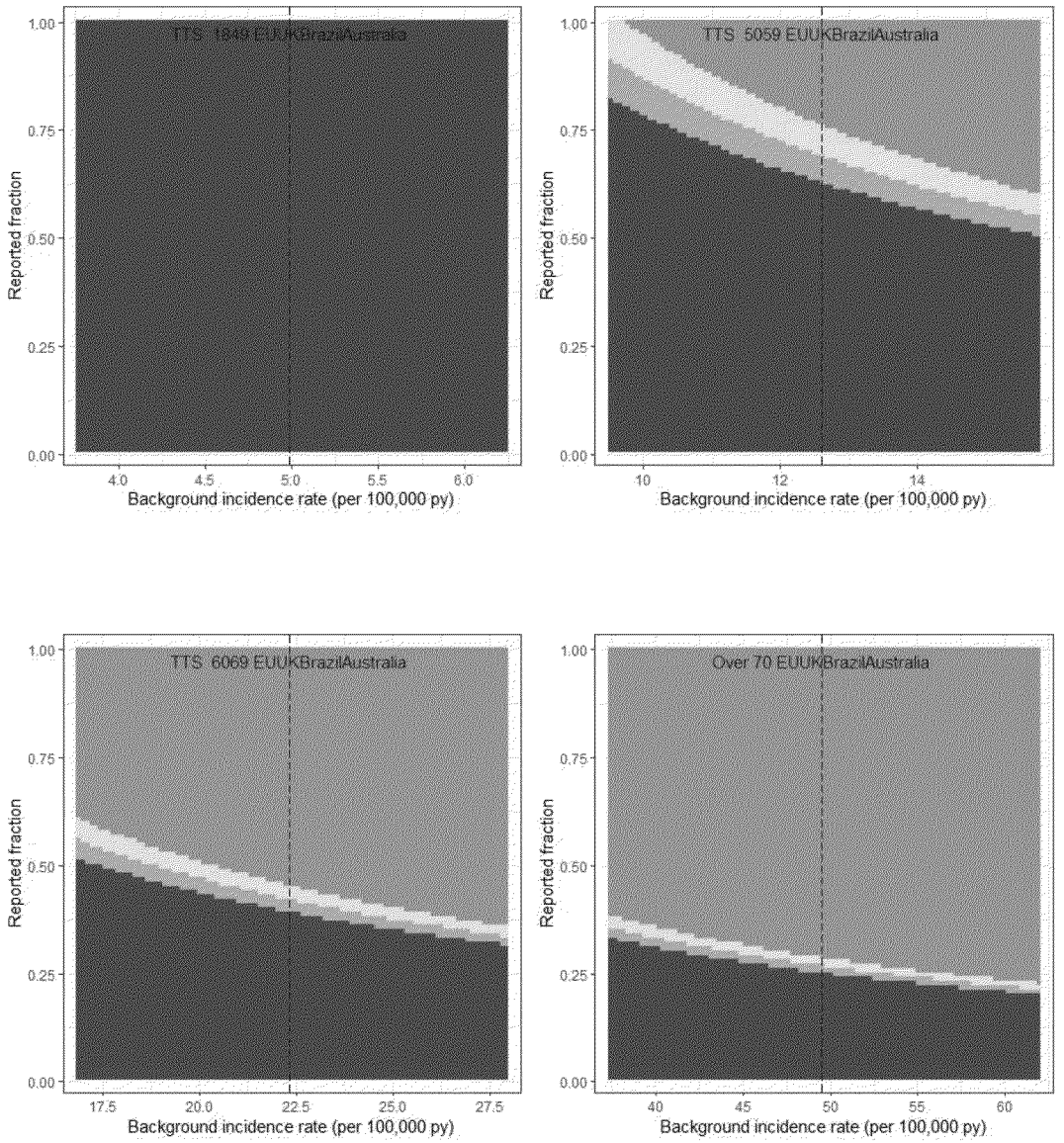
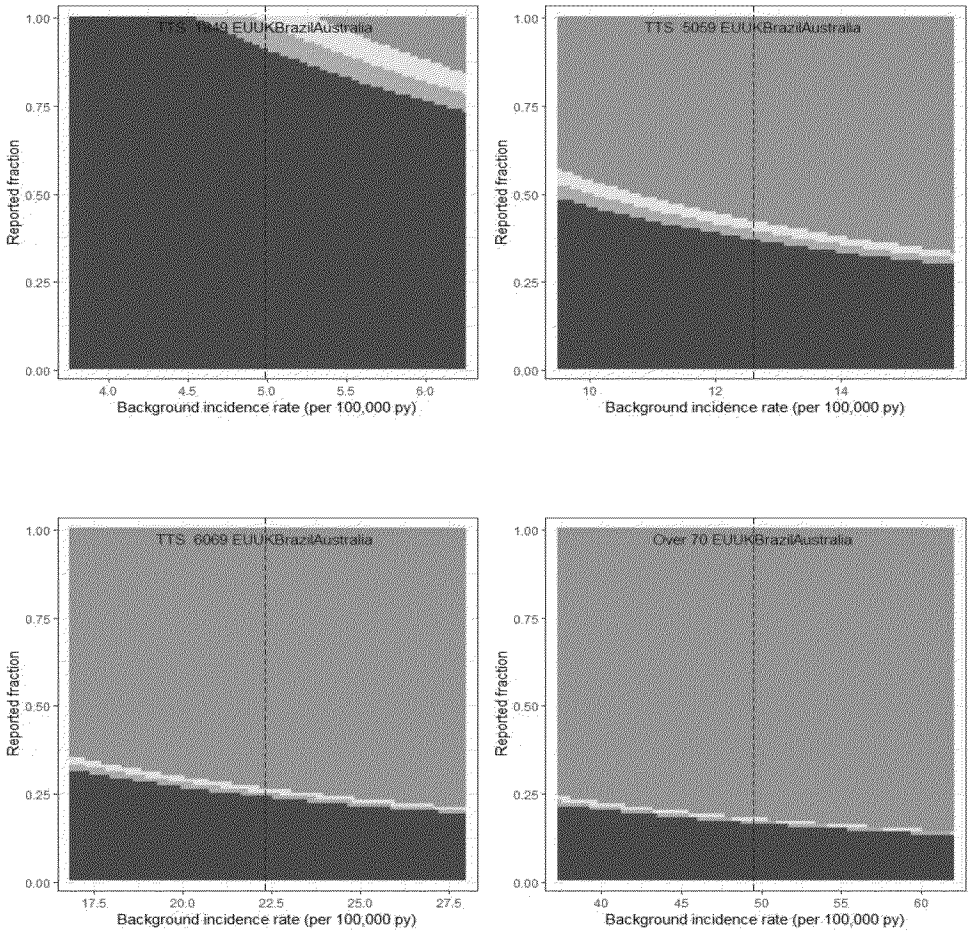

TTS 1849 EUUKBrazilAustralia
TTS 5059 EUUKBrazilAustralia
TTS 6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

Table 66 Observed versus Expected analysis for Thrombosis with thrombocytopenia by age group (EU+UK+Brazil+Australia)

Adverse Events	Observed cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - 18-49	624	631.74	42	4.99	110094983	0.99 (0.91 - 1.07)	Observed < expected
TTS - 50-59	337	845.23	42	12.6	58336094	0.4 (0.36 - 0.44)	Observed significantly < expected
TTS - 60-69	379	1488.3	42	22.33	57960860	0.25 (0.23 - 0.28)	Observed significantly < expected
TTS – Over 70	322	1842.9	42	49.5	32376365	0.17 (0.16 - 0.19)	Observed significantly < expected

Table 66 Observed versus Expected analysis for Thrombosis with thrombocytopenia by age group (EU+UK+Brazil+Australia)

Adverse Events	Observed cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)

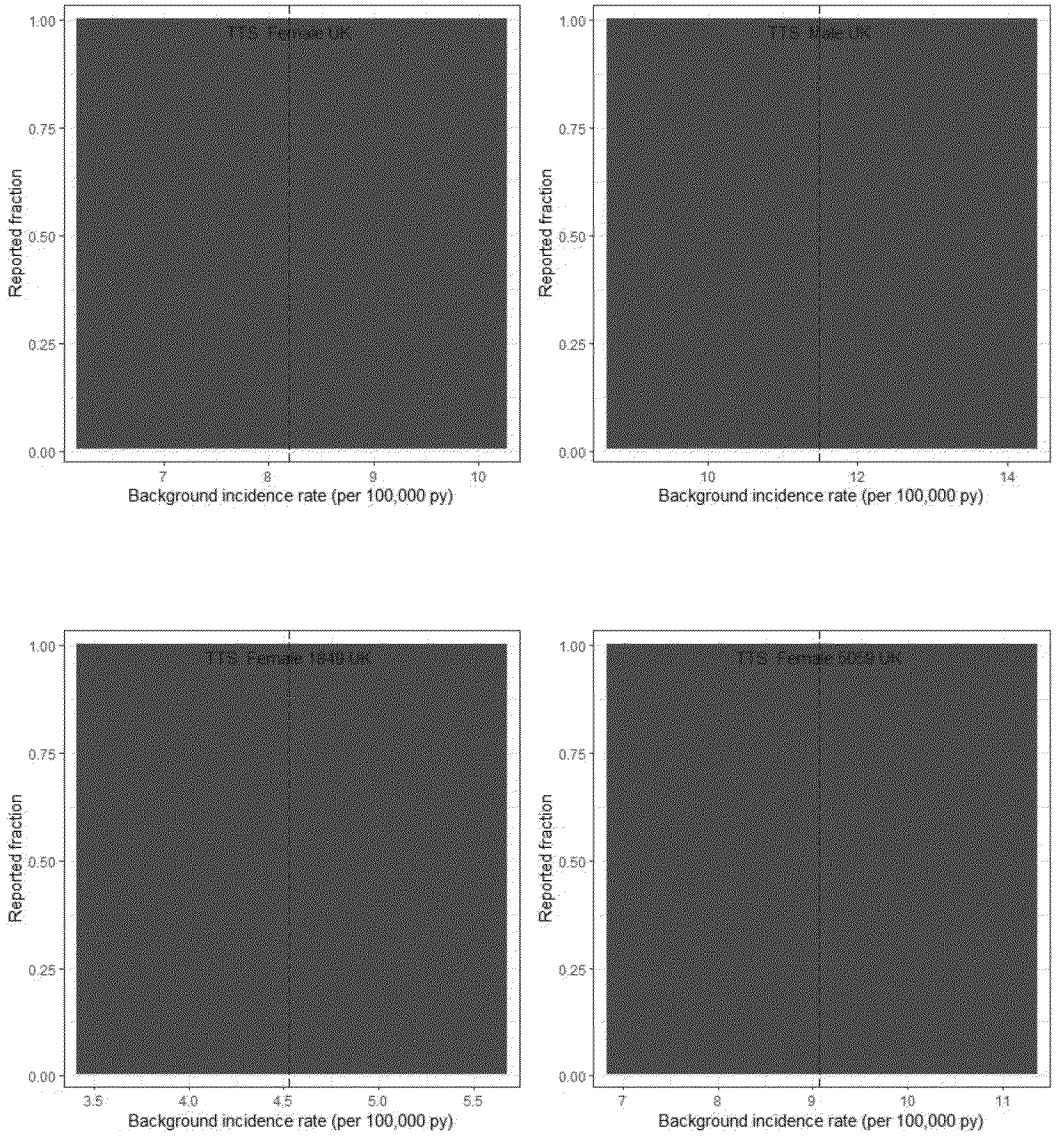


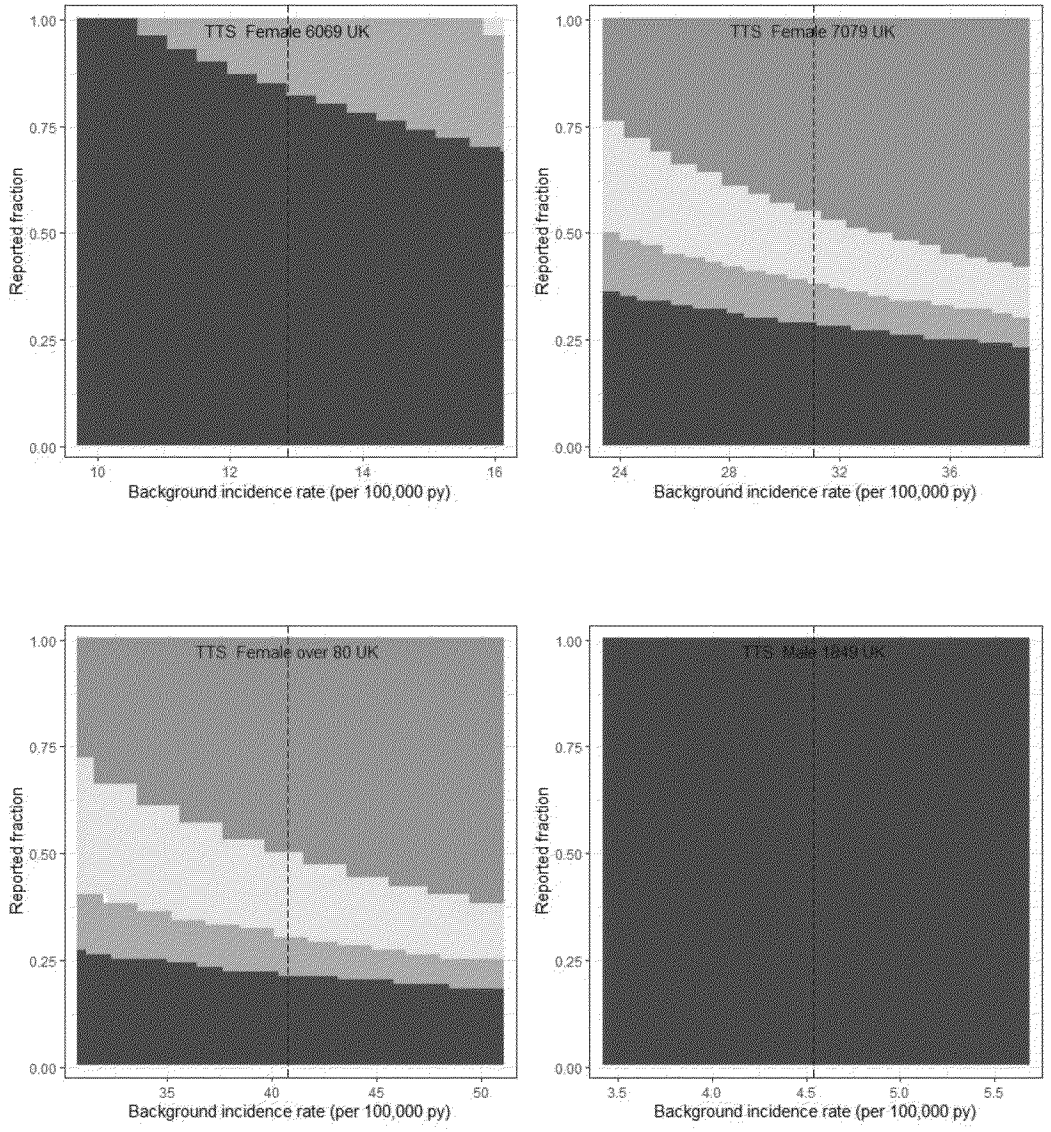
[a] Only cases observed within 0-14, 0-21, and 0-42 days were included; Risk Window: 14, 21, and 42 days.

CI Confidence interval; E Expected; EU European Union; OHDSI Observational Health Data Science and Informatics; O Observed; TCP Thrombocytopenia; TTS Thrombosis with thrombocytopenia syndrome; UK United Kingdom.

Table 67 Observed Versus Expected analysis for Thrombosis with thrombocytopenia by gender and age group (UK)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
Incidence Rate from Truven Market Scan (2019) aligned with the OHDSI TTS algorithm							
TTS - Female UK	216	73.09	14	8.2	23252503	2.96 (2.57 - 3.38)	Observed significantly > expected
TTS - Male UK	199	98.56	14	11.49	22377923	2.02 (1.75 - 2.32)	Observed significantly > expected
TTS - Female 18-49	109	12.87	14	4.53	7414701	8.47 (6.95 - 10.22)	Observed significantly > expected
TTS - Female 50-59	42	20.67	14	9.07	5944683	2.03 (1.46 - 2.75)	Observed significantly > expected
TTS - Female 60-69	29	23.62	14	12.88	4783416	1.23 (0.82 - 1.76)	Observed > expected
TTS - Female 70-79	16	41.37	14	31.05	3475875	0.39 (0.22 - 0.63)	Observed significantly < expected
TTS - Female over 80	8	25.48	14	40.77	1630324	0.31 (0.14 - 0.62)	Observed significantly < expected
TTS - Male 18-49	85	11.77	14	4.54	6766098	7.22 (5.77 - 8.93)	Observed significantly > expected
TTS - Male 50-59	53	29.62	14	11.87	6510960	1.79 (1.34 - 2.34)	Observed significantly > expected
TTS - Male 60-69	22	49.54	14	26.19	4934728	0.44 (0.28 - 0.67)	Observed significantly < expected
TTS - Male 70-79	22	57.99	14	48.22	3137304	0.38 (0.24 - 0.57)	Observed significantly < expected
TTS - Male over 80	7	33.9	14	86.28	1025046	0.21 (0.08 - 0.43)	Observed significantly < expected


TTS Female UK
TTS Male UK
TTS Female 18-49 UK
TTS Female 50-59 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
12
14
3.5
4.0
4.5
5.0
5.5
11


TTS Female 6069 UK
TTS Female 7079 UK
TTS Female over 80 UK
TTS Male 1849 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
10
12
14
16
24
28
32
36
35
40
45
50
3.5
4.0
4.5
5.0
5.5

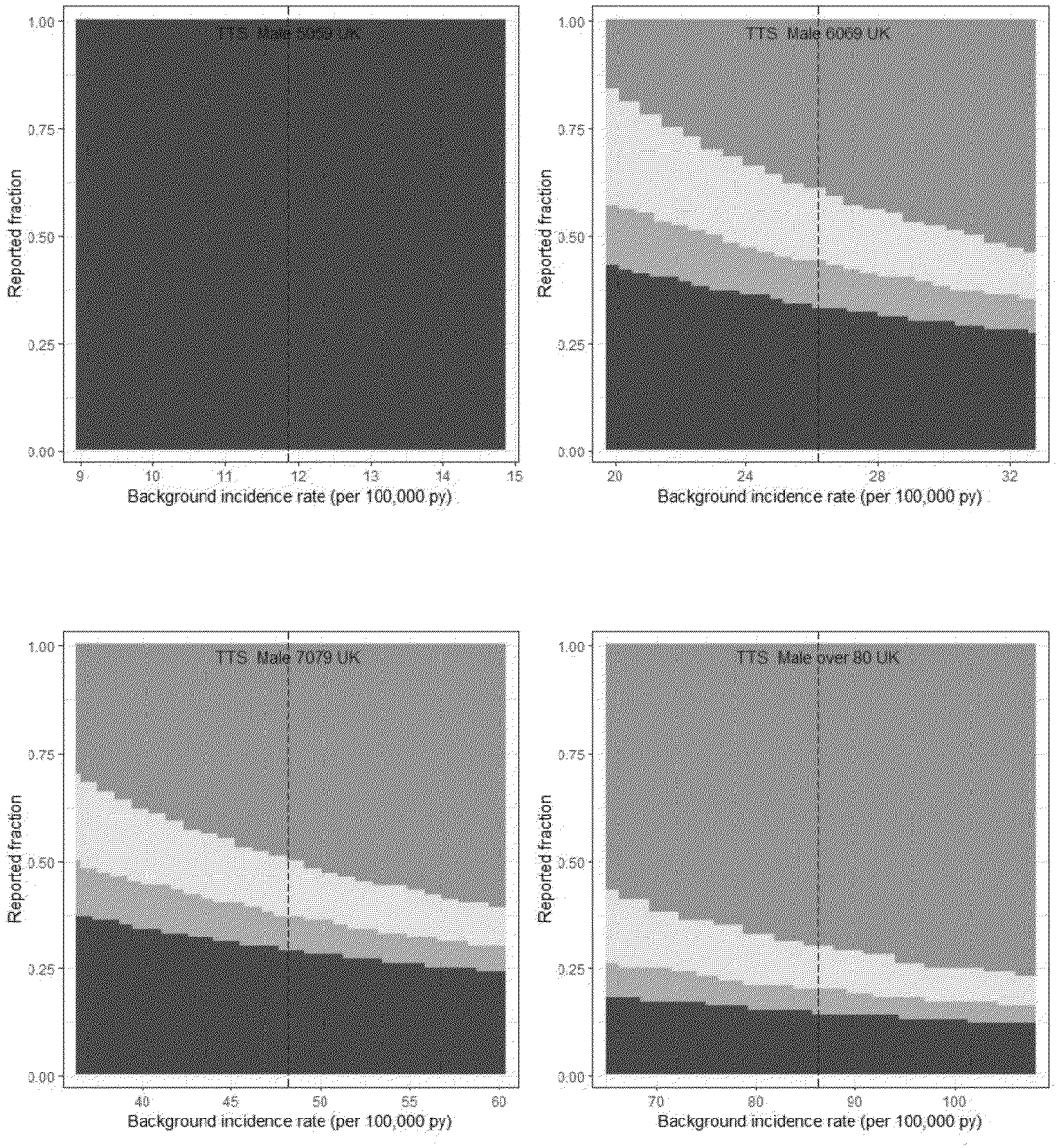
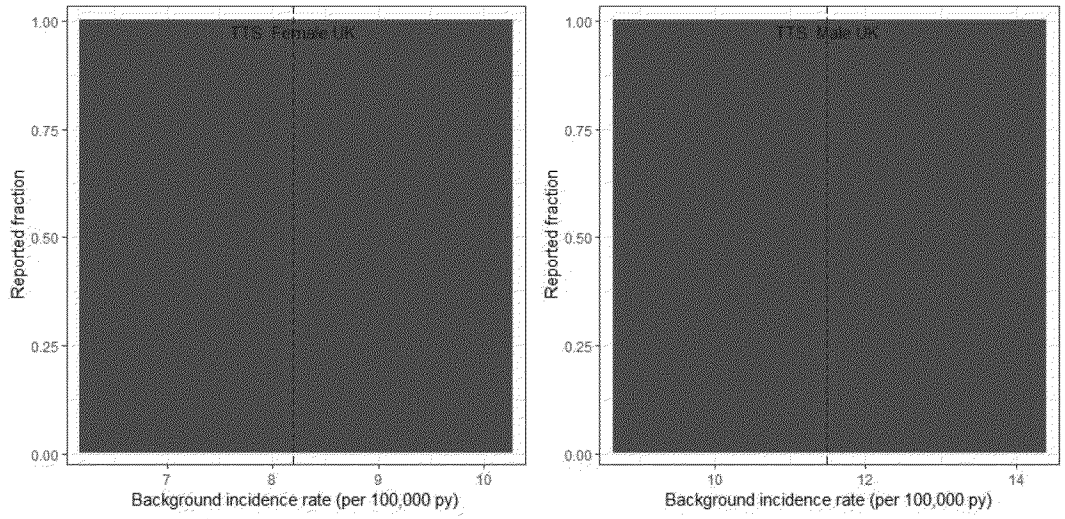
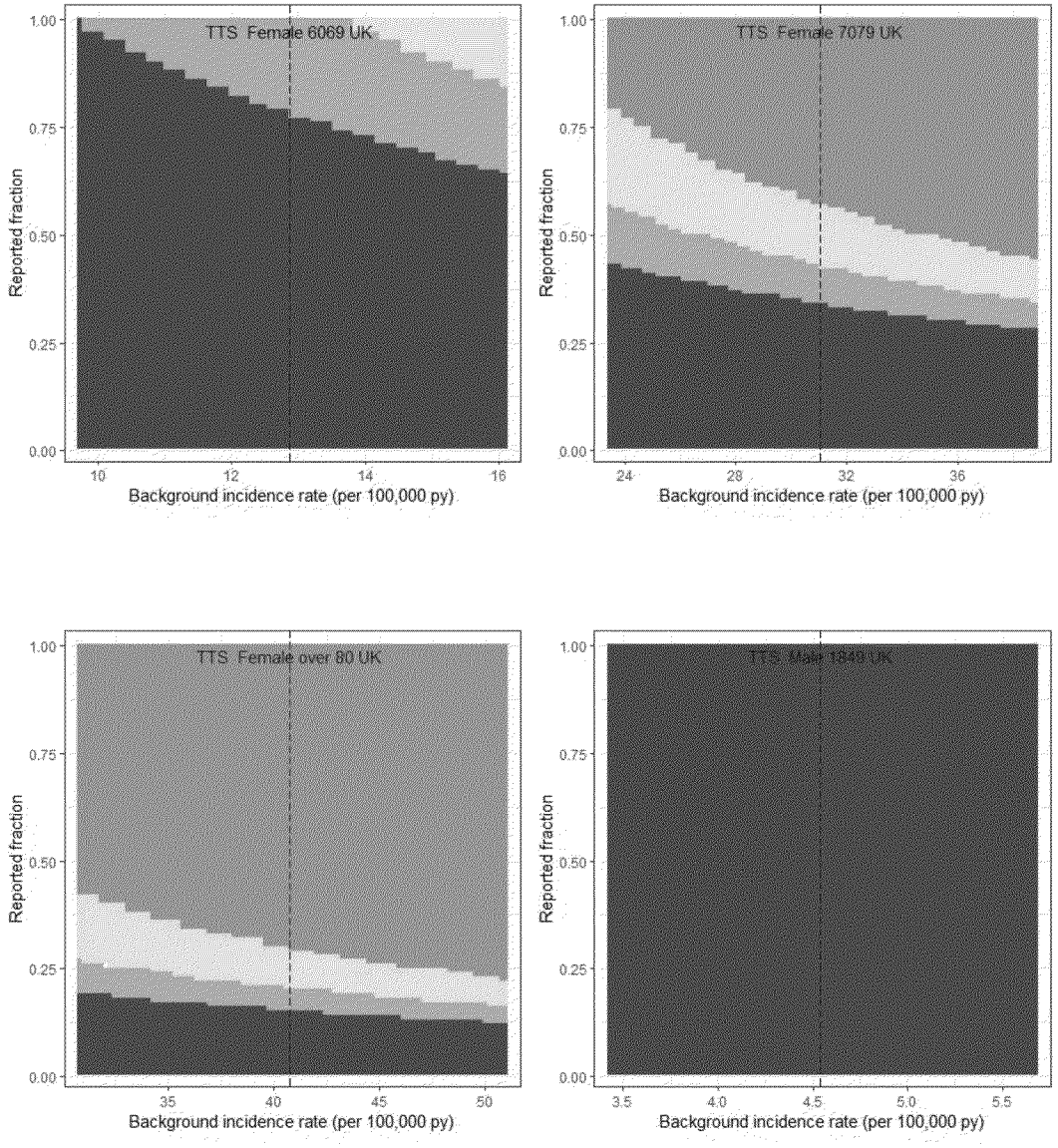

TTS Male 5059 UK
TTS Male 6069 UK
TTS Male 7079 UK
TTS Male over 80 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
14
15
20
24
28
32
40
45
50
55
60
70
80
90
100

Table 67 Observed Versus Expected analysis for Thrombosis with thrombocytopenia by gender and age group (UK)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - Female UK	282	109.63	21	8.2	23252503	2.57 (2.28 - 2.89)	Observed significantly > expected
TTS - Male UK	257	147.84	21	11.49	22377923	1.74 (1.53 - 1.96)	Observed significantly > expected
TTS - Female 18-49	133	19.31	21	4.53	7414701	6.89 (5.77 - 8.16)	Observed significantly > expected
TTS - Female 50-59	59	31	21	9.07	5944683	1.9 (1.45 - 2.46)	Observed significantly > expected
TTS - Female 60-69	38	35.42	21	12.88	4783416	1.07 (0.76 - 1.47)	Observed > expected
TTS - Female 70-79	27	62.05	21	31.05	3475875	0.44 (0.29 - 0.63)	Observed significantly < expected
TTS - Female over 80	8	38.22	21	40.77	1630324	0.21 (0.09 - 0.41)	Observed significantly < expected
TTS - Male 18-49	103	17.66	21	4.54	6766098	5.83 (4.76 - 7.07)	Observed significantly > expected
TTS - Male 50-59	70	44.44	21	11.87	6510960	1.58 (1.23 - 1.99)	Observed significantly > expected
TTS - Male 60-69	34	74.31	21	26.19	4934728	0.46 (0.32 - 0.64)	Observed significantly < expected
TTS - Male 70-79	27	86.98	21	48.22	3137304	0.31 (0.2 - 0.45)	Observed significantly < expected
TTS - Male over 80	8	50.85	21	86.28	1025046	0.16 (0.07 - 0.31)	Observed significantly < expected


TTS Female UK
TTS Male UK
TTS Female 1849 UK
TTS Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
12
14
3.5
4.0
4.5
5.0
5.5
11


TTS Female 6069 UK
TTS Female 7079 UK
TTS Female over 80 UK
TTS Male 1849 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
10
12
14
16
24
28
32
36
35
40
45
50
3.5
4.0
4.5
5.0
5.5

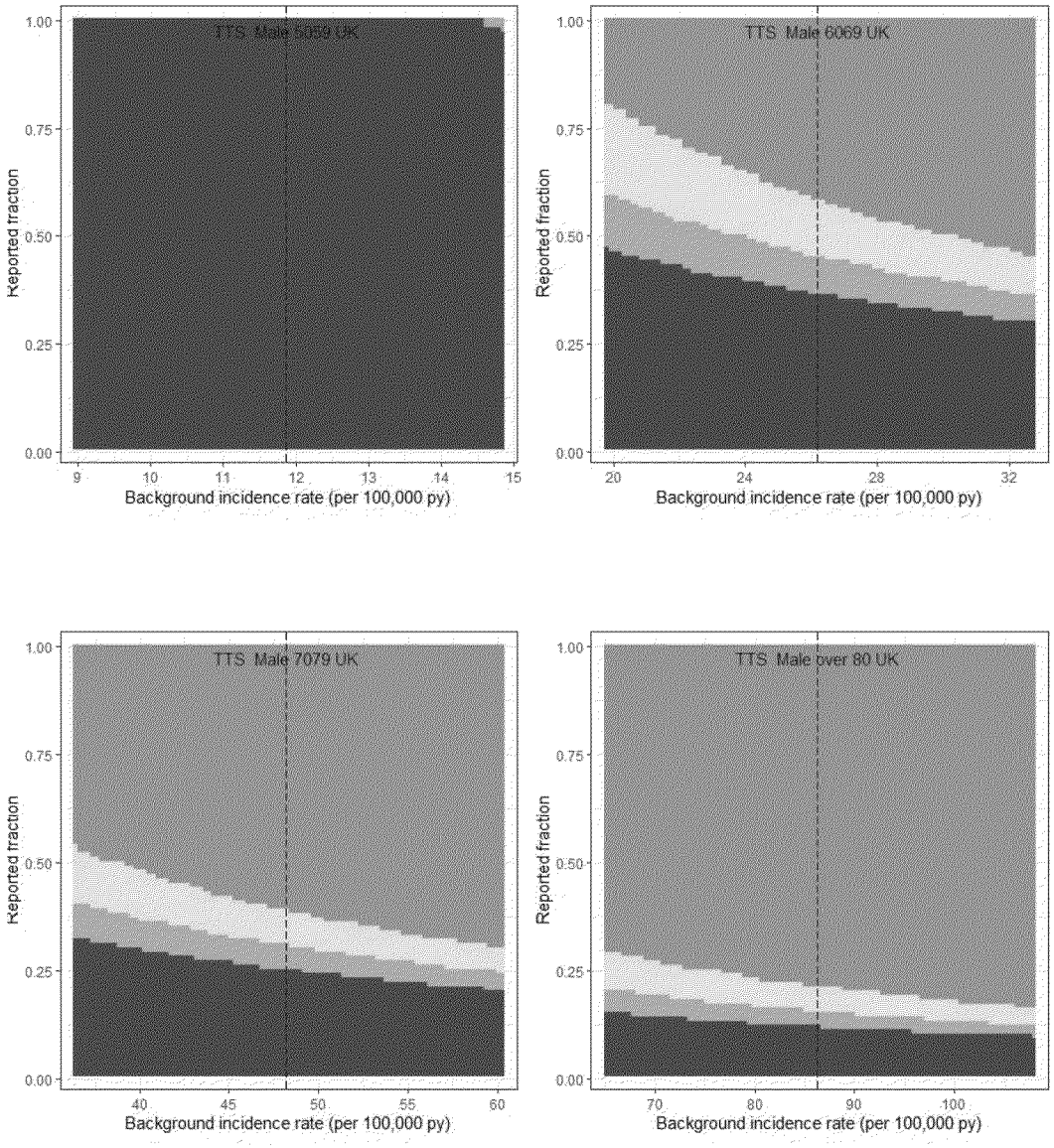
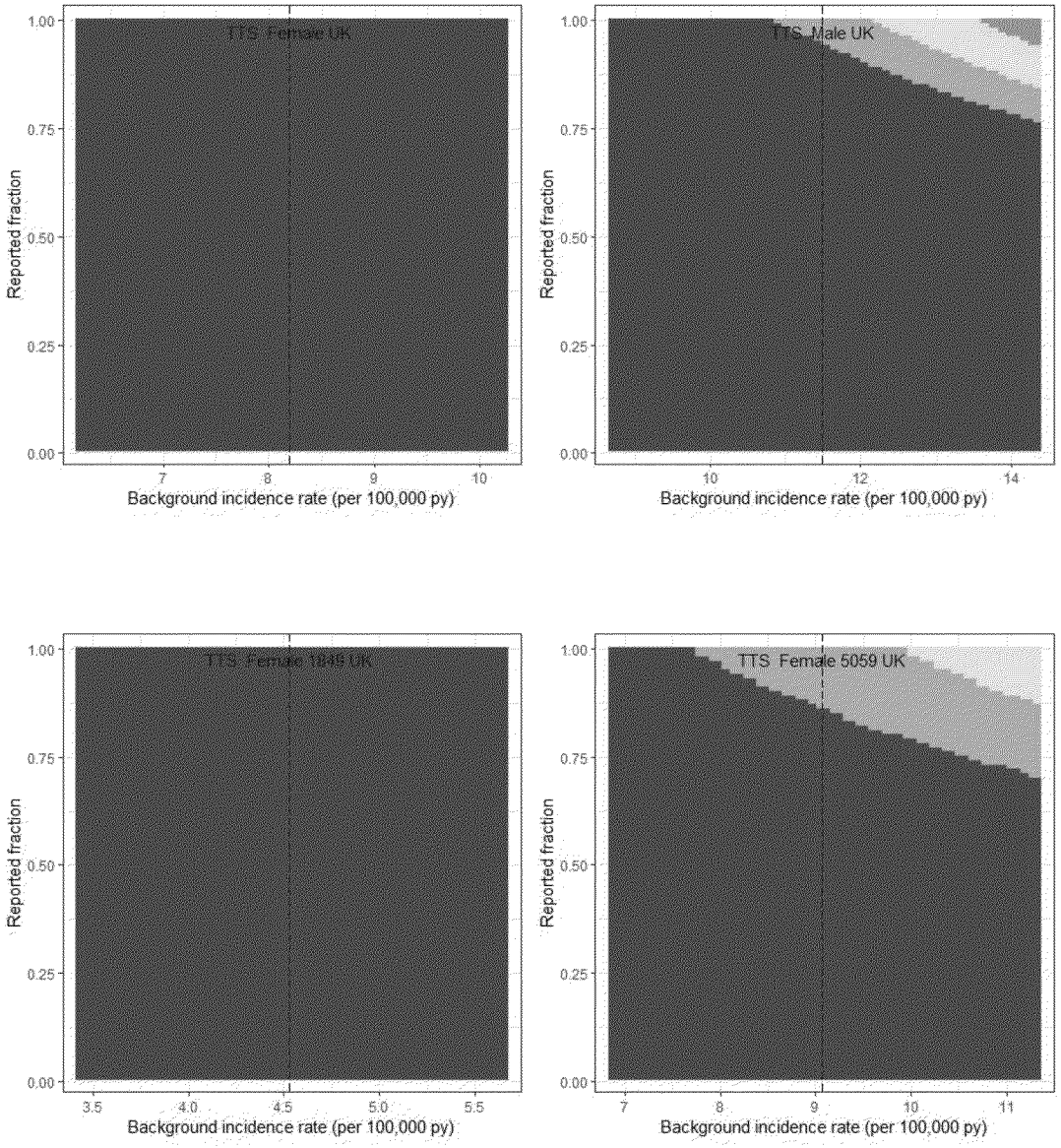
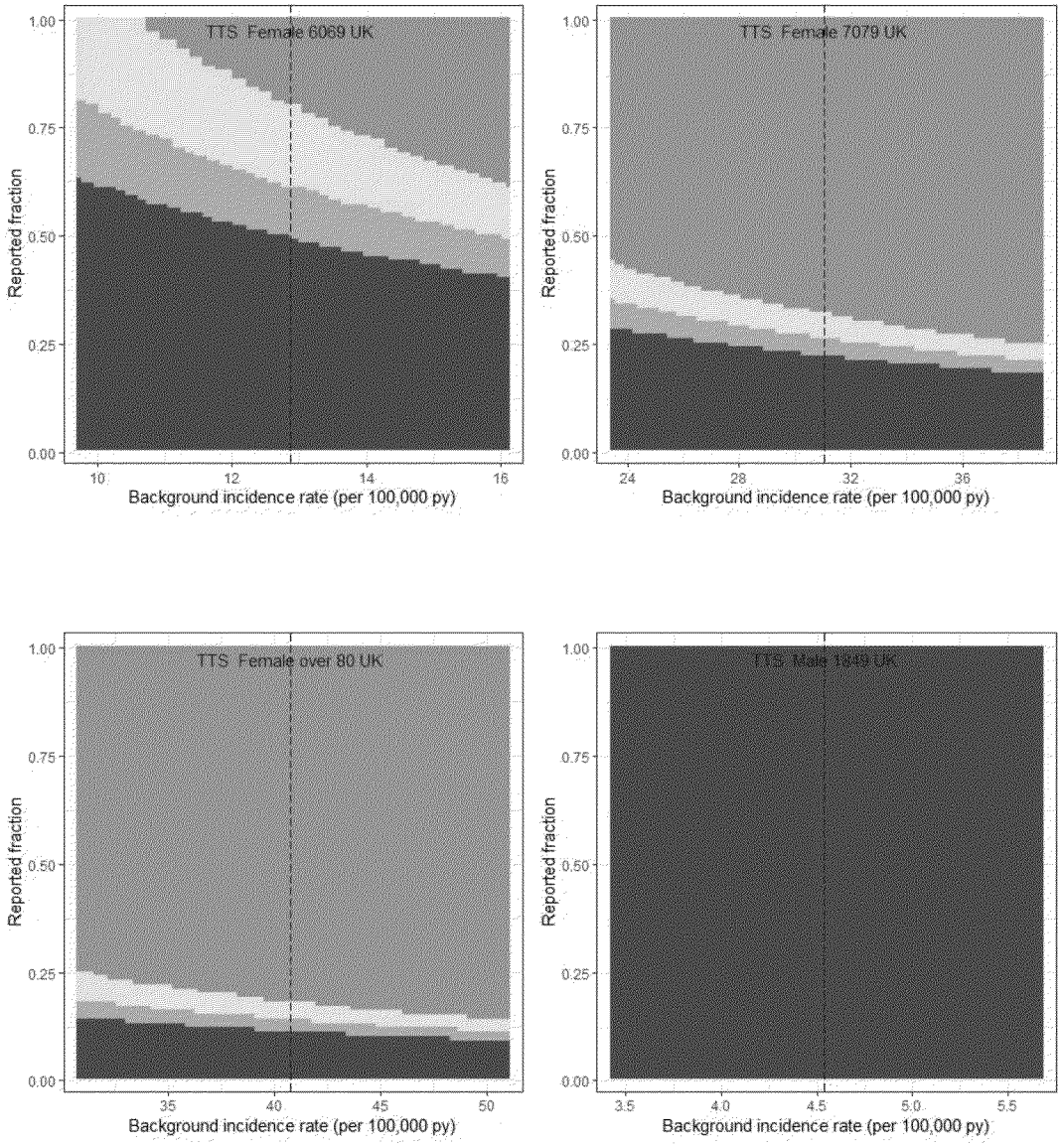

TTS Male 5059 UK
TTS Male 6069 UK
TTS Male 7079 UK
TTS Male over 80 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
14
15
20
24
28
32
40
45
50
55
60
70
80
90
100

Table 67 Observed Versus Expected analysis for Thrombosis with thrombocytopenia by gender and age group (UK)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - Female UK	330	219.26	42	8.2	23252503	1.51 (1.35 - 1.68)	Observed significantly > expected
TTS - Male UK	313	295.67	42	11.49	22377923	1.06 (0.94 - 1.18)	Observed > expected
TTS - Female 18-49	153	38.62	42	4.53	7414701	3.96 (3.36 - 4.64)	Observed significantly > expected
TTS - Female 50-59	68	62	42	9.07	5944683	1.1 (0.85 - 1.39)	Observed > expected
TTS - Female 60-69	44	70.85	42	12.88	4783416	0.62 (0.45 - 0.83)	Observed significantly < expected
TTS - Female 70-79	33	124.11	42	31.05	3475875	0.27 (0.18 - 0.37)	Observed significantly < expected
TTS - Female over 80	11	76.43	42	40.77	1630324	0.14 (0.07 - 0.26)	Observed significantly < expected
TTS - Male 18-49	112	35.32	42	4.54	6766098	3.17 (2.61 - 3.82)	Observed significantly > expected
TTS - Male 50-59	87	88.87	42	11.87	6510960	0.98 (0.78 - 1.21)	Observed < expected
TTS - Male 60-69	47	148.62	42	26.19	4934728	0.32 (0.23 - 0.42)	Observed significantly < expected
TTS – Male 70-79	36	173.96	42	48.22	3137304	0.21 (0.14 - 0.29)	Observed significantly < expected
TTS - Male over 80	11	101.7	42	86.28	1025046	0.11 (0.05 - 0.19)	Observed significantly < expected


TTS Female UK
TTS Male UK
TTS Female 1849 UK
TTS Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
12
14
3.5
4.0
4.5
5.0
5.5
11


TTS Female 6069 UK
TTS Female 7079 UK
TTS Female over 80 UK
TTS Male 1849 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
10
12
14
16
24
28
32
36
35
40
45
50
3.5
4.0
4.5
5.0
5.5

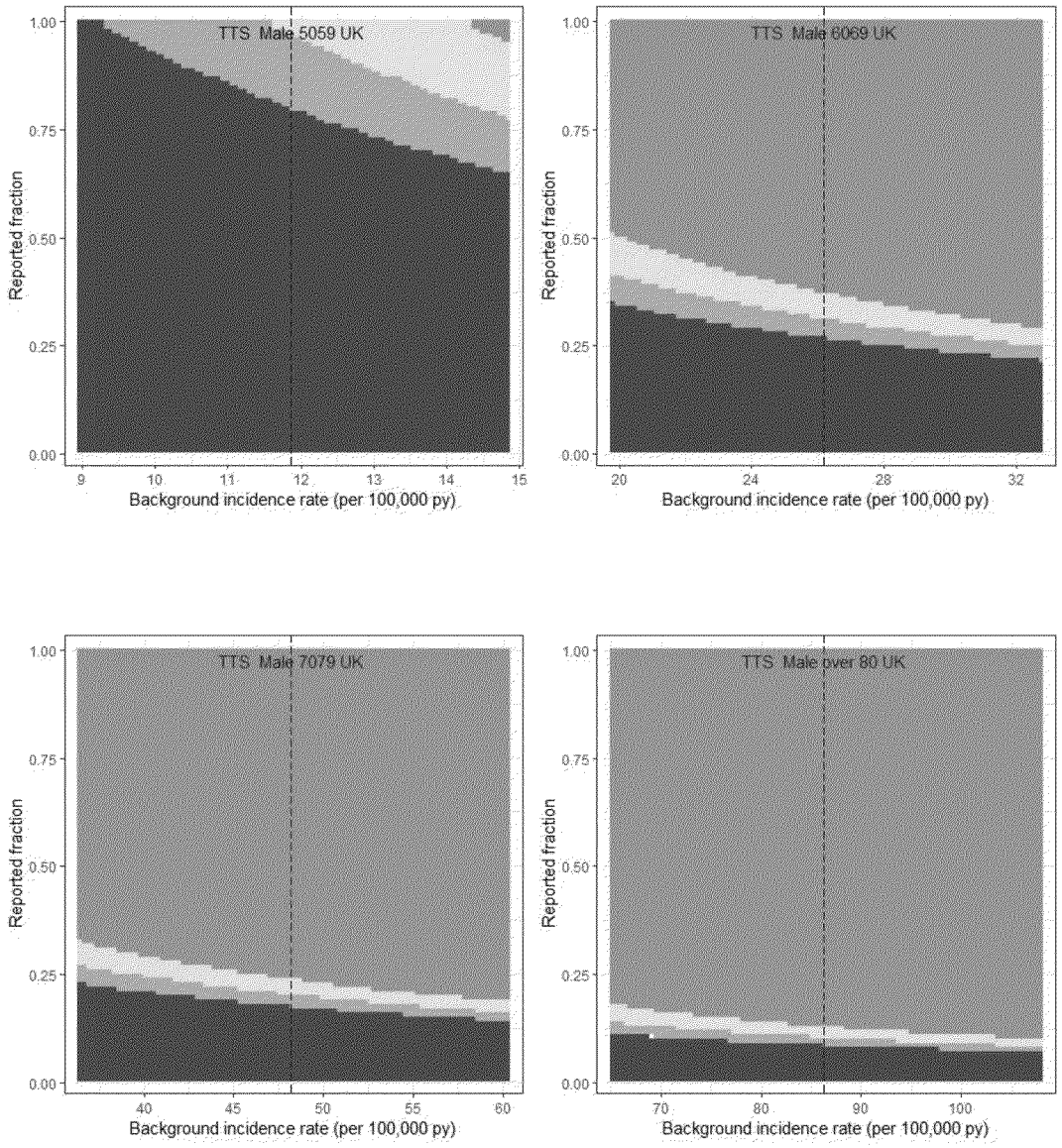
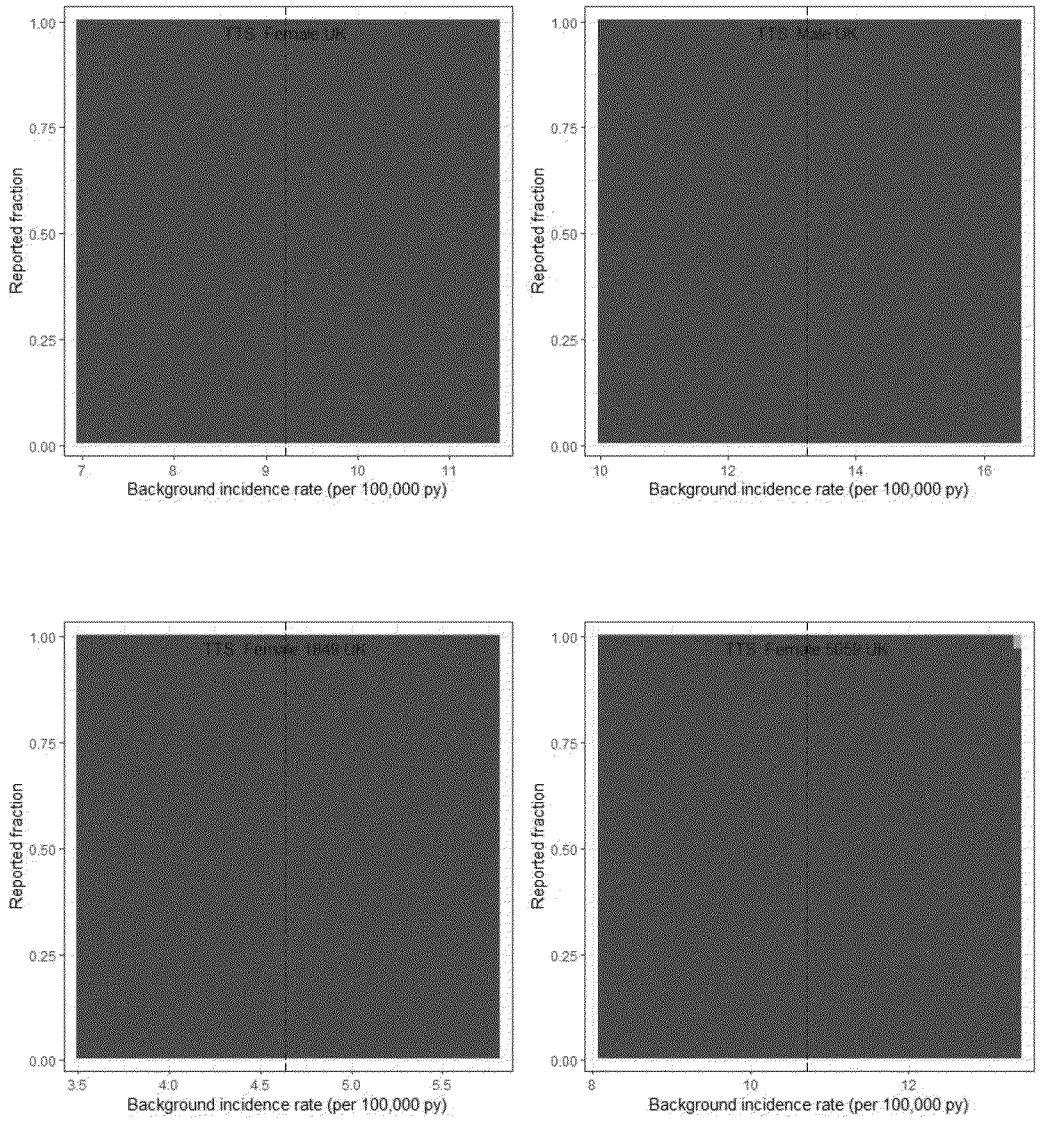
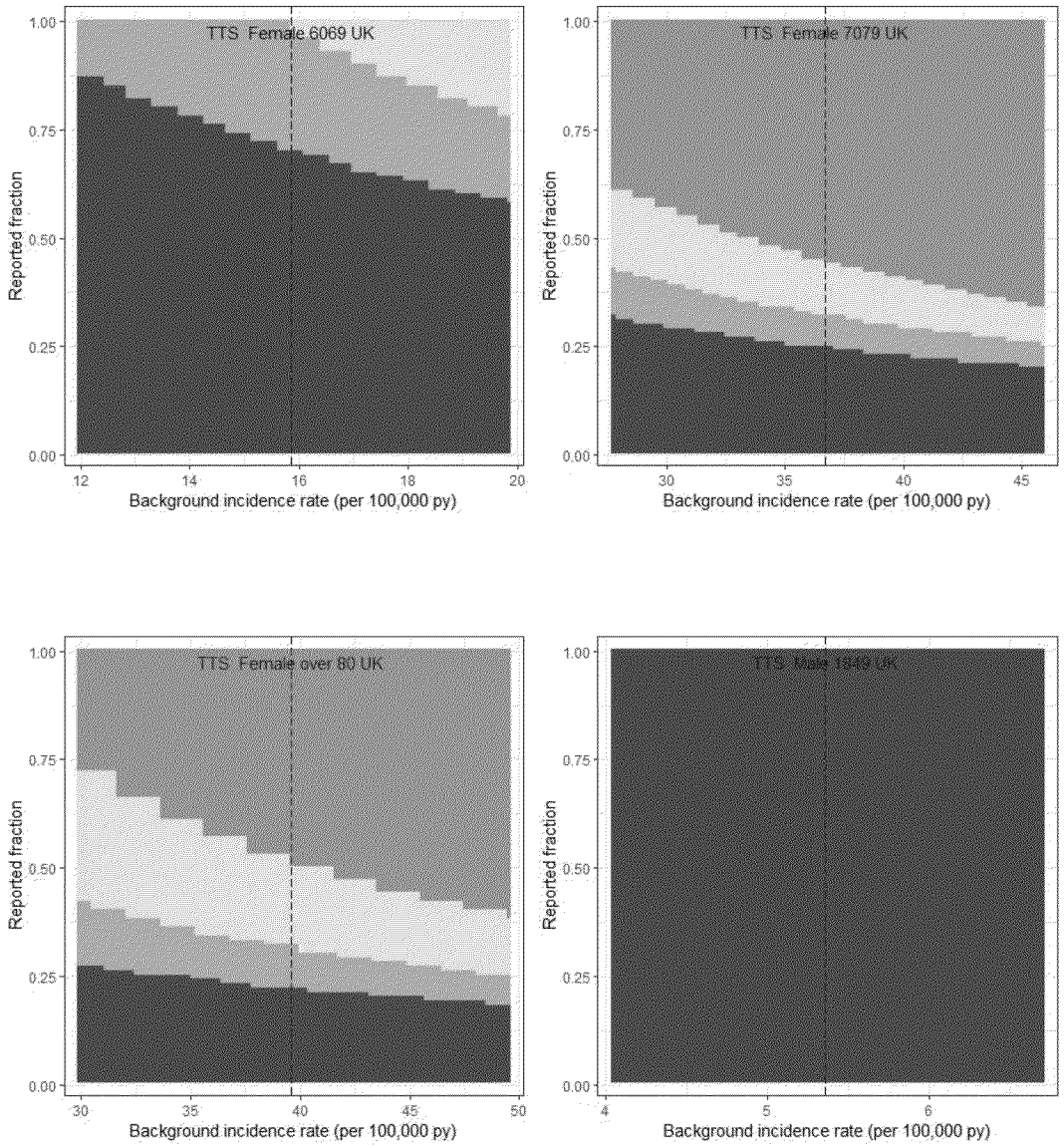

TTS Male 5059 UK
TTS Male 6069 UK
TTS Male 7079 UK
TTS Male over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
9
10
11
12
13
14
15
20
24
28
32
40
45
50
55
60
70
80
90
100
Background incidence rate (per 100,000 py)

Table 67 Observed Versus Expected analysis for Thrombosis with thrombocytopenia by gender and age group (UK)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
Incidence Rate from Truven Market Scan database (2019) aligned with the OHDSI TTS algorithm, updated OHDSI-aligned codelists and washout periods							
TTS - Female UK	216	82.18	14	9.22	23252503	2.63 (2.29 - 3)	Observed significantly > expected
TTS - Male UK	199	113.57	14	13.24	22377923	1.75 (1.52 - 2.01)	Observed significantly > expected
TTS - Female 18-49	109	13.19	14	4.64	7414701	8.26 (6.79 - 9.97)	Observed significantly > expected
TTS - Female 50-59	42	24.4	14	10.71	5944683	1.72 (1.24 - 2.33)	Observed significantly > expected
TTS - Female 60-69	29	29.1	14	15.87	4783416	1 (0.67 - 1.43)	Observed < expected
TTS - Female 70-79	16	48.9	14	36.7	3475875	0.33 (0.19 - 0.53)	Observed significantly < expected
TTS - Female over 80	8	24.75	14	39.61	1630324	0.32 (0.14 - 0.64)	Observed significantly < expected
TTS - Male 18-49	85	13.9	14	5.36	6766098	6.12 (4.88 - 7.56)	Observed significantly > expected
TTS - Male 50-59	53	36.69	14	14.7	6510960	1.44 (1.08 - 1.89)	Observed significantly > expected
TTS - Male 60-69	22	55.82	14	29.51	4934728	0.39 (0.25 - 0.6)	Observed significantly < expected
TTS – Male 70-79	22	64.99	14	54.04	3137304	0.34 (0.21 - 0.51)	Observed significantly < expected
TTS - Male over 80	7	33.25	14	84.62	1025046	0.21 (0.08 - 0.43)	Observed significantly < expected


TTS Female UK
TTS Male UK
TTS Female 1849 UK
TTS Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
11
10
12
14
16
3.5
4.0
4.5
5.0
5.5
8
10
12


TTS Female 6069 UK
TTS Female 7079 UK
TTS Female over 80 UK
TTS Male 1849 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
12
14
16
18
20
30
35
40
45
50
4
5
6

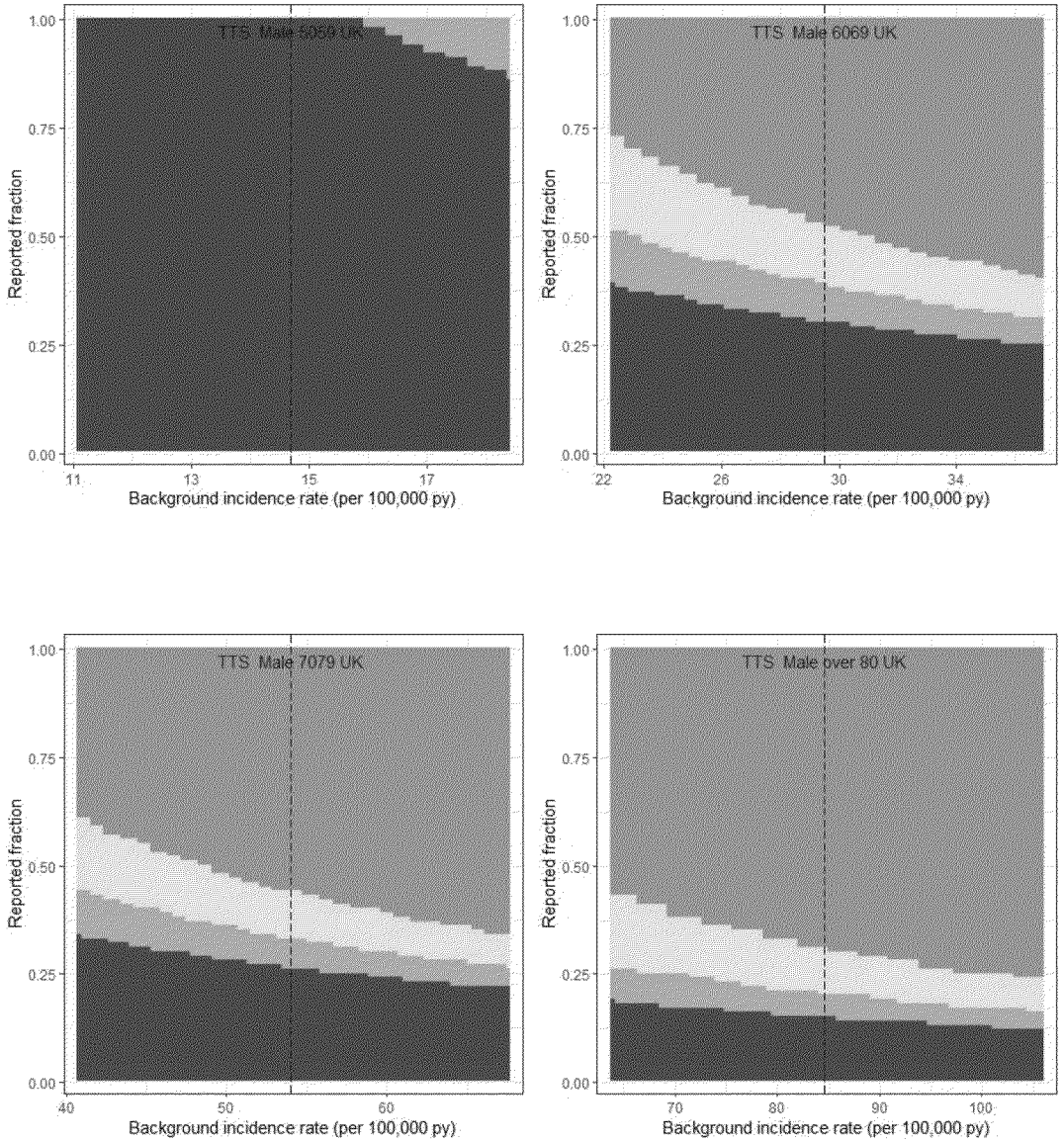
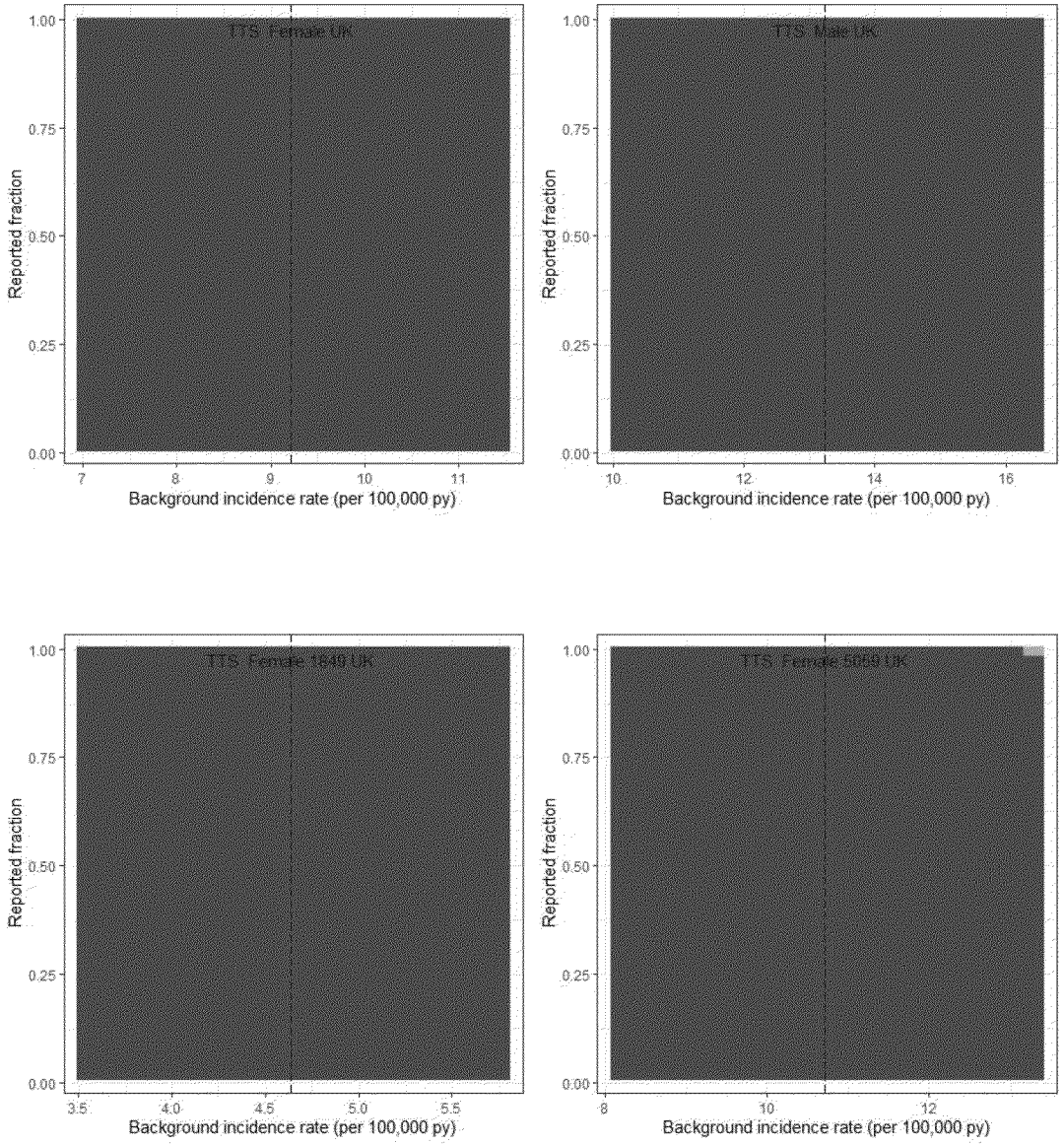
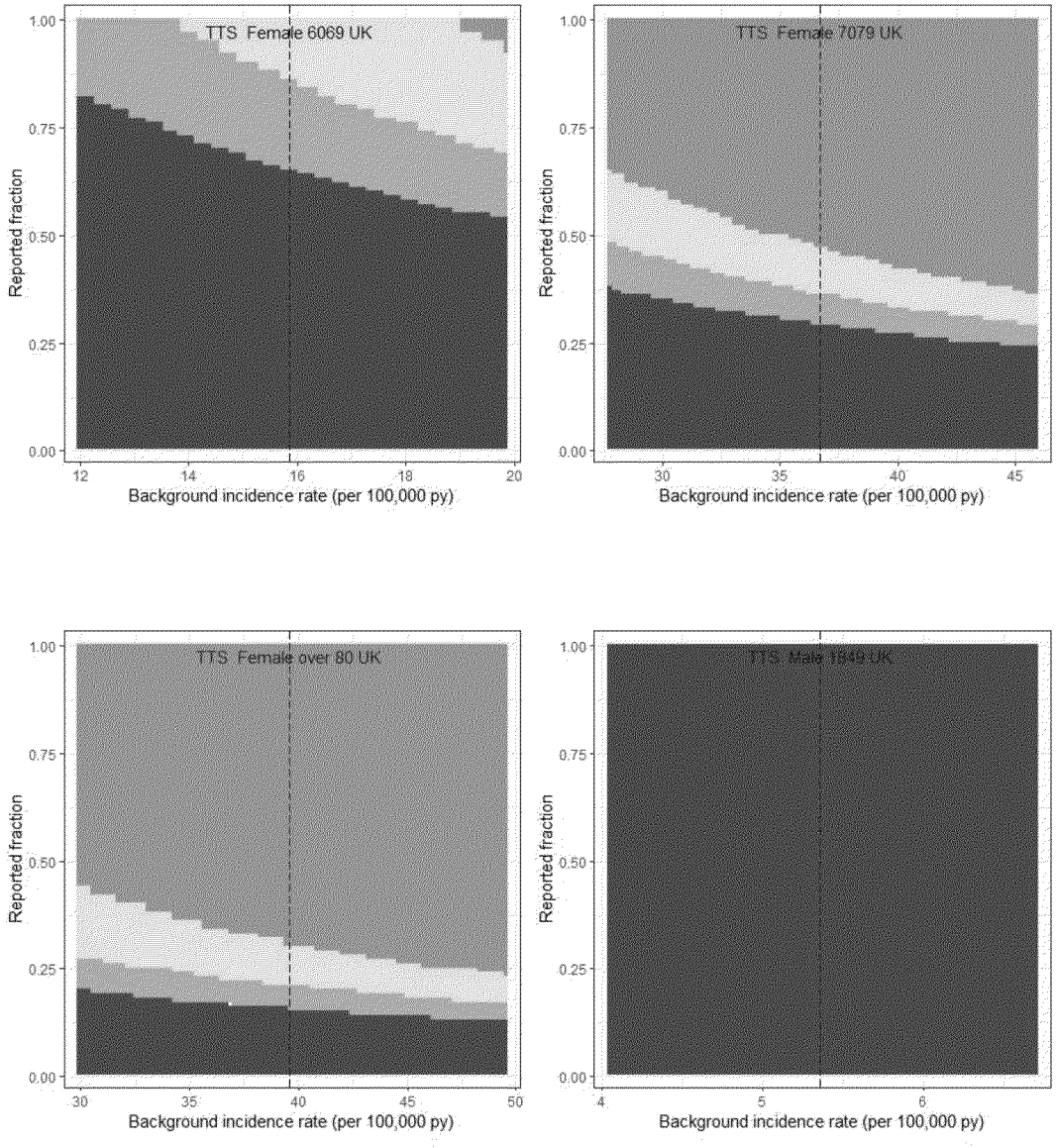

TTS Male 5059 UK
TTS Male 6069 UK
TTS Male 7079 UK
TTS Male over 80 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
11
13
15
17
22
26
30
34
40
50
60
70
80
90
100

Table 67 Observed Versus Expected analysis for Thrombosis with thrombocytopenia by gender and age group (UK)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - Female UK	282	123.26	21	9.22	23252503	2.29 (2.03 - 2.57)	Observed significantly > expected
TTS - Male UK	257	170.35	21	13.24	22377923	1.51 (1.33 - 1.7)	Observed significantly > expected
TTS - Female 18-49	133	19.78	21	4.64	7414701	6.72 (5.63 - 7.97)	Observed significantly > expected
TTS - Female 50-59	59	36.61	21	10.71	5944683	1.61 (1.23 - 2.08)	Observed significantly > expected
TTS - Female 60-69	38	43.65	21	15.87	4783416	0.87 (0.62 - 1.19)	Observed < expected
TTS – Female 70-79	27	73.34	21	36.7	3475875	0.37 (0.24 - 0.54)	Observed significantly < expected
TTS – Female Over 80	8	37.13	21	39.61	1630324	0.22 (0.09 - 0.42)	Observed significantly < expected
TTS - Male 18-49	103	20.85	21	5.36	6766098	4.94 (4.03 - 5.99)	Observed significantly > expected
TTS - Male 50-59	70	55.03	21	14.7	6510960	1.27 (0.99 - 1.61)	Observed > expected
TTS - Male 60-69	34	83.73	21	29.51	4934728	0.41 (0.28 - 0.57)	Observed significantly < expected
TTS – Male 70-79	27	97.48	21	54.04	3137304	0.28 (0.18 - 0.4)	Observed significantly < expected
TTS – Male Over 80	8	49.87	21	84.62	1025046	0.16 (0.07 - 0.32)	Observed significantly < expected


TTS Female UK
TTS Male UK
TTS Female 1849 UK
TTS Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
11
10
12
14
16
3.5
4.0
4.5
5.0
5.5
8
10
12


TTS Female 6069 UK
TTS Female 7079 UK
TTS Female over 80 UK
TTS Male 1849 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
12
14
16
18
20
30
35
40
45
50
4
5
6

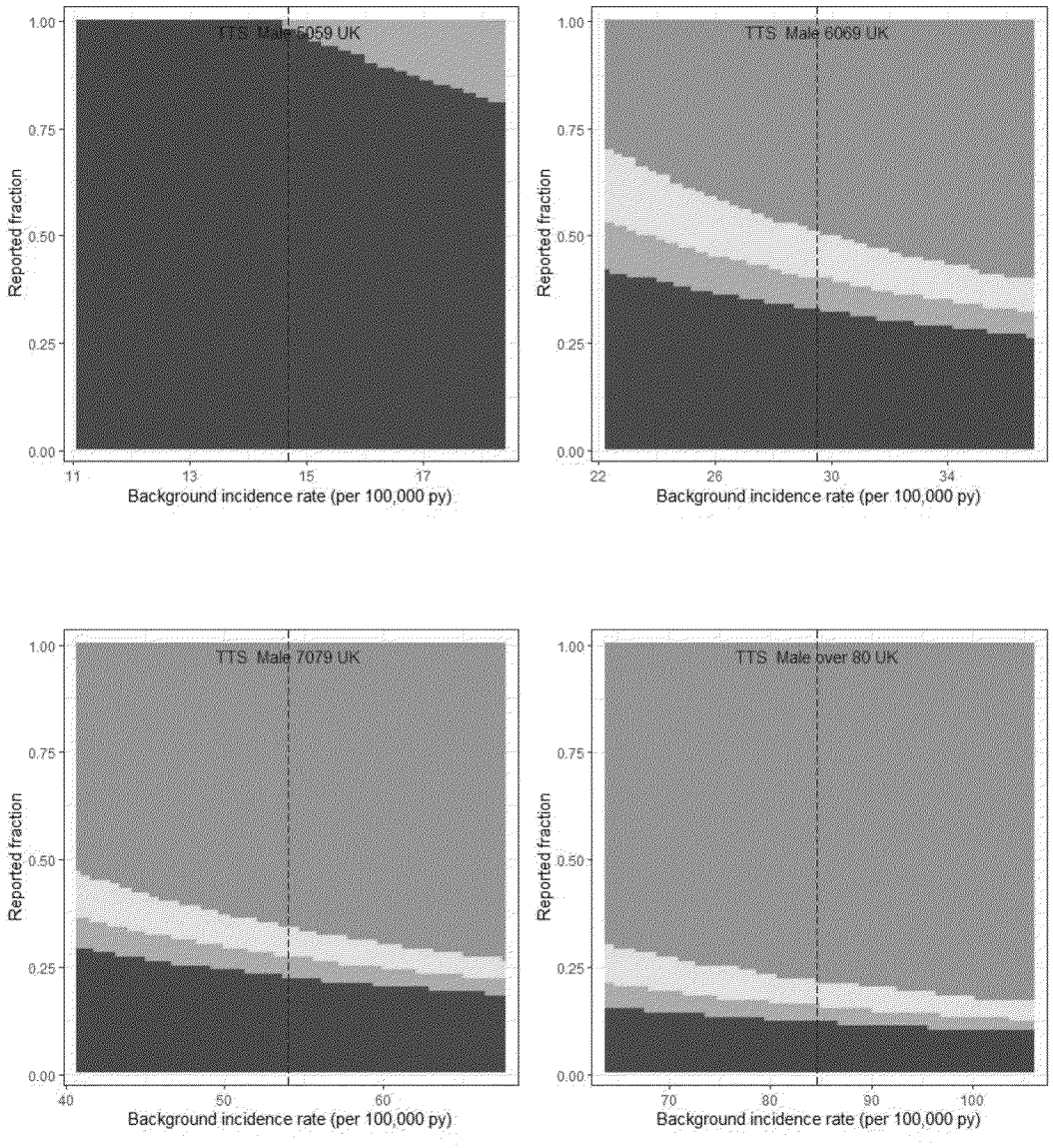
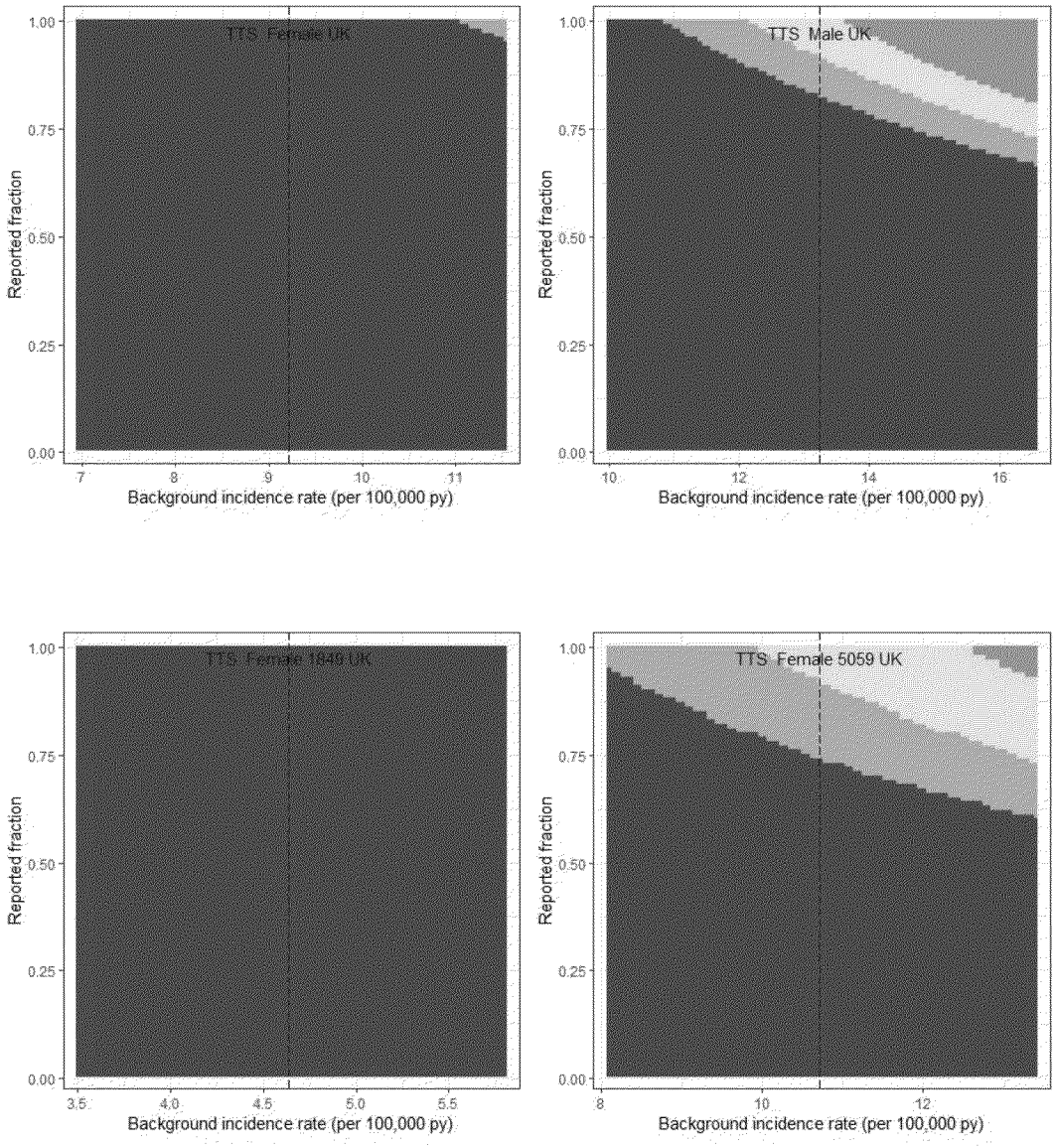
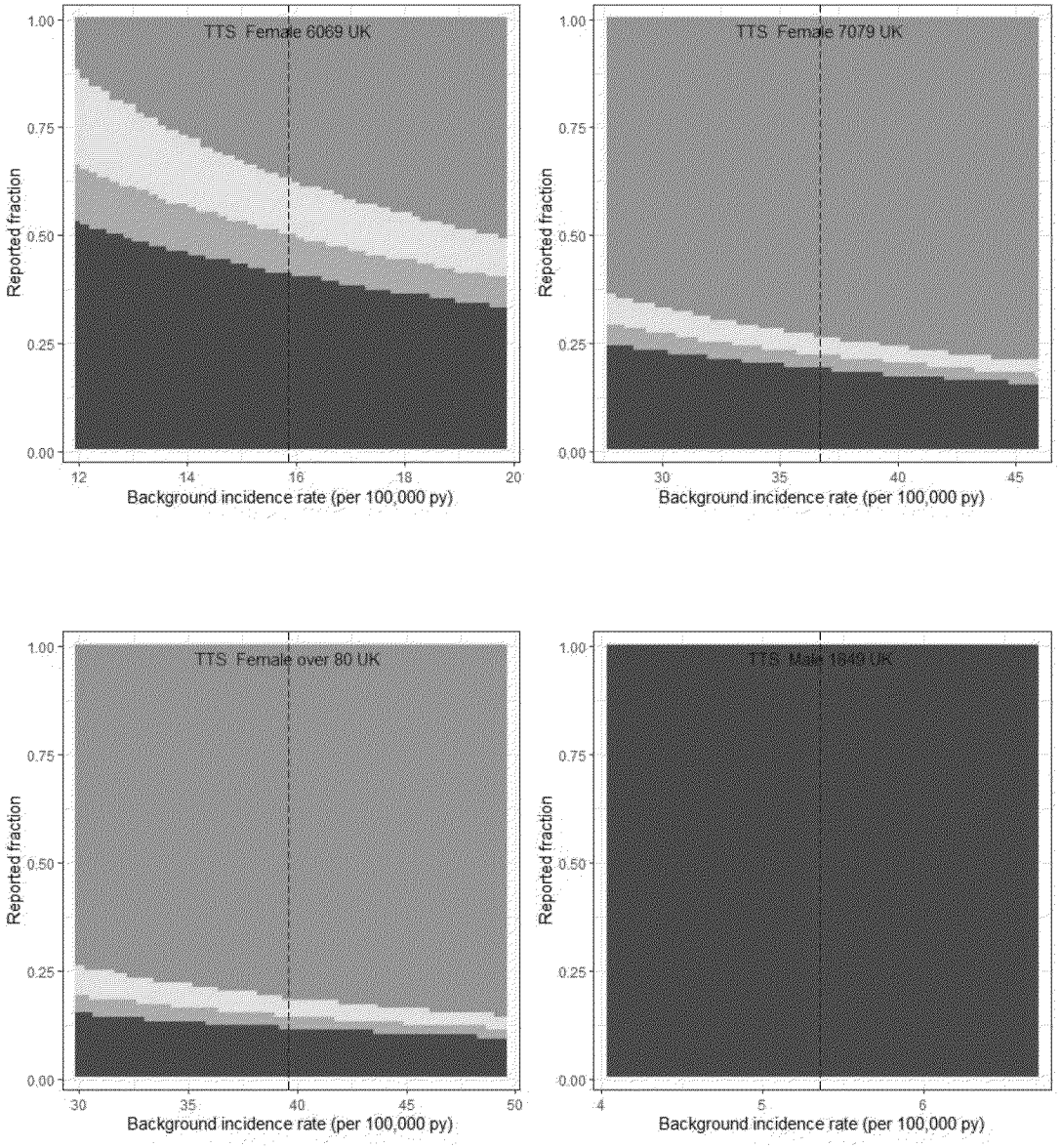
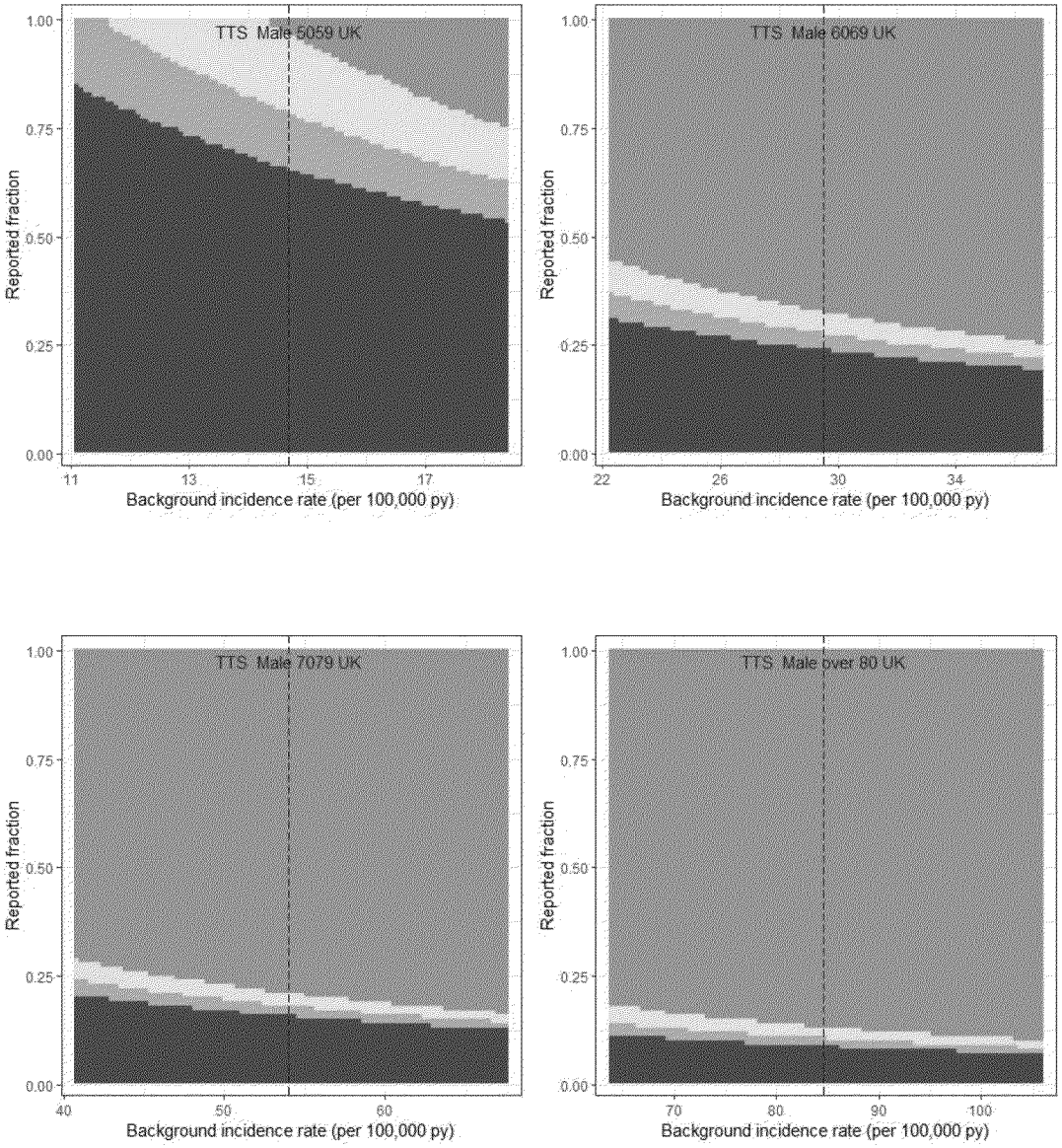

TTS Male 5059 UK
TTS Male 6069 UK
TTS Male 7079 UK
TTS Male over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
11
13
15
17
22
26
30
34
40
50
60
70
80
90
100
Background incidence rate (per 100,000 py)

Table 67 Observed Versus Expected analysis for Thrombosis with thrombocytopenia by gender and age group (UK)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates	Exposure	O over E ratio (95% CI)	
TTS - Female UK	330	246.53	42	9.22	23252503	1.34 (1.2 - 1.49)	Observed significantly > expected
TTS - Male UK	313	340.7	42	13.24	22377923	0.92 (0.82 - 1.03)	Observed < expected
TTS - Female 18-49	153	39.56	42	4.64	7414701	3.87 (3.28 - 4.53)	Observed significantly > expected
TTS - Female 50-59	68	73.21	42	10.71	5944683	0.93 (0.72 - 1.18)	Observed < expected
TTS - Female 60-69	44	87.29	42	15.87	4783416	0.5 (0.37 - 0.68)	Observed significantly < expected
TTS - Female 70-79	33	146.69	42	36.7	3475875	0.22 (0.15 - 0.32)	Observed significantly < expected
TTS - Female Over 80	11	74.26	42	39.61	1630324	0.15 (0.07 - 0.27)	Observed significantly < expected
TTS - Male 18-49	112	41.7	42	5.36	6766098	2.69 (2.21 - 3.23)	Observed significantly > expected
TTS - Male 50-59	87	110.06	42	14.7	6510960	0.79 (0.63 - 0.98)	Observed significantly < expected
TTS - Male 60-69	47	167.46	42	29.51	4934728	0.28 (0.21 - 0.37)	Observed significantly < expected
TTS - Female 70-79	36	194.96	42	54.04	3137304	0.18 (0.13 - 0.26)	Observed significantly < expected
TTS - Female Over 80	11	99.74	42	84.62	1025046	0.11 (0.06 - 0.2)	Observed significantly < expected


TTS Female UK
TTS Male UK
TTS Female 1849 UK
TTS Female 5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
11
12
14
16
3.5
4.0
4.5
5.0
5.5


TTS Female 6069 UK
TTS Female 7079 UK
TTS Female over 80 UK
TTS Male 1549 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
12
14
16
18
20
30
35
40
45
50
4
5
6

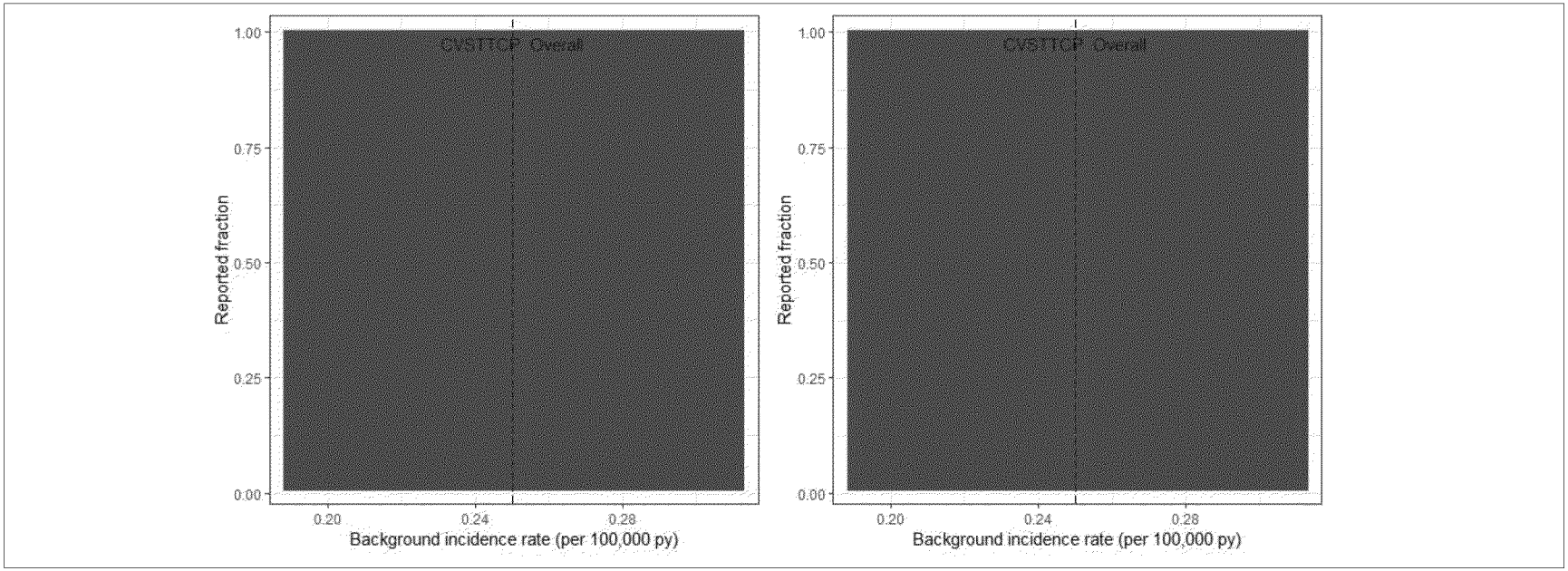

TTS Male 5059 UK
TTS Male 6069 UK
TTS Male 7079 UK
TTS Male over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
11
13
15
17
22
26
30
34
40
50
60
70
80
90
100
Background incidence rate (per 100,000 py)

[a] Only cases observed within 0-14, 0-21, and 0-42 days were included; Risk Window: 14, 21, and 42 days.

CI Confidence interval; E Expected; OHDSI Observational Health Data Science and Informatics; o Observed; TCP Thrombocytopenia; TTS Thrombosis with thrombocytopenia syndrome; UK United Kingdom.

Table 68 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis+ thrombocytopenia (CVST+TCP)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates [b]	Exposure	O over E ratio (95% CI)	
CVST-TCP - Overall	396	44.67	14	0.25	466115644	8.87 (8.01 - 9.78)	Observed significantly > expected
CVST-TCP - Overall	467	67	21	0.25	466115644	6.97 (6.35 - 7.63)	Observed significantly > expected
CVST-TCP - Overall	502	134	42	0.25	466115644	3.75 (3.43 - 4.09)	Observed significantly > expected
CVST TCP Overall (RW14+ Unk TTO)	529	44.67	14	0.25	466115644	11.84 (10.85 - 12.9)	Observed significantly > expected
CVST TCP Overall (RW21+ Unk TTO)	600	67	21	0.25	466115644	8.96 (8.25 - 9.7)	Observed significantly > expected
CVST TCP Overall (RW42+ Unk TTO)	635	134	42	0.25	466115644	4.74 (4.38 - 5.12)	Observed significantly > expected


CVST/TCP Overall
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.20
0.24
0.28
Background incidence rate (per 100,000 py)
CVST/TCP Overall
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.20
0.24
0.28
Background incidence rate (per 100,000 py)

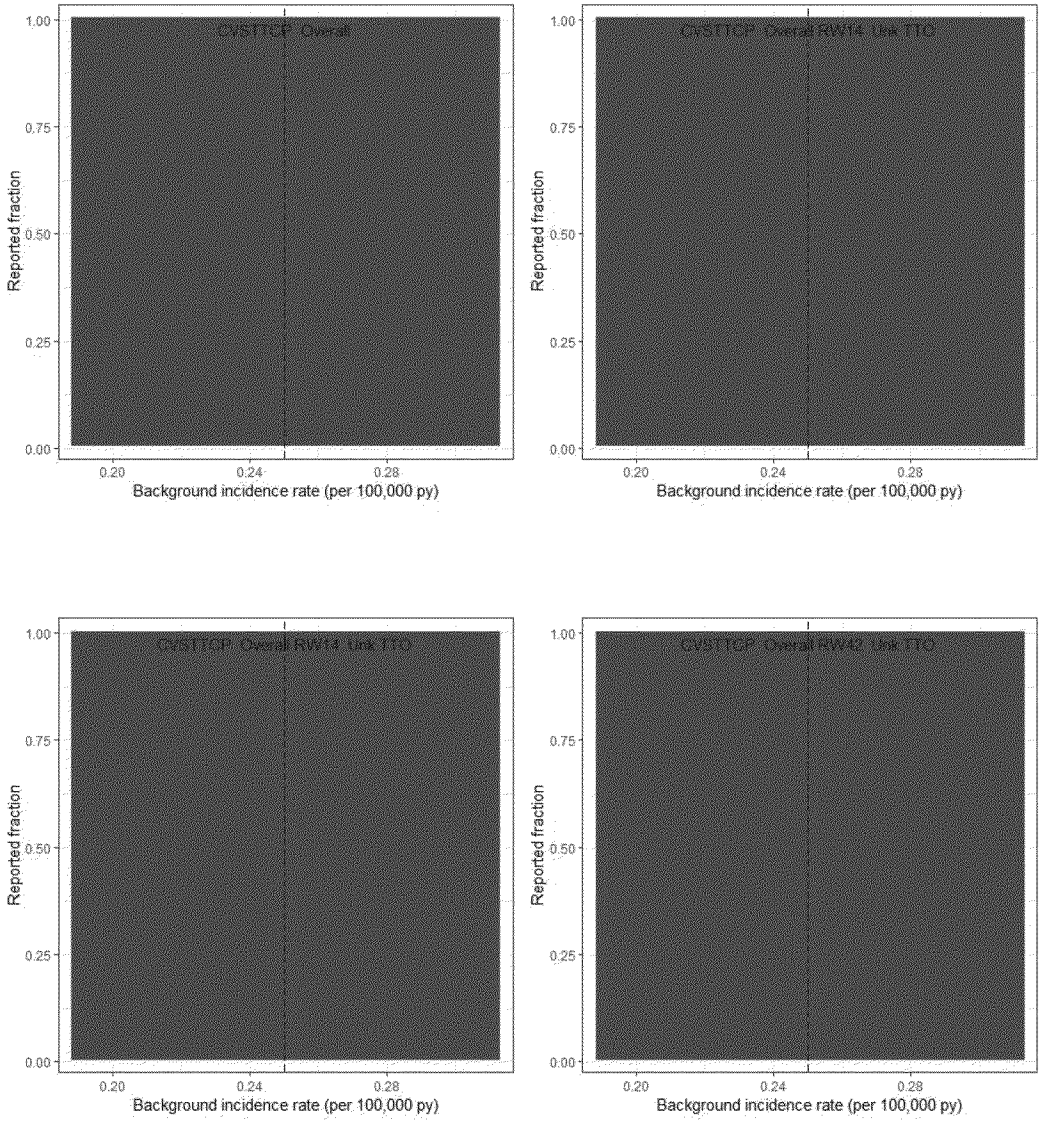

CVSTTCP Overall
CVSTTCP Overall RW14 Unk TTO
CVSTTCP Overall RW14 Unk TTO
CVSTTCP Overall RW40 Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.20
0.24
0.28
Background incidence rate (per 100,000 py)

Table 68 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis+ thrombocytopenia (CVST+TCP)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates [b]	Exposure	O over E ratio (95% CI)	
Observed Versus Expected analysis for CVST+TCP by age group (EU/UK/Brazil/Australia)							
CVST-TCP - 18-49	216	7.17	14	0.17	110094983	30.13 (26.24 - 34.42)	Observed significantly > expected
CVST-TCP - 50-59	62	8.72	14	0.39	58336094	7.11 (5.45 - 9.11)	Observed significantly > expected
CVST-TCP - 60-69	56	7.33	14	0.33	57960860	7.64 (5.77 - 9.92)	Observed significantly > expected
CVST-TCP – 70+	12	2.98	14	0.24	32376365	4.03 (2.08 - 7.03)	Observed significantly > expected

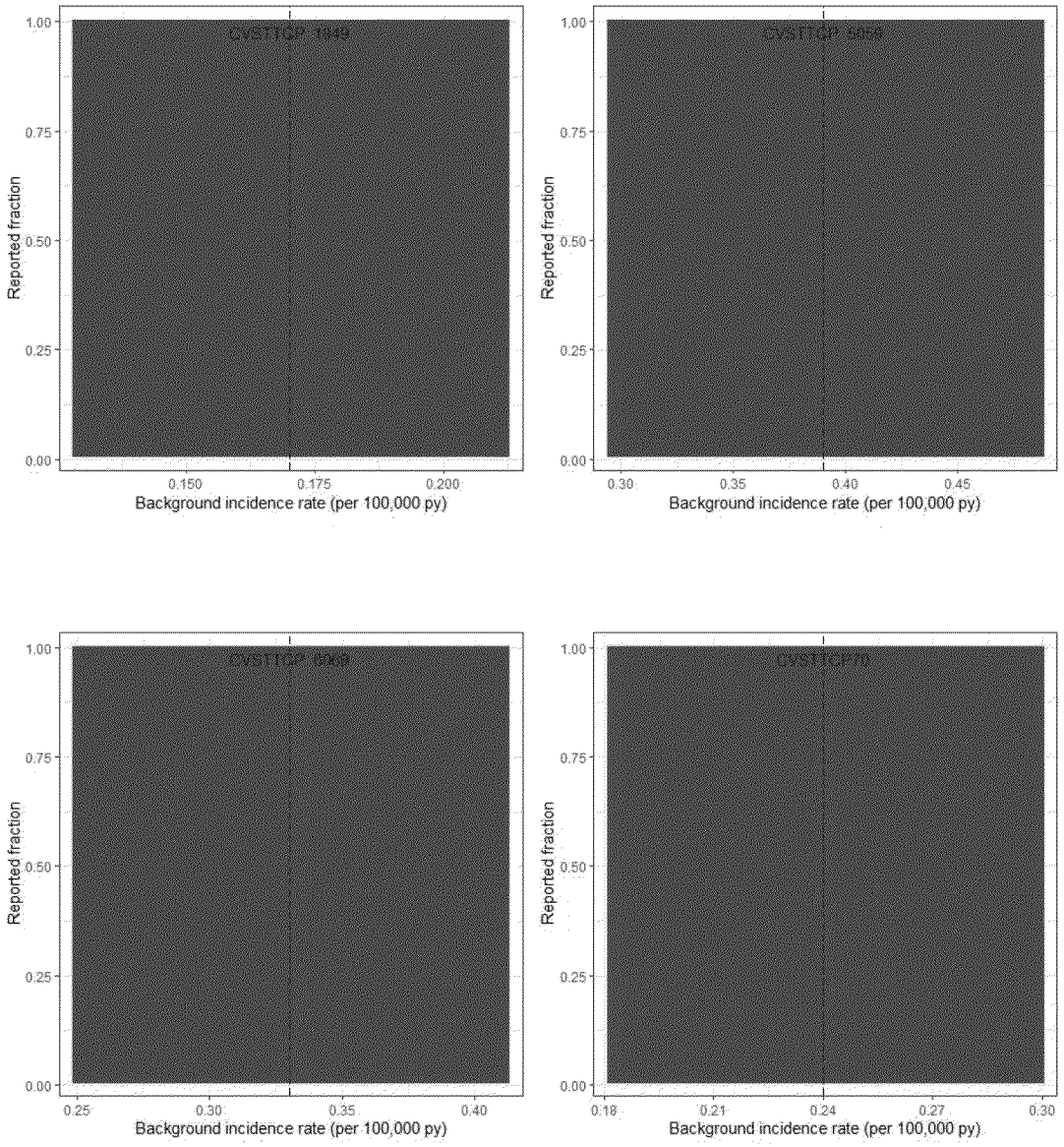

CVSTTCP 1949
CVSTTCP 5858
CVSTTCP 5068
CVSTTCP70
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.150
0.175
0.200
0.30
0.35
0.40
0.45
0.25
0.18
0.21
0.24
0.27
0.30
Background incidence rate (per 100,000 py)

Table 68 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis+ thrombocytopenia (CVST+TCP)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates [b]	Exposure	O over E ratio (95% CI)	
CVST-TCP - 18-49	246	10.76	21	0.17	110094983	22.86 (20.09 - 25.91)	Observed significantly > expected
CVST-TCP - 50-59	81	13.08	21	0.39	58336094	6.19 (4.92 - 7.7)	Observed significantly > expected
CVST-TCP - 60-69	69	11	21	0.33	57960860	6.27 (4.88 - 7.94)	Observed significantly > expected
CVST-TCP – 70+	17	4.47	21	0.24	32376365	3.8 (2.22 - 6.09)	Observed significantly > expected

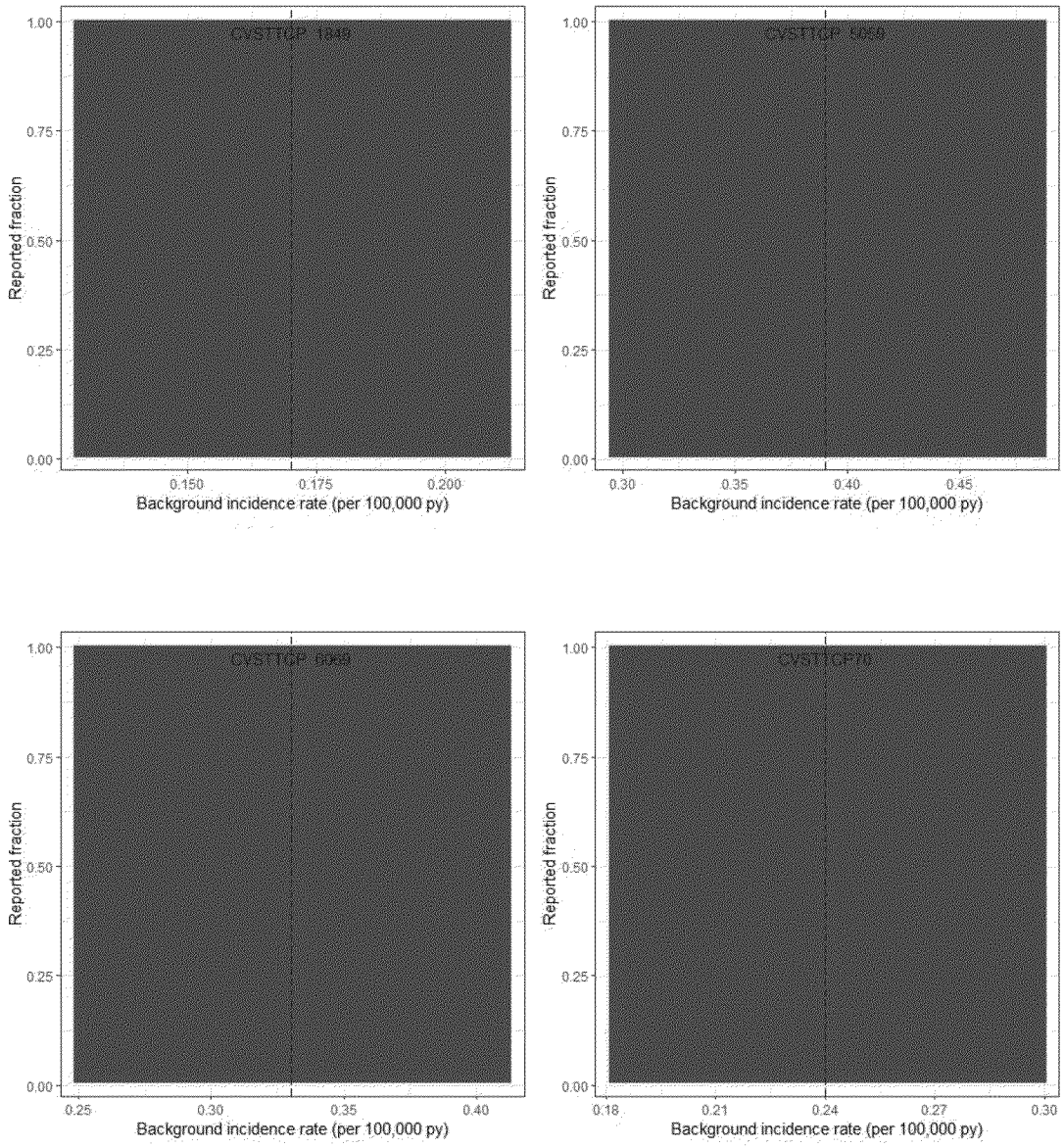
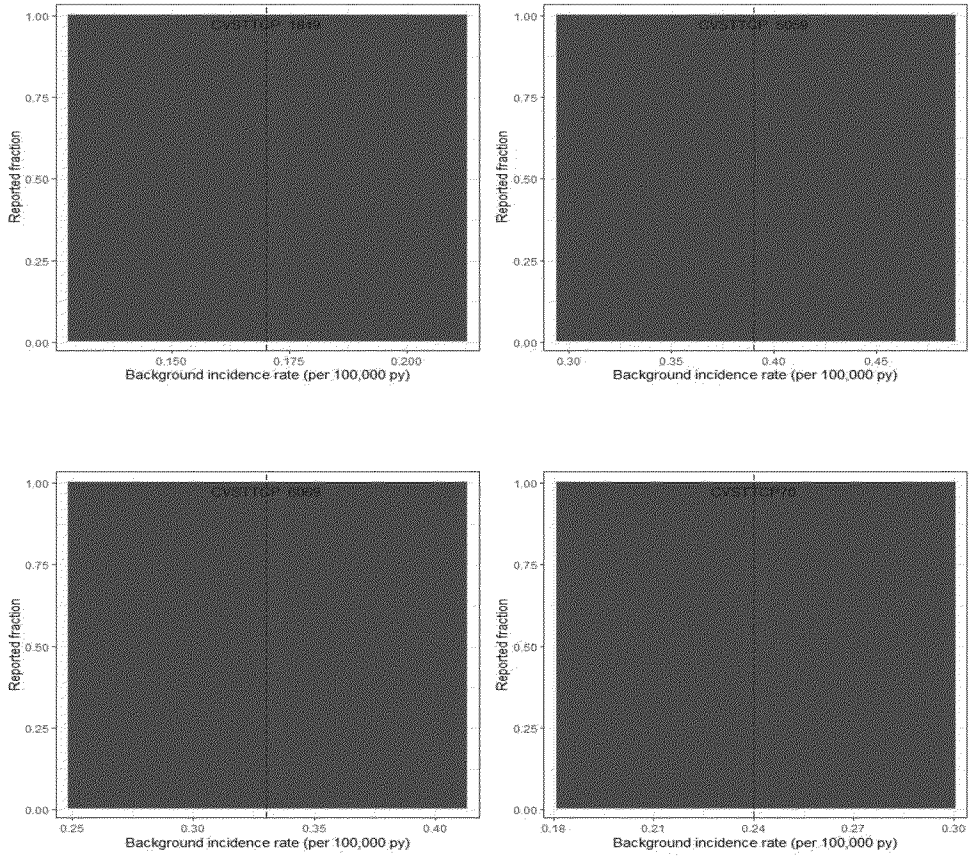

CVST1GP 1849
CVST1GP 5059
CVST1GP 6069
CVST1GP70
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.150
0.175
0.200
0.30
0.35
0.40
0.45
0.25
0.30
0.35
0.40
0.18
0.21
0.24
0.27
0.30

Table 68 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis+ thrombocytopenia (CVST+TCP)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates [b]	Exposure	O over E ratio (95% CI)	
CVST-TCP - 18-49	260	21.52	42	0.17	110094983	12.08 (10.66 - 13.64)	Observed significantly > expected
CVST-TCP - 50-59	88	26.16	42	0.39	58336094	3.36 (2.7 - 4.14)	Observed significantly > expected
CVST-TCP - 60-69	78	21.99	42	0.33	57960860	3.55 (2.8 - 4.43)	Observed significantly > expected
CVST-TCP – 70+	19	8.94	42	0.24	32376365	2.13 (1.28 - 3.32)	Observed significantly > expected

Table 68 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis+ thrombocytopenia (CVST+TCP)

AEs	Observed Cases	Expected cases	Risk window [a]	Background rates [b]	Exposure	O over E ratio (95% CI)	
							

[a] Only cases observed within 0-14, 0-21, and 0-42 days were included; Risk Window: 14, 21, and 42 days.

[b] Incidence Rate (per/100,000 PY) from Truven Market Scan database (2019).

CI Confidence interval; CVST Cerebral venous sinus thrombosis; E Expected; O Observed; TCP Thrombocytopenia; TTO Time to onset; Unk Unknown

Table 69 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases Overall_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Overall	289	192.96	21	0.72	466115644	1.5 (1.33 - 1.68)	Observed significantly > expected
Overall (RW 21+Unk TTO)	454	192.96	21	0.72	466115644	2.35 (2.14 - 2.58)	Observed significantly > expected
Overall	331	275.66	30	0.72	466115644	1.2 (1.07 - 1.34)	Observed significantly > expected
Overall (RW 30+Unk TTO)	496	275.66	30	0.72	466115644	1.8 (1.64 - 1.96)	Observed significantly > expected
Overall	378	385.92	42	0.72	466115644	0.98 (0.88 - 1.08)	Observed < expected
Overall (RW 42+Unk TTO)	543	385.92	42	0.72	466115644	1.41 (1.29 - 1.53)	Observed significantly > expected

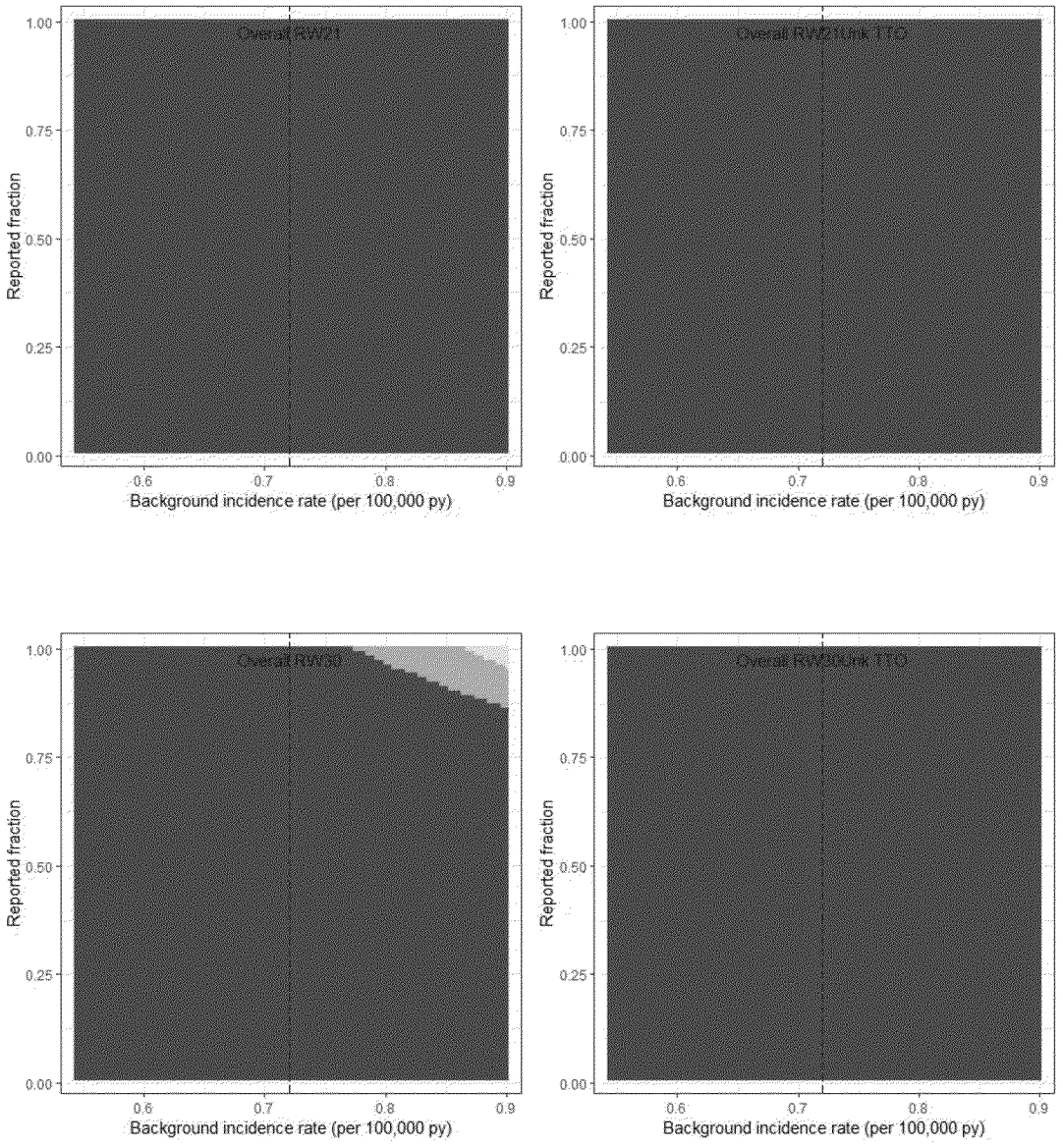
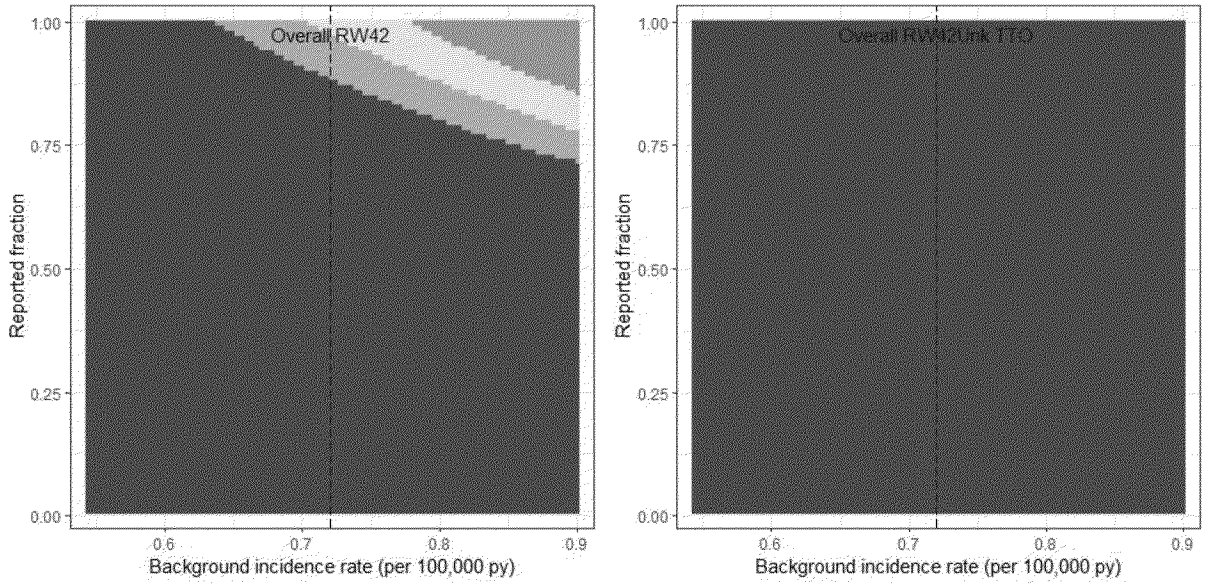

Overall RW21
Overall RW21Unk TTO
Overall RW30
Overall RW30Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9

Table 69 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases Overall_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: SIDIAP PCHOSP rates CI Confidence Interval (Willame et al 2021 [A])

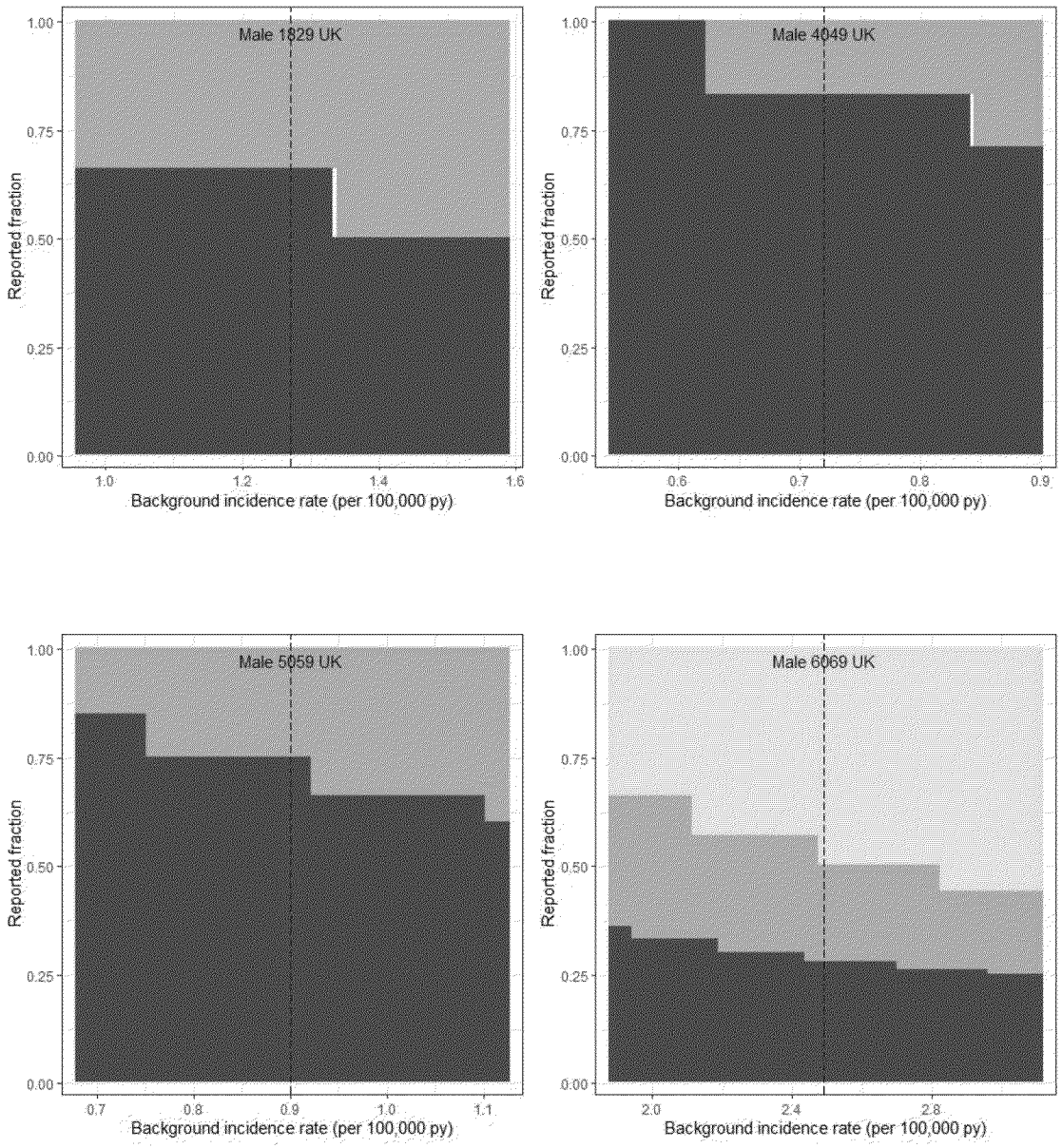
CVST Cerebral Venous Sinus Thrombosis, CI confidence Interval, E Expected; IR Incidence Rate; O Observed, TTO Time to onset, Unk unknown.

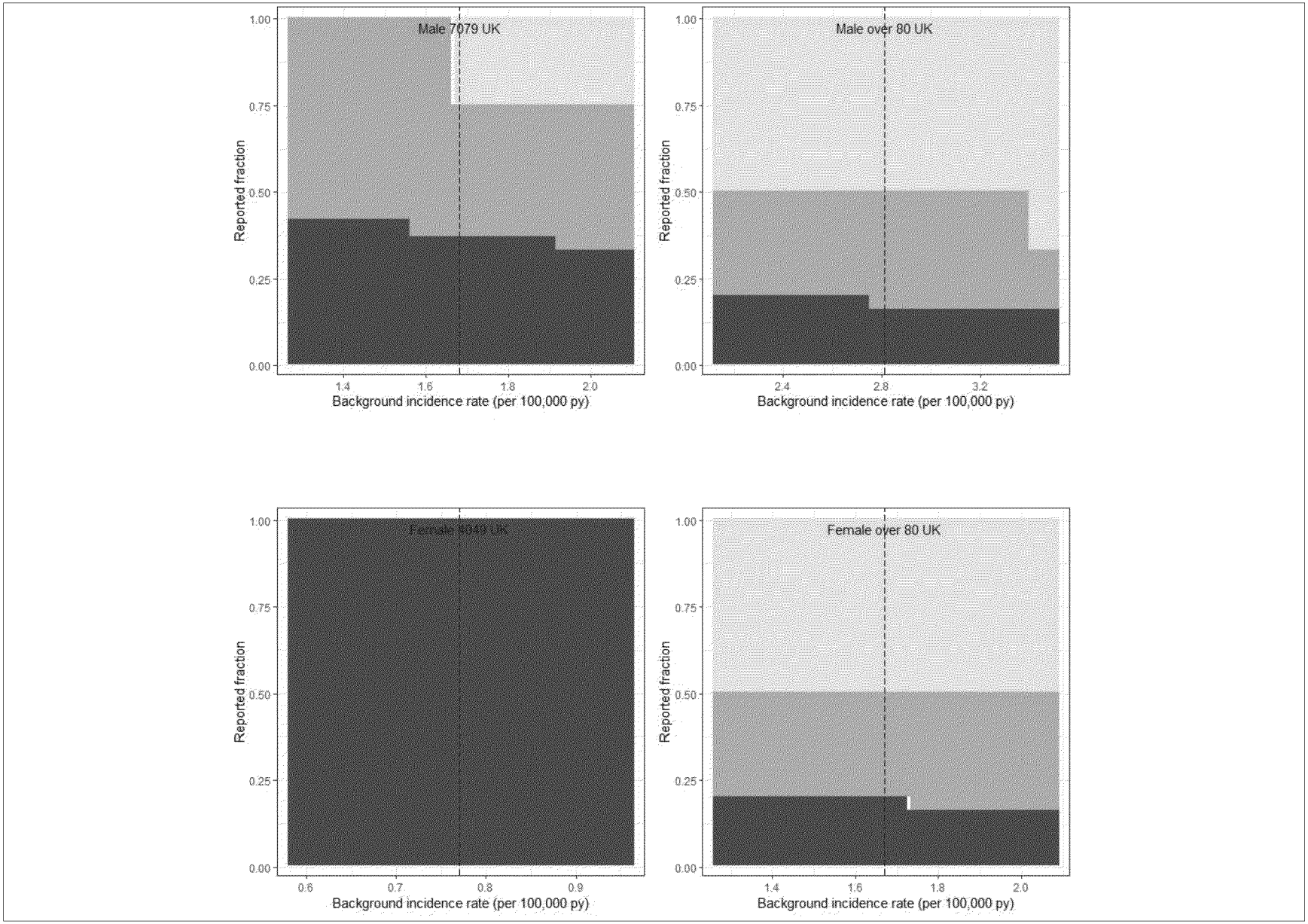
Table 70 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by age and gender from UK_SIDIAP

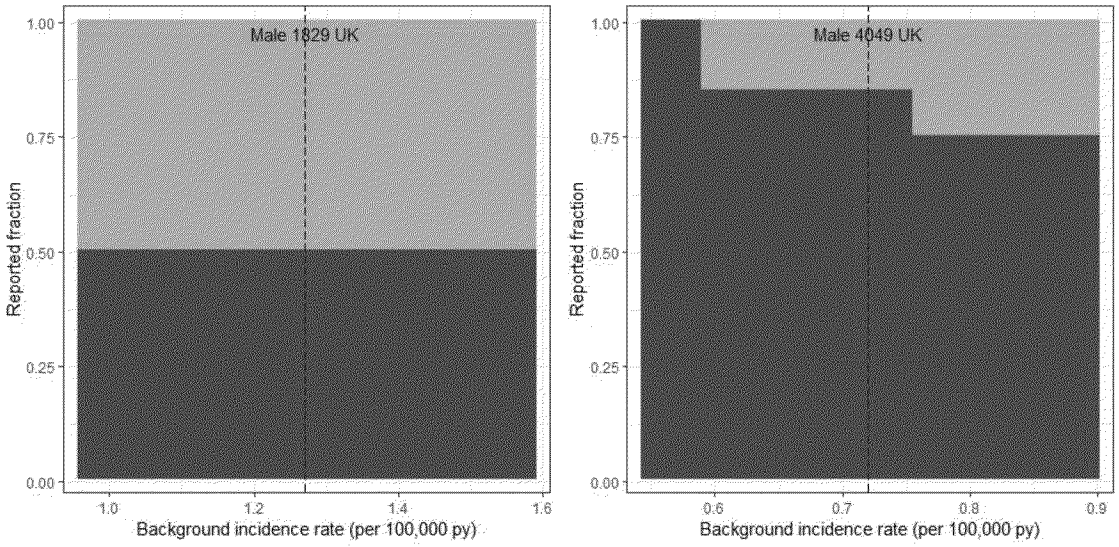
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 18 to 29	2	0.59	21	1.27	808938	3.39 (0.41 - 12.25)	Observed > expected
Male 40 to 49	5	1.88	21	0.72	4542157	2.66 (0.86 - 6.21)	Observed > expected
Male 50 to 59	6	3.37	21	0.9	6510960	1.78 (0.65 - 3.88)	Observed > expected
Male 60 to 69	4	7.06	21	2.49	4934728	0.57 (0.15 - 1.45)	Observed < expected
Male 70 to 79	3	3.03	21	1.68	3137304	0.99 (0.2 - 2.89)	Observed < expected
Male over 80	1	1.66	21	2.81	1025046	0.6 (0.02 - 3.36)	Observed < expected
Female 40 to 49	12	1.95	21	0.77	4412245	6.15 (3.18 - 10.75)	Observed significantly > expected
Female over 80	1	1.57	21	1.67	1630324	0.64 (0.02 - 3.55)	Observed < expected
Male 18 to 29	2	0.84	30	1.27	808938	2.38 (0.29 - 8.6)	Observed > expected
Male 40 to 49	6	2.69	30	0.72	4542157	2.23 (0.82 - 4.85)	Observed > expected
Male 50 to 59	8	4.81	30	0.9	6510960	1.66 (0.72 - 3.28)	Observed > expected
Male 60 to 69	4	10.09	30	2.49	4934728	0.4 (0.11 - 1.02)	Observed < expected
Male 70 to 79	3	4.33	30	1.68	3137304	0.69 (0.14 - 2.02)	Observed < expected
Male over 80	1	2.37	30	2.81	1025046	0.42 (0.01 - 2.35)	Observed < expected
Female 40 to 49	12	2.79	30	0.77	4412245	4.3 (2.22 - 7.51)	Observed significantly > expected
Female over 80	1	2.24	30	1.67	1630324	0.45 (0.01 - 2.49)	Observed < expected
Male 18 to 29	4	1.18	42	1.27	808938	3.39 (0.92 - 8.68)	Observed > expected
Male 40 to 49	7	3.76	42	0.72	4542157	1.86 (0.75 - 3.84)	Observed > expected
Male 50 to 59	12	6.74	42	0.9	6510960	1.78 (0.92 - 3.11)	Observed > expected
Male 60 to 69	6	14.13	42	2.49	4934728	0.42 (0.16 - 0.92)	Observed significantly < expected
Male 70 to 79	3	6.06	42	1.68	3137304	0.5 (0.1 - 1.45)	Observed < expected

Table 70 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by age and gender from UK_SIDIAP

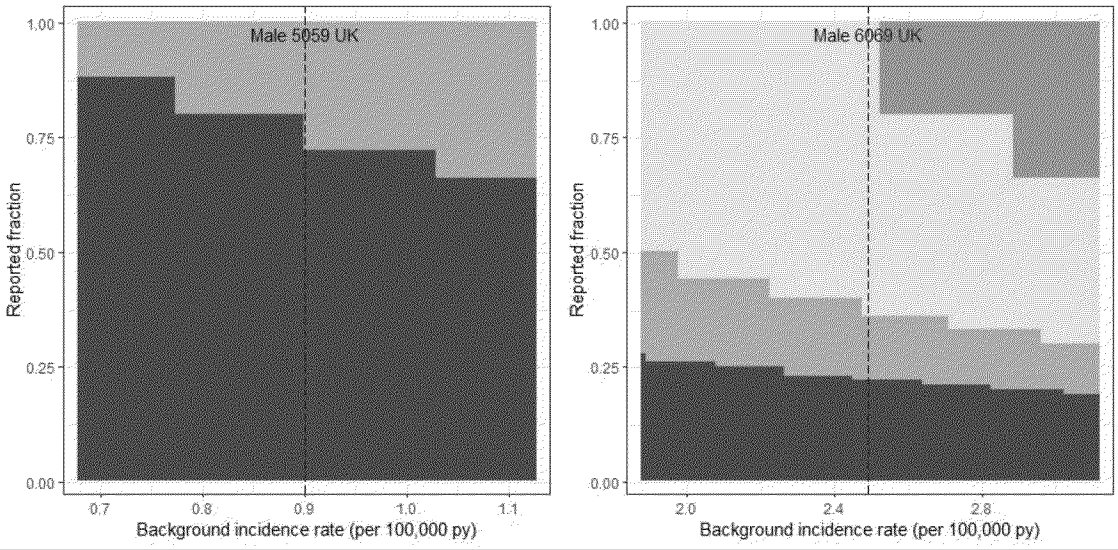
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male over 80	1	3.31	42	2.81	1025046	0.3 (0.01 - 1.68)	Observed < expected
Female 40 to 49	13	3.91	42	0.77	4412245	3.32 (1.77 - 5.69)	Observed significantly > expected
Female over 80	3	3.13	42	1.67	1630324	0.96 (0.2 - 2.8)	Observed < expected


Male 1829 UK
Male 4049 UK
Male 5059 UK
Male 6069 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
0.6
0.7
0.8
0.9
1.1
2.0
2.4
2.8

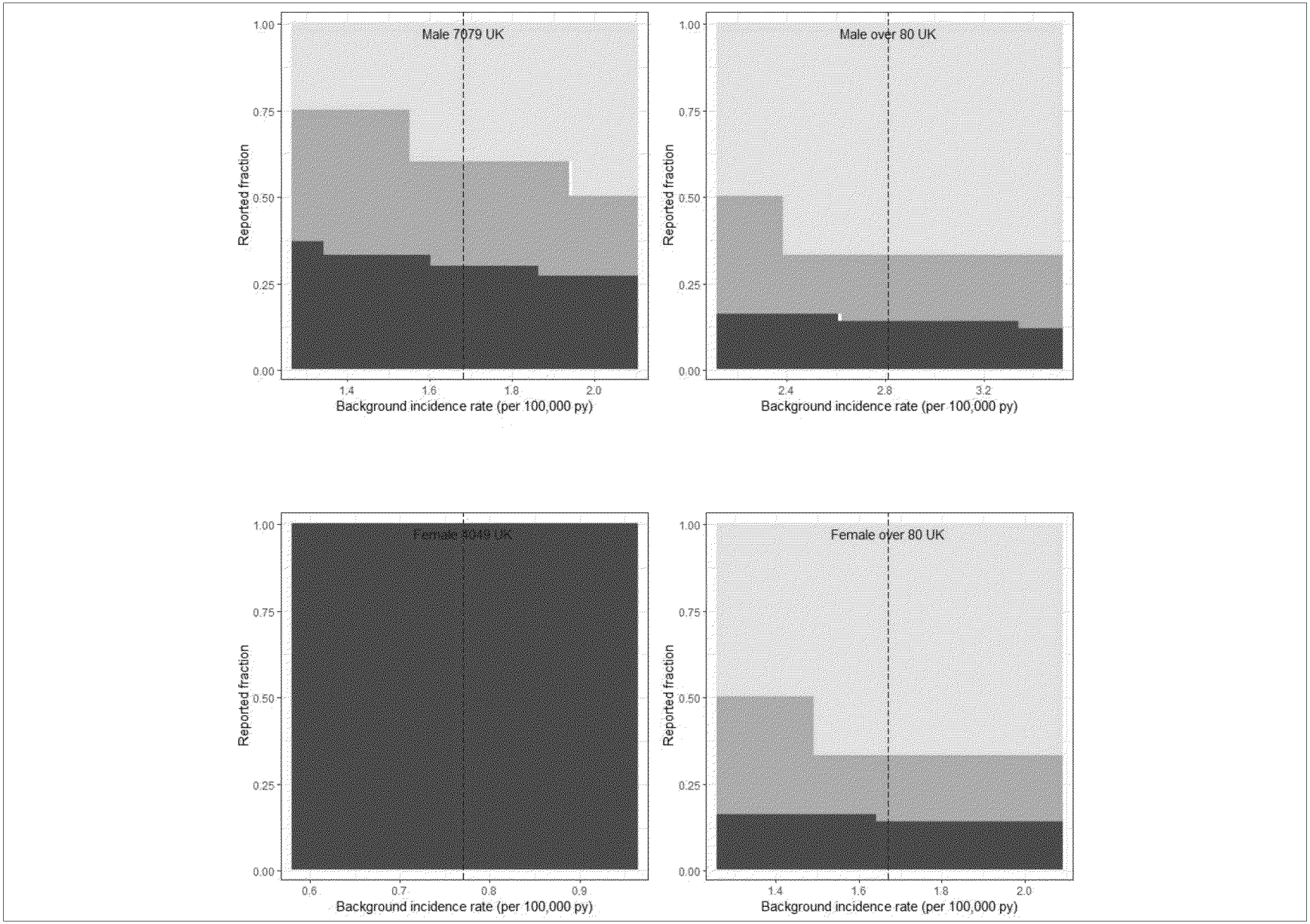

Male 7079 UK
Male over 80 UK
Female 6049 UK
Female over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.4
2.8
3.2
0.6
0.7
0.8
0.9
Background incidence rate (per 100,000 py)


Male 1829 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
Background incidence rate (per 100,000 py)

Male 4049 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
Background incidence rate (per 100,000 py)


Male 5059 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)

Male 6069 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.4
2.8
Background incidence rate (per 100,000 py)


Male 7079 UK
Male over 80 UK
Female 8049 UK
Female over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.4
2.8
3.2
0.6
0.7
0.8
0.9
Background incidence rate (per 100,000 py)

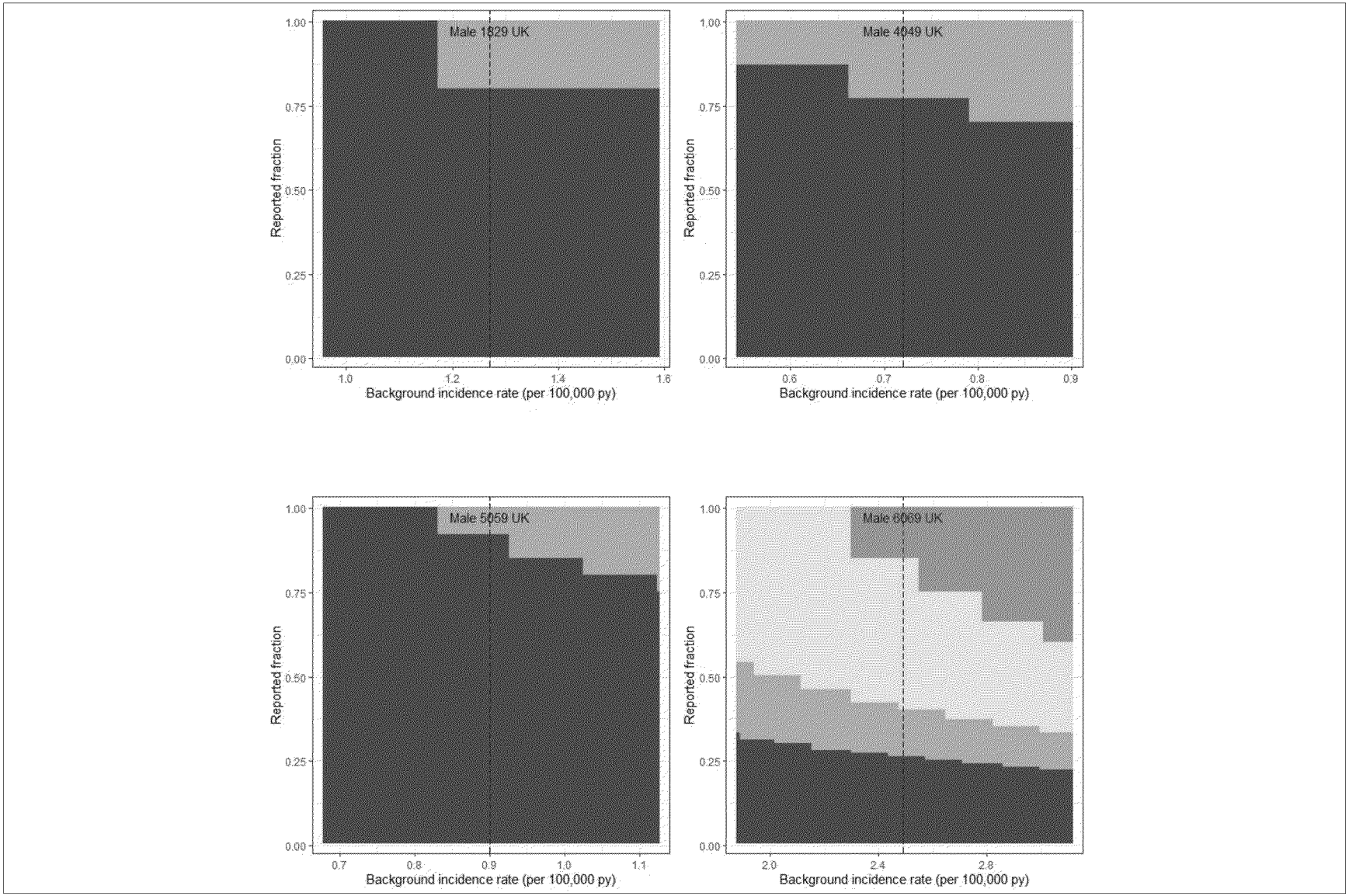
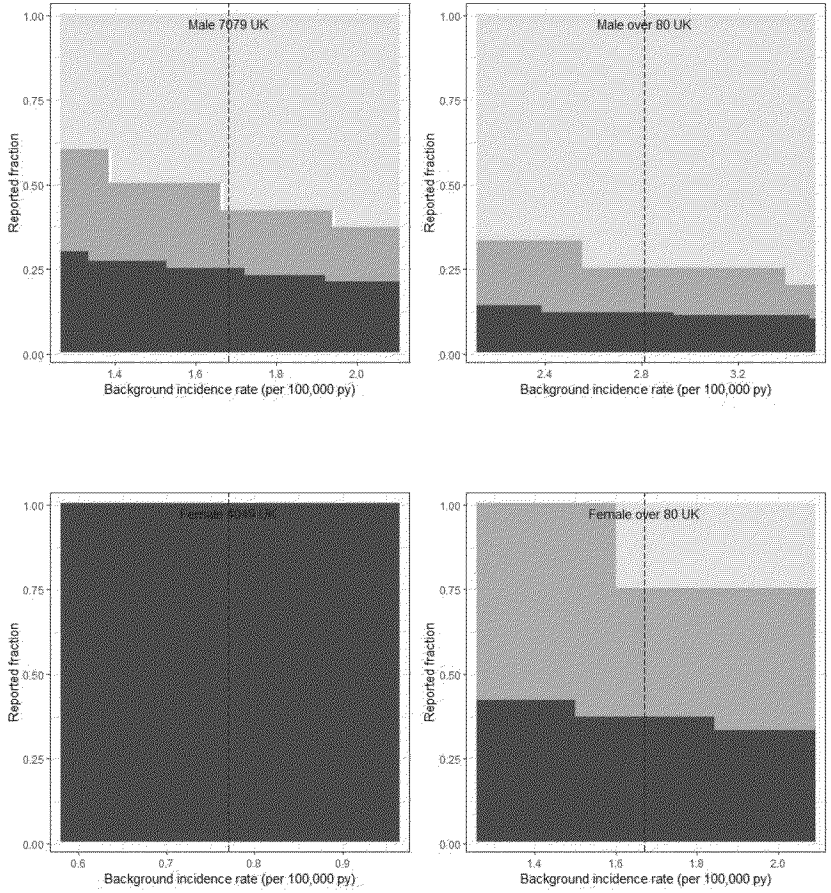

Male 1829 UK
Male 4049 UK
Male 5059 UK
Male 6069 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
0.6
0.7
0.8
0.9
1.1
2.0
2.4
2.8

Table 70 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by age and gender from UK_SIDIAP

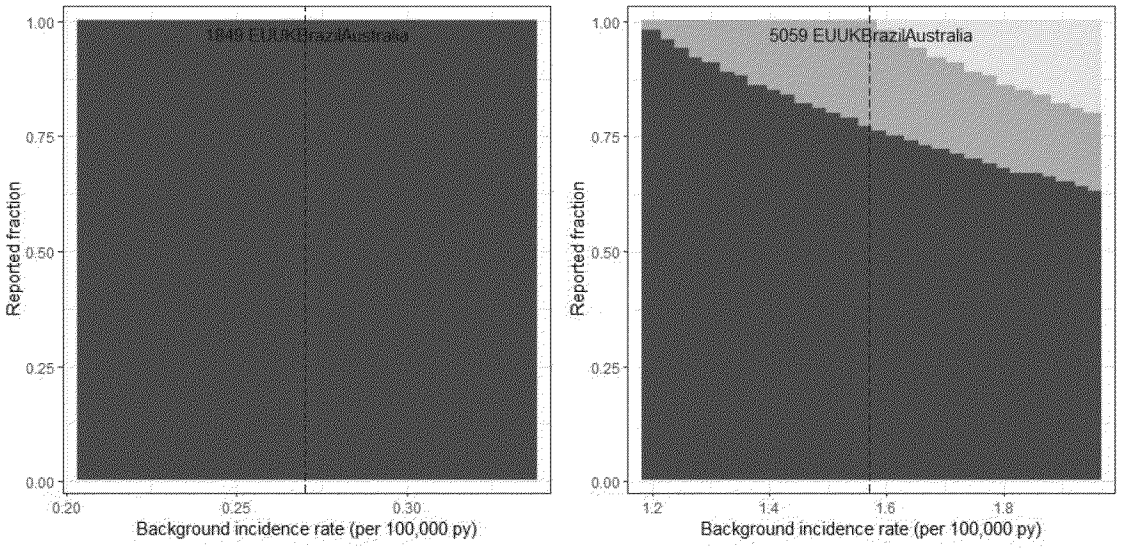
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: SIDIAP PCHOSP rate (Willame et al 2021 [A])

CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset; UK United Kingdom

Table 71 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by age from EU+UK+Brazil+Australia_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18 to 49	124	17.09	21	0.27	110094983	7.26 (6.03 - 8.65)	Observed significantly > expected
50 to 59	53	52.66	21	1.57	58336094	1.01 (0.75 - 1.32)	Observed > expected
60 to 69	58	22.66	21	0.68	57960860	2.56 (1.94 - 3.31)	Observed significantly > expected
Over 70	35	6.33	21	0.34	32376365	5.53 (3.85 - 7.69)	Observed significantly > expected
18 to 49	136	24.42	30	0.27	110094983	5.57 (4.67 - 6.59)	Observed significantly > expected
50 to 59	63	75.23	30	1.57	58336094	0.84 (0.64 - 1.07)	Observed < expected
60 to 69	65	32.37	30	0.68	57960860	2.01 (1.55 - 2.56)	Observed significantly > expected
Over 70	41	9.04	30	0.34	32376365	4.54 (3.25 - 6.15)	Observed significantly > expected
18 to 49	154	34.18	42	0.27	110094983	4.51 (3.82 - 5.28)	Observed significantly > expected
50 to 59	71	105.32	42	1.57	58336094	0.67 (0.53 - 0.85)	Observed significantly < expected
60 to 69	78	45.32	42	0.68	57960860	1.72 (1.36 - 2.15)	Observed significantly > expected
Over 70	46	12.66	42	0.34	32376365	3.63 (2.66 - 4.85)	Observed significantly > expected


1849 EUUKBrazilAustralia
5059 EUUKBrazilAustralia
6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.20
0.25
0.30
1.2
1.4
1.6
1.8
0.6
0.7
0.8
0.30
0.35
0.40

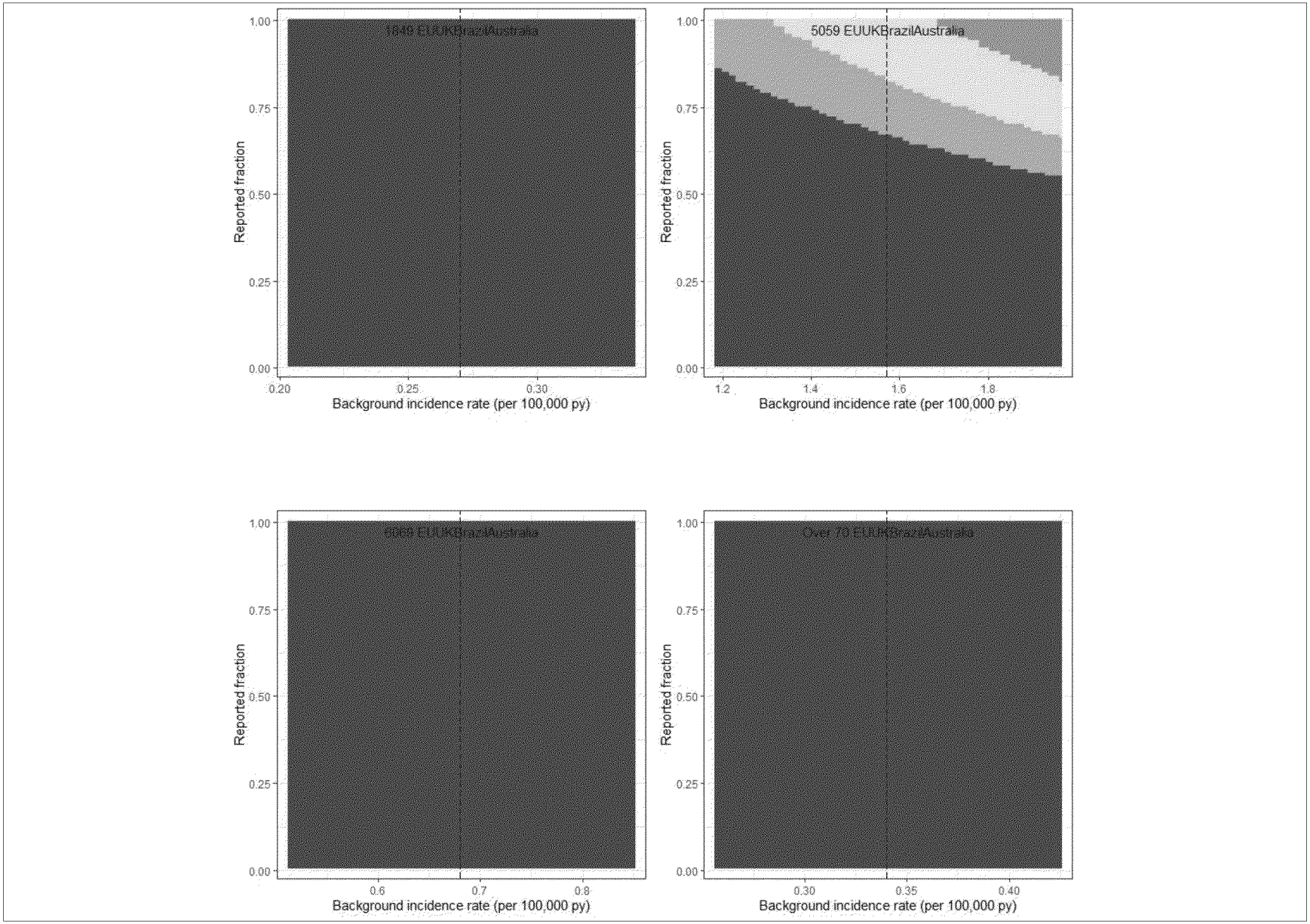
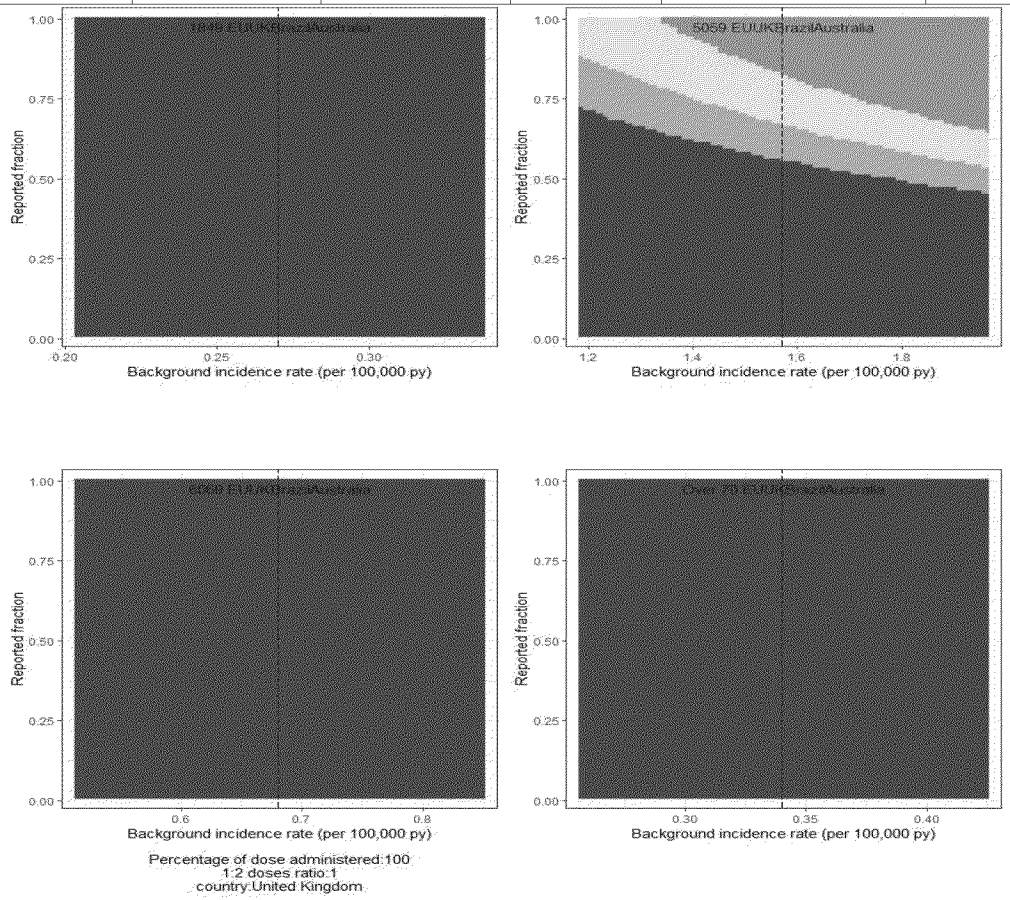

1849 EUUKBrazilAustralia
5059 EUUKBrazilAustralia
6869 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.20
0.25
0.30
1.2
1.4
1.6
1.8
0.6
0.7
0.8
0.30
0.35
0.40

Table 71 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by age from EU+UK+Brazil+Australia_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	

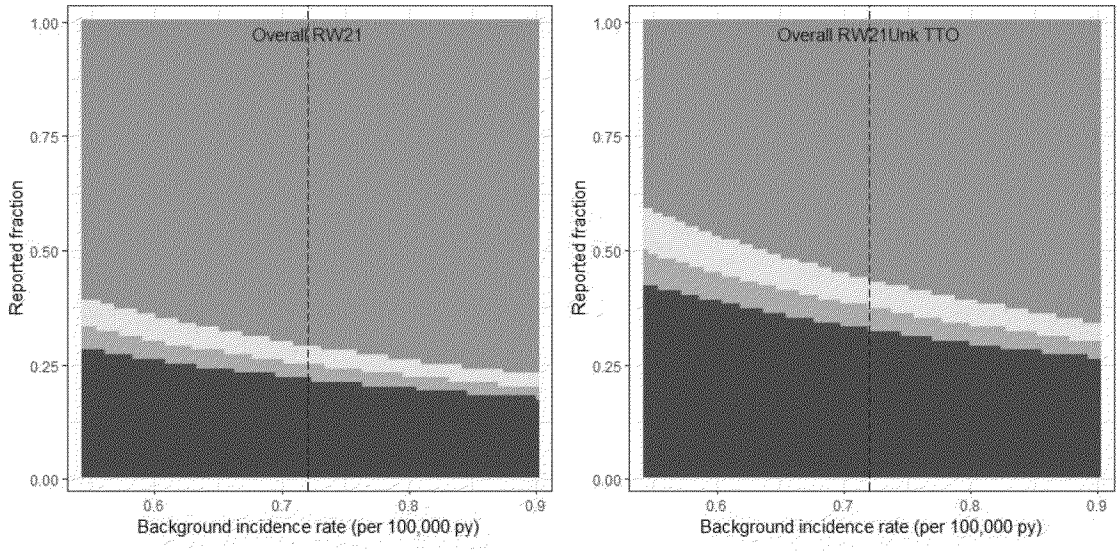


[a] ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: SIDIAP PCHOSP rates (Willame et al 2021 [A])

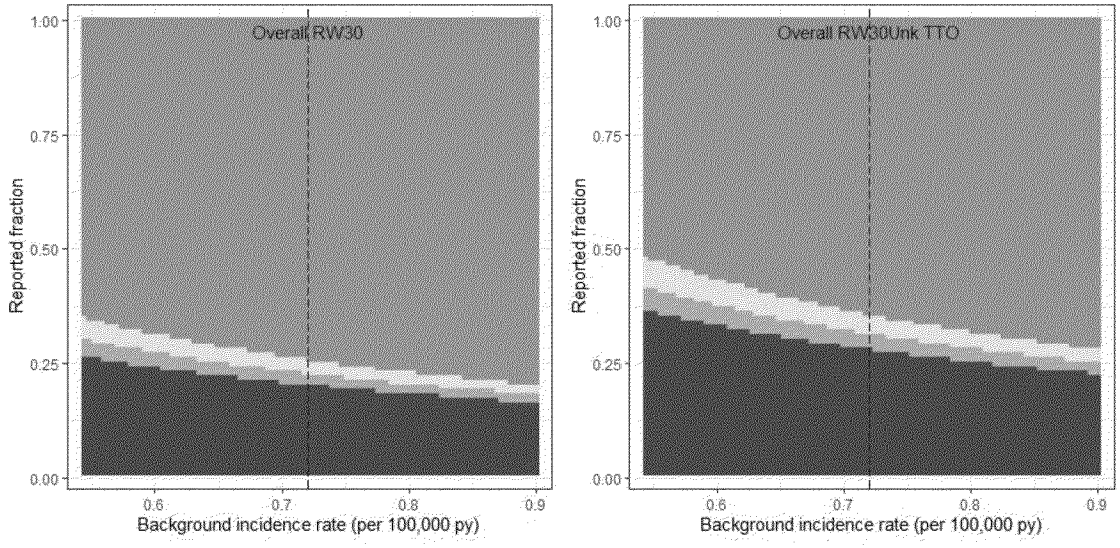
CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; EU European Union; IR Incidence Rate; O Observed, TTO Time to onset; UK United Kingdom.

Table 72 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets Overall_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Overall	49	192.96	21	0.72	466115644	0.25 (0.19 - 0.34)	Observed significantly < expected
Overall (RW21+Unk TTO)	73	192.96	21	0.72	466115644	0.38 (0.3 - 0.48)	Observed significantly < expected
Overall	63	275.66	30	0.72	466115644	0.23 (0.18 - 0.29)	Observed significantly < expected
Overall (RW30+Unk TTO)	87	275.66	30	0.72	466115644	0.32 (0.25 - 0.39)	Observed significantly < expected
Overall	75	385.92	42	0.72	466115644	0.19 (0.15 - 0.24)	Observed significantly < expected
Overall (RW42+Unk TTO)	99	385.92	42	0.72	466115644	0.26 (0.21 - 0.31)	Observed significantly < expected

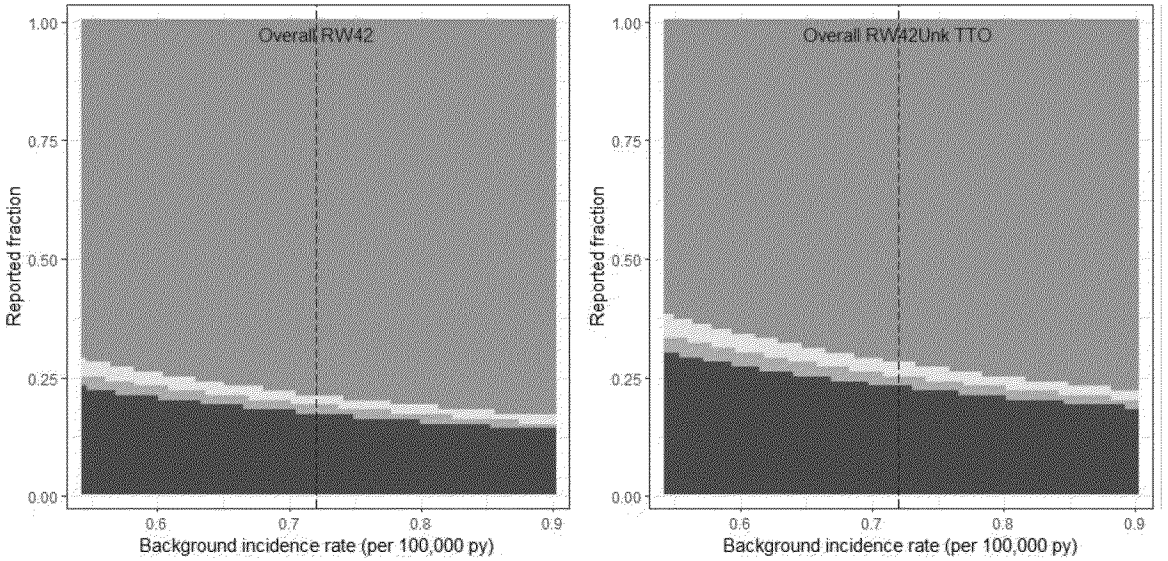

Overall RW21
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
Background incidence rate (per 100,000 py)

Overall RW21Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
Background incidence rate (per 100,000 py)


Overall RW30
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
Background incidence rate (per 100,000 py)

Overall RW30Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
Background incidence rate (per 100,000 py)

Table 72 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets Overall_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: SIDIAP PCHOSP rate (Willame et al 2021 [A])

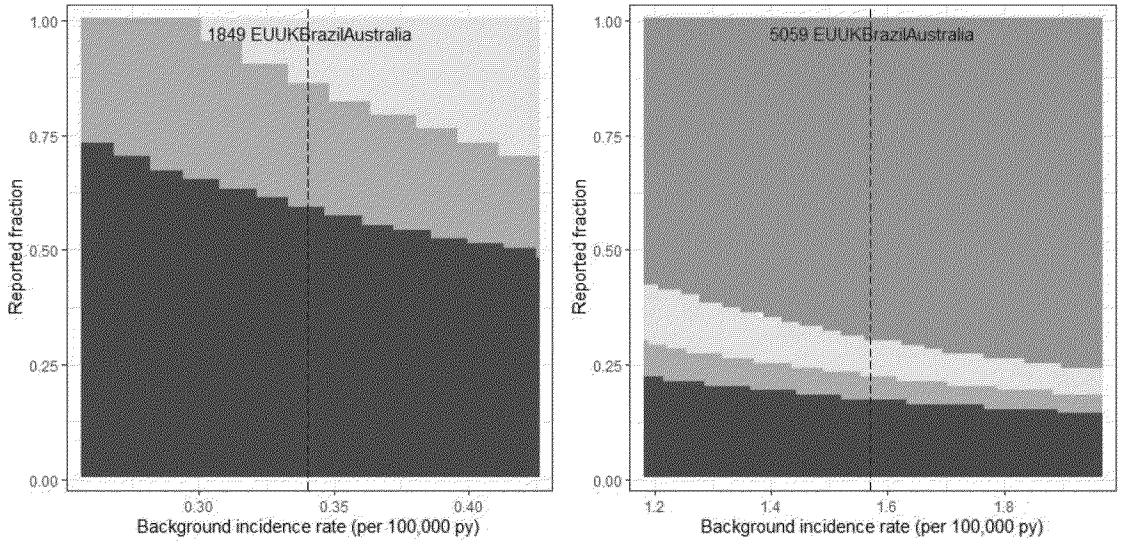
CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, RW Risk Window, TTO Time to onset, Unk Unknown.

Table 73 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by age from EU+UK+Brazil+Australia including unknown TTO_SIDIAP

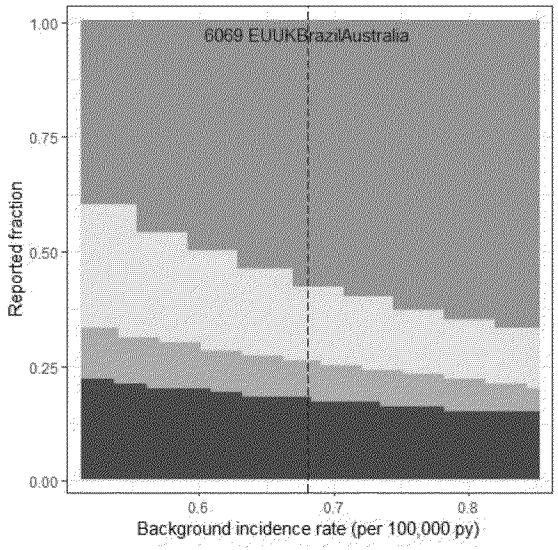
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18-49	19	21.52	21	0.34	110094983	0.88 (0.53 - 1.38)	Observed < expected
50-59	12	52.66	21	1.57	58336094	0.23 (0.12 - 0.4)	Observed significantly < expected
60-69	6	22.66	21	0.68	57960860	0.26 (0.1 - 0.58)	Observed significantly < expected
Over 70	7	6.33	21	0.34	32376365	1.11 (0.44 - 2.28)	Observed > expected
18-49	21	30.75	30	0.34	110094983	0.68 (0.42 - 1.04)	Observed < expected
50-59	17	75.23	30	1.57	58336094	0.23 (0.13 - 0.36)	Observed significantly < expected
60-69	9	32.37	30	0.68	57960860	0.28 (0.13 - 0.53)	Observed significantly < expected
Over 70	10	9.04	30	0.34	32376365	1.11 (0.53 - 2.03)	Observed > expected
18-49	23	43.04	42	0.34	110094983	0.53 (0.34 - 0.8)	Observed significantly < expected
50-59	19	105.32	42	1.57	58336094	0.18 (0.11 - 0.28)	Observed significantly < expected
60-69	12	45.32	42	0.68	57960860	0.26 (0.14 - 0.46)	Observed significantly < expected
Over 70	13	12.66	42	0.34	32376365	1.03 (0.55 - 1.76)	Observed > expected
18-49 (Including Unknown TTO)	26	21.52	21	0.34	110094983	1.21 (0.79 - 1.77)	Observed > expected
50-59 (Including unknown TTO)	16	52.66	21	1.57	58336094	0.3 (0.17 - 0.49)	Observed significantly < expected
60-69 (Including unknown TTO)	8	22.66	21	0.68	57960860	0.35 (0.15 - 0.7)	Observed significantly < expected
Over 70 (Including unknown TTO)	12	6.33	21	0.34	32376365	1.9 (0.98 - 3.31)	Observed > expected

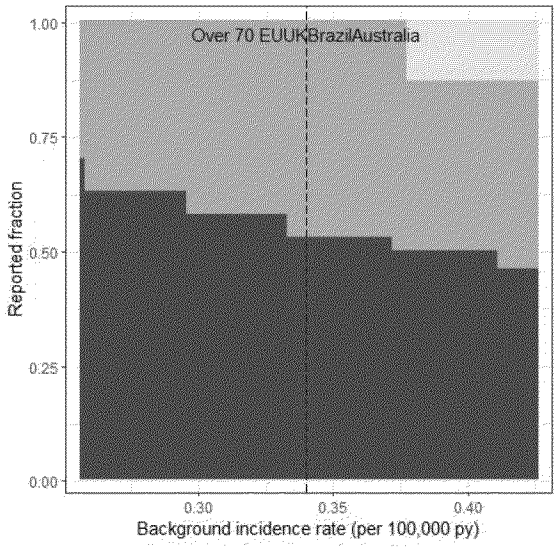
Table 73 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by age from EU+UK+Brazil+Australia including unknown TTO_SIDIAP

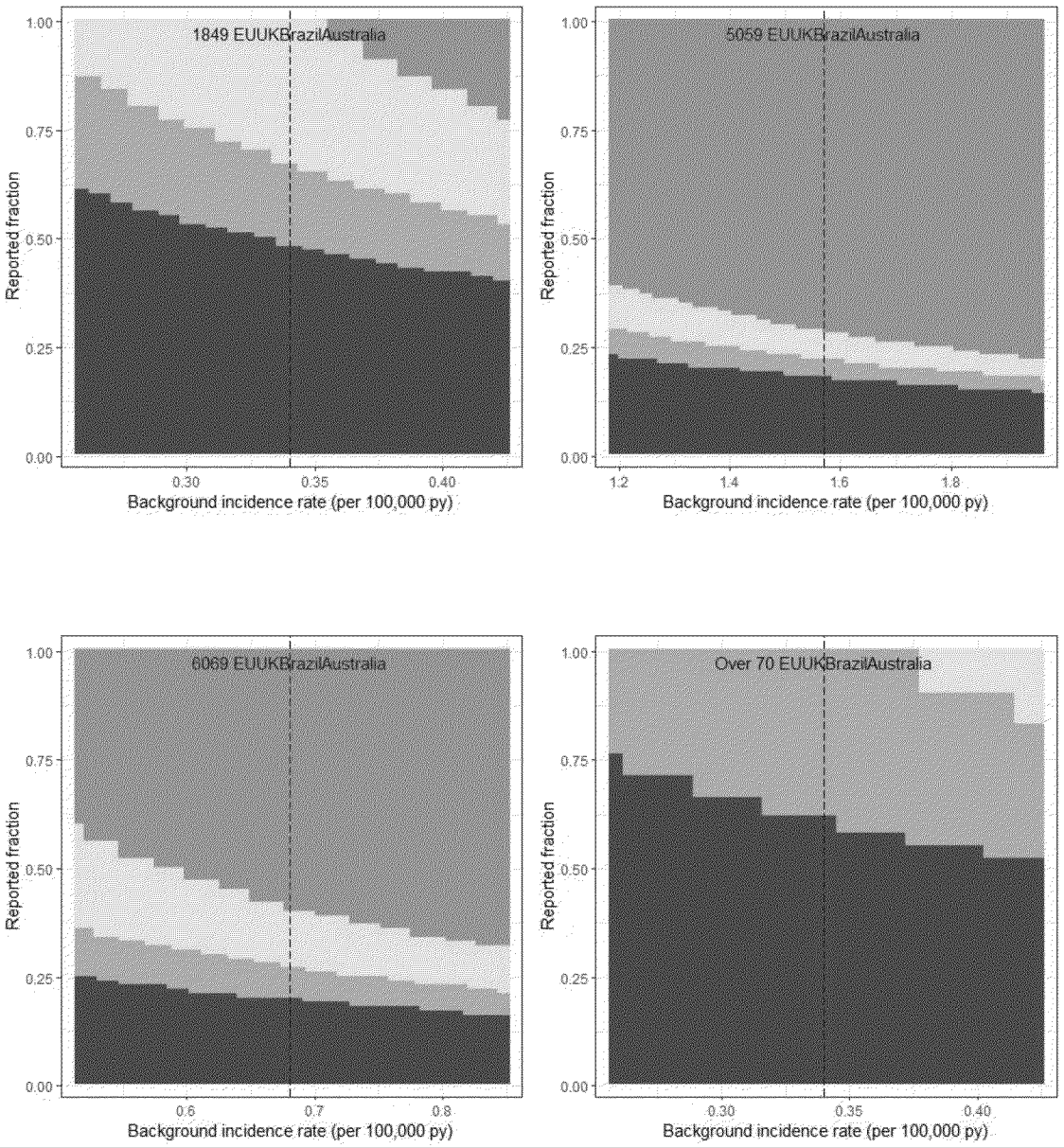
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18-49 (Including unknown TTO)	28	30.75	30	0.34	110094983	0.91 (0.61 - 1.32)	Observed < expected
50-59 (Including unknown TTO)	21	75.23	30	1.57	58336094	0.28 (0.17 - 0.43)	Observed significantly < expected
60-69 (Including unknown TTO)	11	32.37	30	0.68	57960860	0.34 (0.17 - 0.61)	Observed significantly < expected
Over 70 (Including unknown TTO)	15	9.04	30	0.34	32376365	1.66 (0.93 - 2.74)	Observed > expected
18-49 (Including unknown TTO)	30	43.04	42	0.34	110094983	0.7 (0.47 - 1)	Observed significantly < expected
50-59 (Including unknown TTO)	23	105.32	42	1.57	58336094	0.22 (0.14 - 0.33)	Observed significantly < expected
60-69 (Including unknown TTO)	14	45.32	42	0.68	57960860	0.31 (0.17 - 0.52)	Observed significantly < expected
Over 70 (Including unknown TTO)	18	12.66	42	0.34	32376365	1.42 (0.84 - 2.25)	Observed > expected

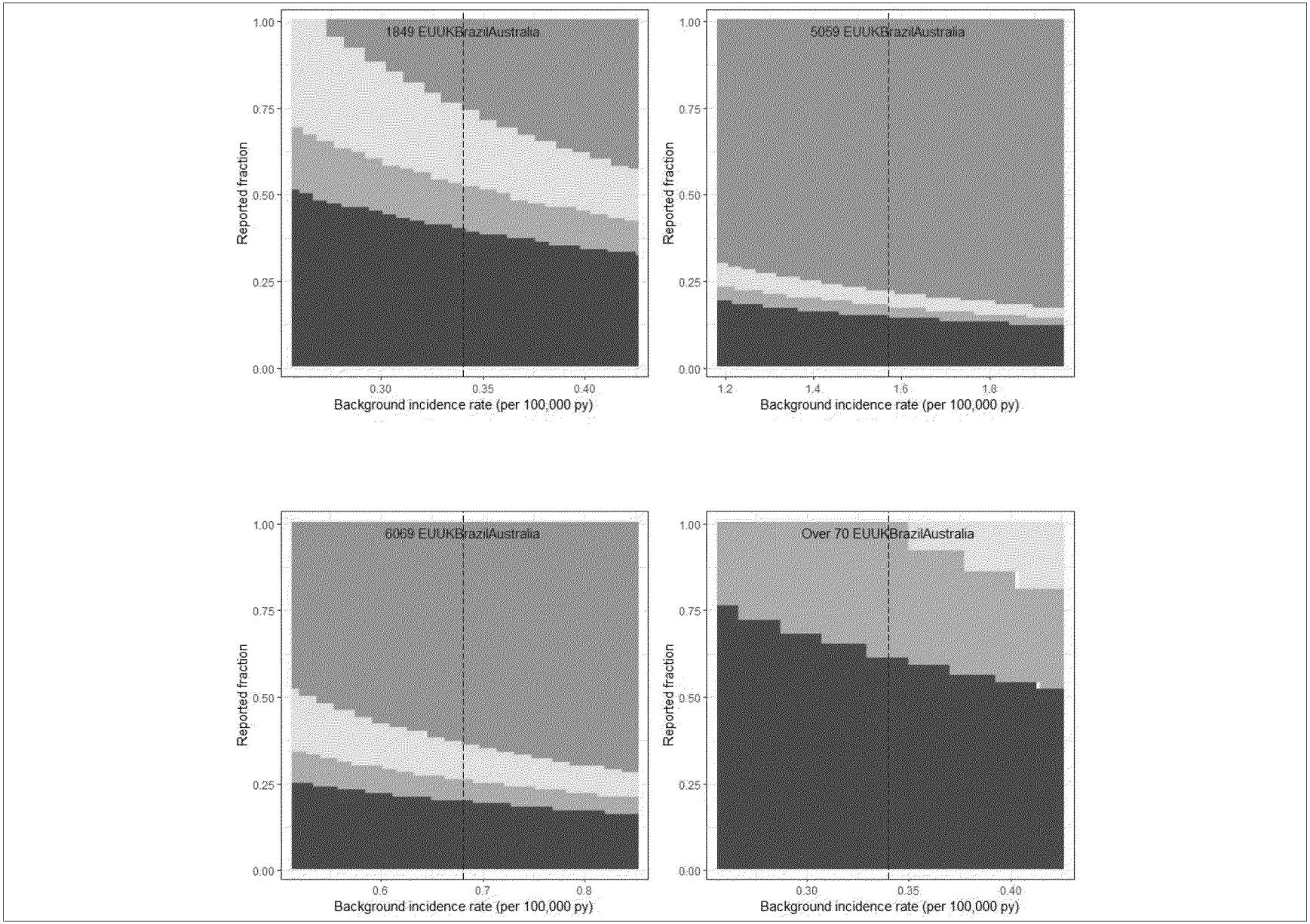

1849 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.30
0.35
0.40
Background incidence rate (per 100,000 py)

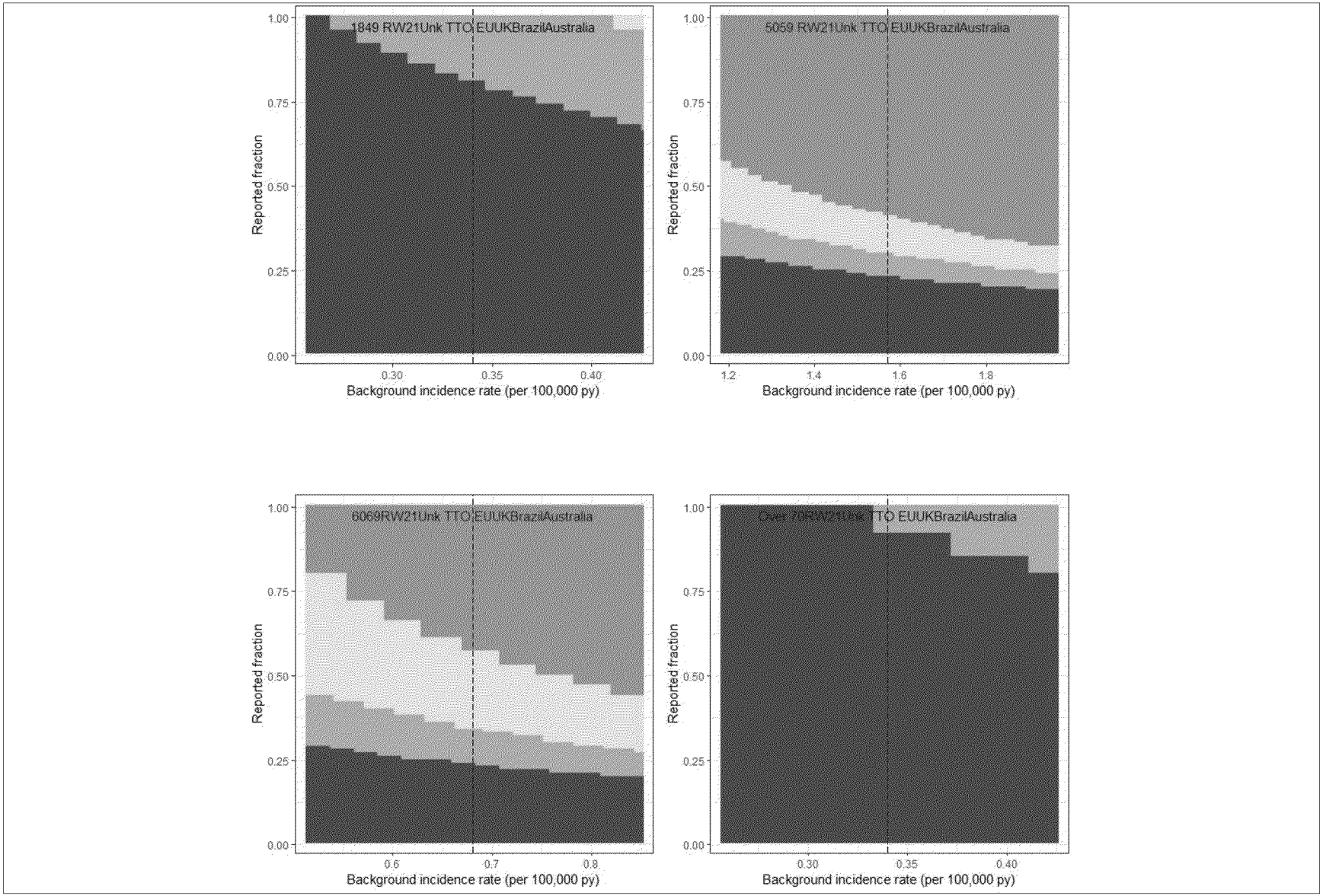
5059 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
1.8
Background incidence rate (per 100,000 py)


6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)


Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.30
0.35
0.40
Background incidence rate (per 100,000 py)


1849 EUUKBrazilAustralia
5059 EUUKBrazilAustralia
6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8
Background incidence rate (per 100,000 py)


1849 EUUKBrazilAustralia
5059 EUUKBrazilAustralia
6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8
Background incidence rate (per 100,000 py)


1849 RW21Unk TTO EUUKBrazilAustralia
5059 RW21Unk TTO EUUKBrazilAustralia
6069RW21Unk TTO EUUKBrazilAustralia
Over 70RW21Unk TTO EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8

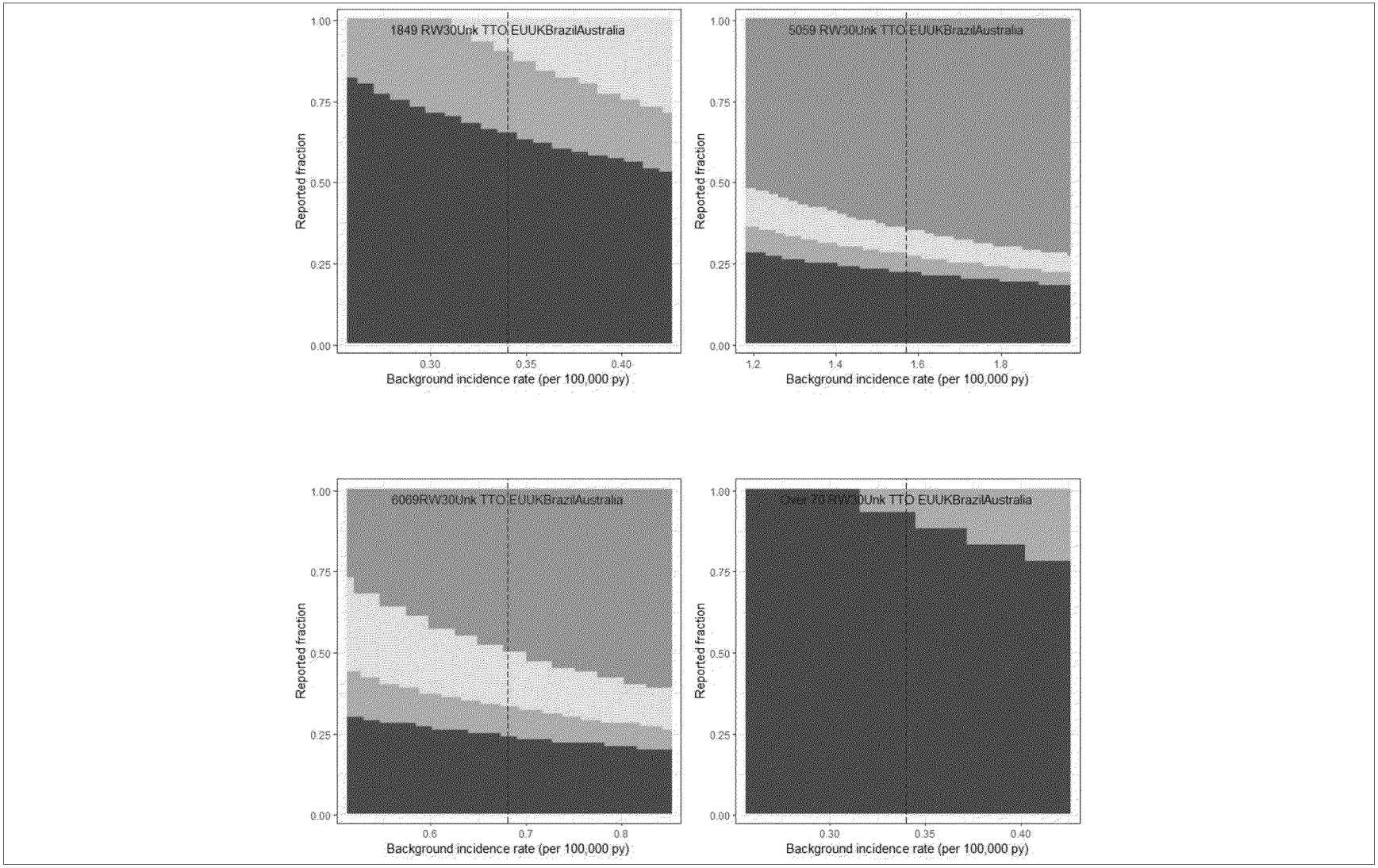
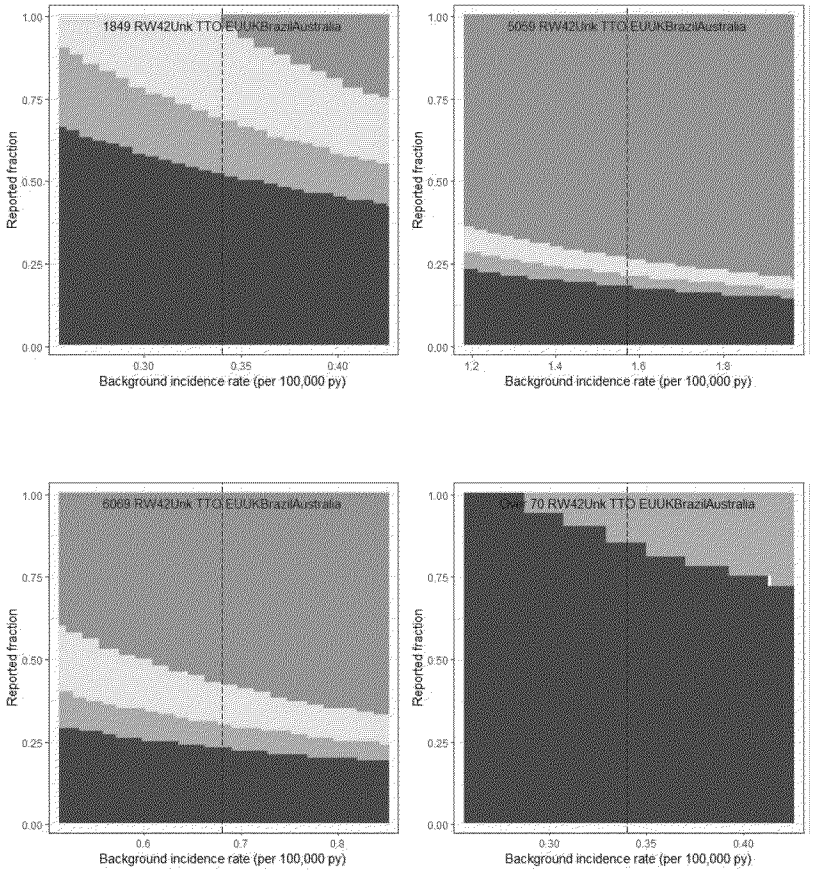

1849 RW30Unk TTO EUUKBrazilAustralia
5059 RW30Unk TTO EUUKBrazilAustralia
6069RW30Unk TTO EUUKBrazilAustralia
Over 70 RW30Unk TTO EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8

Table 73 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by age from EU+UK+Brazil+Australia including unknown TTO_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: SIDIAP PCHOSP rate (Willame et al 2021 [A])

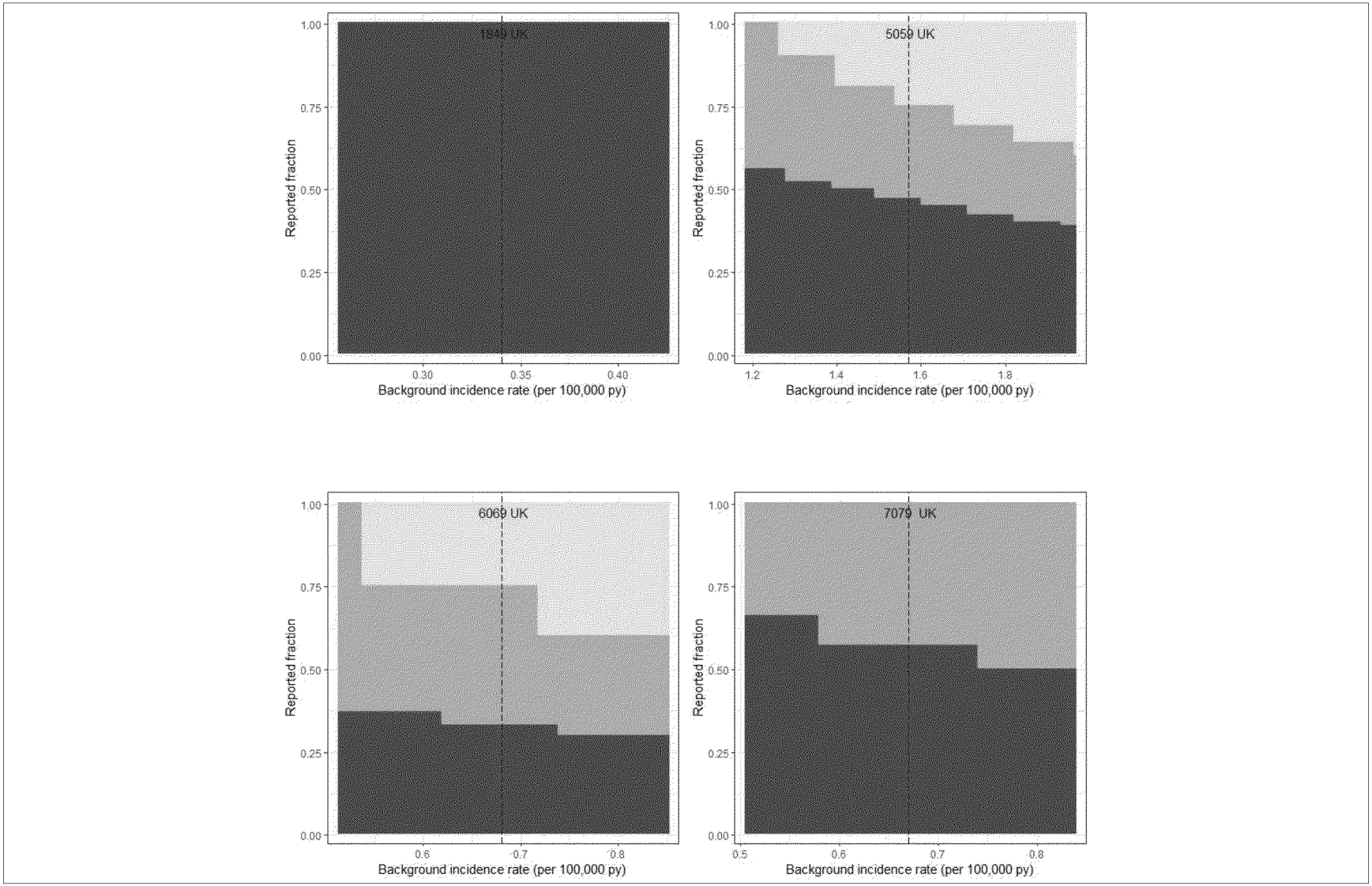
CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; EU European Union; IR Incidence Rate; O Observed, TTO Time to onset.

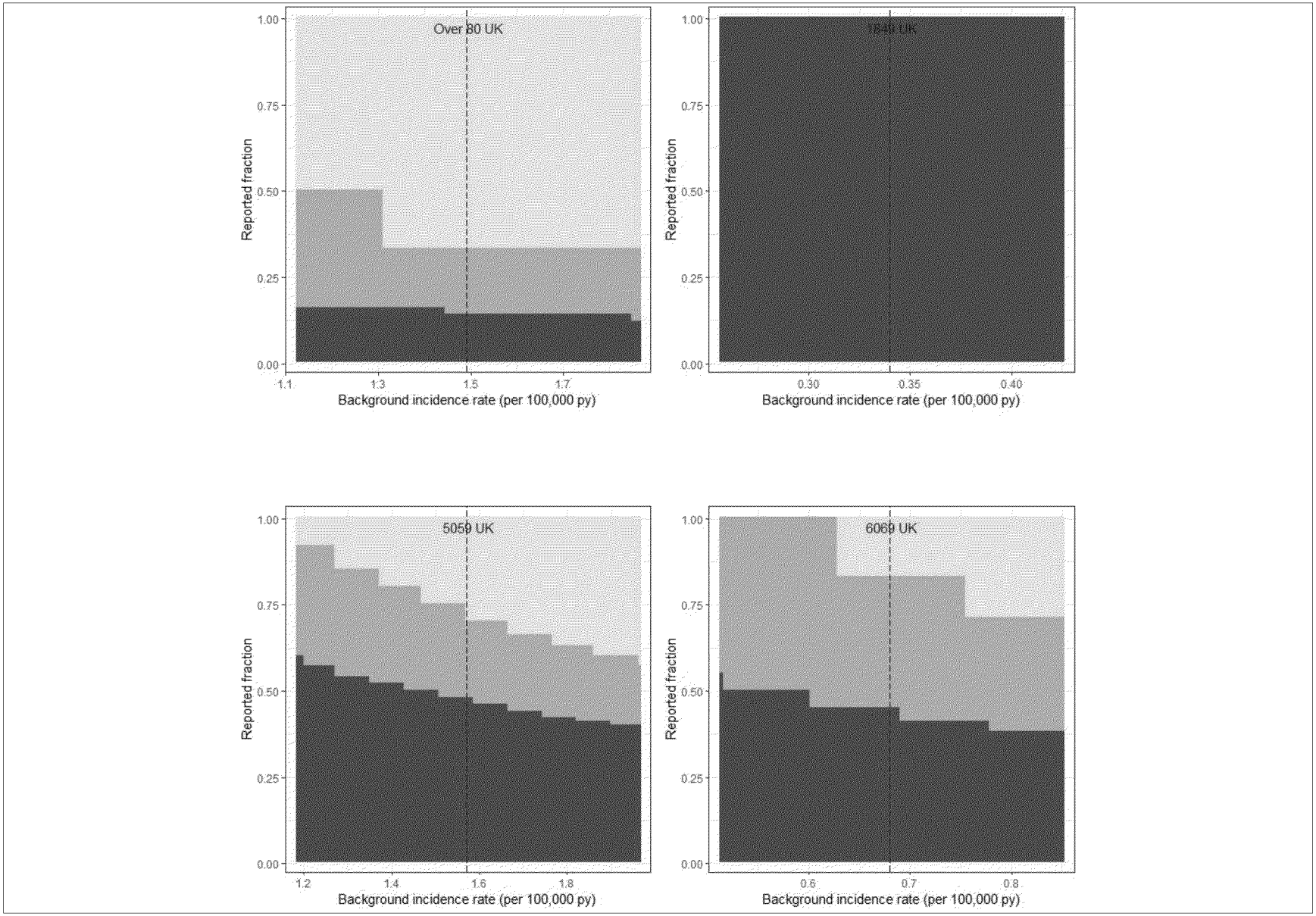
Table 74 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by age from UK including unknown TTO_SIDIAP

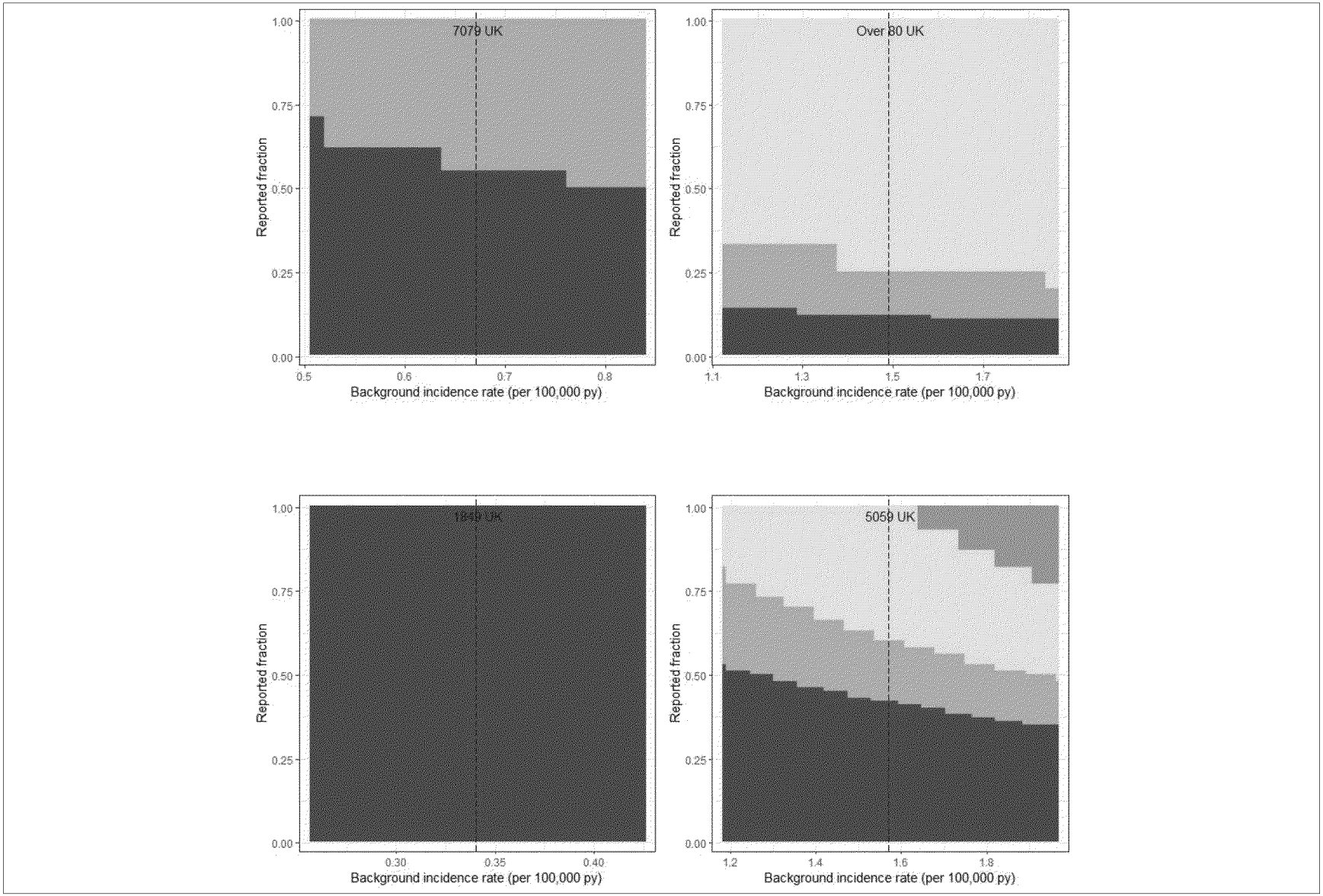
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18-49	12	2.77	21	0.34	14181834	4.33 (2.24 - 7.57)	Observed significantly > expected
50-59	9	11.24	21	1.57	12455887	0.8 (0.37 - 1.52)	Observed < expected
60-69	3	3.8	21	0.68	9718273	0.79 (0.16 - 2.31)	Observed < expected
70-79	4	2.55	21	0.67	6613249	1.57 (0.43 - 4.02)	Observed > expected
Over 80	1	2.27	21	1.49	2655389	0.44 (0.01 - 2.45)	Observed < expected
18-49	13	3.96	30	0.34	14181834	3.28 (1.75 - 5.61)	Observed significantly > expected
50-59	12	16.06	30	1.57	12455887	0.75 (0.39 - 1.31)	Observed < expected
60-69	5	5.43	30	0.68	9718273	0.92 (0.3 - 2.15)	Observed < expected
70-79	5	3.64	30	0.67	6613249	1.37 (0.45 - 3.21)	Observed > expected
Over 80	1	3.25	30	1.49	2655389	0.31 (0.01 - 1.71)	Observed < expected
18-49	15	5.54	42	0.34	14181834	2.71 (1.52 - 4.47)	Observed significantly > expected
50-59	14	22.49	42	1.57	12455887	0.62 (0.34 - 1.04)	Observed < expected
60-69	7	7.6	42	0.68	9718273	0.92 (0.37 - 1.9)	Observed < expected
70-79	5	5.1	42	0.67	6613249	0.98 (0.32 - 2.29)	Observed < expected
Over 80	3	4.55	42	1.49	2655389	0.66 (0.14 - 1.93)	Observed < expected
18-49 (including unknown TTO)	15	2.77	21	0.34	14181834	5.42 (3.03 - 8.93)	Observed significantly > expected
50-59 (including unknown TTO)	13	11.24	21	1.57	12455887	1.16 (0.62 - 1.98)	Observed > expected
60-69 (including unknown TTO)	5	3.8	21	0.68	9718273	1.32 (0.43 - 3.07)	Observed > expected

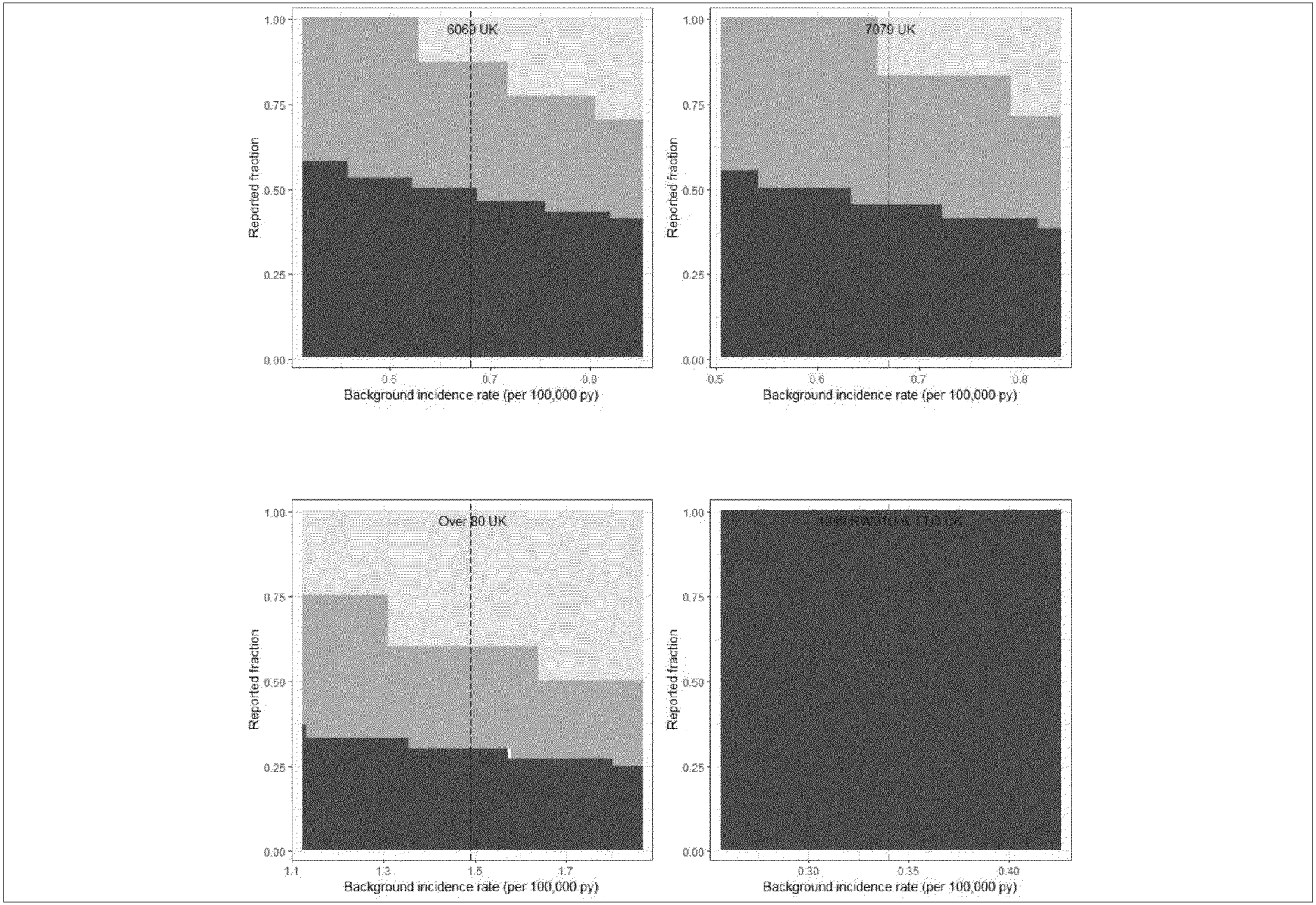
Table 74 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by age from UK including unknown TTO_SIDIAP

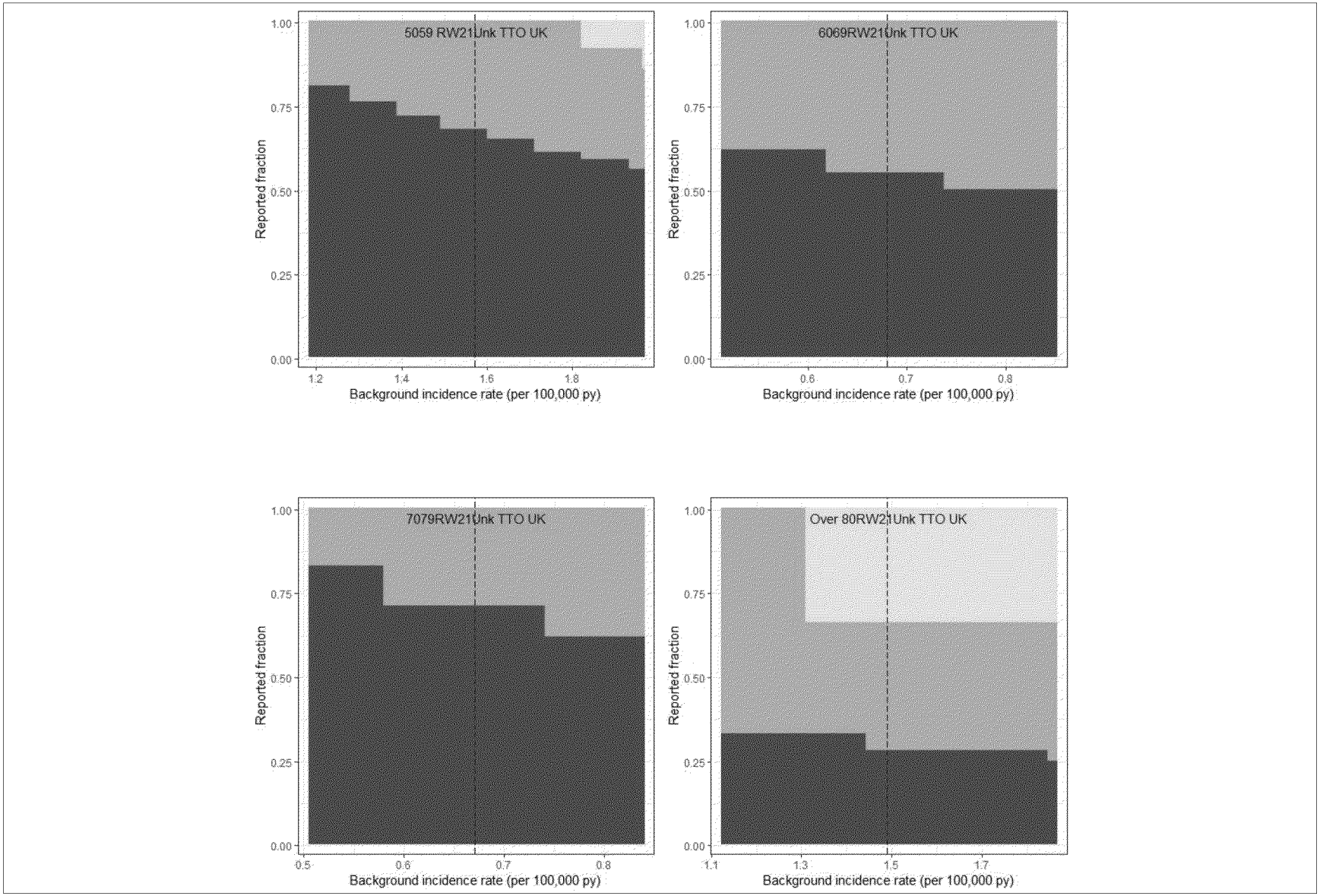
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
70-79 (including unknown TTO)	5	2.55	21	0.67	6613249	1.96 (0.64 - 4.58)	Observed > expected
Over 80	2	2.27	21	1.49	2655389	0.88 (0.11 - 3.18)	Observed < expected
18-49 (including unknown TTO)	16	3.96	30	0.34	14181834	4.04 (2.31 - 6.56)	Observed significantly > expected
50-59 (including unknown TTO)	16	16.06	30	1.57	12455887	1 (0.57 - 1.62)	Observed < expected
60-69 (including unknown TTO)	7	5.43	30	0.68	9718273	1.29 (0.52 - 2.66)	Observed > expected
70-79 (including unknown TTO)	6	3.64	30	0.67	6613249	1.65 (0.6 - 3.59)	Observed > expected
Over 80	2	3.25	30	1.49	2655389	0.62 (0.07 - 2.22)	Observed < expected
18-49 (including unknown TTO)	18	5.54	42	0.34	14181834	3.25 (1.93 - 5.13)	Observed significantly > expected
50-59 (including unknown TTO)	18	22.49	42	1.57	12455887	0.8 (0.47 - 1.26)	Observed < expected
60-69 (including unknown TTO)	9	7.6	42	0.68	9718273	1.18 (0.54 - 2.25)	Observed > expected
70-79 (including unknown TTO)	6	5.1	42	0.67	6613249	1.18 (0.43 - 2.56)	Observed > expected
Over 80	4	4.55	42	1.49	2655389	0.88 (0.24 - 2.25)	Observed < expected

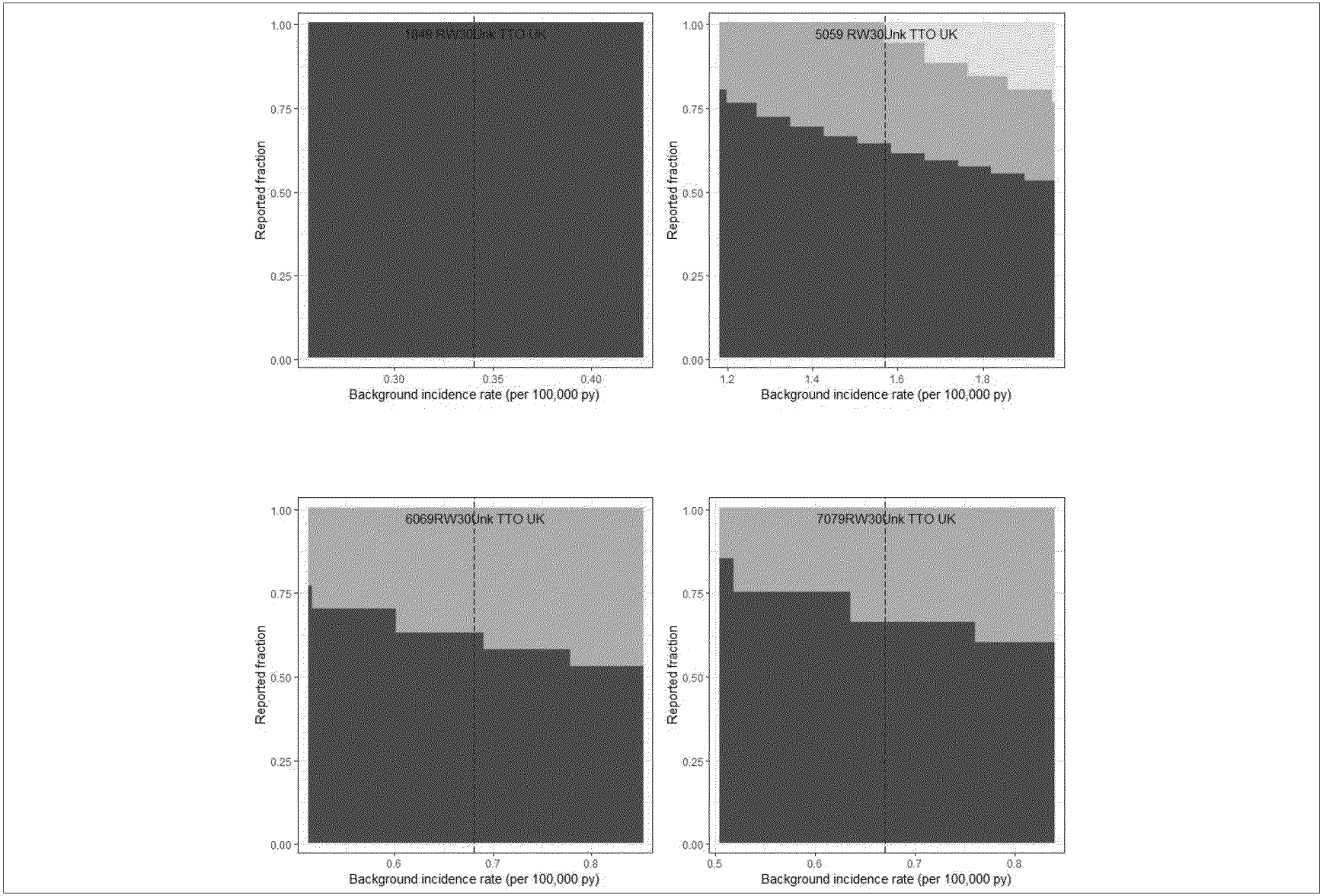

1849 UK
5059 UK
6069 UK
7079 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8
0.5


Over 80 UK
1640 UK
5059 UK
6069 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.1
1.3
1.5
1.7
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8


7079 UK
Over 80 UK
1549 UK
5059 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
0.8
1.1
1.3
1.5
1.7
0.30
0.35
0.40
1.2
1.4
1.6
1.8


6069 UK
7079 UK
Over 80 UK
1849 RW21Risk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
0.8
1.1
1.3
1.5
1.7
0.30
0.35
0.40


5059 RW21Unk TTO UK
6069RW21Unk TTO UK
7079RW21Unk TTO UK
Over 80RW21Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
1.2
1.4
1.6
1.8
0.6
0.7
0.8
0.5
1.1
1.3
1.5
1.7


1849 RW30Unk TTO UK
5059 RW30Unk TTO UK
6069RW30Unk TTO UK
7079RW30Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8
0.5

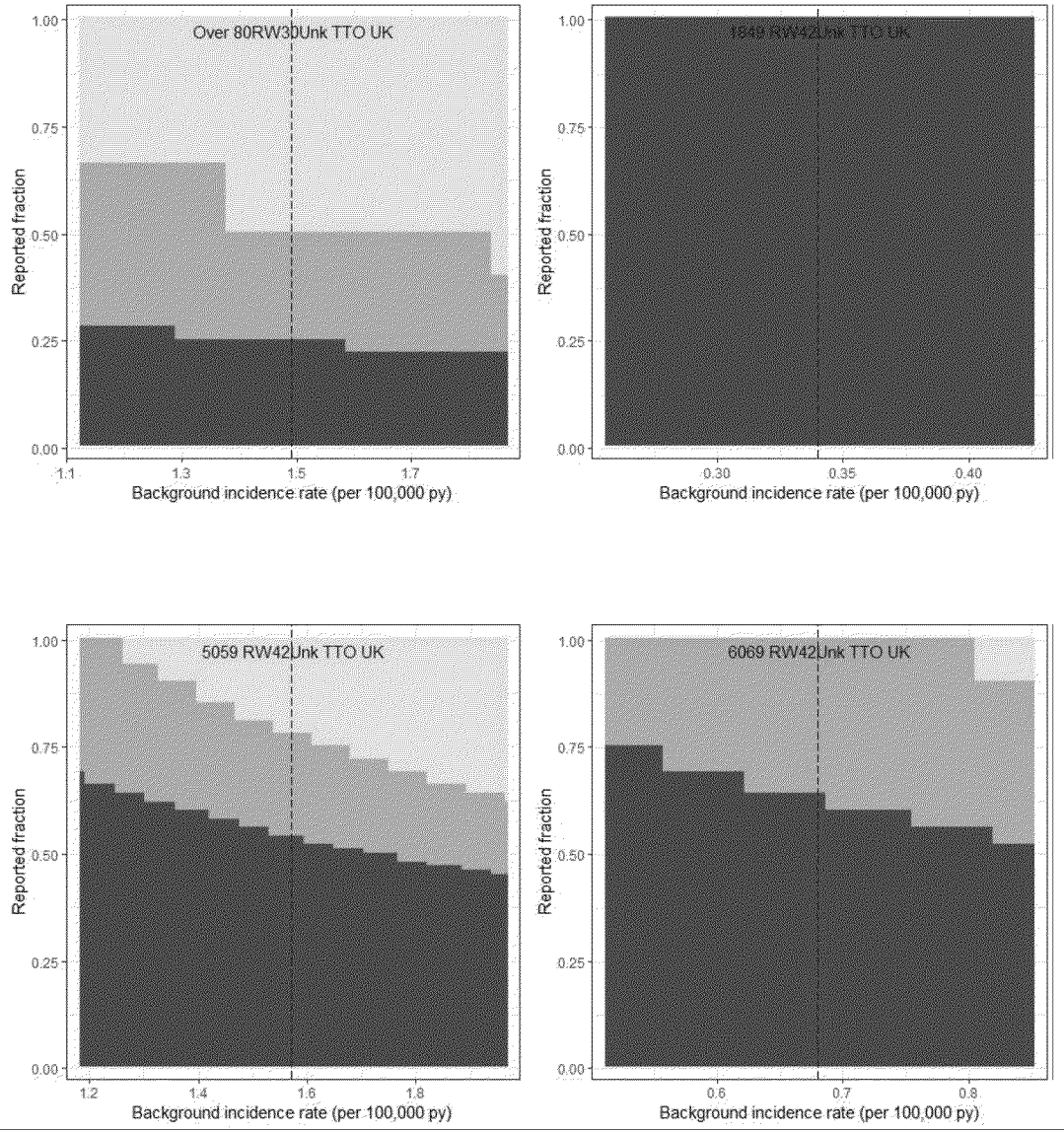
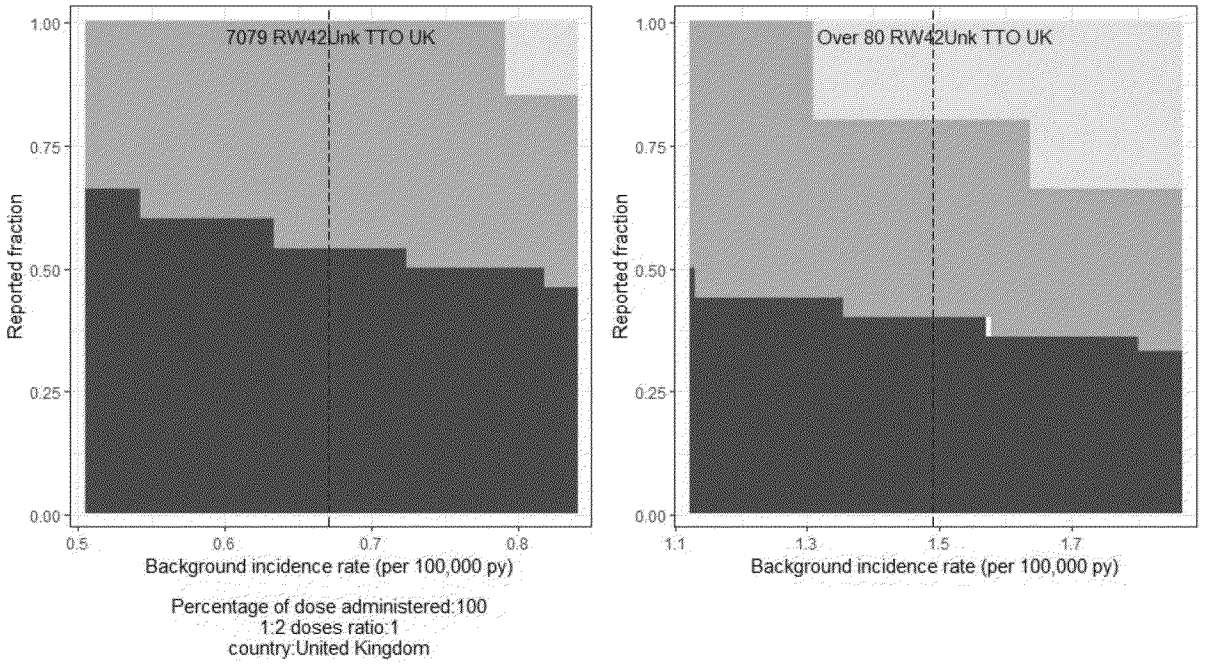

Over 80RW30Unk TTO UK
1849 RW42Unk TTO UK
5059 RW42Unk TTO UK
6069 RW42Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.1
1.3
1.5
1.7
0.30
0.35
0.40
1.2
1.4
1.6
1.8
0.6
0.7
0.8

Table 74 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by age from UK including unknown TTO_SIDIAP

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] ACCESS Background rates of adverse events of special interest (AESIs) for COVID-19 vaccines: SIDIAP PCHOSP rate (Willame et al 2021 [A])

CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, UK United Kingdom

Table 75 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases Overall_TRUVEN 14

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Overall	289	402	21	1.5	466115644	0.72 (0.64 - 0.81)	Observed significantly < expected
Overall (RW21+Unk TTO)	454	402	21	1.5	466115644	1.13 (1.03 - 1.24)	Observed significantly > expected
Overall	331	574.28	30	1.5	466115644	0.58 (0.52 - 0.64)	Observed significantly < expected
Overall (RW30+Unk TTO)	496	574.28	30	1.5	466115644	0.86 (0.79 - 0.94)	Observed significantly < expected
Overall	378	803.99	42	1.5	466115644	0.47 (0.42 - 0.52)	Observed significantly < expected
Overall (RW42+Unk TTO)	543	803.99	42	1.5	466115644	0.68 (0.62 - 0.73)	Observed significantly < expected

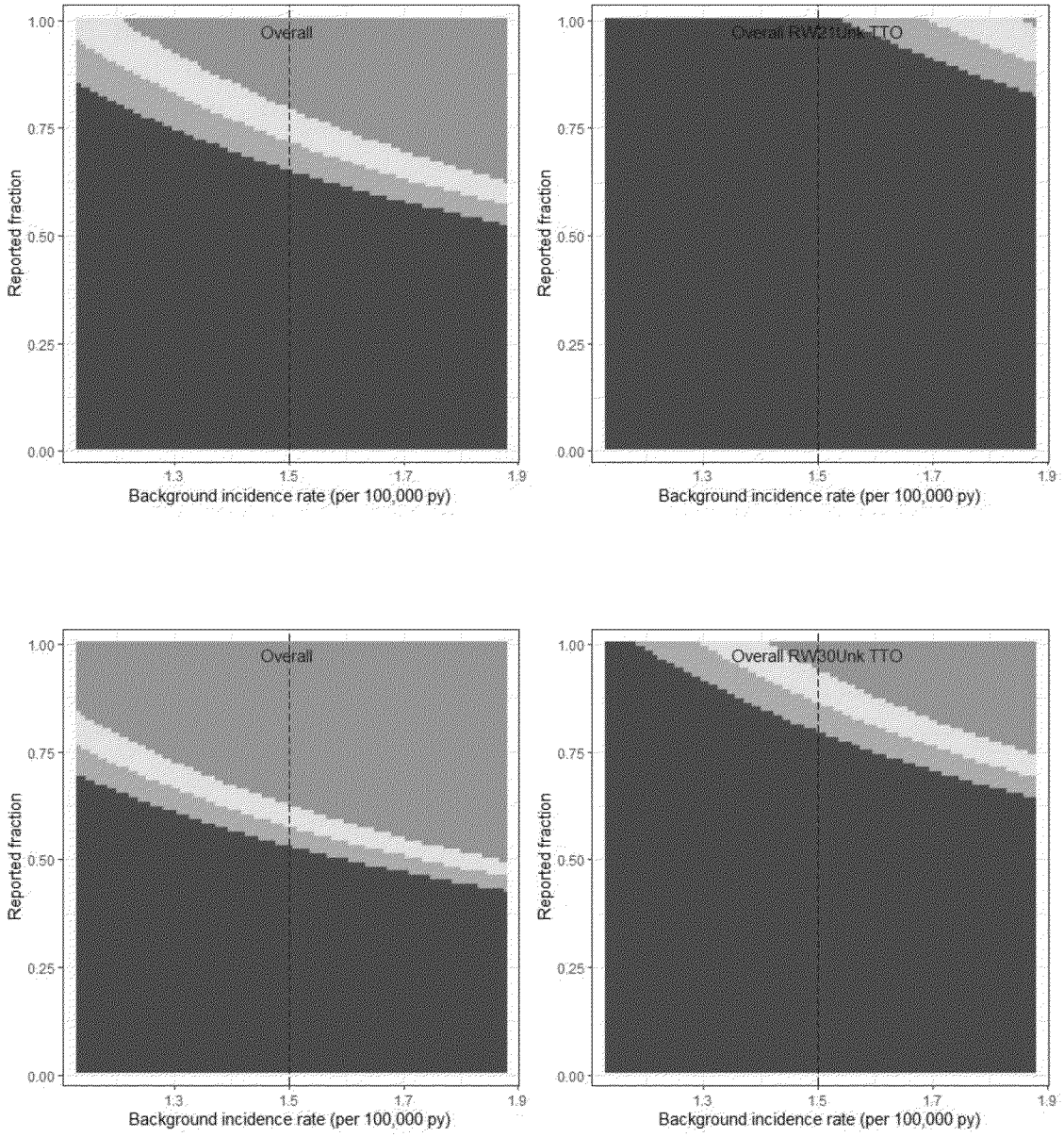
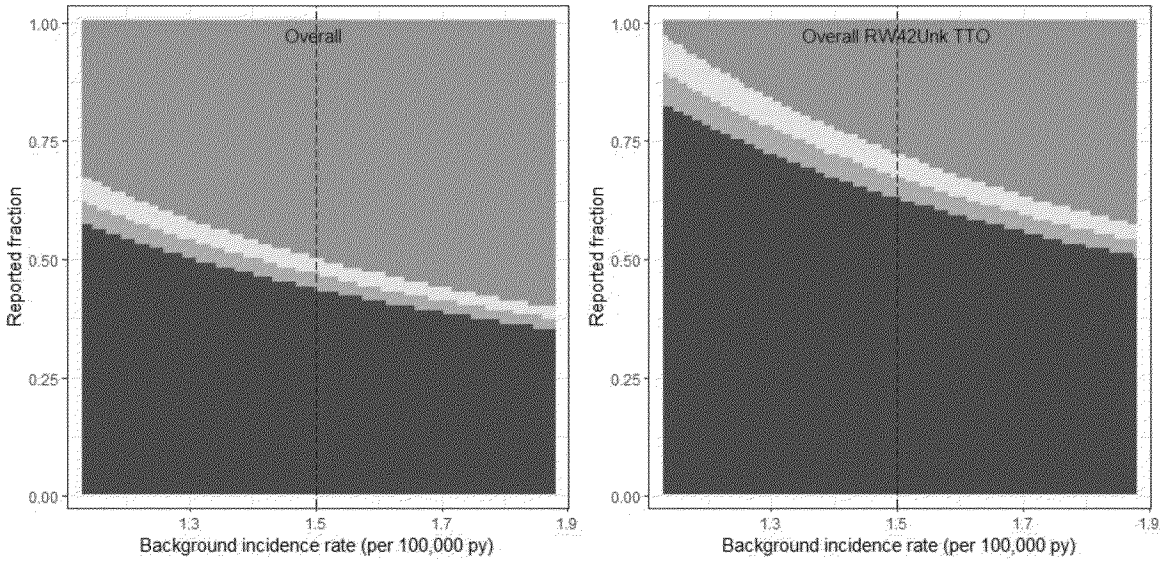

Overall
Overall RW21Unk TTO
Overall
Overall RW30Unk TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.3
1.5
1.7
1.9
Background incidence rate (per 100,000 py)

Table 75 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases Overall_TRUVEN 14

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	



[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

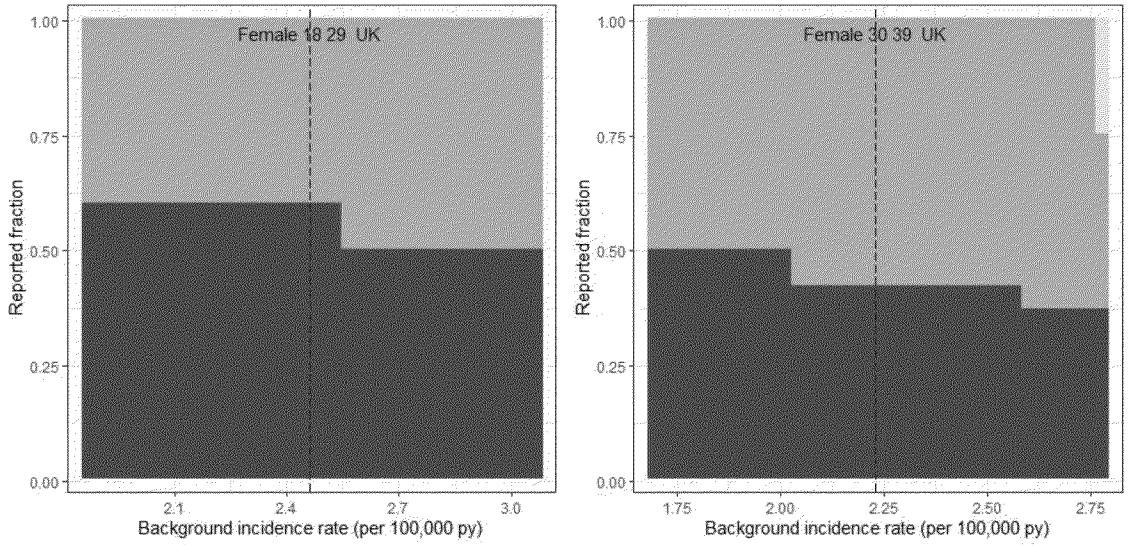
CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, Unk Unknown.

Table 76 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by gender and age from UK_TRUVEN 14

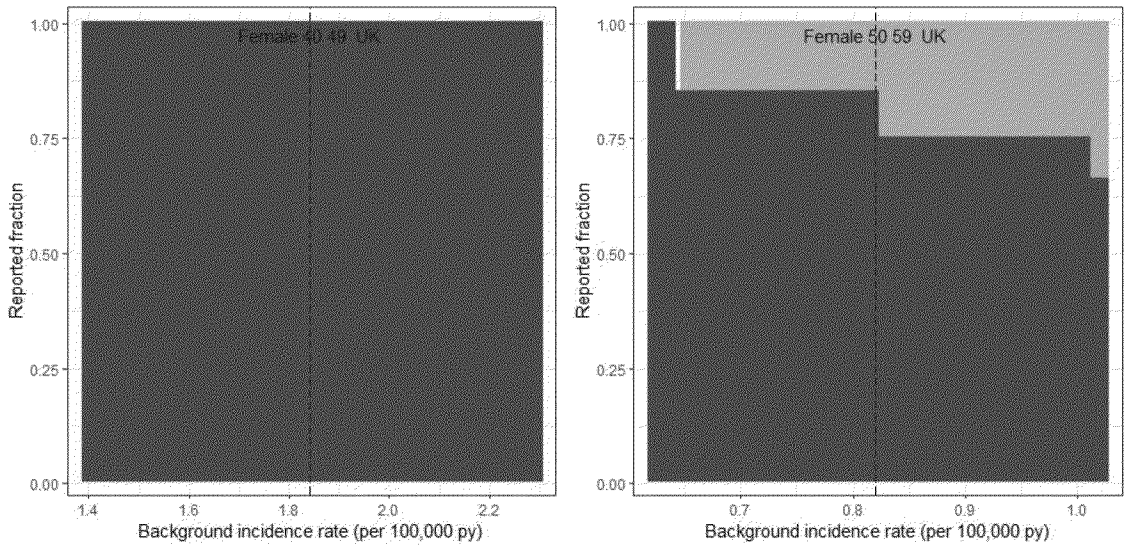
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Female 18-29	3	1.57	21	2.46	1109488	1.91 (0.39 - 5.58)	Observed > expected
Female 30-39	3	2.43	21	2.23	1892968	1.23 (0.25 - 3.61)	Observed > expected
Female 40-49	12	4.67	21	1.84	4412245	2.57 (1.33 - 4.49)	Observed significantly > expected
Female 50-59	6	2.8	21	0.82	5944683	2.14 (0.79 - 4.66)	Observed > expected
Female 60-69	3	3.88	21	1.41	4783416	0.77 (0.16 - 2.26)	Observed < expected
Female 70-79	3	1.42	21	0.71	3475875	2.11 (0.44 - 6.17)	Observed > expected
Female over 80	1	8.74	21	9.32	1630324	0.11 (0 - 0.64)	Observed significantly < expected
Male 18-29	2	0.51	21	1.1	808938	3.92 (0.47 - 14.17)	Observed > expected
Male 30-39	2	0.56	21	0.69	1415003	3.57 (0.43 - 12.9)	Observed > expected
Male 40-49	5	2.25	21	0.86	4542157	2.22 (0.72 - 5.19)	Observed > expected
Male 50-59	6	3.41	21	0.91	6510960	1.76 (0.65 - 3.83)	Observed > expected
Male 60-69	4	5.45	21	1.92	4934728	0.73 (0.2 - 1.88)	Observed < expected
Male 70-79	3	4.49	21	2.49	3137304	0.67 (0.14 - 1.95)	Observed < expected
Male over 80	1	3.91	21	6.64	1025046	0.26 (0.01 - 1.42)	Observed < expected
Female 18-29	4	2.24	30	2.46	1109488	1.79 (0.49 - 4.57)	Observed > expected
Female 30-39	3	3.47	30	2.23	1892968	0.86 (0.18 - 2.53)	Observed < expected
Female 40-49	12	6.67	30	1.84	4412245	1.8 (0.93 - 3.14)	Observed > expected
Female 50-59	8	4	30	0.82	5944683	2 (0.86 - 3.94)	Observed > expected
Female 60-69	5	5.54	30	1.41	4783416	0.9 (0.29 - 2.11)	Observed < expected
Female 70-79	4	2.03	30	0.71	3475875	1.97 (0.54 - 5.05)	Observed > expected
Female over 80	1	12.48	30	9.32	1630324	0.08 (0 - 0.45)	Observed significantly < expected

Table 76 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by gender and age from UK_TRUVEN 14

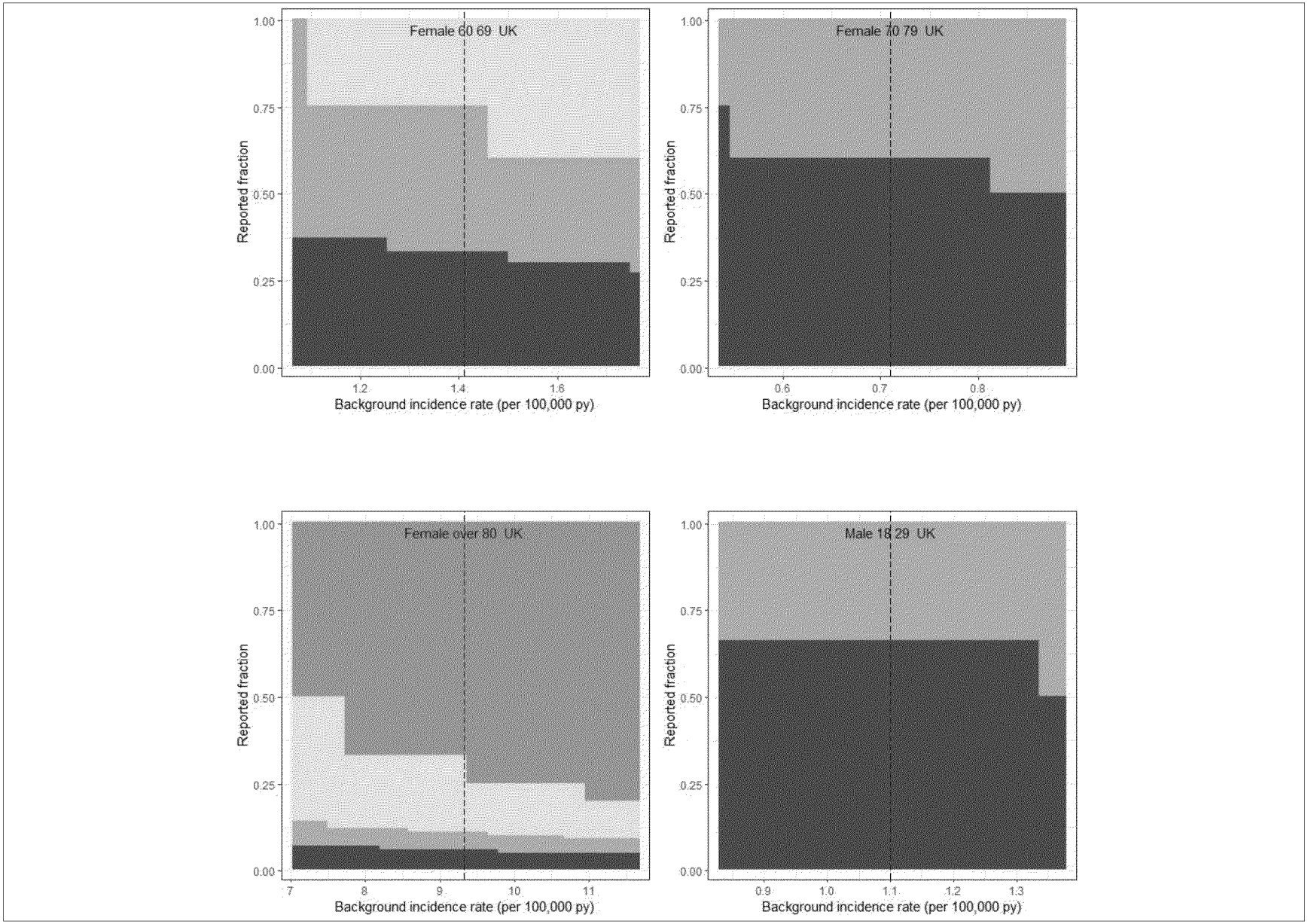
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 18-29	2	0.73	30	1.1	808938	2.74 (0.33 - 9.9)	Observed > expected
Male 30-39	2	0.8	30	0.69	1415003	2.5 (0.3 - 9.03)	Observed > expected
Male 40-49	6	3.21	30	0.86	4542157	1.87 (0.69 - 4.07)	Observed > expected
Male 50-59	8	4.87	30	0.91	6510960	1.64 (0.71 - 3.24)	Observed > expected
Male 60-69	4	7.78	30	1.92	4934728	0.51 (0.14 - 1.32)	Observed < expected
Male 70-79	3	6.42	30	2.49	3137304	0.47 (0.1 - 1.37)	Observed < expected
Male over 80	1	5.59	30	6.64	1025046	0.18 (0 - 1)	Observed significantly < expected
Female 18-29	4	3.14	42	2.46	1109488	1.27 (0.35 - 3.26)	Observed > expected
Female 30-39	5	4.85	42	2.23	1892968	1.03 (0.33 - 2.41)	Observed > expected
Female 40-49	13	9.34	42	1.84	4412245	1.39 (0.74 - 2.38)	Observed > expected
Female 50-59	9	5.61	42	0.82	5944683	1.6 (0.73 - 3.05)	Observed > expected
Female 60-69	6	7.76	42	1.41	4783416	0.77 (0.28 - 1.68)	Observed < expected
Female 70-79	4	2.84	42	0.71	3475875	1.41 (0.38 - 3.61)	Observed > expected
Female over 80	3	17.47	42	9.32	1630324	0.17 (0.04 - 0.5)	Observed significantly < expected
Male 18-29	4	1.02	42	1.1	808938	3.92 (1.07 - 10.04)	Observed significantly > expected
Male 30-39	2	1.12	42	0.69	1415003	1.79 (0.22 - 6.45)	Observed > expected
Male 40-49	7	4.49	42	0.86	4542157	1.56 (0.63 - 3.21)	Observed > expected
Male 50-59	12	6.81	42	0.91	6510960	1.76 (0.91 - 3.08)	Observed > expected
Male 60-69	6	10.9	42	1.92	4934728	0.55 (0.2 - 1.2)	Observed < expected
Male 70-79	3	8.98	42	2.49	3137304	0.33 (0.07 - 0.98)	Observed significantly < expected
Male over 80	1	7.83	42	6.64	1025046	0.13 (0 - 0.71)	Observed significantly < expected

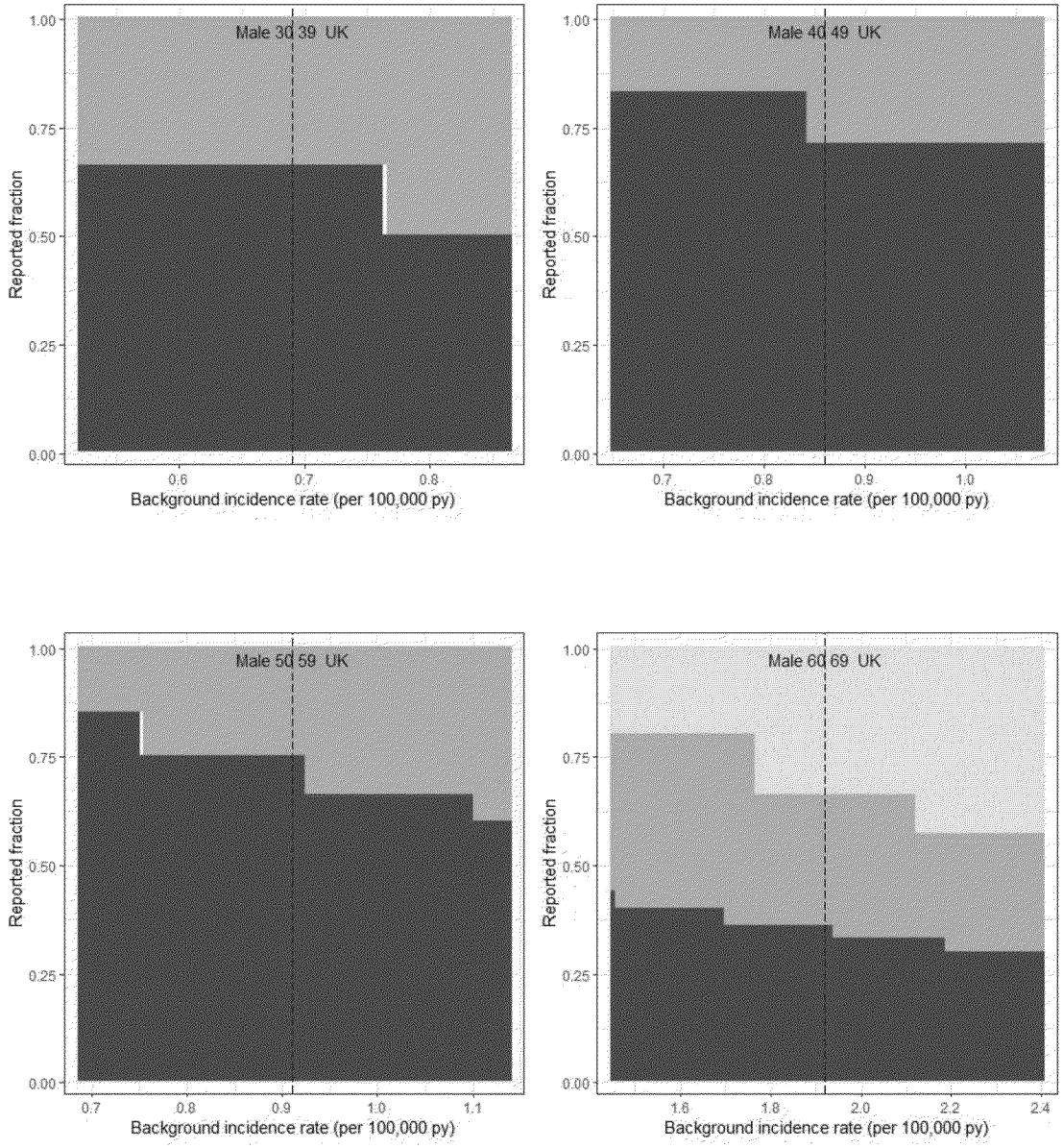

Female 18 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.1
2.4
2.7
3.0
Background incidence rate (per 100,000 py)

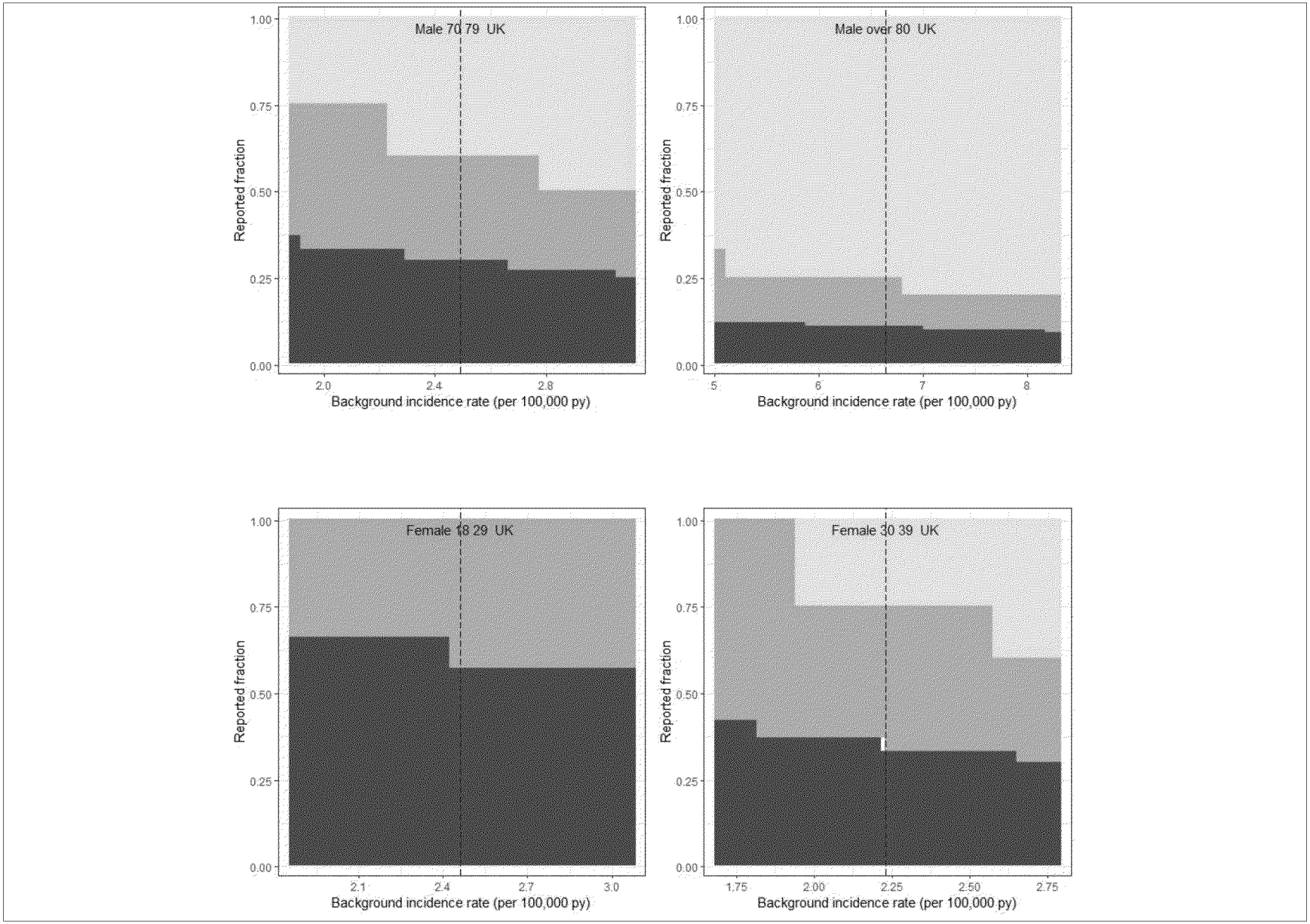
Female 30 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)

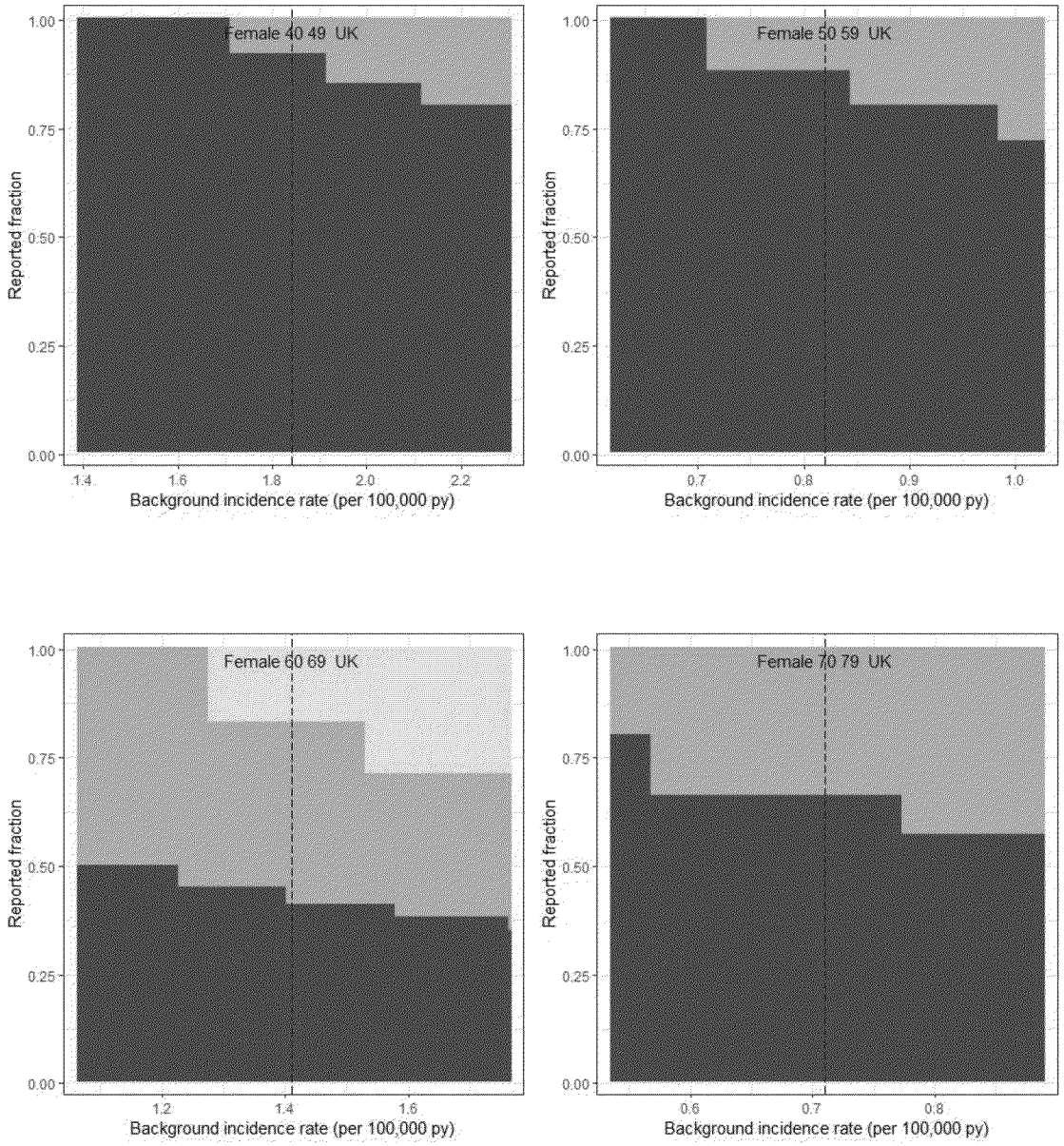

Female 40 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.2
Background incidence rate (per 100,000 py)

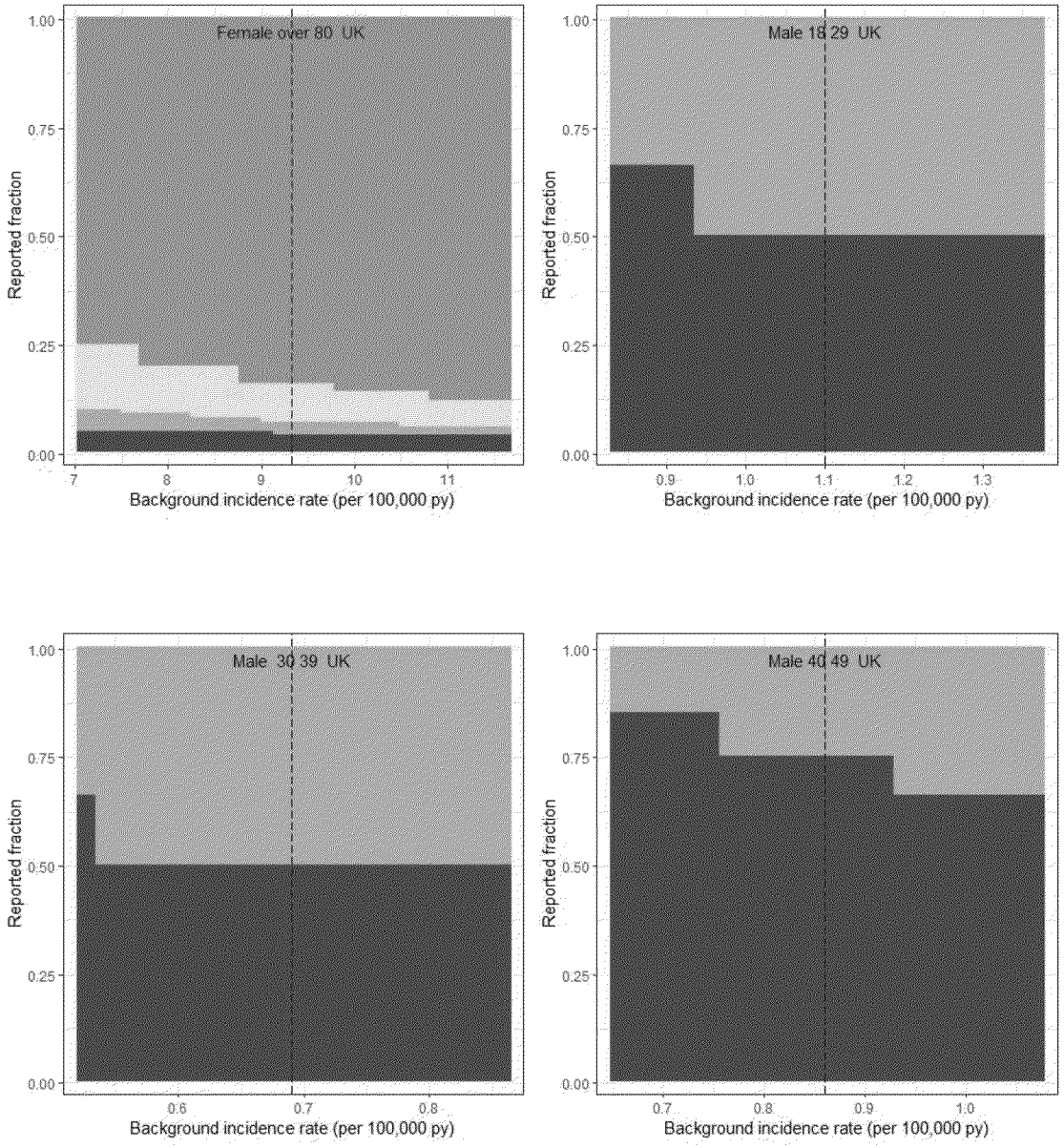
Female 50 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)

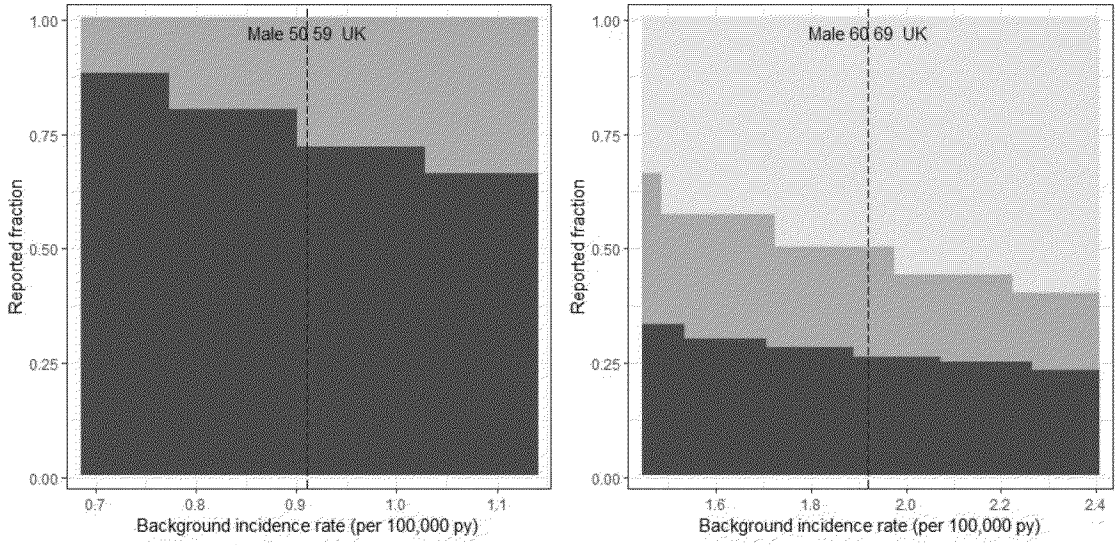

Female 60 69 UK
Female 70 79 UK
Female over 80 UK
Male 18 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
Background incidence rate (per 100,000 py)
1.2
1.4
1.6
0.6
0.7
0.8
7
8
9
10
11
0.9
1.0
1.1
1.2
1.3


Male 30 39 UK
Male 40 49 UK
Male 50 59 UK
Male 60 69 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
0.9
1.0
1.1
1.6
1.8
2.0
2.2
2.4

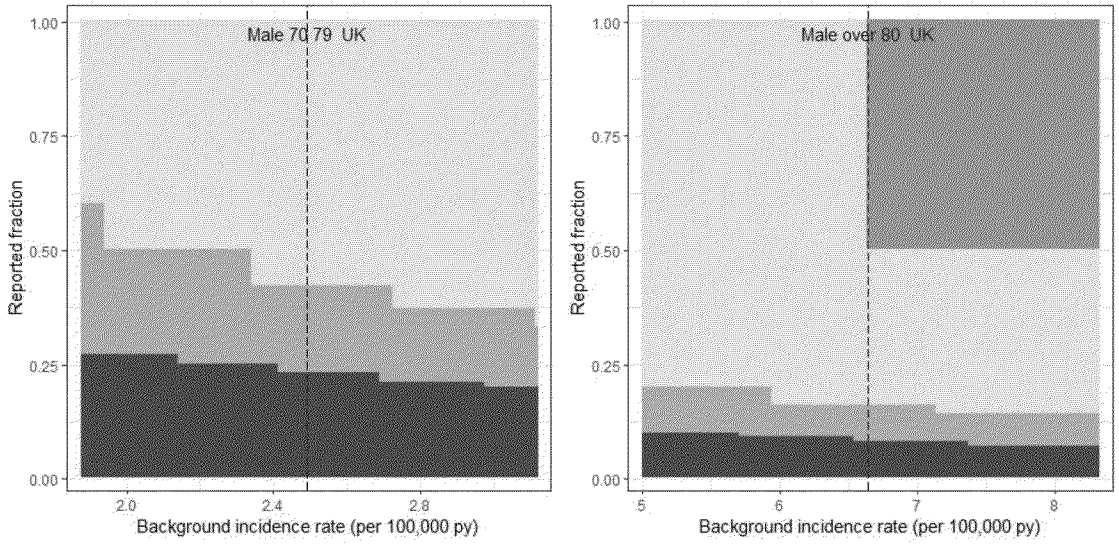

Male 70 79 UK
Male over 80 UK
Female 18 29 UK
Female 30 39 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
2.0
2.4
2.8
5
6
7
8
2.1
2.7
3.0
1.75
2.00
2.25
2.50
2.75


Female 40 49 UK
Female 50 59 UK
Female 60 69 UK
Female 70 79 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.2
0.7
0.8
0.9
1.0
1.2
1.4
1.6
0.6
0.7
0.8

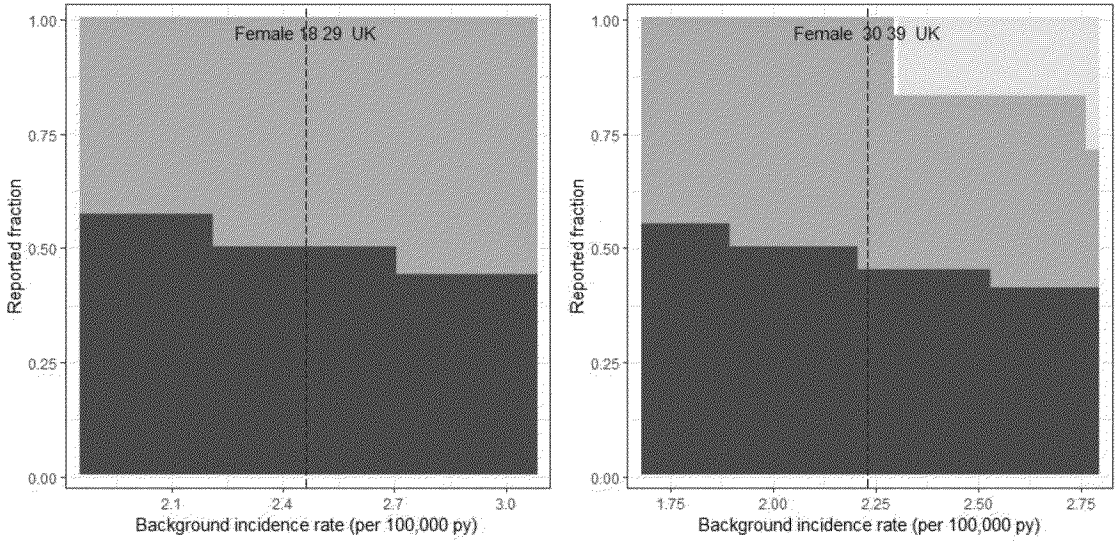

Female over 80 UK
Male 18 29 UK
Male 30 39 UK
Male 40 49 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
7
8
9
10
11
0.9
1.0
1.1
1.2
1.3
0.6
0.7
0.8


Male 50 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)

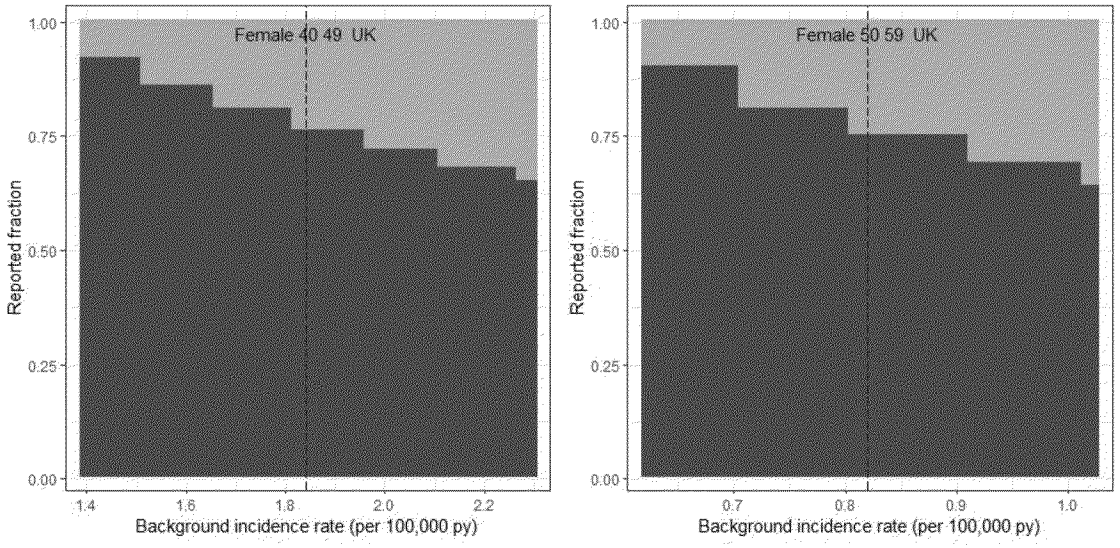
Male 60 69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.6
1.8
2.0
2.2
2.4
Background incidence rate (per 100,000 py)


Male 70 79 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.4
2.8
Background incidence rate (per 100,000 py)

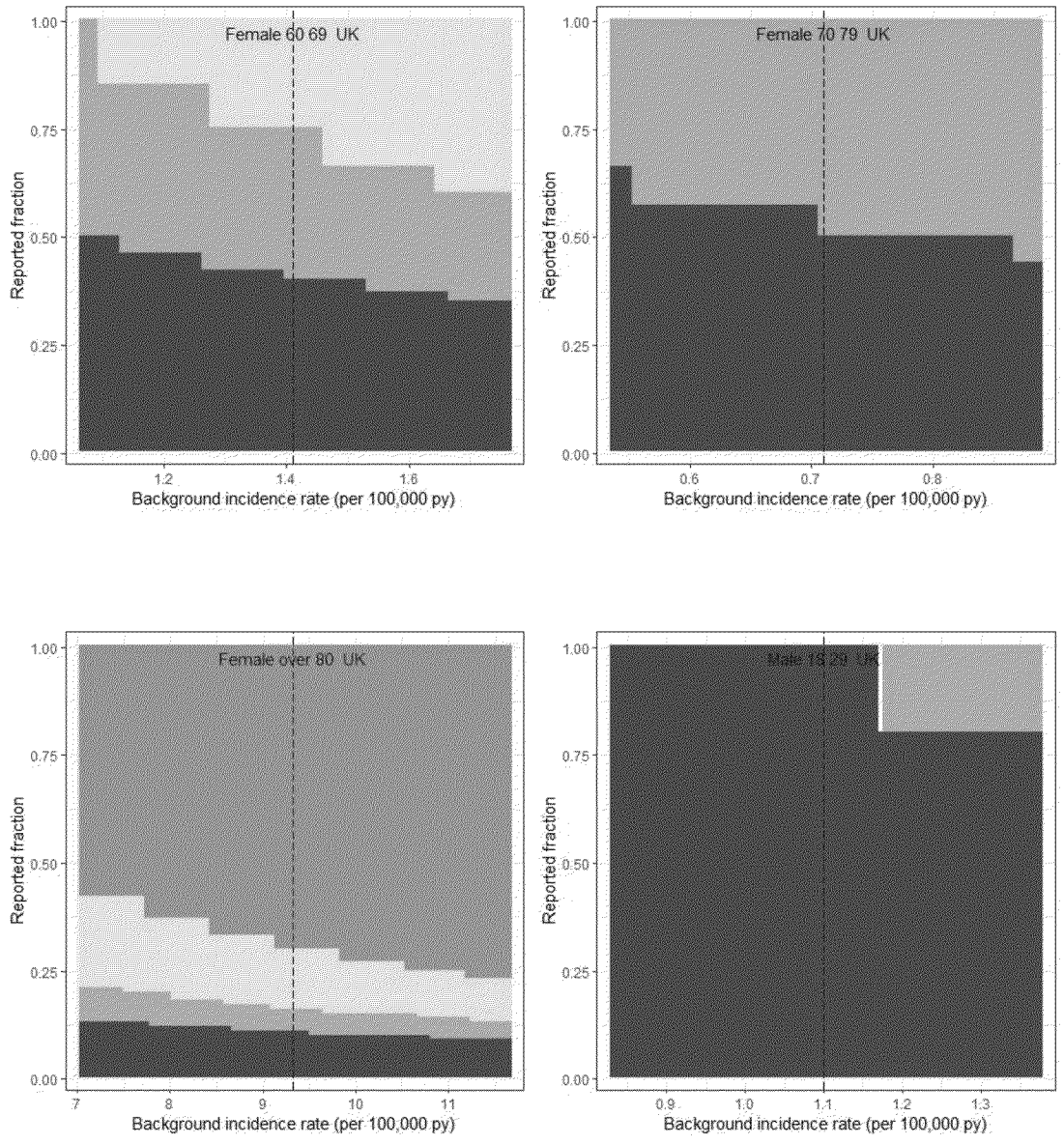
Male over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
8
Background incidence rate (per 100,000 py)


Female 18 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.1
2.4
2.7
3.0
Background incidence rate (per 100,000 py)

Female 30 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)


Female 40 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.2
Background incidence rate (per 100,000 py)

Female 50 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)


Female 60 69 UK
Female 70 79 UK
Female over 80 UK
Male 18 29 UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
0.6
0.7
0.8
7
8
9
10
11
0.9
1.0
1.1
1.2
1.3

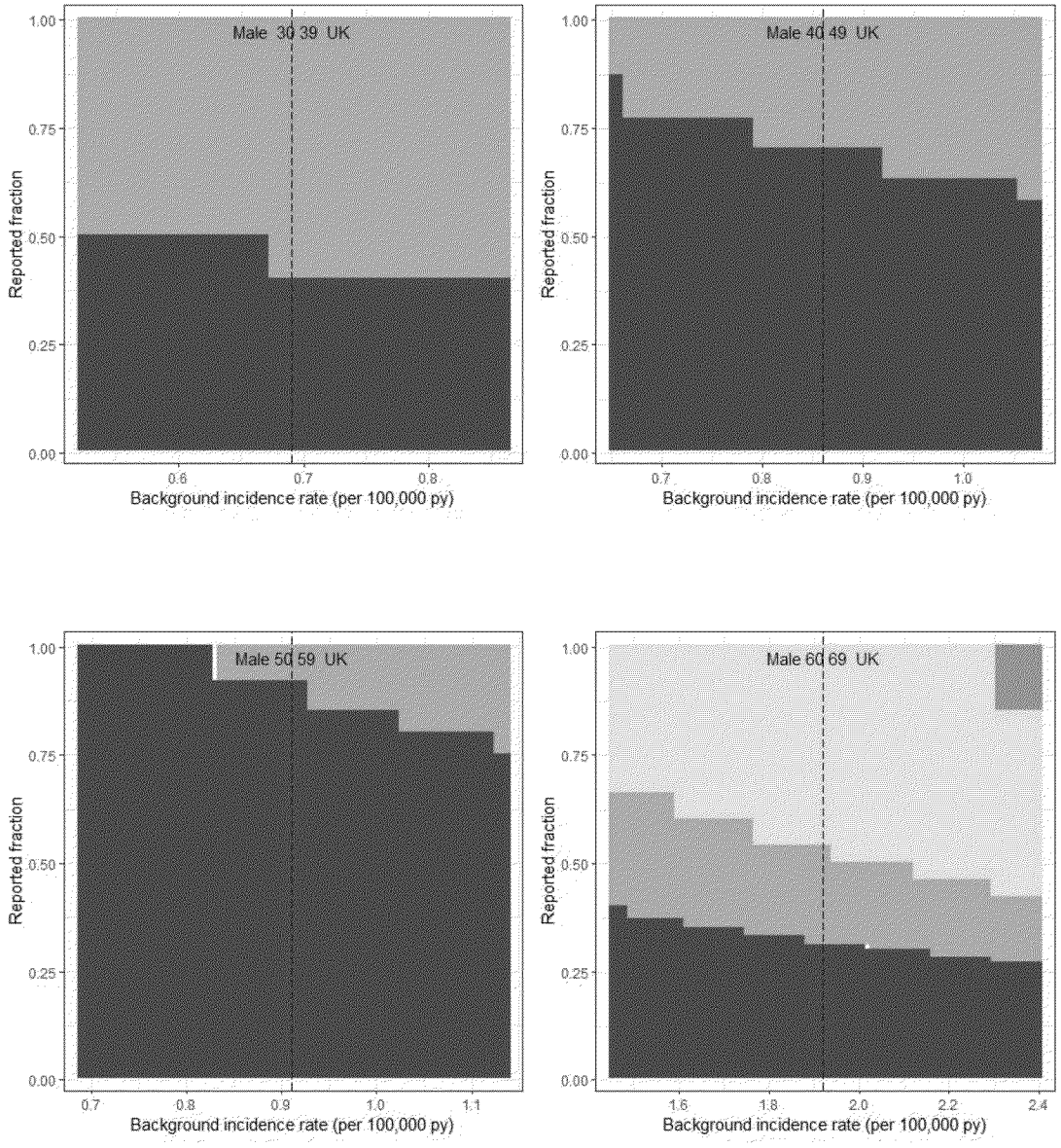
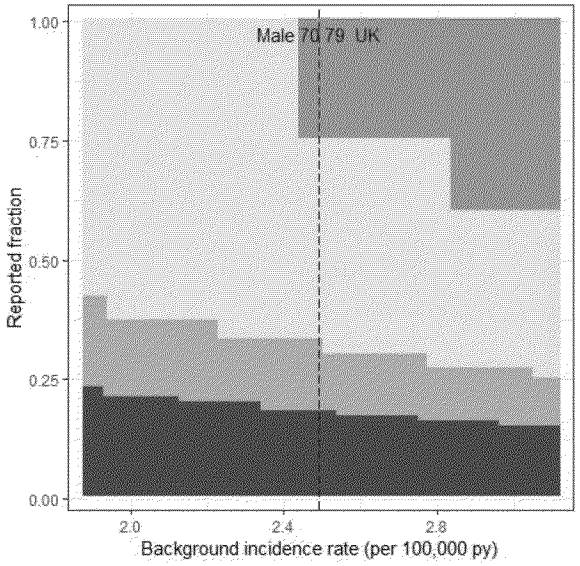
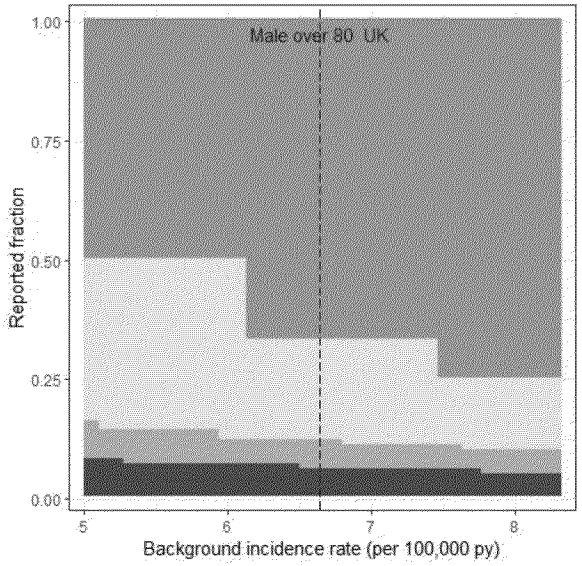

Male 30 39 UK
Male 40 49 UK
Male 50 59 UK
Male 60 69 UK
Reported fraction
Background incidence rate (per 100,000 py)

Table 76 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by gender and age from UK_TRUVEN 14

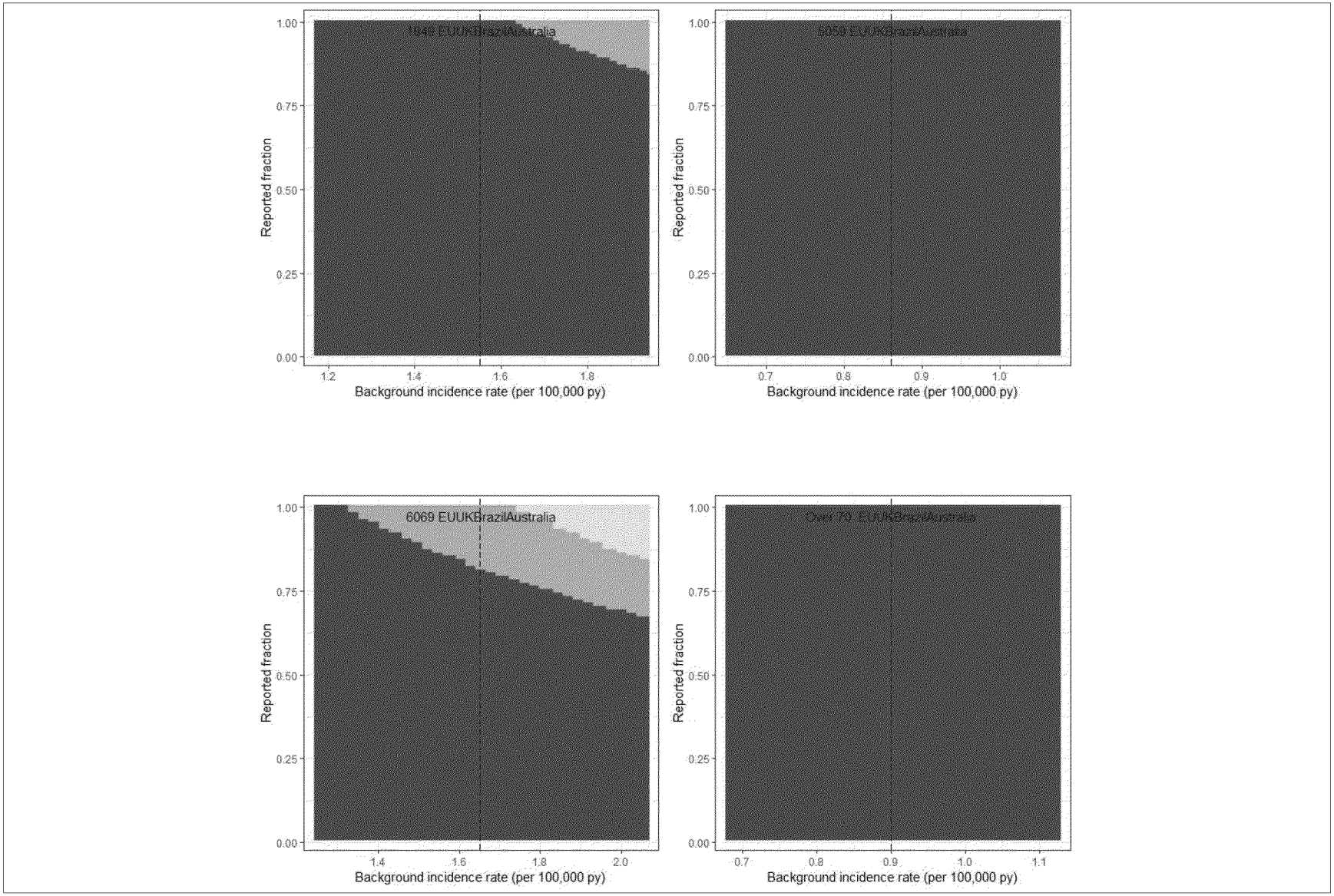
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							
							

[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO time to onset, UK United Kingdom

Table 77 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by age from EU+UK+Brazil+Australia region_TRUVEN 14

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18-49	124	98.12	21	1.55	110094983	1.26 (1.05 - 1.51)	Observed significantly > expected
50-59	53	28.85	21	0.86	58336094	1.84 (1.38 - 2.4)	Observed significantly > expected
60-69	58	54.99	21	1.65	57960860	1.05 (0.8 - 1.36)	Observed > expected
Over 70	35	16.75	21	0.9	32376365	2.09 (1.46 - 2.91)	Observed significantly > expected
18-49	136	140.16	30	1.55	110094983	0.97 (0.81 - 1.15)	Observed < expected
50-59	63	41.21	30	0.86	58336094	1.53 (1.17 - 1.96)	Observed significantly > expected
60-69	65	78.55	30	1.65	57960860	0.83 (0.64 - 1.05)	Observed < expected
Over 70	41	23.93	30	0.9	32376365	1.71 (1.23 - 2.32)	Observed significantly > expected
18-49	154	196.23	42	1.55	110094983	0.78 (0.67 - 0.92)	Observed significantly < expected
50-59	71	57.69	42	0.86	58336094	1.23 (0.96 - 1.55)	Observed > expected
60-69	78	109.97	42	1.65	57960860	0.71 (0.56 - 0.89)	Observed significantly < expected
Over 70	46	33.51	42	0.9	32376365	1.37 (1.01 - 1.83)	Observed significantly > expected


1849 EUUKBrazilAustralia
6059 EUUKBrazilAustralia
6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

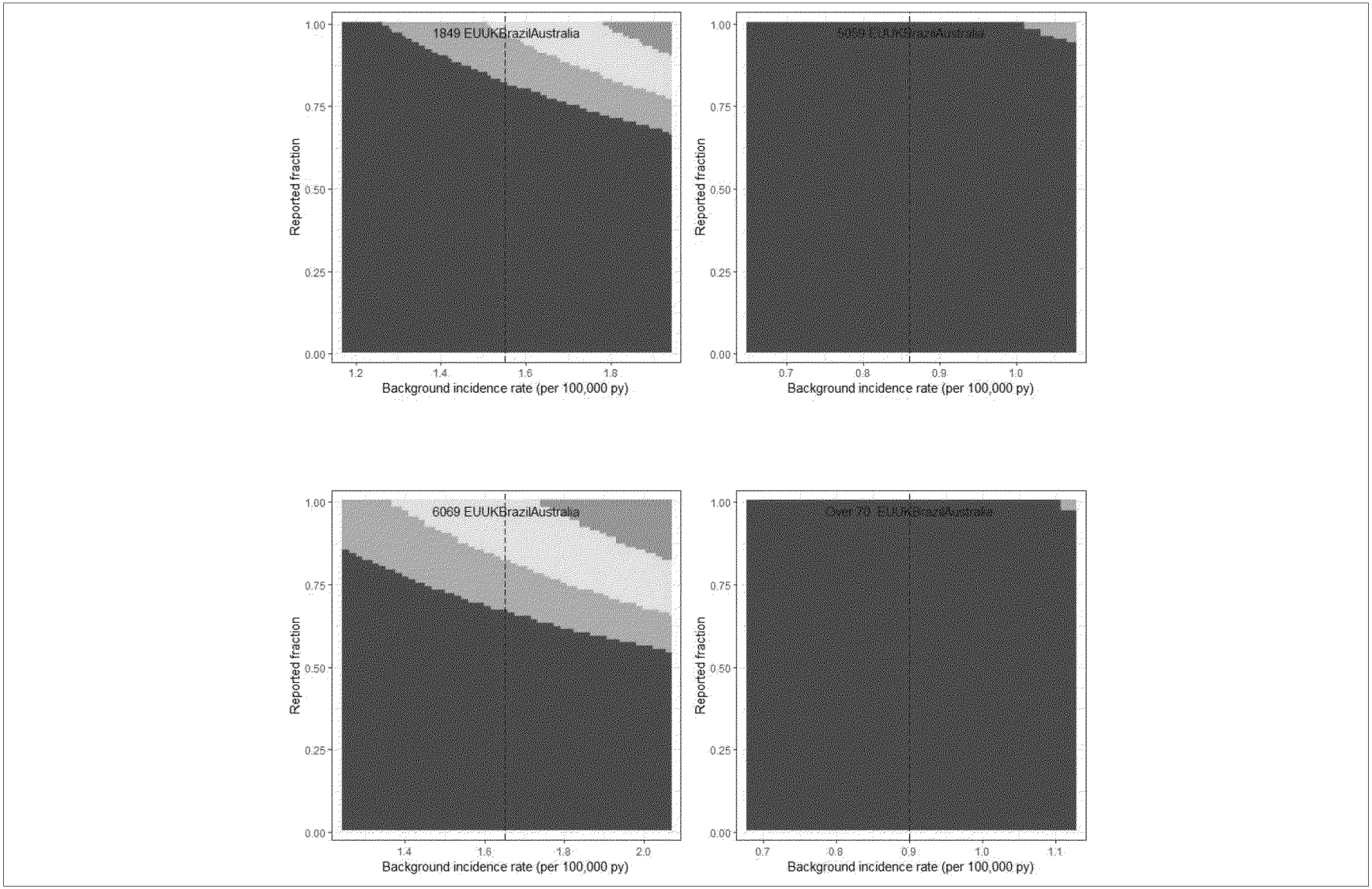
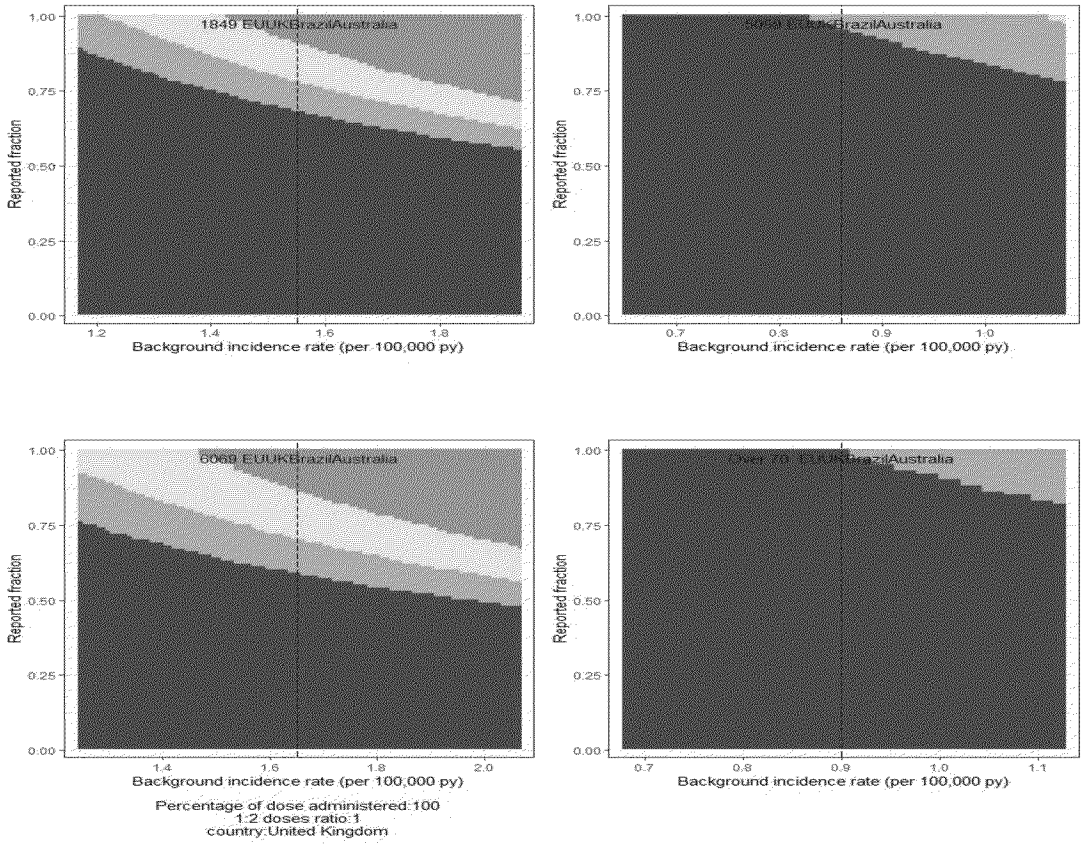

1849 EUUKBrazilAustralia
5069 EUUKBrazilAustralia
6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

Table 77 Observed Versus Expected analysis for CVST without thrombocytopenia cases stratified by age from EU+UK+Brazil+Australia region_TRUVEN 14

Description	Observed Cases	Expected Cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; EU European Union; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, UK European Union, Unk Unknown.

Table 78 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets including unknown TTO_TRUVEN 14 (Overall)

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Overall	49	402	21	1.5	466115644	0.12 (0.09 - 0.16)	Observed significantly < expected
Overall (including unknown TTO)	73	402	21	1.5	466115644	0.18 (0.14 - 0.23)	Observed significantly < expected
Overall	63	574.28	30	1.5	466115644	0.11 (0.08 - 0.14)	Observed significantly < expected
Overall (including unknown TTO)	87	574.28	30	1.5	466115644	0.15 (0.12 - 0.19)	Observed significantly < expected
Overall	75	803.99	42	1.5	466115644	0.09 (0.07 - 0.12)	Observed significantly < expected
Overall (including unknown TTO)	99	803.99	42	1.5	466115644	0.12 (0.1 - 0.15)	Observed significantly < expected

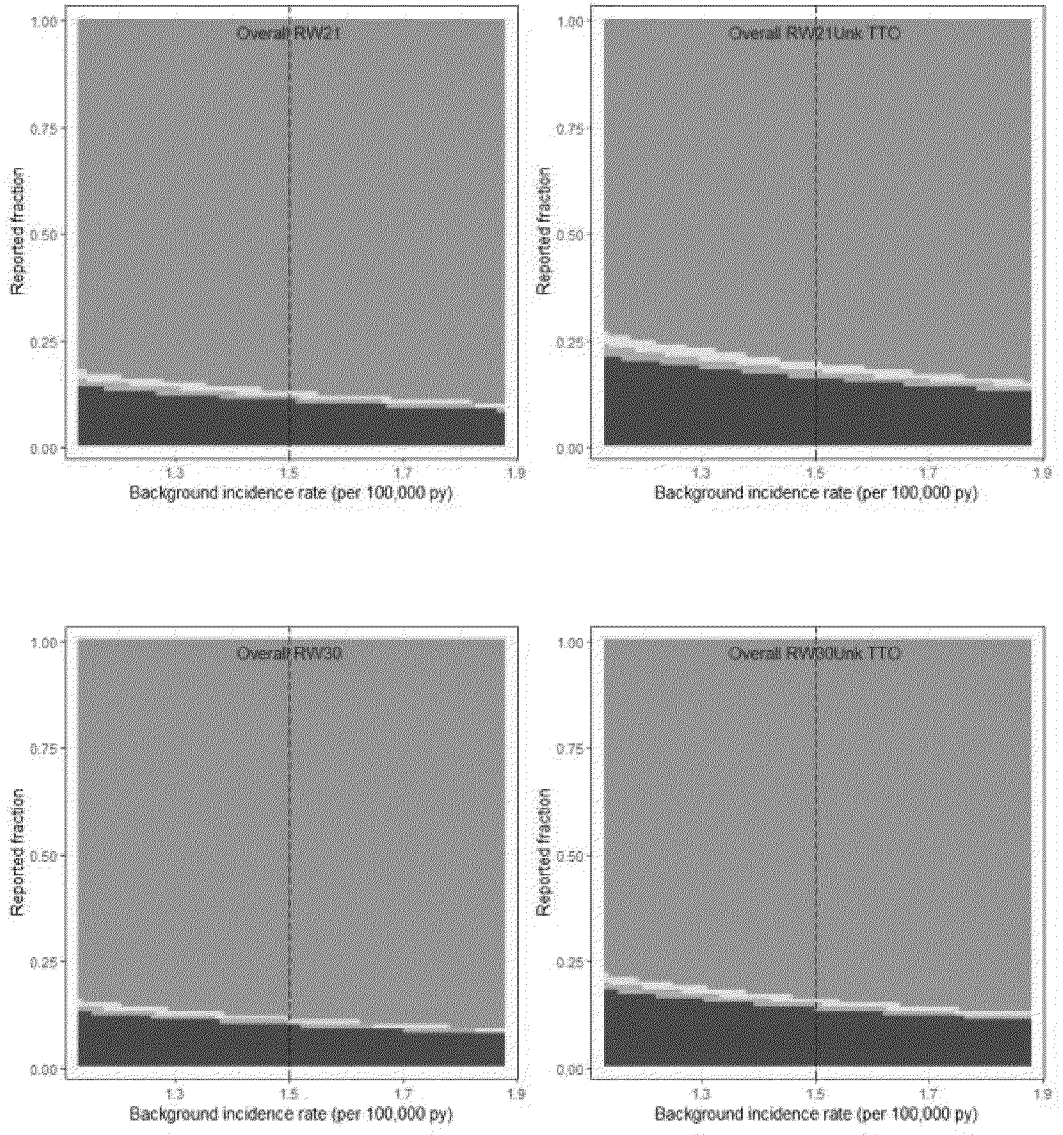
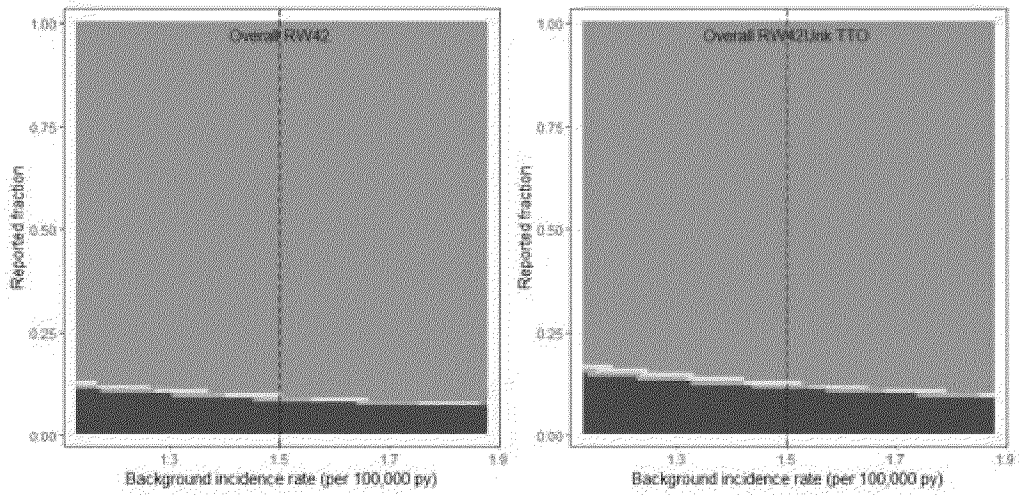

Overall RW21
Overall RW21Unk TTO
Overall RW30
Overall RW30Unk TTO
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.3
1.5
1.7
1.9

Table 78 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets including unknown TTO_TRUVEN 14 (Overall)

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

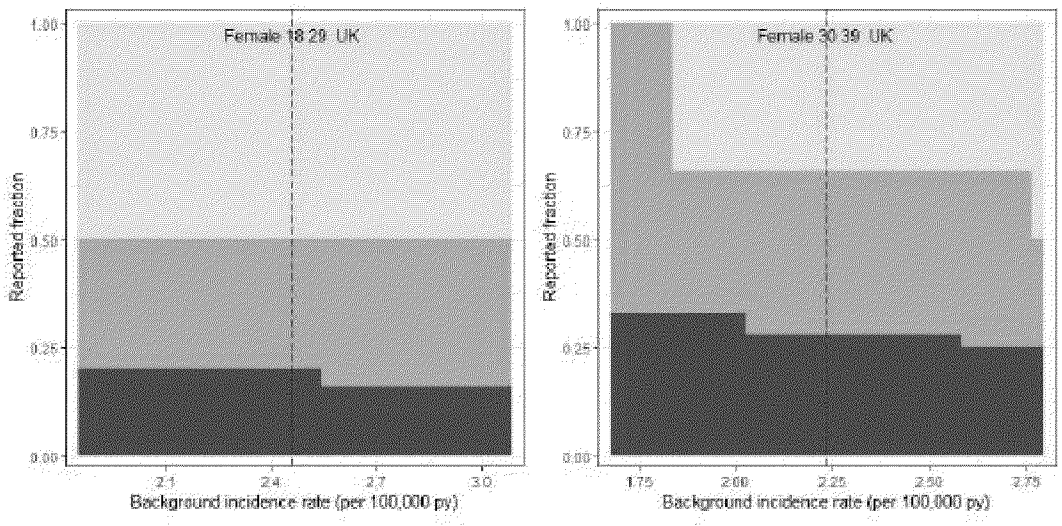
CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset

Table 79 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK_TRUVEN 14

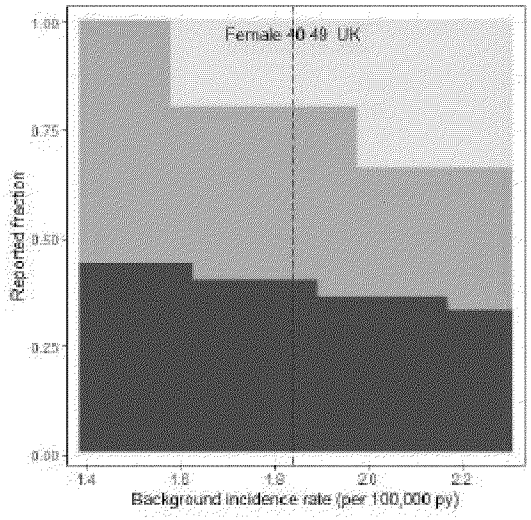
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Female 18-29	1	1.57	21	2.46	1109488	0.64 (0.02 - 3.55)	Observed < expected
Female 30-39	2	2.43	21	2.23	1892968	0.82 (0.1 - 2.97)	Observed < expected
Female 40-49	4	4.67	21	1.84	4412245	0.86 (0.23 - 2.19)	Observed < expected
Female 50-59	4	2.8	21	0.82	5944683	1.43 (0.39 - 3.66)	Observed > expected
Female 60-69	1	3.88	21	1.41	4783416	0.26 (0.01 - 1.44)	Observed < expected
Female 70-79	2	1.42	21	0.71	3475875	1.41 (0.17 - 5.09)	Observed > expected
Female over 80	0	8.74	21	9.32	1630324	0 (0 - 0.42)	Observed significantly < expected
Male 18-29	1	0.51	21	1.1	808938	1.96 (0.05 - 10.92)	Observed > expected
Male 30-39	1	0.56	21	0.69	1415003	1.79 (0.05 - 9.95)	Observed > expected
Male 40-49	3	2.25	21	0.86	4542157	1.33 (0.27 - 3.9)	Observed > expected
Male 50-59	5	3.41	21	0.91	6510960	1.47 (0.48 - 3.42)	Observed > expected
Male 60-69	2	5.45	21	1.92	4934728	0.37 (0.04 - 1.33)	Observed < expected
Male 70-79	2	4.49	21	2.49	3137304	0.45 (0.05 - 1.61)	Observed < expected
Male over 80	1	3.91	21	6.64	1025046	0.26 (0.01 - 1.42)	Observed < expected
Female 18-29	1	2.24	30	2.46	1109488	0.45 (0.01 - 2.49)	Observed < expected
Female 30-39	2	3.47	30	2.23	1892968	0.58 (0.07 - 2.08)	Observed < expected
Female 40-49	4	6.67	30	1.84	4412245	0.6 (0.16 - 1.54)	Observed < expected
Female 50-59	5	4	30	0.82	5944683	1.25 (0.41 - 2.92)	Observed > expected
Female 60-69	3	5.54	30	1.41	4783416	0.54 (0.11 - 1.58)	Observed < expected
Female 70-79	3	2.03	30	0.71	3475875	1.48 (0.3 - 4.32)	Observed > expected
Female over 80	0	12.48	30	9.32	1630324	0 (0 - 0.3)	Observed significantly < expected

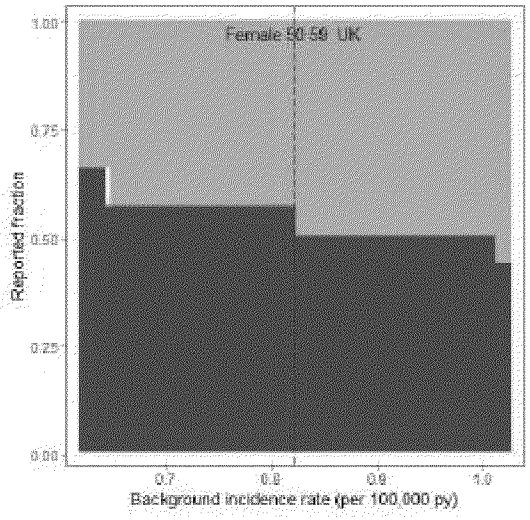
Table 79 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK_TRUVEN 14

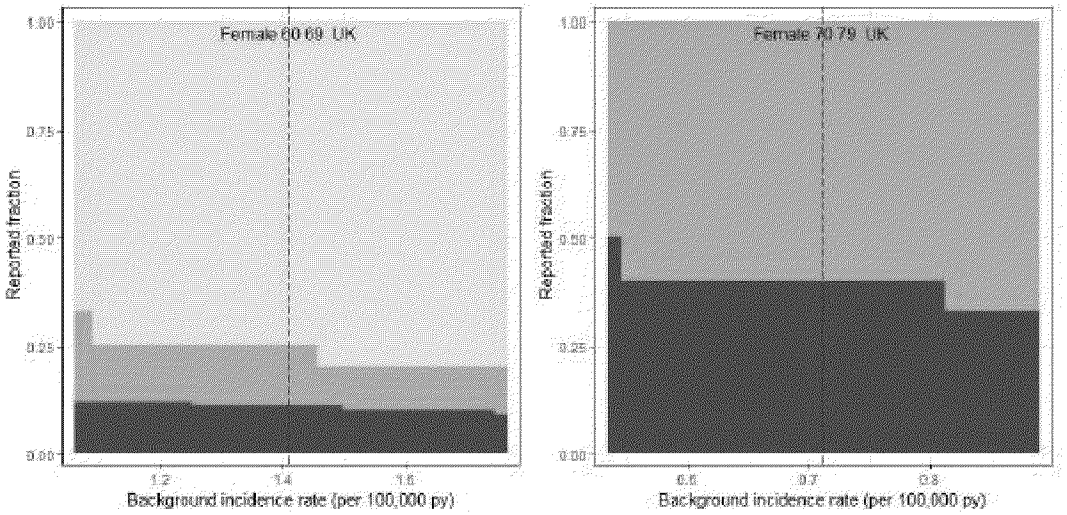
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 18-29	1	0.73	30	1.1	808938	1.37 (0.03 - 7.63)	Observed > expected
Male 30-39	1	0.8	30	0.69	1415003	1.25 (0.03 - 6.96)	Observed > expected
Male 40-49	4	3.21	30	0.86	4542157	1.25 (0.34 - 3.19)	Observed > expected
Male 50-59	7	4.87	30	0.91	6510960	1.44 (0.58 - 2.96)	Observed > expected
Male 60-69	2	7.78	30	1.92	4934728	0.26 (0.03 - 0.93)	Observed significantly < expected
Male 70-79	2	6.42	30	2.49	3137304	0.31 (0.04 - 1.13)	Observed < expected
Male over 80	1	5.59	30	6.64	1025046	0.18 (0 - 1)	Observed significantly < expected
Female 18-29	1	3.14	42	2.46	1109488	0.32 (0.01 - 1.77)	Observed < expected
Female 30-39	2	4.85	42	2.23	1892968	0.41 (0.05 - 1.49)	Observed < expected
Female 40-49	5	9.34	42	1.84	4412245	0.54 (0.17 - 1.25)	Observed < expected
Female 50-59	6	5.61	42	0.82	5944683	1.07 (0.39 - 2.33)	Observed > expected
Female 60-69	4	7.76	42	1.41	4783416	0.52 (0.14 - 1.32)	Observed < expected
Female 70-79	3	2.84	42	0.71	3475875	1.06 (0.22 - 3.09)	Observed > expected
Female over 80	2	17.47	42	9.32	1630324	0.11 (0.01 - 0.41)	Observed significantly < expected
Male 18-29	2	1.02	42	1.1	808938	1.96 (0.24 - 7.08)	Observed > expected
Male 30-39	1	1.12	42	0.69	1415003	0.89 (0.02 - 4.97)	Observed < expected
Male 40-49	4	4.49	42	0.86	4542157	0.89 (0.24 - 2.28)	Observed < expected
Male 50-59	8	6.81	42	0.91	6510960	1.17 (0.51 - 2.31)	Observed > expected
Male 60-69	3	10.9	42	1.92	4934728	0.28 (0.06 - 0.8)	Observed significantly < expected
Male 70-79	2	8.98	42	2.49	3137304	0.22 (0.03 - 0.8)	Observed significantly < expected
Male over 80	1	7.83	42	6.64	1025046	0.13 (0 - 0.71)	Observed significantly < expected


Female 18 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.1
2.4
2.7
3.0
Background incidence rate (per 100,000 py)

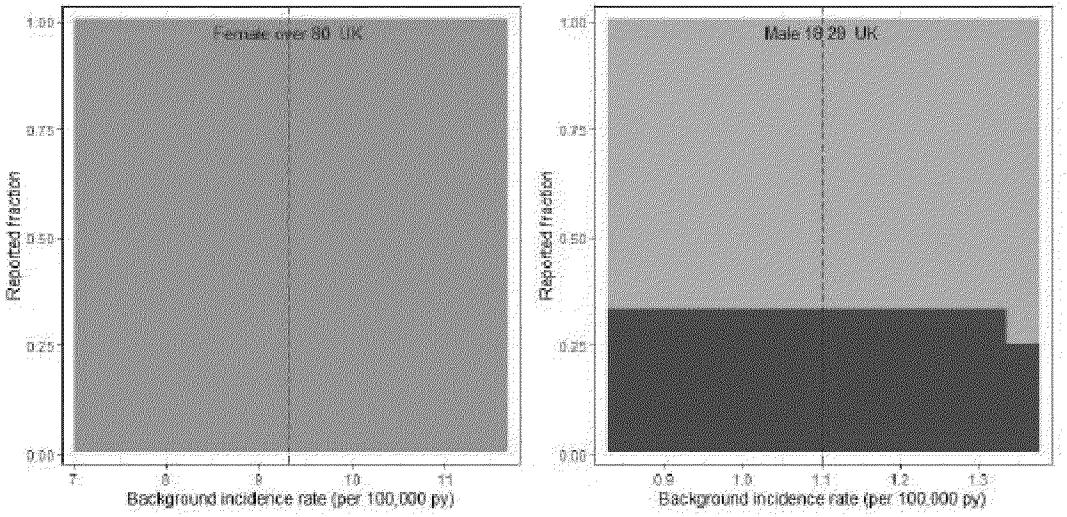
Female 30 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)


Female 40 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.2
Background incidence rate (per 100,000 py)

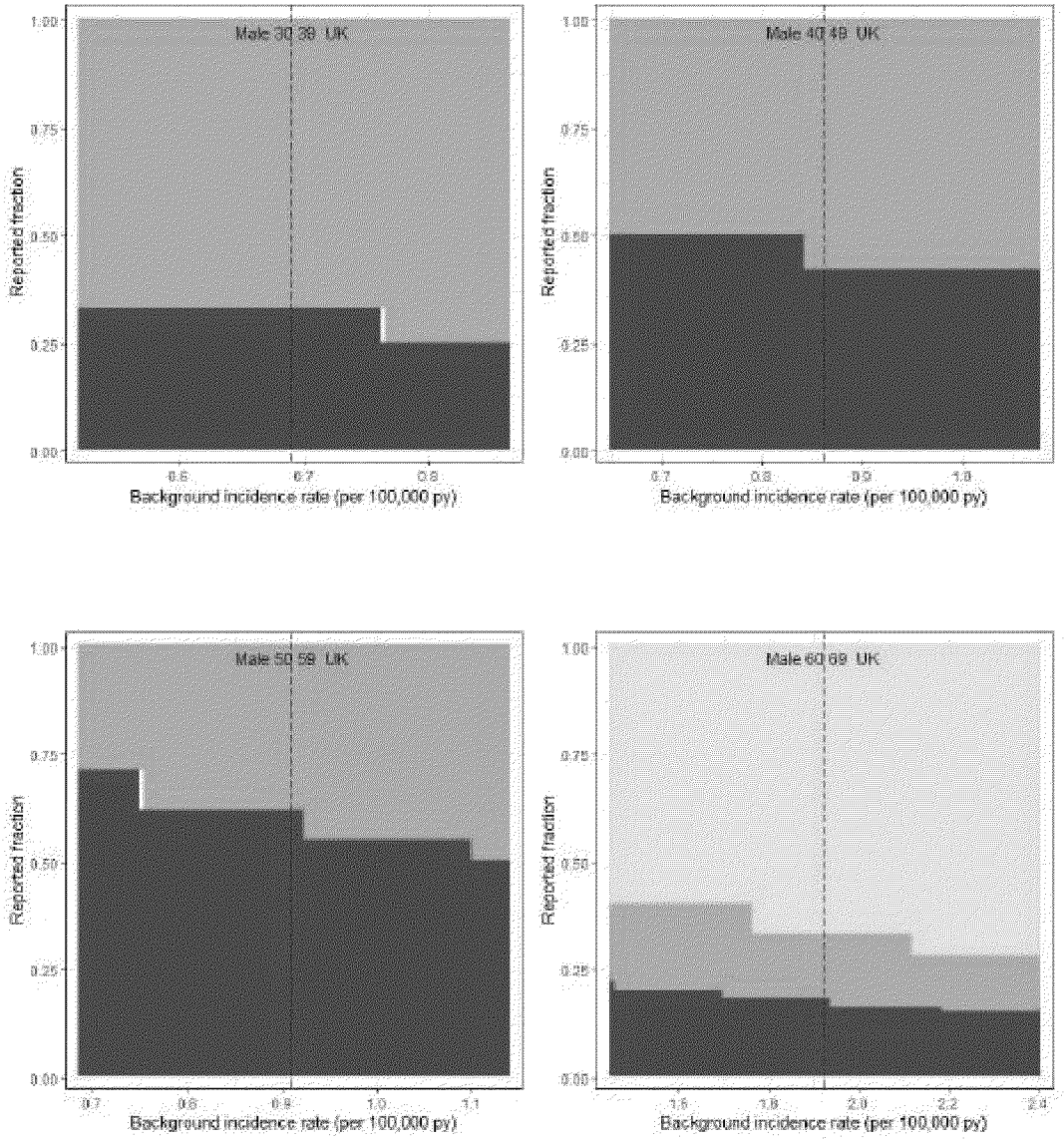

Female 50 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)

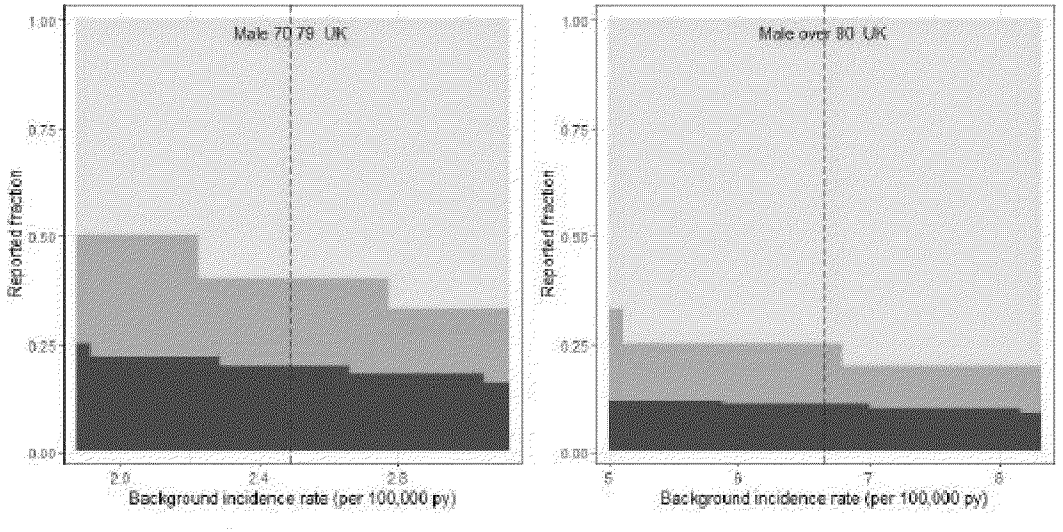

Female 60 69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
Background incidence rate (per 100,000 py)

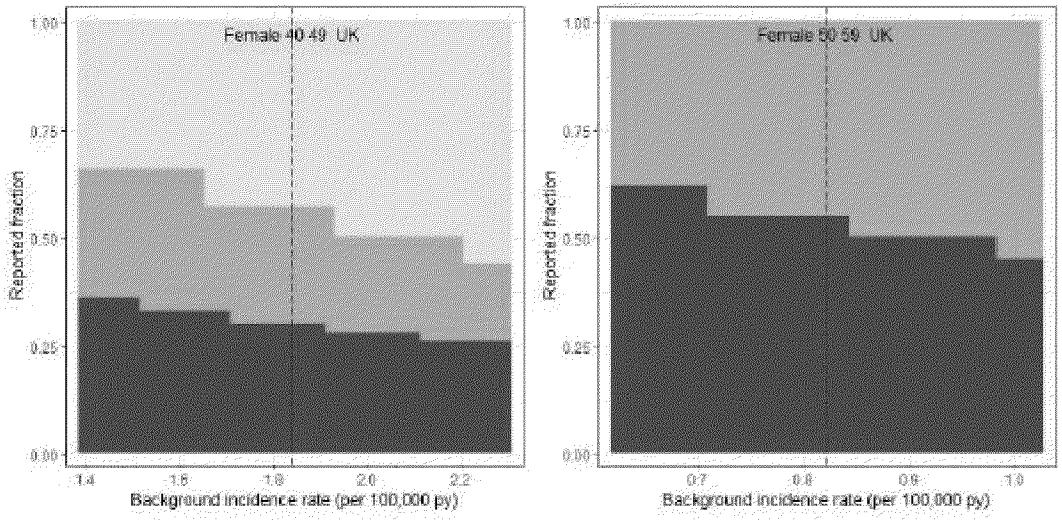
Female 70 79 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)


Female over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
11
Background incidence rate (per 100,000 py)

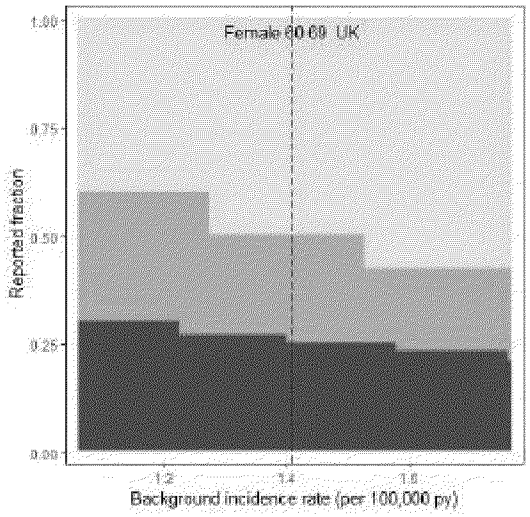
Male 18 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.9
1.0
1.1
1.2
1.3
Background incidence rate (per 100,000 py)

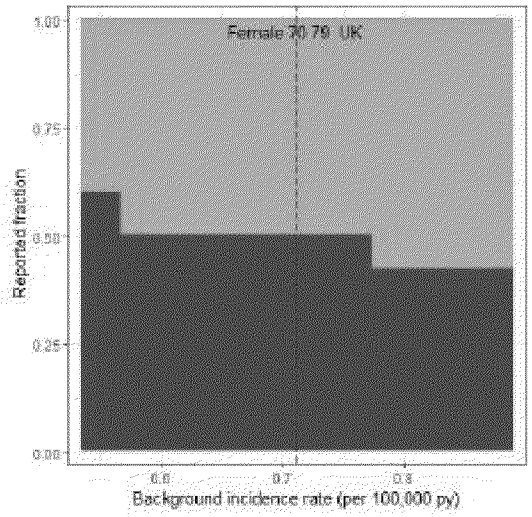

Male 30 39 UK
Male 40 49 UK
Male 50 59 UK
Male 60 69 UK
Reported fraction
Background incidence rate (per 100,000 py)

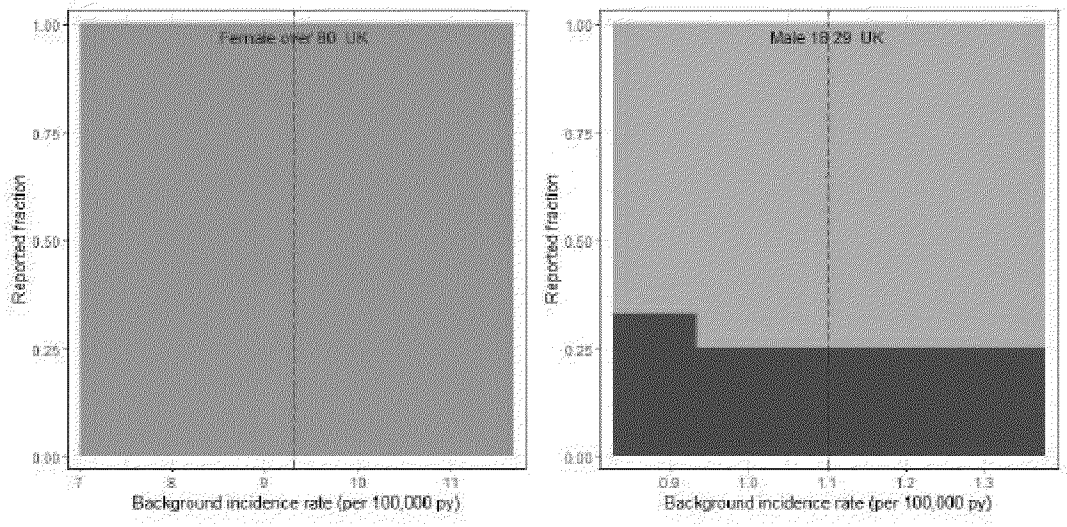

Male 70 79 UK
Male over 80 UK
Female 18 29 UK
Female 30 39 UK
Reported fraction
Background incidence rate (per 100,000 py)

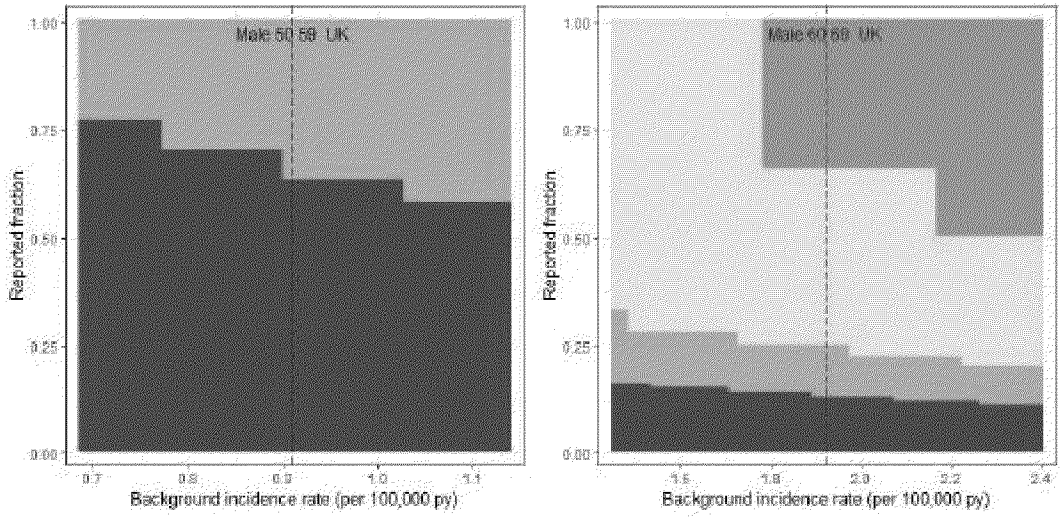

Female 40-49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.2
Background incidence rate (per 100,000 py)

Female 50-59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)

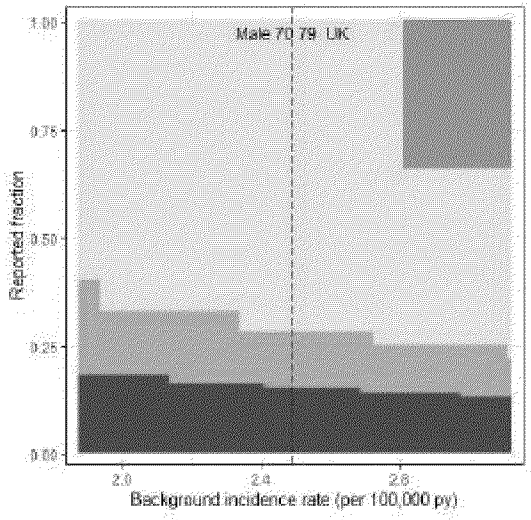

Female 60-69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
Background incidence rate (per 100,000 py)

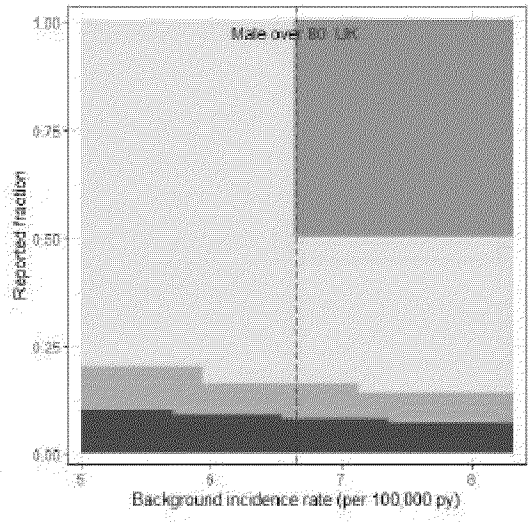

Female 70-79 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)

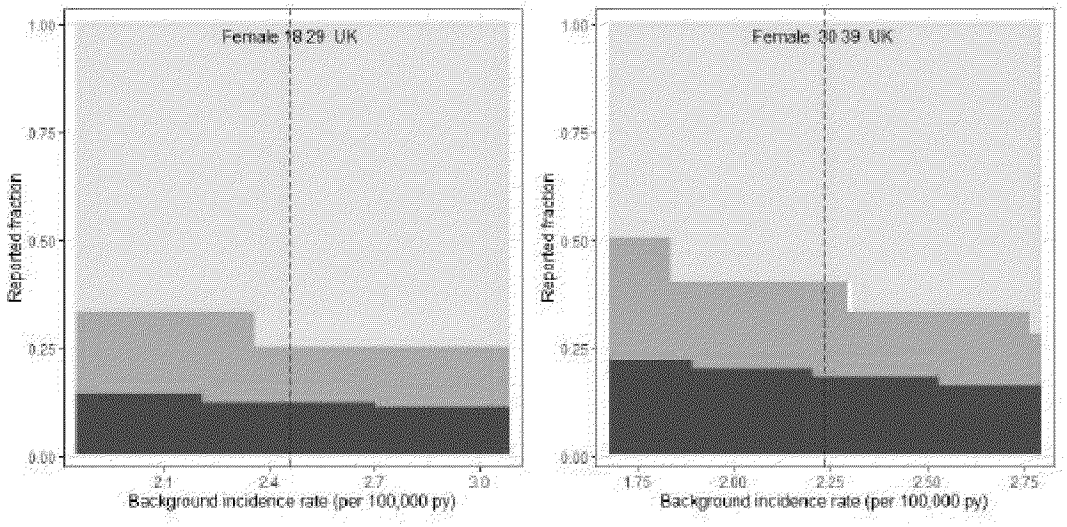

Female over 80 UK
Male 18 29 UK
Male 30 39 UK
Male 40 49 UK
Reported fraction
Background incidence rate (per 100,000 py)


Male 50 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)

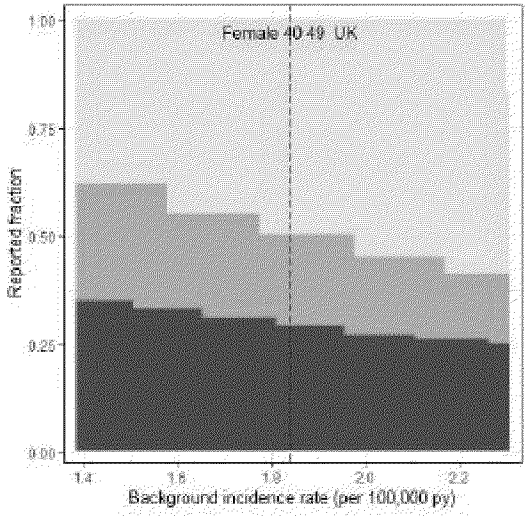
Male 60 69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.6
1.8
2.0
2.2
2.4
Background incidence rate (per 100,000 py)

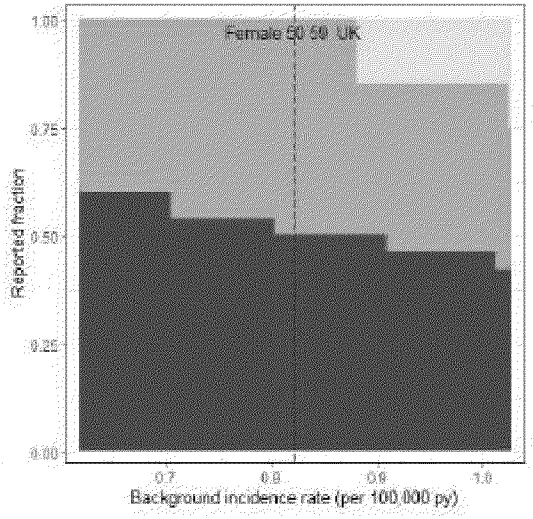

Male 70 79 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.4
2.8
Background incidence rate (per 100,000 py)

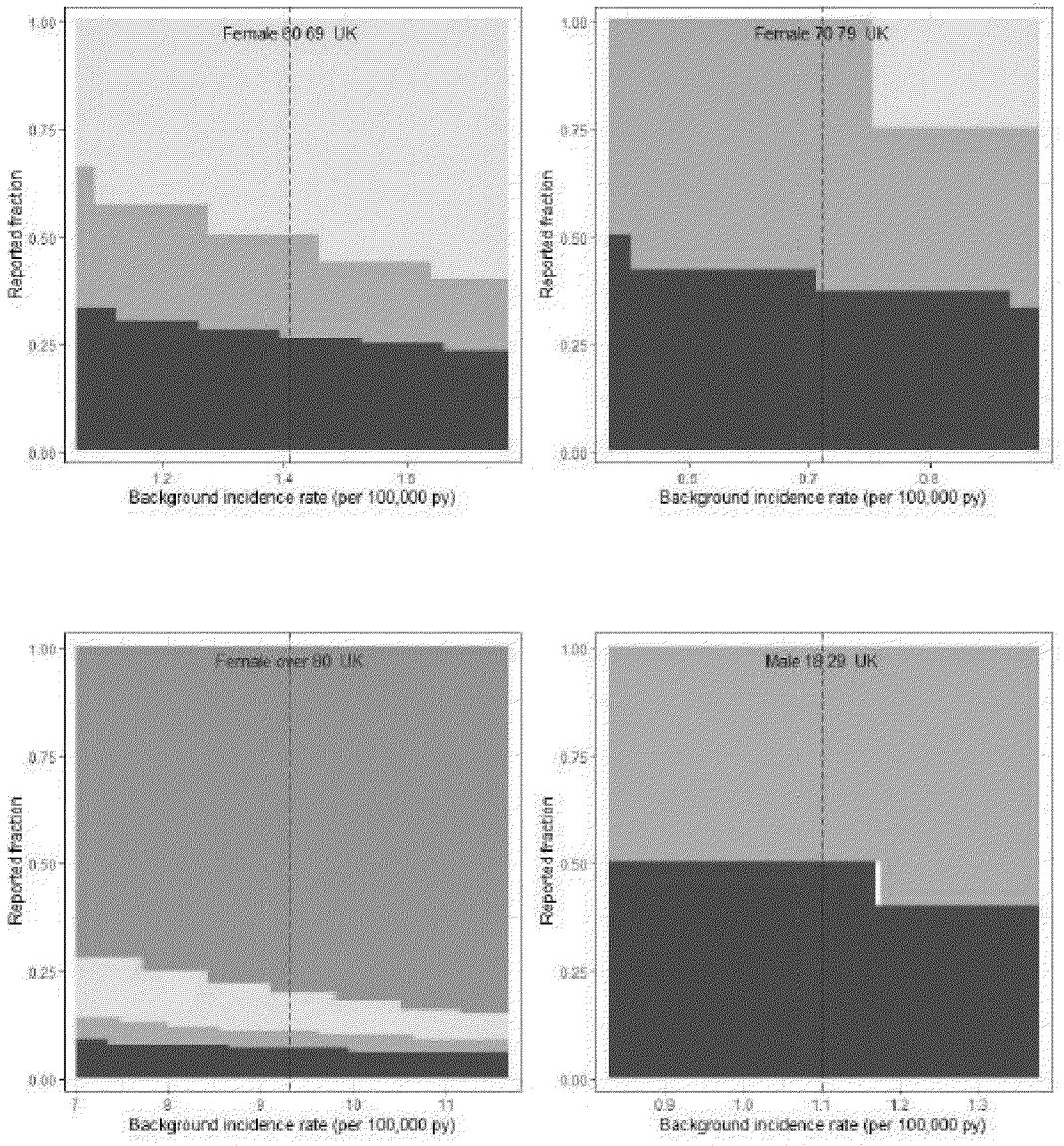

Male over 80 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
8
Background incidence rate (per 100,000 py)

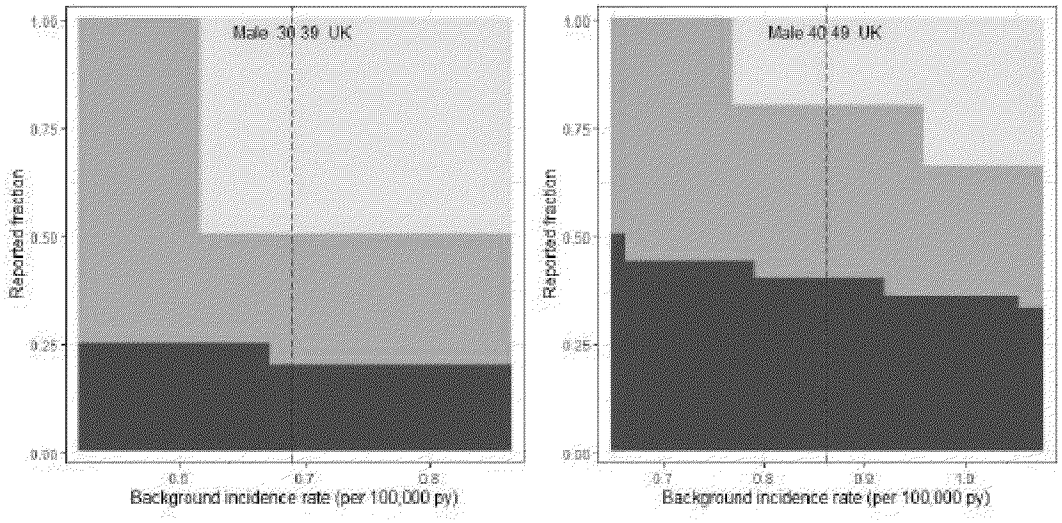

Female 18 29 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.1
2.4
2.7
3.0
Background incidence rate (per 100,000 py)

Female 30 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)

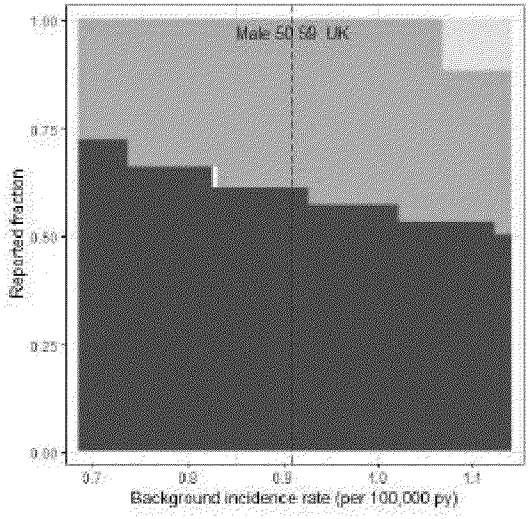

Female 40 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.2
Background incidence rate (per 100,000 py)


Female 50 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)


Female 60 69 UK
Female 70 79 UK
Female over 80 UK
Male 18 29 UK
Reported fraction
Background incidence rate (per 100,000 py)


Male 30 39 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)

Male 40 49 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)


Male 50 59 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)

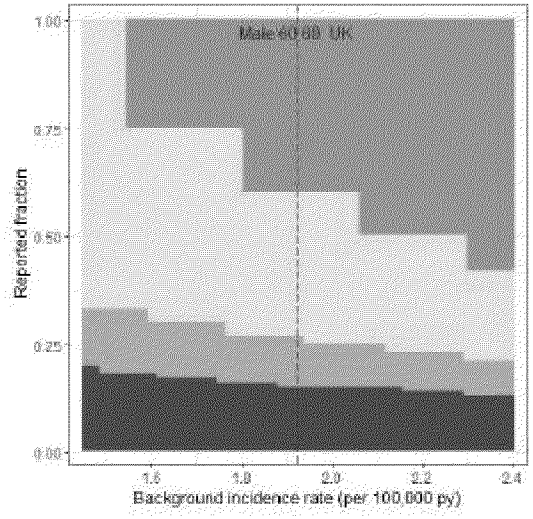
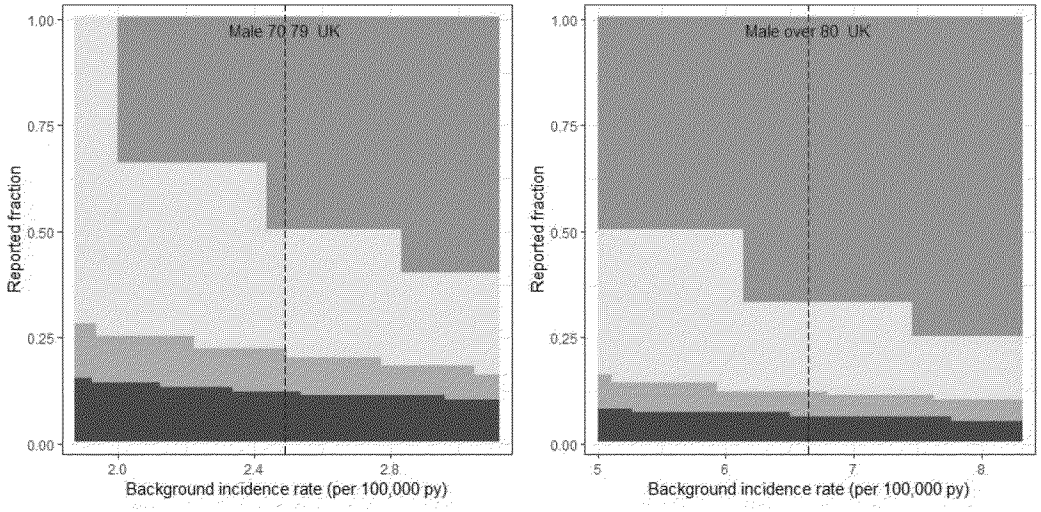

Male 60 69 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.6
1.8
2.0
2.2
2.4
Background incidence rate (per 100,000 py)

Table 79 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK_TRUVEN 14

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

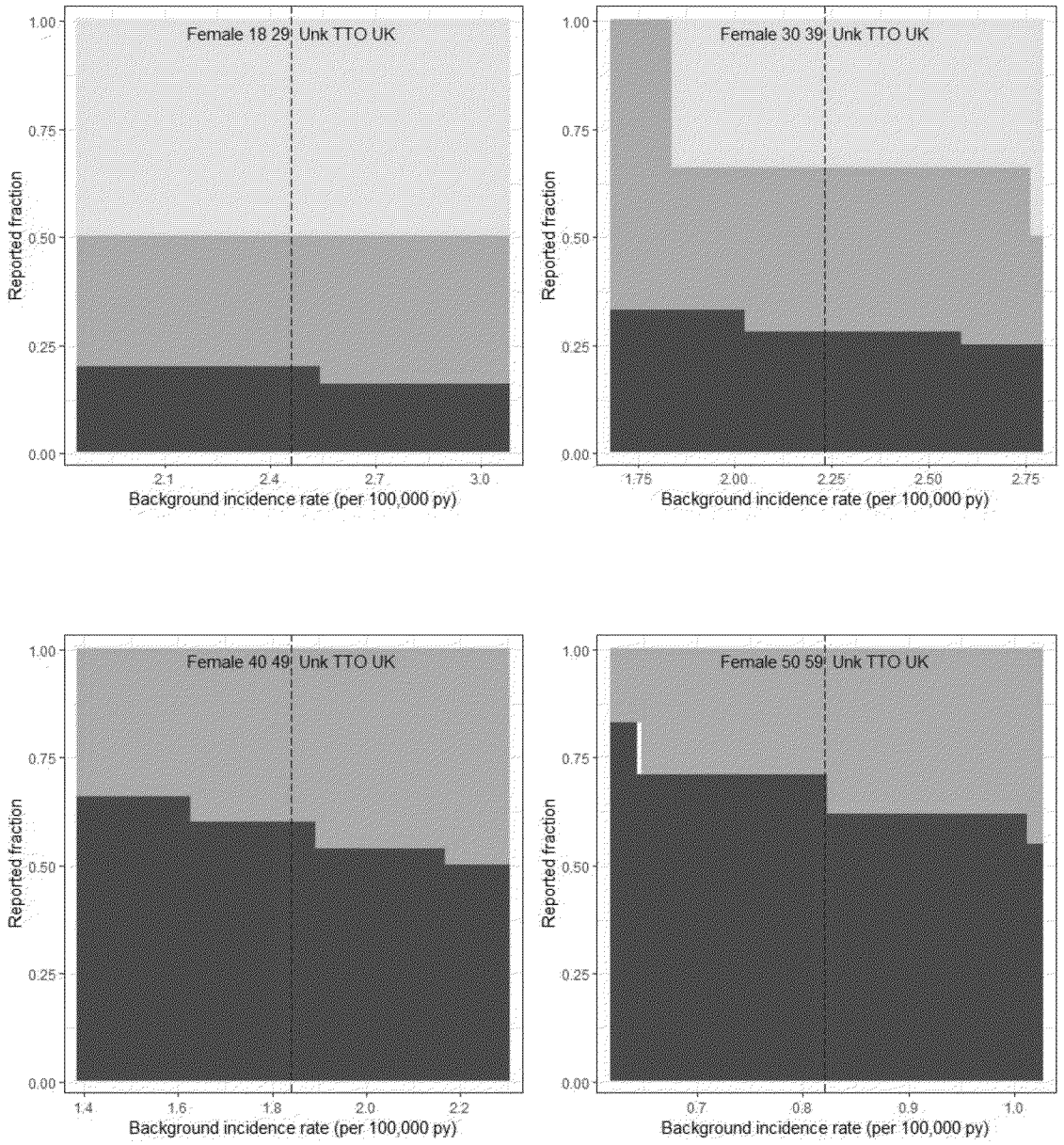
CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO time to onset, UK United Kingdom

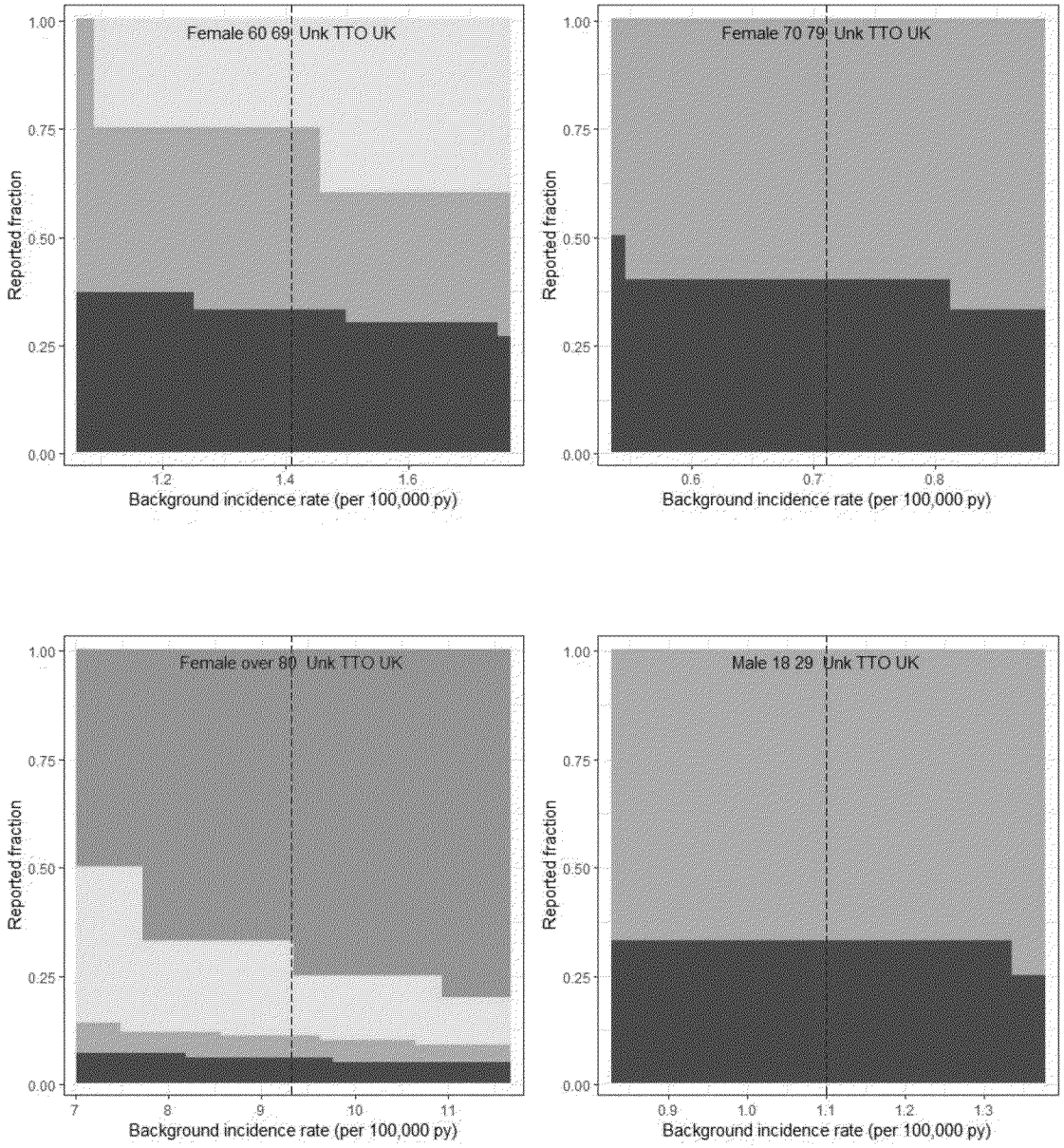
Table 80 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK including unknown TTO_TRUVEN 14

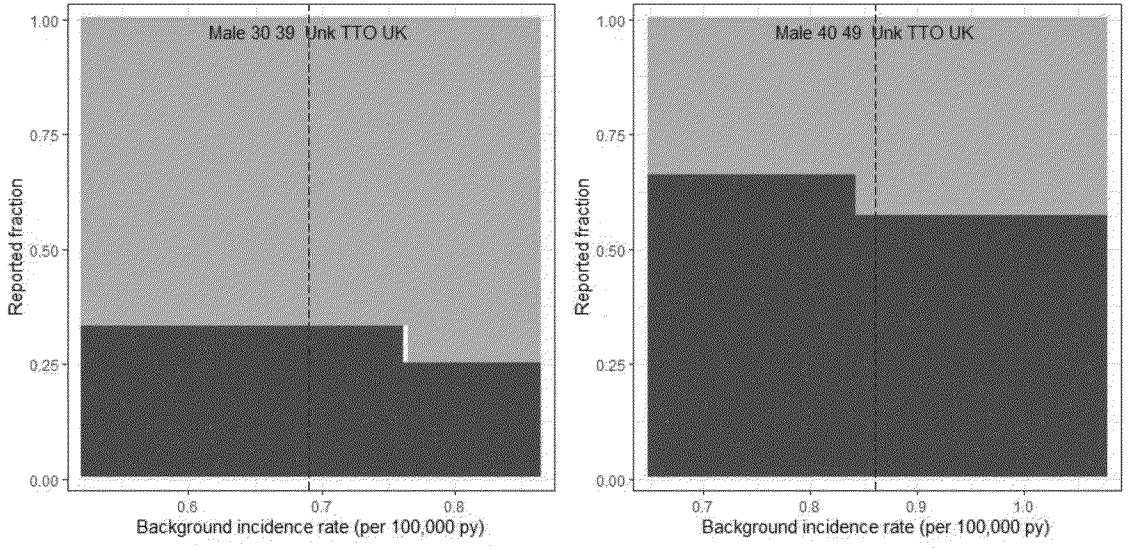
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Female 18-29	1	1.57	21	2.46	1109488	0.64 (0.02 - 3.55)	Observed < expected
Female 30-39	2	2.43	21	2.23	1892968	0.82 (0.1 - 2.97)	Observed < expected
Female 40-49	6	4.67	21	1.84	4412245	1.28 (0.47 - 2.8)	Observed > expected
Female 50-59	5	2.8	21	0.82	5944683	1.79 (0.58 - 4.17)	Observed > expected
Female 60-69	3	3.88	21	1.41	4783416	0.77 (0.16 - 2.26)	Observed < expected
Female 70-79	2	1.42	21	0.71	3475875	1.41 (0.17 - 5.09)	Observed > expected
Female over 80	1	8.74	21	9.32	1630324	0.11 (0 - 0.64)	Observed significantly < expected
Male 18-29	1	0.51	21	1.1	808938	1.96 (0.05 - 10.92)	Observed > expected
Male 30-39	1	0.56	21	0.69	1415003	1.79 (0.05 - 9.95)	Observed > expected
Male 40-49	4	2.25	21	0.86	4542157	1.78 (0.48 - 4.55)	Observed > expected
Male 50-59	8	3.41	21	0.91	6510960	2.35 (1.01 - 4.62)	Observed significantly > expected
Male 60-69	2	5.45	21	1.92	4934728	0.37 (0.04 - 1.33)	Observed < expected
Male 70-79	3	4.49	21	2.49	3137304	0.67 (0.14 - 1.95)	Observed < expected
Male over 80	1	3.91	21	6.64	1025046	0.26 (0.01 - 1.42)	Observed < expected
Female 18-29	1	2.24	30	2.46	1109488	0.45 (0.01 - 2.49)	Observed < expected
Female 30-39	2	3.47	30	2.23	1892968	0.58 (0.07 - 2.08)	Observed < expected
Female 40-49	6	6.67	30	1.84	4412245	0.9 (0.33 - 1.96)	Observed < expected
Female 50-59	6	4	30	0.82	5944683	1.5 (0.55 - 3.26)	Observed > expected
Female 60-69	5	5.54	30	1.41	4783416	0.9 (0.29 - 2.11)	Observed < expected
Female 70-79	3	2.03	30	0.71	3475875	1.48 (0.3 - 4.32)	Observed > expected
Female over 80	1	12.48	30	9.32	1630324	0.08 (0 - 0.45)	Observed significantly < expected

Table 80 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK including unknown TTO_TRUVEN 14

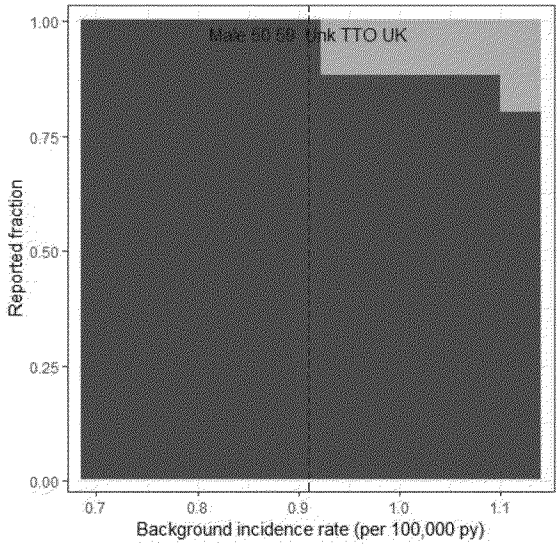
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Male 18-29	1	0.73	30	1.1	808938	1.37 (0.03 - 7.63)	Observed > expected
Male 30-39	1	0.8	30	0.69	1415003	1.25 (0.03 - 6.96)	Observed > expected
Male 40-49	5	3.21	30	0.86	4542157	1.56 (0.51 - 3.63)	Observed > expected
Male 50-59	10	4.87	30	0.91	6510960	2.05 (0.98 - 3.78)	Observed > expected
Male 60-69	2	7.78	30	1.92	4934728	0.26 (0.03 - 0.93)	Observed significantly < expected
Male 70-79	3	6.42	30	2.49	3137304	0.47 (0.1 - 1.37)	Observed < expected
Male over 80	1	5.59	30	6.64	1025046	0.18 (0 - 1)	Observed significantly < expected
Female 18-29	1	3.14	42	2.46	1109488	0.32 (0.01 - 1.77)	Observed < expected
Female 30-39	2	4.85	42	2.23	1892968	0.41 (0.05 - 1.49)	Observed < expected
Female 40-49	7	9.34	42	1.84	4412245	0.75 (0.3 - 1.54)	Observed < expected
Female 50-59	7	5.61	42	0.82	5944683	1.25 (0.5 - 2.57)	Observed > expected
Female 60-69	6	7.76	42	1.41	4783416	0.77 (0.28 - 1.68)	Observed < expected
Female 70-79	3	2.84	42	0.71	3475875	1.06 (0.22 - 3.09)	Observed > expected
Female over 80	3	17.47	42	9.32	1630324	0.17 (0.04 - 0.5)	Observed significantly < expected
Male 18-29	2	1.02	42	1.1	808938	1.96 (0.24 - 7.08)	Observed > expected
Male 30-39	1	1.12	42	0.69	1415003	0.89 (0.02 - 4.97)	Observed < expected
Male 40-49	5	4.49	42	0.86	4542157	1.11 (0.36 - 2.6)	Observed > expected
Male 50-59	11	6.81	42	0.91	6510960	1.62 (0.81 - 2.89)	Observed > expected
Male 60-69	3	10.9	42	1.92	4934728	0.28 (0.06 - 0.8)	Observed significantly < expected
Male 70-79	3	8.98	42	2.49	3137304	0.33 (0.07 - 0.98)	Observed significantly < expected
Male over 80	1	7.83	42	6.64	1025046	0.13 (0 - 0.71)	Observed significantly < expected

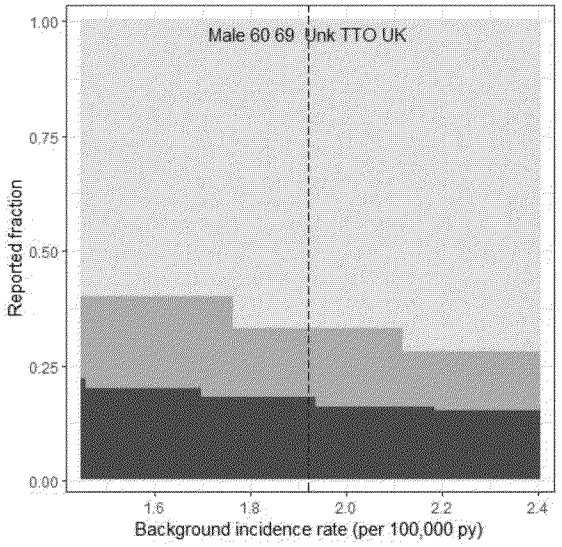

Female 18 29 Unk TTO UK
Female 30 39 Unk TTO UK
Female 40 49 Unk TTO UK
Female 50 59 Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
2.1
2.4
2.7
3.0
1.75
2.00
2.25
2.50
2.75
1.4
1.6
1.8
2.0
2.2
0.7
0.8
0.9
1.0

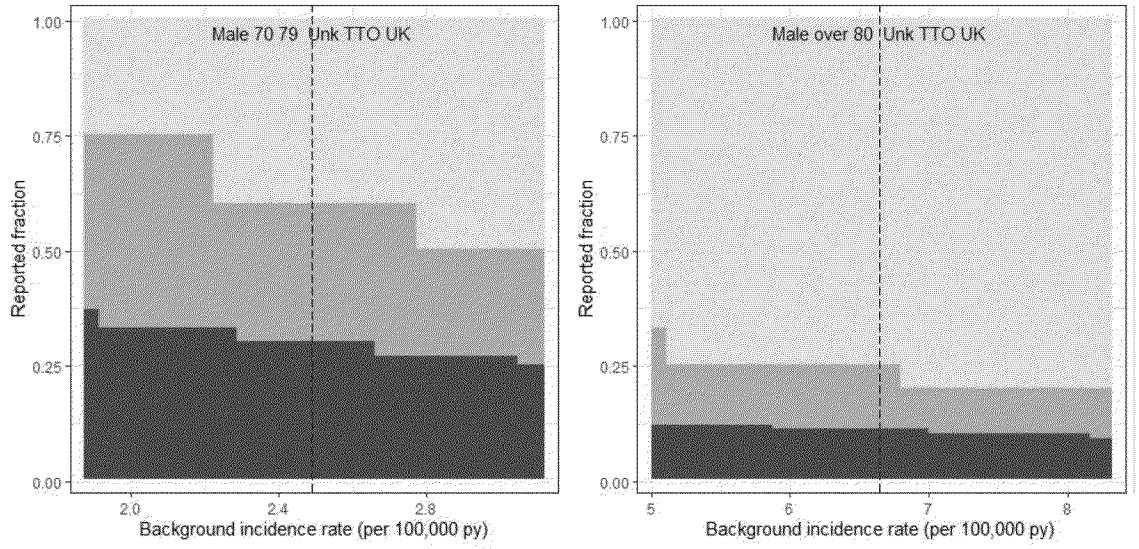

Female 60 69 Unk TTO UK
Female 70 79 Unk TTO UK
Female over 80 Unk TTO UK
Male 18 29 Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
0.6
0.7
0.8
7
8
9
10
11
0.9
1.0
1.1
1.2
1.3


Male 30 39 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)

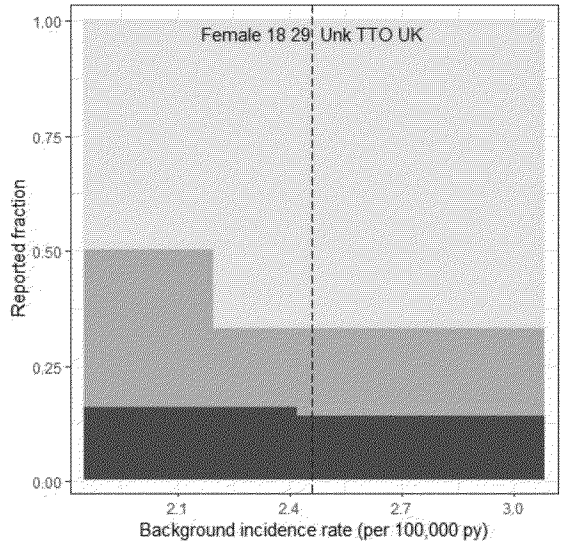
Male 40 49 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)

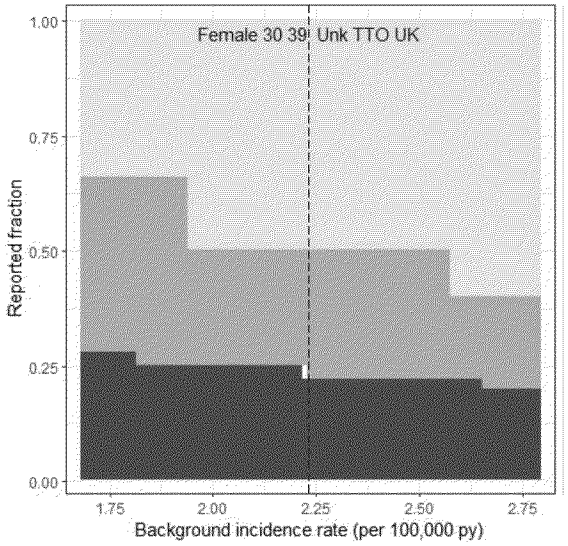

Male 50 59 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)

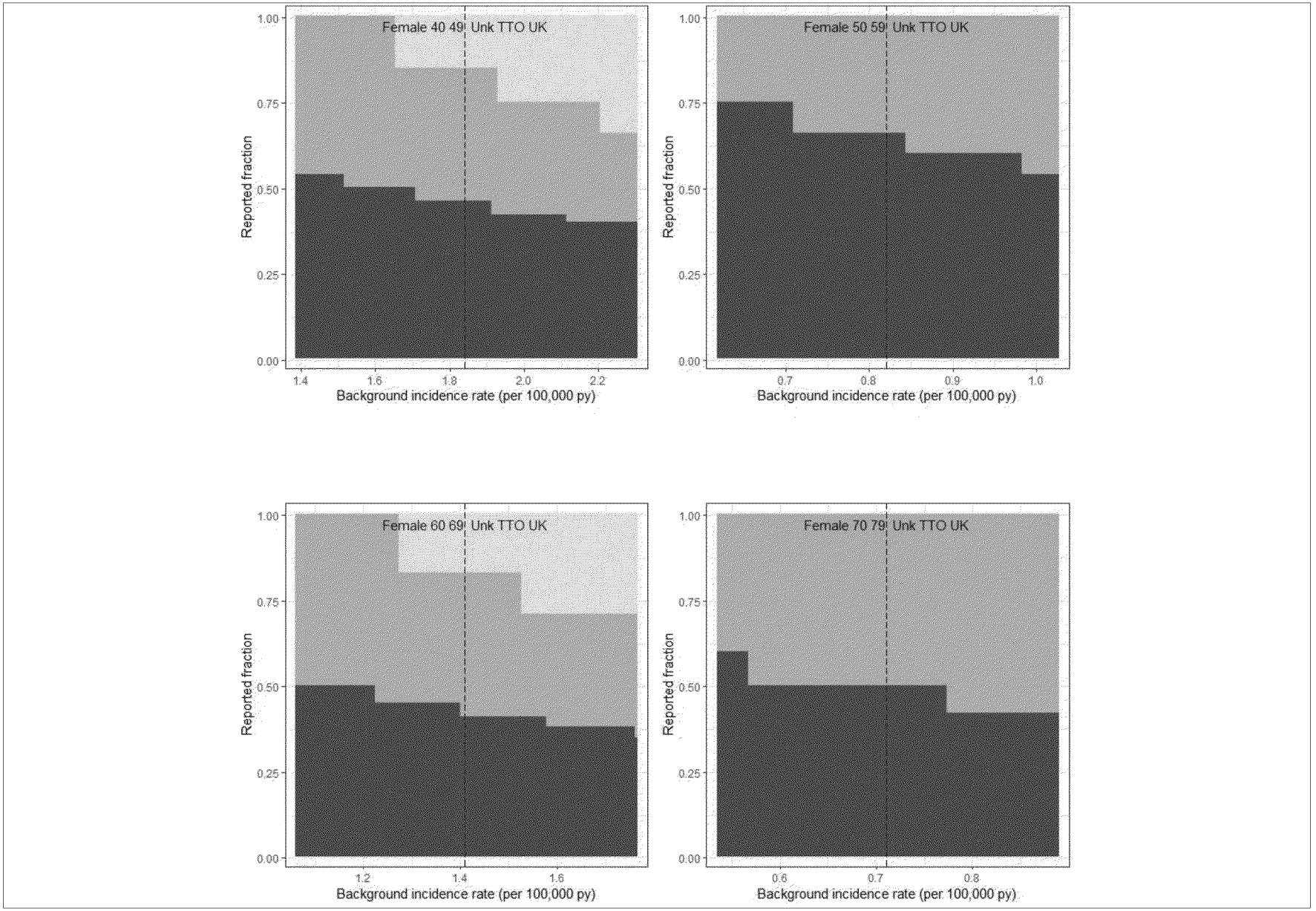

Male 60 69 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.6
1.8
2.0
2.2
2.4
Background incidence rate (per 100,000 py)

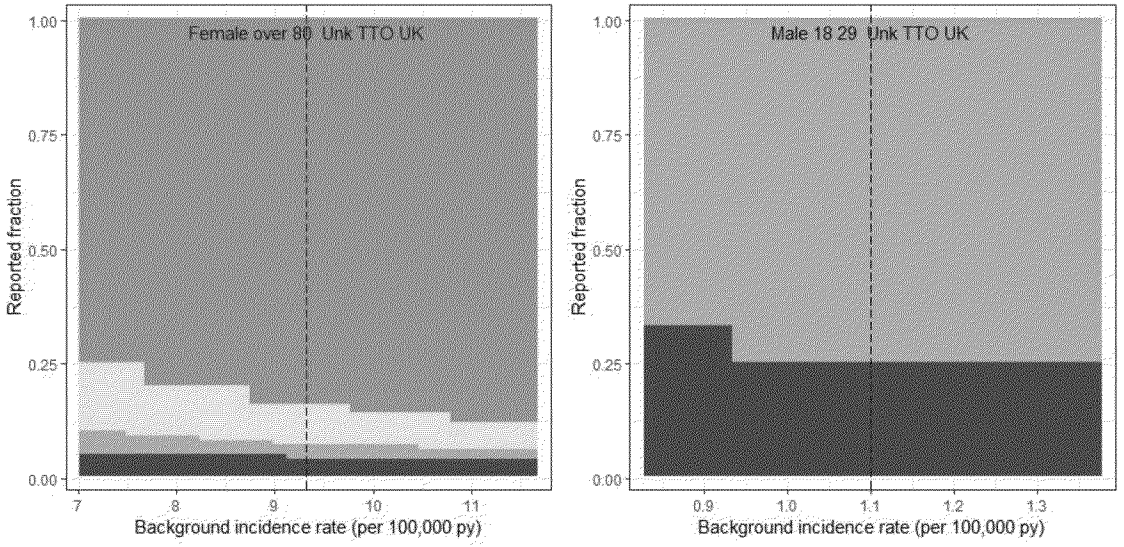

Male 70 79 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.0
2.4
2.8
Background incidence rate (per 100,000 py)

Male over 80 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
8
Background incidence rate (per 100,000 py)

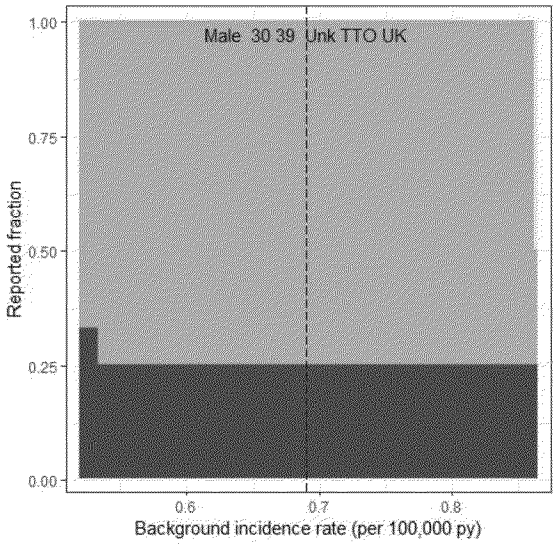

Female 18 29 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.1
2.4
2.7
3.0
Background incidence rate (per 100,000 py)

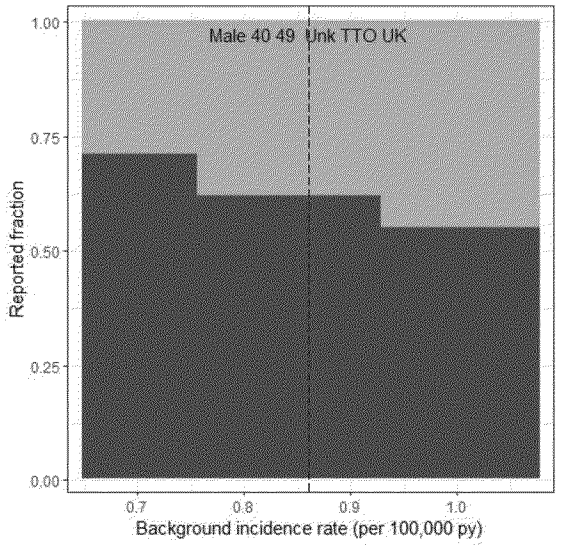

Female 30 39 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.75
2.00
2.25
2.50
2.75
Background incidence rate (per 100,000 py)

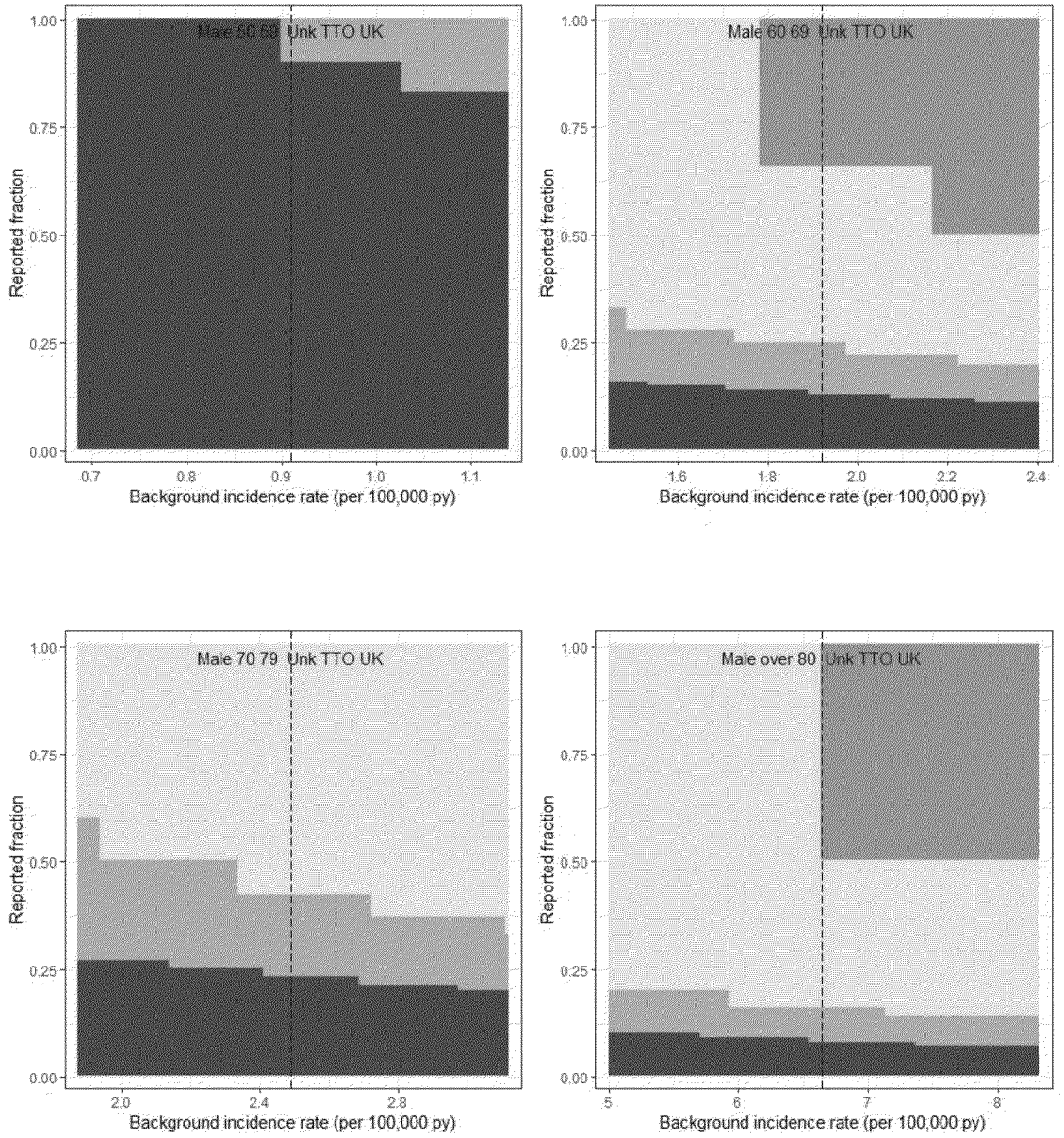

Female 40 49| Unk TTO UK
Female 50 59| Unk TTO UK
Female 60 69| Unk TTO UK
Female 70 79| Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
2.2
0.7
0.8
0.9
1.0
1.2
0.6

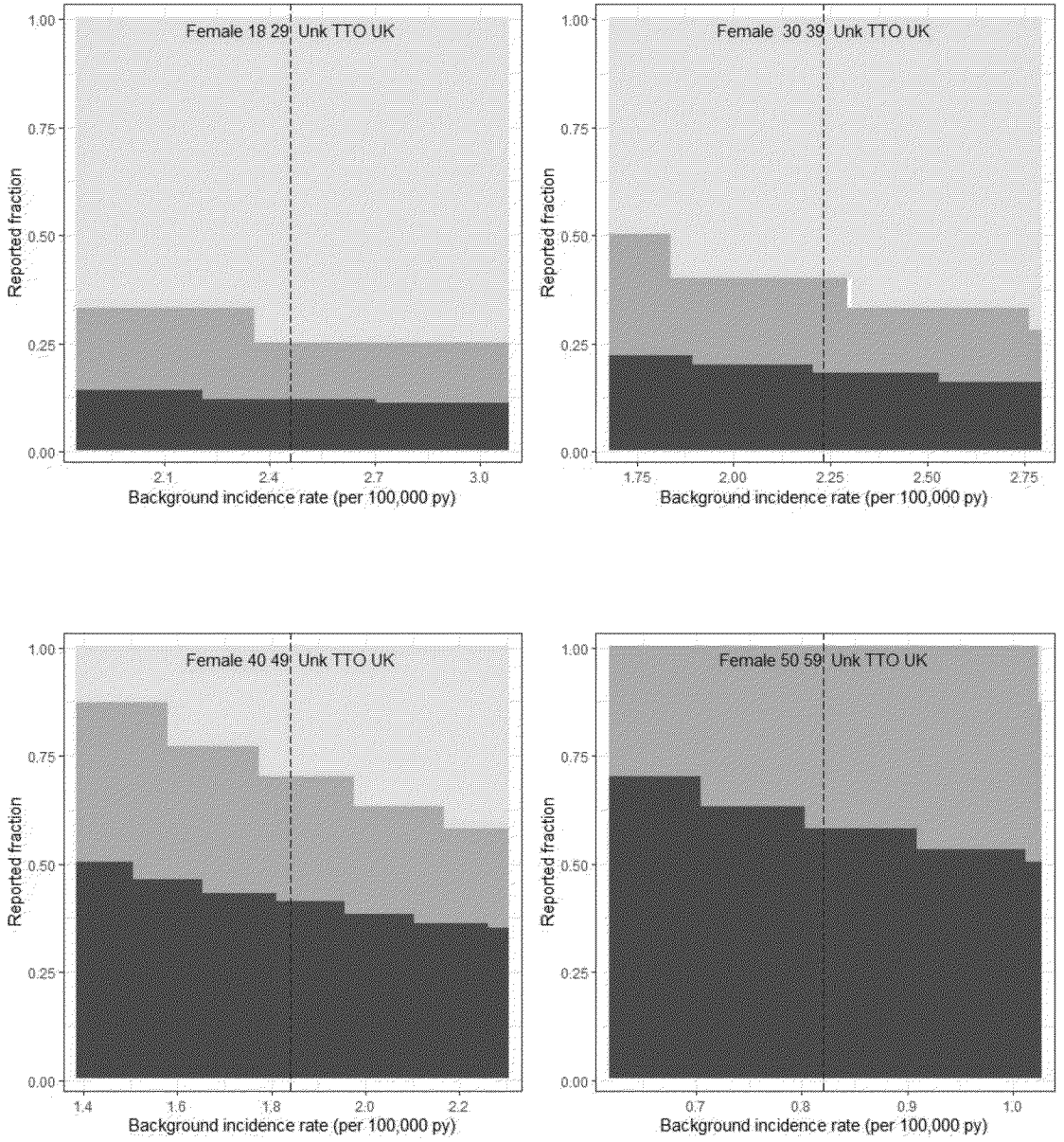

Female over 80 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
7
8
9
10
11
Background incidence rate (per 100,000 py)

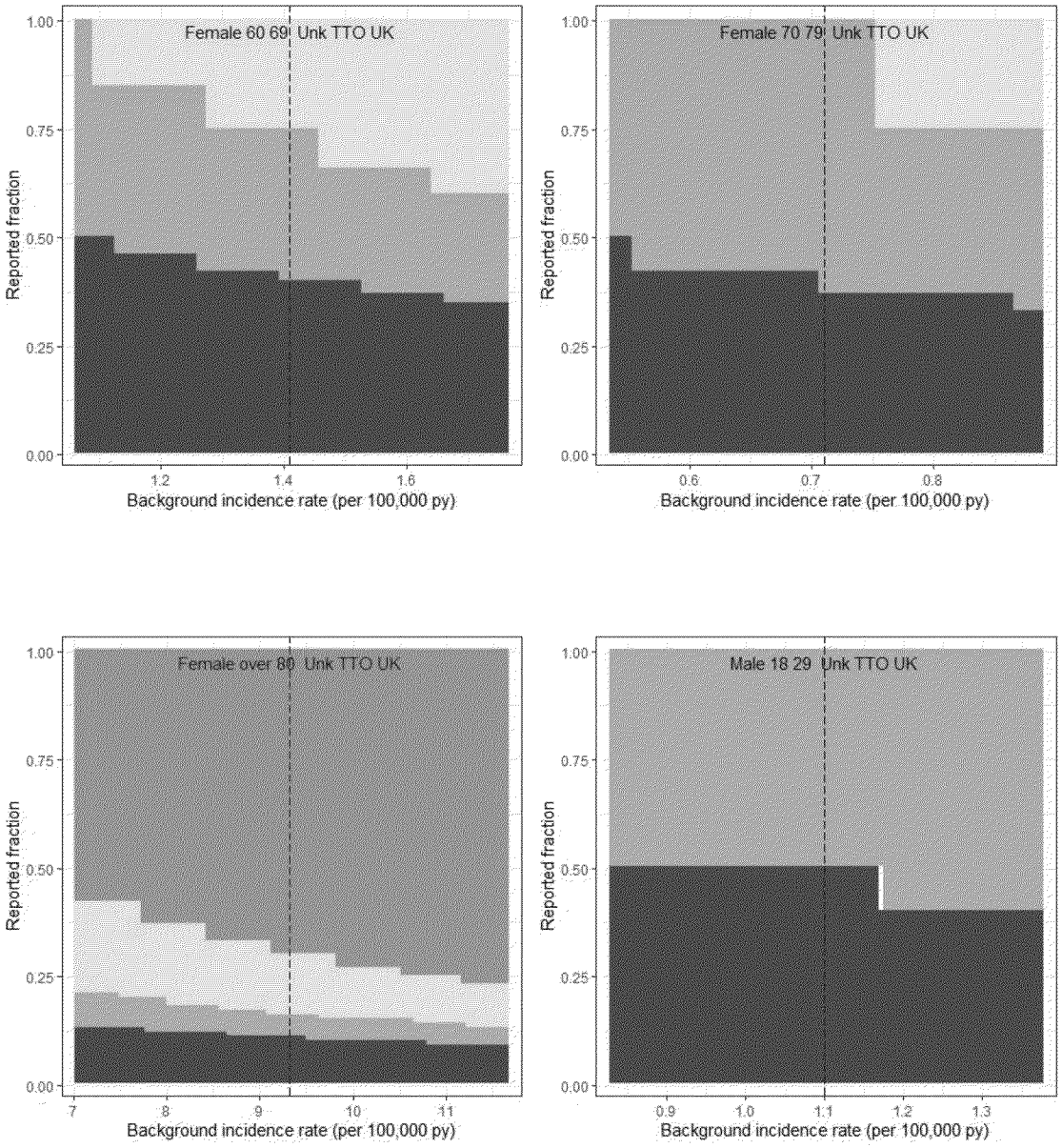
Male 18 29 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.9
1.0
1.1
1.2
1.3
Background incidence rate (per 100,000 py)

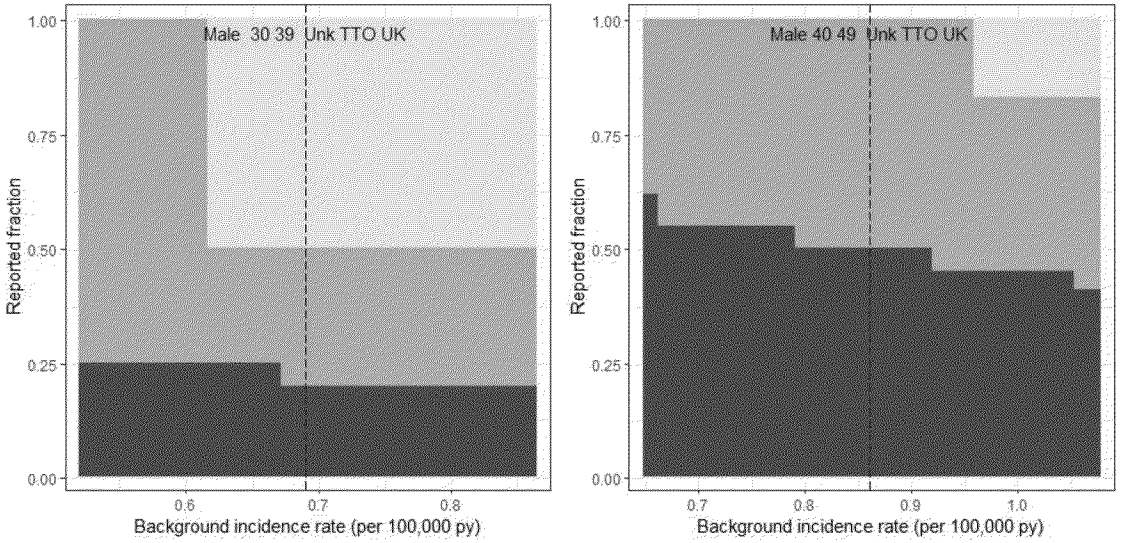

Male 30 39 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)


Male 40 49 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)

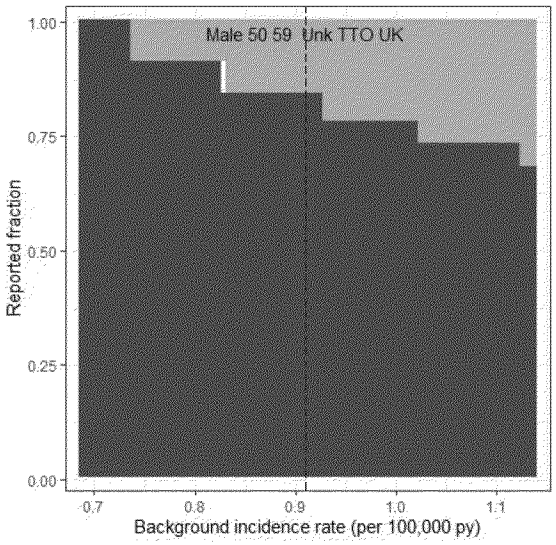

Male 50 59 Unk TTO UK
Male 60 69 Unk TTO UK
Male 70 79 Unk TTO UK
Male over 80 Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
1.6
1.8
2.0
2.2
2.4
2.0
2.4
2.8
5
6
7
8


Female 18 29 Unk TTO UK
Female 30 39 Unk TTO UK
Female 40 49 Unk TTO UK
Female 50 59 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.1
2.4
2.7
3.0
1.75
2.00
2.25
2.50
2.75
1.4
1.6
1.8
2.0
2.2
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)


Female 60 69 Unk TTO UK
Female 70 79 Unk TTO UK
Female over 80 Unk TTO UK
Male 18 29 Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00


Male 30 39 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.6
0.7
0.8
Background incidence rate (per 100,000 py)

Male 40 49 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)


Male 50 59 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)

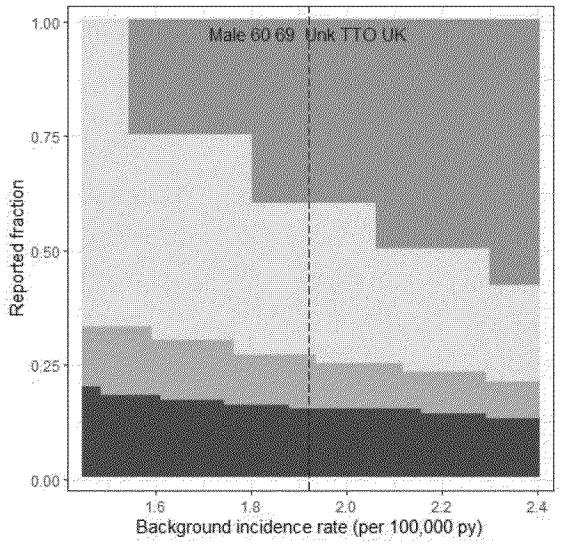
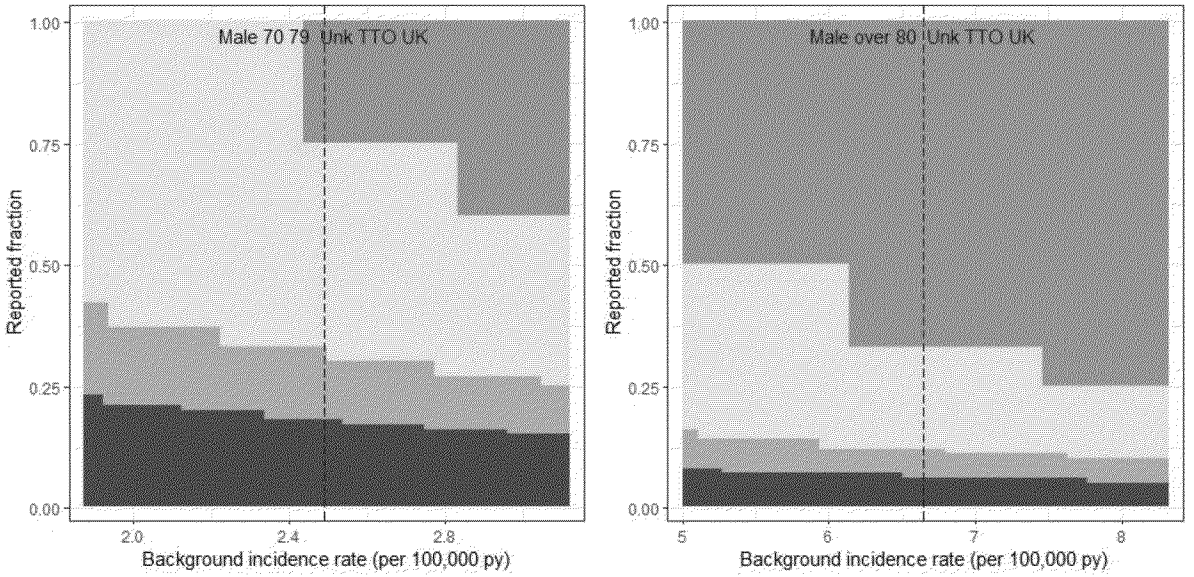

Male 60 69 Unk TTO UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.6
1.8
2.0
2.2
2.4
Background incidence rate (per 100,000 py)

Table 80 **Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK including unknown TTO_TRUVEN 14**

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

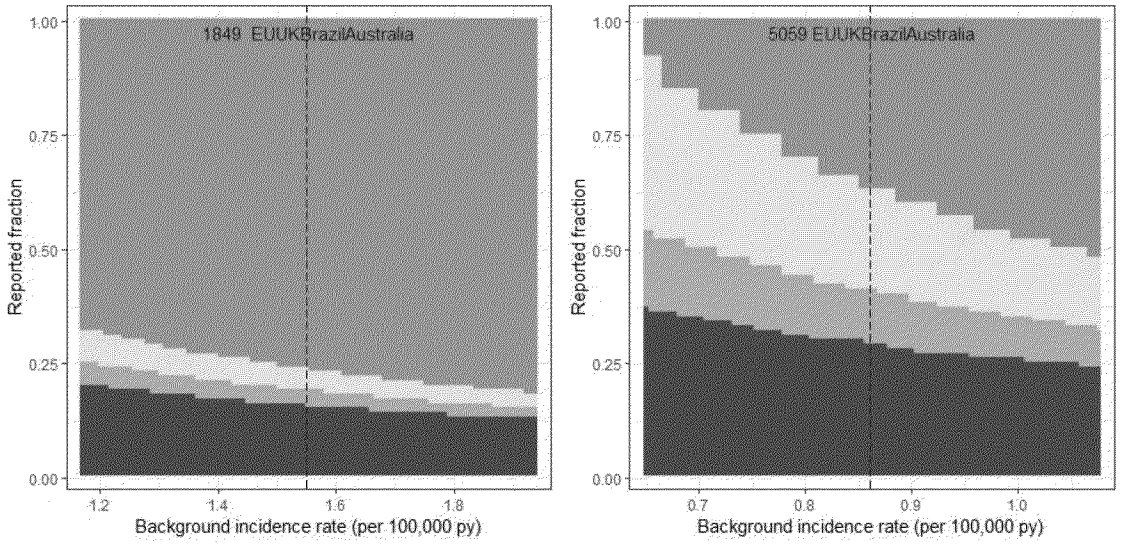
CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, UK United Kingdom

Table 81 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from EEA+UK+Brazil+Australia region including unknown TTO_TRUVEN 14

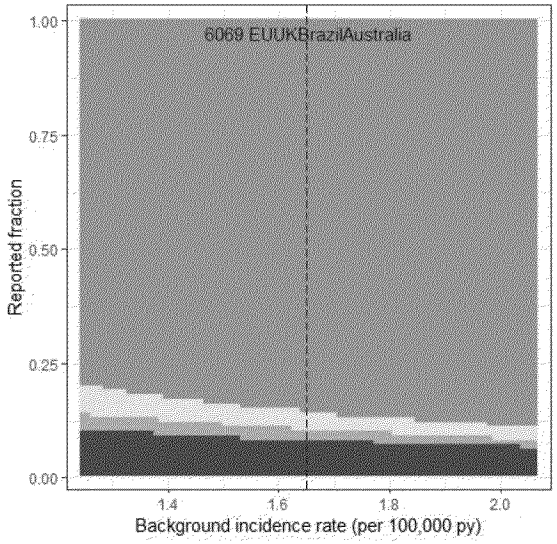
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18 to 49	19	98.12	21	1.55	110094983	0.19 (0.12 - 0.3)	Observed significantly < expected
50 to 59	12	28.85	21	0.86	58336094	0.42 (0.21 - 0.73)	Observed significantly < expected
60 to 69	6	54.99	21	1.65	57960860	0.11 (0.04 - 0.24)	Observed significantly < expected
Over 70	7	16.75	21	0.9	32376365	0.42 (0.17 - 0.86)	Observed significantly < expected
18 to 49	21	140.16	30	1.55	110094983	0.15 (0.09 - 0.23)	Observed significantly < expected
50 to 59	17	41.21	30	0.86	58336094	0.41 (0.24 - 0.66)	Observed significantly < expected
60 to 69	9	78.55	30	1.65	57960860	0.11 (0.05 - 0.22)	Observed significantly < expected
Over 70	10	23.93	30	0.9	32376365	0.42 (0.2 - 0.77)	Observed significantly < expected
18 to 49	23	196.23	42	1.55	110094983	0.12 (0.07 - 0.18)	Observed significantly < expected
50 to 59	19	57.69	42	0.86	58336094	0.33 (0.2 - 0.51)	Observed significantly < expected
60 to 69	12	109.97	42	1.65	57960860	0.11 (0.06 - 0.19)	Observed significantly < expected
Over 70	13	33.51	42	0.9	32376365	0.39 (0.21 - 0.66)	Observed significantly < expected
18 to 49 (including unknown TTO)	26	98.12	21	1.55	110094983	0.26 (0.17 - 0.39)	Observed significantly < expected
50 to 59 (including unknown TTO)	16	28.85	21	0.86	58336094	0.55 (0.32 - 0.9)	Observed significantly < expected
60 to 69 (including unknown TTO)	8	54.99	21	1.65	57960860	0.15 (0.06 - 0.29)	Observed significantly < expected
Over 70 (including unknown TTO)	12	16.75	21	0.9	32376365	0.72 (0.37 - 1.25)	Observed < expected

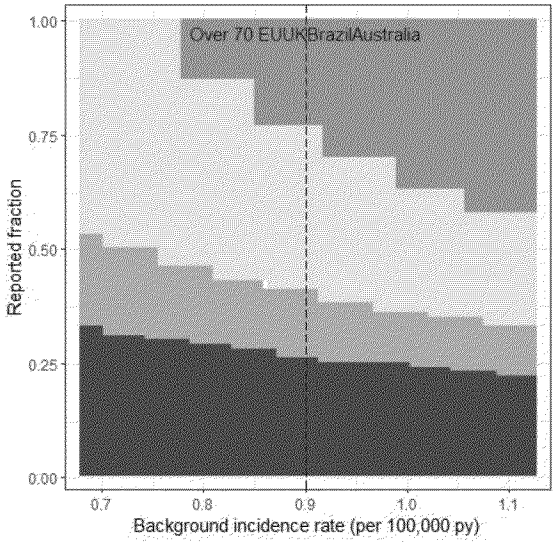
Table 81 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from EEA+UK+Brazil+Australia region including unknown TTO_TRUVEN 14

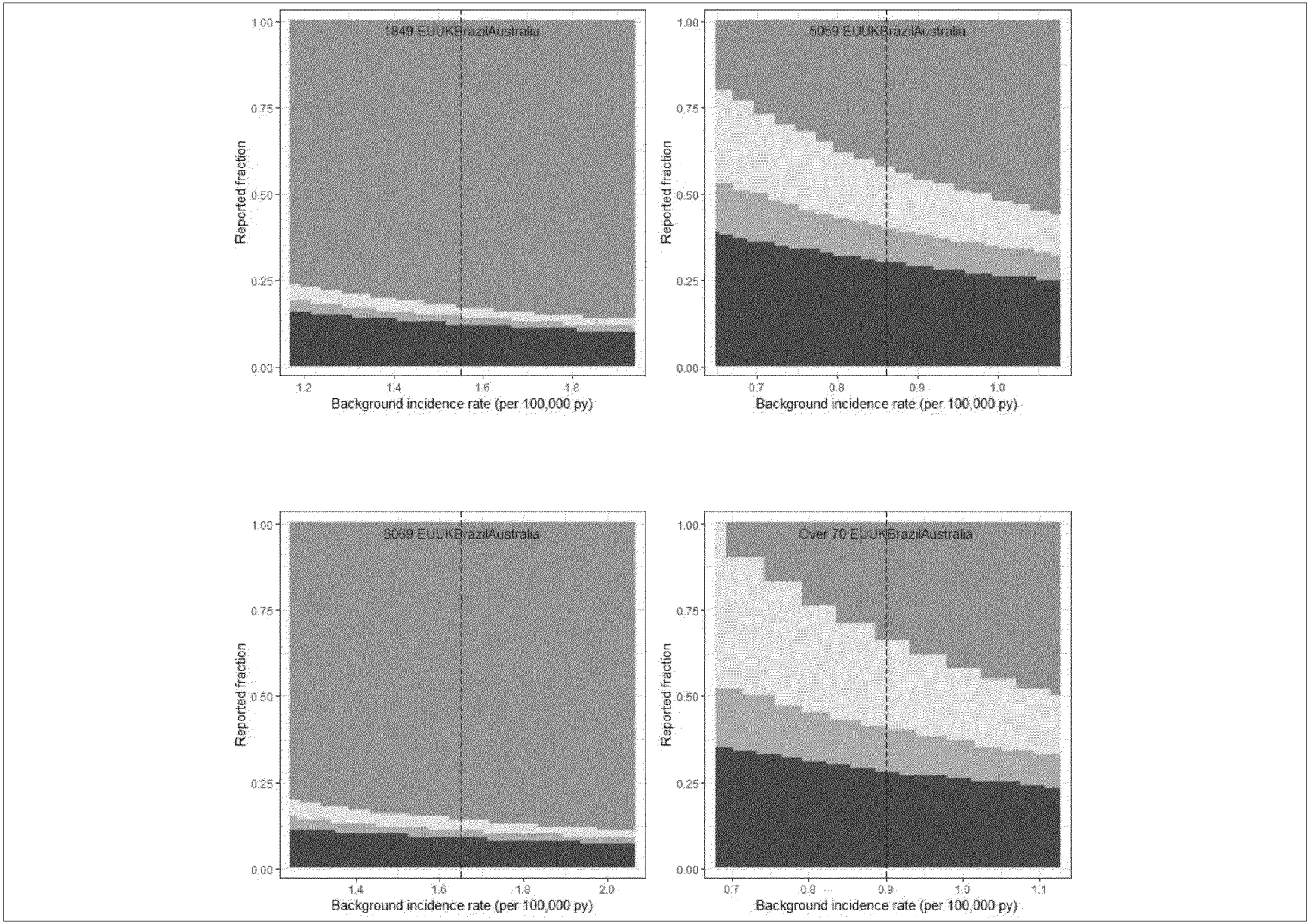
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18 to 49 (including unknown TTO)	28	140.16	30	1.55	110094983	0.2 (0.13 - 0.29)	Observed significantly < expected
50 to 59 (including unknown TTO)	21	41.21	30	0.86	58336094	0.51 (0.32 - 0.78)	Observed significantly < expected
60 to 69 (including unknown TTO)	11	78.55	30	1.65	57960860	0.14 (0.07 - 0.25)	Observed significantly < expected
Over 70 (including unknown TTO)	15	23.93	30	0.9	32376365	0.63 (0.35 - 1.03)	Observed < expected
18 to 49 (including unknown TTO)	30	196.23	42	1.55	110094983	0.15 (0.1 - 0.22)	Observed significantly < expected
50 to 59 (including unknown TTO)	23	57.69	42	0.86	58336094	0.4 (0.25 - 0.6)	Observed significantly < expected
60 to 69 (including unknown TTO)	14	109.97	42	1.65	57960860	0.13 (0.07 - 0.21)	Observed significantly < expected
Over 70 (including unknown TTO)	18	33.51	42	0.9	32376365	0.54 (0.32 - 0.85)	Observed significantly < expected

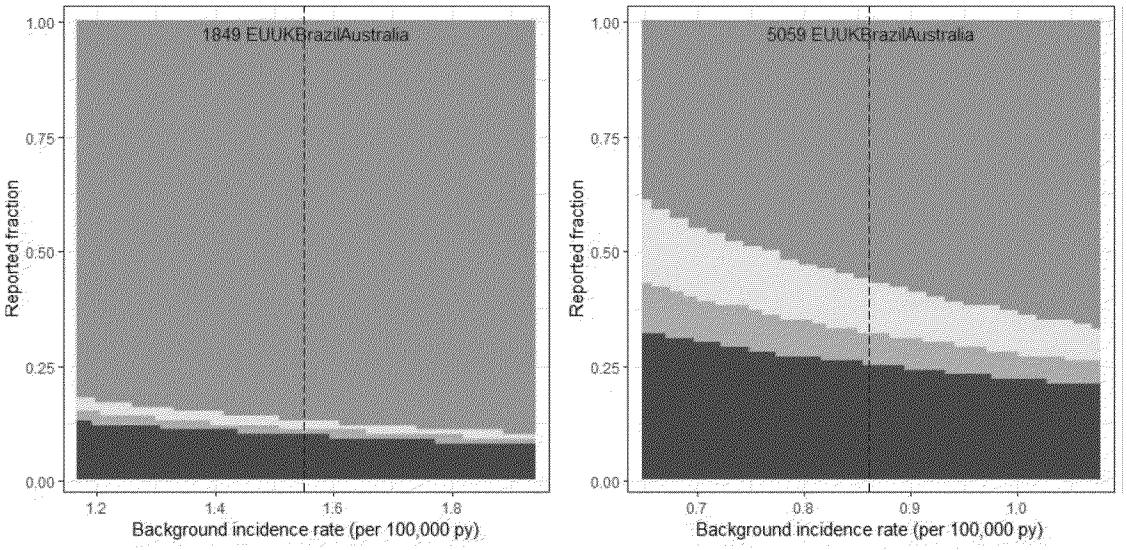

1849 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
1.8
Background incidence rate (per 100,000 py)

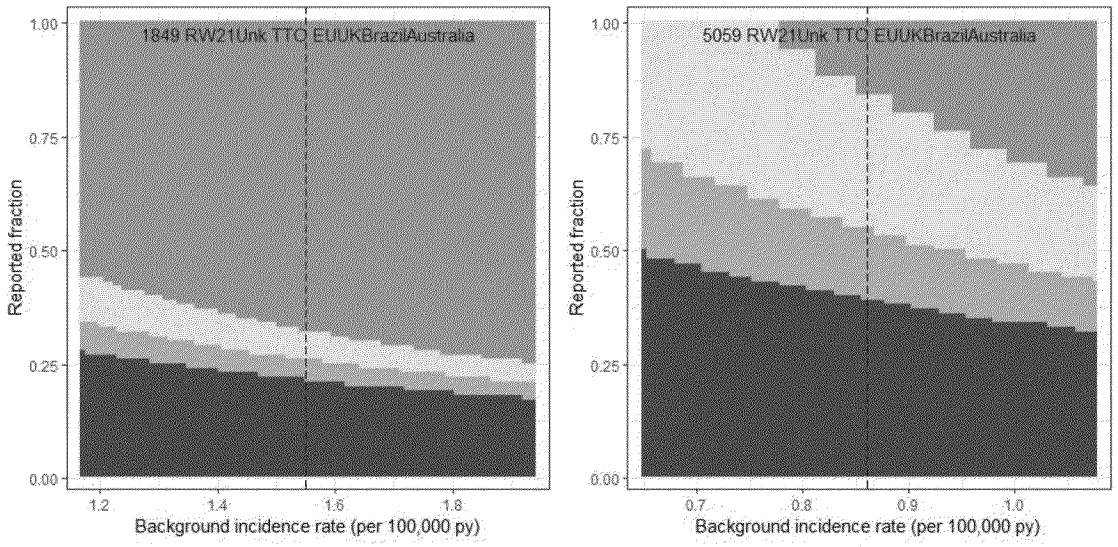
5069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)


6069 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.4
1.6
1.8
2.0
Background incidence rate (per 100,000 py)

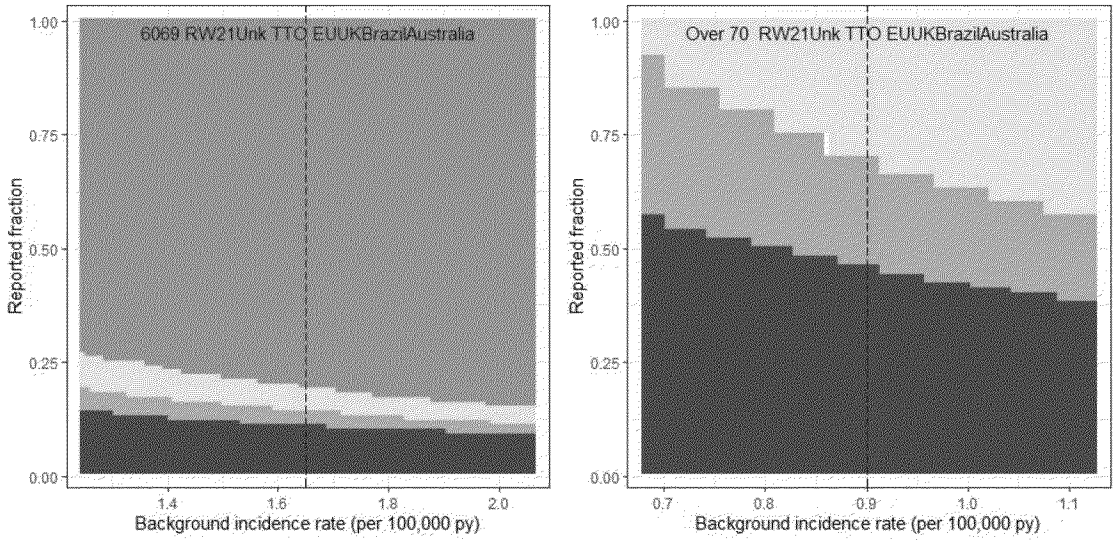

Over 70 EUUKBrazilAustralia
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.1
Background incidence rate (per 100,000 py)


1849 EUUKBrazilAustralia
5059 EUUKBrazilAustralia
6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
1.2
1.4
1.6
1.8
0.7
0.8
0.9
1.0
2.0
1.1


1849 EUUKBrazilAustralia
5059 EUUKBrazilAustralia
6069 EUUKBrazilAustralia
Over 70 EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)


1849 RW21Unk TTO EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

5059 RW21Unk TTO EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)


6069 RW21Unk TTO EUUKBrazilAustralia
Over 70 RW21Unk TTO EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)

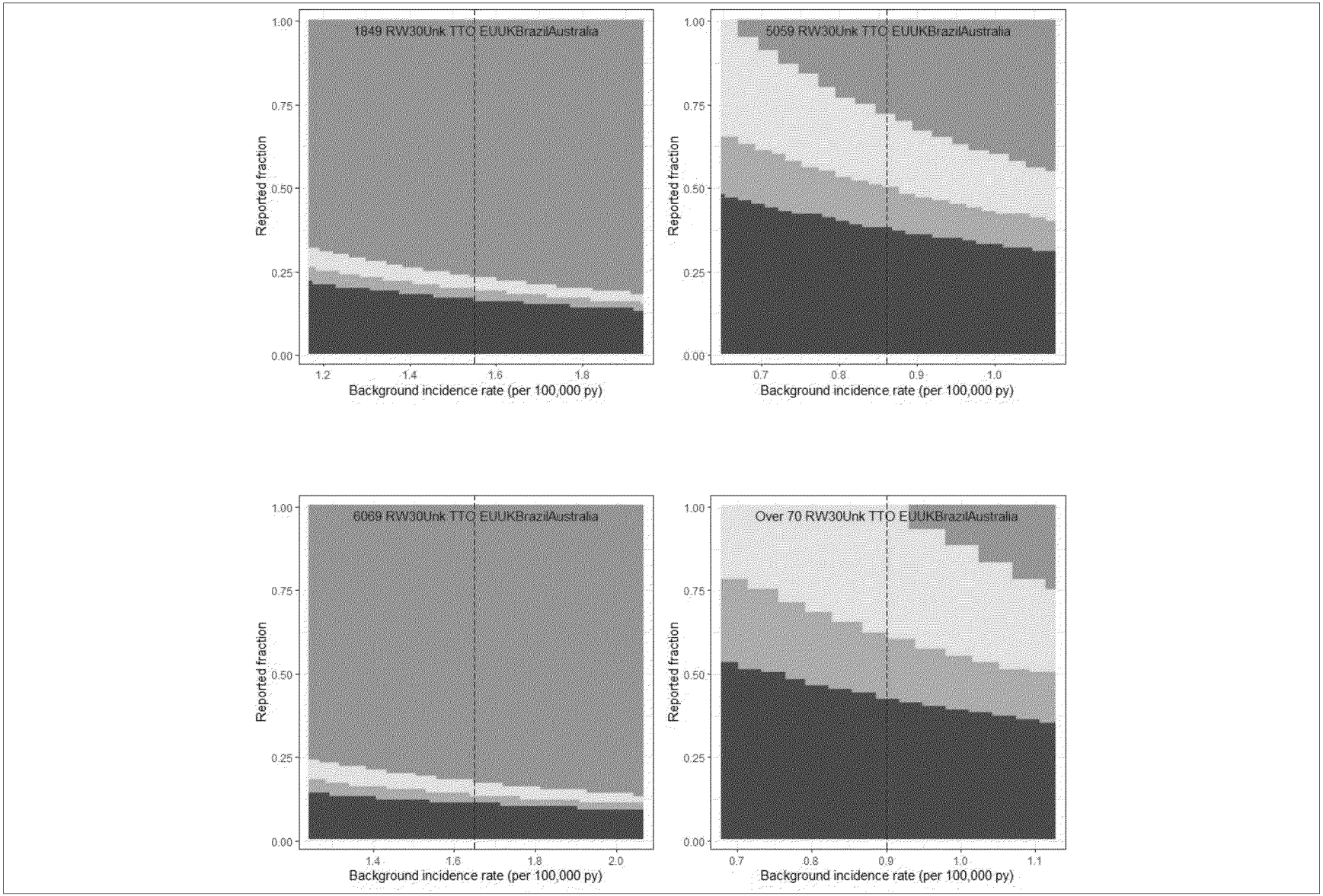
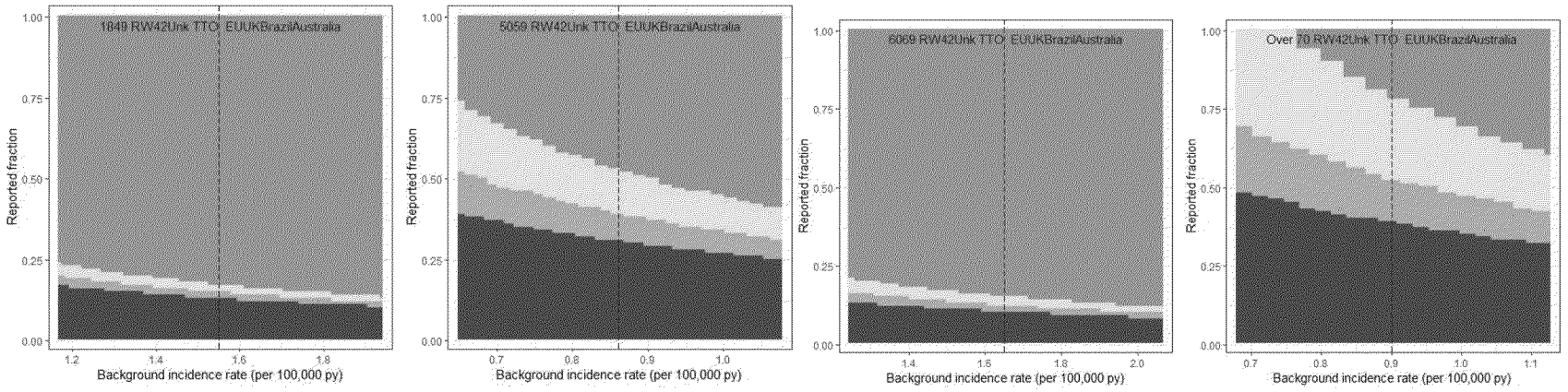

1849 RW30Unk TTO EUUKBrazilAustralia
5059 RW30Unk TTO EUUKBrazilAustralia
6069 RW30Unk TTO EUUKBrazilAustralia
Over 70 RW30Unk TTO EUUKBrazilAustralia
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
1.2
1.4
1.6
1.8
0.7
0.8
0.9
1.0
1.1
2.0

Table 81 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from EEA+UK+Brazil+Australia region including unknown TTO_TRUVEN 14

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; EEA European Economic Area; EU European; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, UK United Kingdom

Table 82 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK including unknown TTO_TRUVEN 14

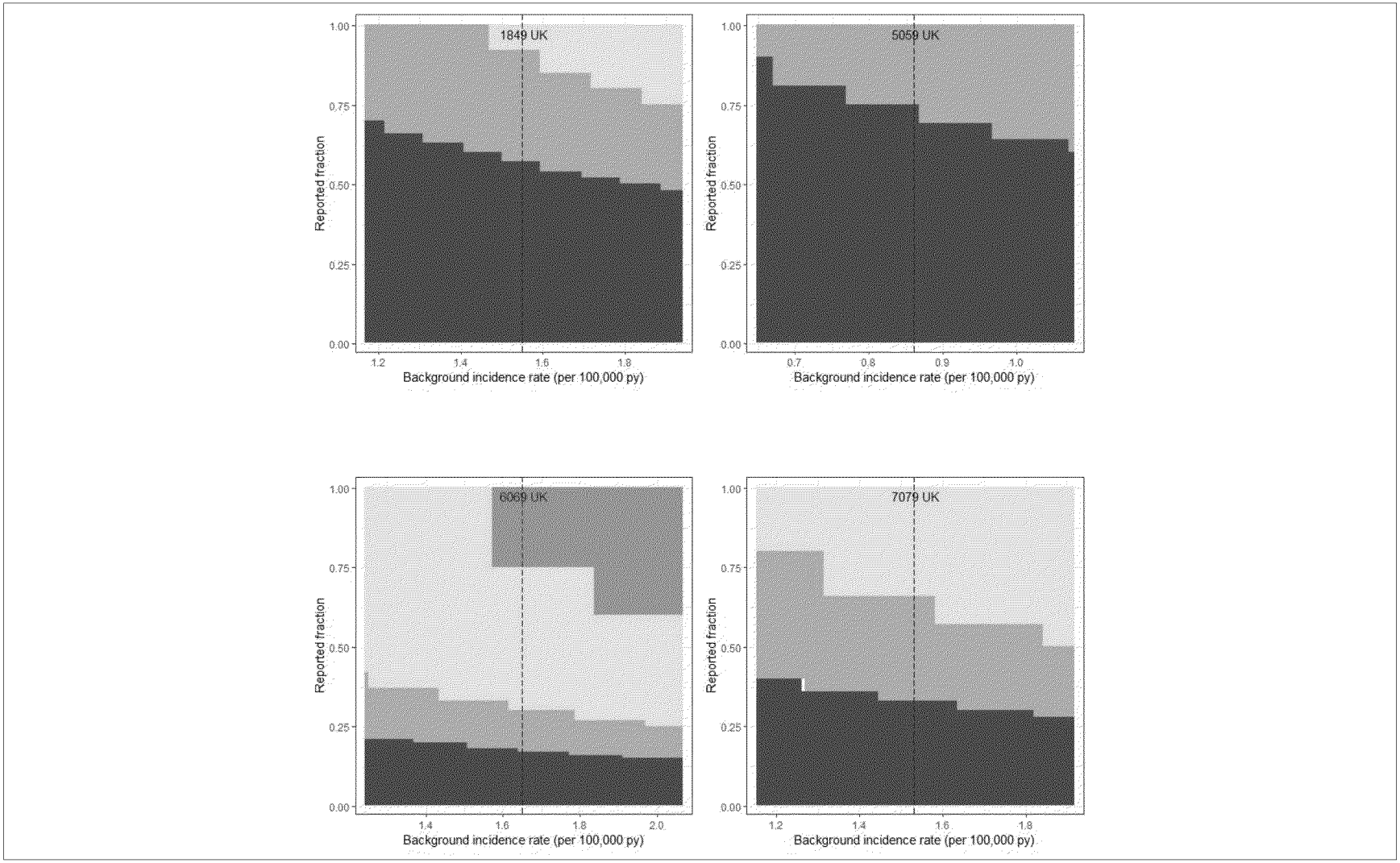
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
18 to 49	12	12.64	21	1.55	14181834	0.95 (0.49 - 1.66)	Observed < expected
50 to 59	9	6.16	21	0.86	12455887	1.46 (0.67 - 2.77)	Observed > expected
60 to 69	3	9.22	21	1.65	9718273	0.33 (0.07 - 0.95)	Observed significantly < expected
70 to 79	4	5.82	21	1.53	6613249	0.69 (0.19 - 1.76)	Observed < expected
Over 80	1	12.53	21	8.21	2655389	0.08 (0 - 0.44)	Observed significantly < expected
18 to 49	13	18.06	30	1.55	14181834	0.72 (0.38 - 1.23)	Observed < expected
50 to 59	12	8.8	30	0.86	12455887	1.36 (0.7 - 2.38)	Observed > expected
60 to 69	5	13.17	30	1.65	9718273	0.38 (0.12 - 0.89)	Observed significantly < expected
70 to 79	5	8.31	30	1.53	6613249	0.6 (0.2 - 1.4)	Observed < expected
Over 80	1	17.91	30	8.21	2655389	0.06 (0 - 0.31)	Observed significantly < expected
18 to 49	15	25.28	42	1.55	14181834	0.59 (0.33 - 0.98)	Observed significantly < expected
50 to 59	14	12.32	42	0.86	12455887	1.14 (0.62 - 1.91)	Observed > expected
60 to 69	7	18.44	42	1.65	9718273	0.38 (0.15 - 0.78)	Observed significantly < expected
70 to 79	5	11.64	42	1.53	6613249	0.43 (0.14 - 1)	Observed < expected
Over 80	3	25.07	42	8.21	2655389	0.12 (0.02 - 0.35)	Observed significantly < expected
18 to 49 (Including unknown TTO)	15	12.64	21	1.55	14181834	1.19 (0.66 - 1.96)	Observed > expected
50 to 59 (Including unknown TTO)	13	6.16	21	0.86	12455887	2.11 (1.12 - 3.61)	Observed significantly > expected
60 to 69 (Including unknown TTO)	5	9.22	21	1.65	9718273	0.54 (0.18 - 1.27)	Observed < expected

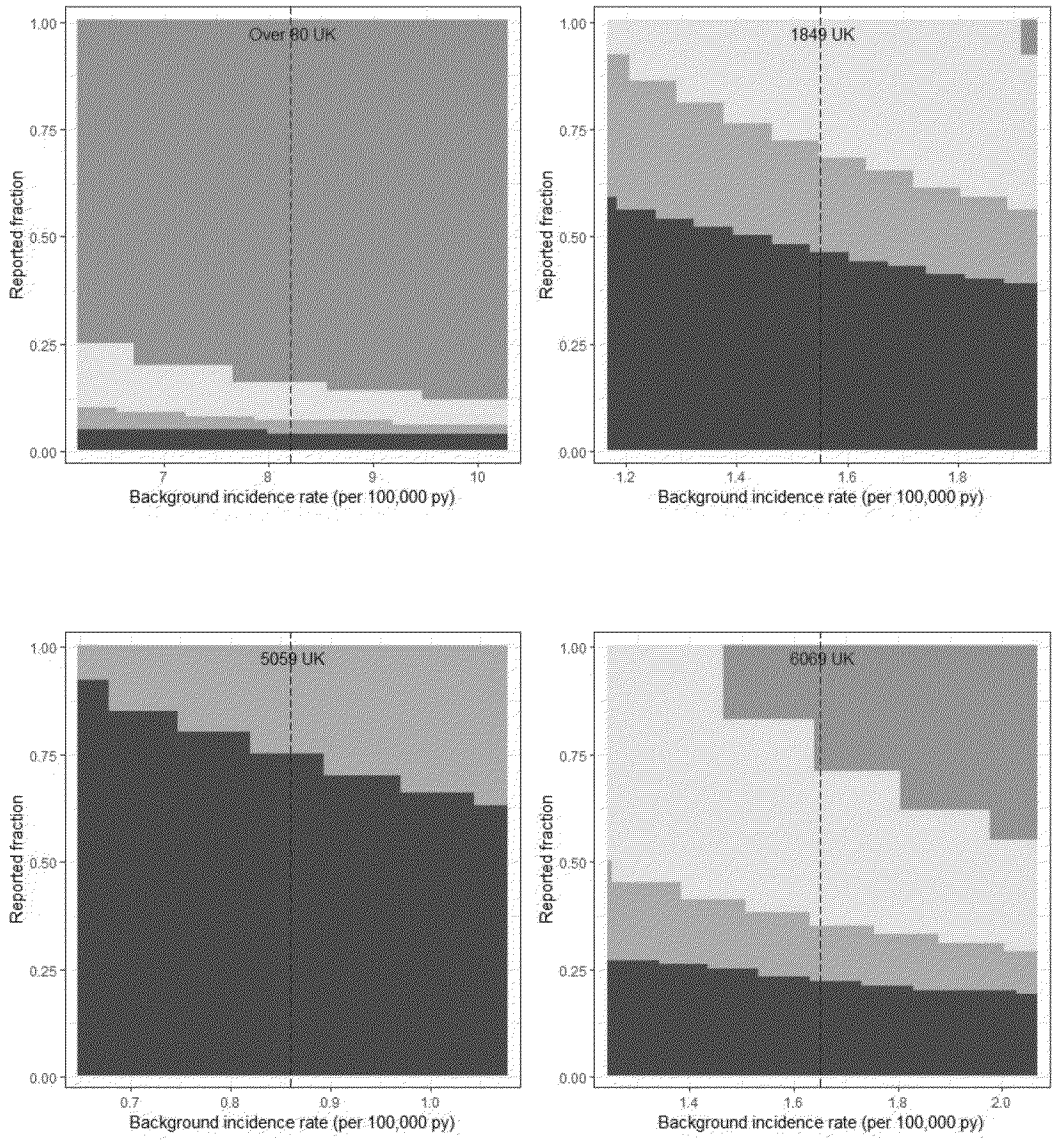
Table 82 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK including unknown TTO_TRUVEN 14

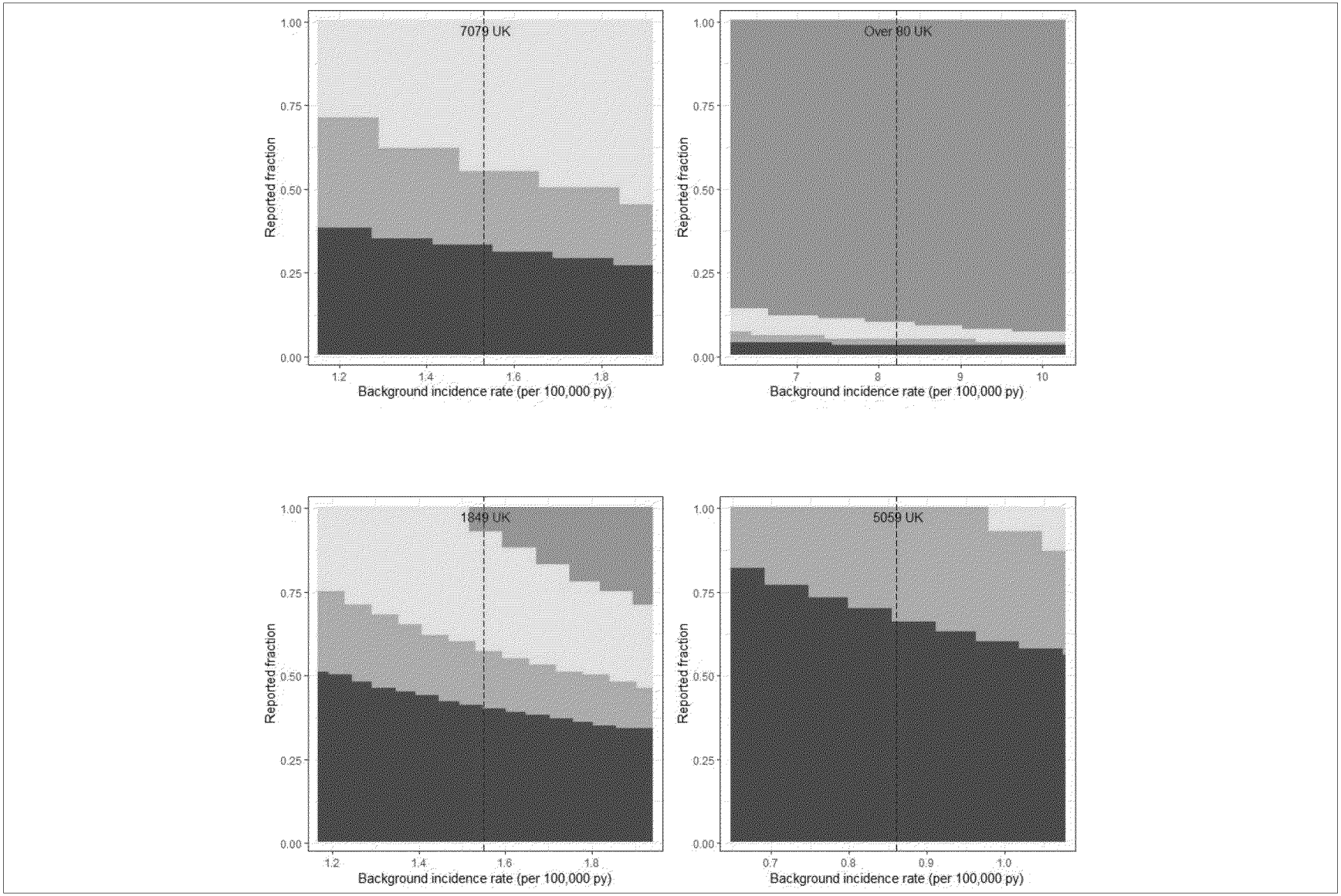
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
70 to (Including unknown TTO)	5	5.82	21	1.53	6613249	0.86 (0.28 - 2)	Observed < expected
Over 80 (Including unknown TTO)	2	12.53	21	8.21	2655389	0.16 (0.02 - 0.58)	Observed significantly < expected
18 to 49 (Including unknown TTO)	16	18.06	30	1.55	14181834	0.89 (0.51 - 1.44)	Observed < expected
50 to 59 (Including unknown TTO)	16	8.8	30	0.86	12455887	1.82 (1.04 - 2.95)	Observed significantly > expected
60 to 69 (Including unknown TTO)	7	13.17	30	1.65	9718273	0.53 (0.21 - 1.1)	Observed < expected
70 to 79 (Including unknown TTO)	6	8.31	30	1.53	6613249	0.72 (0.26 - 1.57)	Observed < expected
Over 80 (Including unknown TTO)	2	17.91	30	8.21	2655389	0.11 (0.01 - 0.4)	Observed significantly < expected
18 to 49 (Including unknown TTO)	18	25.28	42	1.55	14181834	0.71 (0.42 - 1.13)	Observed < expected
50 to 59 (Including unknown TTO)	18	12.32	42	0.86	12455887	1.46 (0.87 - 2.31)	Observed > expected
60 to 69 (Including unknown TTO)	9	18.44	42	1.65	9718273	0.49 (0.22 - 0.93)	Observed significantly < expected
70 to 79 (Including unknown TTO)	6	11.64	42	1.53	6613249	0.52 (0.19 - 1.12)	Observed < expected

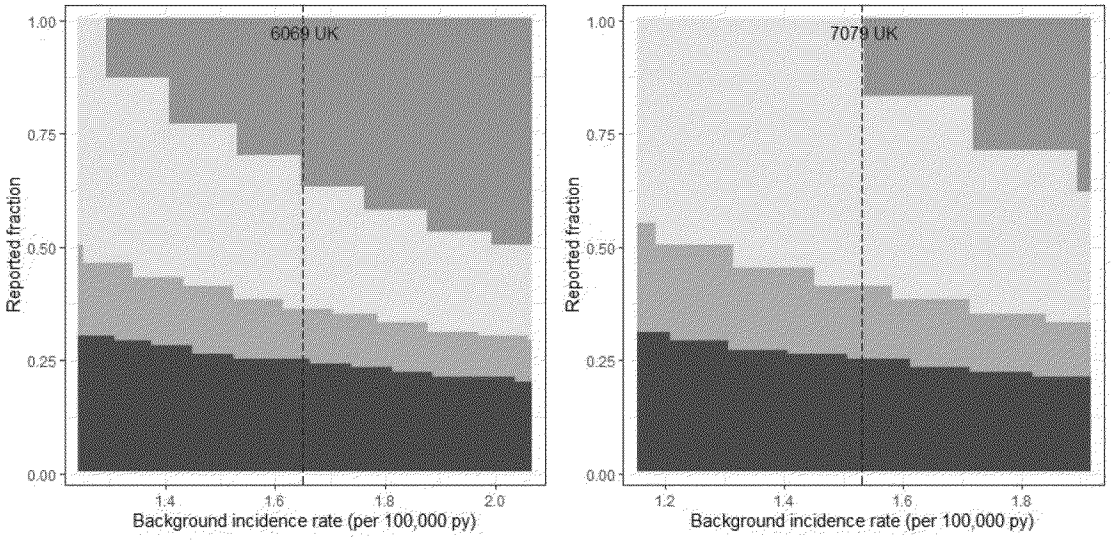
Table 82 Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK including unknown TTO_TRUVEN 14

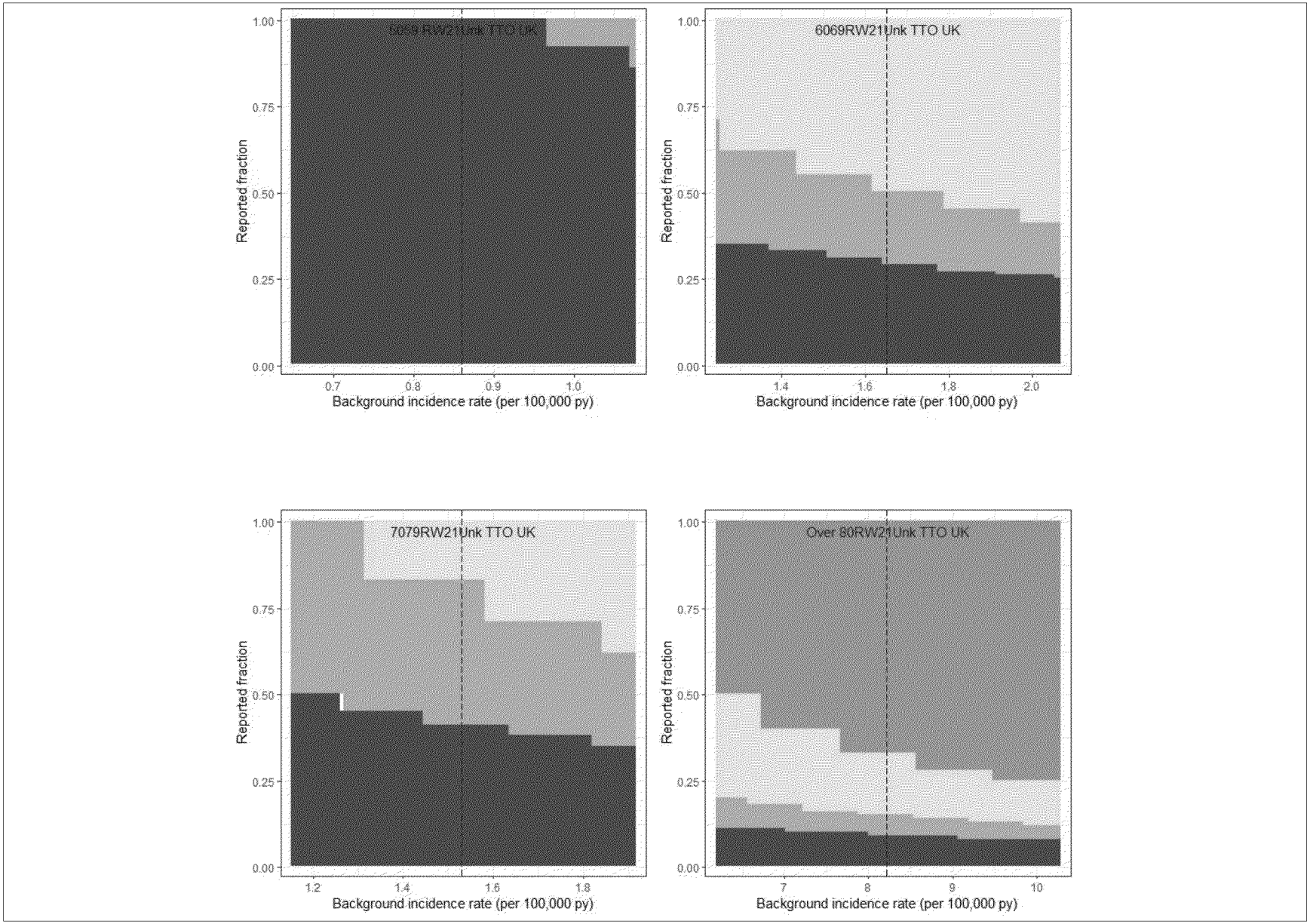
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
Over 80 (Including unknown TTO)	4	25.07	42	8.21	2655389	0.16 (0.04 - 0.41)	Observed significantly < expected

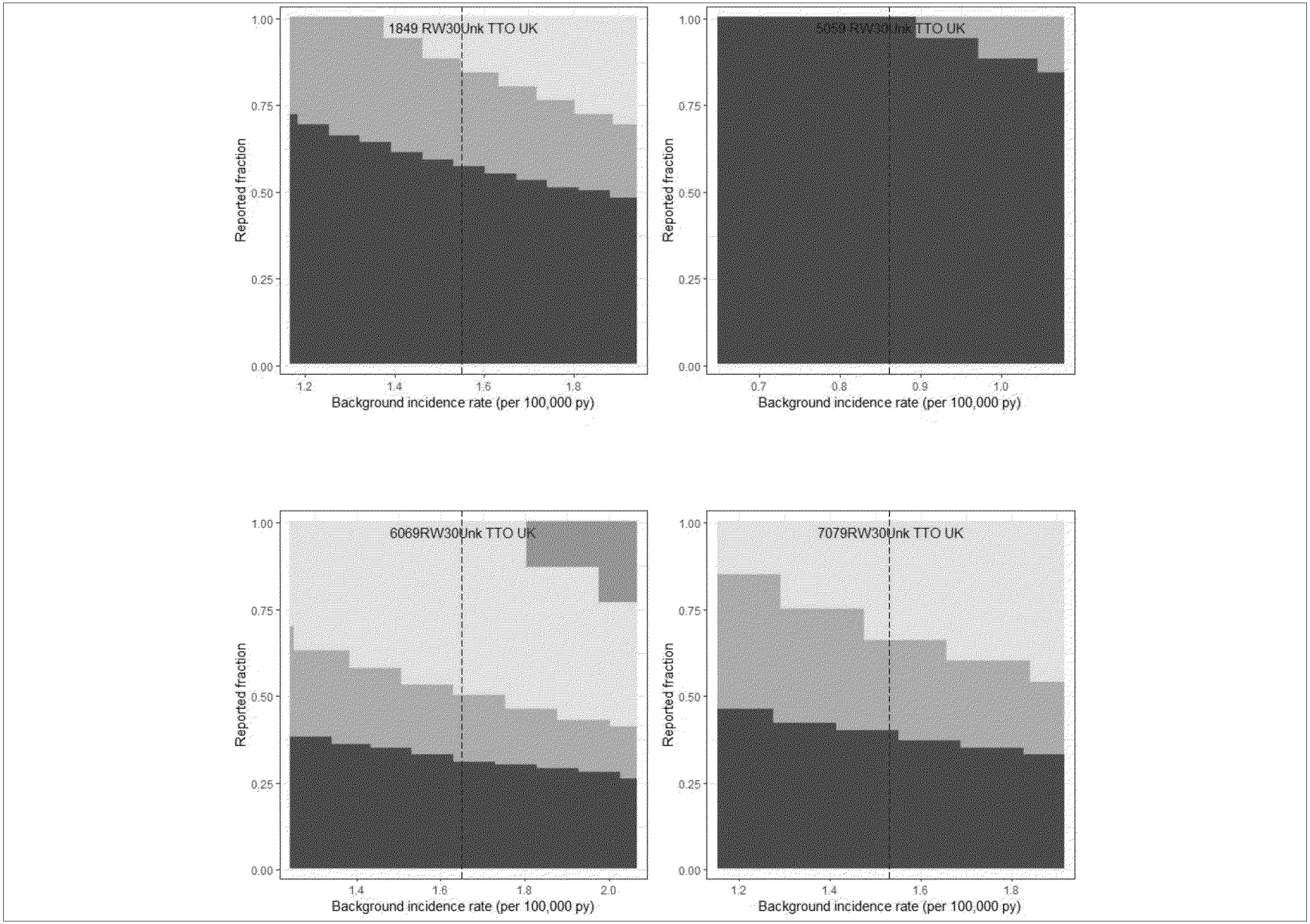

1849 UK
5059 UK
6069 UK
7079 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
1.2
1.4
1.6
1.8
0.7
0.8
0.9
1.0
2.0


Over 80 UK
1849 UK
5059 UK
6069 UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
7
8
9
10
1.2
1.4
1.6
1.8
0.7
0.8
0.9
1.0
2.0


7079 UK
Over 80 UK
1849 UK
5059 UK
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
1.8
7
8
9
10
0.7
0.8
0.9
1.0
Background incidence rate (per 100,000 py)


6069 UK
7079 UK
Over 80 UK
1849 RW21Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
1.4
1.6
1.8
2.0
1.2
7
8
9
10


5059 RW21Unk TTO UK
6069RW21Unk TTO UK
7079RW21Unk TTO UK
Over 80RW21Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
0.7
0.8
0.9
1.0
1.4
1.6
1.8
2.0
1.2
7
8
9
10


1849 RW30Unk TTO UK
5059 RW30Unk TTO UK
6069RW30Unk TTO UK
7079RW30Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
1.2
1.4
1.6
1.8
0.7
0.8
0.9
1.0
2.0

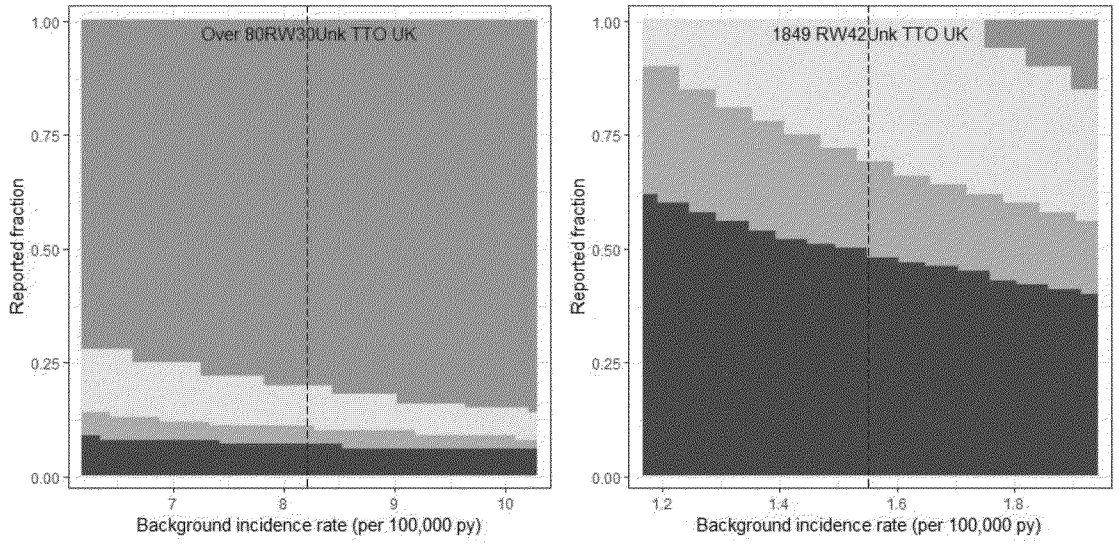
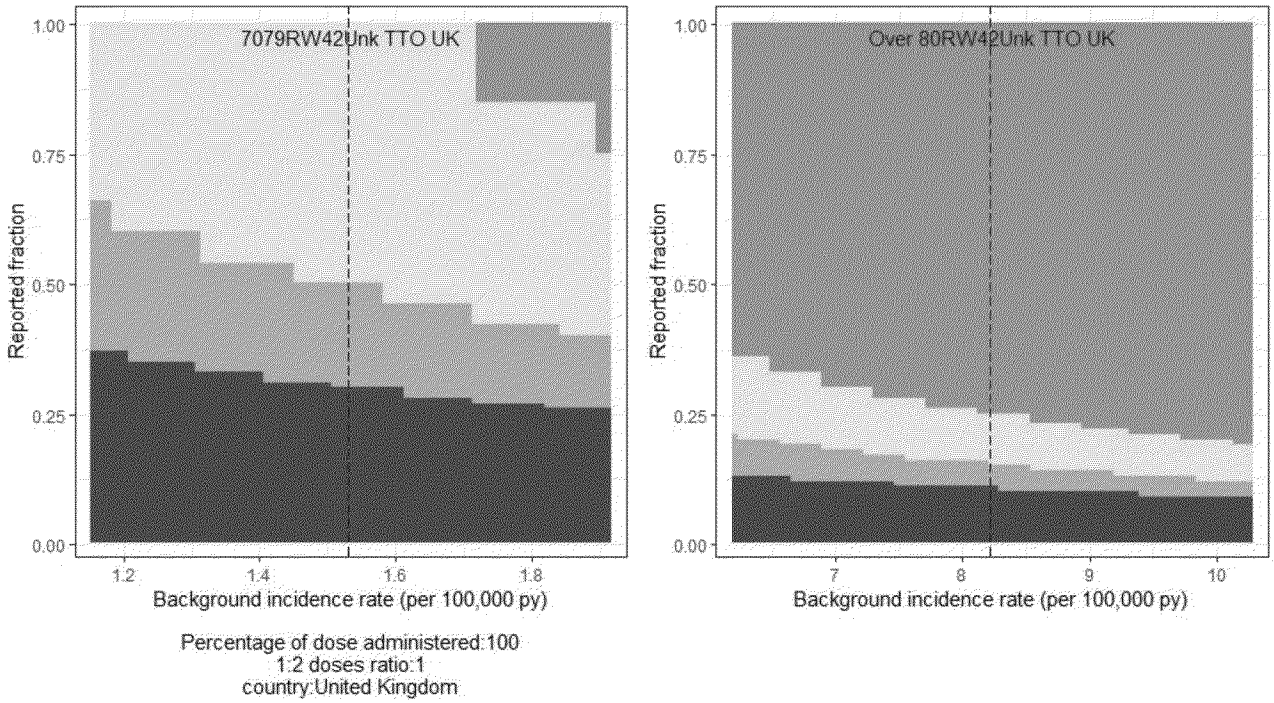

Over 80RW30Unk TTO UK
1849 RW42Unk TTO UK
5059 RW42Unk TTO UK
6069RW42Unk TTO UK
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
7
8
9
10
1.2
1.4
1.6
1.8
0.7
0.8
0.9
1.0
2.0

Table 82 **Observed Versus Expected analysis for Cerebral Venous Sinus Thrombosis (CVST) without thrombocytopenia cases with normal platelets stratified by gender and age from UK including unknown TTO_TRUVEN 14**

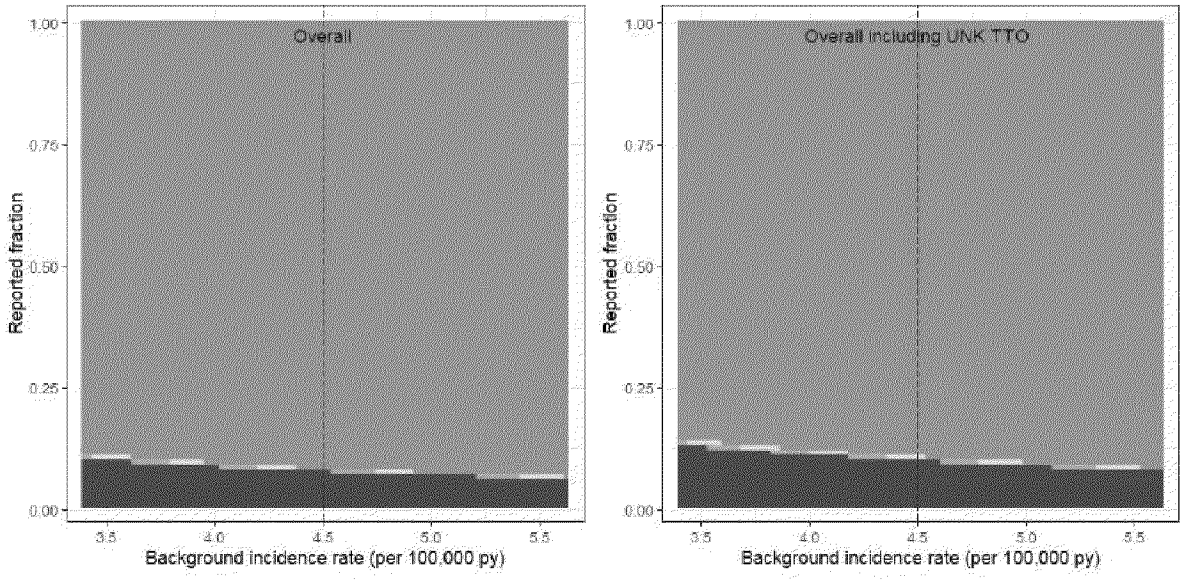
Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Background rates from Truven MarketScan were used - the time window for exclusion of patients with TCP (-1/+14) Included only incident (no CVST claims within 12 months prior to index) inpatient claims.

CVST Cerebral Venous Sinus Thrombosis, CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, UK United Kingdom.

Table 83 Observed Versus Expected analysis for Cutaneous vasculitis

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Overall	195	2319.82	42	4.5	448306152	0.08 (0.07 - 0.1)	Observed significantly < expected
Overall (including Unknown TTO)	247	2319.82	42	4.5	448306152	0.11 (0.09 - 0.12)	Observed significantly < expected



[a] Incidence rate (IR) Source: Arora et al 2014

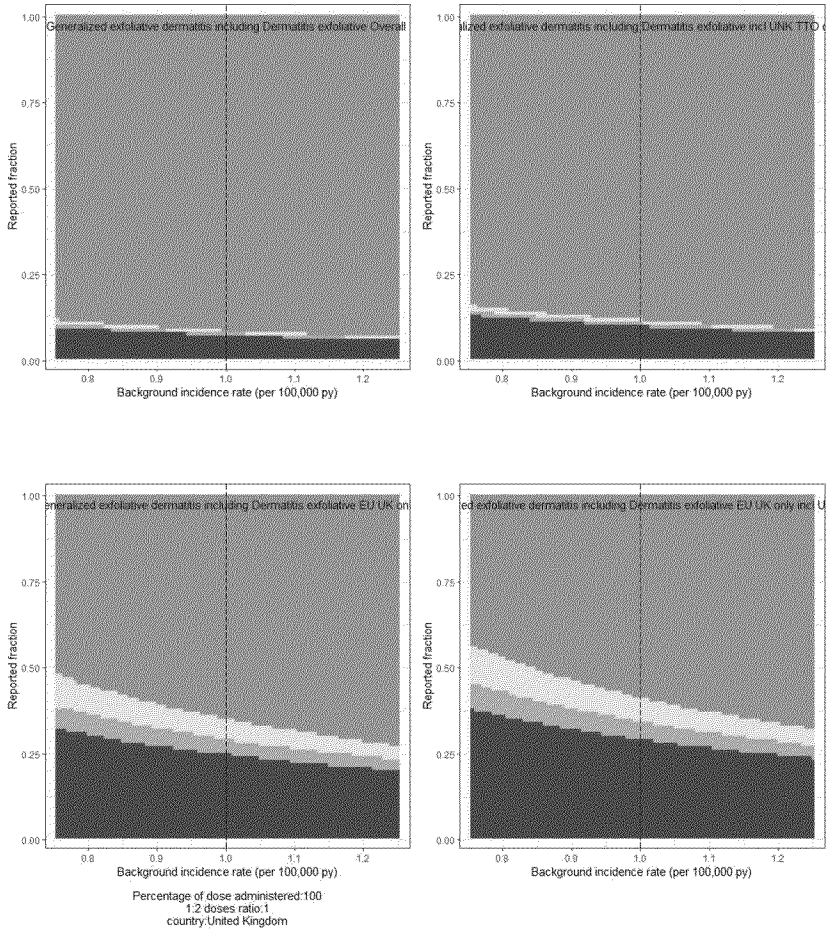
CI Confidence Interval; E Expected; O observed; TTO Time to onset.

Table 84 Observed Vs Expected analysis for Generalized exfoliative dermatitis including Dermatitis exfoliative (Overall)

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Generalized exfoliative dermatitis including Dermatitis exfoliative (Overall)	44	536	42	1	466115644	0.08 (0.06 - 0.11)	Observed significantly < expected
Generalized exfoliative dermatitis including Dermatitis exfoliative incl UNK TTO (overall)	59	536	42	1	466115644	0.11 (0.08 - 0.14)	Observed significantly < expected
Generalized exfoliative dermatitis including Dermatitis exfoliative EU UK only	40	135.37	42	1	117724493	0.3 (0.21 - 0.4)	Observed significantly < expected
Generalized exfoliative dermatitis including Dermatitis exfoliative EU UK only incl UNK TTO	47	135.37	42	1	117724493	0.35 (0.26 - 0.46)	Observed significantly < expected

Table 84 Observed Vs Expected analysis for Generalized exfoliative dermatitis including Dermatitis exfoliative (Overall)

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	



[a] Incidence rate (IR) Source: Truven Marketscan 2019

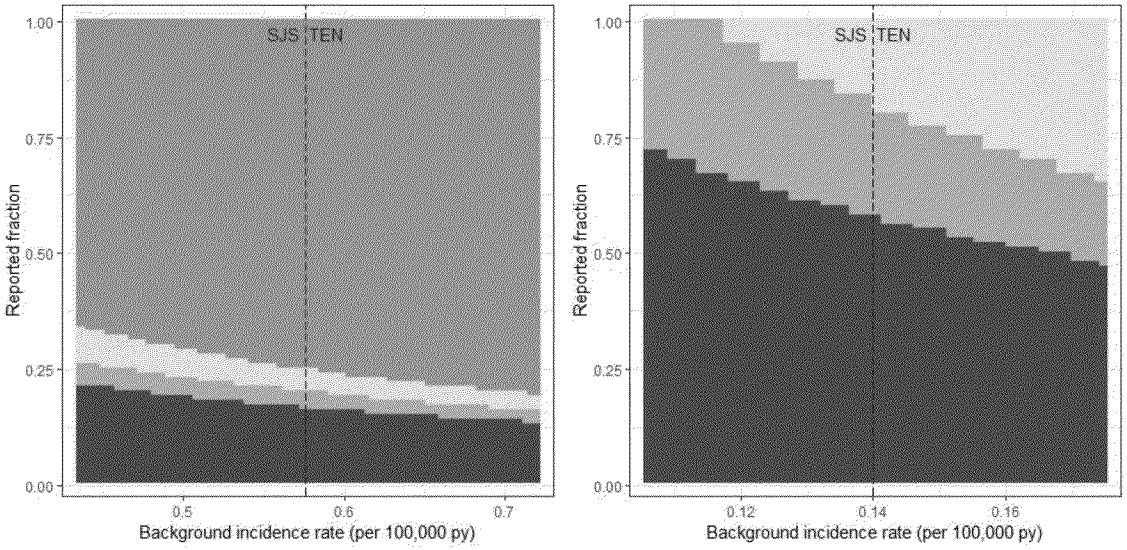
CI Confidence Interval; E Expected; EEA European Economic Area, O observed; TTO Time to onset; Unk Unknown, UK United Kingdom.

Table 85 Observed Vs Expected analysis for Stevens-Johnson syndrome-Toxic epidermal necrolysis (SJS-TEN)

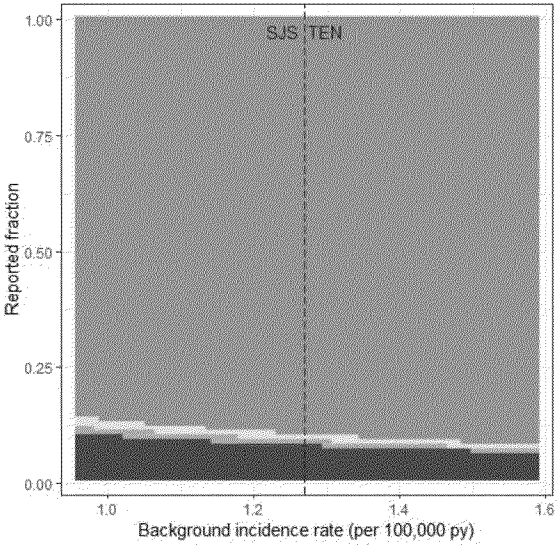
Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
SJS - TEN	21	102.91	14	0.576	466115644	0.2 (0.13 - 0.31)	Observed significantly < expected
SJS - TEN	21	25.01	14	0.14	466115644	0.84 (0.52 - 1.28)	Observed < expected
SJS - TEN	21	226.91	14	1.27	466115644	0.09 (0.06 - 0.14)	Observed significantly < expected
SJS - TEN (incl UNK TTO)	35	102.91	14	0.576	466115644	0.34 (0.24 - 0.47)	Observed significantly < expected
SJS - TEN (incl UNK TTO)	35	25.01	14	0.14	466115644	1.4 (0.97 - 1.95)	Observed > expected
SJS - TEN (incl UNK TTO)	35	226.91	14	1.27	466115644	0.15 (0.11 - 0.21)	Observed significantly < expected
SJS - TEN	24	308.73	42	0.576	466115644	0.08 (0.05 - 0.12)	Observed significantly < expected
SJS - TEN	24	75.04	42	0.14	466115644	0.32 (0.2 - 0.48)	Observed significantly < expected
SJS - TEN	24	680.72	42	1.27	466115644	0.04 (0.02 - 0.05)	Observed significantly < expected
SJS - TEN (incl UNK TTO)	24	308.73	42	0.576	466115644	0.08 (0.05 - 0.12)	Observed significantly < expected
SJS - TEN (incl UNK TTO)	24	75.04	42	0.14	466115644	0.32 (0.2 - 0.48)	Observed significantly < expected
SJS - TEN (incl UNK TTO)	24	680.72	42	1.27	466115644	0.04 (0.02 - 0.05)	Observed significantly < expected
SJS - TEN Overall EU+UK only	12	25.99	14	0.576	117724493	0.46 (0.24 - 0.81)	Observed significantly < expected
SJS - TEN Overall EU+UK only	12	6.32	14	0.14	117724493	1.9 (0.98 - 3.32)	Observed > expected
SJS - TEN Overall EU+UK only	12	57.31	14	1.27	117724493	0.21 (0.11 - 0.37)	Observed significantly < expected

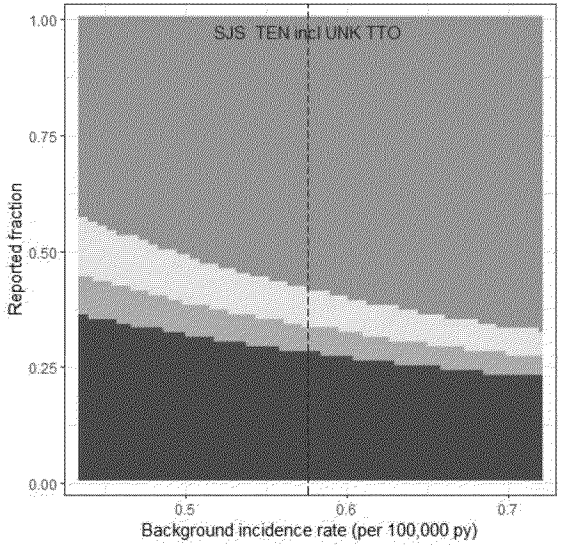
Table 85 Observed Vs Expected analysis for Stevens-Johnson syndrome-Toxic epidermal necrolysis (SJS-TEN)

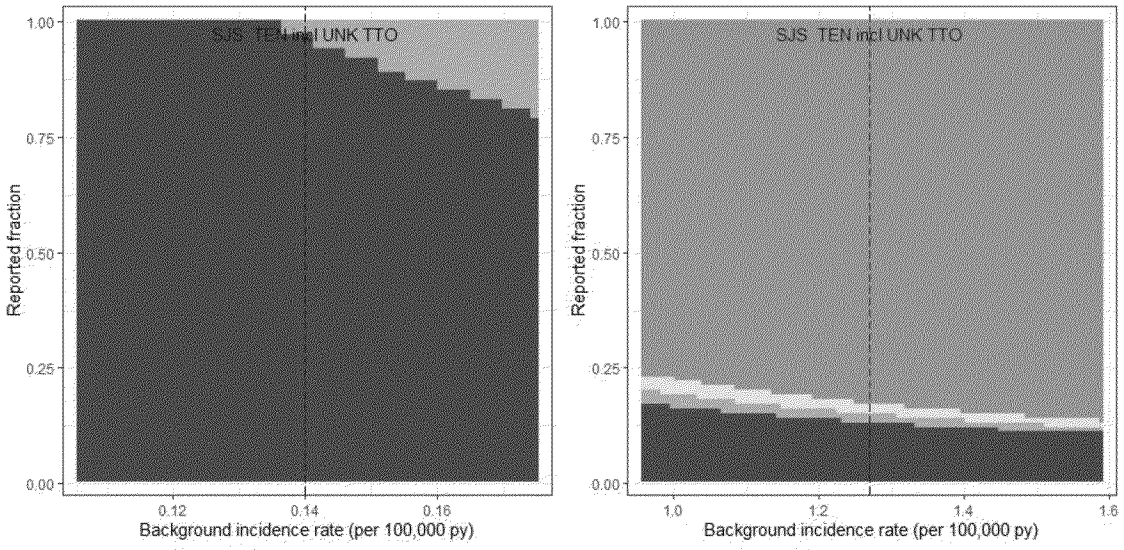
Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
SJS - TEN Overall EU+UK only (incl UNK TTO)	14	25.99	14	0.576	117724493	0.54 (0.29 - 0.9)	Observed significantly < expected
SJS - TEN Overall EU+UK only (incl UNK TTO)	14	6.32	14	0.14	117724493	2.22 (1.21 - 3.72)	Observed significantly > expected
SJS - TEN Overall EU+UK only (incl UNK TTO)	14	57.31	14	1.27	117724493	0.24 (0.13 - 0.41)	Observed significantly < expected
SJS - TEN Overall EU+UK only	14	77.98	42	0.576	117724493	0.18 (0.1 - 0.3)	Observed significantly < expected
SJS - TEN Overall EU+UK only	14	18.95	42	0.14	117724493	0.74 (0.4 - 1.24)	Observed < expected
SJS - TEN Overall EU+UK only	14	171.92	42	1.27	117724493	0.08 (0.04 - 0.14)	Observed significantly < expected
SJS - TEN Overall EU+UK only (incl UNK TTO)	16	77.98	42	0.576	117724493	0.21 (0.12 - 0.33)	Observed significantly < expected
SJS - TEN Overall EU+UK only (incl UNK TTO)	16	18.95	42	0.14	117724493	0.84 (0.48 - 1.37)	Observed < expected
SJS - TEN Overall EU+UK only (incl UNK TTO)	16	171.92	42	1.27	117724493	0.09 (0.05 - 0.15)	Observed significantly < expected


SJS TEN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
Background incidence rate (per 100,000 py)

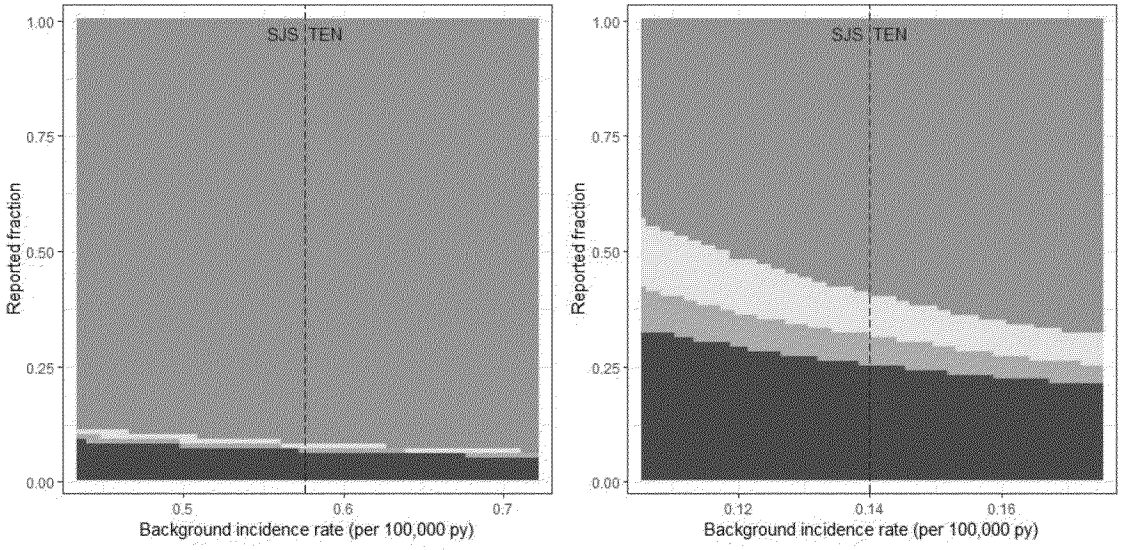
SJS TEN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
Background incidence rate (per 100,000 py)


SJS TEN
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
Background incidence rate (per 100,000 py)

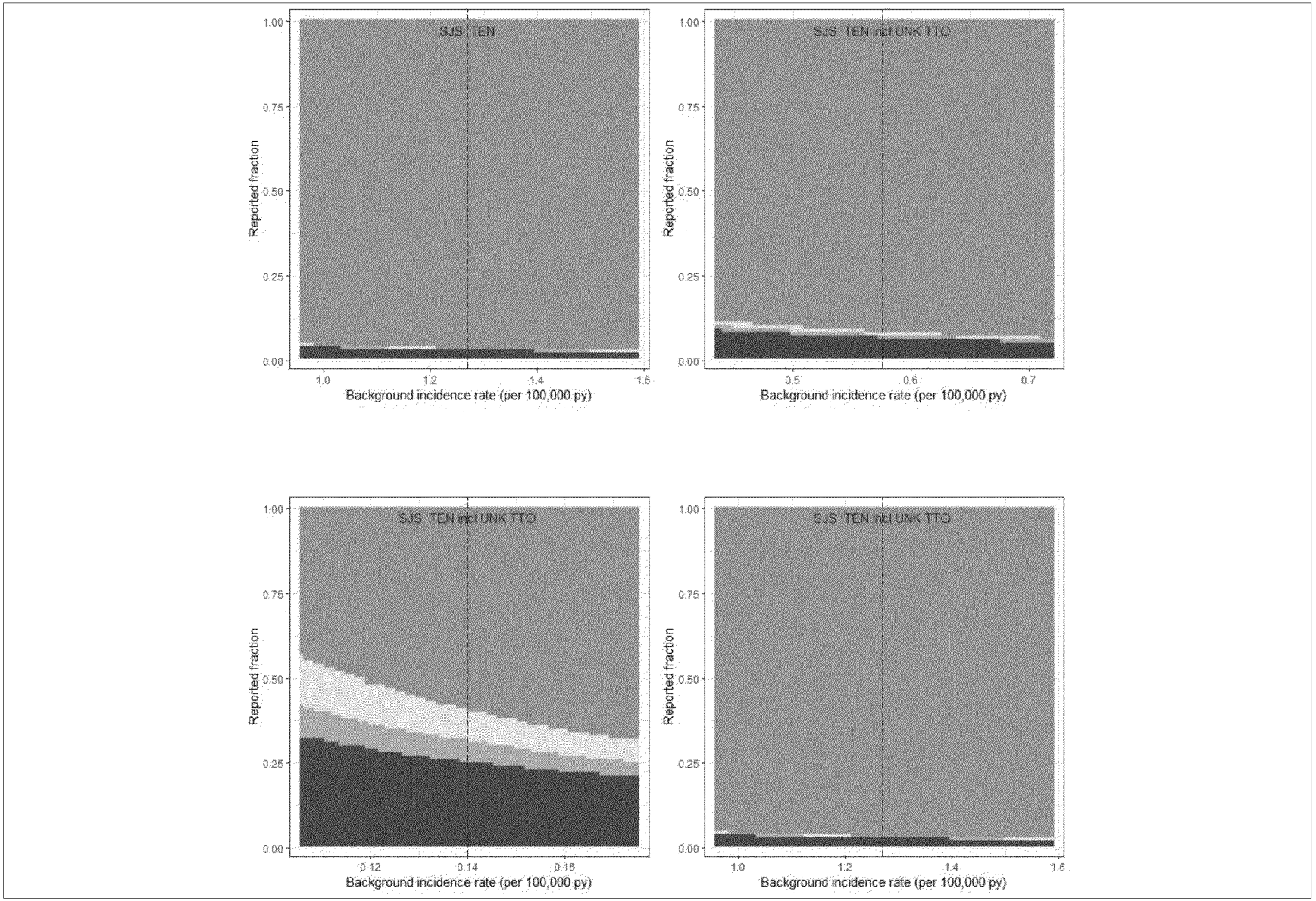

SJS TEN incl UNK TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
Background incidence rate (per 100,000 py)

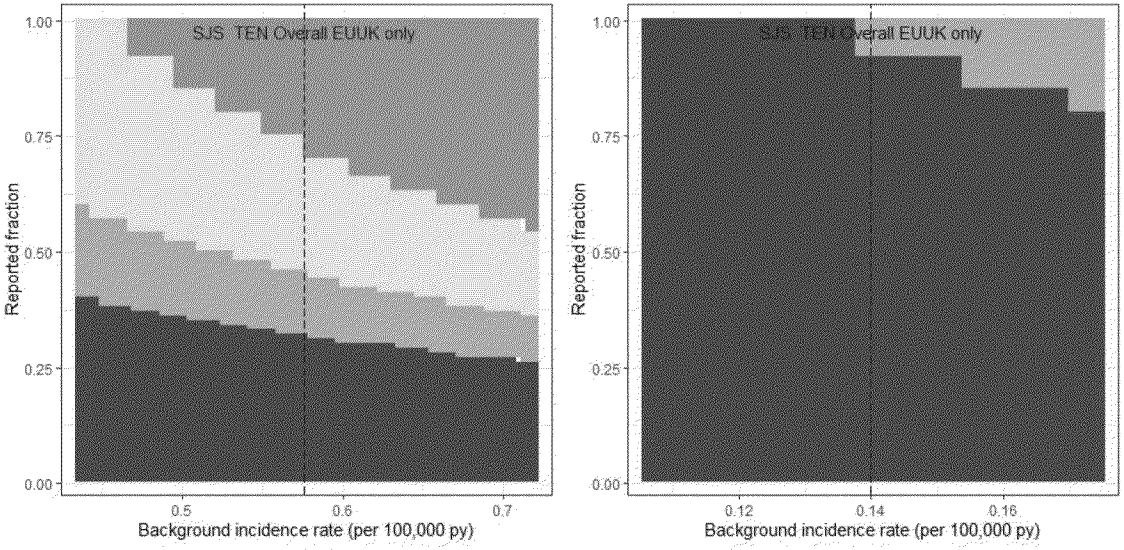

SJS TEN incl UNK TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
Background incidence rate (per 100,000 py)

SJS TEN incl UNK TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
Background incidence rate (per 100,000 py)

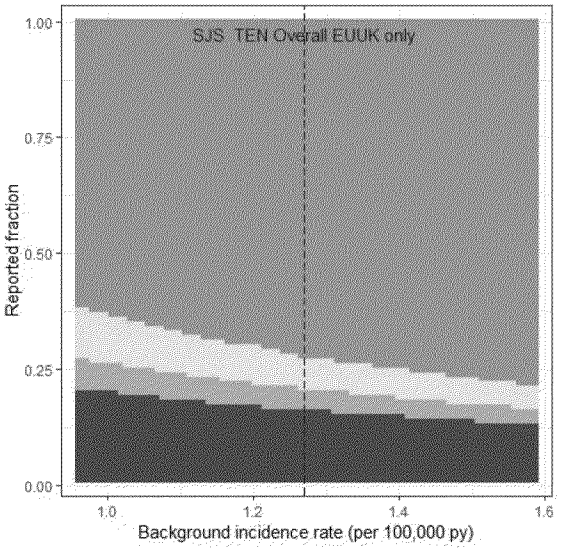

SJS TEN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
Background incidence rate (per 100,000 py)

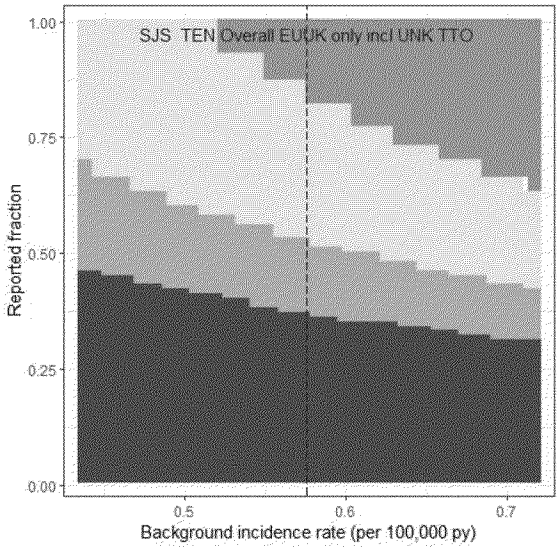
SJS TEN
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
Background incidence rate (per 100,000 py)

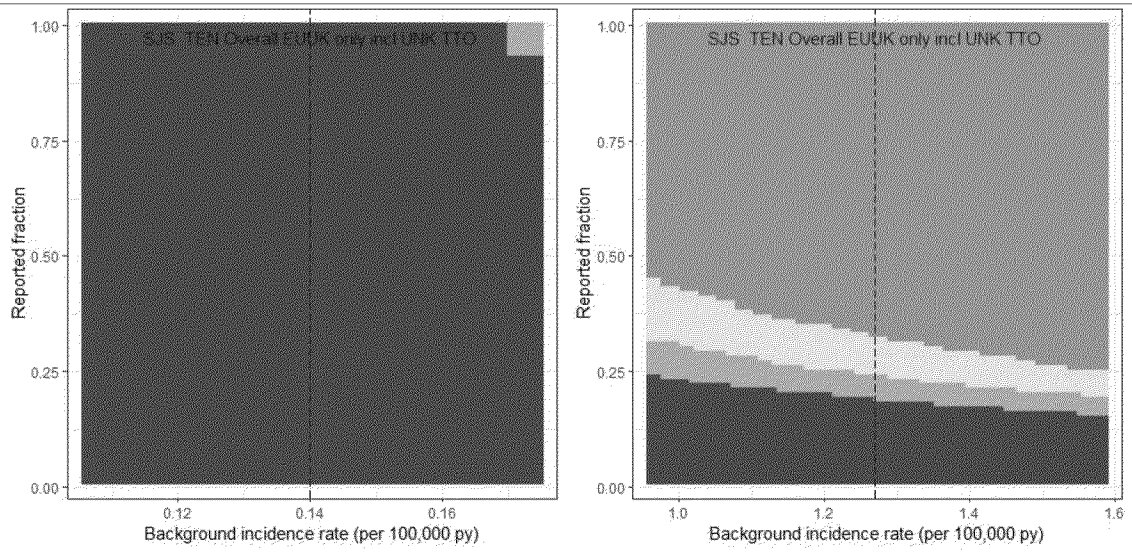

SJS TEN
SJS TEN incl UNK TTO
SJS TEN incl UNK TTO
SJS TEN incl UNK TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
0.5
0.6
0.7
0.12
0.14
0.16
Background incidence rate (per 100,000 py)


SJS TEN Overall EUUK only
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
Background incidence rate (per 100,000 py)

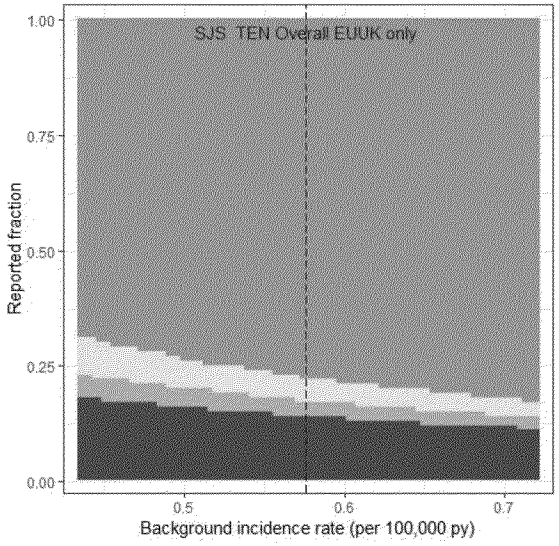
SJS TEN Overall EUUK only
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
Background incidence rate (per 100,000 py)


SJS TEN Overall EUUK only
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
Background incidence rate (per 100,000 py)


SJS TEN Overall EUUK only incl UNK TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
Background incidence rate (per 100,000 py)


SJS TEN Overall EUUK only incl UNK TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
Background incidence rate (per 100,000 py)

SJS TEN Overall EUUK only incl UNK TTO
Reported fraction
1.00
0.75
0.50
0.25
0.00
1.0
1.2
1.4
1.6
Background incidence rate (per 100,000 py)


SJS TEN Overall EUUK only
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.5
0.6
0.7
Background incidence rate (per 100,000 py)

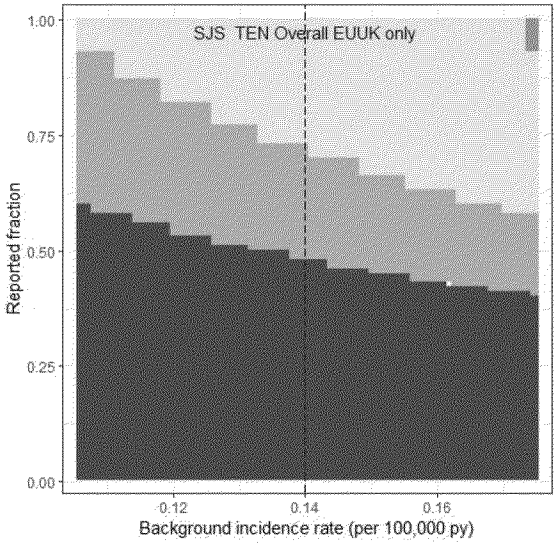
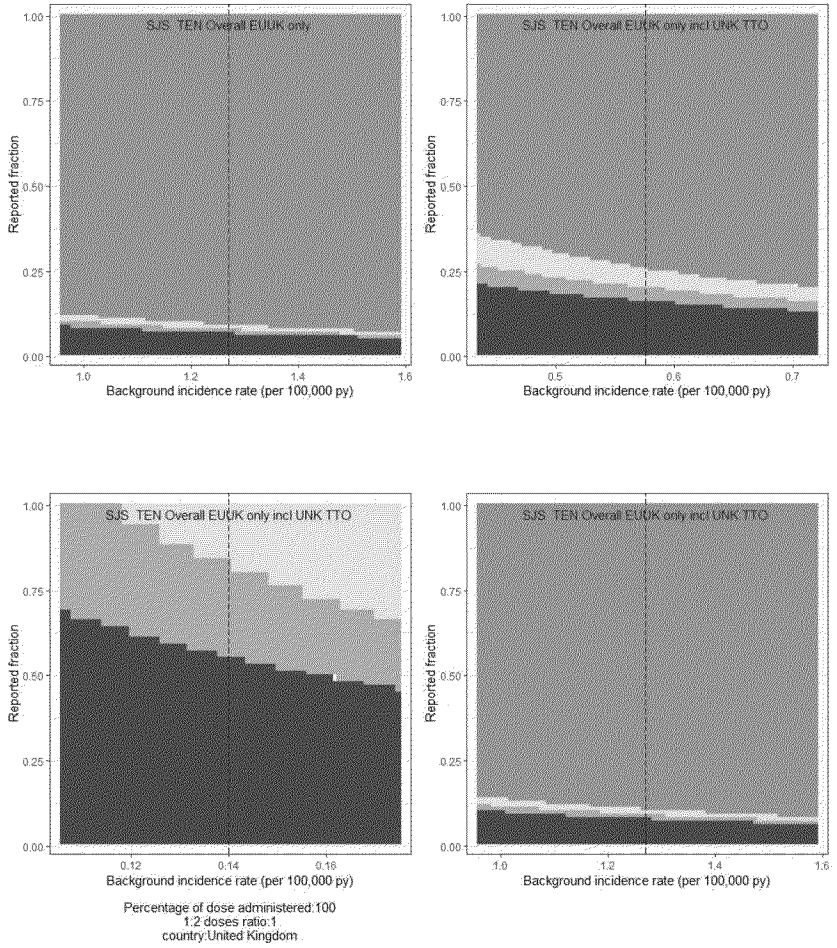

SJS TEN Overall EUUK only
Reported fraction
1.00
0.75
0.50
0.25
0.00
0.12
0.14
0.16
Background incidence rate (per 100,000 py)

Table 85 Observed Vs Expected analysis for Stevens-Johnson syndrome-Toxic epidermal necrolysis (SJS-TEN)

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	

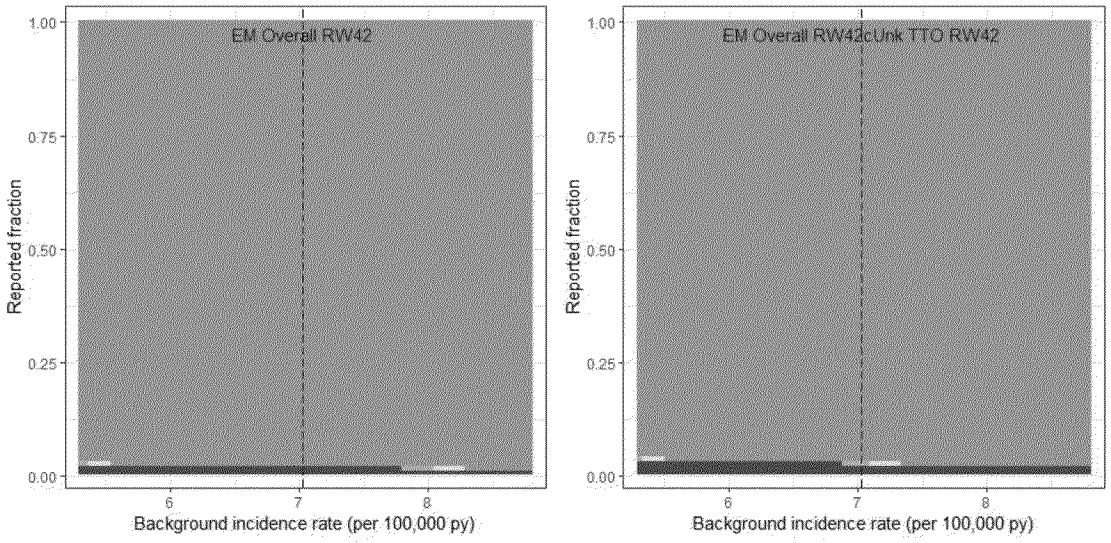


[a] Incidence rate (IR) Source: Truven Marketscan 2019

CI Confidence Interval; E Expected; EEA European Economic Area, O observed; SJS/TEN Stevens-Johnson syndrome/toxic epidermal necrolysis; TTO Time to onset; UK United Kingdom.

Table 86 Observed Vs Expected analysis for Erythema multiforme (EM) overall

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Overall RW42	86	3768.05	42	7.03	466115644	0.02 (0.02 - 0.03)	Observed significantly < expected
Overall RW42 incl Unk TTO	114	3768.05	42	7.03	466115644	0.03 (0.02 - 0.04)	Observed significantly < expected



[a] Incidence rate (IR) Source: Truven Marketscan 2019

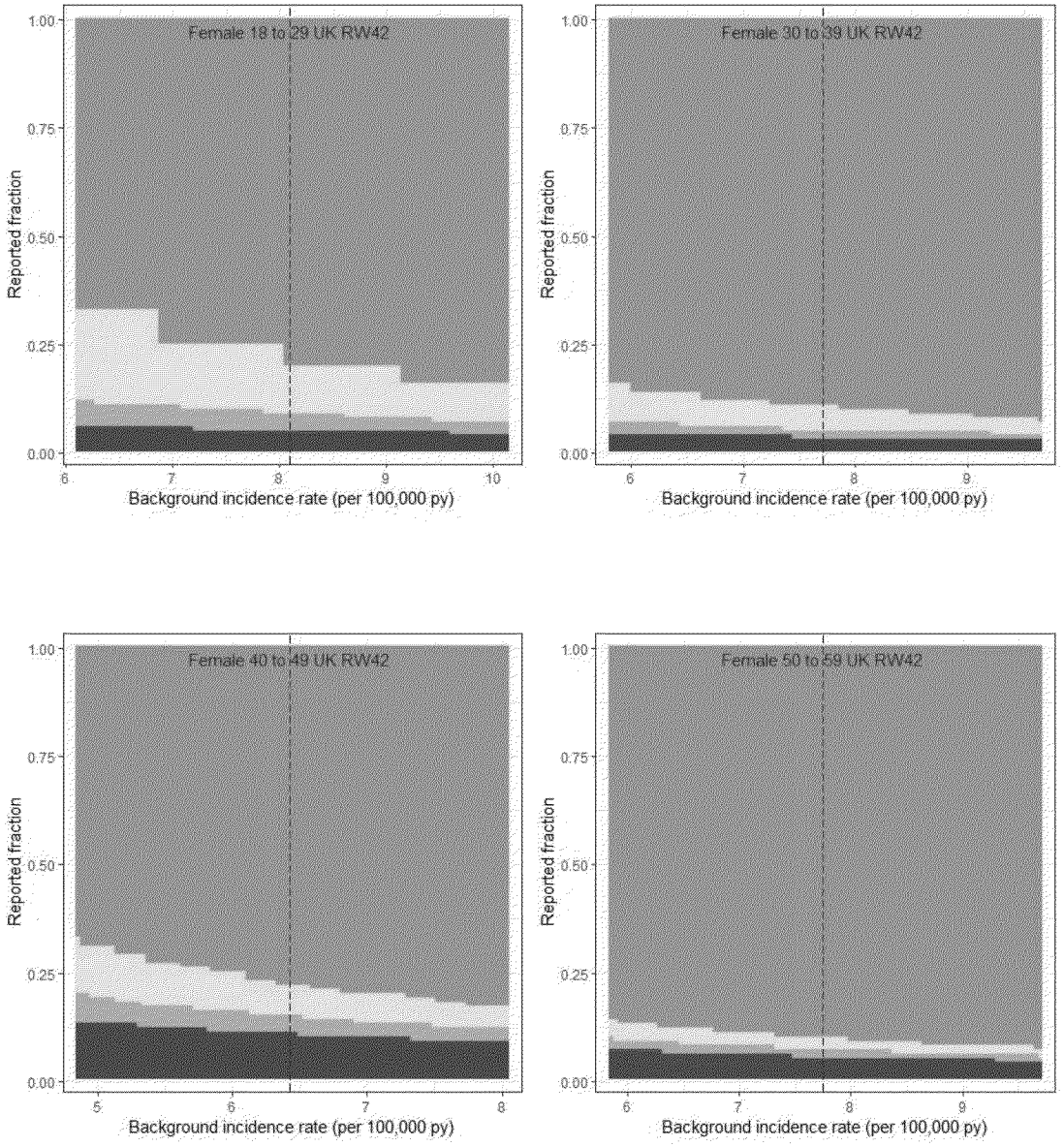
CI Confidence Interval; E Expected; EEA European Economic Area, EM Erythema multiforme; O observed; TTO Time to onset; UK United Kingdom.

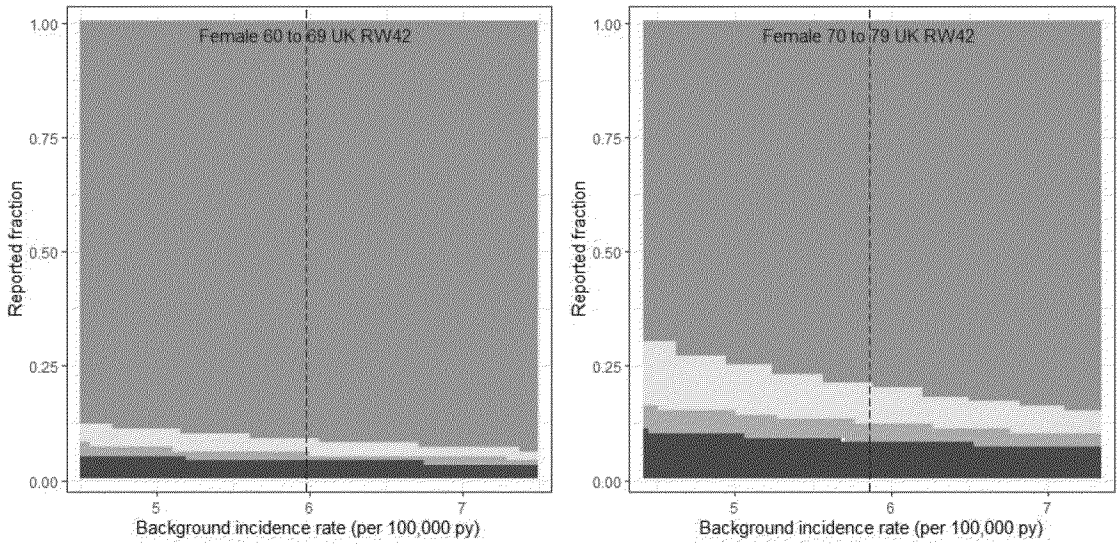
Table 87 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from UK

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Female 18 to 29 UK RW42	1	10.33	42	8.1	1109488	0.1 (0 - 0.54)	Observed significantly < expected
Female 30 to 39 UK RW42	1	16.78	42	7.71	1892968	0.06 (0 - 0.33)	Observed significantly < expected
Female 40 to 49 UK RW42	5	32.62	42	6.43	4412245	0.15 (0.05 - 0.36)	Observed significantly < expected
Female 50 to 59 UK RW42	4	52.98	42	7.75	5944683	0.08 (0.02 - 0.19)	Observed significantly < expected
Female 60 to 69 UK RW42	2	32.89	42	5.98	4783416	0.06 (0.01 - 0.22)	Observed significantly < expected
Female 70 to 79 UK RW42	3	23.42	42	5.86	3475875	0.13 (0.03 - 0.37)	Observed significantly < expected
Female over 80 UK RW42	0	10.18	42	5.43	1630324	0 (0 - 0.36)	Observed significantly < expected
Male 18 to 29 UK RW42	0	3.43	42	3.69	808938	0 (0 - 1.08)	Observed < expected
Male 30 to 39 UK RW42	0	8.93	42	5.49	1415003	0 (0 - 0.41)	Observed significantly < expected
Male 40 to 49 UK RW42	8	19.64	42	3.76	4542157	0.41 (0.18 - 0.8)	Observed significantly < expected
Male 50 to 59 UK RW42	2	36.76	42	4.91	6510960	0.05 (0.01 - 0.2)	Observed significantly < expected
Male 60 to 69 UK RW42	3	23.04	42	4.06	4934728	0.13 (0.03 - 0.38)	Observed significantly < expected
Male 70 to 79 UK RW42	3	23.27	42	6.45	3137304	0.13 (0.03 - 0.38)	Observed significantly < expected
Male over 80 UK RW42	0	9.29	42	7.88	1025046	0 (0 - 0.4)	Observed significantly < expected
Female 18 to 29 including UNK TTO UK RW42	1	10.33	42	8.1	1109488	0.1 (0 - 0.54)	Observed significantly < expected
Female 30 to 39 including UNK TTO UK RW42	2	16.78	42	7.71	1892968	0.12 (0.01 - 0.43)	Observed significantly < expected

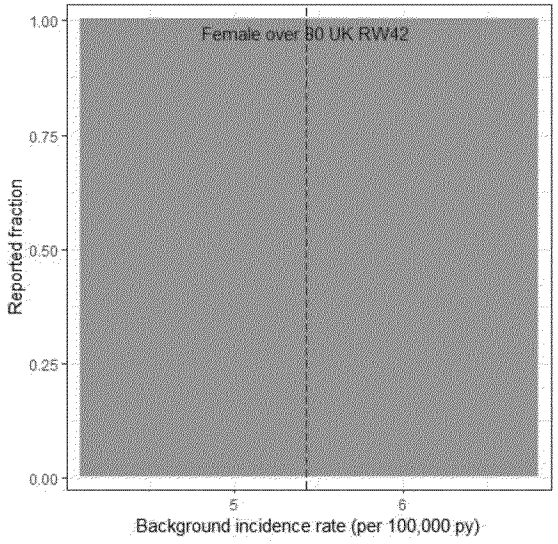
Table 87 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from UK

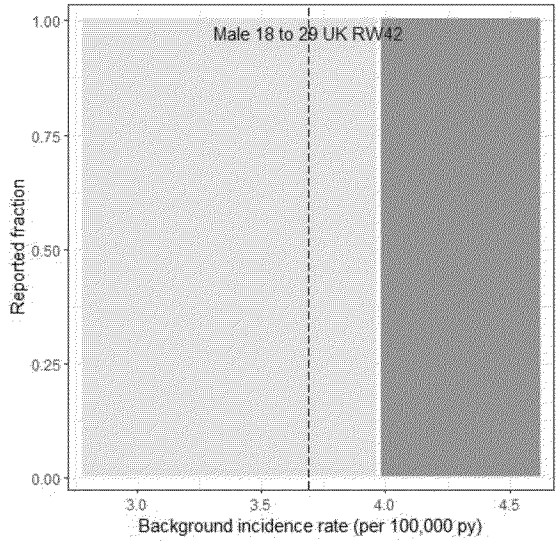
Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Female 40 to 49 including UNK TTO UK RW42	7	32.62	42	6.43	4412245	0.21 (0.09 - 0.44)	Observed significantly < expected
Female 50 to 59 including UNK TTO UK RW42	5	52.98	42	7.75	5944683	0.09 (0.03 - 0.22)	Observed significantly < expected
Female 60 to 69 including UNK TTO UK RW42	2	32.89	42	5.98	4783416	0.06 (0.01 - 0.22)	Observed significantly < expected
Female 70 to 79 including UNK TTO UK RW42	3	23.42	42	5.86	3475875	0.13 (0.03 - 0.37)	Observed significantly < expected
Female over 80 including UNK TTO UK RW42	0	10.18	42	5.43	1630324	0 (0 - 0.36)	Observed significantly < expected
Male 18 to 29 including UNK TTO UK RW42	0	3.43	42	3.69	808938	0 (0 - 1.08)	Observed < expected
Male 30 to 39 including UNK TTO UK RW42	0	8.93	42	5.49	1415003	0 (0 - 0.41)	Observed significantly < expected
Male 40 to 49 including UNK TTO UK RW42	10	19.64	42	3.76	4542157	0.51 (0.24 - 0.94)	Observed significantly < expected
Male 50 to 59 including UNK TTO UK RW42	2	36.76	42	4.91	6510960	0.05 (0.01 - 0.2)	Observed significantly < expected
Male 60 to 69 including UNK TTO UK RW42	4	23.04	42	4.06	4934728	0.17 (0.05 - 0.44)	Observed significantly < expected
Male 70 to 79 including UNK TTO UK RW42	3	23.27	42	6.45	3137304	0.13 (0.03 - 0.38)	Observed significantly < expected
Male over 80 including UNK TTO UK RW42	0	9.29	42	7.88	1025046	0 (0 - 0.4)	Observed significantly < expected

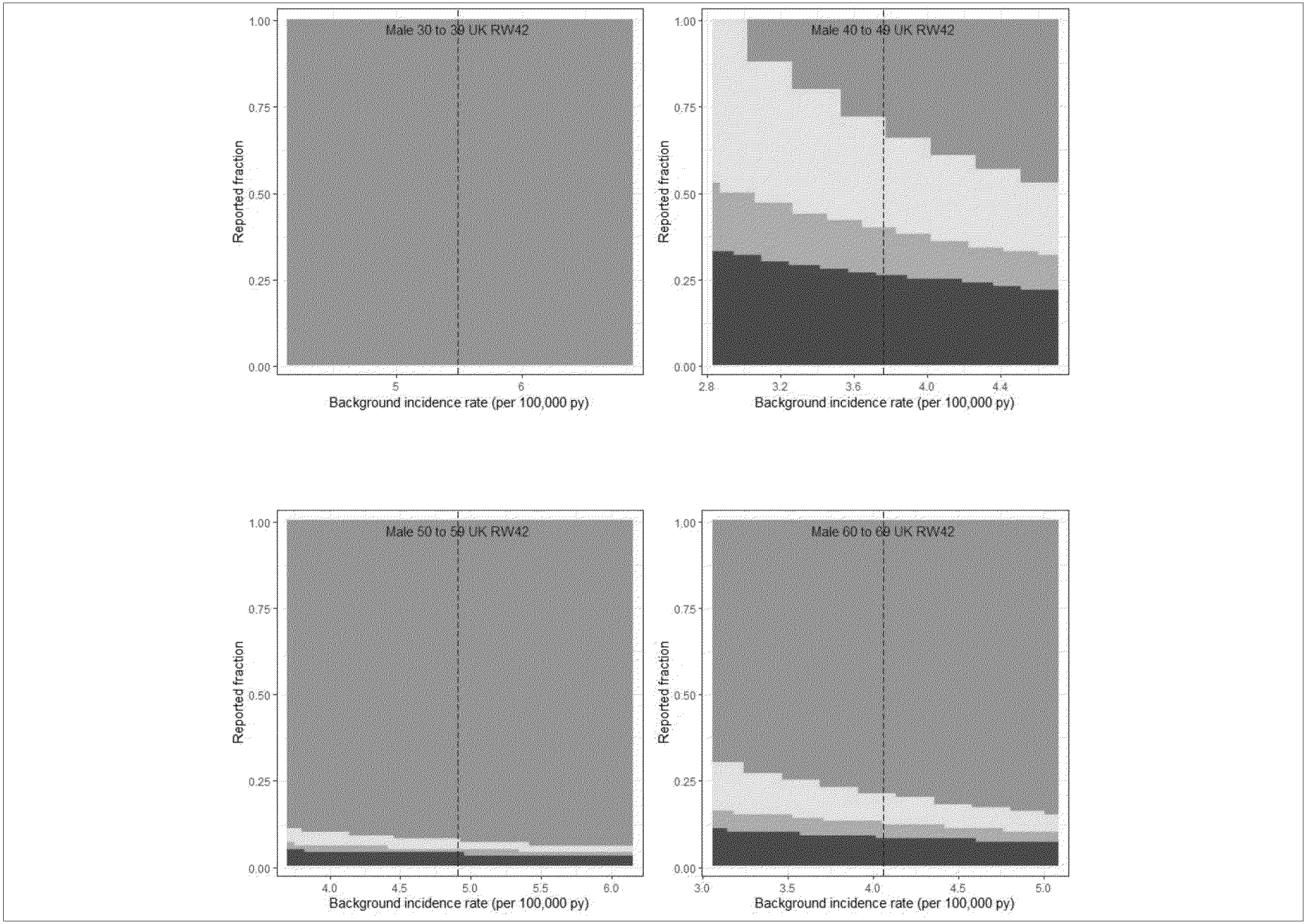

Female 18 to 29 UK RW42
Female 30 to 39 UK RW42
Female 40 to 49 UK RW42
Female 50 to 59 UK RW42
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00

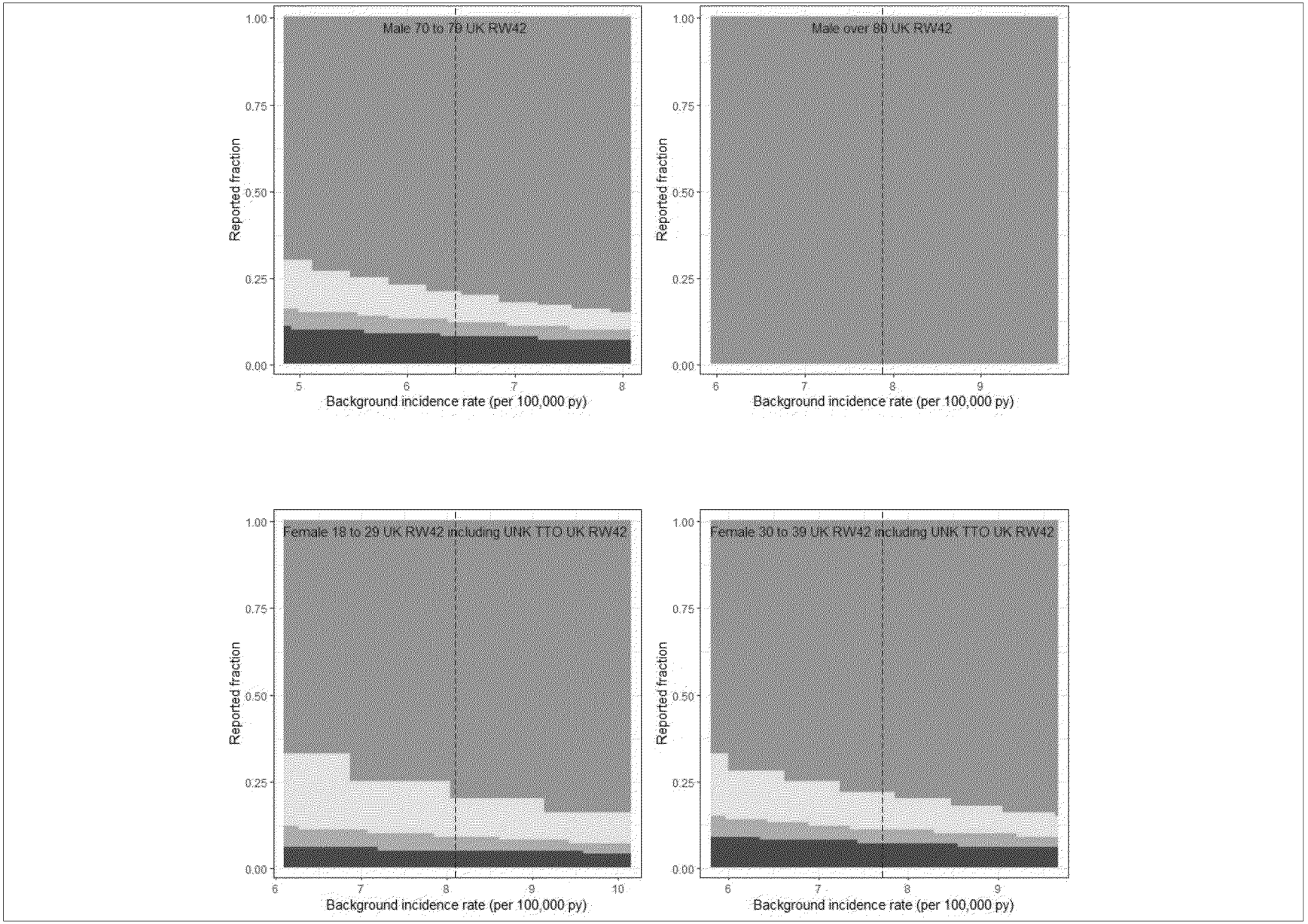

Female 60 to 69 UK RW42
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)

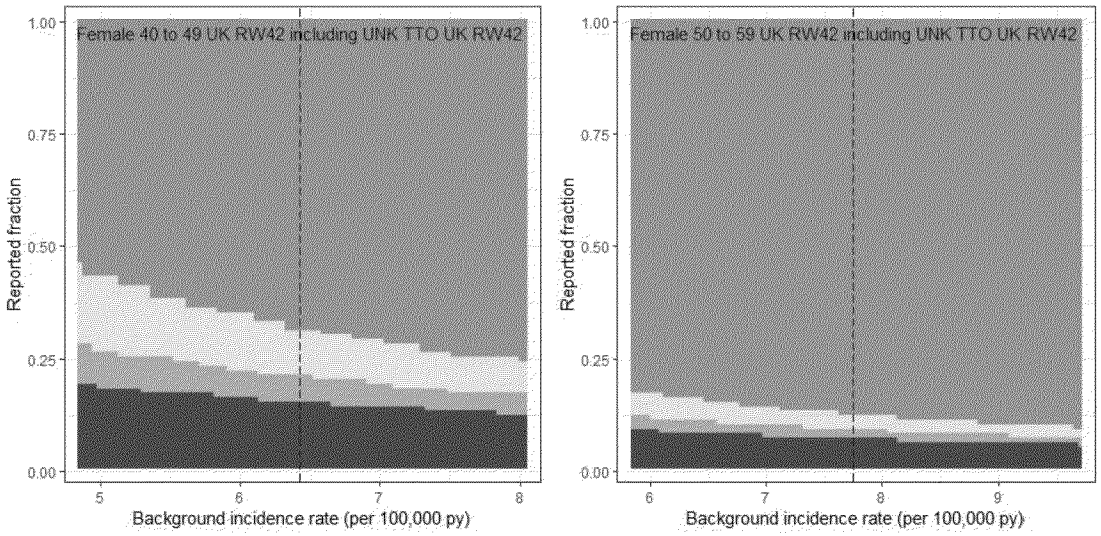
Female 70 to 79 UK RW42
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
Background incidence rate (per 100,000 py)


Female over 80 UK RW42
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
Background incidence rate (per 100,000 py)


Male 18 to 29 UK RW42
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
Background incidence rate (per 100,000 py)


Male 30 to 39 UK RW42
Male 40 to 49 UK RW42
Male 50 to 59 UK RW42
Male 60 to 69 UK RW42
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
5
6
2.8
3.2
3.6
4.0
4.4
4.5
5.0
5.5
6.0
3.0
3.5


Male 70 to 79 UK RW42
Male over 80 UK RW42
Female 18 to 29 UK RW42 including UNK TTO UK RW42
Female 30 to 39 UK RW42 including UNK TTO UK RW42
Reported fraction
Background incidence rate (per 100,000 py)


Female 40 to 49 UK RW42 including UNK TTO UK RW42
Female 50 to 59 UK RW42 including UNK TTO UK RW42
Female 60 to 69 UK RW42 including UNK TTO UK RW42
Female 70 to 79 UK RW42 including UNK TTO UK RW42
Reported fraction
Background incidence rate (per 100,000 py)

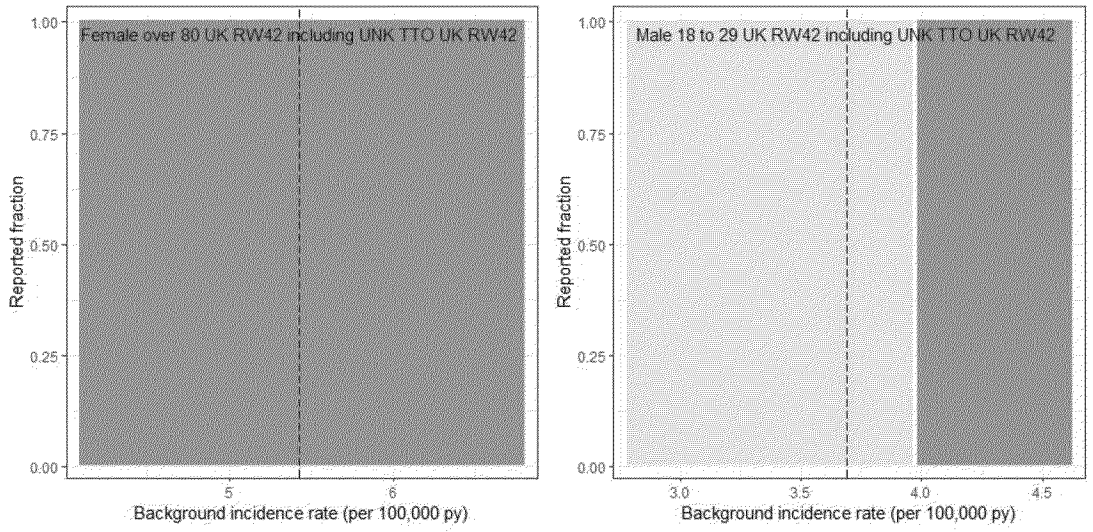
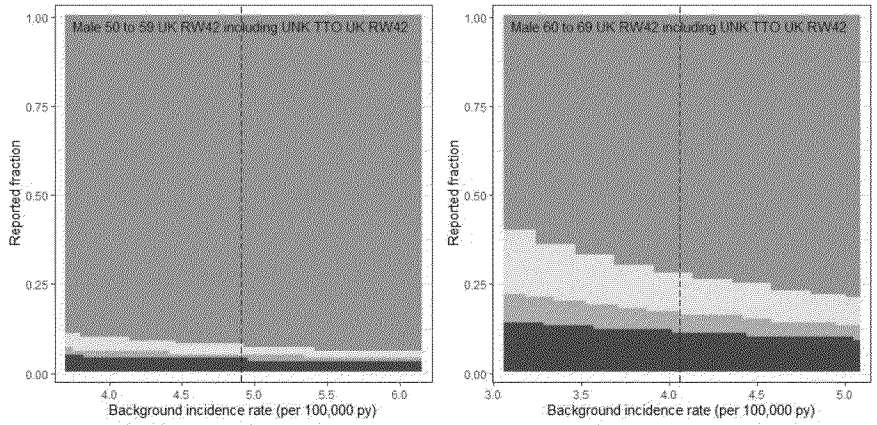

Female over 80 UK RW42 including UNK TTO UK RW42
Male 18 to 29 UK RW42 including UNK TTO UK RW42
Male 30 to 39 UK RW42 including UNK TTO UK RW42
Male 40 to 49 UK RW42 including UNK TTO UK RW42
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
5
6
3.0
3.5
4.0
4.5
2.8
3.2
3.6
4.4

Table 87 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from UK

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) Source: Truven Marketscan 2019

CI Confidence Interval; E Expected; EEA European Economic Area, O observed; TTO Time to onset; UK United Kingdom.

Table 88 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from EU+UK+Brazil+Australia

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
18 to 49	33	896.33	42	7.08	110094983	0.04 (0.03 - 0.05)	Observed significantly < expected
50 to 59	14	449.45	42	6.7	58336094	0.03 (0.02 - 0.05)	Observed significantly < expected
60 to 69	16	337.92	42	5.07	57960860	0.05 (0.03 - 0.08)	Observed significantly < expected
Over 70	13	260.98	42	7.01	32376365	0.05 (0.03 - 0.09)	Observed significantly < expected
18 to 49 incl UNK TTO	44	896.33	42	7.08	110094983	0.05 (0.04 - 0.07)	Observed significantly < expected
50 to 59 incl UNK TTO	16	449.45	42	6.7	58336094	0.04 (0.02 - 0.06)	Observed significantly < expected
60 to 69 incl UNK TTO	20	337.92	42	5.07	57960860	0.06 (0.04 - 0.09)	Observed significantly < expected
Over 70 incl UNK TTO	16	260.98	42	7.01	32376365	0.06 (0.04 - 0.1)	Observed significantly < expected

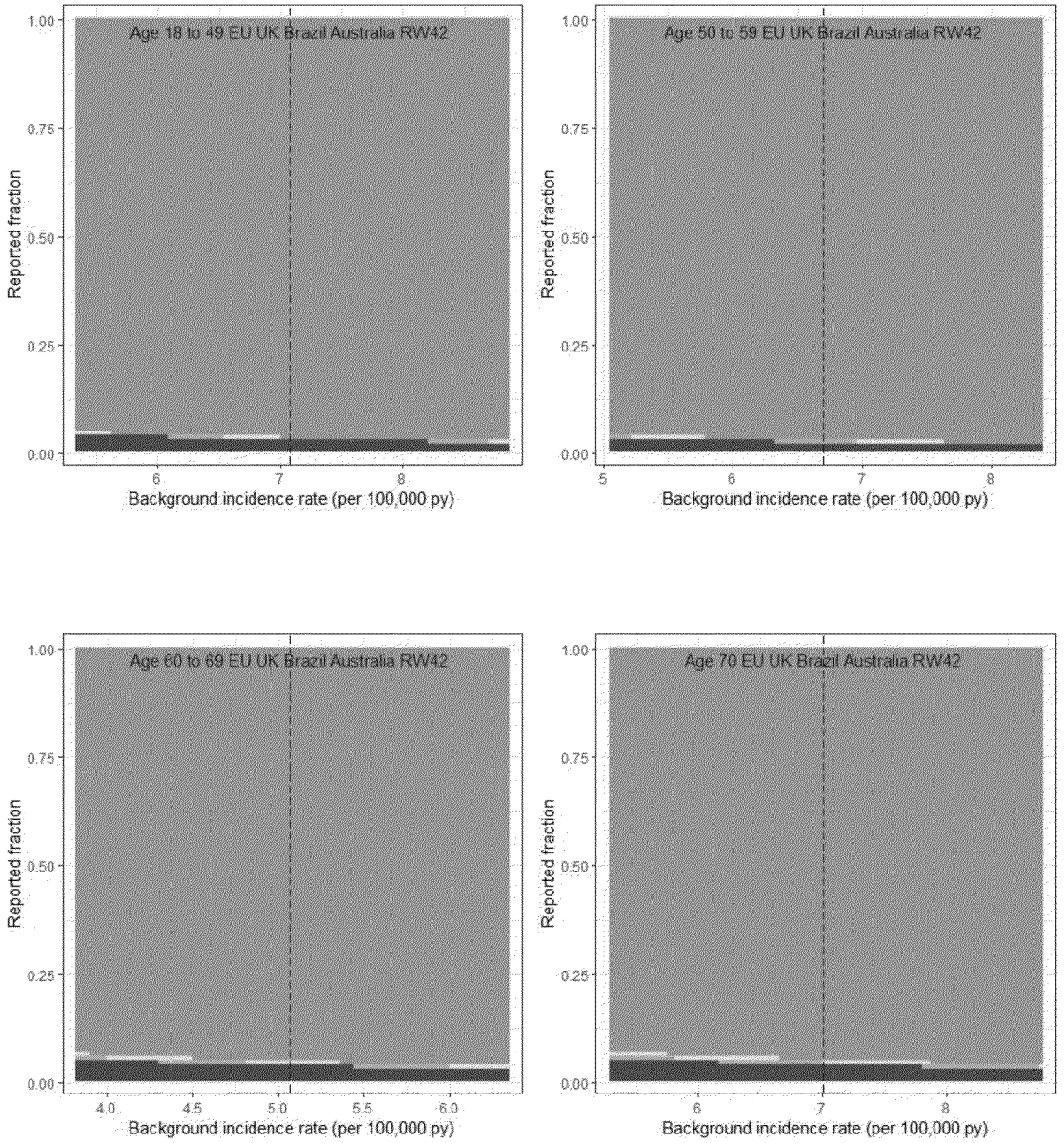
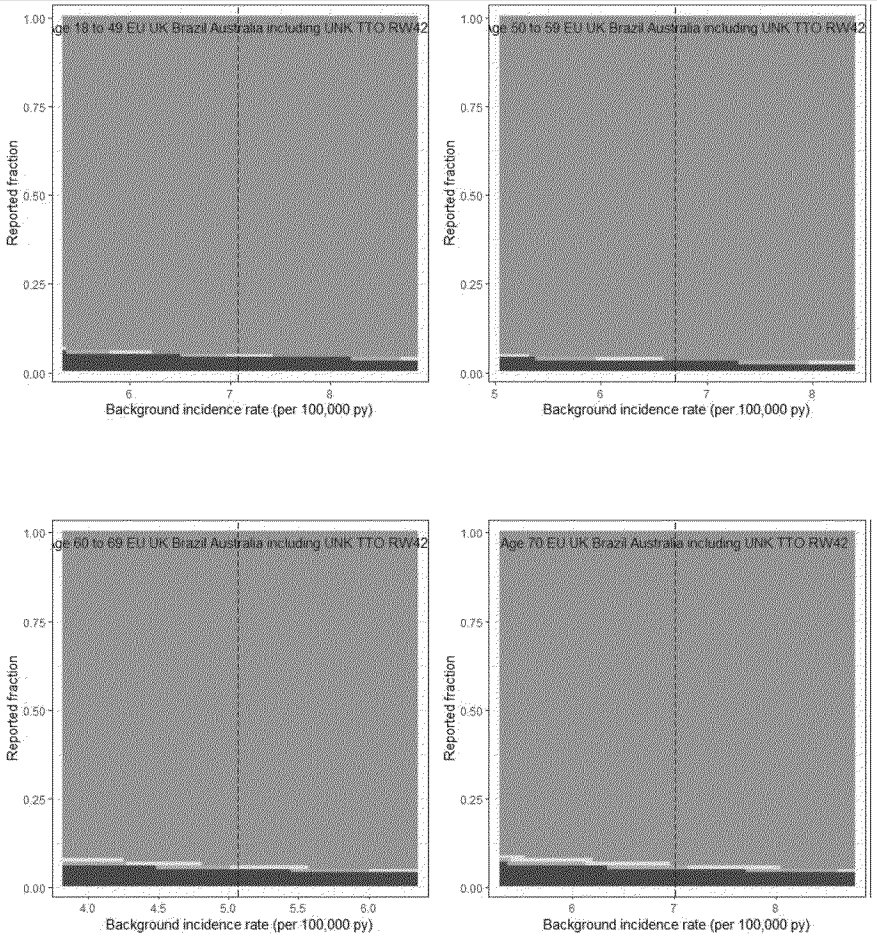

Age 18 to 49 EU UK Brazil Australia RW42
Age 50 to 59 EU UK Brazil Australia RW42
Age 60 to 69 EU UK Brazil Australia RW42
Age 70 EU UK Brazil Australia RW42
Reported fraction
Background incidence rate (per 100,000 py)

Table 88 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from EU+UK+Brazil+Australia

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	

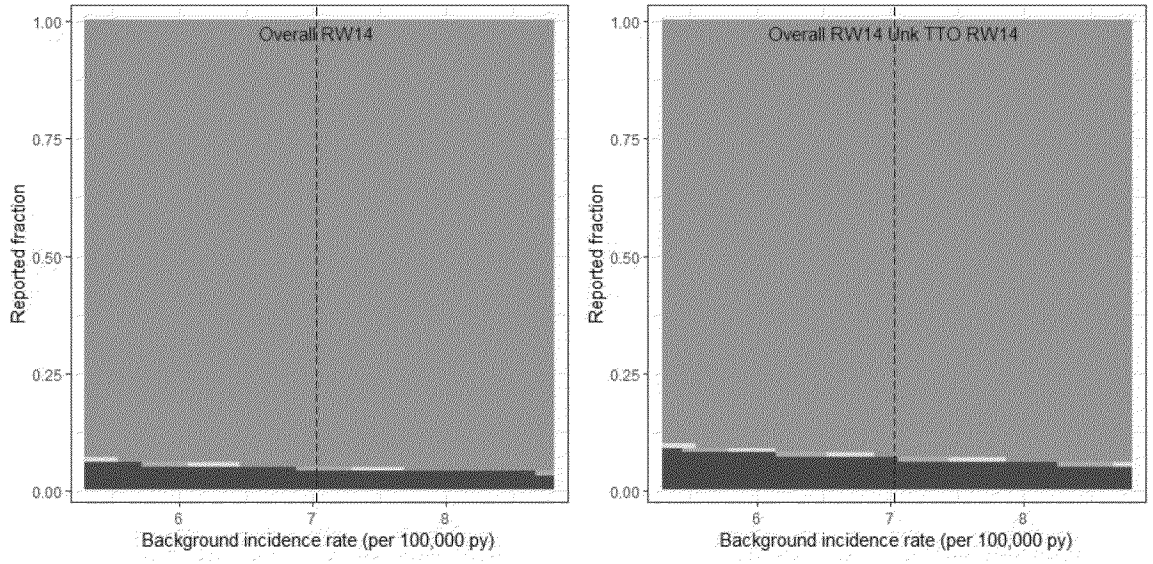


[a] Incidence rate (IR) Source: Truven Marketscan 2019

CI Confidence Interval; E Expected; EEA European Economic Area, O observed; TTO Time to onset; UK United Kingdom.

Table 89 Observed Vs Expected analysis for Erythema multiforme overall

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Overall RW42	65	1256.02	14	7.03	466115644	0.05 (0.04 - 0.07)	Observed significantly < expected
Overall RW42 incl Unk TTO	93	1256.02	14	7.03	466115644	0.07 (0.06 - 0.09)	Observed significantly < expected



[a] Incidence rate (IR) Source: Truven Marketscan 2019

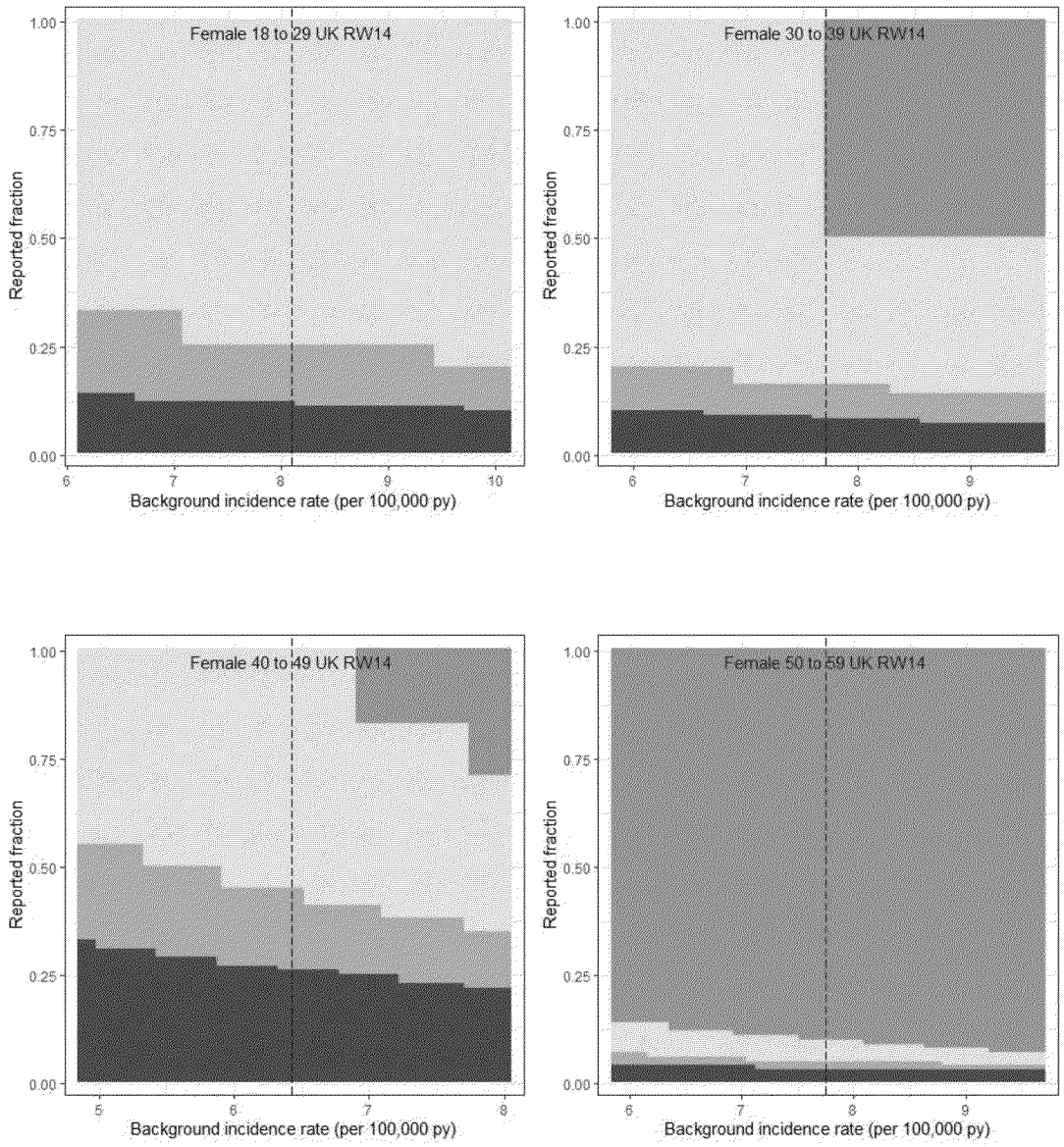
CI Confidence Interval; E Expected; EEA European Economic Area, O observed; TTO Time to onset; UK United Kingdom.

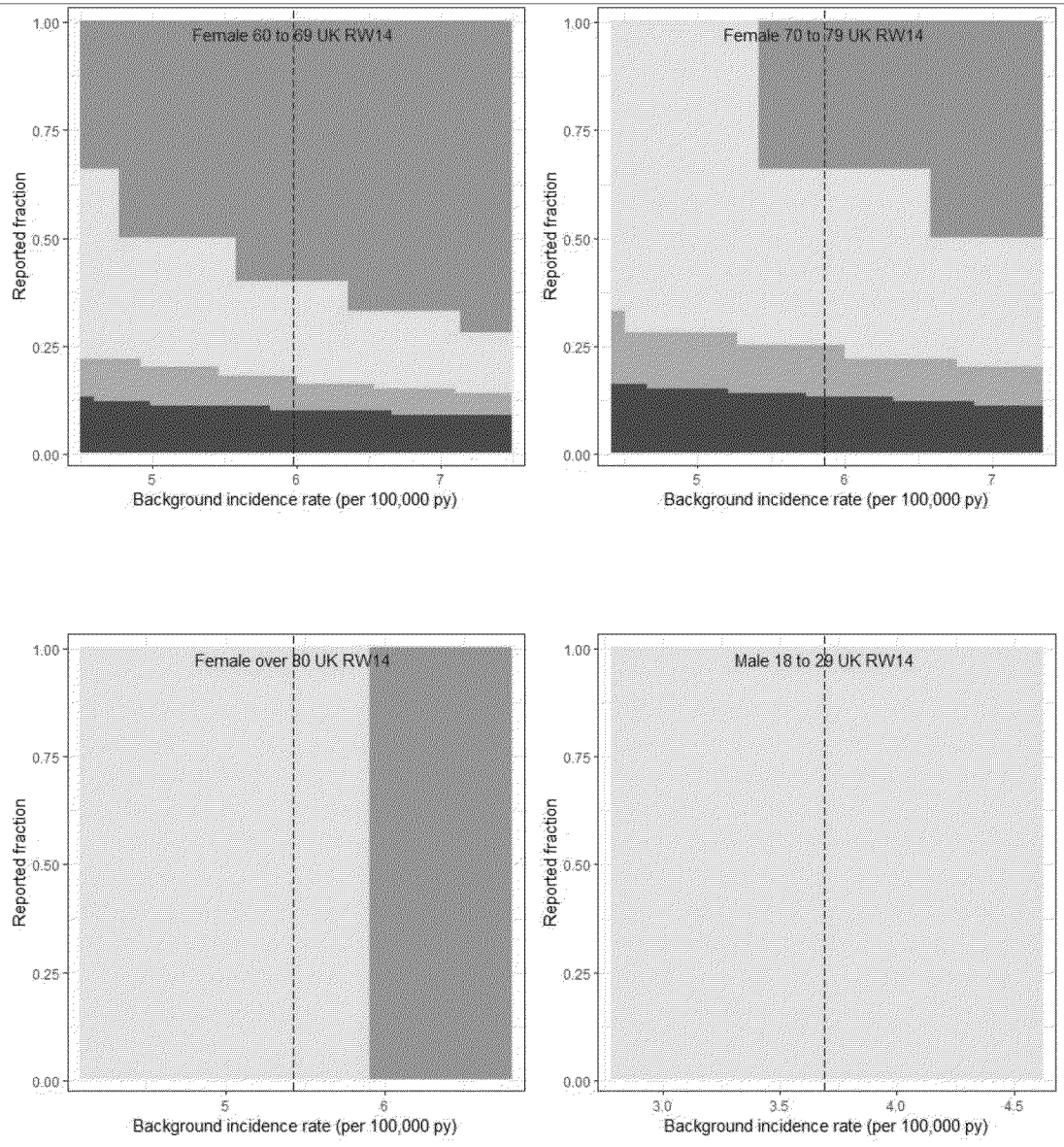
Table 90 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from UK

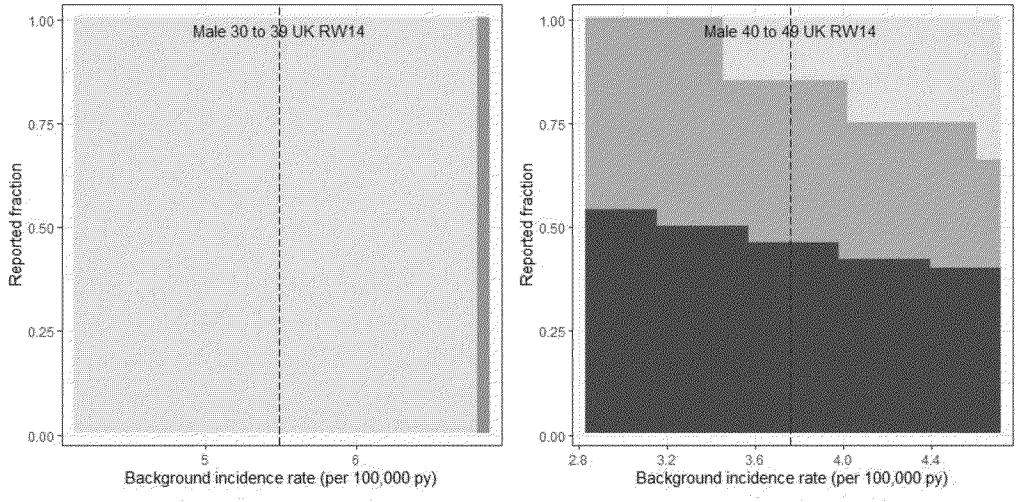
Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Female 18 to 29 UK RW14	1	3.44	14	8.1	1109488	0.29 (0.01 - 1.62)	Observed < expected
Female 30 to 39 UK RW14	1	5.59	14	7.71	1892968	0.18 (0 - 1)	Observed significantly < expected
Female 40 to 49 UK RW14	5	10.87	14	6.43	4412245	0.46 (0.15 - 1.07)	Observed < expected
Female 50 to 59 UK RW14	1	17.66	14	7.75	5944683	0.06 (0 - 0.32)	Observed significantly < expected
Female 60 to 69 UK RW14	2	10.96	14	5.98	4783416	0.18 (0.02 - 0.66)	Observed significantly < expected
Female 70 to 79 UK RW14	2	7.81	14	5.86	3475875	0.26 (0.03 - 0.93)	Observed significantly < expected
Female over 80 UK RW14	0	3.39	14	5.43	1630324	0 (0 - 1.09)	Observed < expected
Male 18 to 29 UK RW14	0	1.14	14	3.69	808938	0 (0 - 3.24)	Observed < expected
Male 30 to 39 UK RW14	0	2.98	14	5.49	1415003	0 (0 - 1.24)	Observed < expected
Male 40 to 49 UK RW14	6	6.55	14	3.76	4542157	0.92 (0.34 - 1.99)	Observed < expected
Male 50 to 59 UK RW14	2	12.25	14	4.91	6510960	0.16 (0.02 - 0.59)	Observed significantly < expected
Male 60 to 69 UK RW14	1	7.68	14	4.06	4934728	0.13 (0 - 0.73)	Observed significantly < expected
Male 70 to 79 UK RW14	2	7.76	14	6.45	3137304	0.26 (0.03 - 0.93)	Observed significantly < expected
Male over 80 UK RW14	0	3.1	14	7.88	1025046	0 (0 - 1.19)	Observed < expected
Female 18 to 29 including UNK TTO UK RW14	1	3.44	14	8.1	1109488	0.29 (0.01 - 1.62)	Observed < expected
Female 30 to 39 including UNK TTO UK RW14	2	5.59	14	7.71	1892968	0.36 (0.04 - 1.29)	Observed < expected

Table 90 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from UK

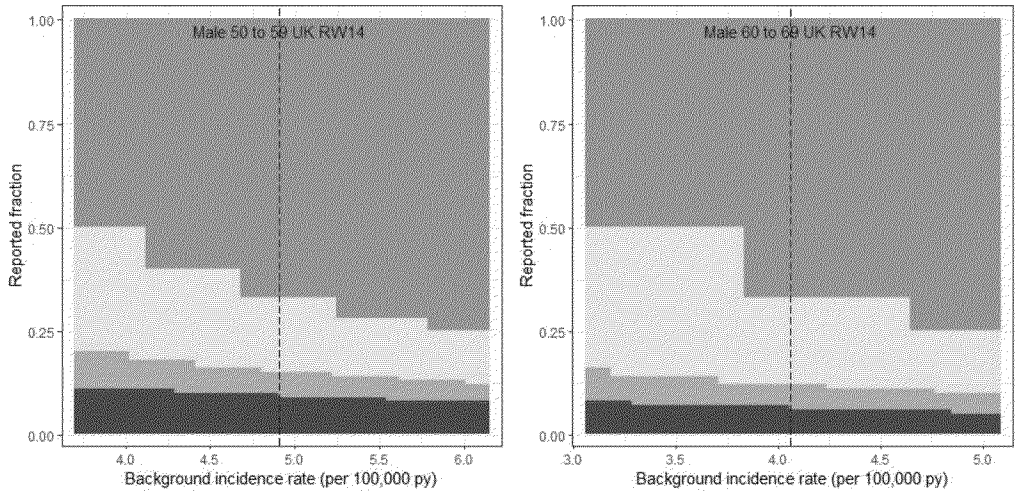
Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
Female 40 to 49 including UNK TTO UK RW14	7	10.87	14	6.43	4412245	0.64 (0.26 - 1.33)	Observed < expected
Female 50 to 59 including UNK TTO UK RW14	2	17.66	14	7.75	5944683	0.11 (0.01 - 0.41)	Observed significantly < expected
Female 60 to 69 including UNK TTO UK RW14	2	10.96	14	5.98	4783416	0.18 (0.02 - 0.66)	Observed significantly < expected
Female 70 to 79 including UNK TTO UK RW14	2	7.81	14	5.86	3475875	0.26 (0.03 - 0.93)	Observed significantly < expected
Female over 80 including UNK TTO UK RW14	0	3.39	14	5.43	1630324	0 (0 - 1.09)	Observed < expected
Male 18 to 29 including UNK TTO UK RW14	0	1.14	14	3.69	808938	0 (0 - 3.24)	Observed < expected
Male 30 to 39 including UNK TTO UK RW14	0	3.81	14	7.03	1415003	0 (0 - 0.97)	Observed significantly < expected
Male 40 to 49 including UNK TTO UK RW14	8	6.55	14	3.76	4542157	1.22 (0.53 - 2.41)	Observed > expected
Male 50 to 59 including UNK TTO UK RW14	2	12.25	14	4.91	6510960	0.16 (0.02 - 0.59)	Observed significantly < expected
Male 60 to 69 including UNK TTO UK RW14	2	7.68	14	4.06	4934728	0.26 (0.03 - 0.94)	Observed significantly < expected
Male 70 to 79 including UNK TTO UK RW14	2	7.76	14	6.45	3137304	0.26 (0.03 - 0.93)	Observed significantly < expected
Male over 80 including UNK TTO UK RW14	0	3.1	14	7.88	1025046	0 (0 - 1.19)	Observed < expected


Female 18 to 29 UK RW14
Female 30 to 39 UK RW14
Female 40 to 49 UK RW14
Female 50 to 59 UK RW14
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00

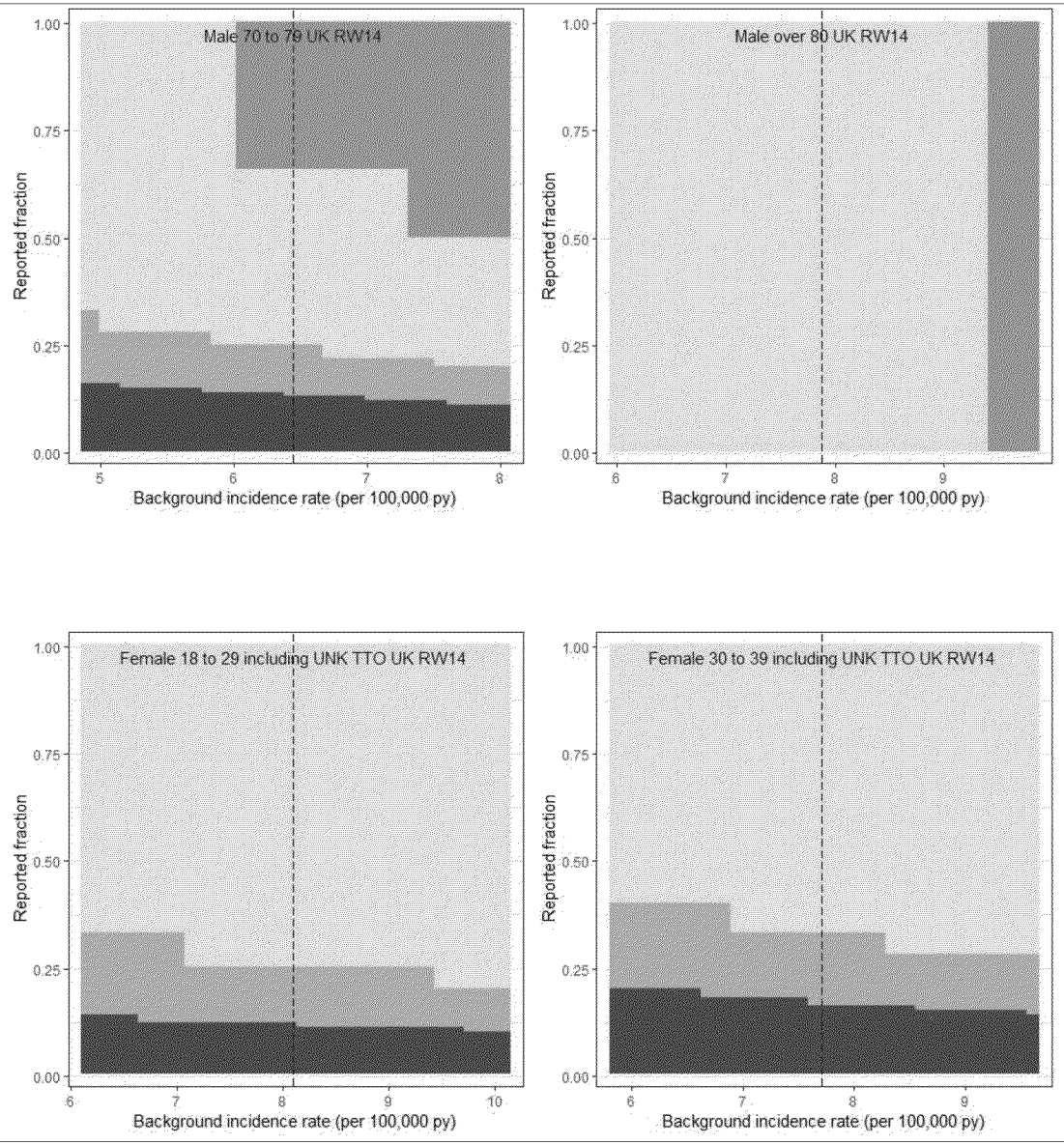

Female 60 to 69 UK RW14
Female 70 to 79 UK RW14
Female over 80 UK RW14
Male 18 to 29 UK RW14
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00
5
6
7
3.0
3.5
4.0
4.5

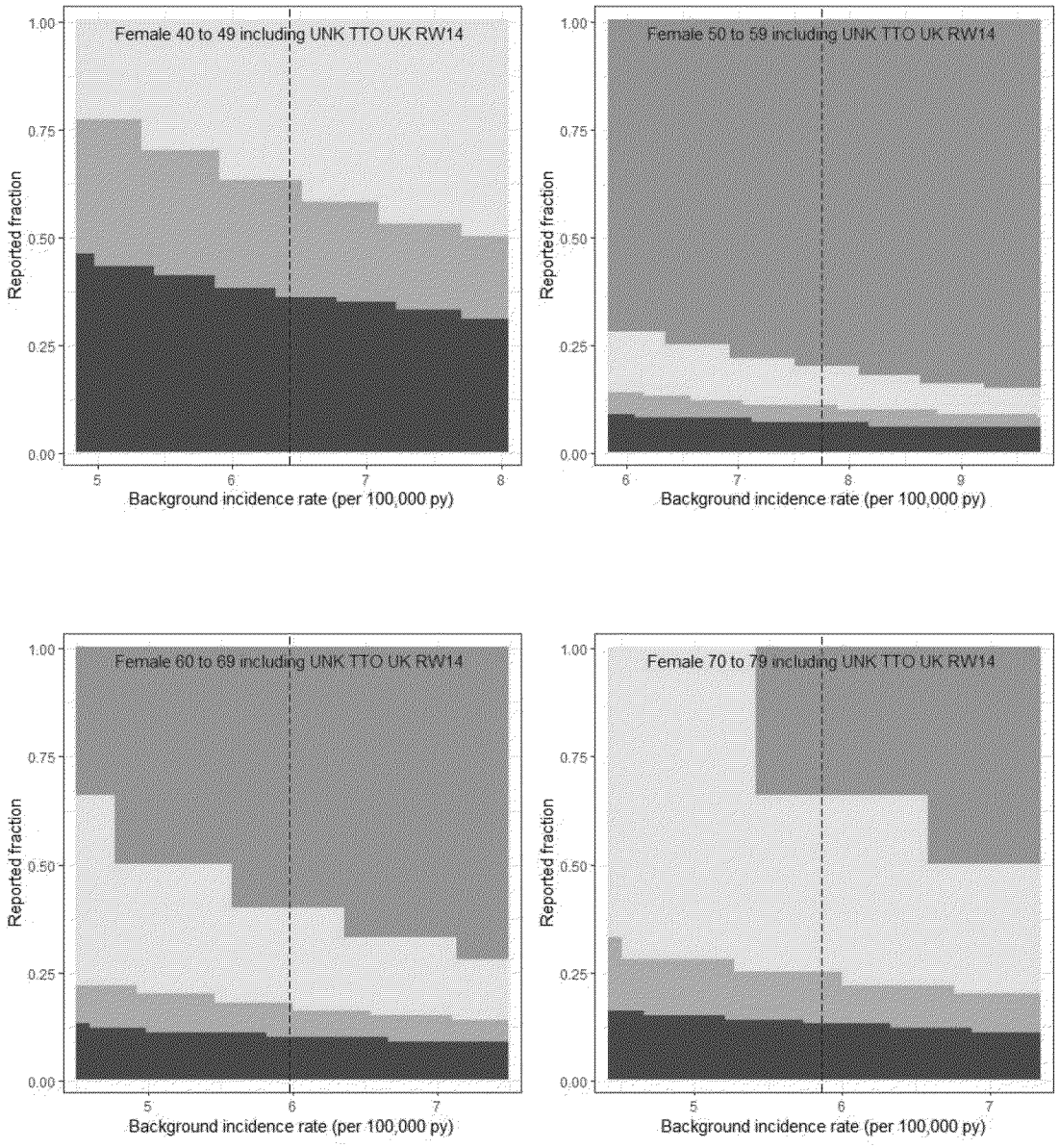

Male 30 to 39 UK RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
Background incidence rate (per 100,000 py)

Male 40 to 49 UK RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
2.8
3.2
3.6
4.0
4.4
Background incidence rate (per 100,000 py)


Male 50 to 59 UK RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
4.0
4.5
5.0
5.5
6.0
Background incidence rate (per 100,000 py)

Male 60 to 69 UK RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
3.0
3.5
4.0
4.5
5.0
Background incidence rate (per 100,000 py)


Male 70 to 79 UK RW14
Male over 80 UK RW14
Female 18 to 29 including UNK TTO UK RW14
Female 30 to 39 including UNK TTO UK RW14
Reported fraction
Background incidence rate (per 100,000 py)


Female 40 to 49 including UNK TTO UK RW14
Female 50 to 59 including UNK TTO UK RW14
Female 60 to 69 including UNK TTO UK RW14
Female 70 to 79 including UNK TTO UK RW14
Reported fraction
Background incidence rate (per 100,000 py)
0.00
0.25
0.50
0.75
1.00

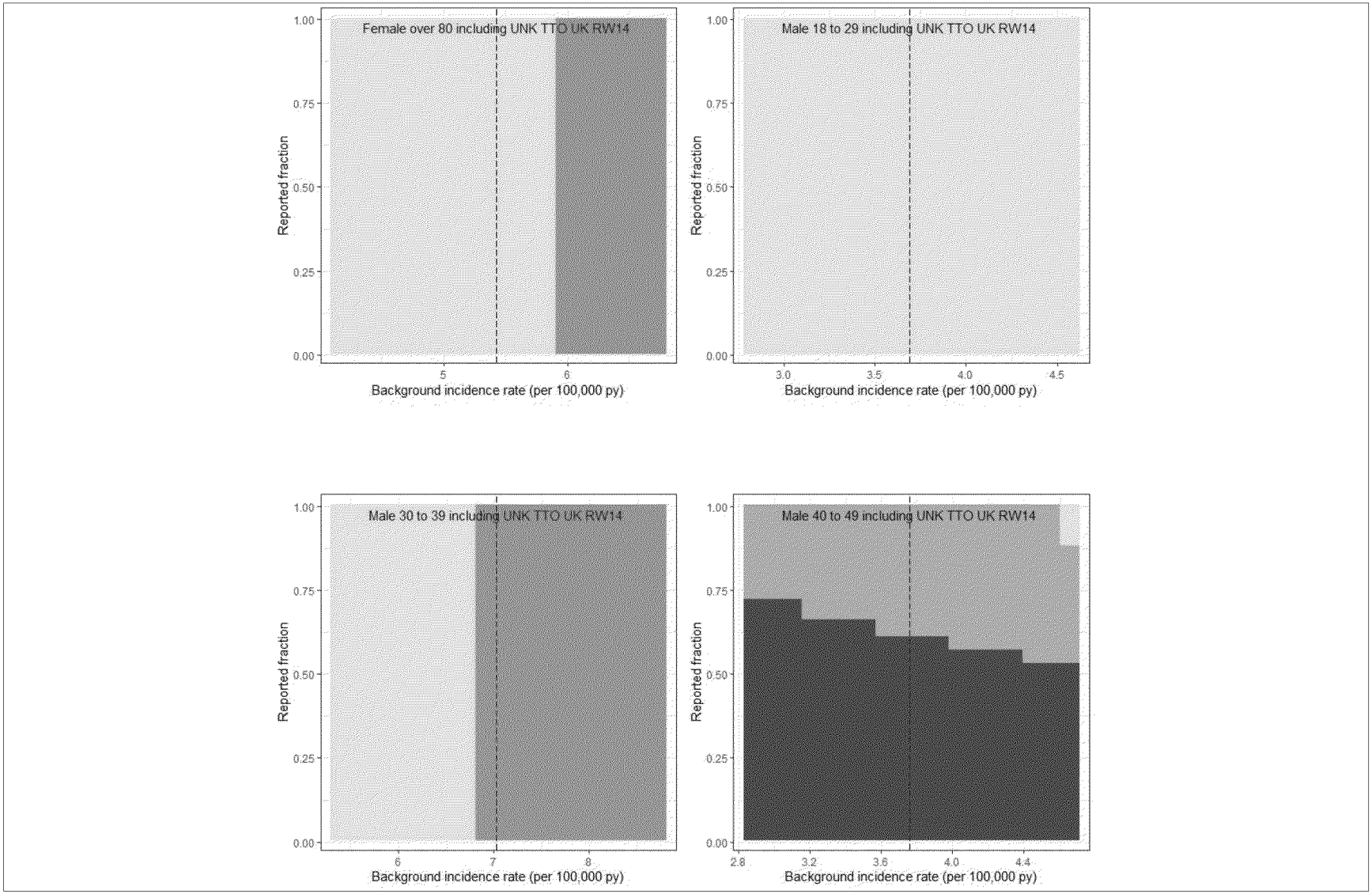
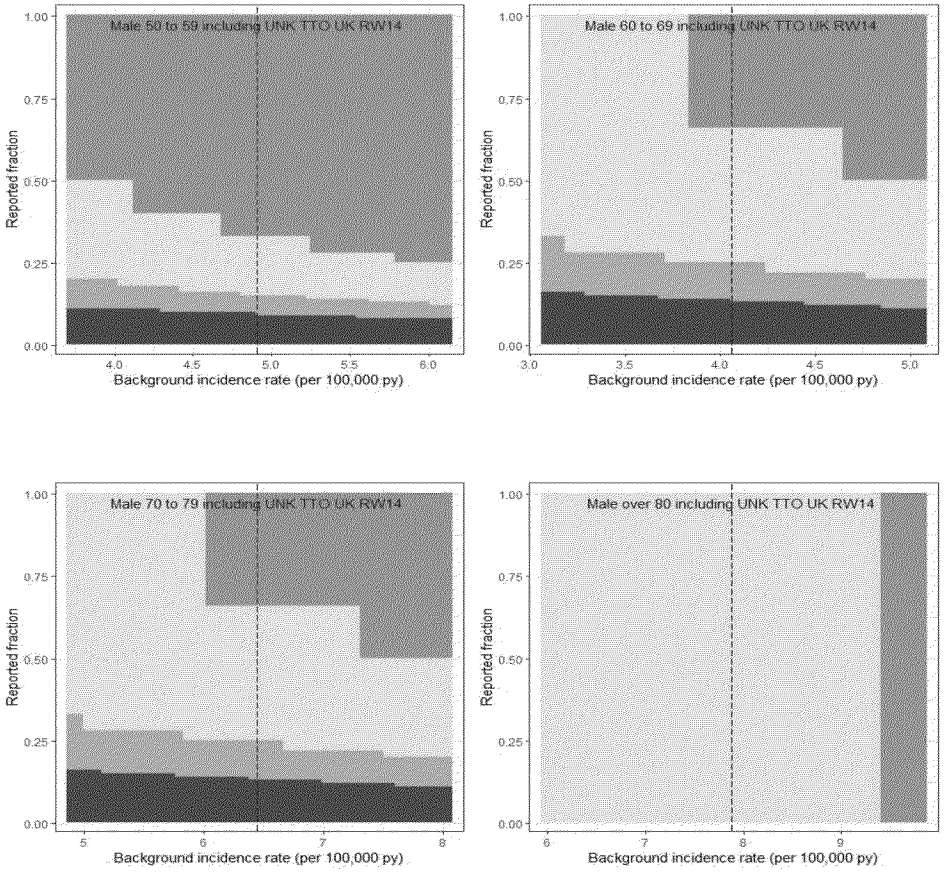

Female over 80 including UNK TTO UK RW14
Male 18 to 29 including UNK TTO UK RW14
Male 30 to 39 including UNK TTO UK RW14
Male 40 to 49 including UNK TTO UK RW14
Reported fraction
Background incidence rate (per 100,000 py)
1.00
0.75
0.50
0.25
0.00
5
6
3.0
3.5
4.0
4.5
7
8
2.8
3.2
3.6
4.4

Table 90 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from UK

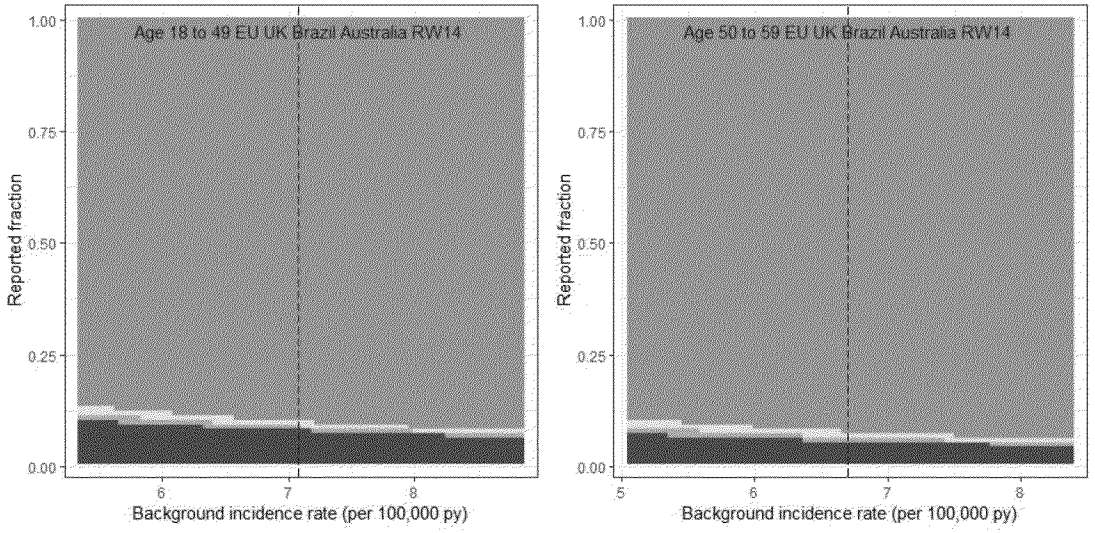
Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)
						

[a] Incidence rate (IR) Source: Truven Marketscan 2019

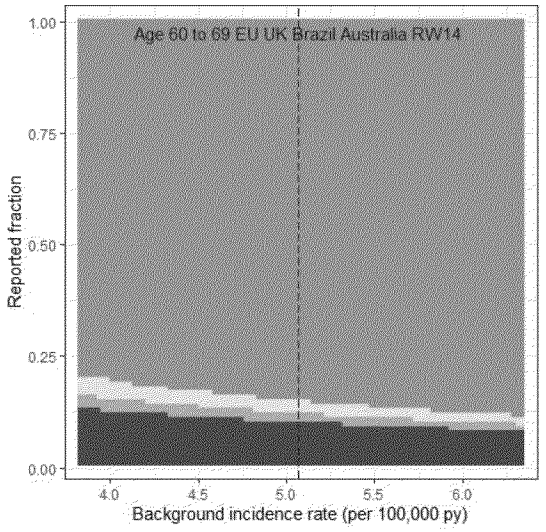
CI Confidence Interval; E Expected; EEA European Economic Area, O observed; TTO Time to onset; UK United Kingdom; UNK unknown

Table 91 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from EU+UK+Brazil+Australia

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)	
18 to 49	27	298.78	14	7.08	110094983	0.09 (0.06 - 0.13)	Observed significantly < expected
50 to 59	10	149.82	14	6.7	58336094	0.07 (0.03 - 0.12)	Observed significantly < expected
60 to 69	14	112.64	14	5.07	57960860	0.12 (0.07 - 0.21)	Observed significantly < expected
Over 70	9	86.99	14	7.01	32376365	0.1 (0.05 - 0.2)	Observed significantly < expected
18 to 49 incl UNK TTO	38	298.78	14	7.08	110094983	0.13 (0.09 - 0.17)	Observed significantly < expected
50 to 59 incl UNK TTO	12	149.82	14	6.7	58336094	0.08 (0.04 - 0.14)	Observed significantly < expected
60 to 69 incl UNK TTO	18	112.64	14	5.07	57960860	0.16 (0.09 - 0.25)	Observed significantly < expected
Over 70 incl UNK TTO	12	86.99	14	7.01	32376365	0.14 (0.07 - 0.24)	Observed significantly < expected


Age 18 to 49 EU UK Brazil Australia RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
Background incidence rate (per 100,000 py)

Age 50 to 59 EU UK Brazil Australia RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
5
6
7
8
Background incidence rate (per 100,000 py)


Age 60 to 69 EU UK Brazil Australia RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
4.0
4.5
5.0
5.5
6.0
Background incidence rate (per 100,000 py)

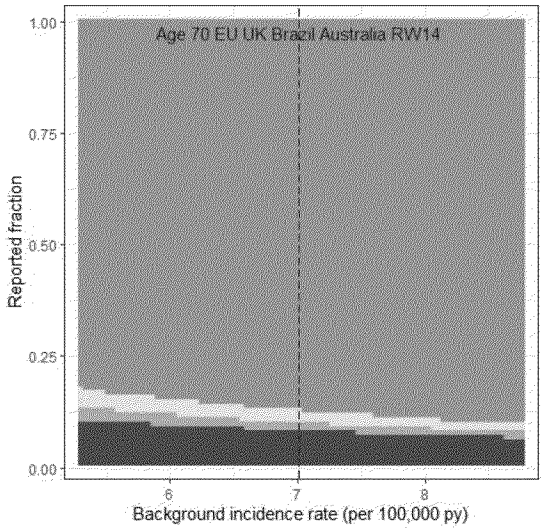
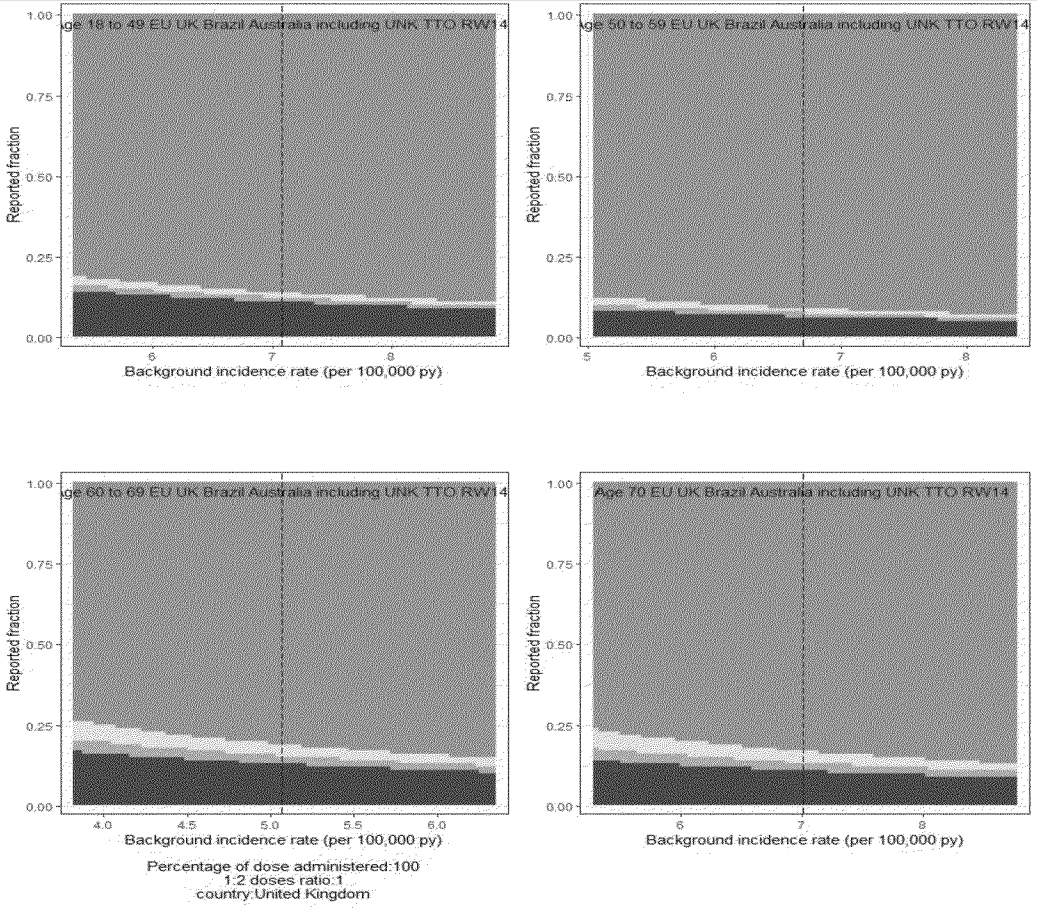

Age 70 EU UK Brazil Australia RW14
Reported fraction
1.00
0.75
0.50
0.25
0.00
6
7
8
Background incidence rate (per 100,000 py)

Table 91 Observed Vs Expected analysis for Erythema multiforme cases stratified by age and gender from EU+UK+Brazil+Australia

Description	Observed Cases	Expected Cases	Risk window	Background rates [a]	Exposure	O over E ratio (95% CI)



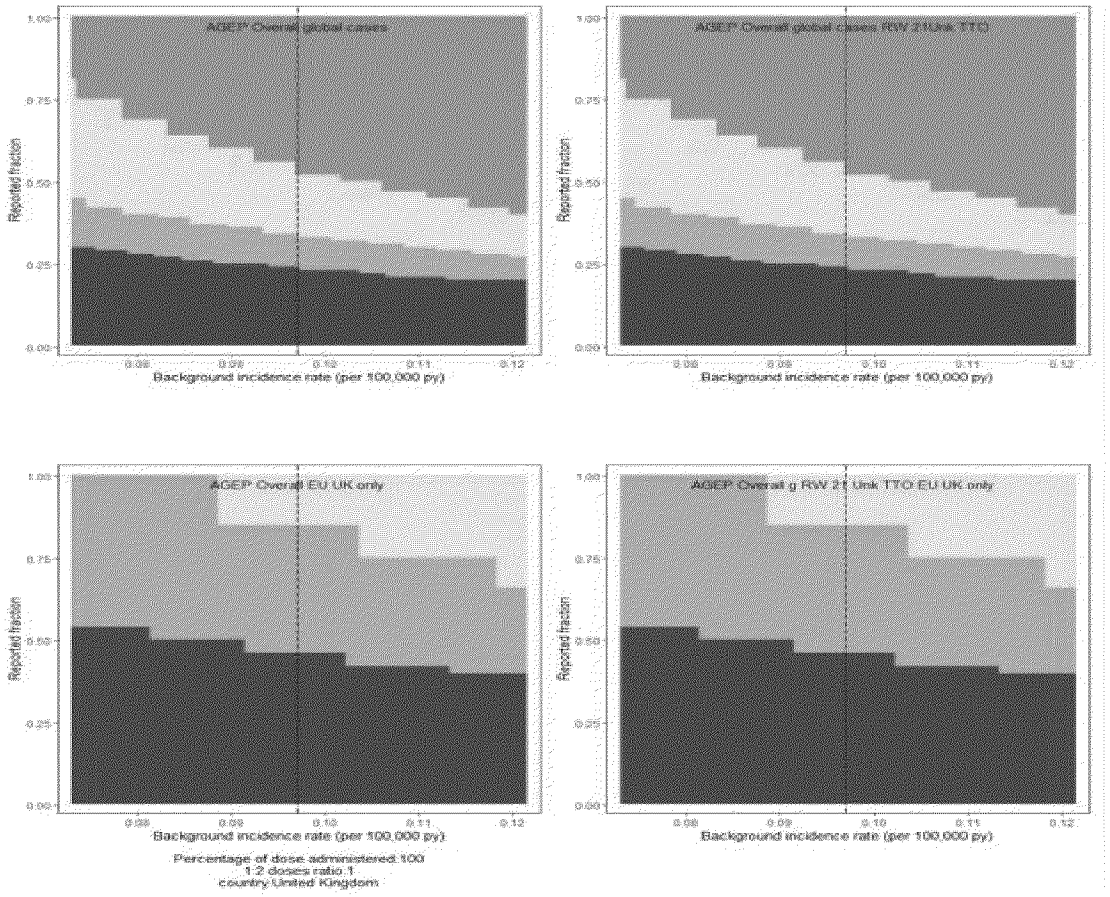
[a] Incidence rate (IR) Source: Willame et al 2021 [A] (Meta-analysis IR from 2010-2013 and 2017-2019 - Erythema multiforme (Narrow)).

CI Confidence Interval; E Expected; EEA European Economic Area; EU European union; O observed; TTO Time to onset; UK United Kingdom.

Table 92 Observed Versus Expected analysis for Acute generalized exanthematous pustulosis (AGEP) (Overall)

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
AGEP Overall global cases	9	26	21	0.097	466115644	0.35 (0.16 - 0.66)	Observed significantly < expected
AGEP Overall global cases RW 21 (Including Unk TTO)	9	26	21	0.097	466115644	0.35 (0.16 - 0.66)	Observed significantly < expected
AGEP Overall EU UK only	6	6.57	21	0.097	117724493	0.91 (0.34 - 1.99)	Observed < expected
AGEP Overall EU UK RW 21 (Including Unk TTO)	6	6.57	21	0.097	117724493	0.91 (0.34 - 1.99)	Observed < expected

Table 92 Observed Versus Expected analysis for Acute generalized exanthematous pustulosis (AGEP) (Overall)

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
							

[a] Incidence rate (IR) Source: Sidoroff et al 2007

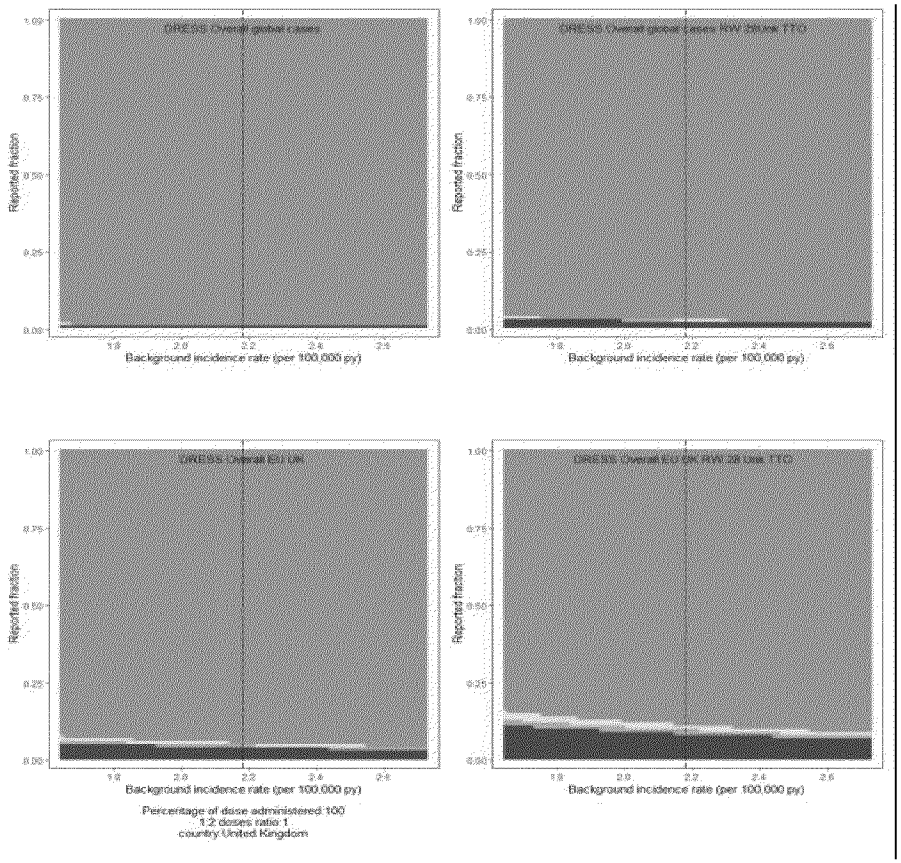
CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, Unk Unknown.

Table 93 Observed Versus Expected analysis for Drug reaction with eosinophilia and systemic symptoms (DRESS) (Overall)

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	
DRESS Overall global cases	11	778.98	28	2.18	466115644	0.01 (0.01 - 0.03)	Observed significantly < expected
DRESS Overall global cases RW 28 (including unknown TTO)	23	778.98	28	2.18	466115644	0.03 (0.02 - 0.04)	Observed significantly < expected
DRESS Overall EU UK	10	196.74	28	2.18	117724493	0.05 (0.02 - 0.09)	Observed significantly < expected
DRESS Overall EU UK RW 28 (including unknown TTO)	20	196.74	28	2.18	117724493	0.1 (0.06 - 0.16)	Observed significantly < expected

Table 93 Observed Versus Expected analysis for Drug reaction with eosinophilia and systemic symptoms (DRESS) (Overall)

Description	Observed Cases	Expected cases	Risk Period/ window (days)	Background rate/100,000 person years [a]	Exposure	O over E ratio (95% CI)	



Incidence rate (IR) Source: Wolfson et al 2018

CI Confidence Interval; E Expected; IR Incidence Rate; O Observed, TTO Time to onset, UK United Kingdom, Unk Unknown.

Appendix A Description of literature background incidence rates

Based on the request from PRAC description of literature references used for background IRs are provided below. Most of the IR used are based on ACCESS protocol and MarketScan, description of literature IR are provided below. The literature search focused on articles in the UK and EU involving vaccinated populations in adults and the elderly.

1 ACUTE ASEPTIC ARTHRITIS

Incidence number	**115**
Unit	100,000 PY
Year of IR	1999–2000
Setting	Population based prospective referral study in an adult population in Kronoberg County in southern Sweden
Follow-up period	A systematic follow up of incoming referrals was conducted up to 31 January 2001.
Data source	The patients were referred from primary healthcare centres to the rheumatology department in Växjö Central Hospital or to the one private rheumatologist in Växjö participating in the study
Number of people observed	132,000
Comments/Notes	
Reference (doi)	Söderlin et al (doi: 10.1136/ard.61.10.911. PMID: 12228162; PMCID: PMC1753904)
Incidence number	**25**
Unit	100,000 PY
Year of IR	2004
Setting	nationwide primary care registry, Spain
Follow-up period	A systematic follow up of incoming referrals was conducted up to 31 January 2001. 6 months after the first rheumatologist visit
Data source	Primary care physicians were instructed in the detection of new cases using a checklist. All cases were evaluated at EA units (EAUs) within 15 days of detection. ACR criteria for the classification of RA were assessed every 6 months thereafter.
Number of people observed	4,642,378
Comments/Notes	
Reference (doi)	Carbonell et al 2008 (doi: 10.1093/rheumatology/ken205. Epub 2008 May 29. PMID: 18511475)

IR Incidence rate, PY Person years

2 ACUTE PANCREATITIS

Incidence number	**56**
Unit	100,000 PY
Year of IR	2018
Reference (doi)	NICE guideline Pancreatitis

IR Incidence rate, PY Person years

3 ANAPHYLAXIS-TYPE REACTIONS

Incidence number	**1**
Unit	1000
Year of IR	2014
Reference (doi)	NICE guideline CG183

IR Incidence rate

4 AUTOIMMUNE THYROIDITIS

Incidence number	**80**
Unit	100,000 PY
Year of IR	1980-2008
Setting	systematic review of literature published between 1980 and 2008 on the incidence of autoimmune thyroid disease; 23 papers were included and critically appraised in this review
Data source	systematic review of published literature
Reference (doi)	McGrogan et al 2008 (DOI: 10.1111/j.1365-2265.2008.03338.x)

IR Incidence rate, PY Person years

5 BELL'S PALSY

Incidence number	**20.2**
Unit	100,000 PY
Year of IR	1992 and 1996
Setting	Survey of all new cases of Bell's palsy occurring between 1992 and 1996 in practices contributing data to the UK General Practice Research Database (GPRD)
Follow-up period	-

Incidence number	**20.2**
Data source	UK General Practice Research Database (GPRD)
Number of people observed	2473
Comments/Notes	The study included any patient for whom first onset was between 1 January 1992 and 31 December 1996 and within the time interval during which the practice was judged to be contributing quality data as defined by the Office for National Statistics. There was no difference in incidence according to sex or season but there were significant changes over time: incidence was higher in the first year of the study period than in subsequent years. There was no clustering of cases in households and no evidence of any tendency for herpes simplex infections to precede Bell's palsy.
Reference (doi)	Rowlands et al 2002 (DOI: 10.1046/j.1468-1331.2002.00343.x)

GPRD General Practice Research Database, IR Incidence rate, PY Person years, UK United Kingdom

6 CHRONIC FATIGUE SYNDROME, FIBROMYALGIA, POST-VIRAL FATIGUE SYNDROME

Incidence number	**Chronic fatigue syndrome=14.8** **post-viral fatigue syndrome=12.2** **fibromyalgia=33.3**
Unit	100,000 PY
Year of IR	2001-2013
Setting	NHS primary care practices in the UK. Patients registered with general practices linked to the Clinical Practice Research Datalink (CPRD) primary care database from January 2001 to December 2013.
Follow-up period	Yearly
Data source	Electronic health records cohort study.
Number of people observed	From the source population in CPRD, 63,683 patients were deemed to have acceptable data and had at least one diagnostic index event during the study period. Of these patients, 48,663 had the event(s) within the practice UTS period, of whom 42,316 patients had at least 12 months of UTS data prior to the index date. FM accounted for half of the diagnoses (49.6%), followed by CFS/ME (23.1%), PVFS (16.3%), and asthenia/debility (9.9%)
Comments/Notes	The average annual incidence of recorded cases of CFS/ME over the whole study period was 14.8 (95% CI 14.5, 15.1) per 100,000 people; for FM, the annual rate per 100,000 people was 33.3 (32.8, 33.8); for PVFS 12.2 (11.9, 12.5),

Incidence number	**Chronic fatigue syndrome=14.8 post-viral fatigue syndrome=12.2 fibromyalgia=33.3**
Reference (doi)	Collin et al 2017 (DOI: 10.1177/0141076817702530)

CPRD Clinical Practice Research Datalink, IR Incidence rate, PY Person years, UK United Kingdom

7 ACUTE TRANSVERSE MYELITIS

Incidence number	**3**
Unit	100,000 PY
Year of IR	1998 to 2004
Setting	This study was conducted within the population of KPNC which is a comprehensive health care organization that serves approximately 3.2 million persons.
Follow-up period	This was a cohort study which included all males and females who were KPNC members for at least 77 of 84 months during the study period from January 1, 1998 to December 31, 2004. In 1998, the subjects in the cohort were aged 10–55 years. In 2004, the maximum age was 62.
Data source	population of KPNC
Number of people observed	153, and 75.7 % were verified after medical record review
Reference (doi)	West et al 2012 (DOI: 10.1055/s-0032-1322586)

IR Incidence rate, PY Person years, KPNC Kaiser Permanente Northern California

8 OPTIC NEURITIS

Incidence number	**3.7**
Unit	100,000 PY
Year of IR	January 1, 1995, to September 1, 2019
Setting	cohort study analyzed data from The Health Improvement Network
Follow-up period	Yearly
Data source	Matched case-control and retrospective cohort studies were performed using data from January 1, 1995, to September 1, 2019, to explore the odds of antecedent diagnosis and hazard of incident diagnosis of 66 IMIDs in patients compared with controls.
Number of people observed	A total of 1962 of 2826 patients (69.4%) with incident ON were female and 1192 of 1290 92.4%) were White, with a mean (SD) age of 35.6 (15.6) years.

Incidence number	**3.7**
Reference (doi)	Braithwaite et al 2020 (doi:10.1001/jamaneurol.2020.3502)

IR Incidence rate, PY Person years

9 MULTIPLE SCLEROSIS

Incidence number	**11**
Unit	100,000 PY
Year of IR	The estimated incidence of MS was calculated for the 9 financial years 2008 to 2009 through to 2016 to 2017
Setting	primary care record
Follow-up period	Yearly
Data source	sample of anonymised primary care records provided by The Health Improvement Network (THIN)[footnote 2] dataset (version January 2018)
Number of people observed	MS estimated prevalence is 190 cases per 100,000 population, with 105,800 individuals in England MS is more than twice as common in females than males, 272 versus 106 per 100,000 population females in the 50 to 59 years age group are 3 times more likely than males of a similar age to have MS (578 and 184 per 100,000 population respectively)
Reference (doi)	Multiple sclerosis UK guidance 2020

IR Incidence rate, MS Multiple-sclerosis, PY Person years, UK United Kingdom

10 POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS)

Incidence number	**6**
Unit	100,000
Year of IR	2016
Setting	POTS in Olmsted County;
Follow-up period	Yearly

Incidence number	**6**
Data source	Using the Rochester Epidemiology Project, we narrowed this search to those who were tested while residents of Olmstead County. The identified records were carefully reviewed to confirm a clinical diagnosis. Census counts for the Olmstead County population from 2000 to 2016 were gathered from government records (www.census.gov).
Number of people observed	A total of 17 years were reviewed (2000–2016) during which we identified 105 unique patients diagnosed with POTS while living in Olmsted County, 91 of which were female (89%). The mean age at diagnosis was 23.4 years. The mean duration of documented orthostatic symptoms was 4.5 years.
Reference (doi)	AbdelRazek et al 2019

IR Incidence rate, PY Person years, POTS postural orthostatic tachycardia syndrome.

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