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The effects of demographic change on disease transmission and vaccine impact in a household structured population

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Abstract

The demographic structure of populations in both more developed and less developed countries is changing: increases in life expectancy and declining fertility have led to older populations and smaller households. The implications of these demographic changes for the spread and control of infectious diseases are not fully understood. Here we use an individual based model with realistic and dynamic age and household structure to demonstrate the marked effect that demographic change has on disease transmission at the population and household level. The decline in fertility is associated with a decrease in disease incidence and an increase in the age of first infection, even in the absence of vaccination or other control measures. Although large households become rarer as fertility decreases, we show that there is a proportionate increase in incidence of disease in these households as the accumulation of susceptible clusters increases the potential for explosive outbreaks. By modelling vaccination, we provide a direct comparison of the relative importance of demographic change and vaccination on incidence of disease. We highlight the increased risks associated with unvaccinated households in a low fertility setting if vaccine behaviour is correlated with household membership. We suggest that models that do not account for future demographic change, and especially its effect on household structure, may potentially overestimate the impact of vaccination.

1 Introduction

The demographic structure of a population is a key determinant of patterns of contact and hence of infectious disease spread, with implications for the design of effective control measures. Households in particular are recognised as an important focus of disease transmission, due to the duration and intensity of contacts occurring within them [27]. Over time, demographic processes such as birth, death, aging, marriage and divorce modify age and household structure. During the 20th century, the populations of more developed countries experienced demographic changes—increases in life expectancy and decreases in fertility—that have led to older populations living in smaller households. Drivers of these demographic changes include improvements to public health, and social and economic transformation associated with the growth of urban industrial societies [39]. Similar trends are occurring, at differing rates, among less developed countries. Understanding how changes in the demographic structure of a population affect disease transmission is a necessary step towards the design of more effective strategies for disease control [34, 41].

Mathematical models can help improve our understanding of how infectious diseases spread and inform decision making about how they can be controlled [2, 35]. To capture the full impact of changes in demography on disease spread, a model must represent age and household structure, as well as how these evolve over an extended period of time. Compartmental models of disease transmission that include either age *or* household structure are well established [24, 26, 29]. However, combining both age *and* household structure in a single model is challenging due to the combinatoric growth in the number of compartments required to capture variations in household composition and disease status. An assumption of many existing models is that population structure exhibits an age distribution that does not change over time (*i.e.*, it is demographically stable). While reasonable over short time frames, for example a single influenza season, this assumption is clearly unrealistic when considering the long term dynamics of an endemic disease, or the long term impacts of vaccination programs. Models that incorporate demographic processes have been proposed, but typically assume either stationary or exponentially growing populations [34], and only rarely include household structure [21]. Models that do incorporate non-stationary age structure have demonstrated significant implications for both patterns of disease and the effectiveness of vaccine programs [10, 16, 18, 31, 38, 41–43, 45, 58].

An alternative approach is individual based models, which explicitly simulate each member of a population together with their demographic characteristics, social contacts and disease status. These models allow much greater flexibility in representing the heterogeneity present in real populations. They have been used for simulating outbreak scenarios in realistically structured (*i.e.*, containing both age and household structure) static and dynamic populations [1, 13, 14, 23, 50]. To date, these models do not explicitly capture the long-term impact of demographic changes to both age and household structure that underpin the contact pat-

terns most relevant to disease transmission.

We have previously described a parsimonious individual based model of household structure and dynamics capable of simulating a range of non-stationary demographic scenarios [19]. Here we use this model to show how demographic processes alter the age and household structure of a population, and the effects this has on patterns of contact, disease transmission and vaccine impact.

2 The model

We model a population of individual people characterised by their age, sex, and the household in which they currently reside. Over time, people are born, age, enter into and leave couples and households, and eventually die. The dynamics of these demographic processes are parameterised using age- and sex-specific mortality and fertility rates, and calibrated against observed patterns of household formation and dissolution (see Supplementary Information for detail). By choosing appropriate rates, a variety of demographic scenarios can be simulated, including stable, exponentially growing, and non-stationary populations [19]. Here we focus on a population moving from a high to a low fertility setting, using current and historical Australian census and survey data to calibrate our model. The key demographic trends included are an increase in life expectancy and a decrease in birth rate, together with social factors such as an increase in the average age of childbearing and an increase in the rate of couple separation.

This demographic model is overlaid with a Susceptible, Infectious, Removed disease transmission model, with contact and transmission simulated in the community and household settings. As our primary focus is the role of household transmission, we aggregate contacts occurring outside of the household—in locations such as schools, workplaces and public spaces—into a matrix of age-specific community contact rates. We assume these contact rates to be age-assortative; that is, people are more likely to come into contact with others of a similar age to themselves [47]. These contact rates are derived from the age structure of the population and empirically observed activity levels [25, 47] (see Supplementary Information for detail). Within the community, we make the standard assumption for large populations that transmission is frequency dependent. As the age structure of the population evolves over time, we recalculate the community contact rates at five yearly intervals. Contacts occurring within households are determined directly by the structure of the model population. The degree to which household transmission is frequency or density dependent is not well-established—and most likely varies by disease [54]—and can be varied within the model.

Thus, the probability of a susceptible person in age class i becoming infected in a given time period depends on the prevalence of disease in their household and in the broader community, and is given by $1 - e^{-\lambda_{i,N_H}}$, where the force of infection λ_{i,N_H} on an individual

in age class i, in a household of size N_H is given by

$$\lambda_{i,N_H} = q_h \frac{I_H}{(N_H - 1)^\alpha} + q_c \sum_j \eta_{ij} \frac{I_j}{N_j} \tag{1}$$

where q_h and q_c are transmission coefficients for household and community transmission, I_H and N_H are, respectively, the number of infectious people and the total number of people in the susceptible person's household, α specifies the degree to which household transmission is frequency ($\alpha = 1$) or density ($\alpha = 0$) dependent, η_{ij} is the average number of community contacts between a person in age class i and people in age class j, and I_j and N_j are, respectively, the number of infectious people and the total number of people in age class j. In addition to endemic transmission, we also allowed for the importation of infection from sources external to the population. At each time step, a susceptible individuals could become infected from an external source with a small probability.

In this study, we parameterised the demography of our population model based on historical Australian census and survey data from 1910 to 2010 [3–6, 11, 57]. As data were only available on the average size of households in the Australian population in 1910, initial household size distributions were estimated using a zero-truncated Poisson distribution [33]. The model is stochastic, and each scenario was simulated ten times; unless otherwise noted, results reported represent means and standard deviations across each set of simulations. Starting populations for all simulations were created by running the model for 200 years, using the earliest available demographic rates, to reach an endemic disease equilibrium. Final population sizes in each simulation were approximately 225,000. Importation of cases from an external source (equivalent to 5×10^{-6} cases per person per week on average) was used to prevent epidemic fade-out due to stochasticity. The model is implemented in Python, and source code is available on request via `http://bitbucket.org/ngeard/simodd`.

3 Results

3.1 Effects of demographic change on population structure and mixing behaviour

The demographic changes modelled here have a marked effect on population structure. Using historic demographic rates, the median age of the model population increases from 23 to 40 years (Figure 1A), while mean household size decreases from 4.5 to 2.6 people (Figure 1B), comparable to both the increase in median age from 22 to 37 years and reduction in mean household size from 4.5 to 2.6 that have been observed in the Australian population during the 20th century [30]. In turn, these shifts affect how people mix in a population. As the population ages, the relative proportion of community contacts that are made with adults increases for all age groups (Figure 2A,B). With data-driven assumptions about rates of

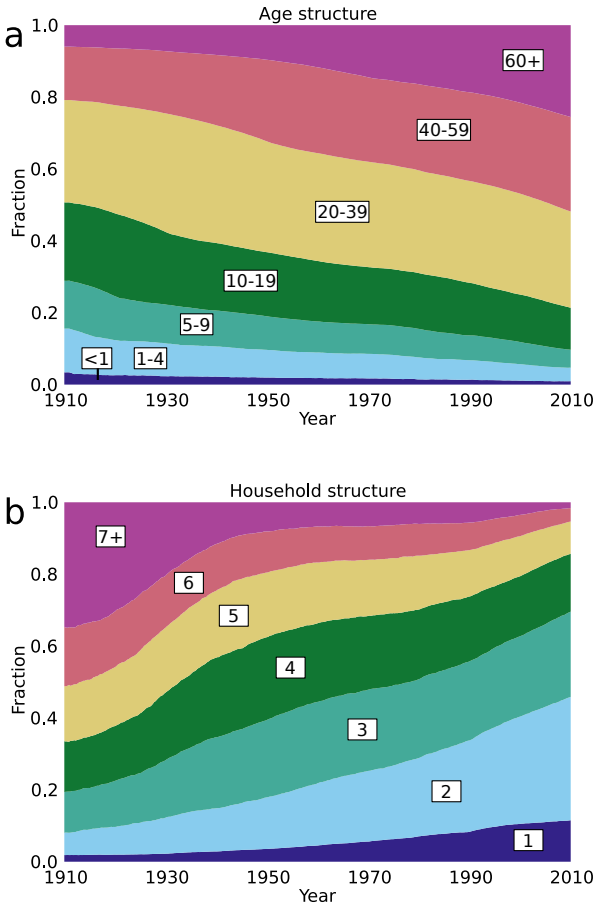


Figure 1: The evolution of (A) age distribution (years) and (B) household size distribution of a simulated population over 100 years, showing the demographic shift towards an older population living in smaller households.

household formation and dissolution, we can also infer how patterns of household contact change as fertility declines (Figure 2C,D). As households become smaller, the overall level of contact occurring in this setting decreases and patterns of contact between age groups change. In particular, children have less contact with siblings and relatively more with their parents.

3.2 Effect of demographic change on disease dynamics

For our baseline scenario, we chose parameters corresponding to a highly transmissible "measles-like" illness. The duration of infection for each case was sampled from an Erlang distribution ($k = 5, \mu = 2$) with a mean duration of two weeks (roughly equivalent to the generation time of measles). Community and household transmission coefficients ($q_c = 0.01$ and $q_h = 0.8$) were chosen such that a randomly selected individual in a fully susceptible population would infect

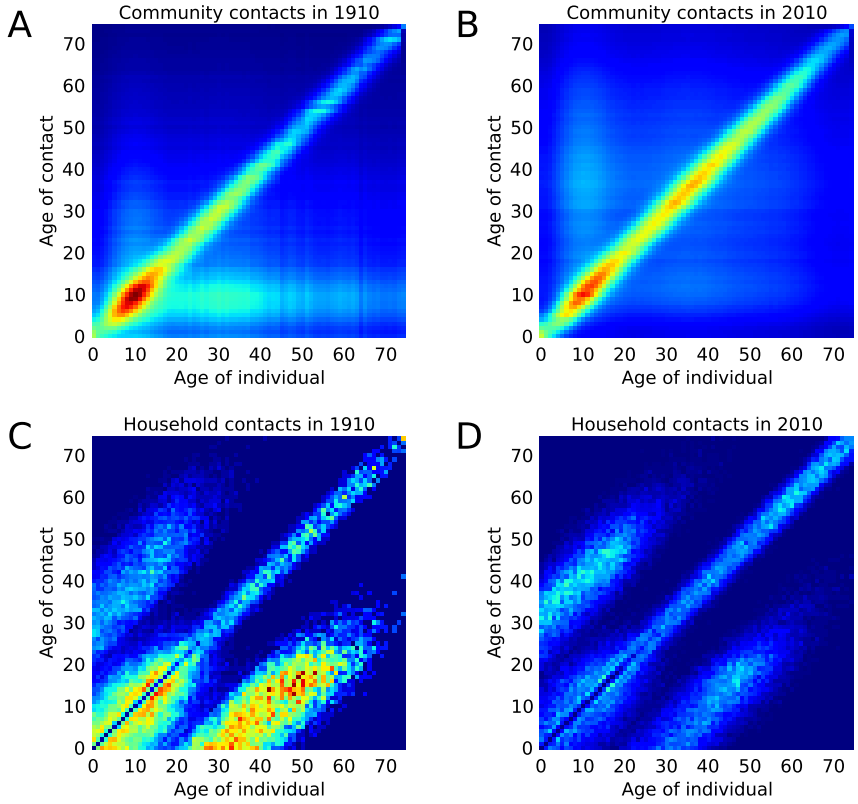


Figure 2: Contact matrices from a sample simulation run showing age-specific rates of contact in the community (A and B) and households (C and D) in the high (A and C) and low (B and D) fertility settings. Equivalent colour scales are used for each pair (A,B and C,D) of matrices. Community contact is age-assortative, and changes in the matrix structure over time reflect the shift towards an older population. The household contact matrices show age-assortative contact between couples and among siblings, as well as inter-generational contact between parents and children. Changes in the matrix structure reflect the shift towards households containing fewer children.

around 17 individuals in total, and 80–100% of their household. We assume that household transmission is frequency dependent ($\alpha = 1$), but also explore the effect of density dependent household transmission. As described above, a key feature of our model is the inclusion of realistic household structure. To establish the independent effect of household mixing on disease dynamics during the shift to a low fertility setting, we compared our baseline scenario to a scenario in which there was no household transmission ($q_h = 0$), and community transmission was recalibrated to ensure that a randomly selected individual in a susceptible population would still infect around 17 individuals ($q_c = 0.017$).

Incidence of disease decreases over the 100 year period simulated, from approximately 25 to 10 cases per 1,000 people annually, in the absence of any vaccination (Supplementary Information, Figure S1A). This decrease in incidence occurs at an equivalent rate in simulations both with and without household mixing, suggesting that declining fertility, rather than change in household structure, is the key driver. As the prevalence of disease in the population falls, it takes longer for a susceptible child to be exposed to infection, and the average age of infection increases from approximately 4.5 to 10.5 years with households and approximately 9 years without households (Supplementary Information, Figure S1B). The decrease in incidence was observed irrespective of whether frequency or density dependent household transmission was used, as could be expected given the high transmissibility associated with the household setting (Supplementary Information, Figure S2).

While overall disease incidence is similar with or without households, the inclusion of household mixing has a stronger effect on the distribution of incidence by age (Figure 3A,B), reducing incidence in infants and children under 5. Children in both scenarios make an equivalent number of daily contacts; however, the inclusion of household structure alters who these contacts are with. Fewer contacts are made with the general pool of predominantly susceptible children in the community, and more are made with household members, including parents, who by virtue of their age are more likely to be immune and hence pose a lower risk. This difference in incidence by age is more pronounced in the low fertility setting (Figure 3B). Smaller households typically contain a greater proportion of adults, which intensifies the potential "cocooning" effect of households.

Disease incidence increases with household size, both with and without household mixing (Figure 3C,D). Larger households are more likely to have experienced recent birth events and hence more likely to contain susceptible infants. The relationship between incidence and household size is stronger in the low fertility setting (Figure 3D). That is, even as large households become less common in the population (Figure 1B), the relative risk of infection associated with being born into them (compared to smaller households) is greater.

The increased risk associated with large households in the low fertility setting is a consequence of changes to patterns of susceptibility in households. In the high fertility setting, disease prevalence is also high and the average age of infection is low. Thus, each child born

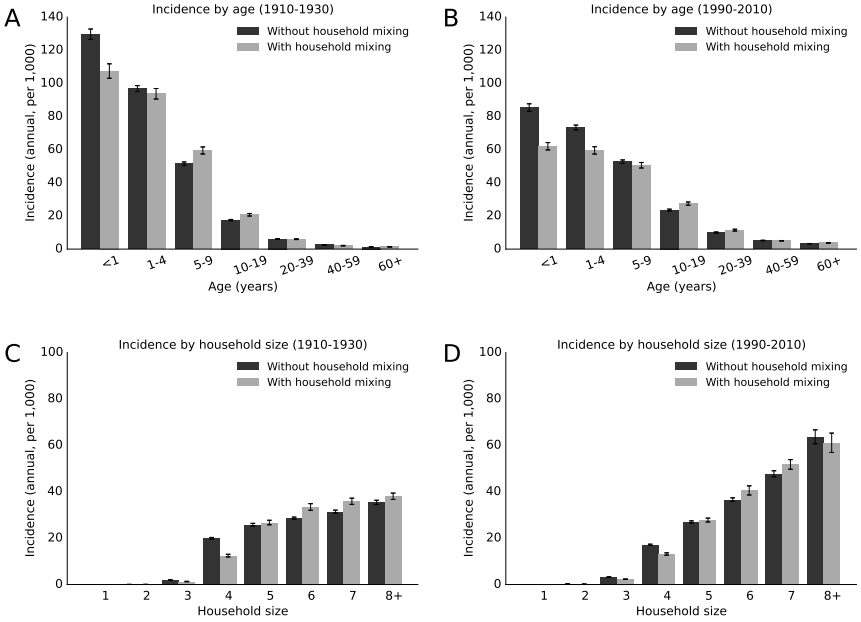


Figure 3: Incidence with and without household mixing by age group (A and B) and household size (C and D) in the high (A and C) and low (B and D) fertility settings. Error bars show standard deviation over 10 independent simulation runs. With household mixing, infants and young children benefit from the 'cocooning' effect of households, particularly in the smaller households that predominate in the low fertility setting. However, while large households are rarer, the risk associated with being born into them is greater.

into a household will tend to be infected before the birth of their younger siblings. By the time subsequent children are born to a household, their older siblings will already have been infected and acquired immunity, so there will be limited opportunity for onward transmission within the household. In contrast, in the low fertility setting, when disease prevalence is lower and the average age of infection is higher, there is a longer window of opportunity for households to accrue additional children prior to the introduction of disease. In high fertility households, this delay enables the accumulation of greater numbers of susceptible children prior to a household outbreak (Figure 4A).

The presence of multiple susceptible children in a household poses two risks. First, there are more opportunities for disease introduction arising from contact between a susceptible household member and infection in the wider community. Second, the clustering of susceptible children provides ideal conditions for onward transmission within the household. Indeed, the proportion of cases for which the source was a household member increases with household size, and also over time (Figure 4B). Thus, in the low fertility and low prevalence setting, more cases will occur in larger households than might be expected, given their relative scarcity in the population.

It is important to note that population-level observations can be misleading as a guide to disease dynamics within households. Over the entire population, the level of transmission within the household appears to remain constant or even decrease slightly over time (Figure 4B, dashed line). However, for a case occurring in a household of a particular size, the probability that the source of infection is a household member actually increases over time, for households of *all* sizes (Figure 4B, solid lines). The apparently contradictory population-level trend reflects the demographic shift towards smaller households (Figure 1B), which experience lower levels of transmission within the household.

3.3 Interactions between demographic change and vaccination

Demographic context can affect vaccine impact [46], and both changing demography and vaccination have contributed to observed reductions in disease such as measles [45]. To ascertain the effect of household structure on vaccination, we compared two control scenarios to the baseline scenario described above. Each control scenario introduced vaccination in year 60 of the simulation, corresponding to the era when uptake of childhood vaccination against disease such as measles and pertussis became widespread in Australia. In the *individual* vaccination scenario, each infant born after vaccine introduction had an independent probability v of being vaccinated and receiving lifelong immunity. In the *household-based* vaccination scenario, the probability of vaccination was evaluated at the household level, recognising that the vaccine status of children from the same household is likely to be correlated [51]. In this scenario, the first infant born into a household after vaccine introduction was vaccinated with probability v. Thereafter, subsequent infants born into a household were vaccinated only if their older

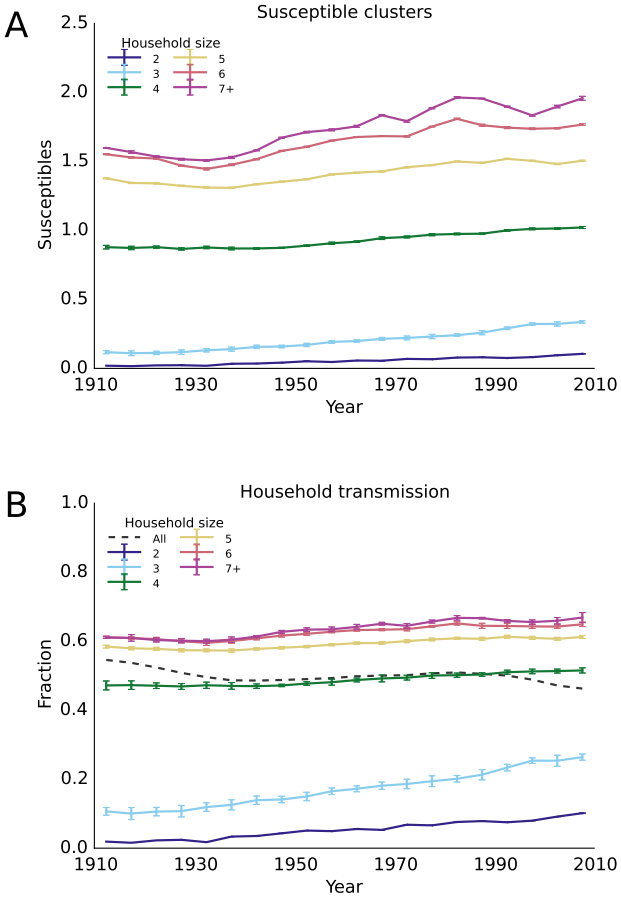


Figure 4: Patterns of susceptibility and transmission within households during the shift from a high to low fertility setting. Each series shows mean values and standard deviations across 10 independent simulation runs. (*A*) The average number of susceptible people in a household at the time of disease introduction (excluding the index case) by household size; (*B*) the proportion of infections for which the source was a household member, over the whole population (dashed line), and by household size (solid lines), estimated using the relative force of infection acting from community and household sources in Equation 1. Overall, larger households accumulate larger susceptible clusters between outbreaks, and experience higher levels of within household transmission. Clustering of susceptibility and household transmission increases in households of all sizes.

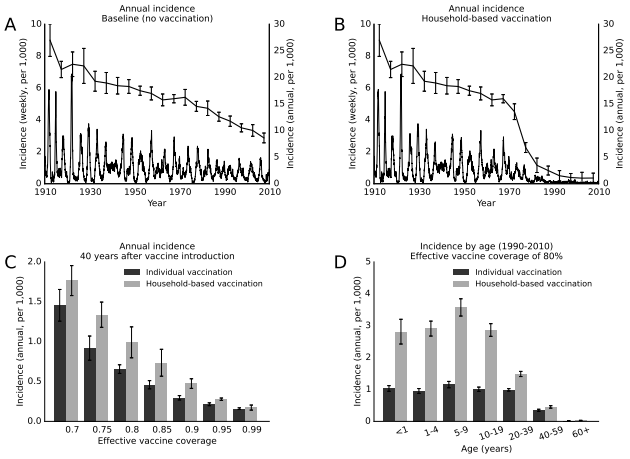


Figure 5: Combined impact of vaccination and demographic change on annual disease incidence. Annual incidence for the baseline scenario with no vaccination (A), and the household vaccination scenario (B), with 80% of children receiving effective vaccination. Also shown are weekly incidence plots for a pair of representative simulation runs (left axis). (C) Vaccine impact in 2010, after 40 years of vaccination, for varying levels of effective vaccine coverage under individual and household vaccination scenarios. (D) Disease incidence by age group, aggregated over the final 20 years of simulation, for 80% coverage under individual and household vaccination scenarios.

siblings were. Across the population, an equal proportion of infants were vaccinated in both scenarios.

The simulated vaccine interventions further reduce population susceptibility, with associated impact on disease incidence (Figures 5A and 5B). However, the impact of the vaccine intervention depends critically upon our assumptions about the households that vaccinated people belong to. If children born to the same household share vaccination status (as in the household-based vaccination scenario), then the reduction in incidence is less than if the decision to vaccinate is made independently for each child, across a range of coverage levels (Figure 5C). The additional disease burden under the household-based vaccination scenario is evident across age classes but is greatest in younger age groups, who may be most likely to experience severe disease (Figure 5D).

These differences are a consequence of the effect that each vaccination scenario has on the distribution of susceptibility across households. Vaccinating children at random, irrespective of the household they belong to, reduces the size of susceptible clusters across households of *all* sizes, reducing the risk of disease introduction and onward transmission (Supplementary Information, Figure S3). In contrast, vaccinating children by household reinforces the clustering of susceptibility observed in the low fertility setting, particularly among larger households (Supplementary Information, Figure S4). Randomly targeted vaccination is unlikely to ever be a realistic policy option [29]; these results illustrate the potential for a vaccine's impact to

be over-estimated if household clustering is not accounted for.

4 Discussion

Demographic change can have a profound impact on the structure of populations, and consequently on mixing patterns, and the spread and control of infectious diseases. Here we have used an individual based model with evolving age and household structure to explore the effects of demographic change on mixing behaviour and disease dynamics. In agreement with existing age-structured models [15, 41, 45], lower fertility levels lead to reduced incidence at the population level and an increase in the average age at infection, even in the absence of vaccination and other factors.

However, because our model explicitly includes households, it also demonstrates how changes in a population's demography affect mixing behaviour and disease incidence at the sub-population level, and it is here that we make three important and perhaps surprising observations. First, even a relatively simple model of contact that includes just household and community locations can produce contact matrices (Figure 2) that recapture key features of empirically observed contact patterns: high levels of household mixing within age groups, corresponding to interactions among siblings (in younger age groups) and between couples (in older age groups), and secondary "wings" reflecting inter-generational contact between parents and children [47]. As populations age and smaller households become more common, the relative contribution of adults to mixing in the household setting increases, both among adults, and between adults and children. The increase in relative contribution of adults to mixing behaviour in the low fertility setting accords with recent observations of the importance of adults as sources of infection in children [32, 49]. Second, even as large households become less common in a population, the risk of infection associated with being born into these households increases (Figure 3D). In the low fertility setting, lower disease prevalence provides increased opportunity for susceptible children to accumulate in large households (Figure 4A). These susceptible clusters increase both the opportunity for infection to enter a household, and the potential size of the resulting outbreak when it does. Finally, the impact of vaccination will be reduced if vaccine status is correlated within households (Figure 5), as observed in previous studies of populations with static household structure [7, 29]. The persistence of susceptible clusters in non-vaccinating households allows higher levels of endemic transmission compared to a scenario in which unvaccinated children are distributed at random in a population. Given the important role of parents in vaccination decisions, both psychological and environmental factors support the likelihood of shared vaccine status among siblings [40, 51].

A major challenge when modelling historical disease scenarios is the absence of data to parameterise mixing behavior, and interpret how changes in the age structure of a population will translate into patterns of contact [41, 45]. Studies aiming to quantify mixing behaviour

related to the transmission of respiratory illness were first conducted in the 1990s [12, 56]. The POLYMOD study provided one of the largest data sets on patterns of contact hitherto gathered [47] and has, as a consequence, become a *de facto* standard for parameterising models of disease spread. However, while broad in scope (covering eight European countries), POLYMOD captures social behaviour in a specific geographic and temporal context, and it is arguably inappropriate to use in earlier time periods or for populations with different social structures. Recent studies in urban and rural regions of China [48], Thailand [52] and Vietnam [28] are starting to improve our understanding of how contact patterns vary across different societies and cultures.

Furthermore, the contact matrices used in compartmental models also typically do not capture variation in the intensity of mixing in different settings, although a recent method for constructing matrices directly from demographic data does allow contacts occurring in different locations to be weighted [17]. Compartmental models also fail to capture the heterogeneity of mixing behaviour within a given age group that arises from the household setting. An entry in a contact matrix describes the *average* level of contact between people in two age classes. However, the real contact patterns of two adults of the same age will be very different if, for example, one lives alone while the other lives with a partner and children. From the other perspective, households of the same size will have very different contact patterns depending on the age of their members. For example, three-person households could consist of two young parents with a newborn infant, two older parents whose youngest child has yet to leave home, or a single parent with two school age children. In each case the mixing behaviour and disease risk are likely to differ.

The individual based model described here addresses these challenges by explicitly simulating how mixing behaviour arises from the demographic structure of populations. Age and household size distributions are often available, or can be estimated, for historical populations. Drawing on census and survey sources, our model enables us to estimate mixing behaviour in a way that captures both a natural and important way in which populations cluster and mix within heterogeneous groups (households), as well as plausible patterns of interaction between those groups, defined in terms of the age-specific patterns of community contact of each of their members. Our model focuses on the changes wrought by demographic change on age and household structure. However, it is likely that, during the 20th century, other social factors would have influenced mixing behaviour, such as changing patterns of travel, work participation and childcare. In the absence of historic contact data, we have assumed that the total number of community contacts that a person makes has remained constant over time, such that all changes to contact patterns are a result of changing age and household structure, and that community contacts are independent of household size. In its current form, our model balances the complexity necessary to produce the household dynamics associated with changing demography against parsimony in choice of model parameters.

Similarly, we have modelled an infection with "measles-like" characteristics in order to illustrate how changes to a population's demographic structure affect the spread of disease. Calibration against historical data could enable more specific predictions about particular diseases, but such calibration efforts must confront two challenges. First, as demonstrated here and elsewhere [42, 45], the dynamics of an infectious disease are dependent on the demographic trajectory of a population. The data, both demographic and epidemiological, required for calibration of disease transmission in the presence of demographic instability are scarce, particularly for historical time periods. Second, historical data that are available can be biased by understanding of disease characteristics at the time of their collection. For example, in the pre-vaccine era, pertussis infection in adults was not commonly recognised, and historic measurements of disease prevalence are likely to underestimate true incidence [22].

Our findings demonstrate the potential for changes in population's demography to affect its experience of disease, with significant interactions between fertility rates and the household size distribution. This important context must be appreciated when interpreting the past and likely future impact of vaccine strategies. Experience with the combined measles, mumps and rubella vaccine has shown that vaccination programs can have unintended long term effects, such as the potential for decreased levels of maternal immunity among children born to vaccinated mothers [44, 55]. Our model further highlights the contribution of changes in population structure to the long-term impact of vaccines. The ability to track patterns of disease and susceptibility at the household level is particularly important when evaluating vaccine strategies that explicitly target households in an effort to provide local herd immunity for young infants, such as maternal immunisation and cocooning [9]. We have used the model described here to compare the effectiveness of alternative antenatal and postnatal vaccination strategies [8].

Households, and their changing structure, could also help in understanding of vector borne diseases. For example, it has been demonstrated that a decrease in prevalence and accompanying increase in average age of dengue haemhorragic fever in Thailand can be accounted for by changes in birth and death rate [10]. However, household clustering of dengue cases has been observed, particularly in rural settings [20], and households are an obvious foci for control measures such insecticides and screening, suggesting that it may be worth exploring the implications of changes in household structure.

In countries with established vaccination programs, our results highlight how the correlation of vaccination status within households can exacerbate the formation of susceptible clusters. We might expect the risk of outbreaks to be further heightened if under-immunisation is associated with larger households, and if these households are geographically co-located. Evidence of this heightened risk can be seen in measles outbreaks occurring among the large family groups prevalent in ultra-orthodox communities in Jerusalem [53]. The recent development of a global Vaccine Confidence Index suggests that addressing trust in vaccination is

a challenge that transcends political and cultural boundaries [36].

Finally, our results highlight the importance of considering future demographic trends when evaluating the introduction of vaccine programs to new countries. It is clear that the decision to introduce a new vaccination program into a country must take into consideration the local factors that may affect it's success. Rubella vaccination is a canonical example, where the benefits associated with vaccination must be balanced against the risks that insufficient coverage may lead to an increase in average age of infection, resulting in an increase in congenital rubella syndroms [37]. Previous studies have focused on the role played by changes in age structure that result from declining fertility, but the implications of household changes have been less frequently considered. The simulations reported here have focused on a vaccine introduced at an advanced stage of demographic transition. Some less developed countries are likely to experience similar patterns of demographic change in the future. If these countries follow a similar path to that experienced by more developed countries, disease incidence may reduce even in the absence of vaccination, but clustering of unvaccinated sub-populations will pose ongoing challenges to control and elimination.

Authors' contributions

NG contributed to the conception and design of the study, performed the experiments, analyzed the data and wrote the manuscript. KG, JMM, ESM, KBK and JM conceived and designed the study and analyzed the data. MJK contributed to interpretation of the data. All authors contributed to critical revision of the manuscript and have seen and approved the final version of the manuscript.

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Supplementary Information

The effects of demographic change on disease transmission and vaccine impact in a household structured population

S1 Model description

S1.1 Outline of the demographic model

We use an individual based model, in which each individual is characterised by age, sex, household of residence, and family ties. Over time, individuals are born, age, form and dissolve couples and household units, and die, with probabilities determined by their sex, current age and life stage. The population demography is updated at each time step of the simulation (in the simulations reported here, at weekly intervals) according to the following procedure:

1. The age of each individual is incremented by the appropriate number of days.
2. For each individual i, one of the following may occur:
   (a) **Death:** with a probability based on i's age and sex, i dies and is removed from the population. An individual j is chosen to be the mother of a replacement individual as follows:
      i. The target age of the mother is determined on the basis of age-specific fertility rates.
      ii. A set of candidate mothers is determined on the basis of age, eligibility to give birth (*i.e.*, not having given birth in the previous 9 month period) and household status (for simplicity, individuals are not eligible to give birth while living with their own parents).
      iii. j is selected at random from the pool of candidate mothers.

      If the death of i results in a household containing only children, these individuals are reallocated as follows:
      i. Any children aged 18 or older form new single-person households.
      ii. Any children aged less than 18 are randomly allocated (fostered) to other households containing at least one child.
   (b) **Couple formation:** if i is currently single, with a probability based on i's age, i forms a couple with an individual j, chosen as follows:
      i. The target age of the partner j is determined on the basis of i's age.

ii. A set of candidate partners is determined on the basis of age, sex, and not currently being a member of a couple.

iii. j is selected at random from the pool of candidate partners.

The households of i and j are merged (along with any children currently residing with them) or, if both previously lived with their parents, a new household of size two is created.

(c) **Leaving home:** if i is currently living with their parents, with a probability based on i's age, i leaves their parents' household and forms a new household of size one.

(d) **Couple separation:** if i is currently in a couple, with a probability based on i's age, i separates from that couple and forms a new household; for simplicity, we assume that any children residing with the couple when they separate join the mother's household.

3. If simulating a growing (or shrinking) population, the number of additional births (or deaths) required to occur in the current time step to match the target growth rate is calculated and additional birth (or death) events are triggered.

S1.2 Summary of parameters and data sources

Mortality: Age-specific mortality rates for Australia during the 20th century were sourced from the Australian Bureau of Statistics [1, 3]. For convenience, we assume that no individual survives beyond 100 years, and the probability of death at 100 years was fixed at 1.0.

Fertility: Age-specific fertility rates for Australia during the 20th centure were sourced from the Australian Bureau of Statistics [1, 2]. These rates were not used directly to generate births in our model, but rather used to estimate relative probabilities of births being attributable to mothers of a particular age. When a birth event was triggered (*e.g.*, by a death, in a scenario with replacement fertility), these relative probabilities were then used to ascertain the age of the mother, and hence the subset of the female population eligible to be randomly chosen as the mother.

Couple formation and separation, leaving home: Probabilities were estimated on the basis of data on the Australian population reported by the Australian Institute of Family studies [5] and the Household Income and Labour Dynamics Survey [12]. This estimation combined data reported both on rates of marriage and divorce with data on rates of de-facto relationships, as the primary focus of our model was the dynamics of household units, rather than the status of relationships. We assume that individuals become eligible to leave their parents' household, either independently or as a member of a couple, at 18 years. As a consequence, individuals also become eligible to separate from a couple at 18 years. We

assume that individuals cease being eligible to form or separate from couples at 60 years. The annual probability of a single individual entering a couple is 0.075. The annual probability of a couple separating is 0.01, increasing to 0.15 over the 100 years corresponding to the period 1910–2010. The annual probability of a single individual leaving home and forming a one person household is 0.01, increasing to 0.1 over the 100 year period.

Population growth: Population growth rates for Australia during the 20th century were sourced from the Australian Bureau of Statistics [4].

It should be noted that the primary aim of the demographic model is intended to capture a reasonable approximation of the size and composition of households in a real population over the last century. Assessment of model performance under a range of demographic scenarios is reported in Geard et al. [6]. It is not intended that the model accurately capture all the complexity of a real population and, as described above, several simplifying assumptions have been made in the name of model parsimony. For example, our model currently simulates dynamics of households containing one or two adults/parents (of opposite sex) and zero or more children (as defined by their familial relationship to the parents in the household; they may themselves be adults who are yet to leave home). Clearly, this does not exhaust the potential types of households observed in real populations. As the disease we are modelling here occurs primarily in children, less common household types containing, for example, groups of unrelated adults, are unlikely to have a large impact on our results. Similarly, we would expect transmission patterns in same-sex households to mimic that of opposite-sex households.

S2 Outline of the disease model

The disease transmission model extends the demographic model described above, tracking the current disease state of each individual. The disesase state of the population is updated at each time step of the simulation (in the simulations reported here, at weekly intervals) according to the following procedure:

1. Population demography is updated, as described in Section S1.1.
2. Periodically (at 5 year intervals in the simulations reported here), the community contact matrix is updated to account for the changing age structure of the population.
3. Individuals born in the current time step are assigned the susceptible disease state.
4. If vaccination is being used, individuals to be vaccinated are assigned the removed disease state.

5. For each individual who is currently susceptible to infection, the force of infection acting on that individual is calculated according to Equation 1 in the main body of the paper, and used to specify the probability of that individual becoming infected in the current time step.

6. The set of susceptible individuals who will become infected is determined stochastically.

7. The disease states of all individuals are updated simultaneously; that is, the state of the population at time $t+1$ is determined by the state of the population at time t. Newly infected individuals are assigned a counter corresponding to their infectious duration. Individuals who are currently infected have their counter decremented. Individuals whose counter reaches zero will recover from infection during the following time step.

S2.1 Contact model and parameterisation

Household contacts: Household structure and contact patterns arise endogenously in the demographic model as a result of the population structure and dynamics. It is important to note that the matrices shown in Figure 2 of the main paper are not used directly to *specify* contact in the model. Rather, they represent the equivalent age-based mixing patterns that result from the household composition and structure captured in the model.

We assume here that mixing and transmission within households is independent of age. While real populations do exhibit age- and sex-dependent transmission characteristics — such as increased levels of transmission between mothers and young children [8, 11] — the effect of these is likely to be diminished at the high levels of household transmission considered in this study (with introduction resulting in 80–100% of susceptible household members becoming infected). For less transmissible pathogens, such as influenza, age- and sex-dependent patterns of within-household mixing are likely to play a more significant role.

Community contacts: In contrast to the household co-location matrix, the community mixing matrix (η_{ij} values) *is* an input parameter of the model. The approach taken here, following Hethcote [7], is to base mixing matrices on age-specific activity levels, using a combination of proportionate and age-assortative mixing, such that the per-capita rate of contact between individuals of ages i and j

$$c_{ij} = \epsilon \frac{a_i a_j}{D} + (1-\epsilon)\frac{a_i}{N_j}\frac{1}{\sqrt{2\pi\sigma^2}}\exp^{\frac{-(j-i)^2}{2\sigma^2}} \quad (1)$$

where ϵ in the interval $[0,1]$ is a convex combination parameter governing the strength of preferential (within age-group) mixing, a_i is the mixing activity, defined as the average number of contacts made by a person of age i, $D = \sum_{k=1}^{m} a_k N_k$ is the total number of contacts made by all people in the population, and σ^2 is the variance in the Gaussian kernel used to smooth

out mixing among nearby ages. As the Gaussian kernel are truncated for some ages, contact rates for each age are normalised such that densities sum to one.

Equation 1 provides per-capita rates of contact. The average number of contact between a person of age i and people of age j is given by $\eta_{ij} = c_{ij}N_j$. While the age of each individual was updated at each time step, contact rates were computed for each year of age from 0 to 100 years.

The values for age-specific levels of contact a_i were derived from Mossong et al. [10] as follows. Mossong et al. [10] report contact data collected in eight European countries, broken down by age of participants and location of contact. They observe that approximately 23% of contacts occur in the home, although this is not further broken down by age. We assume that our model population experiences the same level of contact as that described in Mossong et al. [10], and that contacts occurring within the home are exclusively with other household members. Therefore the level of community mixing is equal to the difference between total number of contacts and number of household contacts (Table S1). This results in 16.2% of contacts occurring in the home. However, if we consider the possibility that contacts occurring in the home could include contacts with people who are *not* members of that household (*i.e.*, visitors), and assume that each person has, on average, contact with one additional person in the home, then home contacts account for 24.1% of contacts, comparable with the level reported in [10]. Activity levels were smoothed across ages by fitting a polynomial of degree 9 to the available data points.

age class	activity	age class	activity
0–4	7.34	40–44	11.47
5–9	11.74	45–49	11.83
10–14	15.07	50–54	10.41
15–19	14.89	55–59	11.02
20–24	11.66	60–64	8.09
25–29	11.71	65–69	8.21
30–34	12.03	70–74	6.08
35–39	11.69	75–79	6.32

Table S1: Age-specific community activity levels, derived from Mossong et al. [10]

Estimating the degree to which *community* mixing is age-assortative or proportionate (*i.e.*, in the absence of household mixing) is challenging, as POLYMOD and similar studies tend not to differentiate between contacts on the basis of context. After initial exploration of parameter space, we chose values of $\epsilon = 0.8$ $\sigma = 10.0$, corresponding to the plausible situation where approximately 36% of an individual's contacts are within three years of their age and 65% are within eight years of their age. Realistically, this value is likely to vary with age and may differ considerably between, for example, school-age students and retirees [9]. A more detailed model could explicitly incorporate multiple mixing locations, such as schools

and workplaces; however, this would come at the cost of additional model and parameter complexity and data to calibrate such a model, particularly for historical time periods, is typically not available.

S2.2 Household and community transmission rates

The force of infection acting on an individual is a linear combination of the prevalence of infection in their household, and in the broader community, weighted by the contact matrix described in Section S2.1 above.

Household and community transmission coefficients (q_h and q_c) were selected to match target levels of household and population transmission. We conducted a two-dimensional parameter sweep over q_h and q_c, seeding a completely susceptible population with a random infectious individual, updating the disease state of the population using a time step equivalent to the generation time of the disease, and recording the proportion of susceptible individuals infected in the seeds household and the total number of individuals infected in the population. This process was repeated 5,000 times for each parameter combination, and the mean number of individuals infected in the household and total population were computed. For the simulations reported here, values of q_h and q_c were selected such that around 80-100% of the seeds household were infected, and around 17 individuals in total across the population were infected.

S2.3 Generating the starting population

In the absence of historical data on household composition, we generate an starting population (*i.e.*, corresponding to the population in 1910 in the simulations reported here) as follows:

1. An initial 'bootstrap' population is created by randomly generating individuals with ages drawn from the target age distribution.

2. These individuals are assigned to households at random according to the target household size distribution. Households of size one or two are assigned one or two adults respectively, while households of size three or greater are assigned two adults and one or more children. This initial population structure will diverge in several ways from a real population; for example, constraints on birth interval and inter-generational age difference will not be respected.

3. **0–100 years:** The model is then run for 100 years, by which time all of these bootstrap individuals and households will have been replaced. At this stage, internal model constraints on population structure such as birth interval and inter-generation age differences will be respected. During this period, we assume that age-specific mortality rates and relative fertility by age are constant over time, and that that the population

grows at a specified rate. During this period, the disease process is not simulated (*i.e.*, the population is susceptible and there is no importation of infection).

4. **100–200 years:** The model is then run for a further 100 years, with disease, to establish a population at (approximately) an endemic disease equilibrium with plausible age-specific patterns of infection and immunity. During this period, age-specific mortality rates and relative fertility by age remain constant over time, and the population size continues to increase; population size is increasing.

5. **200–300 years:** The model is then run for a final 100 years, corresponding to the historical time period 1910–2010. During this period, age-specific mortality rates and relative fertility by age are updated based on available historical rates, and the population size continues to increase. This is the period for which demographic and disease dynamics are collected and reported in this study.

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S3 Supplementary figures

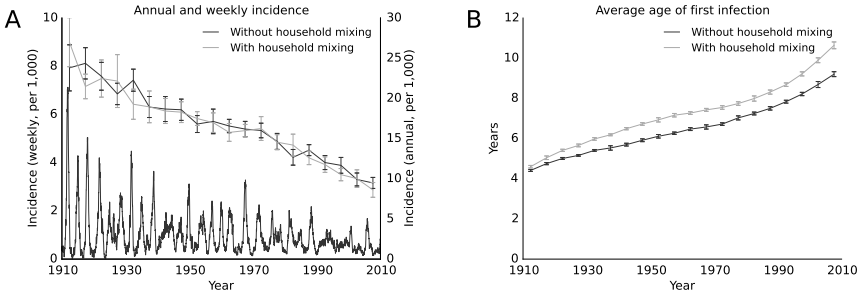


Figure S1: Effect of demographic change on (A) disease incidence and (B) average age of first infection, with and without household mixing and transmission. Error bars show standard deviation over 10 independent simulation runs. In (A), annual disease incidence (right scale), averaged over 5 year intervals is shown for scenarios both with and without household mixing and transmission. Weekly disease (left scale) incidence is shown for the scenario without household mixing, but was qualitatively similar for the scenario with household mixing.

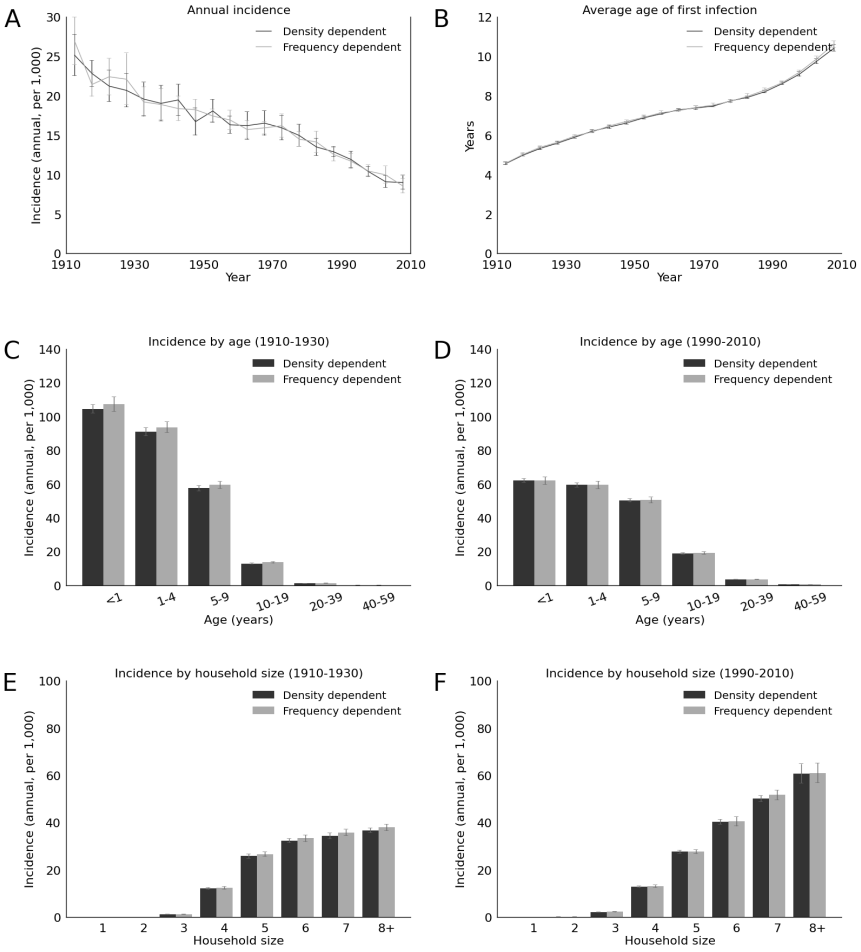


Figure S2: Comparison of the effect of frequency dependent and density dependent household transmission on (A) disease incidence, (B) average age of infection, and incidence by (C and D) age and (E and F) household size in a high (C and E) and low (D and F) fertility setting. Error bars show standard deviation over 10 independent simulation runs.

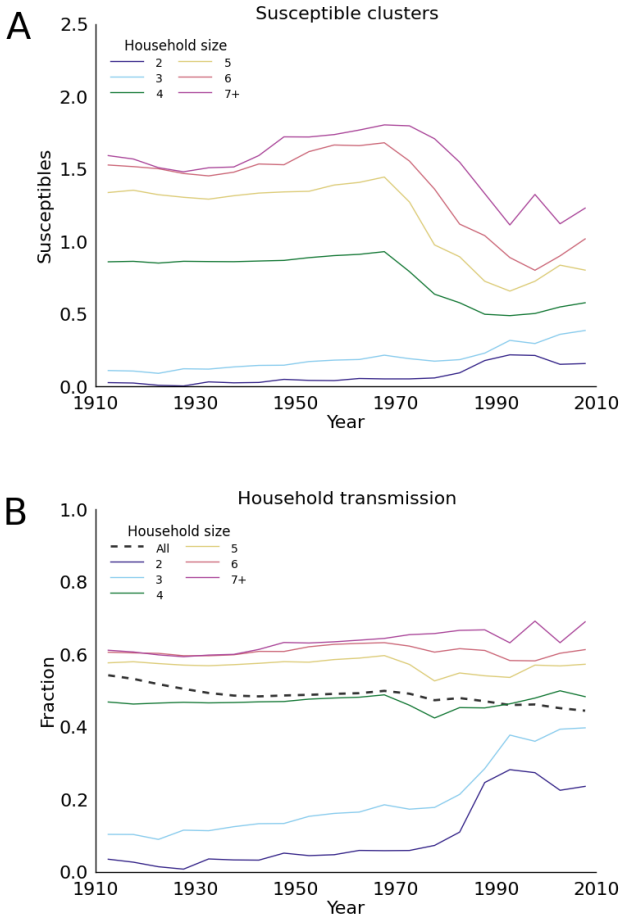


Figure S3: Effect of individual level vaccination on (A) susceptible clusters and (B) proportion of transmission occurring within the household. Series show mean over 10 independent simulation runs. Vaccinating individuals at random, irrespective of household, has the effect of reducing the average number of additional susceptible people in a household at the time of a disease outbreak across households of all sizes, with associated decreases in the proportion of cases attributable to household transmission. Note that the increase in household transmission in households of size 2 and 3 results from the cohort of adults born shortly before the introduction of vaccination. These adults were too old to be vaccinated but, due to the low disease prevalence that followed the introduction of vaccination, also escaped infection and hence remained susceptible until they aged and moved out of home.

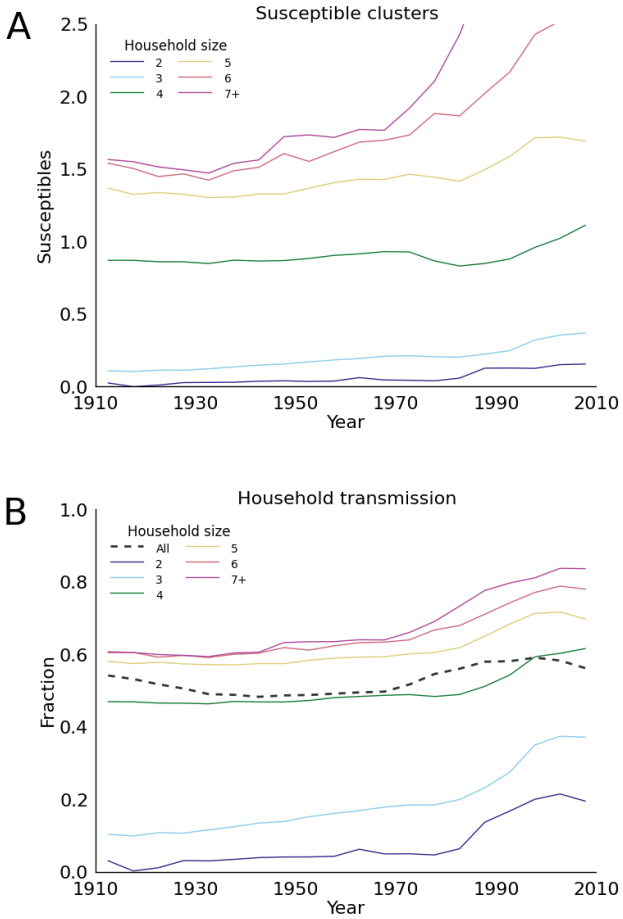


Figure S4: Effect of household level vaccination on (A) susceptible clusters and (B) proportion of transmission occurring within the household. Series show mean over 10 independent simulation runs. In contrast to Figure S3, if vaccination is correlated among household members, the average number of additional susceptible people in a household at the time of a disease outbreak increases dramatically, with associated increases in the proportion of cases attributable to household transmission.