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en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

Appendix: State of Infectious Diseases in the Netherlands, 2013

Appendix RIVM Briefrapport 150205001/2014
P. Bijkerk et al.



National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

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Appendix RIVM Report 150205001/2014
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Colophon

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Contents

Introduction – 4

1	Chlamydia – 7
2	Gonorrhoea – 15
3	Hepatitis B infection – 22
4	Hepatitis C infection – 26
5	HIV infection – 30
6	Syphilis – 33
7	Diphtheria – 38
8	Invasive <i>Haemophilus influenzae</i> infection – 41
9	Invasive meningococcal disease – 45
10	Invasive pneumococcal disease – 48
11	Measles – 51
12	Mumps – 55
13	Pertussis – 58
14	Poliomyelitis – 61
15	Rabies – 64
16	Rubella – 66
17	Tetanus – 72
18	Shigellosis – 75
19	Variant Creutzfeldt-Jakob disease – 80
20	Influenza – 82
21	Legionellosis – 86
22	Q fever – 90
23	Tuberculosis – 94

Introduction

Online appendix

State of Infectious Diseases in the Netherlands 2013

This Appendix provides the outcome trees and disease model parameters (transition probabilities, disability weights and durations) for the various diseases included in the disease burden study. These outcome trees and model parameters were adapted from the disease reports (most recent version available as of 16-06-2014) produced during the Burden of Communicable Diseases in Europe (BCoDE) project. The diseases for which the default BCoDE models were adapted are summarised below.

Changes to default BCoDE disease models

Chlamydia / gonorrhoea

According to Dutch experts, the YLL for chlamydia using the standard BCoDE parameters was unrealistically high. The high YLL was caused by the high risk of mortality due to tubo-ovarian abscess (6%) and ectopic pregnancy (3%) (Gerbase et al. 2000) specified in the BCoDE disease models for both chlamydia and gonorrhoea. Thus, we specified a 0% risk of mortality following tubo-ovarian abscess because disease experts stated that nowadays these abscesses are detected and treated early. The original percentage was adopted from a study published in 1968; however, the quality of health care has markedly increased. Furthermore, for the risk of mortality following ectopic pregnancy we used a CFR of 0.038% (Goldner et al. 1993), which was a more plausible percentage for the Dutch situation.

HIV infection

The risk of symptomatic infection in the BCoDE model for HIV infection of 34-50% (Sterling & Chaisson 2005) was replaced by the range 45-75%, based on the estimated prevalence of undiagnosed HIV infection in the Netherlands (25-55%) (Van Veen et al. 2011). For the HIV burden calculation, we assumed complete reporting of diagnosed infected cases, and so the ratio between prevalent diagnosed infections and prevalent undiagnosed infections is identical to the ratio of symptomatic and asymptomatic infections.

Pertussis

The estimated disease burden of pertussis was judged as being too high compared with other vaccine-preventable diseases, especially with respect to mortality. Therefore, the standard BCoDE model for pertussis was modified by adjusting the proportions of the complicated health states of acute infection to match the number of notified cases (rather than the number of notified cases adjusted by a multiplication factor), because it is unlikely that these complications occurred among non-notified cases.

Legionellosis

For legionellosis, experts had the opinion that the estimated burden derived using the standard BCoDE disease model was unrealistic; namely, mortality was too high. We decided to replace the default acute illness severity proportions with proportions based on Dutch notification data, the estimated number of pneumonia cases in the Netherlands (Dijkstra et al. 2008, Brandsema et al. 2011), and the expected proportion with diagnosed legionellosis (Von Baum et al. 2008). The proportion of mild cases corresponded to the number of cases

visiting a general practitioner, and the proportion of moderate/severe cases corresponded to the number of hospitalised cases. The proportions mild/moderate/severe were changed from 28.5% / 47.7% / 23.8% to 71.5% / 19.0% / 9.5%. Furthermore, the mortality risk for mild cases was reduced from 12% to 0%.

Campylobacteriosis, cryptosporidiosis, giardiasis, hepatitis A infection, listeriosis, norovirus infection, salmonellosis, toxoplasmosis, and infection with STEC O157

For these foodborne diseases, we used Havelaar et al.'s approach (Havelaar et al. 2012, Haagsma et al. 2009) for disease burden estimation. This approach uses the pathogen- and incidence-based DALY methodology, with the same life expectancy values, adjustment for under-estimation of incidence, and similar outcome trees. However, their approach differs from the BCoDE methodology in that additional data sources (i.e., other than notification data) are used to estimate the incident cases for each of the health outcomes in the outcome tree. These sources include data from sentinel laboratory surveillance systems and population-based cohort studies, as well as general practitioner, hospitalisation, and mortality data. Transition probabilities, disability weights, and disability durations were chosen to represent the Dutch situation as much as possible. The disease models for salmonellosis and campylobacteriosis differ from the BCoDE models, in that they additionally include irritable bowel disease (IBD) as a potential sequela. Detailed information regarding the disease models for campylobacteriosis, cryptosporidiosis, giardiasis, hepatitis A infection, listeriosis, norovirus infection, salmonellosis, toxoplasmosis, and infection with STEC O157 are described elsewhere (Havelaar et al. 2012, Haagsma et al. 2009) and are not included in this Appendix.

Additional remark regarding the burden calculation for the poliomyelitis outbreak 1992/1993

During the poliomyelitis outbreak in 1992/1993, 71 cases were reported; note that for three male cases between 40-61 years the exact age was unknown: these cases were included in the age group 60-64 years to give the most conservative estimate.

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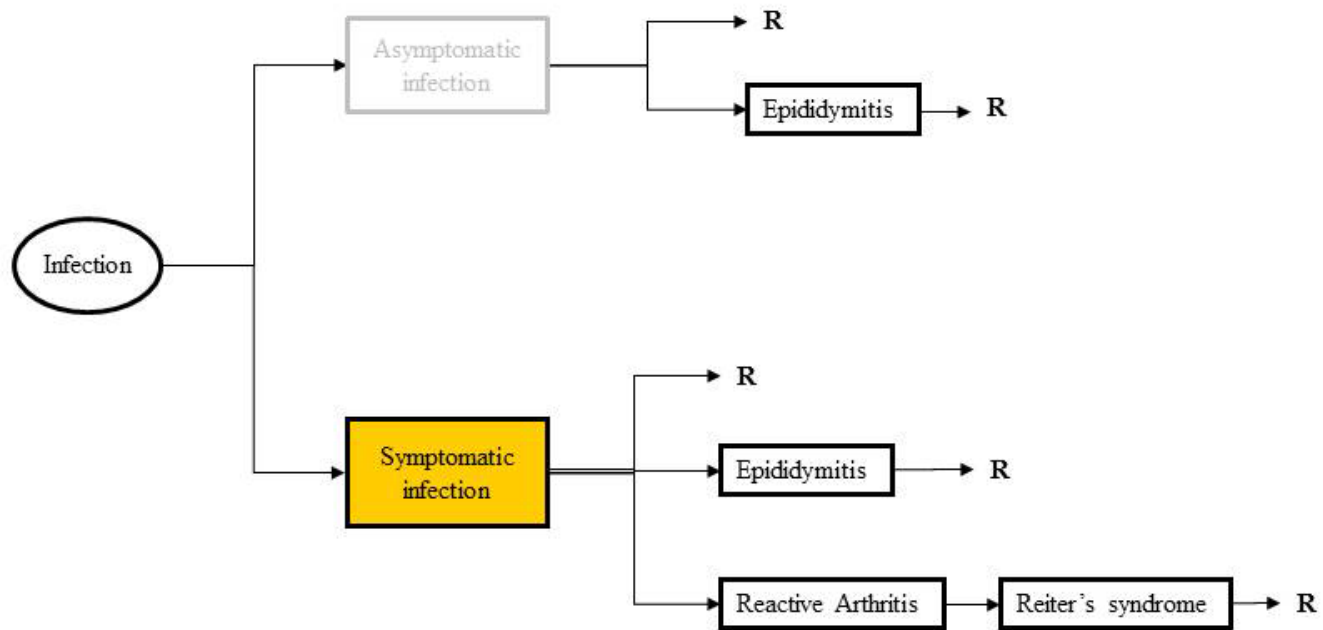
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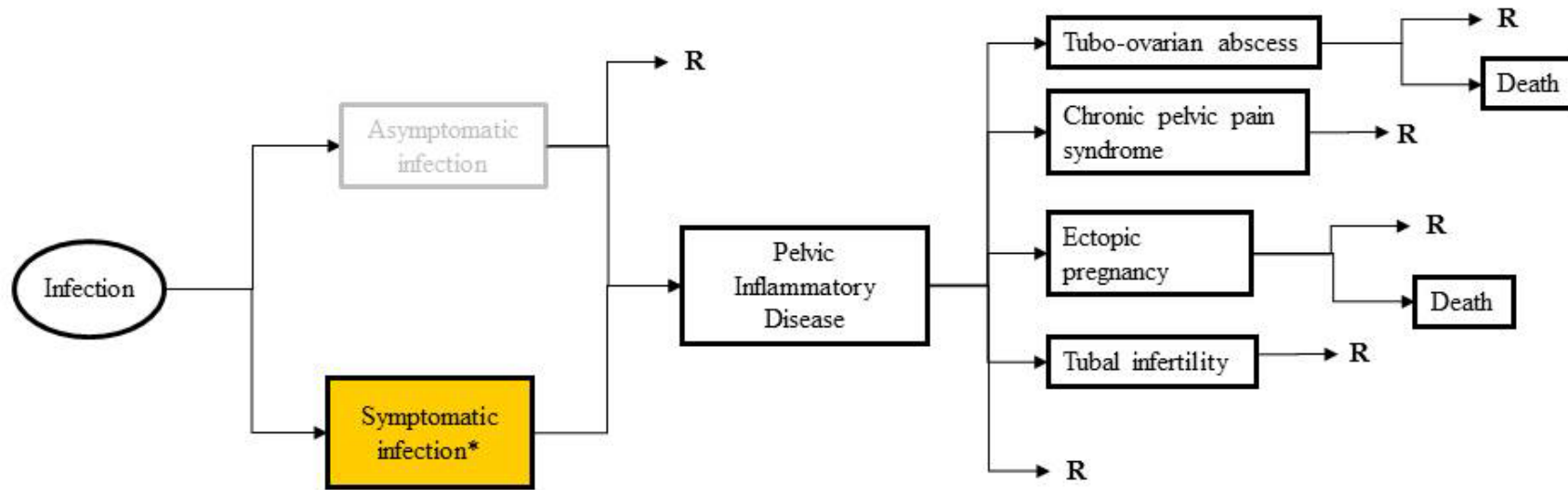
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1 Chlamydia

Outcome tree Chlamydia (men)

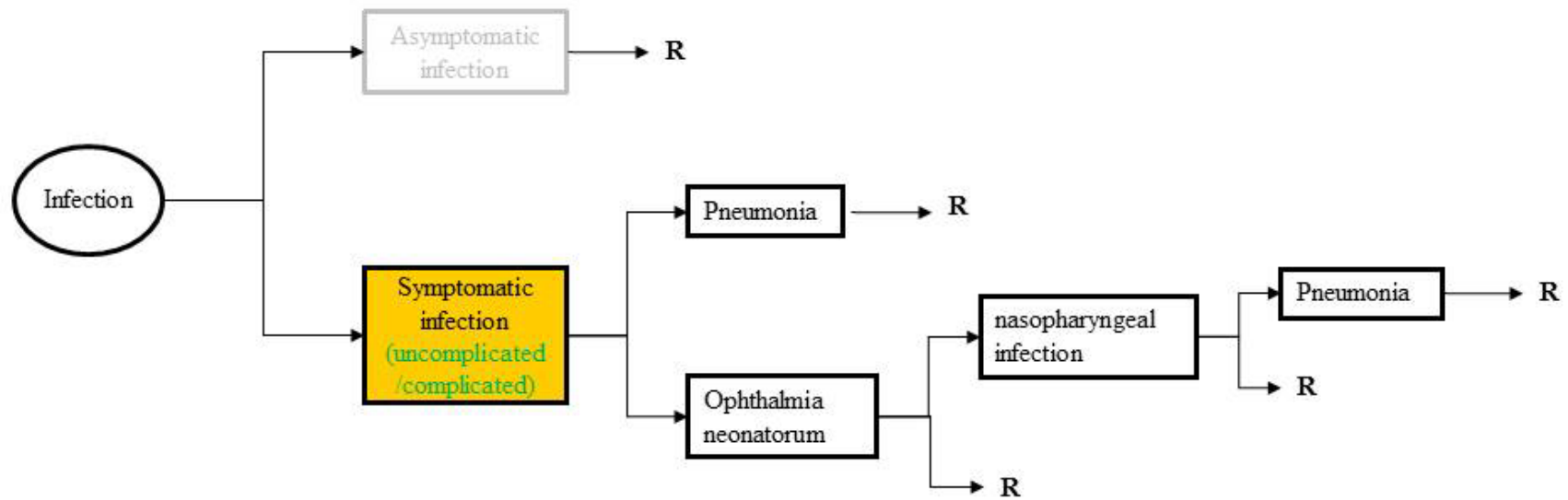


Outcome tree Chlamydia (women)



*presents as Cervicitis/Urethritis

Outcome tree Chlamydia (infants)



Model input: Chlamydia

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Men							
Urethritis		12–50%	Carey & Beagley 2010, McKay et al. 2003	0.067	Murray & Lopez 1996a	0.03	Murray & Lopez 1996b
Epididymitis		10%	Gerbase et al. 2000	0.167	Murray & Lopez 1996a	0.08	Trojian et al. 2009
Reactive arthritis		1%	Stamm et al. 2005	0.197*	Haagsma et al. 2008	0.3	Ozgul et al. 2006
Reiters Syndrome		33%	Stamm et al. 2005	0.377†	Murray & Lopez 1996a	0.41	Miehle 2003
Epididymitis as sequela of asymptomatic infection		1–4%	Gerbase et al. 2000, Welte et al. 2001	0.167	Murray & Lopez 1996a	0.08	Trojian et al. 2009
Women							
Urethritis/Cervicitis		10–30%	Stamm et al. 2005, Gaydos & Quinn 2012, Gaydos et al. 1998; Kalwij et al. 2010, Stamm 1999	0.049	Murray & Lopez 1996a	0.03	Murray & Lopez 1996b
Pelvic Inflammatory Disease (PID)		10% (0.43–16%)	Van Valkengoed et al. 2004, Price et al. 2011, Low 2011	0.169	Murray & Lopez 1996a	0.04	Westrom 1980

Tubo-ovarian abscess		7–16%	Kottman 1995	0.549 (females aged 5- 59 yrs)	Murray & Lopez 1996a	0.08	Murray & Lopez 1996b
Chronic pelvic pain		15%	Rogstad 2008	0.122	Murray & Lopez 1996a	2.8	Sharma et al. 2011
Ectopic pregnancy		0.07%	Van Valkengoed et al. 2004	0.549 (females aged 5- 59 yrs)	Murray & Lopez 1996a	0.08	Female reproductive age 15 – 49; Murray & Lopez 1996b
Tubal infertility		0.02% (0.02–40%)	Van Valkengoed et al. 2004, Westrom et al. 1992	0.18	Murray & Lopez 1996a	4 –34 (age- dependent)	Female reproductive age 15 – 49
Death due to tubo-ovarian abscess		0%**	Based on expert opinion				
Death due to ectopic pregnancy		0.038%**	Goldner et al. 1993				
Infants							
Neonatal pneumonia		5–20%	Hammerschlag 1989	0.28	Murray & Lopez 1996a	0.5	Murray & Lopez 1996b
Ophthalmia neonatorum		20–50%	Hammerschlag et al. 1982	0.18	Murray & Lopez 1996a	0.04	Murray & Lopez 1996b
Nasopharyngeal infection		20–50%	Hammerschlag et al. 1982, Peipert 2003	0.28	Murray & Lopez 1996a	0.5	Murray & Lopez 1996b
Pneumonia from nasopharyngeal infection		30–33%	Hammerschlag et al. 1982, Peipert 2003, Hammerschlag 1989	0.28	Murray & Lopez 1996a	0.5	Murray & Lopez 1996b

* Recalculated from annual profile disability weight (0.059) by dividing by the duration

** Different from BCoDE project where 6% was used for death due to tubo-ovarian abscess and 3% for death due to ectopic pregnancy (Gerbase et al. 2000)

† Multiplicative approach using disability weights for arthritis (0.186), conjunctivitis (0.18), and urethritis (0.067) is calculated as $1 - [(1 - 0.186) * (1 - 0.18) * (1 - 0.067)] = 0.377$

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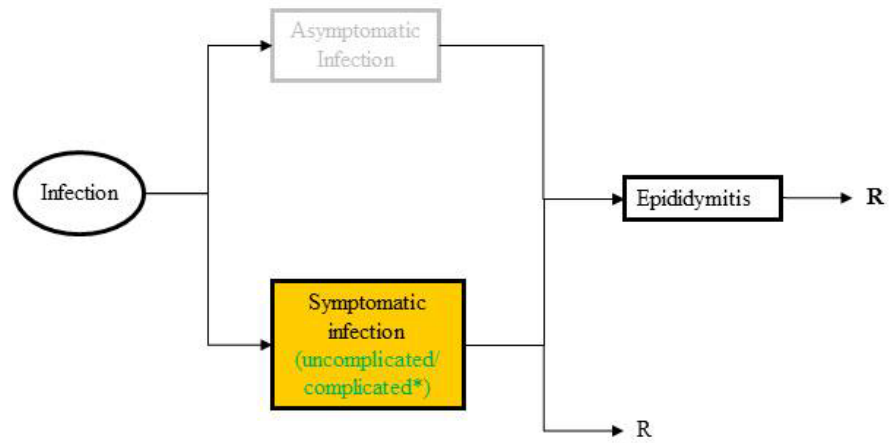
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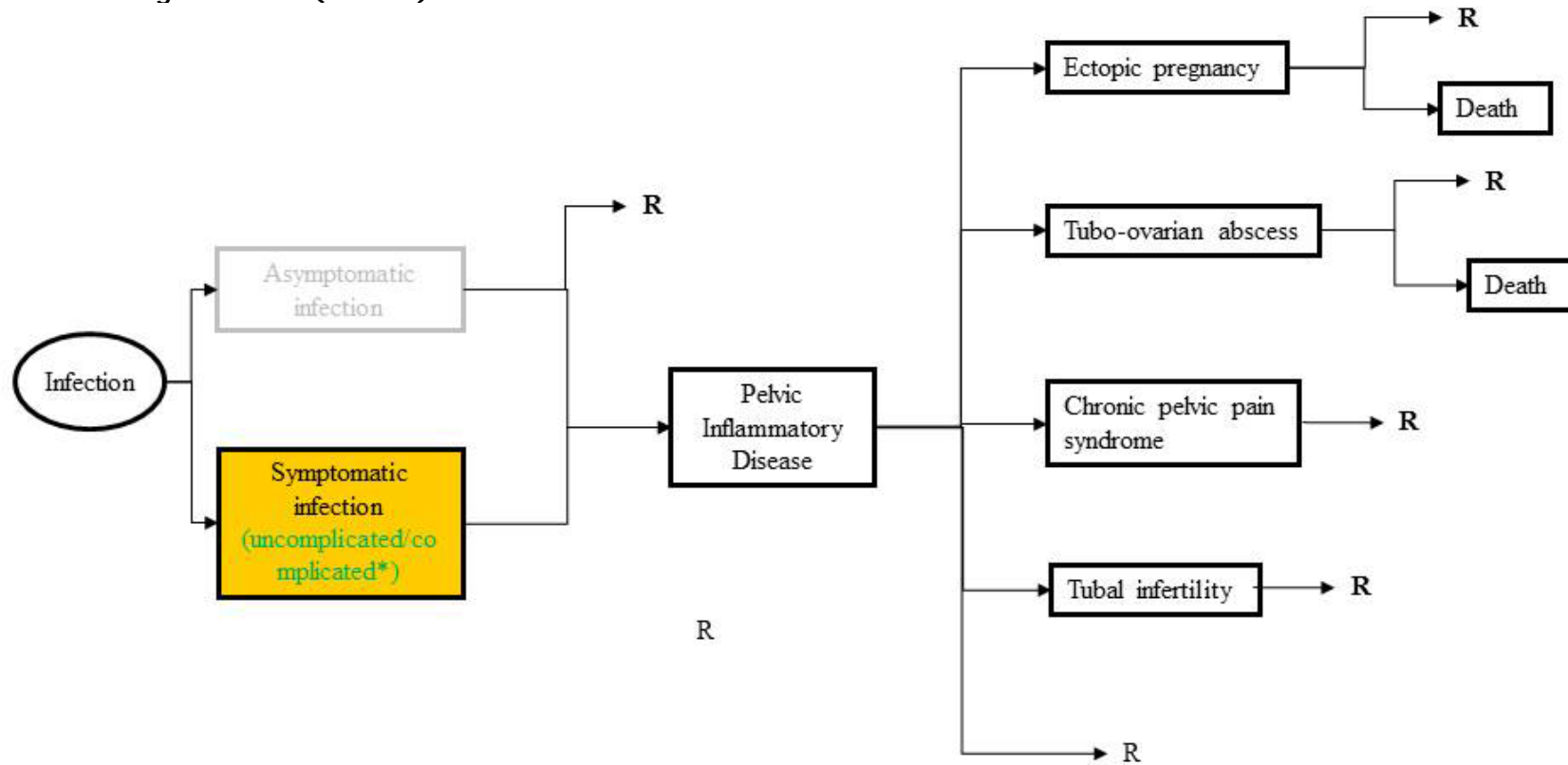
2 Gonorrhoea

Outcome tree gonorrhoea (men)



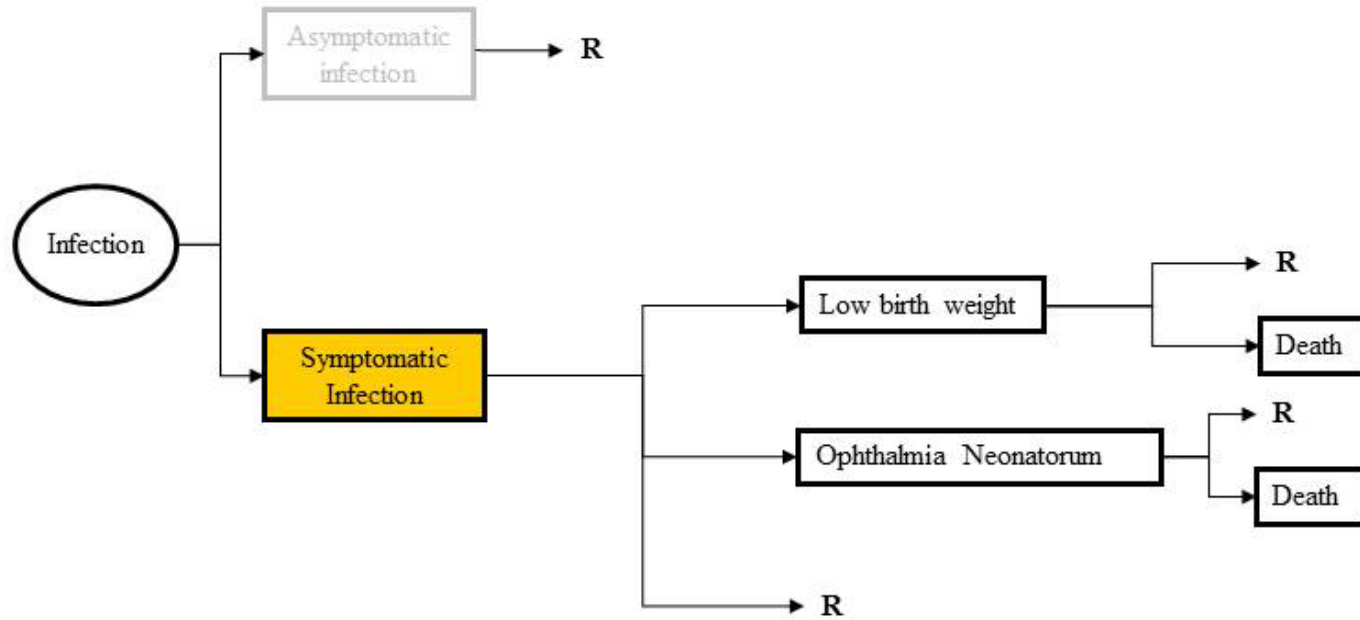
* Complicated cases may present with disseminated gonococcal infections

Outcome tree gonorrhoea (women)



*complicated cases may present with disseminated gonococcal infections

Outcome tree gonorrhoea (infants)



Model input: Gonorrhoea

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Men							
Urethritis	95–99% uncomplicated		Handsfield & Sparling 2005, DeMaio & Zenilman 1998, Nelson 2007, Trojian et al. 2009 Handsfield & Sparling 2005, DeMaio & Zenilman 1998, Nelson 2007, Trojian et al. 2009	0.067	Murray & Lopez 1996a	0.02	Trojian et al. 2009
	0.95–0.99% with disseminated gonococcal infection			0.35†	Murray & Lopez 1996a, Adelman et al. 2002	0.02	Trojian et al. 2009
Epididymitis, from symptomatic and asymptomatic		10%	Nelson 2007, Trojian et al. 2009	0.167	Murray & Lopez 1996a	0.04	Murray & Lopez 1996b
Women							
Cervicitis	20–60% uncomplicated		Handsfield & Sparling 2005, Westrom et al. 1992, Ross 2002 DeMaio & Zenilman	0.049	Murray & Lopez 1996a	0.03	Murray & Lopez 1996b
	0.2–0.6% with disseminated gonococcal infection			0.33*	Murray & Lopez 1996a,	0.03	Murray & Lopez 1996b

			1998, Nelson 2007, Westrom 1980, Westrom et al. 1992		Adelman et al. 2002		
Pelvic Inflammatory Disease (PID) from symptomatic and asymptomatic infection		10–40%	Handsfield & Sparling 2005, Westrom 1980, Ross 2002	0.169	Murray & Lopez 1996a	0.07	DeMaio & Zenilman 1998
Ectopic pregnancy		9.1%	Westrom et al. 1992	0.549 (females aged 5-59 yrs)	Murray & Lopez 1996a	0.08	Female reproductive age 15 – 49; Murray & Lopez 1996b
Tubo-ovarian abscess		15%	Gerbase et al. 2000	0.549 (females aged 5-59 yrs)	Murray & Lopez 1996a	0.01	Goharkhay et al. 2007, Teisala et al. 1990
Chronic pelvic pain syndrome		18%	Bernstein et al. 2006	0.122	Murray & Lopez 1996a	2.8	Sharma et al. 2011
Tubal infertility		16% (10–80%)	Westrom et al. 1992	0.18	Murray & Lopez 1996a	4–34 yrs (age-dependent)	Female reproductive age 15-49 yrs
Death due to ectopic pregnancy		0.038%**	Goldner et al. 1993				
Death due to tubo-ovarian abscess		0%**	Based on expert opinion				
Infants							

Acute illness		100%		0		0	
Ophthalmia neonatorum		30–35%	Nelson 2007, Gerbase et al. 2000, Spencer & Bash 2006	0.180	Murray & Lopez 1996a	0.625	Gerbase et al. 2000
Low birth weight		15%	Gerbase et al. 2000	0	Murray & Lopez 1996a		
Death due to low birth weight		1%	Gerbase et al. 2000				
Death due to ophthalmia neonatorum		0.2%	Gerbase et al. 2000				

† Multiplicative approach using disability weights for urethritis (0.067) and DGI (0.30; combination of osteoarthritis (0.156) and rheumatoid arthritis (0.174)) is calculated as $1 - [(1 - 0.067) * (1 - 0.30)] = 0.35$

* Multiplicative approach using disability weights for cervicitis (0.049) and DGI (0.30; combination of osteoarthritis (0.156) and rheumatoid arthritis (0.174)) is calculated as $1 - [(1 - 0.049) * (1 - 0.30)] = 0.33$

** Different from BCoDE project where 6% was used for death due to tubo-ovarian abscess and 3% for death due to ectopic pregnancy (Gerbase et al. 2000)

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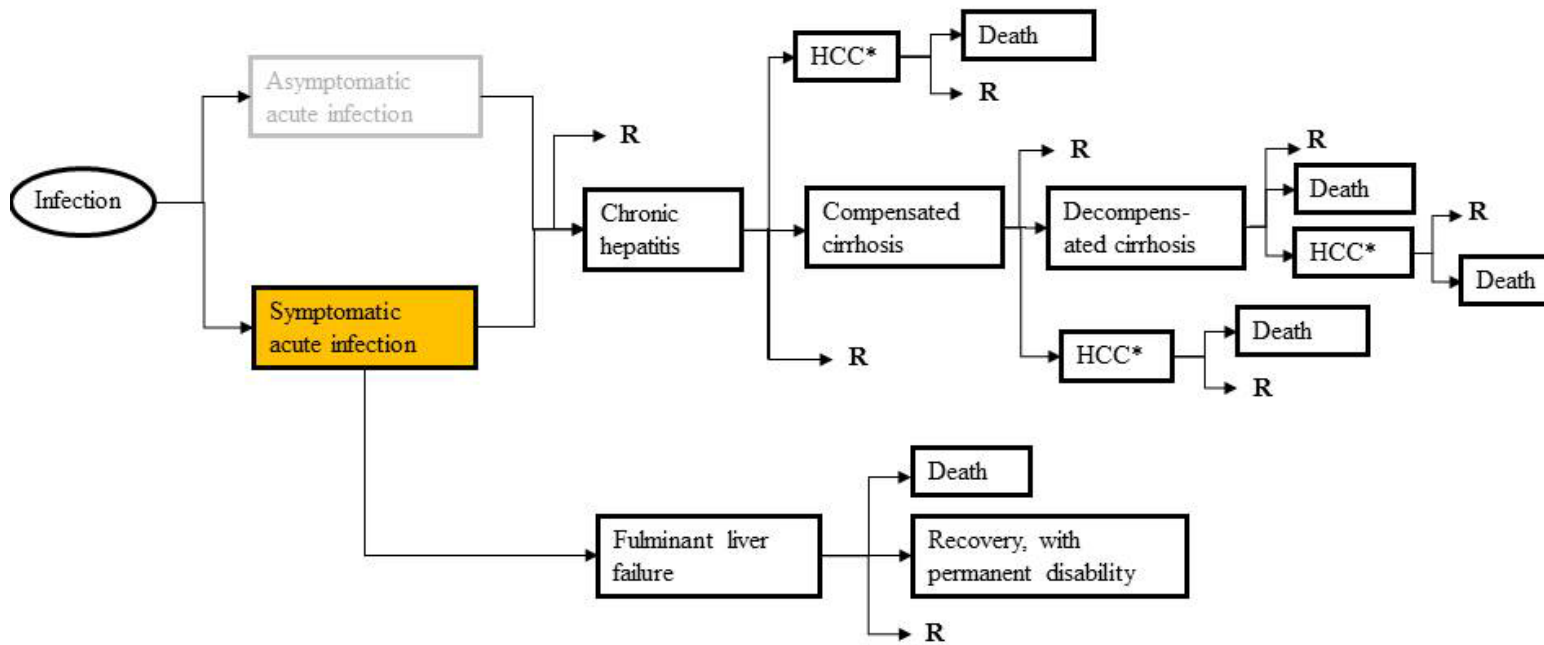
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3 Hepatitis B infection

Outcome tree hepatitis B



* HCC = Hepatocellular carcinoma

Model input: Hepatitis B infection

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Symptomatic infection				0.170– 0.212 (age- dependent)	Murray & Lopez 1996a	0.17	Murray & Lopez 1996b
Chronic hepatitis		(age-dependent)	McMahon et al. 1985	0.06 (no active replication) 0.36 (active virus replication)	Stouthard et al. 1997	33.24 4.5	Virology Online
Fulminant liver failure		0.5–1%	Pappas 1995, Hoofnagle et al. 2007	0.809	Murray & Lopez 1996a	0.0918	Kim et al. 2002
Compensated cirrhosis		2.1%/yr	Chu 2000	0.33	Murray & Lopez 1996a	(age and sex- dependent)	Murray & Lopez 1996b
Decompensated cirrhosis		6%/yr (5–7%/yr)	D'Amico et al. 2006	0.809	Murray & Lopez 1996a	1.429	Calculated as 1/prop. leaving compart.

HCC, <i>following</i> -Chronic hepatitis		5.5%/yr (0.1–1%/yr)	Chu 2000	0.809	Murray & Lopez 1996a	(age and sex-dependent)	Murray & Lopez 1996b
-Compensated cirrhosis		3%/yr	D'Amico et al. 2006				
-Decompensated cirrhosis		3%/yr	D'Amico et al. 2006				
Death, <i>following</i> : -Fulminant liver failure		26.7% (20–33.3%)	Bernuau et al. 1986, Wai et al. 2005				
-Decompensated cirrhosis		67%/yr (57–77%/yr)	D'Amico et al. 2006				
-HCC		49%/yr	D'Amico et al. 2006				

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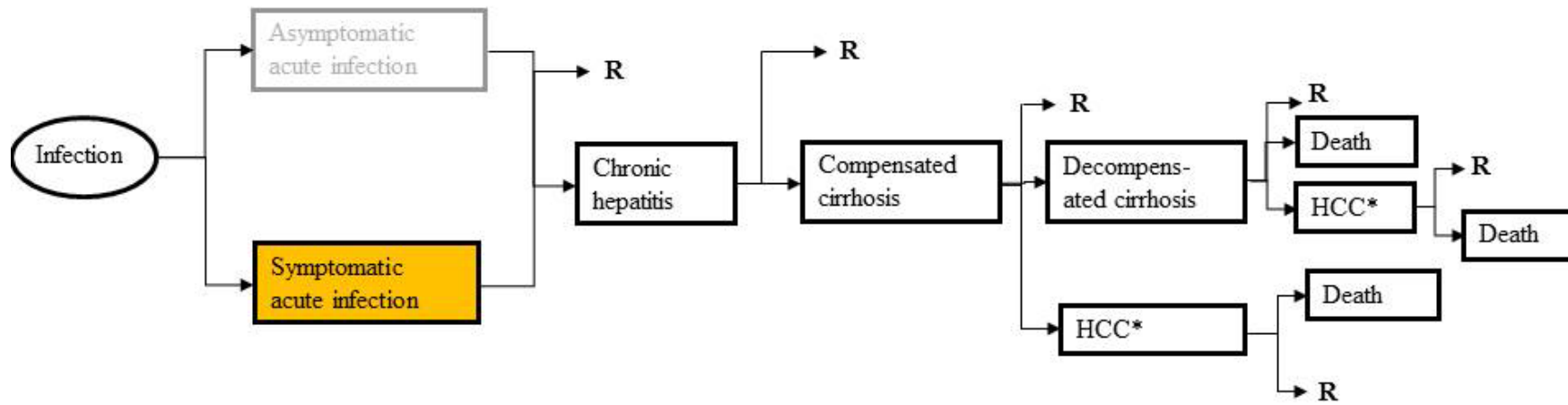
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4 Hepatitis C infection

Outcome tree hepatitis C



* HCC = Hepatocellular carcinoma

Model input: Hepatitis C infection

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Symptomatic infection				0.170–0.212 (age-dependent)	Murray & Lopez 1996a	0.17	Murray & Lopez 1996b
Chronic hepatitis		80% (75–85%)	Alter & Seef 2000, CDC 2011	0.06	Stouthard et al. 1997	36.5	Based on 1.9% annual risk of cirrhosis; Thein et al. 2008
Compensated cirrhosis		1.9%/yr	Thein et al. 2008	0.33	Murray & Lopez 1996a	(age and sex-dependent)	Murray & Lopez 1996b
Decompensated cirrhosis		5-7%/yr	D'Amico et al. 2006	0.809	Murray & Lopez 1996a	3.47	Calculated as 1/prop. leaving compart.
HCC, following -Compensated cirrhosis -Decompensated cirrhosis		3.0%/yr 3.0%/yr	D'Amico et al. 2006 D'Amico et al. 2006	0.809	Murray & Lopez 1996a	(age and sex-dependent)	Murray & Lopez 1996b

Death, <i>following</i> : -Decompensated cirrhosis		13.0–38.5%/yr	Fattovich et al. 1997, Grieve et al. 2006, D'Amico et al. 2006				
-HCC		86%/yr	D'Amico et al. 2006				

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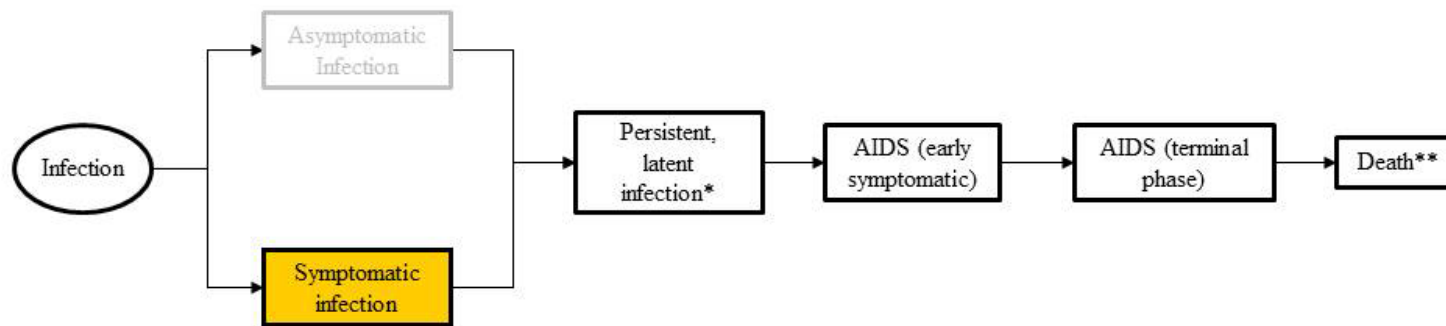
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5 HIV infection

Outcome tree HIV



*In this health outcome the cases are split up in

- a) Rapid progressors (5-15%) duration 2-5 years
- b) Typical progressors (60-90%) duration 8-10 years
- c) Long term non-progressors (5-15%) duration 17.2 years

**Overall death throughout the course of HIV/AIDS Infection

Model input: HIV infection

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute retroviral syndrome (acute HIV)		45-75%*	Van Veen et al. 2011	0.123	Murray & Lopez 1996	0.03	Del Rio & Curran 2005
Persistent (latent) HIV infection	5–15% rapid progressors 60–90% typical progressors 5–15% long-term non- progressors	100%	Assumption, as no cure available Qu et al. 2008 Qu et al. 2008 Herida et al. 2006, Qu et al. 2008	0.2	Van Lier & Havelaar 2007	2–5 8–10 17.2	Qu et al. 2008 Qu et al. 2008 Herida et al. 2006, Qu et al. 2008
AIDS (early symptomatic)		6%	Egger et al. 1997	0.38	Herida et al. 2006	5.36	Herida et al. 2006
AIDS (terminal phase)		100%	Assumption, as no cure available	0.801	Kwong et al. 2010	0.08	Kwong et al. 2010
Death due to AIDS (terminal phase)		100%					

* Different from BCoDE project where 35-50% was used (Sterling & Chaisson 2005)

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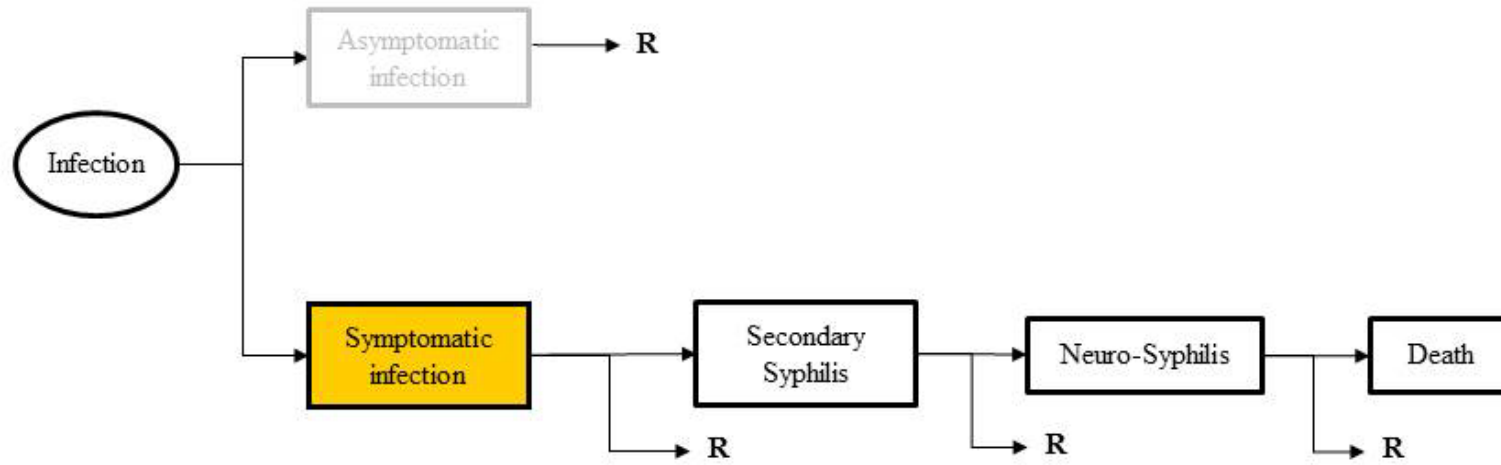
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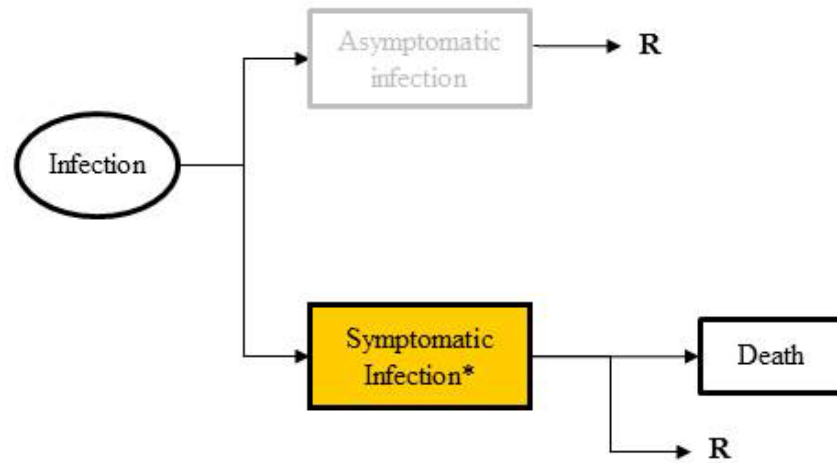
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6 Syphilis

Outcome tree syphilis (adults)



Outcome tree syphilis (infants)



*congenital infection

Model input: Syphilis

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Adults							
Primary syphilis		50%	Robert Koch- Institut 2003	0.015 (1-44 yrs) 0.014 (45+ yrs)	Murray & Lopez 1996a	0.04	Murray & Lopez 1996b
Secondary syphilis		4.5–7.5%	Singh & Romanowski 1999, Weir & Fisman 2002, Gerbase et al. 2000, Golden et al. 2003	0.048 (1-59 yrs) 0.044 (60+ yrs)	Murray & Lopez 1996a	0.07	Murray & Lopez 1996b
Neurosyphilis		0.75–1.88%	Tramont 2005, Zetola et al. 2007, Krause 2006, Gerbase et al. 2000, Golden et al. 2003, Goldmeier & Guallar 2003	0.281	Murray & Lopez 1996a	10	Kwong et al. 2010
Death due to neurosyphilis		15%	Gerbase et al. 2000				
Infants							

Congenital infection		20% (2–64%)	Singh 1999, Saloojee et al. 2004, Genc & Ledger 2000, Gerbase et al. 2000	0.315	Murray & Lopez 1996a	3	Kwong et al. 2010
Death due to congenital infection		1%	Gerbase et al. 2000				

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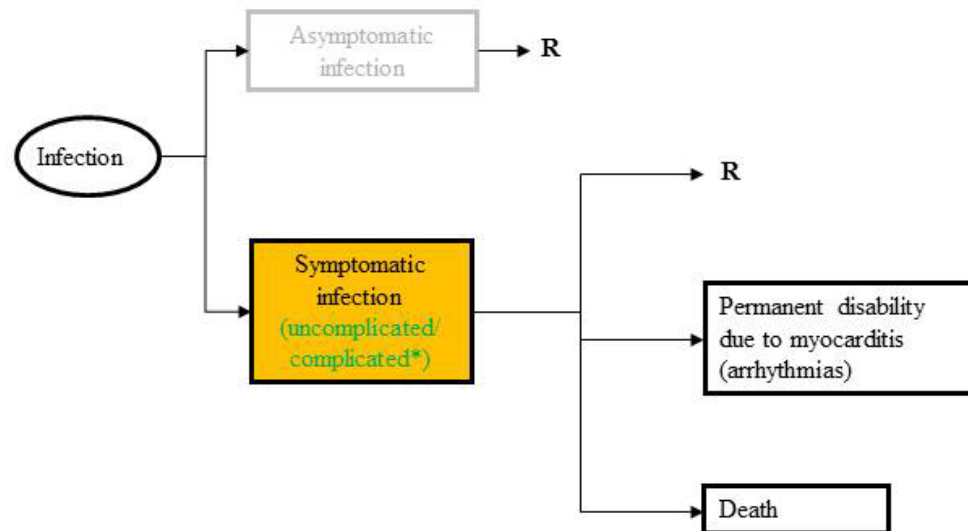
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7 Diphtheria

Outcome tree diphtheria



Note. This outcome tree depicts the **respiratory** variant of diphtheria

* Complicated health states include myocarditis, polyneuropathies/nerve palsies, and systemic toxicity

Model input: Diphtheria

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute respiratory diphtheria	10–25% myocarditis 20% polyneuropathies/nerve palsies		Hadfield et al. 2000	0.231	WHO 2004	0.01918	Estimated from Lodha et al. 2000 10d to 3 mths Mandell et al. 1999 10d to 3 mths Hadfield et al. 2000, Mandell et al. 1999
				0.323	WHO 2004	0.04247	
				0.078	WHO 2004	0.1781	
Permanent disability due to myocarditis (arrhythmias)		0.25%	Mandell et al. 1999	0.171 ^a	WHO 2004	RLE	Mandell et al. 1999
Death following acute illness		2.1–4.2%	Rakhmanova et al. 1996				
Death following myocarditis		2.5–5%	Rakhmanova et al. 1996				
Death following polyneuropathies/nerve palsies		0.25–0.5%	Estimated based on Rakhmanova et al. 1996				

RLE = remaining life expectancy

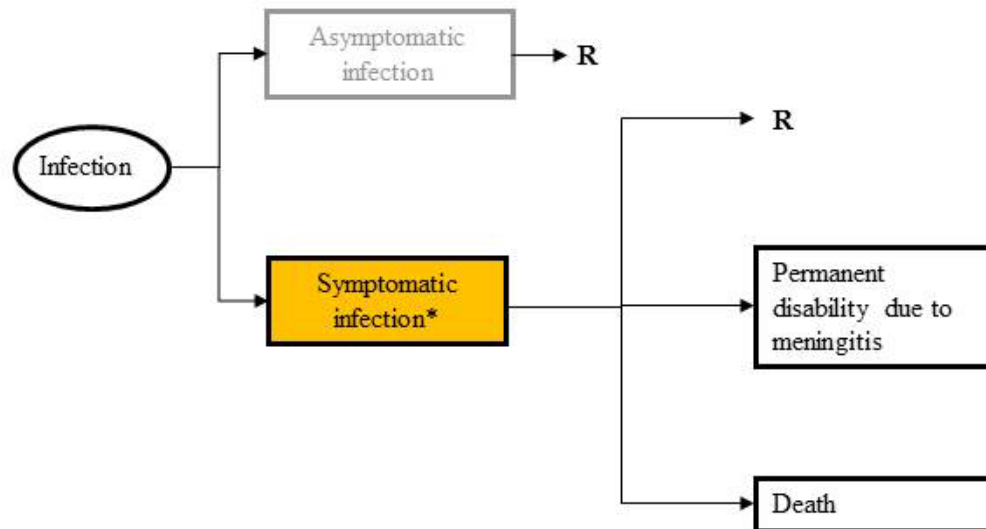
^a Disability weight for rheumatic heart disease was used as a proxy

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8 Invasive *Haemophilus influenzae* infection

Outcome tree invasive *Haemophilus influenzae* infection



* Health states include bone/joint infections and meningitis; further complications can include the non-invasive forms epiglottitis and pneumonia (although no burden is computed for these).

Model input: Invasive Haemophilus influenzae infection

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Invasive <i>H. influenzae</i> disease	3% bone and joint infections 55% (50–60%) meningitis <i>Remaining cases are uncomplicated cases</i>		DiLiberti & Tarlow 1983, Otero Reigada et al. 1998 Funkhouser et al. 1991, Wegner et al. 1999	0.35 ^a	Naghavi et al. 2009	0.00274	1d (estimated)
Permanent disability due to meningitis: Hearing loss or mental retardation		15–30%	Lindberg et al. 1977, Ladhani et al. 2010, Hwang 2010	0.242 ^b	Naghavi et al. 2009	RLE	Lindberg et al. 1977, Naghavi et al. 2009
Death following acute illness		5–10%	Estimated, based on: Dworkin et al. 2007, Cochi et al. 1985, Peltola et al. 1992, CDC 2009, Rathore & Mirza 2010, Thoon et al. 2007				

RLE = remaining life expectancy

^a Disability weight used was Hib septicemia

^b Disability weight used was the average of the disability weights for hearing loss and mental retardation

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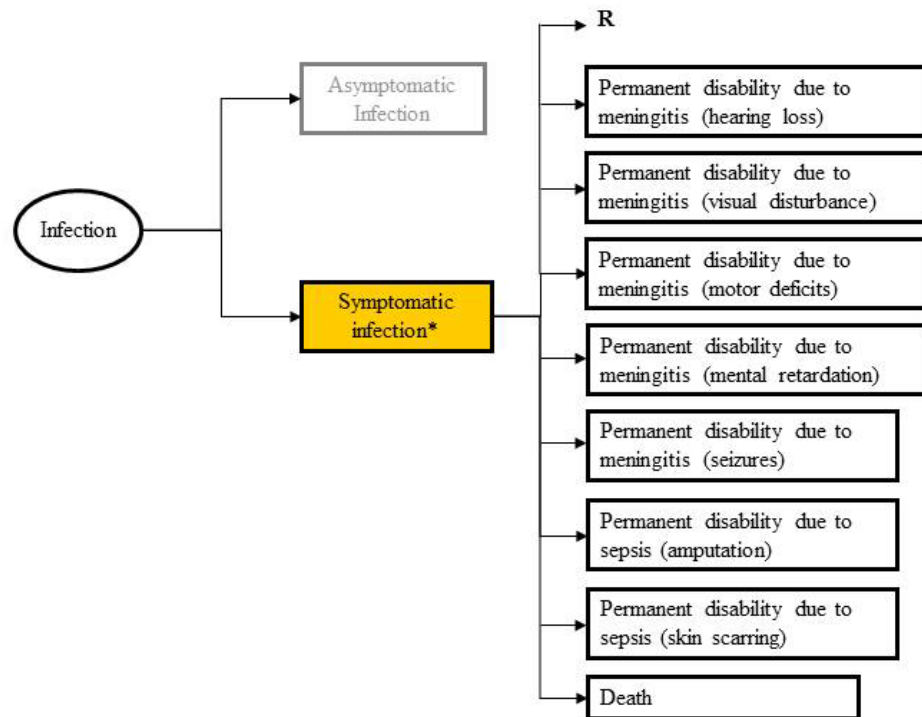
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9 Invasive meningococcal disease

Outcome tree invasive meningococcal disease



* Health states include meningitis and sepsis; further complications can include the non-invasive form pneumonia (although no burden is computed for this).

Model input: Invasive meningococcal disease

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Invasive meningococcal disease	47.3% meningitis 12.5% (5-20%) sepsis <i>Remaining cases are uncomplicated cases</i>		CDC 2009 CDC 2009	0.152	Murray & Lopez 1996	0.0192	Brigham & Sandora 2009
Permanent disability due to meningitis: Hearing loss		2.1% ^a	Smith et al. 2011, Edmond et al. 2010	0.229	Murray & Lopez 1996	RLE	CDC 2009, Mandell et al. 1999
Permanent disability due to meningitis: Visual disturbances		2.1% ^a	Smith et al. 2011, Edmond et al. 2010	0.108	Murray & Lopez 1996	RLE	CDC 2009, Mandell et al. 1999
Permanent disability due to meningitis: Motor deficits		0.8% ^a	Smith et al. 2011, Edmond et al. 2010	0.381	Murray & Lopez 1996	RLE	CDC 2009, Mandell et al. 1999
Permanent disability due to meningitis: Mental retardation		0.4% ^a	Edmond et al. 2010	0.459	Murray & Lopez 1996	RLE	CDC 2009, Mandell et al. 1999
Permanent disability due to meningitis: Seizure disorders		0.5% ^a	Edmond et al. 2010	0.100	Murray & Lopez 1996	RLE	CDC 2009, Mandell et al. 1999
Permanent disability due to sepsis: Amputation		8% ^b	Buyse et al. 2009	0.22*	Murray & Lopez 1996	RLE	Buyse et al. 2009
Permanent disability due to		48% ^b	Buyse et al.	0.001	Murray &	RLE	Buyse et al.

sepsis: Skin scarring			2009		Lopez 1996		2009
Death following acute illness		9–12%	CDC 2009, Mandell et al. 1999				

RLE = remaining life expectancy

^a Only meningitis cases are at risk of developing this sequela.

^b Only sepsis cases are at risk of developing this sequela.

* Average of the disability weights for finger, arm, and leg amputation (0.102, 0.257, 0.300, respectively)

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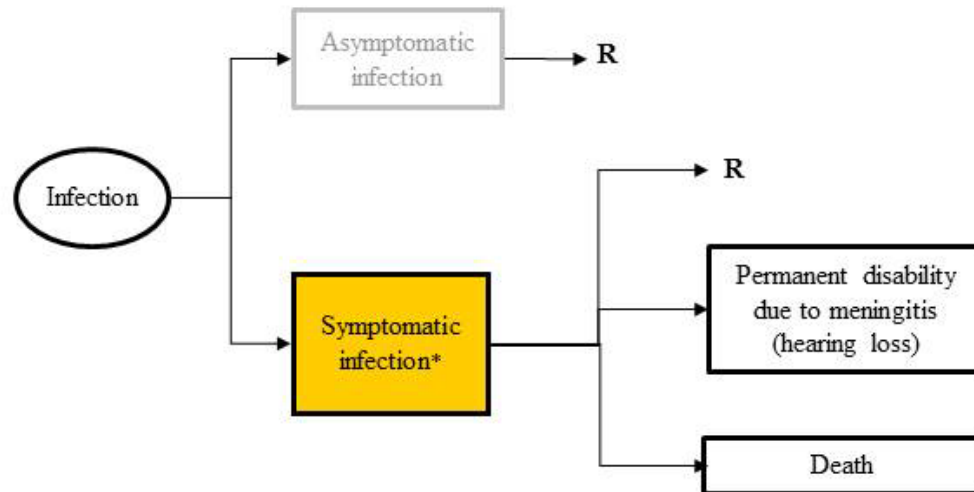
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10 Invasive pneumococcal disease

Outcome tree invasive pneumococcal disease



* Health states include meningitis, bacteraemic pneumonia, and bacteraemia without a focus; further complications can include bacteraemia with a focus (endocarditis, osteomyelitis, and septic arthritis, but these are rare), and also the non-invasive forms pneumonia and otitis media. No burden is calculated for the non-invasive complications.

Model input: Invasive pneumococcal disease

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Invasive pneumococcal disease	75% bacteraemia without a focus/bacteraemic pneumonia 4.5% meningitis <i>Remaining cases are uncomplicated cases</i>		Harper & Flaisher 2010 Muller 2009	0.320*	Estimated	0.01356	2 days: Muller 2009
Permanent disability due to meningitis (hearing loss)		21%	Jit 2010	0.233	Naghavi et al. 2009	RLE	Jit 2010
Death following invasive pneumococcal disease		10–20%	CDC 2009, Rudan & Campbell 2009, Lin et al. 2011, Saldías et al. 2009				

* Disability weight was specified as the weighted mean of the disability weights for the health states bacteraemia and meningitis.

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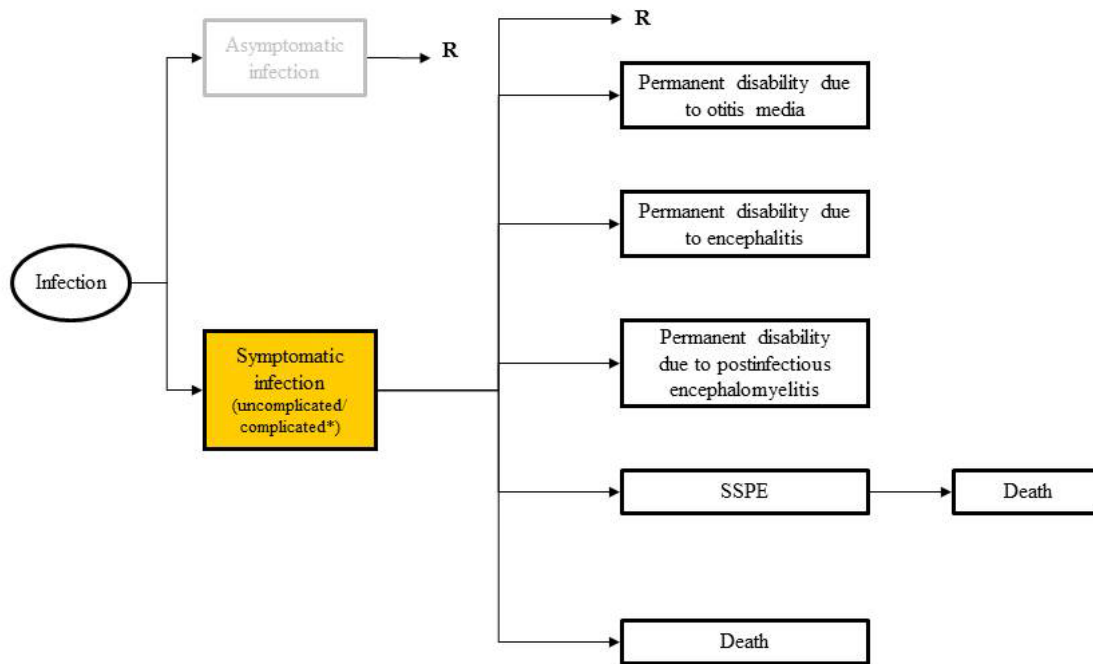
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11 Measles

Outcome tree measles



* Complicated health states include pneumonia, otitis media, convulsions, diarrhea, encephalitis, post-infectious encephalomyelitis

Model input: Measles

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute measles	5–6% pneumonia 8% diarrhea 10% otitis media 5% convulsions 0.1% encephalitis 0.1–0.3% post-infectious encephalomyelitis (PIE) <i>Remaining cases are uncomplicated cases</i>		CDC 1991 CDC 2009 CDC 2011 Miller 1978 Weissbrich et al. 2003, Beutels et al. 2002, Miller et al. 1957 Perry & Halsey 2004	0.152	Murray & Lopez 1996a	0.04	Murray & Lopez 1996b
Permanent disability due to otitis media		0.01%	CDC 1991	0.168– 0.175*	Murray & Lopez 1996a	RLE	
Permanent disability due to encephalitis		20–30%	Beutels et al. 2002, Filia et al. 2007	0.334– 0.390*	Murray & Lopez 1996a	RLE	
Permanent disability due to PIE		25%	CDC 1991	0.334– 0.390*	Murray & Lopez 1996a	RLE	
Subacute sclerosing panencephalitis (SSPE)		0.0081% (<1 yr) 0.0011% (1-4 yrs) 0.001% (> 5 yrs)	Beutels et al. 2002	0.93	Murray & Lopez 1996a	2.0	Garg 2008

Death following SSPE		100%					
Death following acute measles		0.10–0.61%	Based on combined health states; CDC, 2009				

RLE = remaining life expectancy

* Age-dependent disability weights were used

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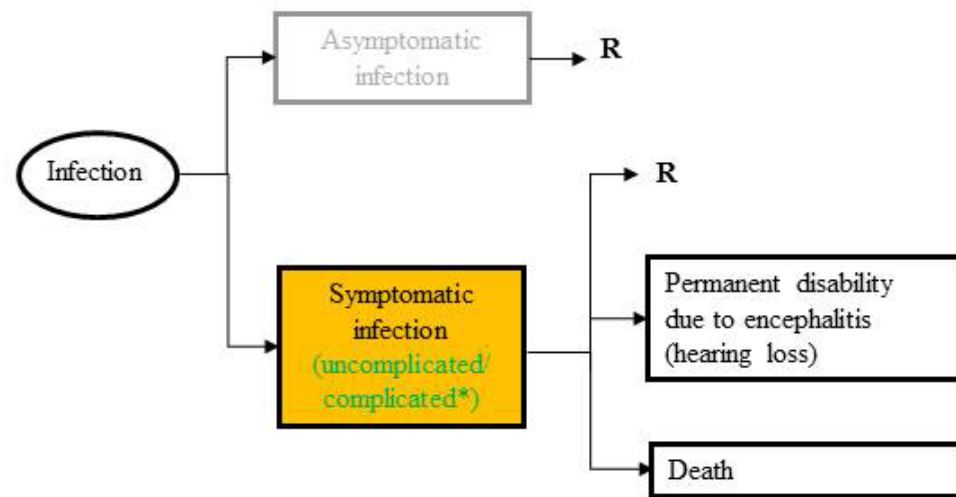
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12 Mumps

Outcome tree mumps



* Complicated health states include orchitis (males only), oophoritis (females only), meningitis, pancreatitis, and encephalitis.

Model input: Mumps

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute mumps	15–30% orchitis (<i>males ≥15 yrs only</i>) 5% oopheritis (<i>females ≥10 yrs only</i>) 1–10% meningitis 0.005–0.1% encephalitis 4% pancreatitis <i>Remaining cases are uncomplicated cases</i>		Hviid et al. 2008 CDC 2009 Hviid et al. 2008 Mandell et al. 1999, Demirci et al. 2011 Vanlioglu & Chua 2011	0.13	Murray & Lopez 1996a	0.03836	Murray & Lopez 1996b
Permanent disability due to encephalitis (hearing loss)		0.005%	Hviid et al. 2008	0.233	Naghavi et al. 2009	RLE	Hviid et al. 2008
Death following encephalitis		1.5%	Hviid et al. 2008				

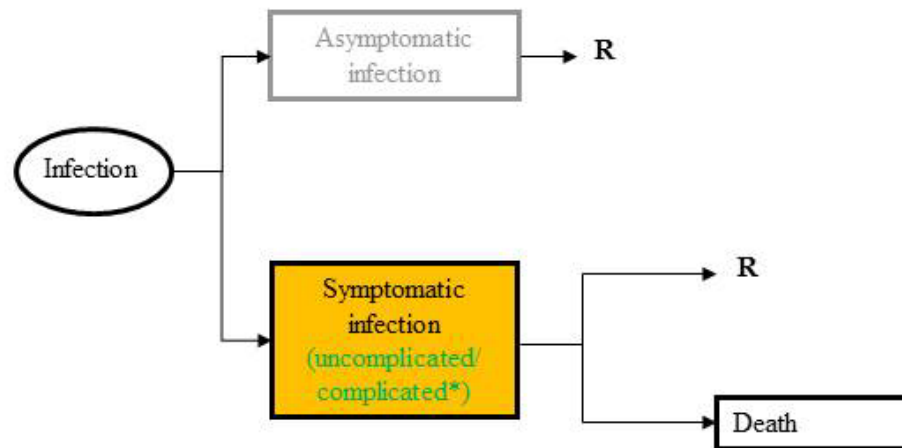
RLE = remaining life expectancy

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13 Pertussis

Outcome tree pertussis



* Complicated health states include pneumonia, otitis media, encephalopathy, and seizures.

Model input: Pertussis

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute pertussis	5.2% pneumonia* 4% otitis media* 0.1% encephalopathy* 0.8% seizures* <i>Remaining cases are uncomplicated cases</i>		CDC 2009 De Serres et al. 2000 CDC 2009 CDC 2009	0.137	Murray & Lopez 1996	0.0767	14 days (estimated)
Death following pneumonia		7.7%	Estimated				
Death following encephalopathy		50%	Estimated				
Death following acute pertussis (health states other than pneumonia or encephalopathy)		0.45% (0-9 yrs) 0.1% (10+ yrs)	Rothstein & Edwards 2005				

* Different from BCoDE project: these percentages were divided by the multiplication factor 21.9 / 25.0 (depending on age) because it is unlikely that these complications occurred among non-notified cases

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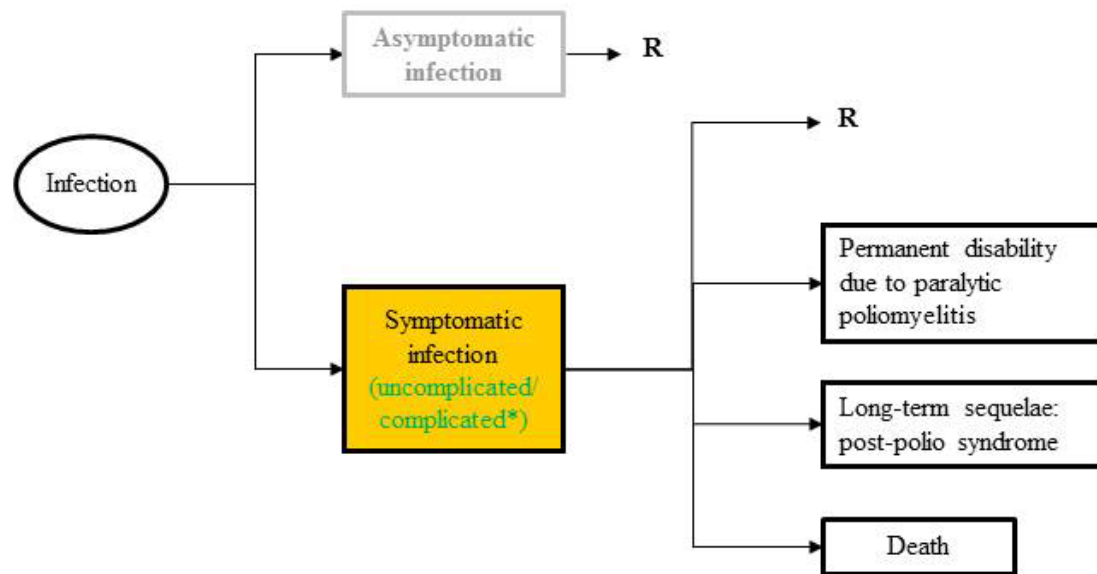
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14 Poliomyelitis

Outcome tree poliomyelitis



* Complicated health states include non-paralytic poliomyelitis and paralytic poliomyelitis.

Model input: Poliomyelitis

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Poliomyelitis	1–2% non-paralytic poliomyelitis		CDC 2009	0.047*	Naghavi et al. 2009	0.01643	CDC 2009
	<1% paralytic poliomyelitis		CDC 2009 Heymann & Aylward 2004	0.280**	Havelaar et al. 2012	0.49315	Farbu 2013
Permanent disability due to paralytic poliomyelitis		0.5%	WHO 2011	0.369	Murray & Lopez 1996	RLE	
Postpolio syndrome		25–50%	Jubelt & Drucket 1999	0.047*	Naghavi et al. 2009)	RLE	
Death following acute illness		10%	American Academy of Pediatrics 2006; Shibuya & Murray 2002				

RLE = remaining life expectancy

* Disability weight for 'influenza episode' was used as a proxy

** Disability weight for 'Guillain-Barre Syndrome (GBS)' was used as a proxy

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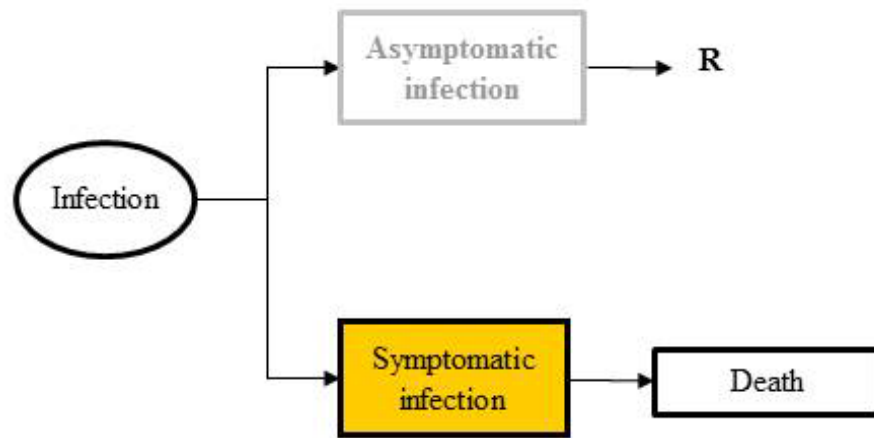
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15 Rabies

Outcome tree rabies



Model input: Rabies

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute rabies	77.5% (70–85%) furious form 22.5% (15–30%) paralytic form		Fishbein 1991, WHO 2010 Fishbein 1991, WHO 2010	0.638*	Knobel et al. 2005	0.056*	Mandell et al. 2000
Death		100%					

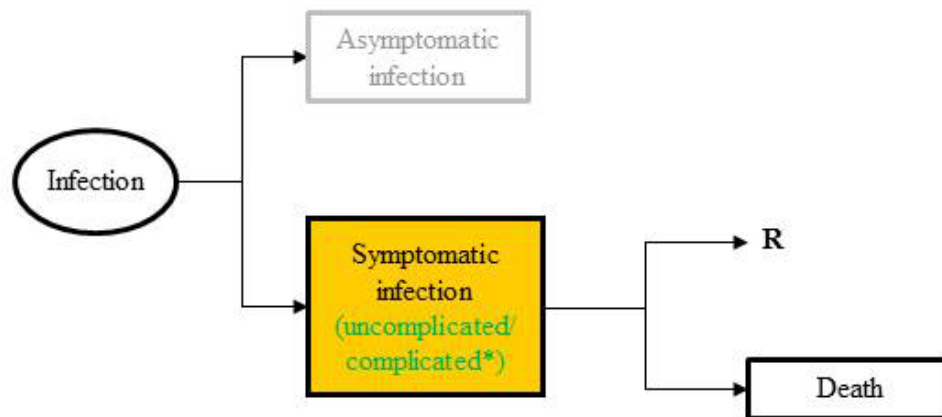
* Derived using multiplicative approach based on average individual health state proportions (77.5% for furious form and 22.5% for paralytic form) and separate disability weights/durations of 0.613/18 days and 0.725/30 days, for the furious and paralytic forms, respectively.

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16 Rubella

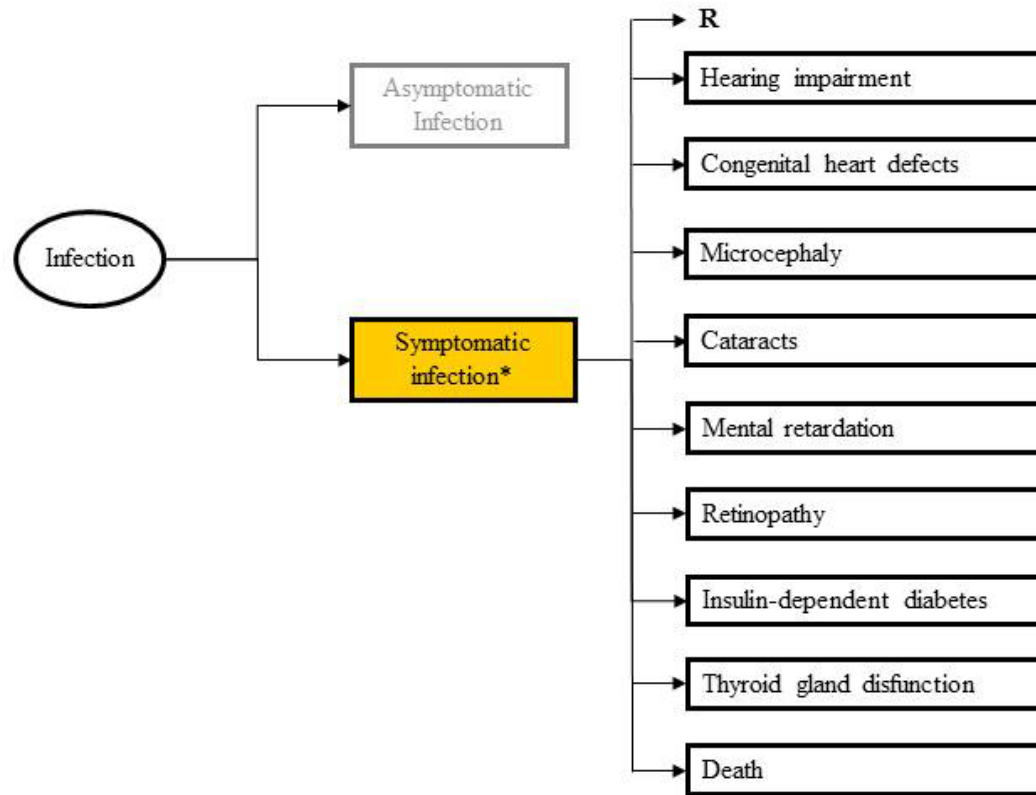
Outcome tree rubella (non-congenital)



NB. Outcome tree is for **non-congenital** rubella.

* Complicated health states include arthritis/arthralgia, thrombocytopenic purpura, and encephalitis.

Outcome tree rubella (CRS)



NB. Outcome tree is for **congenital** rubella only.

* Congenital Rubella Syndrome (CRS)

Model input: Rubella

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Non-congenital rubella							
Acute rubella	Arthritis/arthralgia	30-70% (females only)	CDC 2009, Mandell et al. 1999, Johnson & Hall 1958	0.152	Murray & Lopez 1996	0.008219	3d: CDC 2009
	Thrombocytopenic purpura	0.03%	CDC 2009, White et al. 1985				
	Encephalitis	0.01-0.02%	CDC 2009 Mandell et al. 1999				
	<i>Remaining cases are uncomplicated cases</i>						
Death following thrombocytopenic purpura		4%	White et al. 1985				

Death following encephalitis		20-50%	Gülen et al. 2008, White et al. 1985, Steen et al. 1956, Sherman et al. 1965, Mandell et al. 1999				
<i>Congenital rubella syndrome (CRS; infants)</i>							
Hearing impairment		60%	Reef et al. 2000	0.333 (severe or profound untreated)	Murray & Lopez 1996	RLE	
Heart disease		45%	Reef et al. 2000	0.323	Murray & Lopez 1996	RLE	
Microcephaly		27%	Reef et al. 2000	0.484 (highest burden of mental retardation)	Murray & Lopez 1996	RLE	
Cataract		16-25%	Bloom et al. 2005	0.170	Murray & Lopez 1996	RLE	
Mental retardation		13-25%	Lanzieri et al. 2004, Reef et al. 2000	0.459	Murray & Lopez 1996	RLE	
Retinopathy		5%	Reef et al. 2000	0.552	Murray & Lopez 1996	RLE	

Insulin-dependent diabetes		20-40% (> 35 yrs)	Mandell et al. 1999, Duszak 2009	0.015	Murray & Lopez 1996	RLE	
Thyroid disease		5% (10-19 yrs)	Duszak 2009	0.35*	Naghavi et al. 2009	RLE	
Death due to acute illness		10%	Reef et al. 2000				

RLE = remaining life expectancy

* Disability weight used was for congenital hypothyroidism without diffuse goiter

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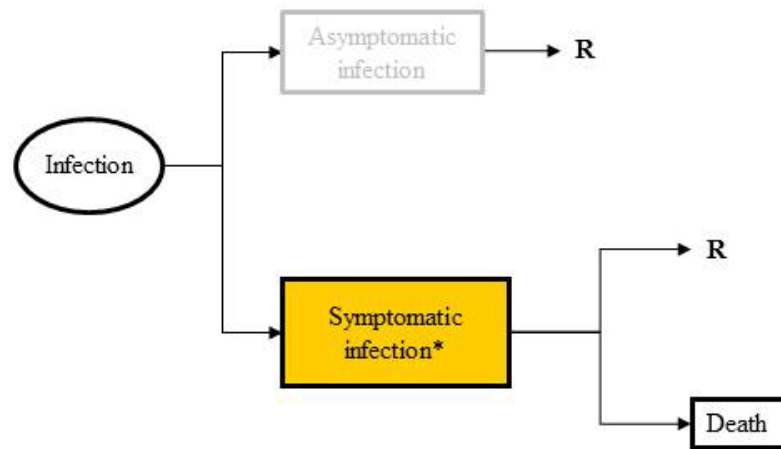
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17 Tetanus

Outcome tree tetanus



*The health-outcome symptomatic infection is split in three forms (health states) of acute infection: "localised", "generalised" and "cephalic"

Model input: Tetanus

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute tetanus	80% generalised		CDC, 2012, Hsu & Groleau 2001	0.640 (0–14 yrs)	Murray & Lopez 1996a	0.04	CDC 2012, Murray & Lopez 1996b
	14% localised		CDC, 2012, Hsu & Groleau 2001	0.610 (15–44 yrs) 0.604 (45–59 yrs) 0.612 (60+ yrs)			
	6% cephalic		Bardenheier et al. 1998	0.78	Murray & Lopez 1996a	0.05*	
Death following: - Generalised tetanus - Localised tetanus - Cephalic tetanus		11% 1% 15–30%	CDC, 2012 CDC, 2012 Hsu & Groleau. 2001				

* Assumed same as for localised tetanus

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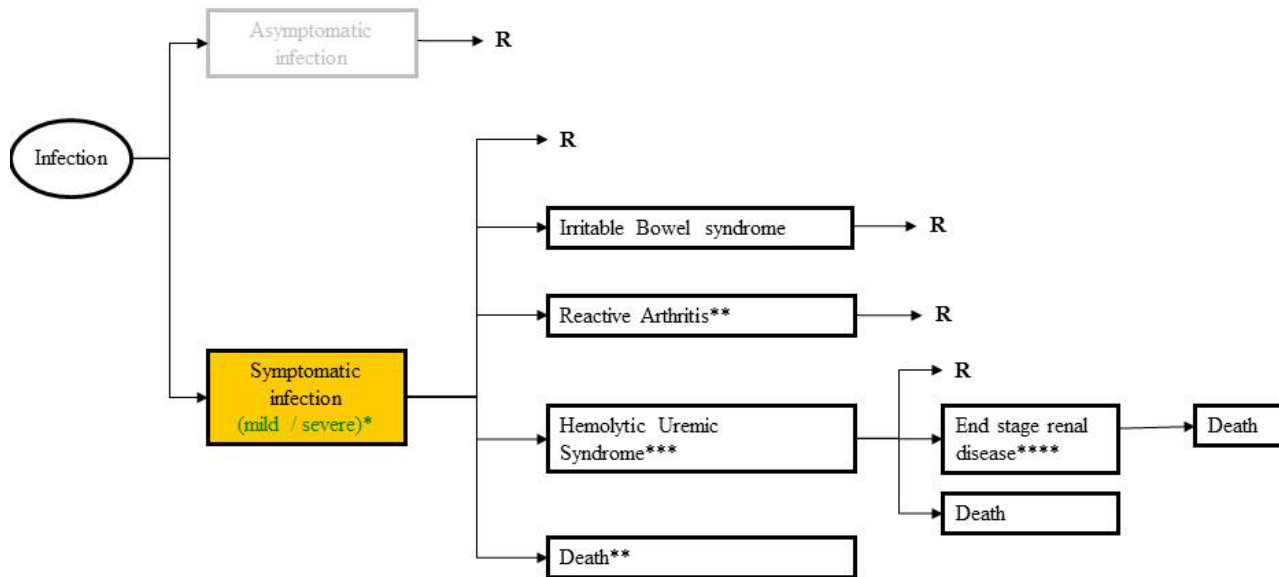
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18 Shigellosis

Outcome tree shigellosis



Note:

* Mild and severe gastroenteritis (GE) are the health states considered

** Only severe GE cases are at risk to develop ReA/at risk of being fatal

*** Only cases with *S.dysenteriae* type1 infection are at risk to develop HUS

**** End-stage renal disease (ESDRD) is distinguished between two health states: early ESRD onset (same year of infection) and late ESRD onset (on average 20 years after infection)

Model input: Shigellosis

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Gastroenteritis	Mean 8.67% (min: 6.40%, max: 11.36%) are severe GE cases* <i>Remaining cases are by definition mild GE cases.</i>		Haagsma et al. 2010. (assuming that notified cases are a proxy for severe GE cases)	0.105	WHO 2004	0.01792	Kemmeren et al. 2006
Death due to gastroenteritis		0-4 yrs: 0.06% 5-64 yrs: 0.09% 65+ yrs: 0.97%	Barton Behravesh et al. 2011				
IBS		8.8% (7.2–10.4%)	Haagsma et al. 2008	0.042	Haagsma et al. 2008	5	Haagsma et al. 2010
ReA*		6.6% (1.2–9.8%)	Hannu et al. 2005, Rees et al. 2004, Townes et al. 2008, Schiellerup et al. 2008	0.4505 ^a	Based on Haagsma et al. 2008, Hannu et al. 2002	0.131	

HUS**		1.6% (1.0-2.9%)	Havelaar et al. 2004, Ternhag et al. 2008, Cressey & Lake 2007	3.21 ^b	Based on Haagsma et al. 2008	0.038	
ESRD		13.4%†	Havelaar et al. 2004, Cressey & Lake 2007	0.154	Based on Haagsma et al. 2008	RLE	
Death following HUS		3.7% (<65 yrs) 56% (≥65 yrs)	Havelaar et al. 2004, Dundas et al. 1999				
Death following ESRD††		13% (0-15 yrs) 17% (16-44 yrs) 45% (45-64 yrs) 88% (≥65 yrs)	Havelaar et al. 2004				

RLE = remaining life expectancy

* Only severe GE cases (proxy: laboratory-confirmed cases) are at risk to die and develop ReA, respectively.

** Only severe (laboratory-confirmed) cases of *S. dysenteriae* type 1 are at risk to develop HUS (Bennish et al. 2006). Based on Ekdahl and Andersson (2005), we assumed that most likely 2% (min. 0% and max. 5%) of Shigella isolates would be *S. dysenteriae*, whereby assuming that 30% are infected with type 1 and therefore at risk of developing HUS (Kotloff et al. 1999).

† Of cases with HUS. 2.9% direct ESRD and 10.5% late ESRD.

†† The majority of fatal cases occur within the first year after starting dialysis. For simplification reasons, we assume that on average ESRD patients are ill for one year before dying.

^a Recalculated from annual profile disability weight (0.059) by dividing by the duration (0.059/0.131)

^b Recalculated from annual profile disability weight (0.123) by dividing by the duration (0.123/0.038)

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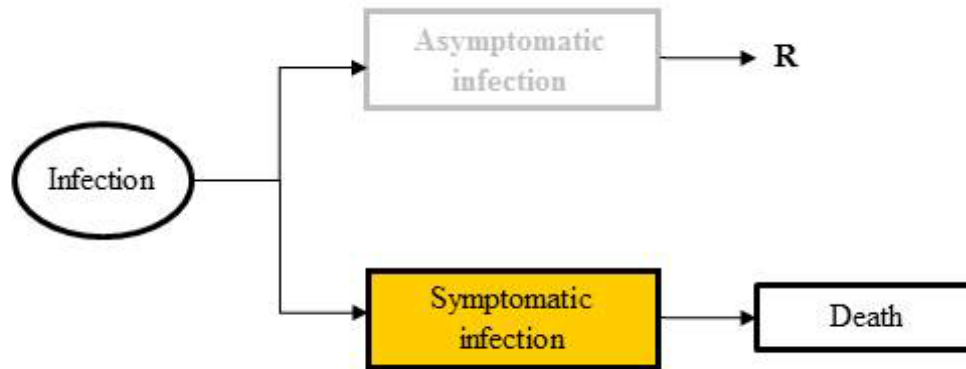
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19 Variant Creutzfeldt-Jakob disease

Outcome tree variant Creutzfeldt-Jakob disease



Model input: Variant Creutzfeldt-Jakob disease

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Symptomatic infection		100%	-	0.616* (0-14 yrs) 0.613 (15+ yrs)	WHO 2004	1.167 (0.5–3.25)	14 mths (6-39 mths): Will & Ward 2004
Death		100%	Henry & Knight 2002				

* Disability weight for bacterial meningitis / Japanese encephalitis was used as a proxy

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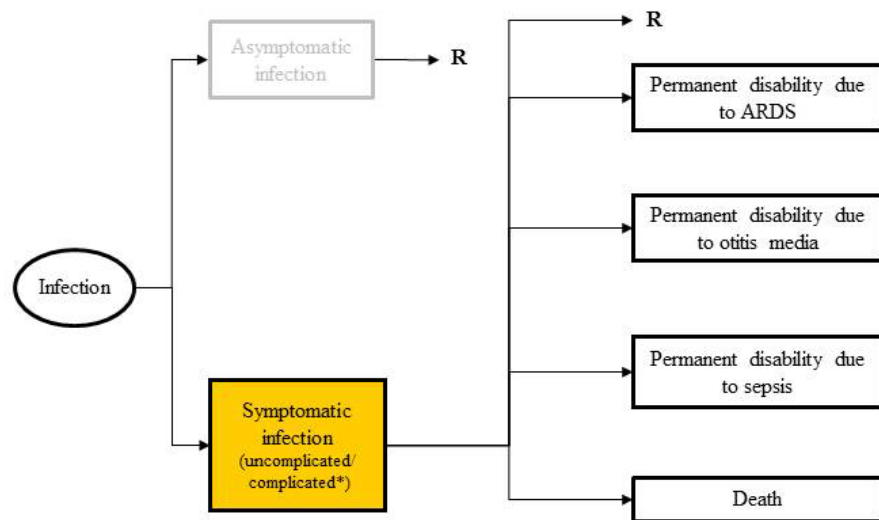
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20 Influenza

Outcome tree influenza



* Complicated health states include Acute Respiratory Distress Syndrome (ARDS), pneumonia, otitis media and sepsis

Model input: Influenza

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute influenza infection	0.023% ARDS 0.36% pneumonia 0.65% otitis media 0.0097% sepsis <i>Remaining cases are uncomplicated cases</i>		Meier et al. 2000, Wielders et al. 2010	0.261*	Stouthard et al. 1997	0.038	(2 wks)
Permanent disability due to Acute Respiratory Distress Syndrome (ARDS)		56%	Wielders et al. 2010, Mikkelsen et al. 2009	0.17 (COPD)	Stouthard et al. 1997	RLE	
Permanent disability due to otitis media (deafness)		0.006%	Meier et al. 2000, Murray & Lopez 1996b	0.175 (0-4 yrs) 0.169 (5-14 yrs) 0.168 (15+ yrs)	Murray & Lopez 1996a	RLE	
Permanent disability due to sepsis		82%	Wielders et al. 2010, Korosec Jagodic et al. 2006	0.28	Melse & Kramers 1998	RLE	

Death following acute influenza		0.13% in total	Meier et al. 2000; age distribution based on vital statistics from Estonia, Germany and the Netherlands				
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* Recalculated from annual profile disability weight (0.01) by dividing by the duration

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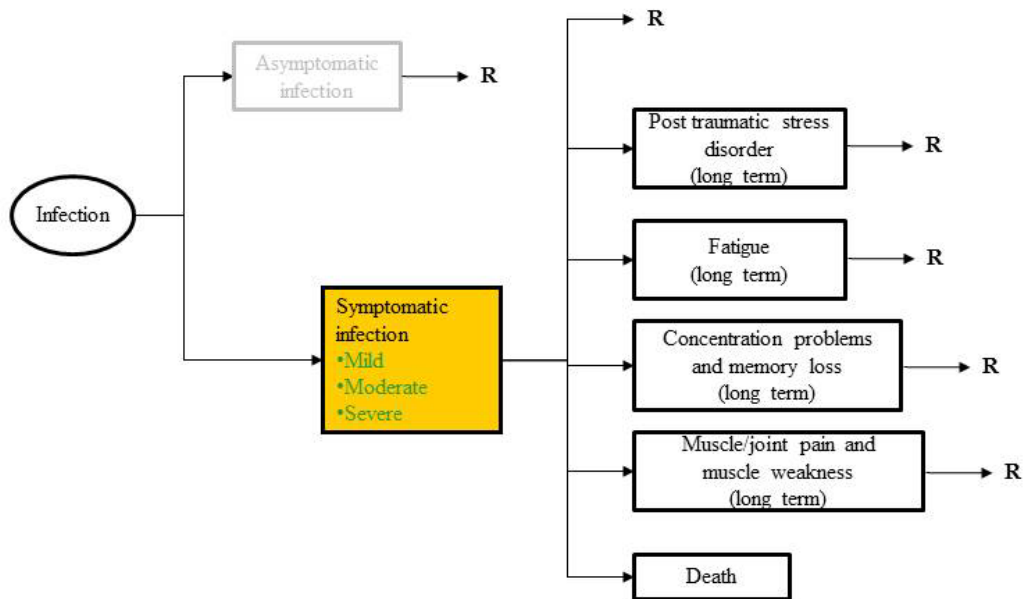
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21 Legionellosis

Outcome tree legionellosis



-Mild cases are considered as outpatient cases or patients not contacting medical services

-Moderate cases are considered as hospitalized cases

-Severe cases are considered as the fraction of hospitalized cases admitted to ICU

Model input: Legionellosis

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Symptomatic infection (Legionnaires' disease)	71.5% mild* 19.0% moderate* 9.5% severe*		Proportions based on notification data, the estimated number of pneumonia cases (Dijkstra et al. 2008, Brandsema et al. 2011), and expected proportion with diagnosed legionellosis (Von Baum et al. 2008)	0.136	Kwong et al. 2010	0.03	Lettinga et al. 2002b
Fatigue		58–81%	Lettinga et al. 2002b, Lattimer et al. 1979	0.14	Stouthard et al. 1997	1.42	Lettinga et al. 2002b

Post-traumatic Stress Disorder		15%	Lettinga et al. 2002b	0.13	Stouthard et al. 1997	1.42	Lettinga et al. 2002b
Concentration problems and memory loss		6.4–81%	Lettinga et al. 2002b, Lattimer et al. 1979	0.14	Stouthard et al. 1997	1.42	Lettinga et al. 2002b
Muscle joint pain and muscle weakness		25–79%	Lettinga et al. 2002b, Lattimer et al. 1979	0.06	Stouthard et al. 1997	1.42	Lettinga et al. 2002b
Death, following - mild - moderate - severe		0%** 5–12.8%; mode=12% 10-30%	EWGLI Lettinga et al. 2002a, Benin et al. 2002, Falco et al. 1991				

* Different from BCoDE project where 28.5% (mild), 47.7% (moderate), and 23.83% (severe) was used (Garcia-Fulgueiras et al. 2003, Lettinga et al. 2002a)

** Different from BCoDE project where the same proportion as for moderate cases (5-12.8%; mode 12%) was used (EWGLI)

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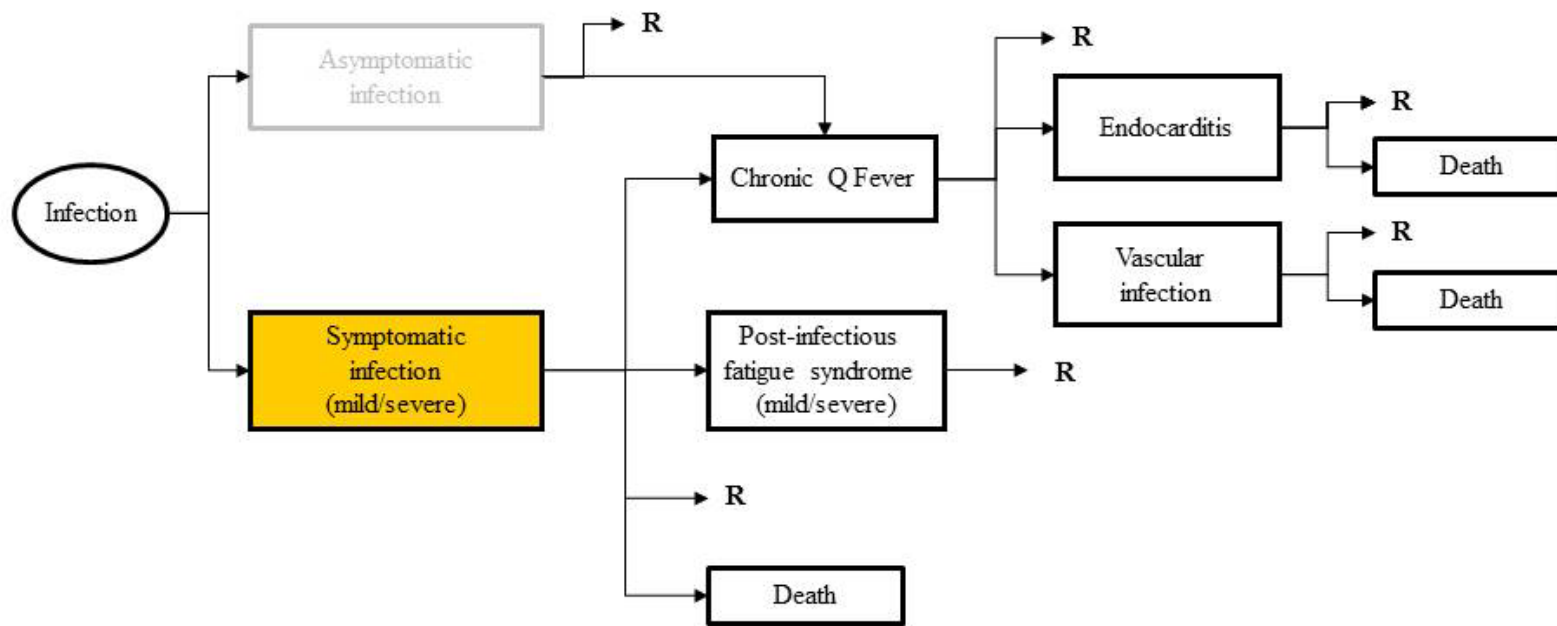
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22 Q fever

Outcome tree Q fever



Model input: Q fever

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Acute illness	<15 yrs: 100% mild ≥15 yrs: 39.3% mild 60.7% severe		Dupuis et al. 1987	0.261†	Stouthard et al. 1997	0.038	(2 wks)
			Maurin & Raoult 1999, Dijkstra et al. 2012	0.261† 2.61†	Stouthard et al. 1997	0.038	(2 wks)
Chronic Q fever		1.6% (1.44–1.76%)*	Van der Hoek et al. 2011	0		2.75	Ayres et al. 1998
Post-infectious fatigue syndrome - mild - severe		27.7–27.8% 16.2–16.3%	Morroy et al. 2011, Ayres et al. 1998	0.14 (depression)	Stouthard et al. 1997	1.5	Morroy et al. 2011
			Wildman et al. 2002	0.14	Stouthard et al. 1997	10	Morroy et al. 2011
Death following acute illness		0.24–0.25%	Kampschreur et al. 2010, van der Hoek et al. 2010				

Endocarditis		73.1% (60–75%)	Raoult et al. 2000, Maurin & Raoult 1999, Gami et al. 2004	0.201	WHO 2004	0.583	Boyle & Hone 1999
Vascular infection		8% (7.2–8.8%)*	Raoult et al. 2000	0.201	WHO 2004	0.583	Boyle & Hone 1999
Death following endocarditis		5%	Raoult et al. 1999				
Death following vascular infection		5%	Raoult et al. 1999				

* Only one point estimate was found in the literature. To reduce artificial certainty, a distribution range was defined as the 90% and 110% multipliers of the point estimate.

† Duration of 2 weeks (=0.038 yrs) for acute illness was specified; disability weights were converted from annual profile weights (0.01 and 0.1, for mild and severe, respectively) to period profile weights by dividing by the duration.

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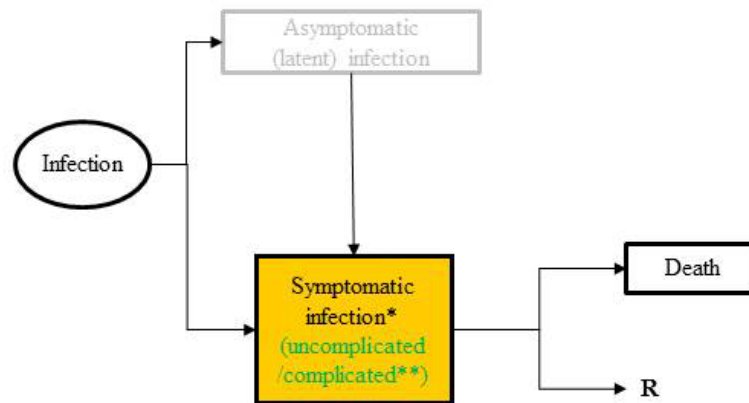
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23 Tuberculosis

Outcome tree tuberculosis



*symptomatic infection may present as pulmonary or extra-pulmonary tuberculosis

**uncomplicated cases include the health state drug-sensitive tuberculosis

complicated cases include the health states multi-drug resistant tuberculosis (MDR) and extensively drug resistant tuberculosis (XDR)

Model input: Tuberculosis

Health outcome (health state)	Distribution of health states in health outcome	Risk to develop that health outcome (most likely)	Sources/ Assumption	Disability weight (w)		Duration	
				w	Source	in years	Source
Active TB (symptomatic infection)	98.7% drug sensitive		Based on Dutch surveillance data (Netherlands Tuberculosis Register)	0.29 (0-44 yrs)	Murray & Lopez 1996a	0.25	Murray & Lopez 1996b
	1.22% MDR			0.264 (45-59 yrs)			
	0.08% XDR			0.274 (60+ yrs)			
				0.29 (0-44 yrs)	Murray & Lopez 1996a	0.25	Murray & Lopez 1996b
			0.264 (45-59 yrs)				
			0.274 (60+ yrs)				
Active TB from latent cases		0.1%/yr	Tseng et al. 2011				

Death, following							
- Drug sensitive TB		3.0% (0-7.4%)	Straetemans et al. 2011				
- MDR TB		12.8-14.2%	Tseng et al. 2011, Straetemans et al. 2011				
- XDR TB		14%	Jassal & Bishai 2009				

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De zorg voor morgen begint vandaag