



Estimating the Burden of COVID-19 in Luxembourg over three years of pandemic, with a focus on the uncertainty associated with PAC

Susanne Schmitz, Jérôme Weiss, Daniel Alvarez-Vaca, Martine Debacker, Guy Weber, Ala'a Alkerwi

Epidemiology and Statistics Unit, Directorate of Health, Ministry of Health and Social Security, Luxembourg

2nd international burden of disease conference
15th March 2024, Trieste



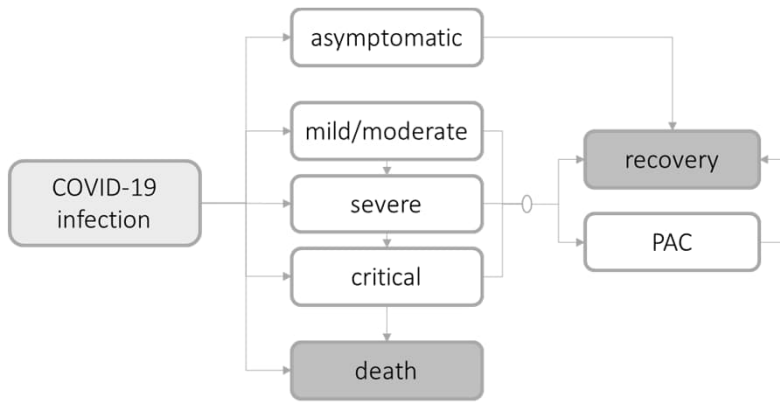
LE GOUVERNEMENT
DU GRAND-DUCHÉ DE LUXEMBOURG
Ministère de la Santé
et de la Sécurité sociale
Direction de la santé



- Evaluate the burden of COVID-19
 - In Luxembourg (resident population)
 - Over 3 years (March 2020 – March 2023)

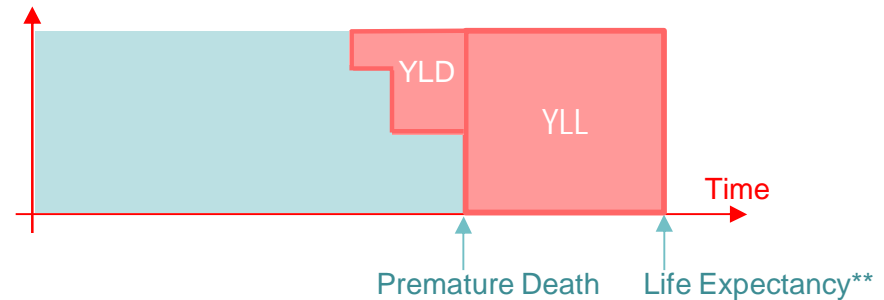
- Uncertainty associated with PAC (post acute consequences)

Methods



Consensus model (burden.eu)

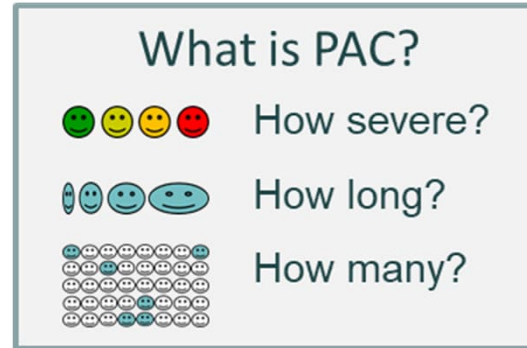
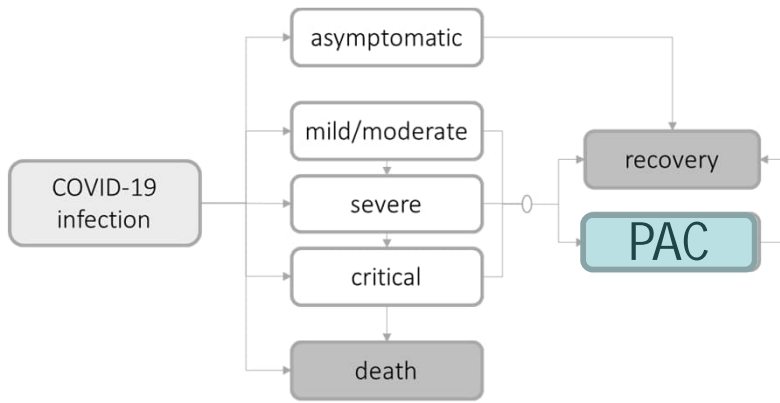
- Data from the national surveillance platform of COVID-19
- Outcome



$$\text{DALY} = \text{YLD} + \text{YLL}$$

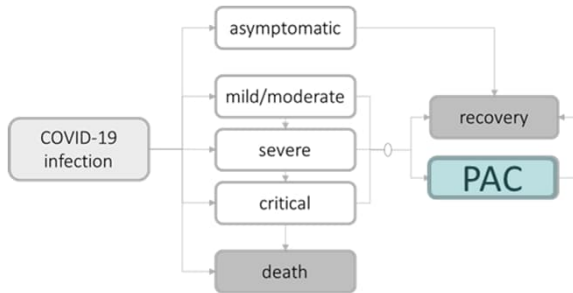
** adjusted for comorbidity profiles using the Charlson comorbidity index

Methods



Consensus model (burden.eu)

Methods



Consensus model (burden.eu)



Disability



PAC specific
DW



Surrogate DW
post acute effect of
an infectious
disease (0.219)
Consensus model

anaemia (0.052 /
0.149 / 0.149) Wyper
et al.



Symptom
related DW

Assign DW to
symptoms, symptom
prevalence for
overall DW. (0.063 /
0.071 / 0.071) Fischer
et al., Howe et al.



Prevalence

- Included **129 studies**.
- The prevalence of long COVID for studies with more than 12 weeks from infection was estimated as 42.1% [6.8%–87.9%].
- Studies using routine healthcare records tended to report lower prevalence (13.6% [1.2% to 68%])

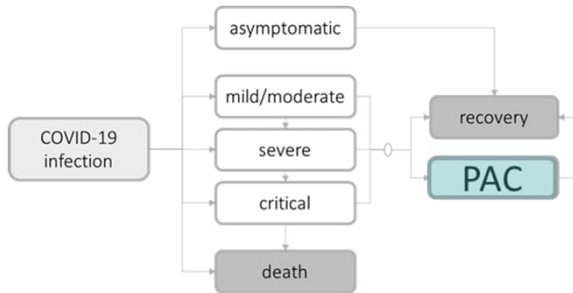
Woodrow et
al. Systematic
Review



Duration

- Duration varies widely across studies from 28 days to 269 days.
- Fischer et al. 2022: 12 months post infection (Luxembourg cohort).
- WHO 2022: development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation.

Methods



Consensus model (burden.eu)



Disability



PAC specific
DW



Surrogate DW
post acute effect of
an infectious
disease (0.219)
Consensus model

anaemia (0.052 /
0.149 / 0.149) Wyper
et al.



Symptom
related DW

Assign DW to
symptoms, symptom
prevalence for
overall DW. (0.063 /
0.071 / 0.071) Fischer
et al., Howe et al.



Prevalence

- Included 129 studies.
- The prevalence of long COVID for studies with more than 12 weeks from infection was estimated as 42.1% [6.8%–87.9%].
- Studies using routine healthcare records tended to report lower prevalence (13.6% [1.2% to 68%])

Woodrow et
al. Systematic
Review



Duration

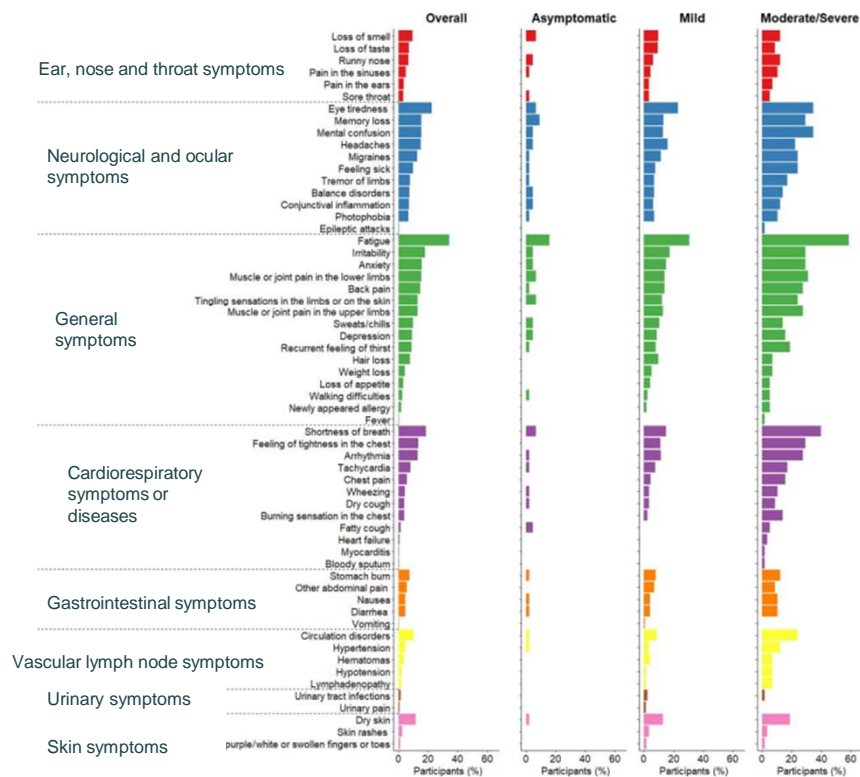
- Duration varies widely across studies from 28 days to 269 days
- Fischer et al. 2022: 12 months post infection (Luxembourg cohort).
- Woodrow et al. 2023: 3 months or more post infection.
- WHO 2022: development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation.

Symptom related DW



Long COVID Symptomatology After 12 Months and Its Impact on Quality of Life According to Initial Coronavirus Disease 2019 Disease Severity

Aurélie Fischer,^{1,2} Lu Zhang,² Abir Elbèji,³ Paul Wilmes,³ Pauline Oustric,⁴ Therese Staub,⁵ Petr V. Nazarov,^{2,6} Markus Ollert,^{6,7} and Guy Fogherazzi^{1,8}

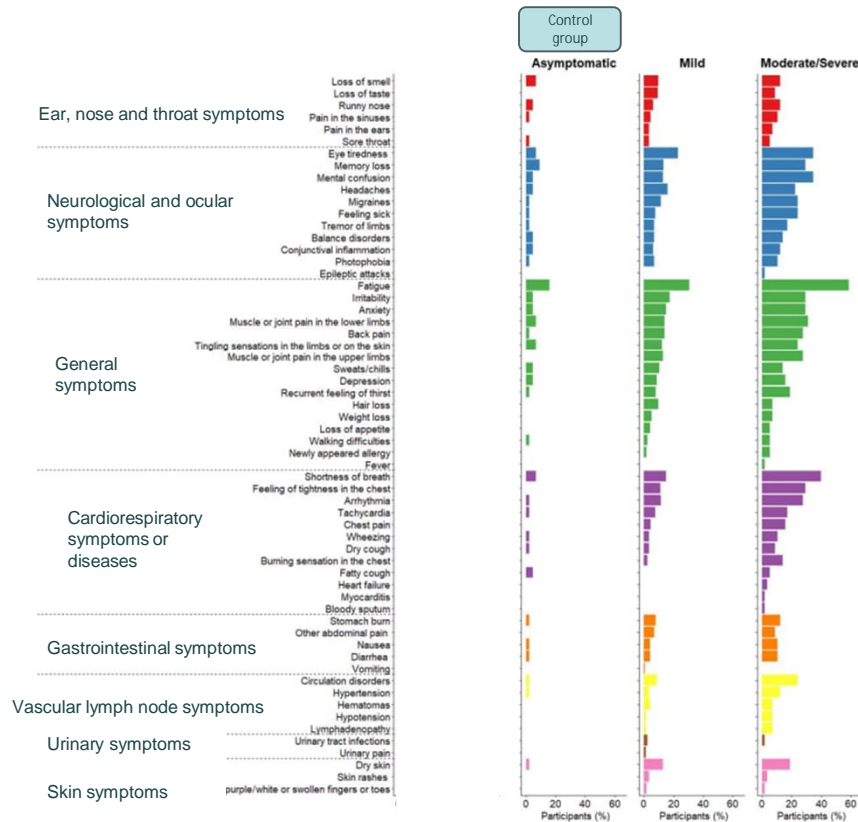


Symptom related DW



Long COVID Symptomatology After 12 Months and Its Impact on Quality of Life According to Initial Coronavirus Disease 2019 Disease Severity

Aurélie Fischer,^{1,6} Lu Zhang,² Abir Elbéji,³ Paul Wilmes,⁷ Pauline Oustric,⁴ Therese Staeh,⁵ Petr V. Nazarov,^{2,6} Markus Ollert,^{4,5} and Guy Fagherazzi^{1,6}



Symptom Profiles:

Comparison 1: Mild vs Control

Comparison 2: Moderate/Severe vs. Control

Disability weights per symptom (use equivalent health state, GBD 2019)

PAC disability weight

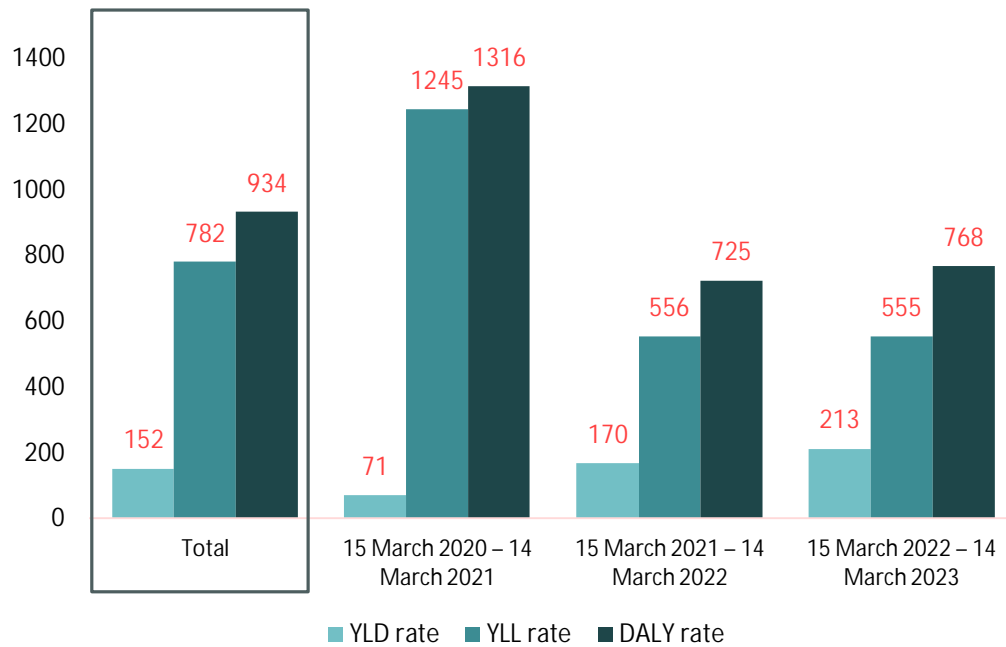
Step 1) calculate average disability weights for each profile, weighted by individual symptom frequencies

Step 2) adjust for number of total symptoms per PAC case (N=2) (Sørensen et al.)

Results

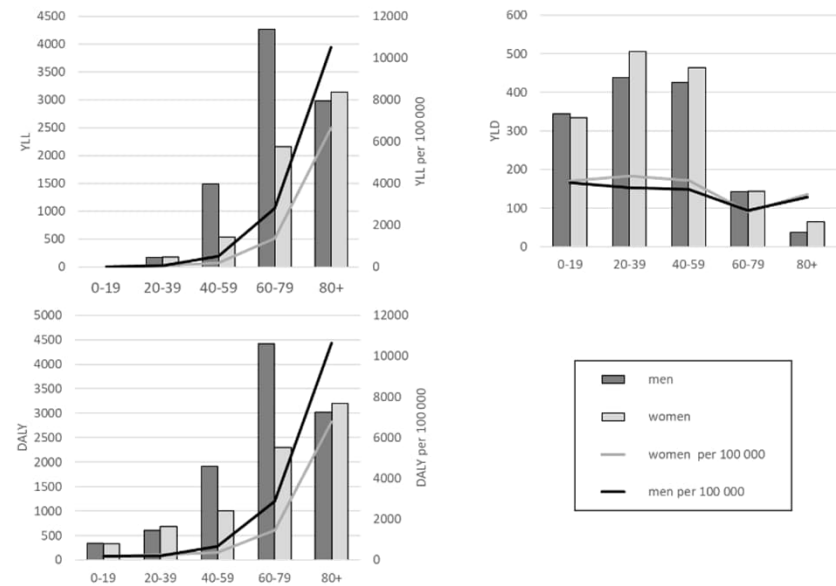


➤ Base Case



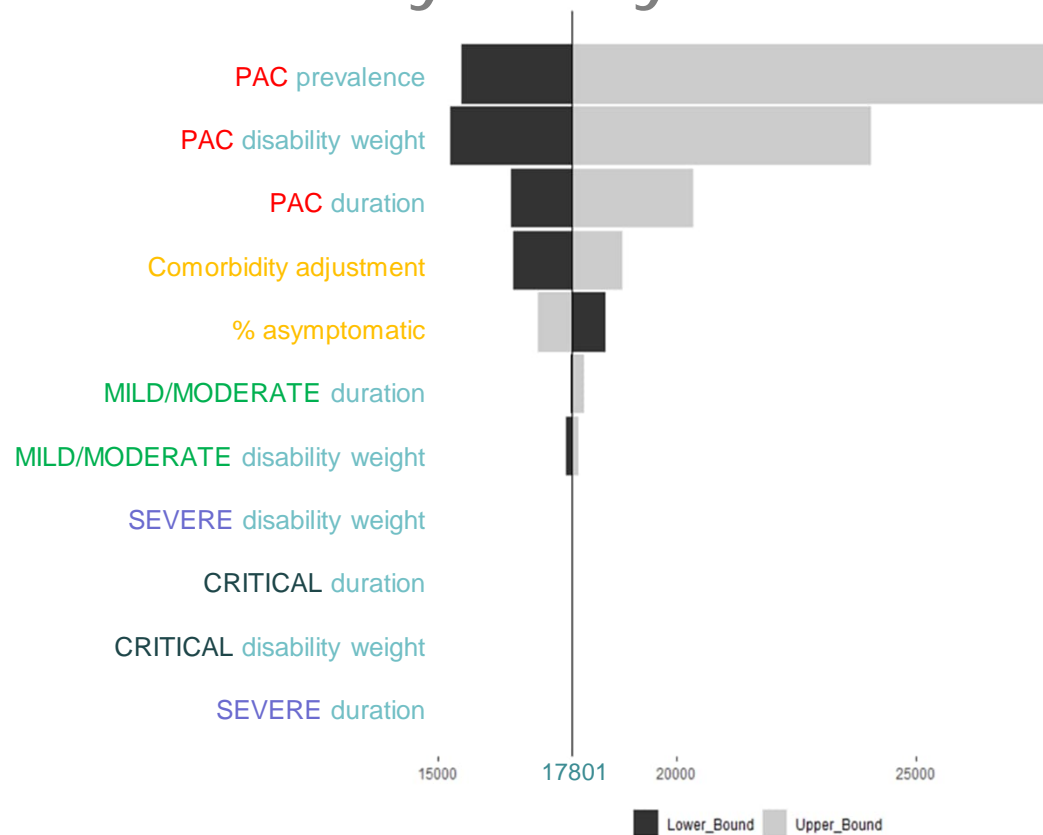
**annual rate per 100 000 population*

Sex and age-specific measures



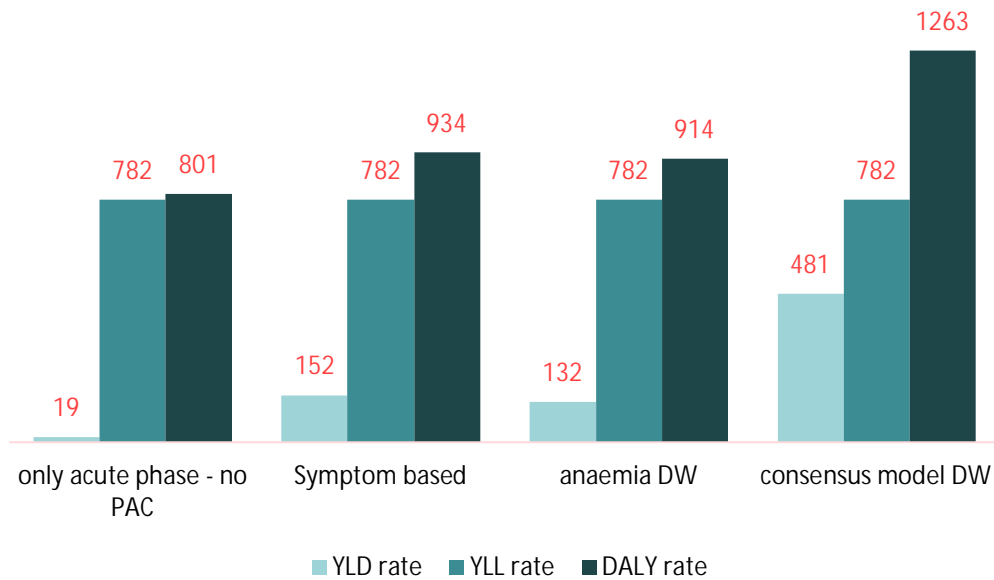


➤ Sensitivity analysis





➤ Scenario Analysis



**annual rate per 100 000 population*

Conclusion



- Over three years: 17 801 DALYs in the resident population in Luxembourg (annual rate per 100 000: 934 DALYs).
- Increasing YLD contribution with time (5% in year 1 to 28% in year 3).
- PAC parameters are key drivers of uncertainty.
 - Urgent need to harmonize; develop PAC specific DW.
 - Until then: Symptom-based approach may be suitable to account for the heterogenous symptoms across patients.

References



- Burden of disease of COVID-19 PROTOCOL FOR COUNTRY STUDIES. [cited 2024 Feb 4]; Available from: <https://www.burden-eu.net/>
- Fischer A, Zhang L, Elbéji A, Wilmes P, Oustric P, Staub T, et al. Long COVID Symptomatology After 12 Months and Its Impact on Quality of Life According to Initial Coronavirus Disease 2019 Disease Severity. Open Forum Infect Dis [Internet]. 2022 Aug 2 [cited 2024 Feb 4];9(8). Available from: <https://dx.doi.org/10.1093/ofid/ofac397>
- Howe S, Szanyi J, Blakely T. The health impact of long COVID during the 2021-2022 Omicron wave in Australia: a quantitative burden of disease study. Int J Epidemiol [Internet]. 2023 Jun 1 [cited 2024 Feb 4];52(3):677–89. Available from: <https://pubmed.ncbi.nlm.nih.gov/37011639/>
- Wyper GMA, McDonald SA, Haagsma JA, Devleeschauwer B, Charalampous P, Maini R, et al. A proposal for further developing fatigue-related post COVID-19 health states for burden of disease studies. Archives of Public Health [Internet]. 2023 Dec 1 [cited 2024 Feb 4];81(1). Available from: [/pmc/articles/PMC10621107/](https://pubmed.ncbi.nlm.nih.gov/37011639/)
- Woodrow M, Carey C, Ziauddeen N, Thomas R, Akrami A, Lutje V, et al. Systematic Review of the Prevalence of Long COVID. Open Forum Infect Dis [Internet]. 2023 Jul 1 [cited 2024 Feb 4];10(7). Available from: <https://dx.doi.org/10.1093/ofid/ofad233>
- Sørensen AIV, Spiliopoulos L, Bager P, Nielsen NM, Hansen JV, Koch A, et al. A nationwide questionnaire study of post-acute symptoms and health problems after SARS-CoV-2 infection in Denmark. Nat Commun [Internet]. 2022 Dec 1 [cited 2024 Feb 4];13(1). Available from: <https://pubmed.ncbi.nlm.nih.gov/35864108/>



Thank you for listening.
Any questions?

Base case table



	YLD		YLL		DALY	
	TOTAL	Rate*	TOTAL	Rate*	TOTAL	Rate*
Total	2898	152	14903	782	17801	934
By pandemic year						
15 March 2020 – 14 March 2021	445	71	7794	1245	8240	1316
15 March 2021 – 14 March 2022	1077	170	3526	556	4603	725
15 March 2022 – 14 March 2023	1376	213	3582	555	4958	768

**annual rate per 100 000 population*

Scenario analysis table



	YLD		YLL		DALY	
	TOTAL	Rate*	TOTAL	Rate*	TOTAL	Rate*
National data (base case)	2898	152	14903	782	17801	934
Only acute phase – no PAC	358	19	14903	782	15260	801
Consensus model approach	9166	481	14903	782	24068	1263
Anaemia-based approach	2520	132	14903	782	17423	914

**annual rate per 100 000 population*

Input parameter table



Parameter	base case	Lower limit	Upper limit	Source	
Disability weights – acute phase					
Mild/Moderate	0.051	0.032	0.074	Burden-eu(16)	
Severe	0.133	0.088	0.190		
Critical	0.655	0.579	0.727		
Duration – acute phase, in days					
Mild/Moderate	7.8	7.0	14.0	Several studies (19–23)	
Severe, by age groups	0-19 years	2.7	2.4	3.1	National surveillance data (mean, 95% confidence interval by bootstrapping)
	20-39 years	5.8	5.2	6.9	
	40-59 years	8.9	8.2	10.1	
	60-79 years	12.3	11.6	13.1	
	80+ years	14.3	13.5	15.1	
Critical, by age groups	0-19 years	9.3	3.3	23.3	National surveillance data (mean, 95% confidence interval by bootstrapping)
	20-39 years	10.7	7.4	18.7	
	40-59 years	15.9	13.8	18.7	
	60-79 years	15.6	13.9	17.7	
	80+ years	9.2	7.9	10.9	
Comorbidity parameters					
RLE reduction coefficient, by age group	0-44 years	1.00	1.00	1.00	RNCD
	45-49 years	0.82	0.57	1.00	
	50-54 years	0.96	0.77	1.00	
	55-59 years	0.94	0.87	1.00	
	60-64 years	0.88	0.76	1.00	
	65-69 years	0.80	0.72	0.88	
	70-74 years	0.91	0.82	0.99	
	75-79 years	0.88	0.81	0.96	
	80-84 years	0.92	0.86	0.97	
	85-89 years	0.92	0.88	0.95	
	90-94 years	0.94	0.90	0.98	
95+ years	0.97	0.91	1.00		
Other input parameters					
Asymptomatic among detected (%)	20%	0%	40%	Hypothesis	

Parameter	base case	Lower limit	Upper limit	Source		
PAC parameters						
Disability weight	Symptom based (by onset severity)	Mild/Moderate	0.063	0.037	0.095	Fischer et al(5),
		Severe	0.071	0.043	0.106	Sørensen et al(24),
		Critical	0.071	0.043	0.106	Burden-eu(16)
	Anaemia (by onset severity)	Mild/Moderate	0.052	0.034	0.076	Wyper et al(25)
		Severe	0.149	0.101	0.209	
		Critical	0.149	0.101	0.209	
Consensus model			0.219	0.148	0.308	Burden-eu(16)
Duration, in months			12	6	24	Fischer et al(5), hypothesis, Woodrow et al(7)
Prevalence			13.6%	1.2%	68%	Woodrow et al(7)