

## Online Supplement

### Title: Future trends in cystic fibrosis demography in 34 European countries

#### The flow method

The flow method was used for estimating the number of children and adults with CF in countries of group A by 2025. This method is based on calculation of the evolution of a known cohort (such as the CF population followed in a national registry) during a period of observation. Entering, exiting and transition flows in a population of CF children and adults from year  $t$  to year  $t+1$  are shown in **Figure 1** of the main manuscript. Each year, exiting cases include deaths (which can occur in paediatric or in adult population) and patients lost to follow-up, whereas entering cases include new diagnoses/referrals of CF based on neonatal screening or clinical diagnosis in children and in adults, and re-tracking of previously lost to follow-up patients. Additionally, transition from the paediatric to adult population occurs in patient aged 18 years.

#### Calculation of entering, exiting and transition flows for countries of group A:

Each year, flows were calculated in each country as follows:

##### Exiting flows:

-death flows:

- death flow in children:  $\frac{O_{c,1}}{C_t}$

- death flow in adults:  $\frac{O_{a,1}}{A_t}$

-losses to follow-up flows:

- - losses to follow-up flow in children:  $\frac{O_{c,2}}{C_t}$

- losses to follow-up flow in adults :  $\frac{O_{a,2}}{A_t}$

##### Entering flows:

- new diagnosis (neonatal screening):  $\frac{I_{c,1}}{C_t}$

- new diagnosis (neonatal screening excluded):
  - paediatric population:  $\frac{I_{c,2}}{C_t}$
  - adult population:  $\frac{I_{a,2}}{A_t}$
- Patient previously lost to follow-up and re-tracked by the registry:
  - paediatric population:  $\frac{I_{c,3}}{C_t}$
  - adult population:  $\frac{I_{a,3}}{A_t}$

### Transition flows

- Transition from year to year in the paediatric population :  $\frac{M_c}{C_t}$
- Transition from year to year in the adult population :  $\frac{M_a}{A_t}$
- Transition from the paediatric to adult population:  $\frac{T_{c,a}}{C_t}$

We computed mean yearly entering, exiting and transition flows in the cohort over a period of time, using longitudinal data, i.e. data linked at patient level for subsequent years of follow-up. Data obtained from the ECFS Patient Registry were used to calculate mean flows for each country. A minimum of 4 years of longitudinal data was considered necessary for calculation of mean yearly flows, to reduce year to year variations in flows. According to data availability, these flows were calculated using 4 to 8 years of follow-up as follows: Czech Republic 4 years (2006-2009), The Netherlands 4 years (2007-2010), United Kingdom 5 years (2008-2012), Belgium and Denmark 7 years (2003-2009), France 8 years (2003-2010). In each of these countries, mean yearly entering, exiting and transition flows over the observation period were used to estimate the number of CF children and adults in 2025. Weighted (based on relative contribution of the country CF population to total CF population in countries of group A) mean flows obtained in these 6 countries were later applied to Registry data of countries of group B for estimating the number of CF children and adults in countries of group B by 2025.

## Weighted mean flows

Weighted (based on relative contribution of the country CF population to total CF population in countries of group A) mean flows obtained in Group A countries were calculated and applied to registry data of countries in group B to estimate their numbers of CF children and adults by 2025. The rationale and method for using weighted mean flow is explained below.

Because it would seem inappropriate that the flows calculated in Belgium (which had 1,129 CF patients in 2009) and in the UK (which had 9,030 CF patients in 2009) would account similarly in the calculation of the mean flow for Group A countries, we calculated the weighted mean flows. The weighted mean is similar to an arithmetic mean, where instead of each of the data points contributing equally to the final average, some data points contribute more than others. In our case, each flow was pondered using the following formula:

$$- \bar{x} = \sum_{j=1}^n f_j x_j \text{ with } f_j = \frac{n_j}{\sum_{j=1}^n n_j} \text{ where } \bar{x} \text{ represents the mean flow and } n_j \text{ the number of patients in}$$

each country.



**Table S1. Mean values of the flows for countries of group A**

Country	Period	Children ( $\leq 17$ yrs)							Adults ( $\geq 18$ yrs)				
		Oc,1	Oc,2	Mc	Tc,a	Ic,1	Ic,2	Ic,3	Oa,1	Oa,2	Ma	Ia,2	Ia,3
Belgium	2003-2009	0.0019	0.0351	0.9139	0.0491	0.0256	0.0629	0.0223	0.0146	0.0312	0.9544	0.0446	0.0229
Czech Republic	2006-2009	0.0052	0.0170	0.9224	0.0572	0.0100	0.0673	0.0069	0.0245	0.0319	0.9478	0.0415	0.0000
Denmark	2003-2009	0.0050	0.0081	0.9221	0.0649	0.0273	0.0442	0.0010	0.0249	0.0066	0.9695	0.0062	0.0009
France	2003-2010	0.0043	0.0368	0.9063	0.0523	0.0491	0.0425	0.0251	0.0220	0.0684	0.9093	0.0376	0.0587
United Kingdom	2008-2012	0.0018	0.0022	0.9321	0.0644	0.0513	0.0433	0.0000	0.0161	0.0079	0.9750	0.0213	0.0001
The Netherlands	2007-2010	0.0017	0.0700	0.8746	0.0537	0.0095	0.1166	0.0143	0.0130	0.1745	0.8156	0.1385	0.1182
Weighted mean*		0.0028	0.0205	0.9183	0.0586	0.0433	0.0483	0.0107	0.0178	0.0381	0.9438	0.0304	0.0258

\*Weighted means were calculated based on the relative contribution of the country CF population to total CF population in countries of group A

**Abbreviations:**

Oc,1 and Oa,1: deaths in paediatric and adult populations, respectively

Oc,2 and Oa,2: losses to follow-up in paediatric and adult population, respectively

Mc: staying in the paediatric population

Ma: staying in the adult population

Tc,a: transition from paediatric to adult population

Ic,1: new diagnosis by neonatal screening

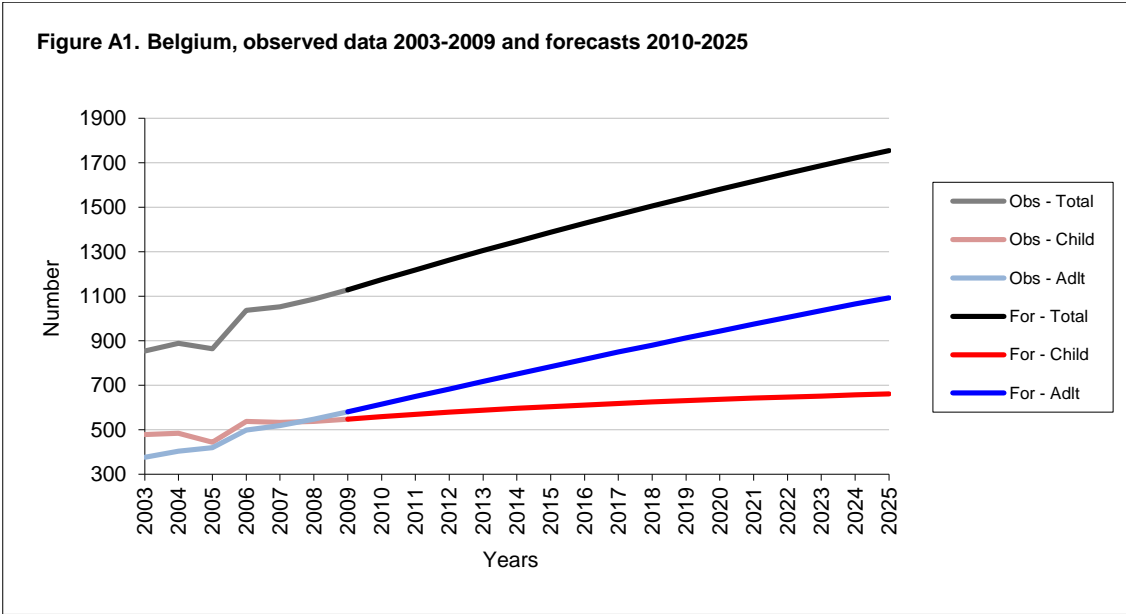
Ic,2 and Ia,2: new diagnosis in the paediatric and adult populations, respectively

Ic,3 and Ia,3: re-tracked by the Registry (patients previously lost to follow-up) in paediatric and adult populations, respectively.

**CF population forecasts in groups A and B, by country**

Table A1. CF population forecasts for Belgium (country group: A)

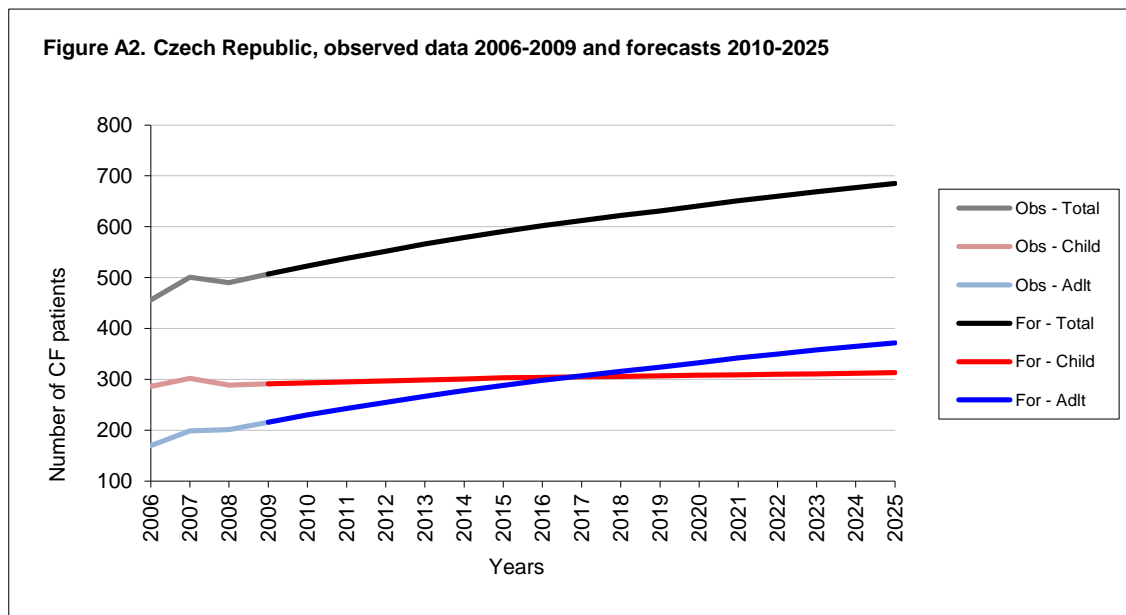
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
observed	2003	478	376	854
	2004	484	404	888
	2005	444	420	864
	2006	537	499	1,036
	2007	533	519	1,052
	2008	538	548	1,086
	2009	548	581	1,129
forecasts	2010	559	615	1,174
	2011	569	649	1,218
	2012	579	683	1,262
	2013	588	717	1,305
	2014	596	750	1,346
	2015	604	783	1,387
	2016	611	816	1,427
	2017	618	849	1,467
	2018	625	880	1,505
	2019	631	912	1,543
	2020	637	943	1,580
	2021	642	974	1,616
	2022	647	1,005	1,652
	2023	651	1,035	1,686
	2024	656	1,065	1,721
	2025	661	1,093	1,754



Obs: observed  
For: forecasts

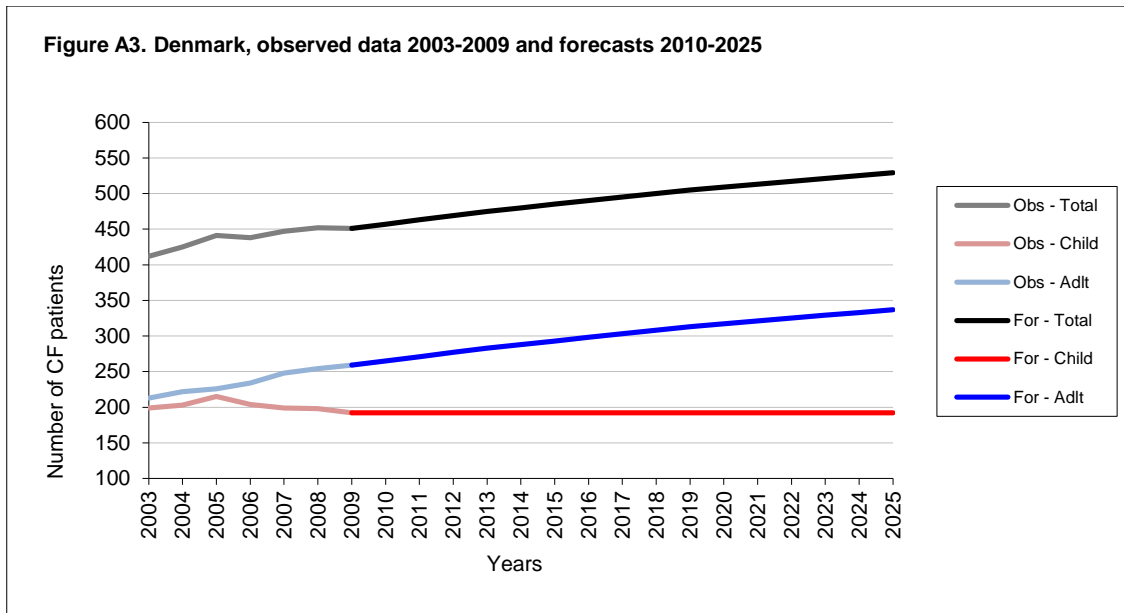
Table A2. CF population forecast for Czech Republic, (Country group: A)

Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2006	286	170	456
	2007	302	199	501
	2008	289	201	490
	2009	291	216	507
	2010	293	230	523
	2011	295	243	538
	2012	297	255	552
	2013	299	267	566
	2014	301	278	579
Forecasts	2015	303	288	591
	2016	304	298	602
	2017	305	307	612
	2018	306	316	622
	2019	307	324	631
	2020	308	333	641
	2021	309	342	651
	2022	310	350	660
	2023	311	358	669
	2024	312	365	677
	2025	313	372	685



Obs: observed  
For: forecasts

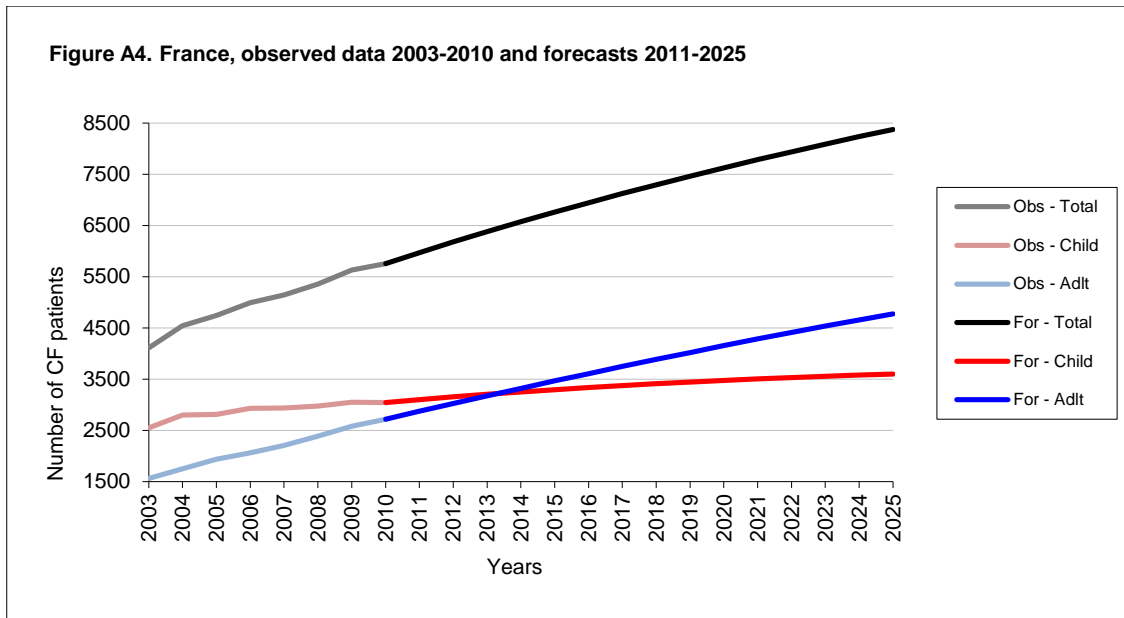
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2003	199	213	412
	2004	203	222	425
	2005	215	226	441
	2006	204	234	438
	2007	199	248	447
	2008	198	254	452
	2009	192	259	451
Forecasts	2010	192	265	457
	2011	192	271	463
	2012	192	277	469
	2013	192	283	475
	2014	192	288	480
	2015	192	293	485
	2016	192	298	490
	2017	192	303	495
	2018	192	308	500
	2019	192	313	505
	2020	192	317	509
	2021	192	321	513
	2022	192	325	517
	2023	192	329	521
	2024	192	333	525
	2025	192	337	529



Obs: observed  
For: forecasts

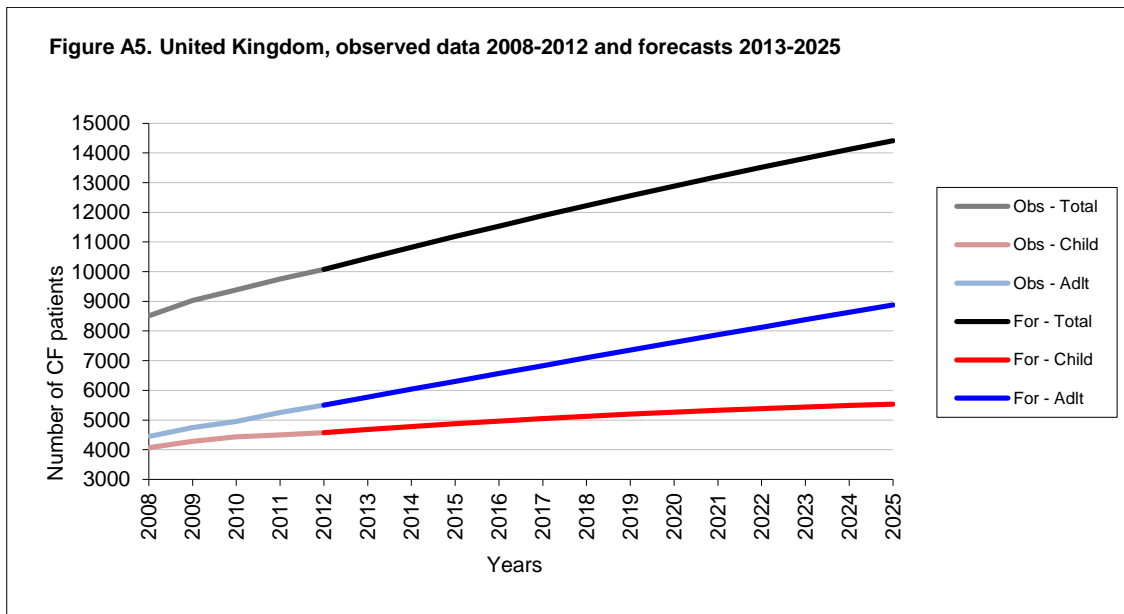


Table A4. CF population forecasts for France (country group: A)					
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total	
Observed	2003	2,550	1,561	4,111	
	2004	2,799	1,745	4,544	
	2005	2,812	1,933	4,745	
	2006	2,932	2,062	4,994	
	2007	2,935	2,205	5,140	
	2008	2,971	2,386	5,357	
	2009	3,049	2,579	5,628	
	2010	3,040	2,718	5,758	
	Forecasts	2011	3,098	2,872	5,970
		2012	3,153	3,024	6,177
2013		3,204	3,173	6,377	
2014		3,251	3,320	6,571	
2015		3,295	3,465	6,760	
2016		3,336	3,607	6,943	
2017		3,374	3,747	7,121	
2018		3,410	3,884	7,294	
2019		3,443	4,019	7,462	
2020		3,473	4,152	7,625	
2021		3,502	4,283	7,785	
2022		3,529	4,410	7,939	
2023		3,554	4,535	8,089	
2024		3,577	4,657	8,234	
2025		3,599	4,776	8,375	



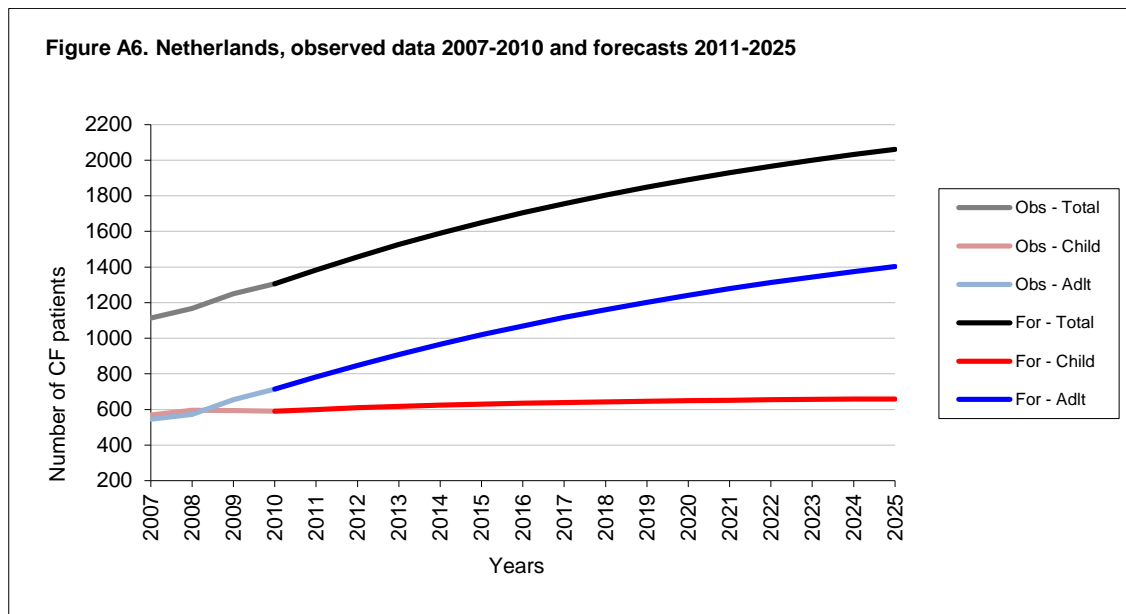
Obs: observed  
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Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2008	4,067	4,446	8,513
	2009	4,283	4,747	9,030
	2010	4,435	4,950	9,385
	2011	4,499	5,250	9,749
	2012	4,572	5,507	10,079
Forecasts	2013	4,682	5,772	10,454
	2014	4,784	6,037	10,821
	2015	4,879	6,303	11,182
	2016	4,968	6,568	11,536
	2017	5,051	6,832	11,883
	2018	5,128	7,095	12,223
	2019	5,200	7,356	12,556
	2020	5,267	7,616	12,883
	2021	5,329	7,873	13,202
	2022	5,387	8,128	13,515
	2023	5,441	8,380	13,821
	2024	5,492	8,629	14,121
	2025	5,539	8,876	14,415



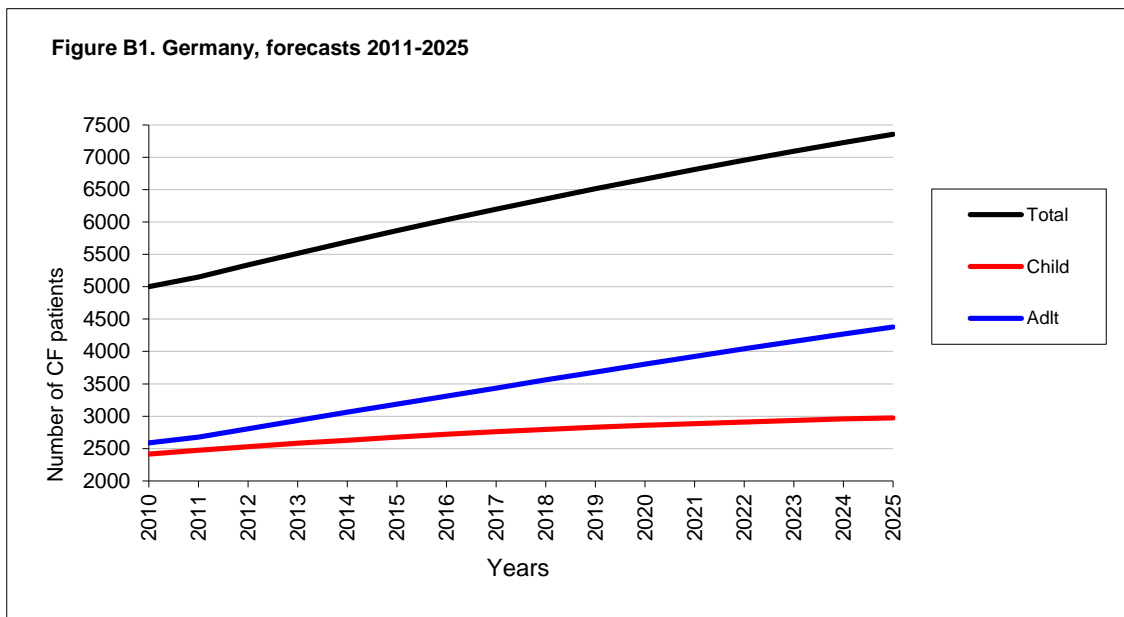
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Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2007	568	545	1,113
	2008	596	572	1,168
	2009	594	655	1,249
	2010	591	715	1,306
	2011	600	783	1,383
	2012	609	848	1,457
	2013	617	909	1,526
	2014	624	965	1,589
	2015	630	1,019	1,649
	2016	635	1,069	1,704
Forecast	2017	639	1,116	1,755
	2018	643	1,160	1,803
	2019	646	1,202	1,848
	2020	649	1,241	1,890
	2021	652	1,278	1,930
	2022	654	1,312	1,966
	2023	656	1,344	2,000
	2024	658	1,374	2,032
	2025	659	1,402	2,061



Obs: observed  
For: forecasts

Table B1. CF population forecasts for Germany (country group: B)				
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2010	2,413	2,590	5,003
	2011	2,473	2,677	5,150
	2012	2,529	2,807	5,336
	2013	2,581	2,935	5,516
	2014	2,629	3,064	5,693
	2015	2,678	3,187	5,865
	2016	2,722	3,311	6,033
Forecasts	2017	2,762	3,435	6,197
	2018	2,797	3,560	6,357
	2019	2,830	3,682	6,512
	2020	2,860	3,803	6,663
	2021	2,886	3,924	6,810
	2022	2,911	4,041	6,952
	2023	2,936	4,155	7,091
	2024	2,958	4,267	7,225
	2025	2,976	4,380	7,356



Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2010	339	218	557
	2011	344	241	585
	2012	349	262	611
	2013	352	284	636
	2014	357	304	661
	2015	361	325	686
	2016	365	345	710
	2017	368	365	733
Forecasts	2018	371	384	755
	2019	373	404	777
	2020	376	422	798
	2021	378	440	818
	2022	380	457	837
	2023	382	474	856
	2024	385	489	874
	2025	388	506	894

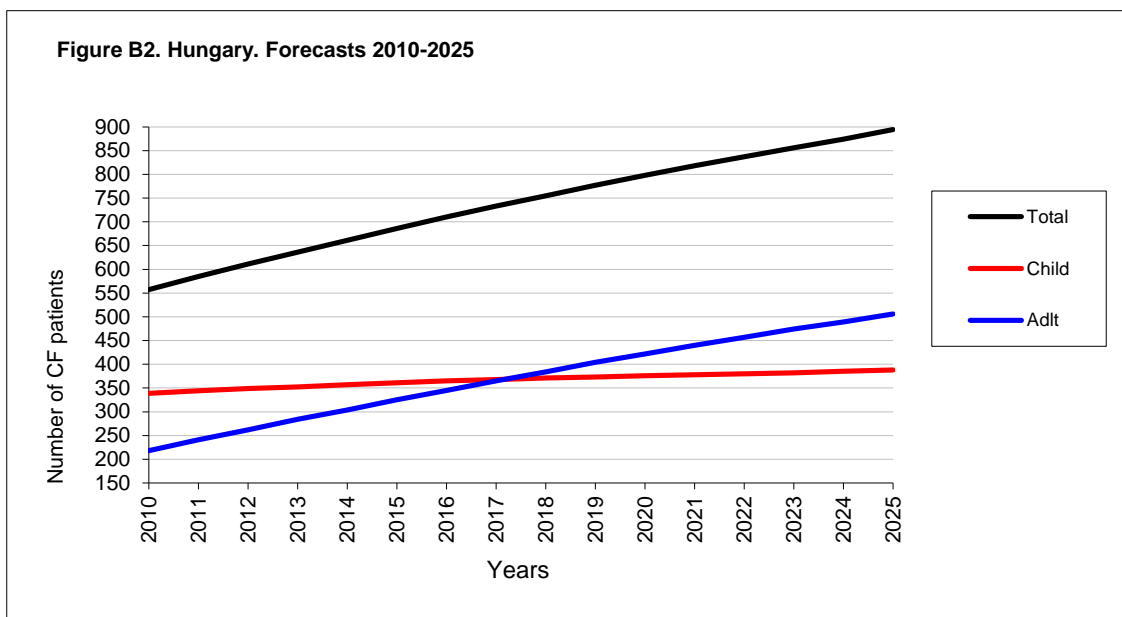


Table B3. CF population forecasts for Ireland, (country group: B)					
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total	
Observed	2008	504	517	1,021	
	2009	514	529	1,043	
	2010	527	554	1,081	
	2011	540	579	1,119	
	2012	551	605	1,156	
	2013	562	630	1,192	
	2014	572	655	1,227	
	2015	580	681	1,261	
	2016	588	707	1,295	
	Forecasts	2017	595	731	1,326
		2018	601	756	1,357
		2019	607	781	1,388
		2020	613	804	1,417
		2021	620	827	1,447
		2022	626	849	1,475
		2023	632	871	1,503
2024		635	894	1,529	
2025		640	915	1,555	

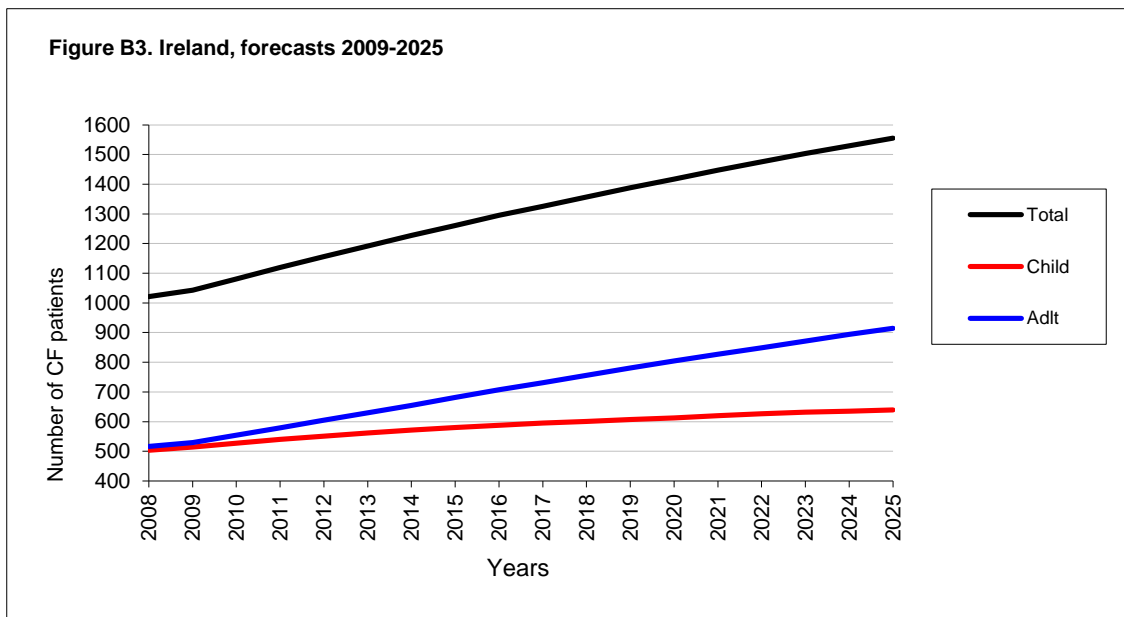


Table B4. CF population forecasts for Israel, (country group: B)				
Type of data	Year	Children ( $\leq 17$ )	Adults ( $\geq 18$ )	Total
Observed	2009	261	272	533
	2010	268	284	552
	2011	274	298	572
	2012	281	311	592
	2013	286	325	611
	2014	292	338	630
	2015	296	352	648
	2016	301	364	665
Forecasts	2017	305	377	682
	2018	308	391	699
	2019	312	403	715
	2020	316	414	730
	2021	319	427	746
	2022	321	440	761
	2023	324	451	775
	2024	326	464	790
	2025	327	476	803

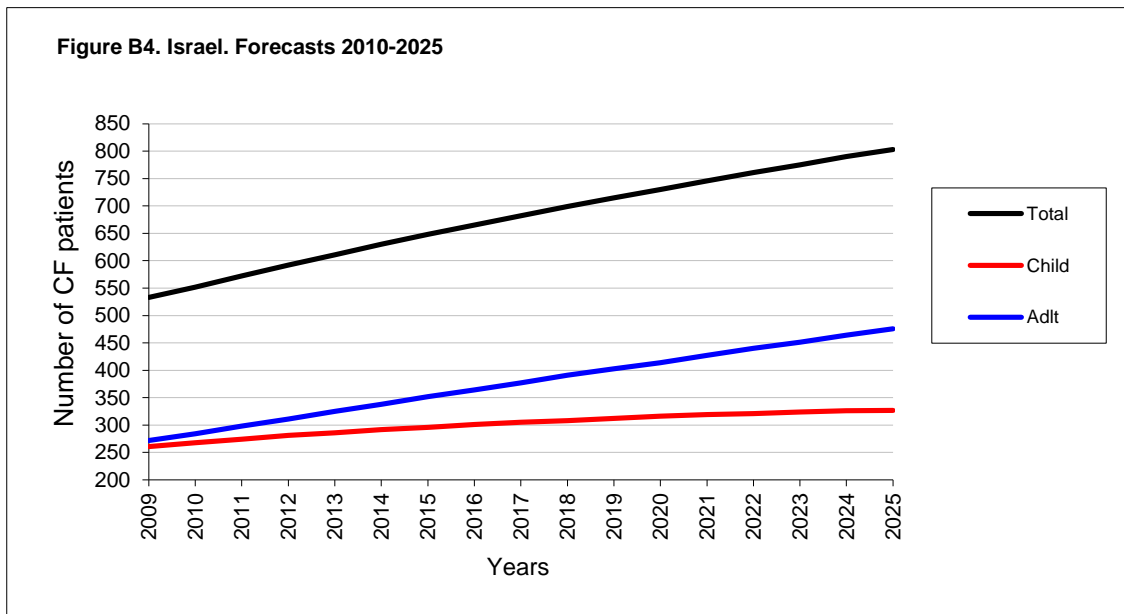
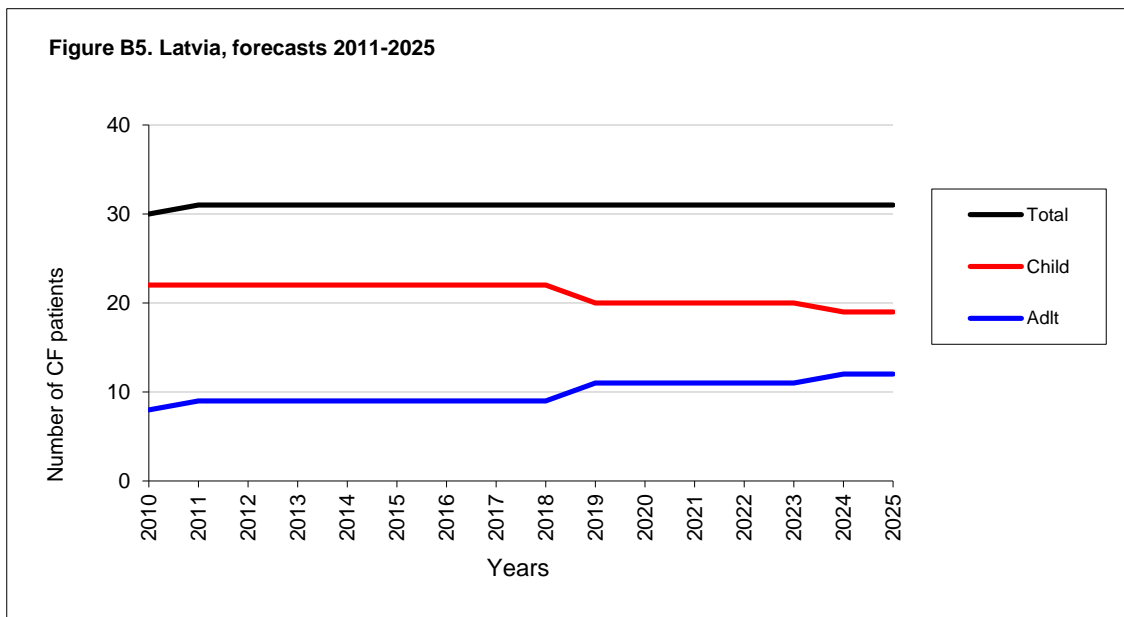
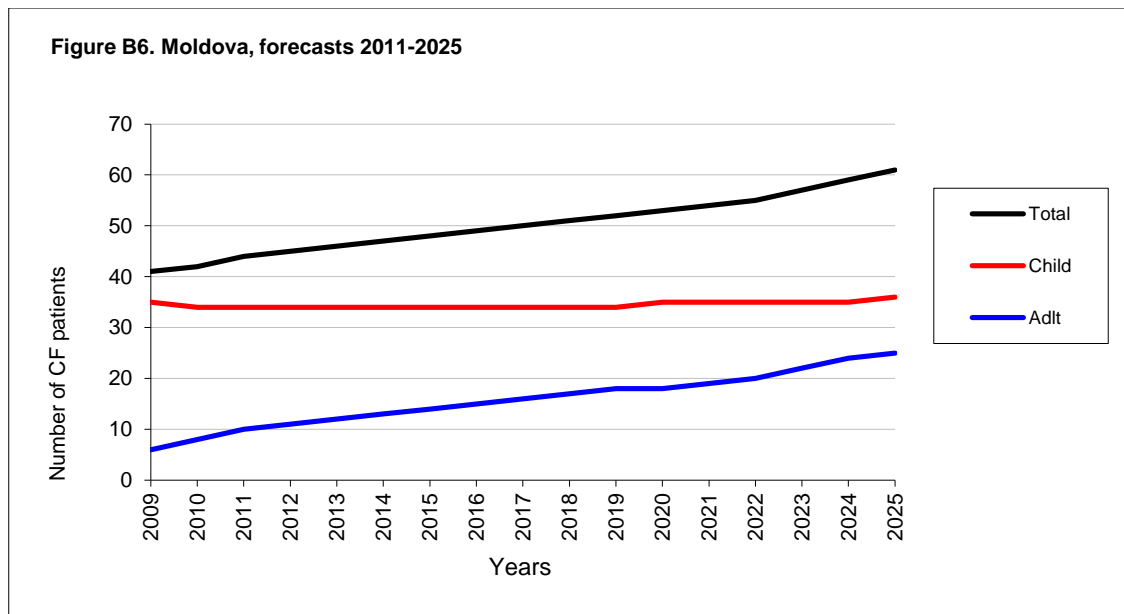


Table B5. CF population forecasts for Latvia (country group: B)				
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2010	22	8	30
	2011	22	9	31
	2012	22	9	31
	2013	22	9	31
	2014	22	9	31
	2015	22	9	31
	2016	22	9	31
	2017	22	9	31
Forecasts	2018	22	9	31
	2019	20	11	31
	2020	20	11	31
	2021	20	11	31
	2022	20	11	31
	2023	20	11	31
	2024	19	12	31
	2025	19	12	31





Type of data	Year	Children ( $\leq 17$ years)	Adults ( $\geq 18$ years)	Total
Observed	2009	35	6	41
	2010	34	8	42
	2011	34	10	44
	2012	34	11	45
	2013	34	12	46
	2014	34	13	47
	2015	34	14	48
	2016	34	15	49
Forecasts	2017	34	16	50
	2018	34	17	51
	2019	34	18	52
	2020	35	18	53
	2021	35	19	54
	2022	35	20	55
	2023	35	22	57
	2024	35	24	59
	2025	36	25	61



Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2010	86	35	121
	2011	87	38	125
	2012	90	42	132
	2013	92	47	139
	2014	94	50	144
	2015	96	54	150
	2016	97	59	156
	2017	98	65	163
Forecasts	2018	100	69	169
	2019	102	73	175
	2020	105	76	181
	2021	106	80	186
	2022	107	84	191
	2023	108	87	195
	2024	108	91	199
	2025	109	94	203

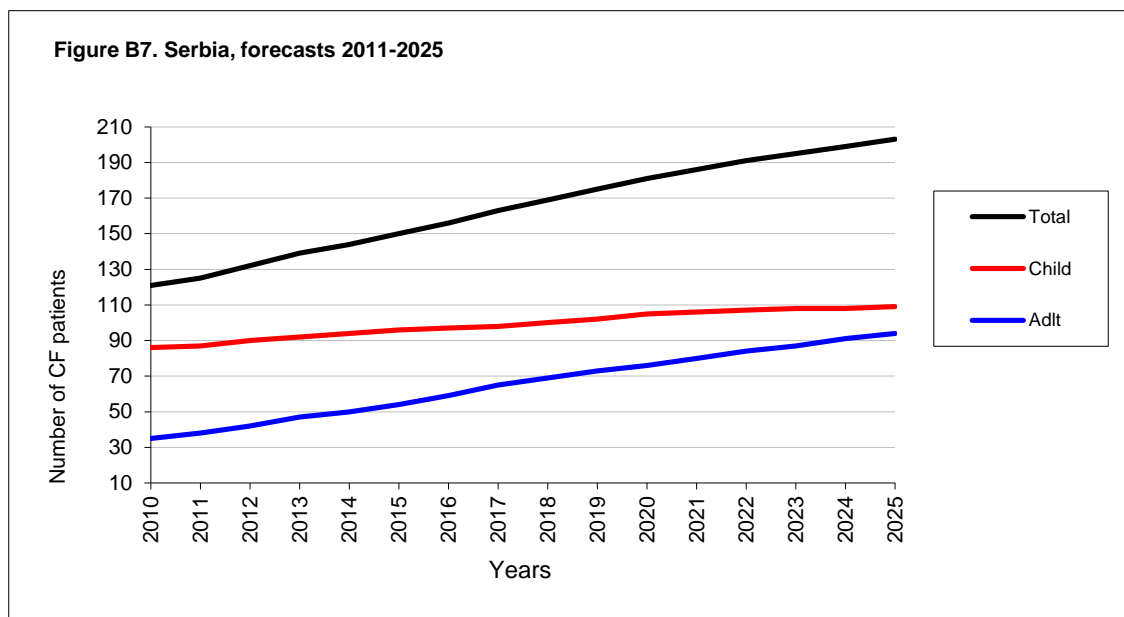


Table B8. CF population forecasts for Sweden (country group: B)					
Type of data	Year	Children ( $\leq 17$ )	Adults ( $\geq 18$ )	Total	
Observed	2009	256	322	578	
	2010	264	329	593	
	2011	270	342	612	
	2012	276	356	632	
	2013	281	369	650	
	2014	286	382	668	
	2015	290	397	687	
	2016	293	411	704	
	Forecasts	2017	297	424	721
		2018	301	436	737
		2019	303	449	752
		2020	305	463	768
		2021	307	476	783
		2022	309	488	797
		2023	311	501	812
		2024	313	513	826
2025		315	523	838	

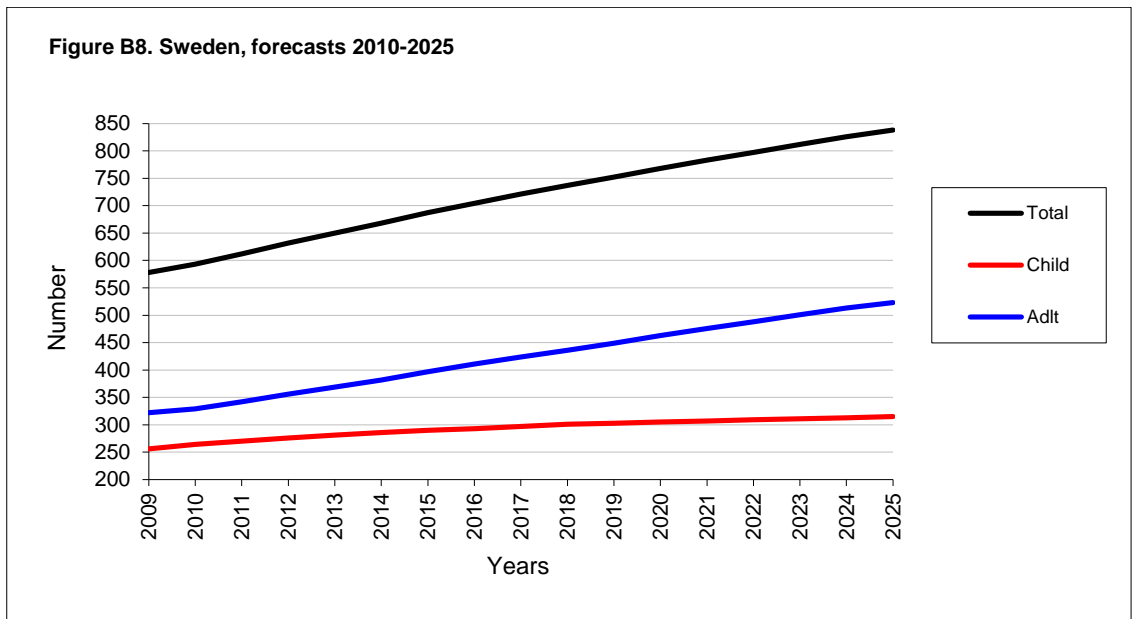


Table B9. CF population forecasts for Slovenia (country group: B)				
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2010	55	25	80
	2011	58	28	86
	2012	60	30	90
	2013	61	34	95
	2014	63	37	100
	2015	64	41	105
	2016	66	44	110
Forecasts	2017	69	46	115
	2018	70	48	118
	2019	71	50	121
	2020	72	52	124
	2021	72	55	127
	2022	72	58	130
	2023	73	60	133
	2024	74	63	137
	2025	74	66	140

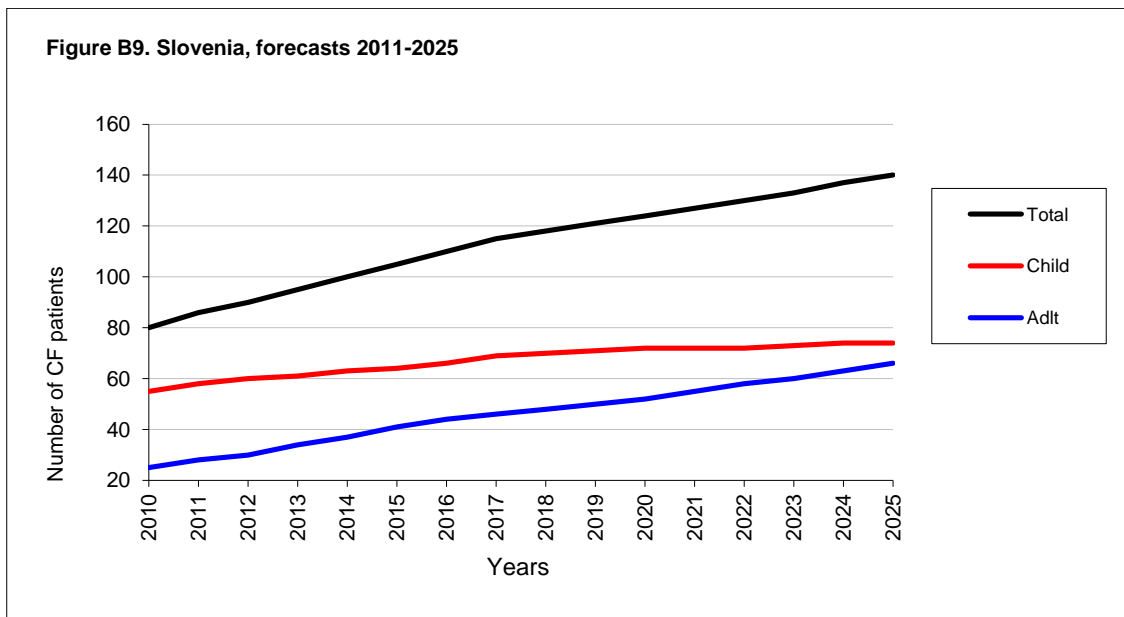


Table B10. CF population forecasts for Slovakia (country group: B)				
Type of data	Year	Children (≤17 years)	Adults (≥18 years)	Total
Observed	2010	151	182	333
	2011	157	189	346
	2012	162	196	358
	2013	168	202	370
	2014	172	210	382
	2015	177	216	393
	2016	181	224	405
	2017	186	230	416
Forecasts	2018	188	239	427
	2019	191	247	438
	2020	193	254	447
	2021	195	262	457
	2022	197	269	466
	2023	199	277	476
	2024	200	285	485
	2025	202	292	494

