Rapid communications

What will the next influenza season bring about: seasonal influenza or the new A(H1N1)v? An analysis of German influenza surveillance data

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For the next influenza season (winter 2009-10) the relative contributions to virus circulation and influenza-associated morbidity of the seasonal influenza viruses A(H3N2), A(H1N1) and B, and the new influenza A(H1N1)v are still unknown. We estimated the chances of seasonal influenza to circulate during the upcoming season using data of the German influenza sentinel scheme from 1992 to 2009. We calculated type and subtype-specific indices for past exposure and the corresponding morbidity indices for each season. For the upcoming season 2009-10 our model suggests that it is unlikely that influenza A(H3N2) will circulate with more than a low intensity, seasonal A(H1N1) with more than a low to moderate intensity, and influenza B with more than a low to median intensity. The probability of a competitive circulation of seasonal influenza A with the new A(H1N1)v is low, increasing the chance for the latter to dominate the next influenza season in Germany.

Background

A new influenza A(H1N1) variant has spread globally since its first appearance in April 2009 [1] and its transmissibility has been estimated in a range similar to that known from seasonal influenza. Nevertheless it is unclear if this new influenza A(H1N1)v will replace seasonal influenza A or there may be co-circulation or successive circulation, in particular considering that A(H1N1)v has been circulating very early, ahead of the season. Cross immunity of the new influenza A(H1N1)v with seasonal influenza viruses is very low and probably negligible except for elderly people [2]. Hence a general susceptibility of the population to the new A(H1N1)v is assumed, even though not immunity-based mechanisms may additionally influence susceptibility [3,4]. For seasonal influenza A partial immunity of the population due to previous infections can be assumed. A rather constant drift with significant antigenetic changes - when a new successful lineage evolves - allows the virus to overcome this immunity [5]. The imbalance of population immunity and drift is seen as a driving force for intense virus circulation. The exact correlate of molecular or antigenic drift - as characterised by laboratory methods - on this balance is unknown.

In most European countries primary care sentinel surveillance systems are used to estimate the "intensity" of seasons and laboratory testing of a sub-sample indicates the viruses circulating. These data do not provide exact measurements of virus circulation and subsequent population immunity. However, assuming a stable relationship between population immunity and virus circulation, the latter can serve as a proxy measure of type- and subtype-specific population immunity. For the upcoming season a seasonal influenza vaccine and a vaccine against the new influenza A(H1N1)v will be available with some remaining uncertainties regarding the amount of each. Therefore anticipating the circulation of the different seasonal influenza viruses - still present in the population - and the new A(H1N1)v virus may be helpful for setting up the vaccination strategy.

Materials and methods

We calculated type- and subtype-specific indices of past exposures and morbidity indices by season. We used data of the German influenza sentinel system (AGI) which has been registering acute respiratory tract infections in the winter seasons since 1992 (available at http://influenza.rki.de/). In this system the presence of influenza viruses is monitored through syndromic sentinel surveillance and, additionally, a sub-group of participating physicians swab patients with acute respiratory tract infections and send samples for testing to the national influenza reference centre (NIC).

In order to allow the calculation of indices for as many seasons as possible, in addition, virological data from NIC for the five seasons before 1992-3 were used.

For each season we estimated the total influenza-associated morbidity from weekly excess consultations (as percentage above baseline) during periods of laboratory-confirmed influenza activity [6]. Splitting this total excess morbidity by the percentages of detected influenza types and subtypes gave the type- and subtype-specific morbidity index for each season.

To calculate indices of past exposure we used the morbidity indices of the five preceding seasons. However, it is unclear for how long immunity acquired during past exposures persists. We therefore used weighting factors to adjust for the decreasing influence of more distant seasons. Each of the five included seasons was weighted with a factor that was kept constant for all calculations. The set of weighting factors giving the best linear

correlation for all seasons between the morbidity index of each season and the morbidity indices of the respective five preceding seasons was chosen. The sum of the five weighted morbidity indices gave the past exposure index for the respective season.

Results

The figures show the distribution of the value pairs of the estimated past exposure and morbidity indices for each season (1992-3 to 2008-9), by influenza type and subtype. Estimates obtained using data exclusively of the NIC are plotted in grey, estimates obtained using data of the AGI are in blue, and the estimate for the past exposure index for the upcoming season (2009-10) is plotted as a blue arrow. For influenza A(H3N2) and B the best linear correlation (-0.55 for A(H3N2) and -0.62 for B) was seen when the morbidity index of just the directly preceding

season was used to estimate the past exposure index. For seasonal influenza A(H1N1) the best correlation (-0.46) was obtained with weighting factors that left a greater relative contribution to more distant seasons (preceding season: weighting factor = 1; two years ago = 1.4^{-1}; three years ago = 1.9^{-1}; four years ago = 2.7^{-1}; five years ago = 3.8^{-1}).

For all seasonal influenza viruses the distribution pattern is similar: the probability of a high excess morbidity - as correlate of intense virus circulation - is low when the past exposure index is high. For median past exposure indices low to moderate seasons can be expected and for low past exposure indices severe seasons may but do not need to occur. These distributions of the value pairs (past exposure and morbidity indices) are typical of distributions which reflect a limiting influence, i.e the past exposure indices represent a kind of upper bound for the morbidity indices of the corresponding seasons. Seasons with no measurable intensity are rare for influenza A(H3N2), frequent for seasonal A(H1N1) and occur with intermediate frequency for influenza B.

Influenza A(H3N2) reaches the highest indices of past exposure and morbidity. However, direct comparability of past exposure indices is only given between influenza A(H3N2) and influenza B. Their respective past exposure indices are based on the same number of seasons and the identical weighing factors.

For the next influenza season in Germany the results of our model suggest that it is very unlikely that influenza A(H3N2) will circulate with more than a low intensity. The same can be concluded for seasonal A(H1N1) with a slight chance to reach a moderate intensity level. Influenza B may circulate with up to a median intensity.

Discussion

Predictions of the circulation of influenza viruses in upcoming seasons are highly desirable but generally accepted models are still lacking [7-9]. This is mainly due to the multitude of factors involved and limited data availability and quality. The data we used on

FIGURE 1

Estimates of past exposure and morbidity indices of influenza A(H3N2), Germany, 1992-3 to 2008-9
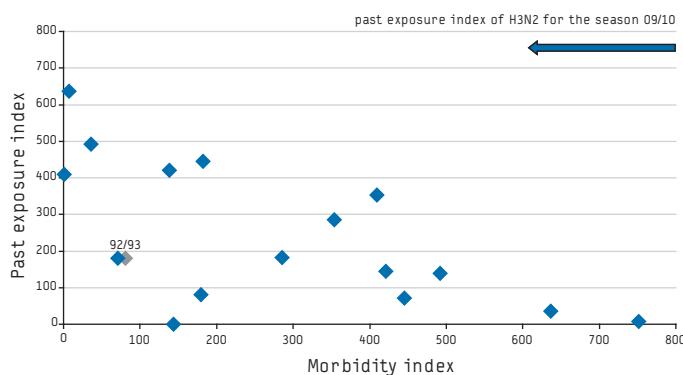
Note: Estimates obtained using only virological data from the national influenza reference centre (NIC) are plotted in grey, estimates obtained using data of the influenza sentinel system (AGI) are in blue, and the estimate for the past exposure index for the upcoming season (2009-10) is plotted as a blue arrow.

FIGURE 2

Estimates of past exposure and morbidity indices of seasonal influenza A(H1N1), Germany, 1992-3 to 2008-9
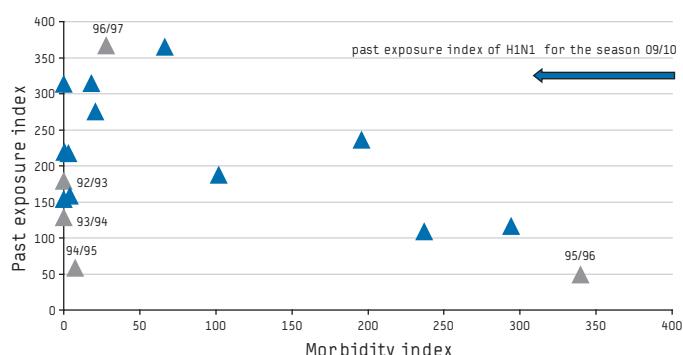
Note: Estimates obtained using only virological data from the national influenza reference centre (NIC) are plotted in grey, estimates obtained using data of the influenza sentinel system (AGI) are in blue, and the estimate for the past exposure index for the upcoming season (2009-10) is plotted as a blue arrow.

FIGURE 3

Estimates of past exposure and morbidity indices of influenza B, Germany, 1992-3 to 2008-9
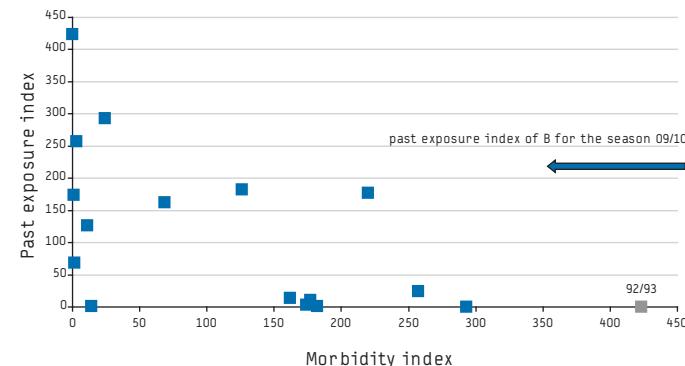
Note: Estimates obtained using only virological data from the national influenza reference centre (NIC) are plotted in grey, estimates obtained using data of the influenza sentinel system (AGI) are in blue, and the estimate for the past exposure index for the upcoming season (2009-10) is plotted as a blue arrow.

morbidity and virus circulation have been collected systematically for 17 years, thus providing a reasonable basis for the approach we used.

This analysis is based on the assumption of a type- and subtype-specific link between past exposure and virus circulation in the following season. In our results for influenza A(H3N2) and B a short lived "protection" of past exposure is suggested. These results are in line with a short-lived strain overlapping immunity as suggested by modelling studies [7].

We consider the chances for the seasonal influenza viruses to lead to considerable morbidity during the upcoming influenza season 2009-10 to be very low. Should the A(H1N1)v virus circulation during the upcoming season 2009-10 be high enough, the expected low seasonal activity may lead to a rapid total replacement, as seen in previous pandemics (except for the 1977 H1N1). However, if the activity of the A(H1N1)v during the season 2009-10 is a pre-wave and a severe circulation of A(H1N1)v will be seen in the following season 2010-1, the possibly low past exposure index for the 2010-1 season in Germany may hamper a total replacement [7].

This model has several limitations. Regional differences in virus circulation are not taken account of. The frequency of laboratory testing varies during one season and, additionally, depends on type- and subtype-specific disease severity, thus potentially biasing the relative contributions of the different virus types and subtypes. In addition, a relatively short time series (17 value pairs for each type/subtype) limit the applicability of complex statistics.

In conclusion, our systematic approach may reduce the unpredictability of influenza activity and thus contribute to strategic planning, e.g. regarding vaccination priorities. These results should be confirmed with data obtained from different surveillance systems. Further improvements of this model may then address its current limitations and additionally offer the possibility to include other factors, such as weather conditions [8], holidays or historical experiences regarding timing and trend [9].

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