Age-location differentiated dynamic model for influenza

Introduction

Seasonal influenza causes significant global health and economic burdens, with millions of severe cases and hundreds of thousands of deaths annually. Older adults, especially those over 65, face the highest risks. Vaccination strategies tailored by age, living conditions, and vaccine effectiveness are essential for improving cost-effectiveness of potential vaccination policies and the resulting health outcomes. Notably, vaccine effectiveness might decrease by age and location of vaccination, such as nursing homes; yet such aspects have so far not been included in cost-effectiveness analyses. In the absence of these aspects, increasing coverage and lowering age limits have been found to be cost-effective.

An age-stratified dynamic transmission model for influenza, accounting for decreasing vaccine effectiveness by age and location, was developed to evaluate vaccination strategies in the Netherlands compared to the current vaccination scheme were people over 60 and risk groups are vaccinated. The model simulates different adult vaccination scenarios' health and economic outcomes, including cost-effectiveness expressed in the incremental cost-effectiveness ratio (ICER) across age groups. Key features include age-group stratification, location (in particular, nursing homes), and varying vaccine effectiveness across age groups.

The model was based on a previous age-stratified model for COVID-19. The model consists of two interacting layers, a vaccinated a non-vaccinated group. Each layer has five main health states, susceptible, infectious, asymptomatic, symptomatic, and recovered. There is a common health state for death. The symptomatic state is subdivided into substates in which patients require home-, regular in-patient-, and intensive care unit (ICU) care. The nursing homes are a separate compartment and internally run as a susceptible, infectious, recovered, death (SIRD) model.

The model accommodated an open population cohort including births, migration, and background mortality as well as shifts between age groups due to aging. Model input parameters were stratified by ten distinct age groups, (0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, 90 and older). Notably, this approach reflects a much higher level of granularity in age grouping than previously applied. A time horizon of 30 years was considered to be able to capture the effects of changes in vaccination strategies and 10 years run-in period was used to start the simulation in a stable epidemiological situation.

The model was designed to incorporate numerous age-specific parameters, such as length of hospitalization, productivity loss and vaccine effectiveness, to provide more precise estimates of the outcomes for each age group. This unique feature was specifically utilized to gain insights into the incremental costs and effects associated with immunosenescence and age-specific vaccine effectiveness against infection and to observe the differences between a constant value applied uniformly across all age groups and various levels of decreasing age-specific vaccine effectiveness.

Key parameters

Label	Explanation
Share in population	Fraction of number of persons within the age group compared to the total populations
Population size	Total population
Number of years in age group	Width of the age groups in years
Contacts with different age j groups	Contact matrix
Birth rate fraction (yearly)	Average expected yearly birth rate births/person
Background mortality rate fraction (year)	Background (all cause) mortality rate
Net migration rate (year)	Net migration rate
Disease name	Name disease
Simulation duration fraction (days)	Duration of the simulation in days
Report report_duration fraction (days)	Duration of the report (i.e. end of the simulation duration)
Year vaccination will start in simulation	Year of vaccination start
Start date of simulation	Date of simulation start
Season multiplier (0= no seasonality)	Cyclical calibrator
Season shifter (>0, the higher the more intense)	Cyclical height calibrator
time step (days) OBSOLETE	Obsolete
CFR symptomatic	Case-fatality rate symptomatic persons
Fraction in NH	Fraction population in nursing homes
CFR symptomatic without NH deaths	CFR symptomatic for population excluding nursing home residents
CFR symptomatic with NH deaths	CFR symptomatic all population
Basic reproduction number	Basic reproduction number
Infectious period	Duration infectious period
Fraction that is symptomatic	Fraction that is symptomatic
Fraction of symptomatic recovering at home	Fraction of symptomatic recovering at home
Fraction of symptomatic recovering in hospital	Fraction of symptomatic recovering in hospital
Fraction of symptomatic recovering in ICU	Fraction of symptomatic recovering in ICU
Duration recovering period asymptomatic	Duration recovering period asymptomatic

Duration recovering period home	Duration recovering period home
Duration recovering period in patient	Duration recovering period in patient
Duration recovering period in ICU	Duration recovering period in ICU
Length Immunity by infection	Length Immunity by infection
Length Immunity by vaccination	Length Immunity by vaccination
First day vaccination within year (999=off)	Day within the year that vaccination starts, for vaccination spreading
Fraction willing to vaccinate	Vaccination coverage/uptake
Mortality effectiveness vaccine	Fraction averted mortality due to vaccination
Vaccine effectiveness infection	Fraction averted infections due to vaccination
Vaccine effectiveness hospitalization	Fraction averted hospitalization due to vaccination
Vaccine effectiveness on Length of stay	Fraction averted hospitalization stay duration due to vaccination
Years between vaccination	Period between vaccinations in years
Nursing home time infection to death	Nursing home time infection to death
Nursing case-fatality rate due to disease	Nursing case-fatality rate due to disease
Nursing homes R0	Nursing homes R0
Number of nursing homes	Number of nursing homes
Number of persons per nursing homes	Number of persons per nursing homes
Other than influenza mortality (yearly)	Other than influenza mortality (yearly)
Utility nursing home resident	Utility nursing home resident
Fraction normal population visiting NH	Fraction normal population visiting NH
Nursing home length of immunity (days)	Nursing home length of immunity (days)
Vaccine uptake in nursing home	Vaccine uptake in nursing home
Cost stay at Home (day)	Health care cost per day at home
Cost of stay in-patient (day)	Health care cost per day as in-patient
Cost of stay in ICU (day)	Health care cost per day in ICU
Productivity loss at home (per day)	Productivity loss ill at home per day
Productivity loss Inpatient (per day)	Productivity loss ill in-patient per day

Productivity loss in ICU (per day)	Productivity loss in ICU per day
Productivity loss premature death	Productivity loss due to premature death due to influenza
Utility healthy	Health related utility of a normal person
Relative health utility home	Relative utility ill at home
Relative health utility in-patient	Relative utility ill in-patient
Relative health utility ICU	Relative utility ill in ICU
Discount rate effect	Discount rate of the effects (QALYs)
Discount rate financial	Discount rate of economic
Cost of vaccination	Total cost of vaccination per person
Inflation for costs and productivity loss (yearly)	Inflation (not used for fixed prices)