PREPSHIELD

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Nature of the Deliverable		
R	Document, report (excluding the periodic and final reports)	X
DEM	Demonstrator, pilot, prototype, plan designs	
DEC	Websites, patents filing, press & media actions, videos, etc.	
OTHER	Software, technical diagram, etc.	

Dissemination Level		
PU	Public, fully open, e.g. web	X
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Project Summary

PREPSHIELD aims to foster a more holistic and citizen-centric approach to health crisis preparedness and management, by co-creating policy recommendations, methods and an AI-powered platform for crisis management to better prepare for and address health emergencies from a social and societal perspective. To reach this objective, PREPSHIELD will rely on the participation of public authorities, citizens (specifically from vulnerable and non-compliant groups), CSOs, DROs and healthcare institutions. Based on the needs of these groups, PREPSHIELD will develop recommendations for health crisis preparedness, management and communication as well as tools to simulate future crises through an iterative process, involving various pilots for their evaluation. These pilots will include a communication pilot, tabletop exercises and an online exercise, which will include all these stakeholders and take place at different scales in different countries: local (Hamburg, DE), regional (Piedmont, IT) and national (Romania). The online exercise will rely on a PREPSHIELD platform and app (built on the proven CRIMSON platform) to reproduce real-life crisis communication conditions and provide decision-makers with simulations and feedback on the behaviour, wellbeing, capacities, and resources of the other stakeholders. The project brings together a complementary consortium of five universities, two public authorities, one RTO, two non-profit organizations, one SME and two large enterprises from seven European Union countries (and Switzerland)

Document Objective and Executive Summary

List Of Partners

N°	Participant organisation name	Acronym	Country
1	UNIVERSITA DEGLI STUDI DEL PIEMONTE ORIENTALE AMEDEO AVOGADRO	UPO	IT
2	RIJKSUNIVERSITEIT GRONINGEN	UG	NL
3	UNIVERSITETET I OSLO	UiO	NO
4	TECHNISCHE HOCHSCHULE KOELN	THK	DE
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List of Abbreviations

BMI	Body Mass Index
CI	Confidence Interval
EIP	Extrinsic incubation period
IAV	Alpha influenza viruses
ILI	Influenza like illness
IQR	Interquartile range
NPI	Non-pharmaceutical interventions
OR	Odd Ratio
PHEIC	Public Health Emergency of International Concern
R0	Basis Reproductive number
RNA	Ribonucleic Acid
RR	Risk ratio
USA	United States of America
WHO	World Health Organization

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Introduction

This report is the outcome of Task 2.1, 'Scenario Definition for Pilots', of the PREPSHIELD project, led by the University of Zurich (UZH), and makes a significant contribution to Task 2.4, 'AI-powered multi-agent simulation models'. The aim of this work and the resulting report and deliverable, 'D2.1 – Forward-looking health crisis scenarios', was not to predict the next pandemic or develop a new pandemic action plan. Rather, the intention was to design a few selected and realistic outbreak scenarios on which the pilots and exercises later in the project could be based.

This report is the outcome of Task 2.1, 'Scenario Definition for Pilots', of the PREPSHIELD project, led by the University of Zurich (UZH), and makes a significant contribution to Task 2.4, 'AI-powered multi-agent simulation models'. This work and the resulting report and deliverable, 'D2.1 – Forward-looking health crisis scenarios', did NOT aim to predict the next pandemic or develop a new pandemic action plan. Rather, the intention was to design a few selected and realistic outbreak scenarios on which the pilots and exercises later in the project could be based.

1 Determination of pathogens that could lead to a major outbreak

Our choice of pathogens is mostly based on the 2024 “Pathogens Prioritization” framework from the World Health Organization (WHO). This document is based on conclusions from over 200 scientists reviewing the evidence on viral and bacterial families comprising over 1,600 pathogens. We decided to have two very different scenarios, with pathogens belonging to different viral families, having a different transmission mode, and different epidemiologic parameters. Both scenarios are based on pathogens estimated to have high Public Health Emergency of International Concern (PHEIC) potential, including in the European region. The PHEIC is the strongest global alert from the WHO and designates “an extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response”[1] and, when declared, is associated with legal obligations for outbreak response under international health regulations (2005). In addition, both pathogens have a “One Health” component, with the One health approach integrating human and animal health, as well as the environment. We non-systematically reviewed the literature on past influenza pandemics in the world (focusing on the 1918 and the 2009 pandemics) and recent dengue outbreaks in Europe (2010-23), to retrieve epidemiological parameters for each scenario. This includes for instance the incidence, hospitalization rate or mortality rate.

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1.1 First scenario - Influenza A pandemic

Alpha influenza viruses (IAV) belong to the *Orthomyxoviridae* family. There actually exists three genera of influenza viruses (A, B, and C), but only IAV have caused pandemics up to now. Influenza is a respiratory virus which is transmitted by droplets among animals, from animal to human (and vice versa), and among humans. Their viral genome consists of 8 strands of ribonucleic acid (RNA), including the haemagglutinin (H) and neuraminidase (N) antigens, which code for glycoproteins and give the nomenclature to each strain of influenza. There exists 18 H (H1-H18) and 11 N (N1-N11) subtypes. The combination of H and N defines the influenza variant, with for instance H1N1 and H3N2 strains. A new strain can appear in two ways: mutations in the genes that code for the H and N proteins occurring naturally, thereby leading to slight changes in these H and/or N proteins (e.g., antigenic drift), or reassortment (e.g., antigenic shift) which occurs when two or more strains of influenza combine by exchanging some of their RNA strands to create a new subtype (e.g., strain) of influenza, with a novel H and N combination. New influenza strains can emerge rapidly through RNA antigenic shift and drift, posing both a PHEIC and a pandemic risk [2], since the population has no previous immunity against these novel strains.

Influenza is a zoonotic disease, and influenza A viruses circulate in various animals including aquatic and domestic avian species as well as domestic mammals. The 2009 influenza H1N1 pandemic (A(H1N1)pdm09) appeared due to reassortment between human, avian, and swine strains [3].

Influenza pandemics have occurred regularly in history (H1N1 in 1918, H2N2 in 1957-58, H3N2 in 1968-69, and A(H1N1)pdm09 in 2009-10). In addition, the intensification of farming and the global travel patterns of a highly-connected world make viral spread easier. Indeed, there are regularly sporadic cases of human influenza infection with new viruses, with potential for person-to-person transmission, posing a threat to human health. Therefore, future influenza pandemics are likely to occur.

1.1.1 Summary of epidemiological parameters

Studies on the 1918 and the 2009 influenza pandemics were considered, because these are probably the pandemics associated with the highest numbers of publications, but also because the 1918 had the highest death toll (50-100 million deaths worldwide based on the highest estimations [4]) and the 2009 is the most recent one. The 1957 and 1968 pandemics were not included due to their comparatively lower impact in terms of morbidity and mortality. While global in scope, the 1957 influenza pandemic (H2N2) resulted in

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significantly fewer deaths and has received comparatively limited scientific attention. Similarly, the 1968 pandemic (H3N2) caused moderate mortality and disruption, but did not trigger the same level of public health response or long-term impact as the 1918 and 2009 pandemics.

The overall incidence rates of the two pandemics were close (median of 17-18%, Table 1 and Table 2). However, the incidence rates in 1918 are greatly underestimated. It is estimated that two-thirds of the population fell ill that year. However, the fatality rate and hospitalization rate among ill people were much higher during the historical pandemic than the more recent one (3.8% and 4% (Table 1) vs. 0.02% and 1.5% (Table 2), respectively). A systematic review noted that the median reproductive number R_0 of the 1918 pandemic was 1.80 [interquartile range (IQR) 1.47 to 2.27], based on 24 studies, while that of the 2009 pandemic was 1.46 [IQR 1.30 to 1.70], based on 57 studies); for the two pandemics, the reproductive number was similar across the waves [5]. This systematic review also noted that the median generation time (or serial interval) was 3.3 days with a mean ranging from 1.5 to 6 days for the 1918 pandemic, and median 2.8 days with a mean ranging from 1.9 to 7 days for the 2009 pandemic [5]. The incubation period of influenza A subtypes ranges from 1.34 to 2.1 days [6].The incubation time in the 2009 pandemic was lower for those <15 years (mean 1.2 days) compared to those ≥15 years (1.9 days) [7].

Table 1 Summary estimates of epidemiological parameters of the 1918-20 influenza pandemic, based on the literature. *d: days. Incidence: proportion of the population who gets ill; Mortality rate: proportion of the population who dies, Fatality rate: proportion of ill people who dies; Clinical infection: proportion of ill people who develop symptoms; R0: reproduction number; Latency: time from infection to symptoms; Infectious period: time from infection to recovery infectious, Generation time: interval from infection of one individual to when their contacts are infected. Epidemiological parameters are summarized depending on the pandemic wave. For the "overall" part, this summarizes studies which either assessed the effect during the whole pandemic, or did not specify in which wave they focused on.*

	Incidence (%)	Mortality rate (/1000)	Fatality rate (%)	Hospitalisation rate (% population)	Hospitalisation rate (% ill)	Tranmission rate (/d)	R0	Latency (d)	Infectious period (d)	Generation time (d)
median	17.94	9.59	3.80	0.80	4.00	5.75	3.20	1.45	2.80	4.50
mean	16.91	15.38	3.57	0.80	4.00	5.75	2.96	1.45	2.96	4.50
min	5.15	4.10	2.00	0.80	4.00	5.75	1.49	0.70	0.25	3.00
max	25.00	55.60	5.35	0.80	4.00	5.75	5.40	1.90	6.00	6.00

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Table 2 Summary estimates of epidemiological parameters of the 2009-10 influenza pandemic, based on the literature. *d: days. Incidence: proportion of the population who gets ill; Mortality rate: proportion of the population who dies, Fatality rate: proportion of ill people who dies; R0: reproduction number, Latency: time from infection to symptoms, Incubation period: time from exposure to infectiousness, Infectious period: time from infection to recovery infectious, Generation time: interval from infection of one individual to when their contacts are infected.*

	Incidence (%)	Mortality rate (/1000)	Fatality rate (%)	Hospitalisation rate (% population)	Hospitalisation rate (% ill)	R0	Latency (d)	Incubation period (d)	Infectious period (d)	Symptoms duration (d)	Generation time (d)
median	16.50	2.63	0.03	0.10	3.00	1.52	2.62	1.65	3.38	6.50	2.75
mean	16.50	2.63	0.12	0.10	3.00	2.51	2.62	2.36	6.99	6.50	3.15
min	9.00	0.46	0.02	0.10	1.50	1.09	2.62	1.43	2.60	6.00	2.60
max	24.00	4.80	0.30	0.10	4.50	5.96	2.62	4.00	15.00	7.00	4.50

1.1.2 Transmissibility of influenza

Directly measuring the probability of infection given a contact between an infectious person (I) and a susceptible person (S) is not possible. It can however be estimated based on household surveys, using the secondary attack rate. This is "the probability that an infected person in the household will infect another person in the household during the infectious period" [8]. In the US it was estimated that the household secondary attack rate during the early stage of A(H1N1)pdm09 was 27.3% [95% confidence interval (CI) 12.2 to 50.5%] [8]: each index case has a 27% probability of infecting a household member. A web-based participatory cohort survey estimated an odds ratio (OR) of 1.87 [95% CI 1.40 to 2.50] for getting influenza-like illnesses (ILI) after contact with infected persons in the three previous days [9]. The probability of transmission varies depending on the contact groups, with higher probability of transmission in households compared to schools and communities, and among children (80%) compared to between a child and an adult or among adults (30-40%) of the same household [10]. Within a household, the probability of transmission decreases with increasing size of the household (because people share their time with all household members), from 28% for two-member households to 9% for six-member households [11].

1.1.3 Vulnerable groups

During the seasonal flu, it is usually the infants and the elderly that are at a high risk of severe symptoms. However, concerning the 1918-1920 pandemic, while the very young and elderly remained vulnerable, young adults (20-40 years old) were also severely affected [12].

On the other hand, the antigenic imprinting theory states that early immunological memory of one influenza strain can weaken the immune response to significantly different strains later in

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life, thereby increasing the risk of death[13–16]. Therefore, the age-mortality or age-hospitalization pattern will depend on the specific type of influenza strain. In the PREPSHIELD project, we do not aim at predicting which influenza strain could evolve to become a pandemic. Therefore, and for simplicity reasons, we chose the influenza strain for scenario 1 to have a similar age-hospitalization and age-mortality pattern to the seasonal flu (e.g., the infants and elderly would be the most affected).

During seasonal epidemics, the ≥65 years old experience much higher excess mortality (14.27/100 000) while those 25-44 a lower one (0.16/100 000) [17]. The case fatality rate of the A(H1N1)pdm09 was the highest for those ≥ 85 years old (2.51% [95%CI 2.09 to 2.94%]). Between 55 and 84 years old, the risk was multiplied by 2.5 for each 5 years of age increase [18]. Infants also have a higher risk of hospitalization, with children <2 years old infected by influenza A(H1N1) pdm09 having an OR of 13.8 [95%CI 1.7 to 106.4] compared to children aged 2-18 years old [19].

There is some evidence that men had a higher risk of severe complications and death, as for instance during the 2009 pandemic: the age-standardized mortality rate among men was 0.54 compared to 0.37/100 000 among women [20].

Few studies investigated the risk factors for developing severe influenza during the 2009 pandemic, but obesity and pregnancy have been noted as important risk factors [21]. Martin et al. found that obesity was associated with a higher risk of hospitalization for influenza in 2009-2011 compared to both outpatient cases and to outpatient controls; this was also the case for continuous BMI (Body Mass Index) (OR=1.11 [95%CI 1.07 to 1.16] compared to outpatient cases, and OR 1.04 [95%CI 1.01 to 1.07] compared to outpatient controls. The population attributable fraction of hospitalization by influenza due to BMI was 9-22% [22]. Being underweight might also be a risk factor for being hospitalized after influenza infection (OR 5.20 [95%CI 1.67 to 16.01], compared to normal weight), even more so than overweight or obesity [23]. A case-control study from Brazil found that after contracting A(H1N1) pdm09, obesity was a risk factor for developing severe compared to mild symptoms, among women only (OR 3.84 [1.06 to 13.83]) [21]. A meta-analysis reported that severely obese patients (BMI ≥40kg/m2) with A(H1N1)pdm09 infection had a twofold increase of intensive care unit admission (OR 2.01 [95%CI 1.29 to 3.12]) [24].

Pregnancy is an important risk factor for developing a severe illness and for being hospitalized following seasonal or pandemic influenza [25–27]. During the 1918-1920 pandemic, contemporary studies reported death rates ranging from 27% to 62% among pregnant women presenting at hospitals [28–32]. Pregnant individuals also had a higher risk of adverse

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pregnancy outcomes during the 2009 pandemic, including higher risks of stillbirth [33,34], low birth weight (<2,500g) [35] and preterm birth [34,35]. The rates of stillbirth and neonatal mortality appear to have peaked during the 1918-1920 pandemic [36,37]. Several reports from 1918-1920 also noted frequent preterm birth or pregnancy loss in the case of maternal influenza [28–30,32], and a recent paper showed higher risks of preterm birth and low birth weight [38]. Therefore, influenza during pregnancy is associated with adverse outcomes for both the pregnant individual and the unborn infant.

1.1.4 Choice of scenarios

Based on the literature, we decided on two sub scenarios: a mild one and a severe one.

Table 3 Influenza A- pandemic scenarios

Parameter	Mild scenario	Severe scenario
Incidence (%)	9	18 (up to 60-70%)
Hospitalisation rate (% ill)	0.2	2.3
Case Fatality Rate (%)	0.02	0.7
Vulnerable groups	Pregnant persons, persons up to 2 weeks postpartum, infants under 59 months, individuals younger than 19 years on long-term aspirin- or salicylate containing medications, individuals with a body mass index of 40 or higher, individuals with underlying health conditions, individuals with low socioeconomic status, elderly individuals	

1.2 Second scenario – Dengue

The second pathogen is the dengue virus, which belongs to the *Flaviviridae* family, and that could lead to a local outbreak. Dengue is a vector-borne virus that is mostly transmitted by the mosquitoes *Aedes aegypti* and *Aedes albopictus*. Among the flaviviruses, this pathogen was chosen because dengue infection is the most common arboviral infection (e.g., transmitted by arthropods such as mosquitoes, ticks, and sandflies) in the world, with more than a hundred million of infections and about ten thousand deaths every year [39], and because of increasing numbers of recent outbreaks in Europe [40].

Indeed, the geographical distribution is shifting to Southern Europe because of warming temperatures. A recent systematic review and meta-analysis estimated that almost sixty thousand dengue cases occurred in Europe between 2000 and 2023, with 5% of them being

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autochthonous (locally acquired) [40]. Only 12 of these cases were reported to have resulted in death, but the outcome was only reported in 73% of cases. Of note, there was a very large dengue outbreak in Madeira (Portuguese island) in 2012 that resulted in 2218 cases. Furthermore, dengue virus prevalence in travelers returning to Europe that have suggestive symptoms was 6% [95%CI 4; 10%], which is higher compared to the prevalence of Zika and Chikungunya viruses [40]. The numbers of autochthonous (e.g., locally acquired) and imported cases of dengue in Europe in the last two decades can be seen in Figure 1.

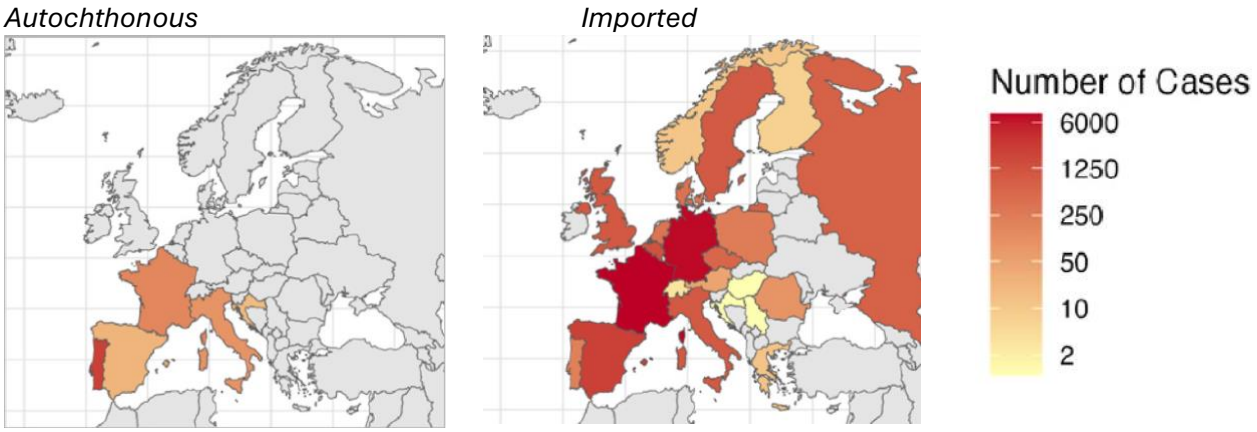

Figure 1 Dengue virus cases in Europe between 2000 and 2023. *Figure adapted from "Hedrich, N., Bekker-Nielsen Dunbar, M., Grobusch, M. P. & Schlagenhauf, P. Aedes-borne arboviral human infections in Europe from 2000 to 2023: A systematic review and meta-analysis, Travel Medicine and Infectious Disease vol. 64"* [40]

The risk of dengue autochthonous transmission will continue to increase in the future due to important international travel but also due to climate change: warmer temperatures and wetter climate contribute to *Aedes* mosquitoes spread, survival, and overwintering, as well as higher viral replication [40].

1.2.1 Summary of epidemiological parameters

Based on the historical dengue outbreak in Greece in 1928, and since the reappearance of dengue in Europe in 2010, the range, mean and median of key parameters have been summarized in Table 4. In addition, more detailed parameters (not necessarily based on European outbreaks) are detailed in Table 5. After biting a viremic (e.g., with virus present in the blood) human host, the vector becomes infectious within 8-12 days (extrinsic incubation period, EIP). The EIP period depends on climatic factors, with higher temperatures associated with a faster replication of dengue viruses and thus a lower EIP.

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Table 4 Summary of epidemiologic parameters based on dengue outbreaks in Europe, 2010-2023 (+ the 1928 outbreak in Greece) *d: days. Hosp: Hospitalisation, incidence: proportion of the population who gets ill; fatality rate: proportion of ill people who dies; clinical infection: proportion of ill people who develop symptoms; R_0: reproduction number; generation time: interval from infection of one individual to when their contacts are infected; sampling delay: from symptom onset to laboratory test; reporting delay: from laboratory test to the health authorities*

	Number of cases	Incidence (%)	Number of deaths	Fatality rate (%)	Clinical infections (%)	Hosp. rate (% ill)	R0	Infectious period (d)	Symptoms duration (d)	Generation time (d)	Symptom onset to hosp. (d)	Hosp. duration (d)	Sampling delay (d)	Reporting delay (d)
median	8	50.00	0	0.00	95.56	15.39	2.66	4	6	19	5	2	10.5	9
mean	5190	44.08	88	0.01	95.56	19.87	2.32	4	6.75	19.77	3.71	2.33	14.94	11.9
min	2	10.82	0	0.00	91.11	0	1.31	4	5	18.3	0	1	1	0.5
max	65000	71.43	1061	0.16	100.00	50	3	4	65	22	7	4	57	30

Table 5 summary of epidemiologic/incubation parameters of dengue

Parameter	Definition or details	Value	References
Viremia in the human	Period during which the vector can get infected while biting a human	2-5 days	[41,42]
Extrinsic incubation period	Period for the vector to become infectious after biting a viremic human host	8-12 days	[43]
		5-33 (mean 15 days) at 25°C, 2-15 (mean 6.5 days) at 30°C	[44]
		3-10 days (mean 4 days)	[45]
Intrinsic incubation period	Time between human infection and symptom onset	7 days (range 4 to 10)	[43]
		5.9 days, [95% CI 3 to 10]	[44]
	If nocosomial/occupational exposure	2-14 days	[46–48]
Symptoms	Description %	Classic: high fever, cephalgia, muscle and joint pain, skin rash	[43,49,50]
		Rare & severe, dengue hemorrhagic fever (e.g., vomiting, weakness, plasma leakage, organ failure). Higher risk if secondary infection. Can be fatal.	

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Parameter	Definition or details	Value	References
	Duration of high grade fever (if dvped)	2 to 7 days	
	Asymptomatic/mild flu-like symptoms	25 to 70%	[40]
		40 to 80% of the cases. But this varies across geographic areas: 19% [17 to 21%] in Eastern Mediterranean region, to 93% [89 to 98%] in South East Asia	

1.2.2 Vulnerable groups

There exist four distinct serotypes of dengue, from DEN-1 to DEN-4 [43]. A primary infection corresponds to infection with one of the four serotypes, which confers lifelong immunity only to that specific serotype. A subsequent infection with a different serotype from the first infection (e.g., secondary infection), can lead to severe disease due to antibody-dependent enhancement. Therefore, those previously infected with one dengue serotype that is different from the circulating serotype are a vulnerable group. People coming from endemic areas, such as migrants, refugees, or tourists, who may have already been infected by a dengue serotype while abroad, would then be at a high risk if infected by another serotype during a European outbreak. In Latin America, the risk of severe dengue was increased by 17% in the case of a secondary dengue infection (OR 1.17 [1.04 to 1.29]) [51], but other meta-analyses have reported two to threefold increased risk [52–54].

Females have a higher risk of severe dengue than males (OR 1.13 [95%CI 1.01 to 1.26] [54]. Regarding age, children have a higher risk of severe dengue (OR 1.96 [95%CI 1.22 to 3.13] [55]. Among children, obesity further enhances the risk of dengue virus infection (OR 1.21 [95%CI 1.03 to 1.42][56], severe dengue (OR 1.33 [95%CI 1.04 to 1.70 compared to normal weight children][57], and severe respiratory failure (OR 2.3 [95%CI 1.31 to 4.06] [58].

Cardiovascular disease appears as an important risk factor for developing severe dengue (OR 2.71-2.79) [54,59]. Diabetes is also associated with a higher risk of both severe dengue (OR 2.88-4.42 [52–54]) and death (OR 3.70 [95%CI 1.20 to 11.43] [55]); renal disease seems like a very important risk factor (OR 4.54-4.67 for severe dengue)[53,54].

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1.2.3 Choice of scenarios

The mild scenario is a combination of low-risk factors: rather low temperatures, introduction of the virus late in the year, only one dengue serotype circulating. The introduction of dengue in late summer or in autumn means that the epidemic will die out quickly because of the drop in temperatures, which will not sustain the transmission of dengue [60]. On the other hand, the severe scenario is a combination of high-risk factors: warm temperatures, introduction of the virus earlier in the year, and at least two different dengue serotypes circulating. For instance, the slightly warm summer of 2012, compared to a typical year in Madeira contributed to the epidemic potential of the dengue outbreak[61]. The introduction of dengue in spring/early summer means that there is a higher potential for the epidemic to last longer. The risk of major size (>1000 cases) compared to any-size (>3) outbreak is higher for an introduction of dengue during the summer months, because the climate will drive the increasing of R_0 until late summer [61].

Based on the literature[60,62–67], we decided on two sub scenarios: a mild one and a severe one:

Table 6 Dengue outbreak scenarios based

	Mild scenario	**Severe scenario**
Serotypes	Only one	At least two
Beginning of the epidemic	late summer/autumn	Spring/early summer
Temperature	~25°C -> incubation time ~15days in mosquitoes	~30°C -> incubation time ~6 to 7days in mosquitoes
Incidence (%)	1	10 (local hotspots)
Hospitalisation rate (% infected)	1	15
Fatality rate (%)	0	0.5
Groups at risk of severe symptoms/hospitalisation	refugees/migrants coming from endemic dengue areas (already infected)	those already infected with one serotype (also includes refugees/migrants coming from endemic dengue areas)

1.2.4 Potential for outbreaks in the selected study sites

A. albopictus is widely distributed and survives winter in temperate regions (dormancy state), while *A. aegypti* is only established in Madeira, Cyprus, and parts of Russia [40]. *Aedes*

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mosquitoes seem to be established in the three study sites, Romania, Italy, and Germany [68]. However, although sporadic cases have also occurred in the three countries, local transmission of dengue has so far only been documented in Italy [40,69].

2 Prevention measures and treatment

2.1 Influenza

2.1.1 Vaccines

The effectiveness of seasonal and A(H1N1)pmd09 vaccines against illness and hospitalization due to the A(H1N1)pdm09 is summarized in Table 7. It seems that the effectiveness of influenza vaccines against laboratory-confirmed illness or hospitalization is higher for adjuvanted vaccines compared to unadjuvanted ones. Vaccine effectiveness against both illness and hospitalization are lower among adults than among children. Overall, A(H1N1)pdm09 vaccines are more effective than seasonal ones which only elicit a cross-immunity: the rapid development of a new vaccine in the case of a pandemic is crucial [70,71]. A systematic review concluded that pandemic vaccines were effective across age groups in preventing infection [71]. Regarding the target population for vaccination, a simulation study estimated that vaccinating 80% of the children has almost the same effectiveness on lowering influenza incidence as vaccinating 80% of the whole population [72].

Among healthcare workers in the Netherlands, an immunization program against the seasonal and pandemic influenza in three intervention hospitals in 2009 was associated with higher vaccination uptake than in the control hospitals (12% higher for the seasonal vaccine uptake and 21-24% higher for the pandemic vaccine uptake) [73]. Furthermore, hospitalized patients in hospitals where the program was implemented had significantly lower rates of nosocomial influenza and pneumonia at the internal medicine departments (risk ratio (RR)=0.47 [95%CI 0.3 – 0.9]) but not at the pediatrics departments (RR=2.1 [95%CI 0.7. 6.7]).

For simplicity and in view of the objective of our scenarios as a basis for the exercises, we assume no prior immunity from previous seasonal influenza. This is because a pandemic scenario involves a novel or long-absent pathogen, meaning the population has little to no pre-existing immunity. Interventions focus solely on the pandemic vaccine, which is assumed to become available after the outbreak begins. For the 2009 A(H1N1)pdm09 pandemic the vaccine was available after 5-6 month after the new strain of influenza virus was identified[74]. However newer technologies can shorten the timeline to 2-3 months[75].

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Table 7 Effectiveness of influenza vaccines against A(H1N1)pdm09 illness and hospitalization, mostly based on three meta-analyses and an original study [70,76–78]

	Type of vaccine/ vaccinated group	Range
Against lab-confirmed illness A(H1N1)pdm09	A(H1N1)pmd09 vaccines, adjuvanted and non-adjuvanted	73-86%
	A(H1N1)pmd09 vaccines adjuvanted	80-90%
	A(H1N1)pmd09 vaccines non-adjuvanted	66-89%
	A(H1N1)pmd09 vaccines, adjuvanted and non-adjuvanted among <18yo	76%
	A(H1N1)pmd09 vaccines, adjuvanted and non-adjuvanted among >18yo	49%
	A(H1N1)pmd09 vaccines, adjuvanted among <18yo	88%
	A(H1N1)pmd09 vaccines, non-adjuvanted. among <18yo	45%
	seasonal Trivalent Influenza Vaccine	19%
	seasonal Trivalent Influenza Vaccine, only studies with low level of bias	34%
Against hospitalisation due to A(H1N1)pdm09	A(H1N1)pmd09 vaccines, adjuvanted and non-adjuvanted	61-72%
	A(H1N1)pmd09 vaccines adjuvanted	82%
	A(H1N1)pmd09 vaccines non-adjuv.	50%
	A(H1N1)pmd09 vaccines, adjuv. and non-adjuv. among <18yo	86%
	A(H1N1)pmd09 vaccines, adjuv. and non-adjuv. among >18yo	48%
	seasonal Trivalent Influenza Vaccine	48-50%
	seasonal IV, 16-64 yo	55%
	seasonal IV, >65 yo	54%

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2.1.2 Protection of vulnerable groups

While there are several studies on the immunogenicity of the A(H1N1)pdm09 vaccines among pregnant women, very few studies actually compare their effectiveness in preventing ILI or hospitalization. In a study where pregnant women received the A(H1N1) 2009 monovalent vaccination, those who were vaccinated in the first or second trimesters and who had a higher post-vaccination hemagglutination inhibition (HI) titer (≥1:40, i.e., an "antibody efficacy", concerning *n*=109/125, 87% of participants) had an adjusted OR of 0.09 [95%CI 0.004 to 0.93] for medical visits due to respiratory illness, compared to those who had a titer <1:40 (concerning *n*=16/125, 13% of participants) [79]. This implies that the vaccine effectiveness in preventing medical visit due to respiratory illness was 79% (91% antibody efficacy * 0.87 (87% of participants). Vaccination of infants below 6 months is not effective and not recommended. Some studies report on infant outcomes after maternal vaccination: a small-sample sized (*n*= 196) study from Japan reported that infants below 6 months of age whose mother had been vaccinated against pandemic influenza (i.e., trivalent vaccine which included the pandemic vaccine) while pregnant had a lower incidence of influenza (*n*= 0/106 in the group whose mother had been vaccinated, *n*= 5/90 in the "control" group) [80]. However, these infants were born between November 2010 and April 2011, when the influenza strain was not pandemic anymore. A prospective case-control study from the US reported that the effectiveness of maternal vaccination during pregnancy in preventing influenza-associated hospitalization was 39% [95%CI 12 to 58%] in infants <6 months, and 53% [95%CI 30 to 68%] in infants <3months, with higher effectiveness for third-trimester vaccination [81]. Of note again, this concerned only seasonal influenza years after the 2009 pandemic. The WHO's SAGE recommend following priority groups for influenza vaccinations: pregnant persons, healthcare workers, children, elderly,people with underlying medical conditions and people living in institutionalized settings[82]. The influenza vaccination dose schedule depends on age, health status, and previous vaccination history. A single dose of the vaccine is suitable for children aged 9 years and older, as well as healthy adults. Detailed information on dosing schedules for influence vaccines depends also on specific manufacturers and national regulators [82]

2.1.3 Antivirals

There exist different types of antivirals against influenza A: adamantanes (which inhibit the viral replication by preventing the fusion between the viral capsid and the cell plasma membrane, and by fixating to the ionic protein-canal of viral capsid) such as amantadine and rimantadine, and neuraminidase inhibitors, such as zanamivir and oseltamivir [72]. They have

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different efficacies, and viral resistance occurs more often for adamantanes, especially if it is used as a treatment compared to as a prophylaxis [72]. Antivirals can thus either be used in preventively (to avoid illness) or as a treatment (to reduce the risk of clinical illness or transmission in the case of infection).

During the 2009 pandemic, neuraminidase inhibitor treatment among patients admitted to the hospital was effective in preventing mortality [83]. The timing of treatment initiation was crucial, with early treatment reducing mortality to a bigger extent compared to no treatment at all[83,84]. In a simulated epidemical model, only early treatment within a day of symptom onset was effective in reducing transmission [85]. The efficacy and effectiveness of antivirals during the 2009 pandemic is detailed in Table 8, while the theoretical effectiveness based on simulation models is displayed in Table 9. A study estimated the impact of prophylactic antiviral use in the case of an outbreak of an influenza A H2N2. If 80% of the population would take prophylaxis for 8 weeks, the attack rate would decrease from 33% to 2%, and the death rate would decrease from 0.58/1000 to 0.04/1000. Such an effect would be almost as effective as vaccinating 80% of the population.

Table 8 : Effectiveness of antivirals during the A(H1N1)pdm09 pandemic against illness, hospitalization and mortality, based on metanalyses [70,76–78]

Name antiviral	Outcome	Effectiveness
Neuraminidase inhibitor (NI)	mortality of patients admitted to hospital and treated	19% [95%CI 7-30%]
		50% [95%CI 33 to 63%] if early treatment (within 2 days of symptom onset), compared to no treatment
	mortality of patients >=16 admitted to hospital and treated	25% [95%CI 13 to 36%]
	mortality of patients <16 admitted to hospital and treated	18% [-17 to 42%]
	mortality of pregnant women admitted to hospital and treated	54% [95%CI 11-77%]
	hospital admission among treated	76% [95%CI 70 to 80%]
	hospital admission among treated adults >=16	74% [65 to 81%]

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Name antiviral	Outcome	Effectiveness
	Hospital admission among treated children <16	75% [95%CI 66 to 82%]
Oseltamivir (NI)	Pneumonia in treated adult	45% [95%10 to 67%]
	Pneumonia in treated children	-4% [-83 to 38%]
	Hospital admission among treated adults	8% [-50 to 43%]
	Symptomatic flu in individuals receiving prophylaxis	55% [33 to 70%]
	Mortality in adult treatment	10% [-20 to 33%]
Zanamivir (NI)	Symptomatic flu in individuals receiving prophylaxis	61% [30 to 78%]
	Pneumonia in adult receiving prophylaxis	70% [20 to 99%]

Table 9 Theoretical effectiveness of antivirals as a prophylaxis on illness, hospitalization and mortality, based on simulation studies [72,86]

Pandemic/Subtype	Outcome	Effectiveness
1918-like flu	Infection	22%
2009-like flu		22%
H2N2 (1957-58 like)	Clinical attack rate if 80% exposed (cases and relatives) had prophylaxis for 4 weeks	79.70%
	Death rate if 80% exposed (cases and relatives) had prophylaxis for 4 weeks	81.67%
	Clinical attack rate if 80% exposed (cases and relatives) had prophylaxis for 8 weeks	93.11%
	Death rate if 80% exposed (cases and relatives) had prophylaxis for 8 weeks	93.33%

2.1.4 Non-pharmaceutical interventions

Non-pharmaceutical interventions (NPIs), such as hand hygiene and mask use, remain crucial tools, especially in the early stages of a pandemic before vaccines or antiviral

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treatments become available. A meta-analysis of ten studies found that hand hygiene was significantly associated with reduced influenza transmission when combined with facemask use (RR 0.73 [95% CI 0.53 to 0.99]) [87]. Although only one of these studies was conducted during the 2009 pandemic and did not find statistically significant effects for hygiene or facemasks alone on laboratory-confirmed influenza (RR 0.64 [95% CI 0.32 to 1.99]) or ILI (RR 0.52 [95% CI 0.21 to 1.29]), other evidence supports their value. A separate meta-analysis reported that frequent handwashing reduced the spread of respiratory viruses by 46% (OR 0.54 [95% CI 0.44 to 0.67]) [88]. Furthermore, the same study showed that wearing N95 respirators offered greater protection than other types of masks (OR 0.17 [95% CI 0.07 to 0.46] compared to 0.32 [95% CI 0.26 to 0.39] for any mask type).

Overall, school closures may help reduce the burden on health services, although their exact impact remains difficult to quantify [89]. A review of 57 simulation studies across various influenza pandemics estimated that school closures reduced contact rates among children by 30–78%, though the heterogeneity of models and outcomes precluded a formal meta-analysis. Historical evidence from the 1918 pandemic in a Swiss region suggests that school closures, along with restrictions on mass gatherings, were associated with substantial reductions in influenza incidence rates (RR 0.16 [95% CI 0.15 to 0.17] for school closures and RR 0.57 [95% CI 0.54 to 0.61] for gathering restrictions) [90].

Historical analyses of the 1918 influenza pandemic in United States (USA) cities provide strong evidence that early, sustained, and layered implementation of NPIs such as school closures, bans on public gatherings, and quarantine was associated with significantly lower peak death rates, delayed epidemic peaks, and reduced cumulative mortality[91,92]. In studies of 17[92] and 43[91] cities, those that implemented multiple NPIs early experienced up to 50% lower peak death rates and flatter epidemic curves, with trends toward reduced overall mortality despite most NPIs being maintained for fewer than six weeks. While no single intervention was consistently linked to better outcomes, the combination and timing of measures were crucial. These findings underscore the vital role of NPIs in mitigating pandemic impact and emphasize their importance as complementary tools alongside vaccine and antiviral development in future pandemic preparedness[93].

This study of the 1918–1920 influenza pandemic in Zurich demonstrates that public health measures like bans on gatherings and school closures played a key role in reducing disease transmission and mitigating the pandemic's impact. It highlights the importance of sustained implementation and compliance with these interventions to effectively control multi-wave outbreaks and reduce overall disease burden beyond just mortality[93].

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Analyses of the 1918 influenza pandemic in Switzerland reveal the significant impact of public health interventions on controlling disease spread[94,95]. In the canton of Bern[95], a study across 473 municipalities showed that school closures and restrictions on mass gatherings during the first wave significantly slowed epidemic growth. However, hesitant responses and premature relaxation of restrictions in the second wave were linked to a resurgence of cases. Similarly, in Zurich[94], bans on gatherings and school closures were associated with decreases in incidence, hospitalizations, and mortality during the 1918–1920 pandemic waves, while lifting or non-compliance with these measures corresponded with increases in reported cases. These findings underscore the critical role of early, sustained, and layered public health interventions in mitigating pandemic severity.

For the 2009 pandemic, studies on social distancing and lockdowns are limited. However, research during COVID-19 has consistently shown that national lockdowns rapidly reduce transmission. Flexman et al.[96] reported an approximate 80% reduction in European countries, while Prem et al. [97] found reductions of up to 92%.

The WHO provides recommendations for NPI[98]. Table 10 gives an overview about the most important interventions and the effects they have.

Table 10 Summary of influenza interventions

Intervention	Estimated Reduction	Advantages	Disadvantages
Lockdown	0.5-0.7	- Strong suppression of transmission - Buys time to strengthen health system capacity	- Severe economic/social impact - Unsustainable long-term
Mask-wearing (general public)	0.3-0.7 (depending on mask type, fit, and adherence)	- Inexpensive and scalable - Protects others and self	- Requires compliance - Lower effectiveness if improperly used
Masks for symptomatic individuals only	0.2-0.4 (depending on mask type, fit, and adherence)	- Targets those most likely to transmit - Conserves mask supply	- May miss asymptomatic or pre-symptomatic spread - Relies on honest self-reporting

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Intervention	Estimated Reduction	Advantages	Disadvantages
School closure	0.2–0.4	- Reduces cluster spread in youth - Protects families indirectly	- Disrupts learning and childcare - Unequal access to remote learning and may widen inequalities
Work-from-home	0.5	- Maintains economic activity - Reduces commuting-related contacts	- Not possible for all jobs - May widen inequalities (tech access, job type)
Shielding elderly	0.4	- Protects high-risk populations - Can reduce hospital burden	- Risk of isolation and mental health decline -Hard to fully implement at scale
Travel advice/restrictions	0.1–0.3 (higher early in outbreak)	- Slows geographic spread - Buys time for preparedness	- Economic impact on tourism/trade - Limited long-term effectiveness
Isolation of sick individuals	0.4–0.6 (if enforced and supported)	- Directly removes sources of transmission - Easy to understand messaging	- Needs support (paid leave, space) - Risk of stigma or underreporting
Quarantine of exposed individuals	0.3 -0.5	- Prevents presymptomatic and asymptomatic spread - Effective when testing is limited	- Requires monitoring and compliance - May disrupt work/life balance
Contact tracing	0.3 - 0.5	- Breaks transmission chain - Enables targeted response	- Labor- and tech- intensive - Privacy concerns
Avoiding crowding	0.3 - 0.5	- Reduces super-spreader risk	- Difficult enforcement - Affects events and businesses
Border closure	0.2 -0.5 (if early)	- Delays international spread - Buys time for preparation	- Economic costs - Politically sensitive

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Intervention	Estimated Reduction	Advantages	Disadvantages
Modifying humidity	0.1-0.3	- May reduce virus survival - Supports respiratory health	- Hard to control consistently - Evidence still limited
Increased ventilation (indoors)	0.2–0.5	- Reduces airborne transmission indoors - Long-term public health benefit	- May require retrofitting or upgrades - Harder in cold climates
Vaccination	0.5–0.7	- High effectiveness - Critical for outbreak control	- Requires rapid development and rollout - Availability constrains

2.1.5 Combining interventions

A study which simulated an influenza outbreak in Great Britain or in the USA [85] (Table 11) concluded that border/travel restrictions would only delay viral spread by 2-3 weeks, and only if travel restrictions would be highly effective (~90%). Treating clinical cases and providing AV prophylaxis to their household members would be effective in reducing attack rates. Case isolation and quarantining household members would also have an impact, but may also be unethical if no AV is provided (because quarantining would put the household members at a higher risk). The best option would thus be a combination of both prophylaxis and quarantining of household members (40-50% efficacy of reducing the attack rates). School closure would only be efficient in reducing peak attack rate, which would be useful to lower the pressure on healthcare systems, but would not lower much the overall attack rate. AV prophylaxis among school and workplaces where a case is identified would have a great efficacy on attack rates but requires important AV stockpile. Overall, this study emphasizes the importance of coupling measures.

Admission to the hospital: during the 2009 pandemic, among patients admitted to the hospital, those who died had been admitted late after symptom onset (4 days) compared to those who survived (2 days) -> importance of early hospitalization [83].

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Table 11Effectiveness of different interventions on clinical attack and peak attack rates, based on two scenarios with different transmissibility*. A generation time of 2.6 days is assumed, and it is assumed that 50% of all cases are clinical. This is based on the study by Fergusson et al.* [85]

Intervention	Clinical Attack Rate (%)		Efficiency on Clinical Attack Rate (%)		Peak Attack Rate (%)		Efficiency on Peak Attack Rate (%)	
Baseline	72.0	34.0			1.2	1.9		
90% clinical cases treated and household members have AV prophylaxis	17.0	22.0	37.0	35.3	0.6	1.0	50.0	47.4
Quarantine of HH with clinical cases for 14 days (assumptions: 50% HH comply, external contact rates reduced by 75% and within-HH contact rated increased by 100%)	24.0	30.0	11.1	11.8	0.9	1.5	25.0	21.1
Combination of the above two previous policies	15.0	20.0	44.4	41.2	0.5	0.9	58.3	52.6
Reactive school closure (closing 100% schools and 10% workplaces for 3 weeks from the day the case is detected. Assumptions: contact rates in affected HH increase by 50% and community contact rates in absent staff/pupils by 25%)	24.0	32.0	11.1	5.9	0.9	1.4	25.0	26.3

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Intervention	Clinical Attack Rate (%)		Efficiency on Clinical Attack Rate (%)		Peak Attack Rate (%)		Efficiency on Peak Attack Rate (%)	
Reactive school closure (closing 100% schools and 50% workplaces for 3weeks from the day the case is detected. Assumptions: the same	23.0	31.0	14.8	8.8	0.8	1.3	33.3	31.6
School/workplace prophylaxis (requires high AV stockpiles)	7.6	13.0	71.9	61.8	0.1	0.3	91.7	84.2

2.2 Dengue

As no antiviral treatment is available, dengue treatment is symptomatic and includes the use of analgesic and rehydration [43]. In the case of severe dengue, red blood cells transfusion, assisted ventilation and dialysis are possible [43].

2.2.1 Vaccines

There are two commercially available vaccines: Dengvaxia and Qdenga. Dengvaxia is only recommended for those who previously had dengue fever or in populations in which most people have already previously been infected, and requires a vaccination test to confirm previous dengue infection. However, due to a lack of demand on the global market, Dengvaxia will stop being manufactured by Sanofi-Pasteur [99]. Qdenga is also recommended for those who have not previously been infected, and has recently been approved by the European Medicines Agency[100]. The WHO's SAGE currently recommends that only individuals with confirmed evidence of a previous dengue infection should receive the vaccine. In cases where pre-vaccination screening is not feasible, vaccination should be restricted to regions with recent data indicating a seroprevalence rate of at least 80% by the age of 9 years[101]. The dengue vaccine is administered in three doses, with six months between each dose. It is recommended for people aged 9 to 45 years - in some countries, depending on national approval, up to 60 years - who live in areas where dengue fever is endemic[101].

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2.2.2 Non-pharmaceutical interventions

In addition to vaccination, there are various measures to prevent mosquitoes from reproducing and transmitting the infection. A promising method is the Wolbachia method, which can reduce dengue cases by up to 80%[102,103]. The Wolbachia method involves releasing mosquitoes infected with the Wolbachia bacteria into the wild. These bacteria reduce the mosquitoes' ability to transmit viruses like dengue. Wolbachia also spreads through mosquito populations by affecting their reproduction, helping to lower disease transmission naturally and sustainably without harmful chemicals. However, this method is suitable for prevention or use after an outbreak. During an outbreak, methods such as fogging[104,105] or larviciding [106](e.g., process of applying chemicals or biological agents specifically targeting mosquito larvae in their breeding sites like stagnant water) rapidly reduce the number of cases. Furthermore, it is extremely important to involve the population. This means, for example, that the population should empty and cover containers that can collect water, regularly change the water in vases or bowls, and keep water storage containers properly covered[107,108]. In addition, people should use mosquito repellents, wear long-sleeved clothing, and use bed nets - especially for infants or those resting during the day. If a large portion of the population takes part in these measures, it can significantly reduce mosquito reproduction and the spread of infection[109]. Table 12 gives an overview about the possible interventions and the effects they have. The most effective intervention is the integrated vector management which combines different tools and strategies to prevent and control dengue [110,111].

Table 12 Summary of dengue interventions

Category	Interventions	Estimated Reduction	Advantages	Disadvantages
Vector Control	- Larviciding - Source reduction - Fogging - Wolbachia	Wolbachia: 60–85% Larviciding/source reduction: 20–40% Fogging: <10%	- Directly targets mosquito population - Effective in outbreaks (fogging) - Wolbachia is self-sustaining	- Fogging has short-lived effect - Insecticide resistance - Cost and logistics for Wolbachia

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Category	Interventions	Estimated Reduction	Advantages	Disadvantages
Personal Protection	- Repellents - Bed nets - Protective clothing	20–30% (with high adherence)	- Easy to implement at household level - Protects individuals immediately	- Requires constant compliance - May be expensive - Less effective during the day (Aedes bites)
Public Education	- Media campaigns - School awareness - Community engagement	25–35% (with strong participation)	- Empowers local communities - Increases uptake of other NPIs	- Effects vary by community - Impact may take time - Needs tailored messages
Urban Planning	- Drainage - Waste removal - Covered storage	30–50% (long-term impact)	- Sustainable control - Prevents breeding permanently	- Requires infrastructure investment - Difficult in informal settlements
Legislation	- Anti-breeding laws - Construction codes - Housing regulation	15–30% (with enforcement)	- Provides legal framework for control - Encourages compliance	- Needs enforcement mechanisms - Can face public resistance if punitive
Surveillance	- Case detection - Health worker visits - GIS tracking	~15% (indirectly, faster control response)	- Enables early outbreak detection - Informs targeted interventions	- Requires strong health infrastructure - Often reactive, not preventive

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3 Simulation of epidemiological models

As a contribution to Task 2.4, 'AI-powered multi-agent simulation models' and to simulate the spread and outcomes of influenza and dengue pandemics compartmental epidemiological model will be used. A compartmental epidemiological model is a mathematical framework used to study how infectious diseases spread within a population. It divides the population into different “compartments” based on health status - being susceptible, exposed, infected, hospitalized, recovered or deceased - and models the transitions between these states over time. Each compartment is represented by a variable, and the changes in these compartments are modelled using ordinary differential equations, which will be explained in more detail in the following sections.

3.1 Influenza

To simulate influenza outbreaks, we assume the following transition states:

S: Susceptible - can catch the disease

E: Exposed - infected, not yet infectious

I: Infected - can transmit the disease

H: Hospitalized - receiving care

R: Recovered - no longer infectious

D: Deceased - died from the disease

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S → E: Exposure to the virus (infection occurs through contact with infectious individuals)

E → I: Progression from exposed to infectious (after the incubation period)

I → R: Recovery without hospitalization

I → D: Death without hospitalization

I → H: Hospitalization of infectious individuals

H → R: Recovery after hospitalization

H → D: Death after hospitalization

To simulate the transition states the following parameters need to be defined (estimated or assumed from previous pandemics, literature etc.):

R_0: Basic reproduction number

incubation period: Time from exposure to infectiousness in days

infectious period: Time from infection to recovery infectious in days

p_{id}: Probability of dying directly I → D

p_{hosp}: Probability an infectious individual is hospitalized I → H

p_{hd}: Probability of dying in hospital H → D

Time in hospital: Average hospital stay in days

Given the above assumptions following parameters can be calculated:

Recovery rate γ

$$\gamma = \frac{1}{infectious\ period}$$

Incubation rate σ

$$\sigma = \frac{1}{incubation\ period}$$

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Transmission rate β

$$\beta = R_0 * \gamma$$

Mortality rate in hospital μ

$$\mu_{hosp} = p_{hd} * Time\ in\ hospital$$

Recovery rate in hospital ρ

$$\rho = (1 - p_{hd}) * Time\ in\ hospital$$

Once all parameters are defined and calculated, the transition states can be described by the following ordinary differential equations:

Susceptible:

$$\frac{dS}{dt} = -\beta * \frac{S * I}{N}$$

Exposed:

$$\frac{dE}{dt} = \beta * \frac{S * I}{N} - \sigma * E$$

Infected:

$$\frac{dI}{dt} = \sigma * E - \gamma * I$$

Hospitalized:

$$\frac{dH}{dt} = p_{hosp} * \gamma * I - (\rho + \mu_{hops}) * H$$

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Recovered:

$$\frac{dR}{dt} = (1 - p_{hosp}) * \gamma * I + \rho * H$$

Deceased:

$$\frac{dD}{dt} = p_{id} * \gamma * I + \mu_{hosp} * H$$

3.1.1 Simulation of mild and severe scenarios - basic model

Using the formulas above, the compartmental model can now be simulated. For this, parameters are assumed for both a mild and a severe influenza outbreak based on the literature review.

In the first simulation, we apply the same parameters across all age groups. It is assumed that all parameters remain constant over time and that the population size is 100,000. Lifelong immunity and a stable population are also assumed. All cases are observed, with no asymptomatic infections. Since a pandemic scenario is modeled, no prior immunity is assumed, as pandemics involve novel or long-absent pathogens to which the population has little or no pre-existing immunity.

In chapter 3.1.2, these parameters are adjusted to reflect differences between age groups (parameters different for age groups). Subsequently, NPIs are implemented in chapter 3.1.3 to flatten the curve (parameters change over time), followed by the introduction of vaccination (parameters change over time) in chapter3.1.4.

Table 13 Assumption for simulation for a mild and severe influenza pandemic

Parameter	Mild	Severe	Description
R_0	1.5	3	Basic reproduction number
p_{id}	0.17%	0.70%	Percentage of death directly after infection
p_{hosp}	0.23%	3%	Percentage of infectious getting hospitalized
p_{hd}	15%	25%	Percentage of hospitalized individuals who die
Incubation Period	2 days	2 days	Time from exposure to infectiousness
Infectious Period	5 days	5 days	Time from infection to recovery

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Parameter	Mild	Severe	Description
Hospital Stay	10 days	10 days	Average hospital stay

Figure 2 shows the simulation results for both mild and severe scenarios, based on prior assumptions. In the mild scenario, the epidemic peak occurs later, and the curves are flatter. In the severe scenario, the number of cases, hospitalizations, and deaths is significantly higher, with a more compressed and earlier peak.

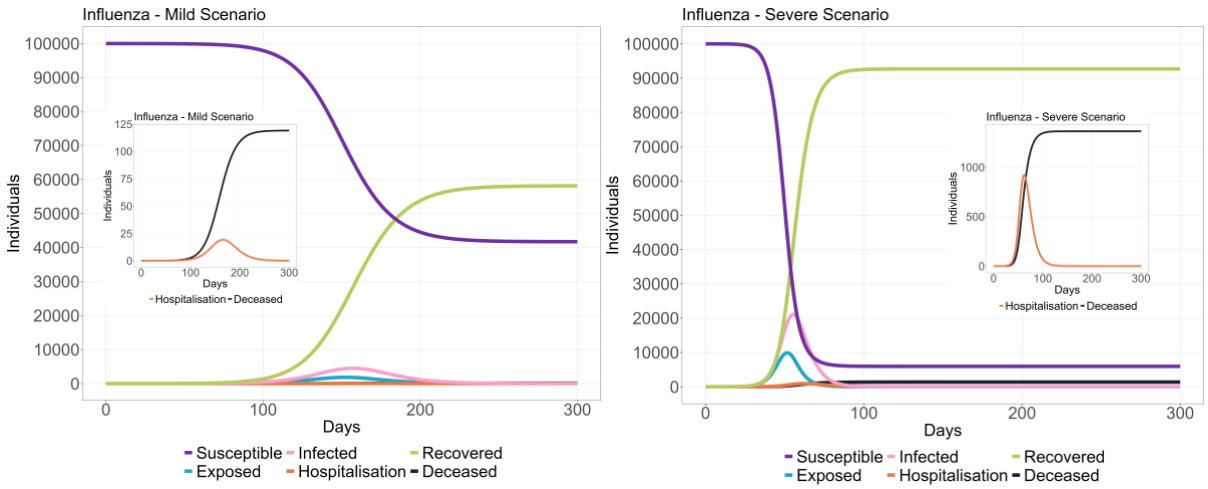

Figure 2 Simulation of a mild and severe influenza outbreak given the above-mentioned assumptions*. The smaller figures zoom in into the hospitalized and deceased individuals.*

3.1.2 Simulation of age groups

The next step is to look at the age distribution. The following age distribution is assumed: 0-18 years = 20%, 19-64 years = 60% and ≥ 65 years = 20%. The assumptions in Table 13 are now age dependent. Table 14 shows the parameter of the age group. The mean values of these parameters result in the values in Table 13.

Table 14 Age-dependent parameter assumptions

Parameter	Scenario	0-18	19-64	≥ 65
R_0	Mild	1.8	1.5	1.2
	Severe	3.5	3	2.5
p_{id}	Mild	0.00002	0.0002	0.005

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Parameter	Scenario	0-18	19-64	≥ 65
	Severe	0.0001	0.0003	0.02
p_{hosp}	Mild	0.001	0.002	0.004
	Severe	0.01	0.03	0.05
p_{hd}	Mild	0.002	0.15	0.3
	Severe	0.02	0.25	0.5
Incubation Period	Both	2	2	2
Infectious Period	Both	5	5	5
Hospital Stay	Both	10	10	10

A contact matrix is required to simulate an age-structured compartmental model. A contact matrix describes the average number of daily contacts between different age groups in a population. Table 15 shows the contact matrix used for this simulation. It is obvious that younger people have more contact with each other than older people. This high contact rate increases the risk of infection.

Table 15 Contact matrix used to simulate age-structured compartmental models

	0-18 years	19-64 years	≥ 65 years
0-18 years	8	4	1
19-64 years	3	6	2
≥ 65 years	1	2	3

The absolute number of individuals getting infected, hospitalized or are deceased are shown in Figure 3. The highest number of infections and hospitalizations occurs among individuals aged 19-64, while the highest number of deaths is observed in the age group 65 and older. However, this only shows the absolute figures, so it is not surprising that the age groups with the highest population also have the highest incidence and hospitalization rate. Looking at the rate per 100,000 (Figure 4), it is clear that the older population has the highest hospitalization rate. As also indicated in the assumptions.

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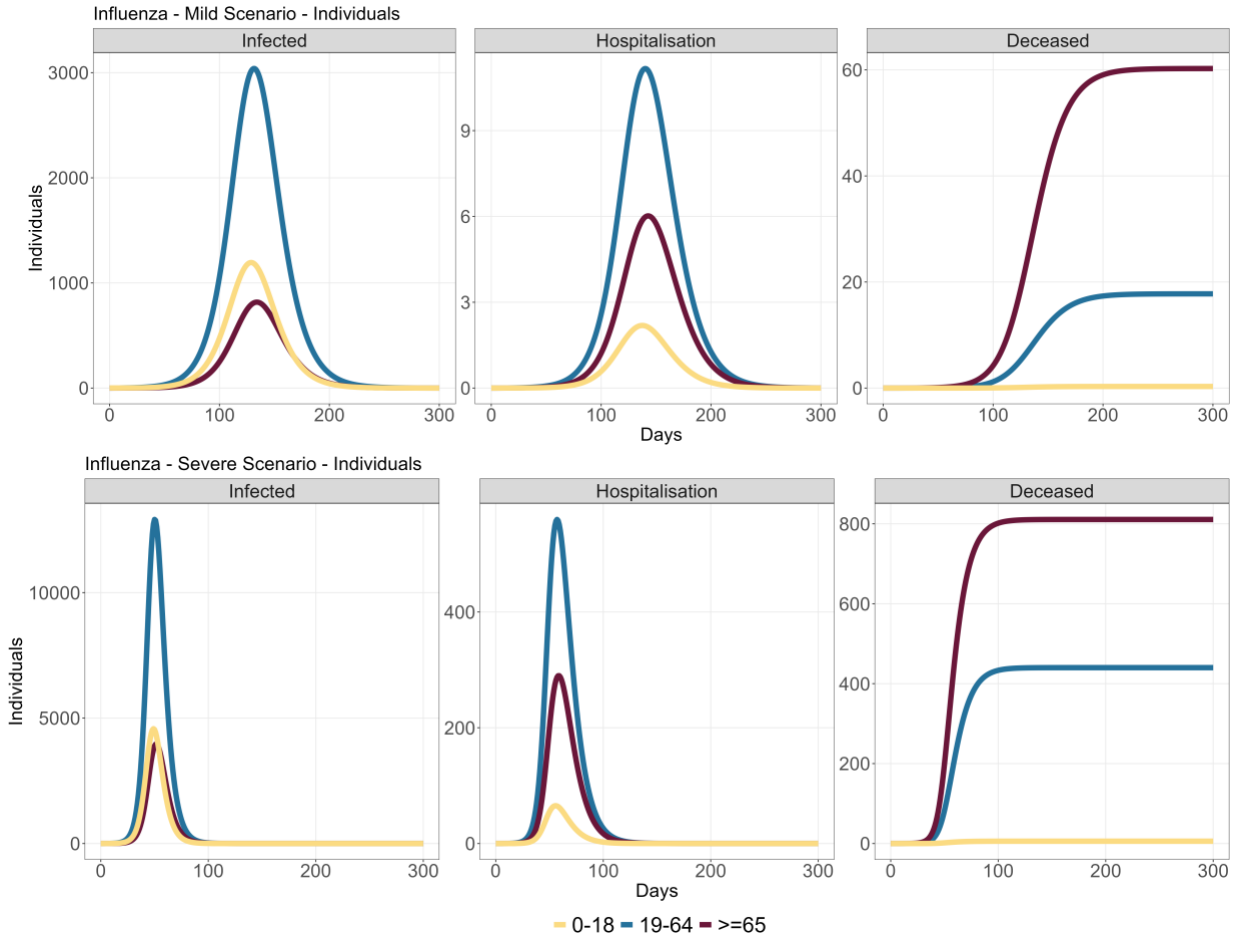

Figure 3 Absolute number of individuals being infected, hospitalized and deceases over time for the mild and sever scenario.

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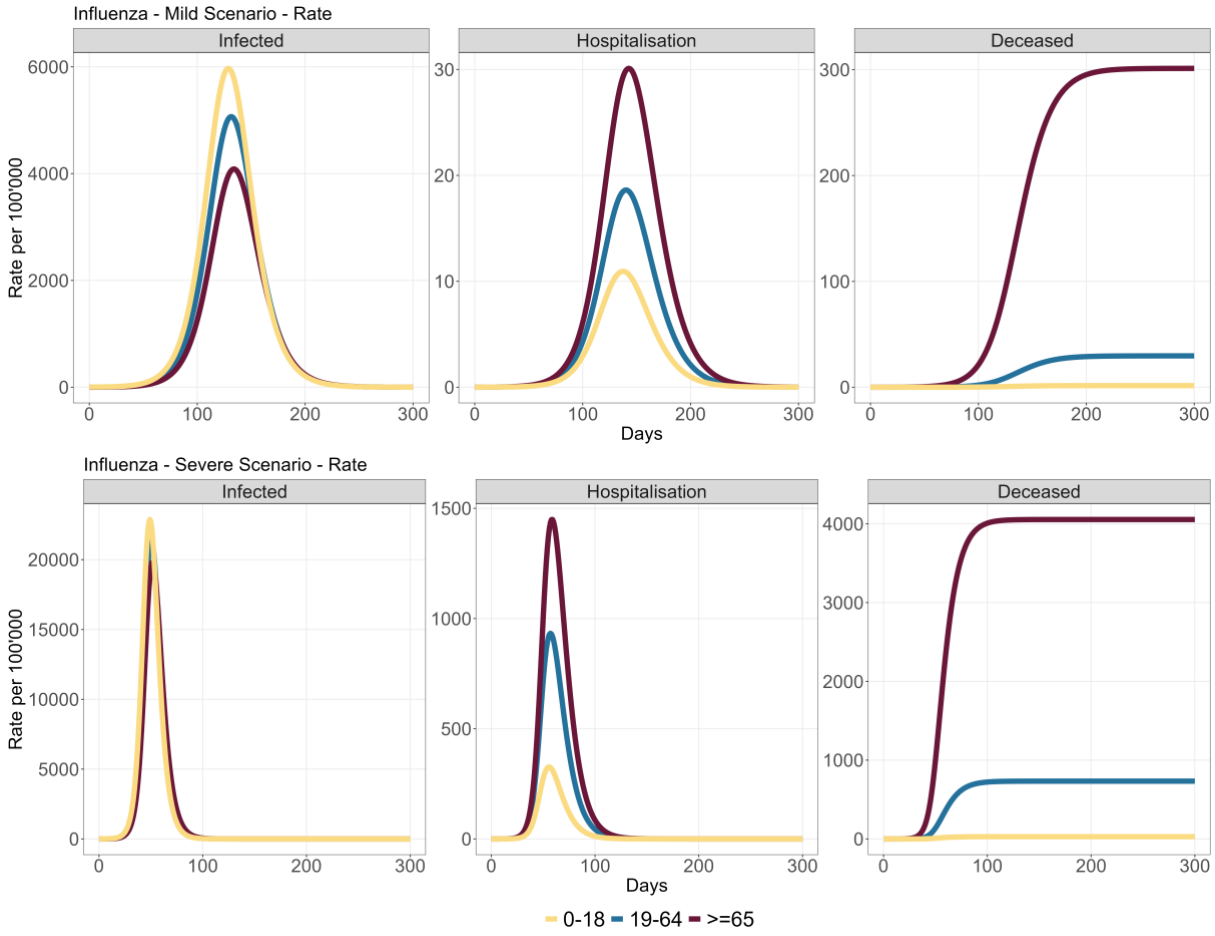

Figure 4 Rates per 100'000 inhabitants of being infected, hospitalized and deceases over time for the mild and sever scenario.

3.1.3 Simulation of non-pharmaceutical interventions

Until now, constant parameters were assumed. In the next model, non-pharmaceutical interventions (NPIs) will be introduced which will have an influence of the given parameter. For NPIs to have an impact on the course of the pandemic, contacts (as defined in the contact matrix Table 15) must be reduced. This can be achieved through measures such as lockdowns and social distancing (e.g., people no longer meet), school closures (e.g., fewer young people interact), or the use of medical masks (which reduce transmission and thereby lower the number of people who can become infected). Table 16 shows the reduction factor of the most common NPIs. The reduction factors are multiplied by the basic contact matrix (Table 15).

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Table 16 Reduction factors of the most common NPIs

NPIs	Reduction factor	Applies to
Lockdown	0.3–0.5	All contacts
Mask-wearing	0.7	Transmission probability (not contact)
School closure	0.2–0.4 (among youth)	young → young, young → adult
Work-from-home	0.5	adult → adult, adult → elderly
Shielding elderly	0.4 (among elderly)	elderly ↔ other groups

For the simulation following NPIs are assumed.

Table 17 NPIs which are included in the compartmental model.

Time (days)	NPIs	Reduction factor	Impact
0–29	No intervention	1	Normal contact rates
30–89	Strong lockdown	0.2	Significant contact reduction
90–149	Partial reopening	0.5	Moderate contact reduction
150–179	Strong lockdown	0.2	Reintroduction of strong measures
180–209	Partial reopening	0.5	Moderate contact reduction
210+	All open, but still wearing mask	0.7	Contact reduction due to protective effect

All other parameters remained the same as defined in Table 14. The basic contact matrix is the same as in Table 15.

Figure 5 illustrates the epidemic curves following the introduction of NPIs. The mild scenario is shown for completeness, though strong NPIs are generally not implemented in such cases. The

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focus is therefore on the severe scenario. Rates are not displayed, as decision-makers are primarily interested in absolute numbers (e.g., for hospital bed capacity). The curve clearly flattens during strict lockdowns but rises again when measures are relaxed. With mask use alone, case numbers increase more slowly compared to having no interventions (compare Figure 3). In the simulation without NPIs, the pandemic peaks after approximately two months, with over 12,000 active cases and nearly 600 hospitalizations (Figure 3). By introducing NPIs the pandemic peaks later with a reduced number of infection (ca. 4500) and with a lower utilization of the hospitals. This simulation is intended to illustrate how the course of the pandemic can be slowed down with NPIs and thus the utilization of hospital capacity can be controlled. It is also clear how the number of cases increases again with a total opening. The measures help to control the capacity limits of hospitals and reduce the number of deaths. But without further measures, such as vaccinations, etc., the curve will rise again each time the measures are abolished until herd immunity occurs. The next step shows how the curves change when a vaccination is introduced.

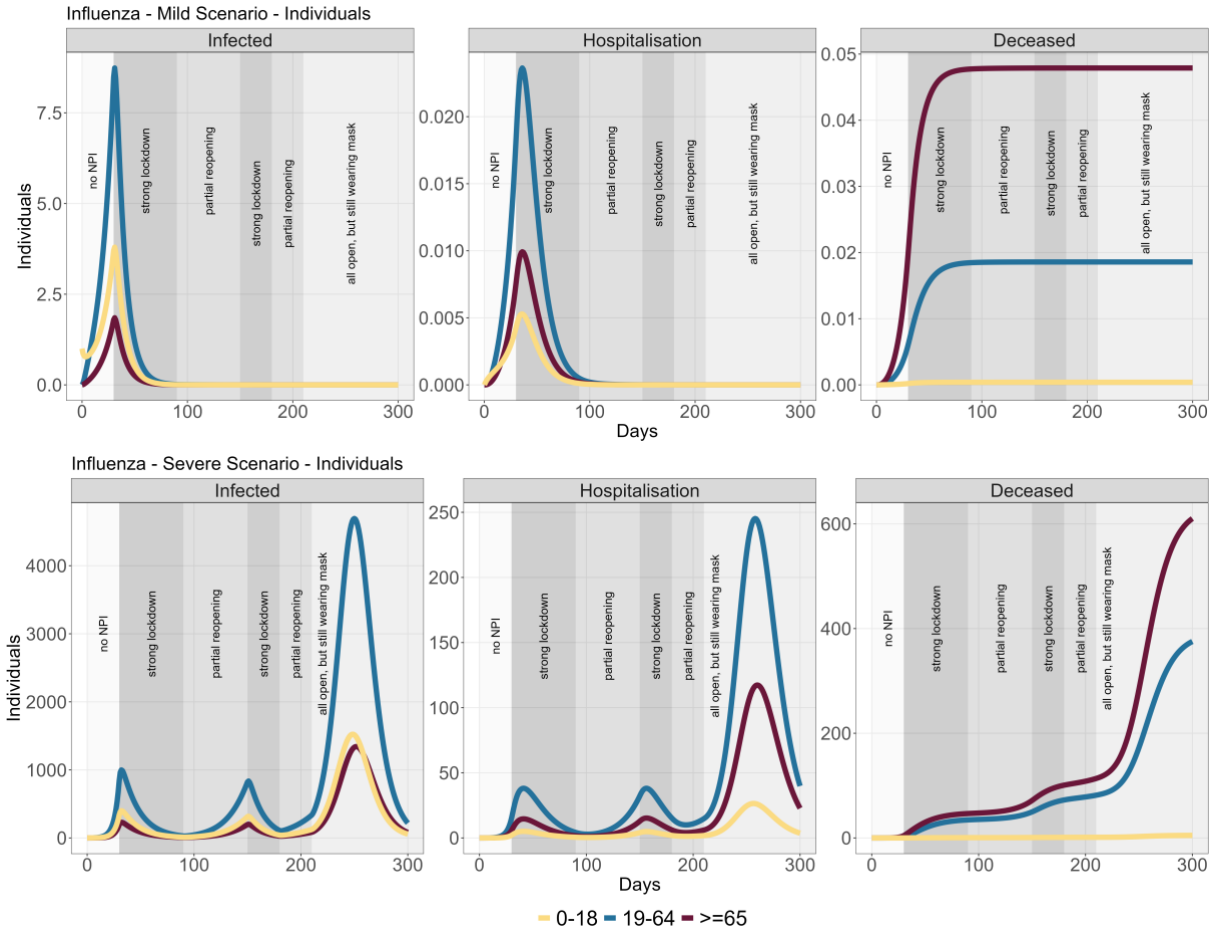

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Figure 5 Absolute number of infected persons, hospitalizations and deaths over time for the mild and severe scenarios after the introduction of the NPI

3.1.4 Simulation of vaccination

The last simulation shows how the epidemic curves may develop after the introduction of the vaccination. Once again, all parameters and assumptions from Table 13 and Table 14 are used. The first 90 days follow the same pattern as in Figure 5, where only NPIs were implemented. From day 90 onward, a phased vaccination rollout begins – starting with the elderly, followed by adults aged 19–64, and finally including all age groups (Table 18).

Table 18 NPIs and vaccination rate which are included in the compartmental model

Time (Days)	NPI and Vaccination Phase	Reduction Factor	Vaccination per Day (0–18 / 19–64 / ≥65)	Impact
0–29	No intervention	1	0 / 0 / 0	Normal contact rates, no immunity
30–89	Strong lockdown	0.2	0 / 0 / 0	Significant contact reduction, no immunity
90–119	Partial reopening + elderly vaccinated	0.5	0 / 0 / 1000	Moderate contact reduction, protecting elderly
120–149	Mask wearing + adults vaccinated	0.7	0 / 1000 / 1000	Contact reduction due to protective effect, more immunity (19-64 years old)
≥150	Restrictions lifted + all vaccinated	1	1000 / 1000 / 1000	Full contact resumes, population gaining protection

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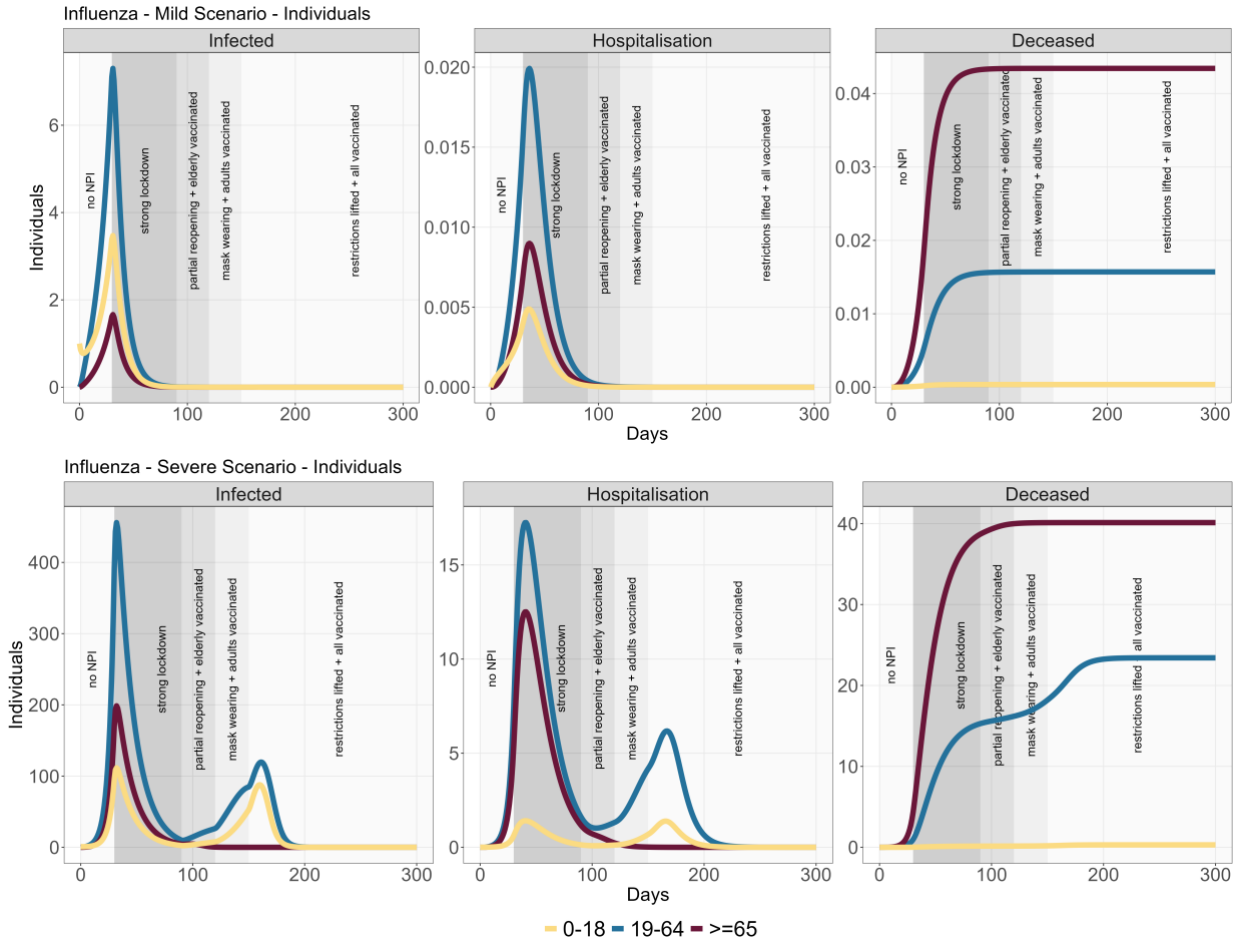

Figure 6 Absolute number of infected persons, hospitalizations and deaths over time for the mild and severe scenarios after the introduction of the NPI and vaccination

Figure 6 shows the epidemic curves after NPI and vaccination introduction. The mild scenario is shown again for completeness, but the focus remains again on the severe scenario. The first 90 days behaves like in Figure 5, after it the vaccine was introduced for individuals aged ≥65. At the same time, the lockdown was partially lifted. However, due to vaccination, the curve no longer rises for the elderly – only for individuals aged 0-64. After an additional 30 days, vaccination was extended to individuals aged 19–64. As this group represents the largest share of the population (60%) and the vaccination rate is assumed to be 1,000 per day, the curves continue to rise – though significantly flattened – until sufficient immunity (due to infection and vaccination) is achieved within this age group. Finally, the youngest age group is vaccinated, leading to a decline in cases across all age groups. Since the elderly were vaccinated first, the number of deaths drops significantly, and hospital occupancy also decreases.

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3.1.5 Summary

This simulation illustrates which parameters influence the course of an epidemic and how various measures can alter its trajectory and flatten the curve. Changing assumptions such as age distribution or parameter values will also change the outcome. The simulation serves as an example, using values based on previous pandemics. In a new pandemic, many of these parameters are initially unknown and must be estimated during the early weeks, based on observed cases, deaths, and hospitalizations. Since an influenza pandemic is assumed here, the parameters are considered realistic for an initial scenario, but they should remain adjustable as new data becomes available.

3.2 Dengue

To simulate dengue outbreaks, we need to assume the transition states of the humans and the mosquitos. For the humans the transitions states are the same as for influenza:

S: Susceptible – can catch the disease

E: Exposed – infected, not yet infectious

I: Infected – can transmit the disease

H: Hospitalized – receiving care

R: Recovered – no longer infectious

D: Deceased – died from the disease

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S → E: Exposure to the virus (infection occurs through contact with infectious individuals)

E → I: Progression from exposed to infectious (after the incubation period)

I → R: Recovery without hospitalization

I → D: Death without hospitalization

I → H: Hospitalization of infectious individuals

H → R: Recovery after hospitalization

H → D: Death after hospitalization

For the mosquitos there are additional transition stages:

S → E: Mosquito bites an infectious human and becomes exposed (infected, not yet infectious).

E → I: After an incubation period the mosquito becomes infectious.

I → D: The mosquito dies while infectious, no recovery.

To simulate the transition states following parameters need to be defined (estimated or assumed from previous pandemics, literature etc.)

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β_{mh}: Transmission rate mosquito → human

β_{hm}: Transmission rate: human → mosquito

incubation period mosquito: Time from exposure to infectiousness in days for mosquito

incubation period human: Time from exposure to infectiousness in days for humans

infectious period: Time from infection to recovery infectious in days only human

p_{id}: Probability of dying directly I → D

p_{hosp}: Probability an infectious individual is hospitalized I → H

p_{hd}: Probability of dying in hospital H → D

Time in hospital: Average hospital stay in days

hmr: Human-mosquito ratio

p_m: Probability that the mosquito dies

N_h: Population humans

Given the above assumptions following parameters can be calculated. h denotes humans and m mosquitoes.

Recovery rate γ

$$\gamma = \frac{1}{infectious\ period}$$

Incubation rate σ_h

$$\sigma_h = \frac{1}{incubation\ period\ human}$$

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Incubation rate σ_m

$$\sigma_m = \frac{1}{incubation\ period\ mosquito}$$

Mortality rate in hospital μ_{hosp}

$$\mu_{hosp} = p_{hd} * Time\ in\ hospital$$

Recovery rate in hospital ρ

$$\rho = (1 - p_{hd}) * Time\ in\ hospital$$

Population of mosquito

$$N_m = N_h * hmr$$

Rate at which susceptible humans become infected by mosquitoes

$$\lambda_h = \beta_{mh} * \frac{I_m}{N_m}$$

Rate at which susceptible mosquitoes become infected by biting infectious humans

$$\lambda_m = \beta_{hm} * \frac{I_h}{N_h}$$

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Mosquito population (assumption that the population is constant, mosquito births balance out deaths)

$$N_m = S_m + E_m + I_m$$

$$birthrate_m = p_m * N_m$$

Once all parameters are defined and calculated, the transition states can be described by the following ordinary differential equations:

Susceptible:

$$\frac{dS_h}{dt} = -\lambda_h * S_h$$

$$\frac{dS_m}{dt} = birthrate - \lambda_m * S_m - p_m * S_m$$

Exposed:

$$\frac{dE_h}{dt} = \lambda_h * S_h - \sigma_h * E_h$$

$$\frac{dE_m}{dt} = \lambda_m * S_m - \sigma_m * E_m - p_m * E_m$$

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Infected:

$$\frac{dI_h}{dt} = \sigma_h * E_h - \gamma * I_h$$

$$\frac{dI_m}{dt} = \sigma_m * E_m - p_m * I_m$$

Hospitalized (only human):

$$\frac{dH}{dt} = p_{hosp} * \gamma * I_h - (\rho + \mu_{hosp}) * H$$

Recovered (only human):

$$\frac{dR}{dt} = (1 - p_{hosp}) * \gamma * I + \rho * H$$

Deceased (only human):

$$\frac{dD}{dt} = p_{id} * \gamma * I + \mu_{hosp} * H$$

3.2.1 Simulation of mild and severe scenarios – basic model

Using the formulas above, the compartmental model can now be simulated. For this, parameters are assumed for both a mild and a severe dengue outbreak based on the literature review. In the first simulation, we apply the same parameters across all age groups. It is assumed that all parameters remain constant over time and that the population size is 100,000. Moreover, the mosquito population remains constant over time, assuming the same temperature over time. All cases are observed, with no asymptomatic infections. Moreover, it is assumed that the first case starts with a human (however, the course would be the same by starting with an infected mosquito).

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In chapter 3.2.2, these parameters are adjusted to reflect differences between age groups (parameters different for age groups). Subsequently, NPIs are implemented in chapter 3.2.3 to simulate how the curves flatten (parameters and the population of mosquitos change over time).

Table 19 Assumption for simulation for a mild and severe dengue pandemic

Parameter	Mild	Severe	Description
β_{mh}	0.3	0.5	Transmission rate mosquito → human
β_{hm}	0.3	0.5	Transmission rate human → mosquito
p_{id}	0.001%	0.5%	Percentage of death directly after infection
p_{hosp}	1%	15%	Percentage an infectious individual is hospitalized
p_{hd}	1%	10%	Percentage of hospitalized individuals who died
Incubation Period h	15 days	8 days	Time from exposure to infectiousness humans
Incubation Period m	5 days	5 days	Time from exposure to infectiousness mosquito
Infectious Period	5 days	5 days	Time from infection to recovery
Hospital Stay	7 days	7 days	Average hospital stay

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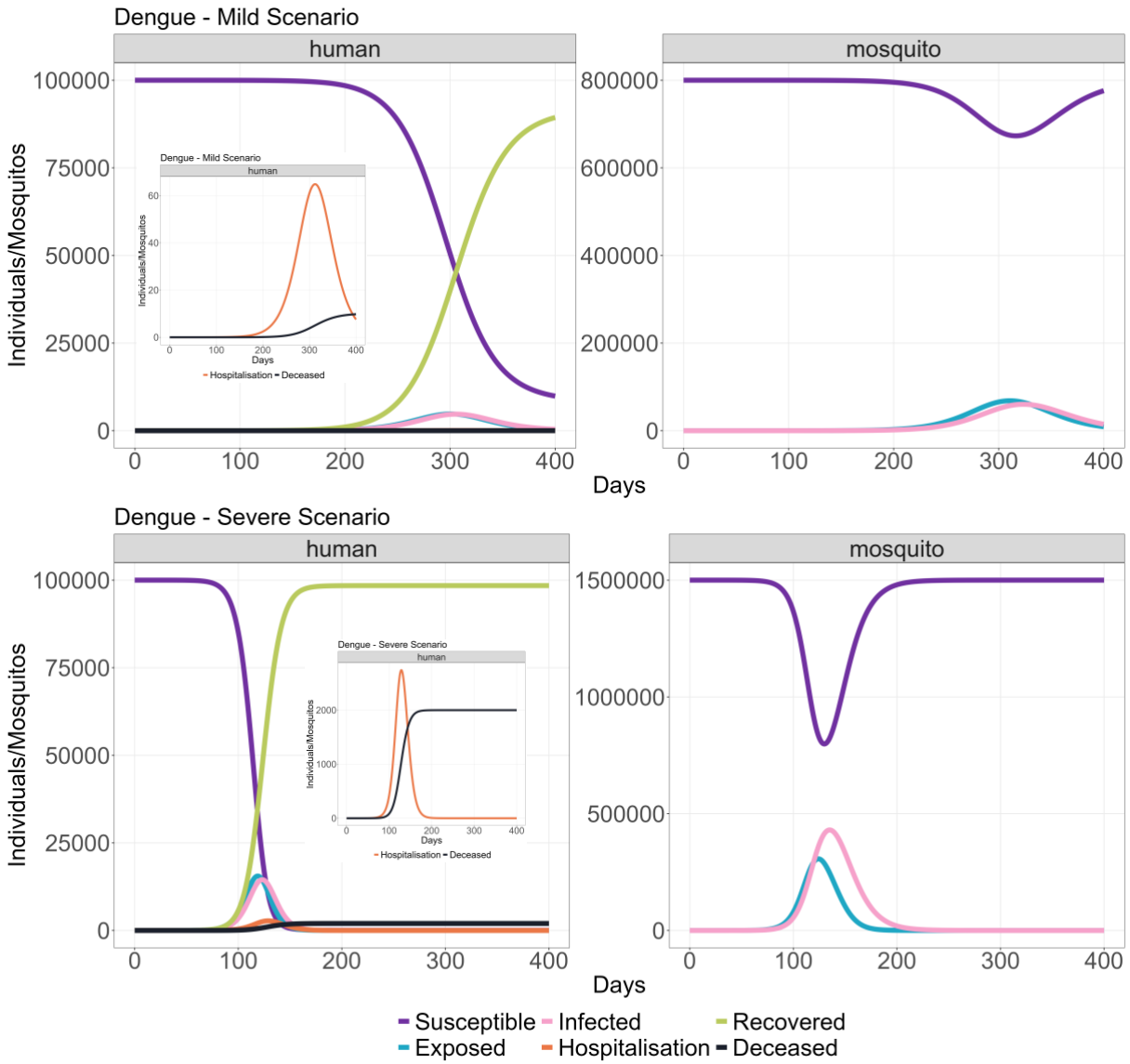

Figure 7 Simulation of a mild and severe dengue outbreak given the above-mentioned assumptions. *The smaller figures zoom in into the hospitalized and deceased individuals.*

Figure 7 shows the simulation results for both mild and severe scenarios, based on prior assumptions. In the mild scenario, the epidemic peak occurs later, and the curves are flatter. In the severe scenario, the number of cases, hospitalizations, and deaths is significantly higher, with a more compressed and earlier peak. The population of mosquitos remains stable over time, which means the total number always sum up to 8'000'000 and 15'000'000, respectively.

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3.2.2 Simulation of age groups

The next step is to look at the age distribution. The following age distribution is assumed: 0-18 years = 20%, 19-64 years = 60% and ≥ 65 years = 20%. The assumptions in Table 19 are now age-dependent. Table 14 shows the parameter of the age group. The mean values of these parameters result in the values in Table 20.

Table 20 Age-dependent parameter assumptions

Parameter	Scenario	0-18	19-64	≥ 65
β_{mh}	Mild	0.35	0.30	0.25
	Severe	0.55	0.50	0.45
β_{hm}	Mild	0.35	0.3	0.25
	Severe	0.55	0.50	0.45
p_{id}	Mild	0.00004	0.0006	0.002
	Severe	0.2	0.5	0.8
p_{hosp}	Mild	0.5	1	1.5
	Severe	1	10	20
p_{hd}	Mild	0.002	0.15	0.3
	Severe	0.02	0.25	0.5
Incubation Period m	Mild	15	15	15
	Severe	8	8	8
Incubation Period h	Both	5	5	5
Infectious Period	Both	5	5	5
Hospital Stay	Both	10	10	10

Figure 8 shows the absolute number of individuals who became infected, were hospitalized, or died. The highest numbers are observed among individuals aged 19–64. However, since these are absolute figures, it is expected that the age group with the largest population also shows the highest counts. When looking at rates per 100,000 population (Figure 9), it becomes clear that the elderlies have the highest hospitalization and death rates, as

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outlined in the assumptions. Die course of the mosquito population is the same as in Figure 7.

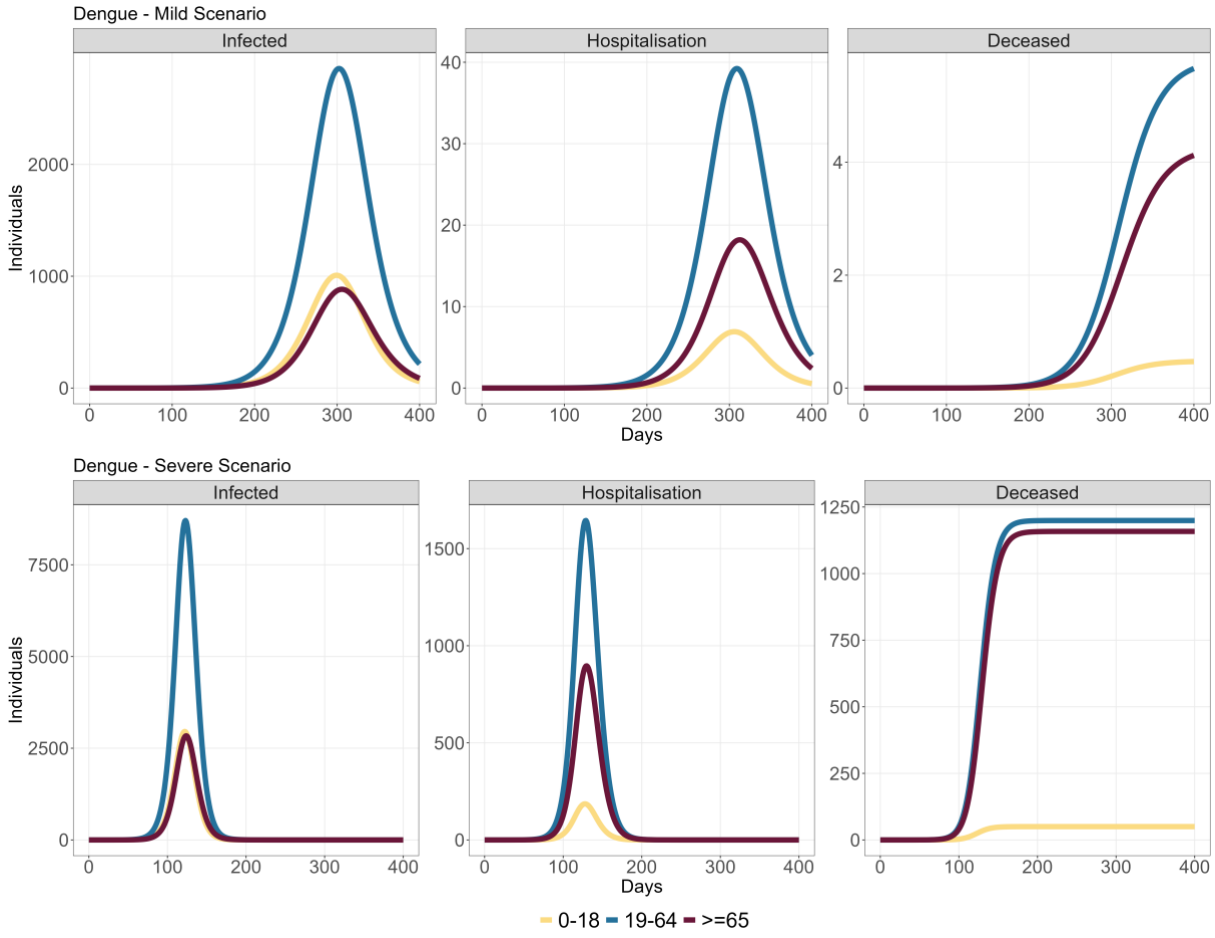

Figure 8 Absolute number of individuals being infected, hospitalized and deceases over time for the mild and sever scenario.

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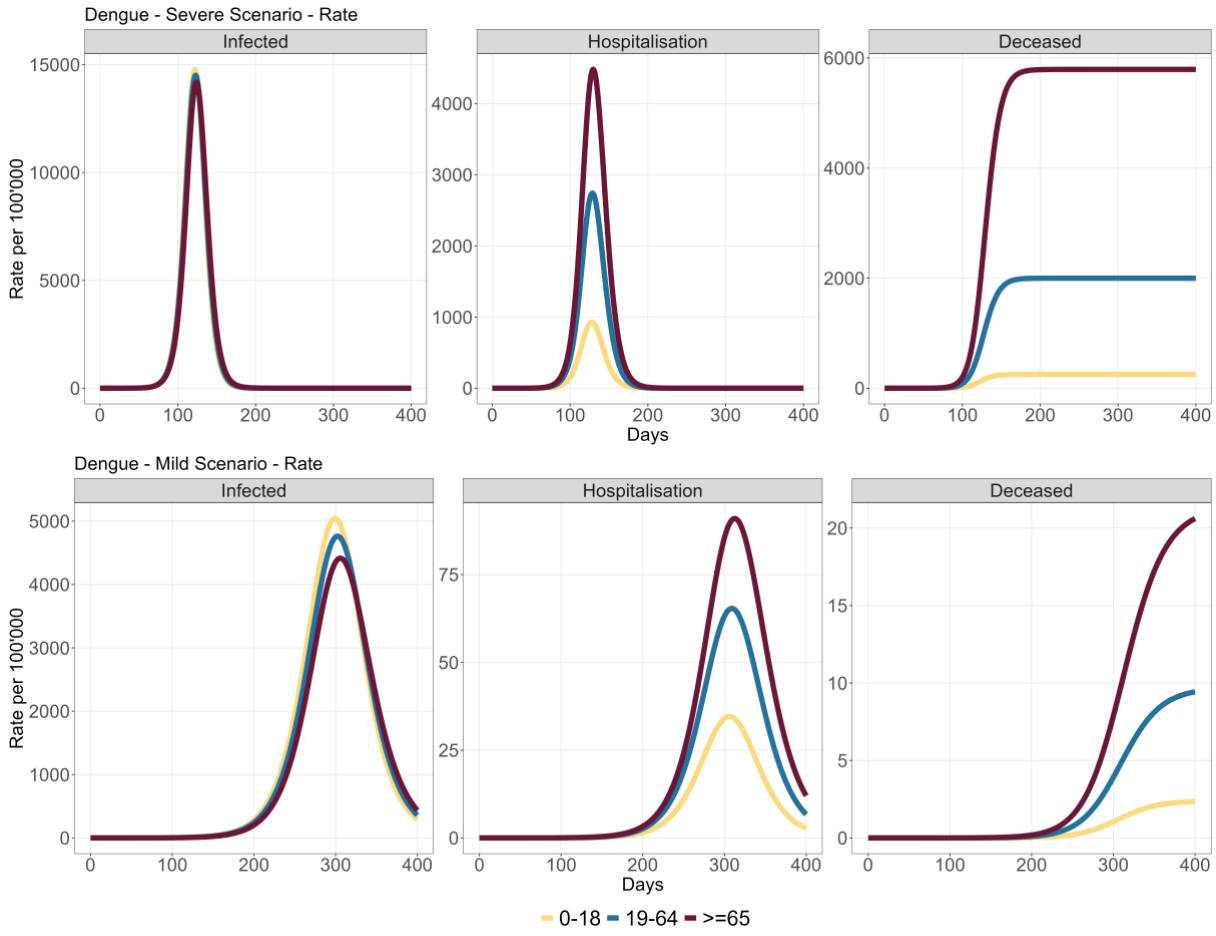

Figure 9 Rates per 100'000 inhabitants of being infected, hospitalized and deceases over time for the mild and sever scenario.

3.2.3 Simulation of non-pharmaceutical interventions

To reduce the number of infected humas, the number of mosquitoes must be reduced. There are different methods for it as described in Chapter 0. For that simulation, an integrated vector management consistent of thermal fogging, source reduction (removal of breeding sites) and public messaging (behavioural changes, public education, etc.). This integrated management approach will result in an immediate 40% reduction in mosquitoes through thermal fogging, followed by an additional 30% gradual reduction over time through source reduction and public messaging. The simulation is carried out for the introduction of interventions after 100, 80, 60 and 40 days. Since there are only very few cases for the mild scenario, only the severe scenario is shown here.

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Figure 10 illustrates how the timing of intervention implementation affects the course of the epidemic. It is obvious that the early introduction of interventions will quickly reduce the number of cases. Figure 11 shows how the population of mosquitos decrease after interventions and how the number of infected mosquitos rapidly decrease by early implementations. The simulations highlight the importance of rapid response to contain vector-borne disease outbreaks promptly.

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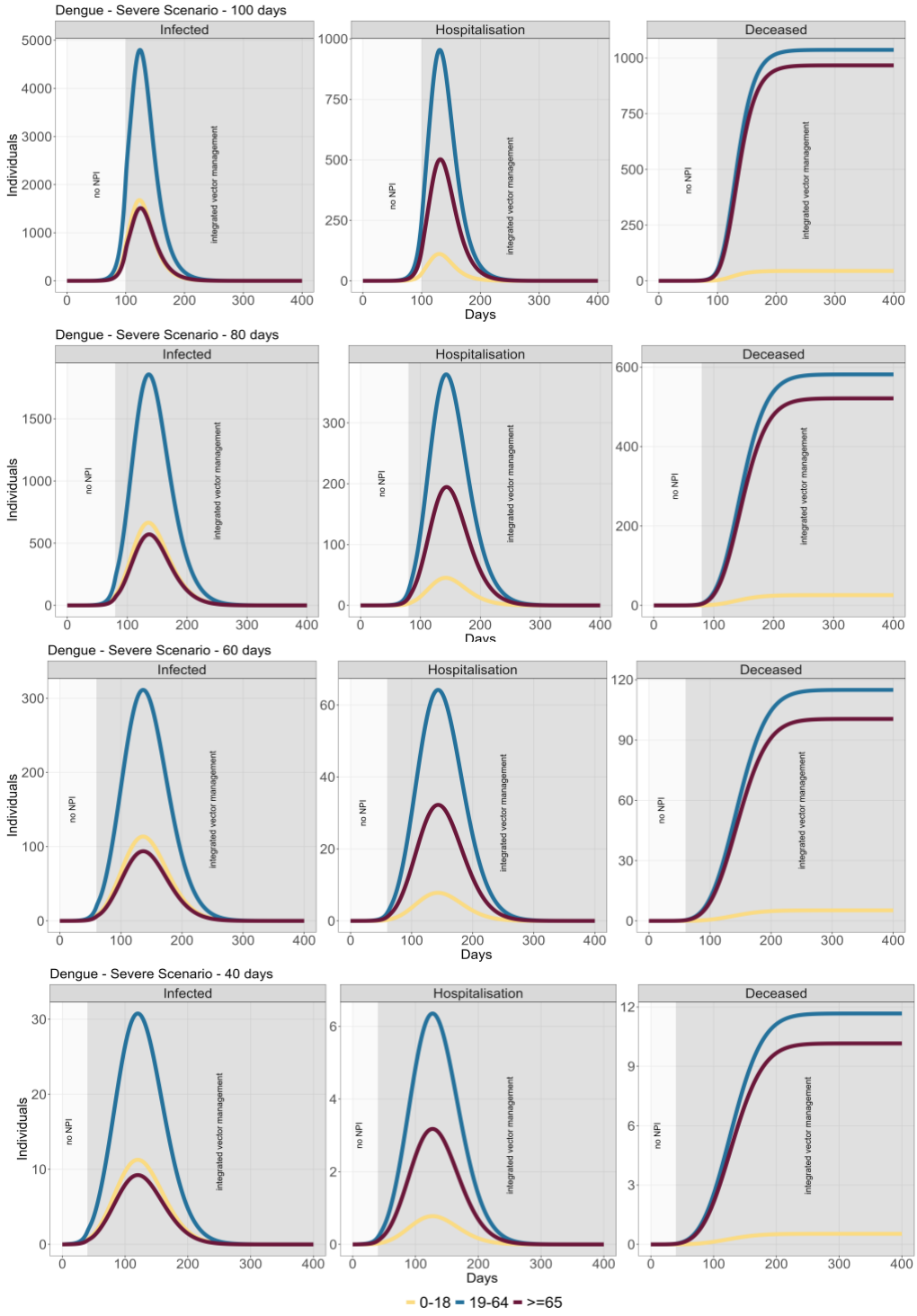

Figure 10 Absolute number of infected individuals, hospitalizations and deaths over time for the severe scenarios after the introduction of the interventions

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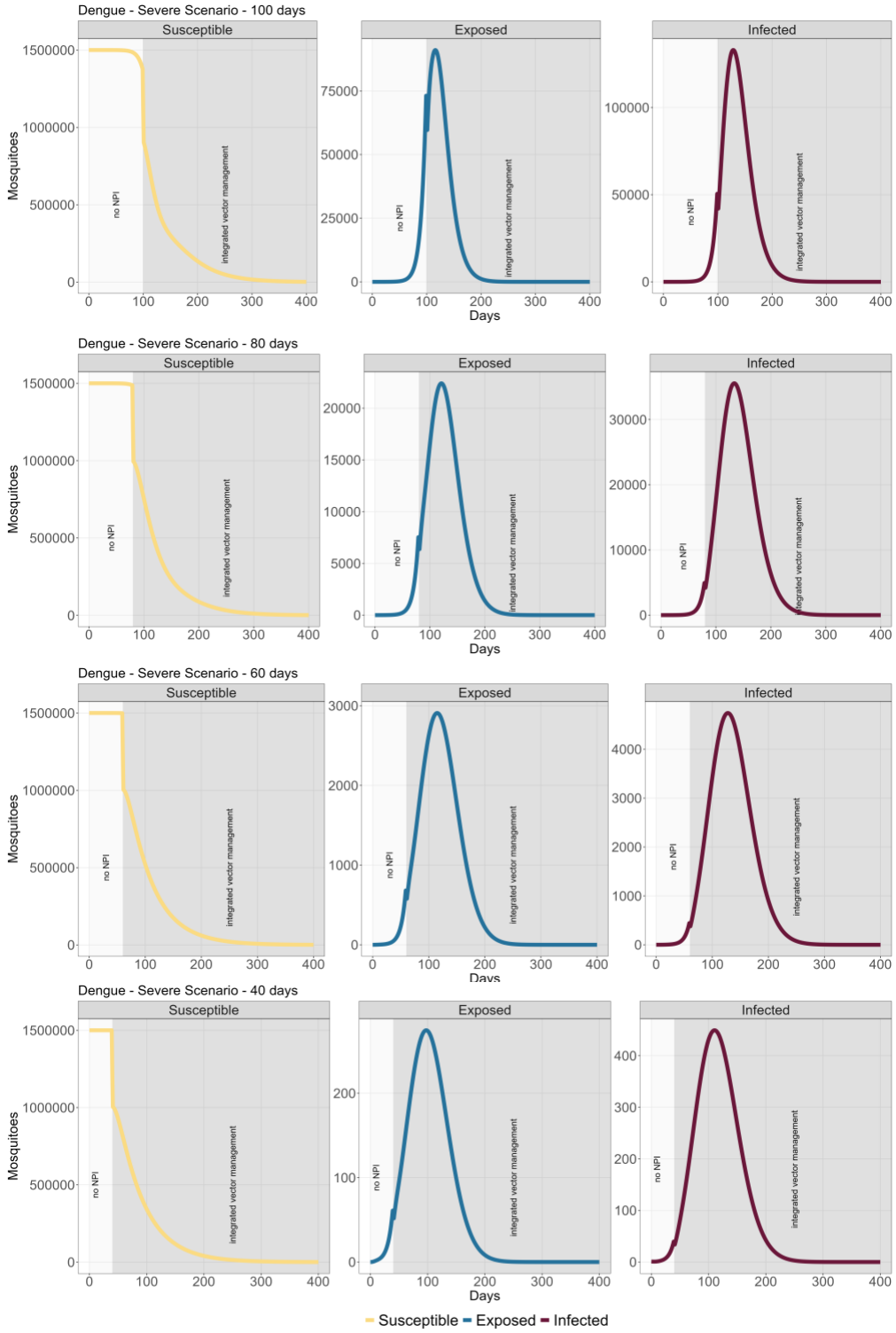

Figure 11 Number of infected mosquitos, hospitalizations and deaths over time for the severe scenarios after the introduction of the interventions

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3.2.4 Summary

These simulations illustrate how dengue outbreaks may unfold. Containment largely depends on the intervention strategy, and thermal fogging in particular has limitations if overused or improperly applied. The severity of an outbreak also strongly depends on how many people have been previously infected with a different dengue virus serotype, as this increases the risk of severe disease. The success of many of these interventions also depends on the will of the population and how much they are included and educated.

4 Summary of the forward-looking health scenarios

This chapter provides a summary of the scenario and the underlying assumptions.

4.1 Influenza

For influenza, two scenarios are considered: a mild scenario and a severe scenario. The parameters used for each are summarized in Table 21. We assume that the course of influenza is most severe for the age group ≥65. This means that the larger the proportion of the population in this age group, the higher the proportion of hospitalized and deceased individuals.

Table 21 Parameters for severe and mild influenza

Parameter	Scenario	0-18	19-64	≥ 65
R_0	Mild	1.8	1.5	1.2
	Severe	3.5	3	2.5
p_{id}	Mild	0.00002	0.0002	0.005
	Severe	0.0001	0.0003	0.02
p_{hosp}	Mild	0.001	0.002	0.004
	Severe	0.01	0.03	0.05
p_{hd}	Mild	0.002	0.15	0.3
	Severe	0.02	0.25	0.5
Incubation period in days	Both	2	2	2
Infectious period in days	Both	5	5	5
Hospital stay in days	Both	10	10	10

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The following interventions the related reduction factors are assumed for both scenarios. We have set the introduction of the vaccination program for the 90th day, with a phased introduction: first for people aged 65 and older, then for those aged 19 to 64 and finally for the 0 to 18 age group. The influenza course changes if vaccination starts earlier or later, if the number of vaccinations administered increases or decreases, or if all age groups are vaccinated at the same time from the beginning.

Table 22 Reduction factors for NPI and vaccination

Time (Days)	NPI and Vaccination Phase	Reduction Factor	Vaccination per Day (0–18 / 19–64 / ≥65)	Impact
0–29	No intervention	1	0 / 0 / 0	Normal contact rates, no immunity
30–89	Strong lockdown	0.2	0 / 0 / 0	Significant contact reduction, no immunity
90–119	Partial reopening + elderly vaccinated	0.5	0 / 0 / 1000	Moderate contact reduction, protecting elderly
120–149	Mask wearing + adults vaccinated	0.7	0 / 1000 / 1000	Contact reduction due to protective effect, more immunity (19-64 years old)
≥150	Restrictions lifted + all vaccinated	1	1000 / 1000 / 1000	Full contact resumes, population gaining protection

For a population of 100,000 with an age distribution of 20% aged 0–18, 60% aged 19–64, and 20% aged 65 and older, the outcomes are illustrated in Chapter 3.1.4. If the size of the population and the distribution of age groups changes, the course of influenza will also change. All these parameters are flexible and the course of influenza and the number of hospitalized and deceased depends on the given population, the introduction of NPI and vaccination. Table 23 gives a synthetic overview of the intervention for an influenza pandemic and

Table **24** of the population to be considered.

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Table 23 Overview of intervention of influenza pandemic

Category	Type
Vaccines	Development depends on the circulating strain
Medication	Neuraminidase inhibitor (NI)
Medication	Oseltamivir (NI)
Medication	Zanamivir (NI)
Medication	Analgesics
Medication	Hydration
Regulations	Complete lockdown
Regulations	Partial lockdown
Regulations	Mandatory mask wearing
Regulations	Masks for symptomatic individuals only
Regulations	School closure
Regulations	Work from home
Regulations	Shielding elderly
Regulations	Travel advice/restrictions
Regulations	Isolation of sick individuals
Regulations	Quarantine of exposed individuals
Regulations	Contact tracing
Regulations	Avoiding crowding
Regulations	Border closure
Regulations	Modifying humidity
Regulations	Increased ventilation (indoors)

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Table 24 Vulnerable groups to be "tracked"

Vulnerable groups
Pregnant persons
Persons up to 2 weeks postpartum
Infants under 59 months of age
Individuals younger than 19 years on long-term aspirin- or salicylate containing medications
Individuals with a body mass index of 40 or higher
Individuals with underlying health conditions
Individuals with low socioeconomic status
Elderly people

4.2 Dengue

For dengue, also two scenarios are considered: a mild scenario and a severe scenario. The parameters used for each are summarized in Table 25. We assume that the course of dengue is most severe for the age group ≥65. This means that the larger the proportion of the population in this age group, the higher the proportion of hospitalized and deceased individuals. But the transmission rate is highest for the youngest age group, since they spend more time outside, children play near breeding sides, the probably is lower that there are previously exposed to dengue, etc.

Table 25 Parameters for severe and mild influenza

Parameter	**Scenario**	**0-18**	**19-64**	**≥ 65**
β_{mh}	Mild	0.35	0.30	0.25
	Severe	0.55	0.50	0.45
β_{hm}	Mild	0.35	0.3	0.25
	Severe	0.55	0.50	0.45
p_{id}	Mild	0.00004	0.0006	0.002
	Severe	0.2	0.5	0.8

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Parameter	Scenario	0-18	19-64	≥ 65
p_{hosp}	Mild	0.5	1	1.5
	Severe	1	10	20
p_{hd}	Mild	0.002	0.15	0.3
	Severe	0.02	0.25	0.5
Incubation Period m	Mild	15	15	15
	Severe	8	8	8
Incubation Period h	Both	5	5	5
Infectious Period	Both	5	5	5
Hospital Stay	Both	10	10	10

To reduce the number of infected humas, the number of mosquitoes must be reduced. Therefor integrated management approach will be used, which result in an immediate 40% reduction in mosquitoes through thermal fogging, followed by an additional 30% gradual reduction over time through source reduction and public messaging. For a population of 100,000 with an age distribution of 20% aged 0–18, 60% aged 19–64, and 20% aged 65 and older, the outcomes are illustrated in chapter 3.2.3. Also, here as for influenza, all these parameters are flexible and the course of dengue and the number of hospitalized and deceased depends on the given population, the introduction of NPI and how early there are implemented.

Table 26 gives a synthetic overview of the intervention for a dengue outbreak and

Table **27** of the population to be considered.

Table 26 Overview of intervention of a dengue outbreak

Category	Type
Vaccines	Dengvaxia (only recommended for those who previously had dengue fever)
Vaccines	Qdenga (only recommended for those who previously had dengue fever)
Vector controls	Larviciding
Vector controls	Soure reduction
Vector controls	Fogging

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Category	Type
Vector controls	Wolbachia
Personal Protection	Repellents
Personal Protection	Bed nets
Personal Protection	Protective clothing
Regulation	Media campaigns
Regulation	School awareness
Regulation	Community engagement
Regulation	Waste removal
Regulation	Covered storage
Regulation	Housing regulation
Regulation	Drainage
Surveillance	Case detection
Surveillance	GIS tracking

Table 27 Vulnerable groups to be "tracked"

Vulnerable groups
Persons already infected with one serotype
Individuals with underlying medical conditions
Pregnant persons

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