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Vaccination of high-risk patients against influenza: impact on primary care contact rates during epidemics Analysis of routinely collected data

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ABSTRACT
A general practice (GP) based retrospective cohort study was conducted to assess the effects of influenza vaccination on the primary care contact rate during influenza epidemics. Given the rising workload of family physicians, particularly due to ageing of the population, it is very relevant to know to whether influenza vaccination of high-risk patients reduces the contact rate during epidemics. No effect of vaccination was found on the contact rate of GP during a mild epidemic period. During a 'normal' influenza epidemic, the workload was reduced through fewer contacts by patients with cardiovascular or diabetic diseases. Epidemic periods severe enough to show contact rate reduction occurred approximately every other year.

1. INTRODUCTION

Influenza is an acute respiratory illness with high morbidity and significant mortality that occurs in epidemic proportions almost every winter and is a threat to public health, especially in patients with co-morbidity [1–3]. Influenza-related mortality and morbidity have considerable economic consequences [4]. To reduce the impact of influenza, immunoprophylaxis with conventional inactivated (i.e. killed virus) influenza vaccine is the main option [5]. Most influenza vaccination programmes are targeted at citizens aged 65 years or older, or those with high-risk conditions regardless of age [3,6,7]. Previous research has shown that variation in vaccination acceptance depends almost entirely on differences between risk patients rather than on differences between practices [8].

Little is known about the frequency at which different groups contact the general practice (GP) when suffering from certain illnesses [9], or about the differences in consultation rates between vaccinated and unvaccinated patients. Most studies on the effectiveness of large-scale vaccination have been conducted on subsections of the total population, particularly on the elderly [10]. Consistently, reductions in the traditionally used endpoints, such as mortality and hospitalisation, were shown [11–14]. We can therefore expect that vaccinating high-risk patients in primary care will also reduce consultation rates. Given the rising workload of family physicians, particularly due to ageing of the population, this is a very relevant issue in daily practice. The winter season is well-known for its raised workload in primary care and it would be welcome if some reduction could be established through vaccinating high-risk influenza patients. GPs in The Netherlands are partly paid by capitation (for about 60% of their patients) and partly by fee-for-service. One of the advantages of capitation payment mentioned in the literature [15] is that it provides an incentive for family physicians to invest in preventive care. If preventive care is successful, family physicians would have less work for the same capitation payment. It has never been shown that family physicians indeed make these calculations, nor has it been shown that investing in preventive care leads to subsequent reductions in workload. Preventive care services tend to be remunerated separately, also in systems with capitation fees, such as The Netherlands [16] and the UK. Apparently, returns for investing in preventive care are not perceived as being large enough to induce family physicians to perform them without extra payment. Therefore, we conducted a study to determine the difference in use of primary care between vaccinated and unvaccinated patients. We also explored whether a difference in the type of risk resulted in different use of care.

To our knowledge, no previous research has been conducted into the relationship between immunising high-risk patients and subsequent primary care contact (during an epidemic period). This retrospective cohort study addressed differences in utilisation of primary care during influenza epidemic periods (in terms of the total number of contacts with family physicians or their practice assistants) by vaccinated and unvaccinated high-risk patients in The Netherlands from November 1999 to March 2002. Adjustment was made for differences between vaccinated and unvaccinated high-risk patients in non-epidemic periods.

2. METHODS

2.1. Study population

The study population was identified within a large computerised GP based network in The Netherlands, i.e. the National Information Network of GPs (LINH). In this network, the GP staff routinely record encoded patient information using a computerised medical record system (CMRS). To ensure completeness of data, participating practices must have a (nearly) paperless office. In the vaccination years 1999–2001, the family physicians at these practices invited all their high-risk patients for annual immunisation in accordance with the immunisation guidelines of the Dutch College of General Practitioners [1,17].

2.2. Measurements

Eligible patients for an influenza vaccination in 1999 and 2001 were identified by means of a software module that searches through the CMRS and uses ICPC codes, indication tags and prescriptions to identify high-risk patients. Elected patients were registered by means of an influenza indication tag. Details of the stepwise selection procedure have been reported previously [18]. Box 1 describes the Dutch influenza programme.

All relevant data were extracted from the CMRS using specially developed software. All data were collected on a patient level. Contacts were defined as events in which a patient received professional advice or help from the family physician or practice assistant, including consultations, phone calls and home visits. Additional data were gathered on age, gender, type of health insurance (social health insurance or private health insurance), indications for vaccination according to the Dutch guidelines [17] (high-risk (co-) morbidity and/or age 65 years or older) and vaccination status.

Box 1. The Dutch influenza vaccination programme In The Netherlands, primary health care is mainly provided by GP and nearly all Dutch inhabitants are listed with a GP. The GP staff keep a record of the vast majority of persons, including demographic and medical information.

In the Dutch influenza immunisation guidelines [17] vaccination is recommended for persons: aged 65 years or older, with cardiovascular disease, pulmonary or renal disease, diabetes or other immunerelated disease at any age. Influenza vaccination is free of charge for all Dutch high-risk patients. There is a fee-for-service for the GPs who select, invite and vaccinate the population at risk, and document the vaccinations in the patients' medical records.

Annual influenza surveillance monitoring has been carried out by the National Influenza Centre in collaboration with the Sentinel Practice Network since 1970 [19]; since 1996, vaccination rates have been monitored yearly by the National Information Network of GPs (LINH) [28].

2.3. Data analysis

Descriptive statistics were used to compare characteristics of the patients listed (total population) with the national population.

To determine whether the vaccination of high-risk patients affected the number of contacts with the GP, we compared the contact rate of vaccinated patients in the epidemic periods to that of non-vaccinated patients. In The Netherlands, the annual influenza surveillance is carried out by the National Influenza Center in collaboration with the Sentinel Practice Network. This institute is linked to the 'European Influenza Surveillance Scheme' (EISS), their data are representative for Dutch figures. One objective of their surveillance is to describe the impact of influenza periods on populations and for our study we adopted their periods marked. The clinical data cohere with isolations of influenza viruses in samples of patients from the sentinel practices. The National Influenza Center uses the following definition of an epidemic period: when more than four per 10,000 inhabitants per week have influenza-like-illnesses (ILI) [19]. So in accordance with The Netherlands annual influenza surveillance, the influenza season in 1999–2000 was marked as follows: the epidemic occurred from week 50 in 1999 through week 6 in 2000. In 2000–2001, no epidemic occurred (and no data were collected), while in 2001–2002, the epidemic occurred from week 4 through week 10 in 2002 (see Fig. 1) [19,20]. In 1999–2000, the highest weekly incidence of patients with influenza (-like illness) was 32 per 10,000; in 2001–2002, the highest weekly incidence was 13 [21].

[FIGURE 1]

Research has shown that illness and patient characteristics differ between vaccinated and unvaccinated patients [8]. These features can affect the consultation rate. Patients at risk often belong to more than one risk group, thereby increasing their risk. Moderate-risk groups have a relatively lower vaccination rate than high-risk groups [8]. Diabetics, who visit their GP frequently, have a higher vaccination rate than patients with mild pulmonary diseases. Membership to more than one risk group increases the chance of vaccination, with the exception of diabetic patients with co morbid pulmonary disease. In addition to the medical factors, demographic characteristics (age, gender and type of health insurance) can also affect the contact rate. Patients who generally seek less health care (namely young people, men and privately insured persons) are less likely to be vaccinated [22,23]. To assess which of these characteristics were associated with vaccination status, we calculated odds ratios using the chi-square method. To estimate the probability of vaccination in each individual patient in the full data-set, we made use of a 'propensity score'. The propensity score method, which is a powerful tool, was used to correct for 'confounding by indication' [24,25]. This technique enables assessment of the association between vaccination and medical consumption in patients with an equal probability of being vaccinated. The propensity score represents this probability of vaccination.

Multiple logistic regression analyses with the forward stepwise method were performed to assess which variables needed to be included in the propensity score as predictors of vaccination probability. Vaccination status was the dependent variable. The fit of the model (propensity score) included age (continuous), type of health insurance (social health insurance or private), indication for pulmonary disease, indication for cardiovascular disease, indication for diabetes mellitus and the total number of contacts with the GP in the 6 months before vaccination.

We compared the number of contacts of the vaccinated patients during the *epidemic period* to that of the unvaccinated patients by performing linear regression twice (for the 1999–2000 and the 2001–2002 epidemic periods) and adjusting for confounding with the propensity score. To be able to see whether there was a difference in vaccination effect between the different high-risk groups, we performed separate analyses on the four most prevalent subgroups by indication (aged 65 years and older; younger than 65 years of age; patients with diabetic diseases; patients with cardiovascular diseases; patients with pulmonary diseases). The propensity score was adjusted for each sub-analysis by removing the indication variable of the subgroup from the model. The epidemic in 2001–2002 was much more severe in the southern part of The Netherlands; therefore we performed a sub-group analysis on high-risk patients in this region. We used a *P*-value of 0.05 to indicate statistical significance.

3. RESULTS

3.1. Study population and patients at risk

The study population (i.e. all the patients listed at the GPs) was representative of the general Dutch population in both study years (Table 1). There were two samples of high-risk patients studied: 25,533 patients from 30 GPs in 1999–2000 and 38,483 patients from 40 GPs in 2001–2002.

[TABLE 1]

3.2. Association between influenza vaccination and number of primary care contacts

Table 2 shows the associations between vaccination and several patient characteristics in terms of odds ratios. In both study periods (1999–2000 and 2001–2002), the strongest predictors of vaccination were the indication cardiovascular disease and the total number of primary care contacts in the 6 months before vaccination. Owing to the low mean age of the patients with pulmonary diseases, this Odds Ratio was less than one. The mean age of the patients with pulmonary diseases was 44.3 years, whereas the mean age of the total high-risk group was 58.6 years). Fig. 2 shows the mean number of contacts by the vaccinated and unvaccinated patients from week 49 through week 13 during the influenza seasons of 1999–2000 and 2001–2002. In both periods, the vaccinated patients had more primary care contacts than their unvaccinated counterparts. The mean number of contacts per week was more or less stable over the whole period: about 0.2 contacts per week by the vaccinated high-risk patients, versus about 0.1 contacts per week by the unvaccinated patients.

[TABLE 2]
[FIGURE 2]

3.3. Mean number of contacts during the influenza season 1999–2000

After excluding 1297 patients due to missing information about the number of contacts, 24,236 records were available for analysis (94.9%). In 1999, the mean propensity score (=mean vaccination rate) of the total population at high-risk for influenza was 0.78 (S.D. 0.11; 95% CI 0.78–0.78).

The vaccinated high-risk patients had significantly more contacts with their GP during the epidemic period than the unvaccinated high-risk patients. After correction for confounding (with the propensity technique), the trend was a lower number of contacts during the epidemic period by the total group of vaccinated high-risk patients and by all the subgroups compared to the unvaccinated patients. There was a statistically significant reduction in primary care contacts by vaccinated patients with cardiovascular diseases (−0.26 contact (adjusted)) and by vaccinated diabetic patients (−0.29 contact (adjusted)) (Table 3).

[TABLE 3]

3.4. Mean number of contacts during the influenza season 2001–2002

In 2001, 85 patients had to be excluded due to missing information about the number of contacts. Thus, 38,398 records were available for analysis (99.8%). The mean propensity score of the total high-risk population was 0.75 (S.D. 0.12; 95% CI 0.75–0.75). The same variables were included in the model as for the 1999–2000 epidemic. Table 4 shows the mean number of primary care contacts by vaccinated and unvaccinated patients during the 2001–2002 influenza epidemic. After correction for confounding with the propensity technique, no significant differences were found.

[TABLE 4]

The epidemic in the influenza season 2001–2002 was of moderate severity. However, it was much more severe in the southern part of The Netherlands. Therefore, we did a sub-analysis on the high-risk patients (9733 high-risk patients from seven practices) in this region of The Netherlands. The patient characteristics at the seven practices were comparable with those at the 40 participating practices and therefore with those of the total Dutch population. We used the same propensity score used as that for the total population in the influenza season 2001–2002. No significant differences were found between the vaccinated and unvaccinated high-risk patients.

4. DISCUSSION

We studied whether vaccinating high-risk patients against influenza had impact on the utilisation of primary care services during two influenza epidemics. There seemed to be an increase in the number of GP contacts by unvaccinated high-risk patients only when the epidemic was severe (like in 1999–2000 in The Netherlands, maximum of 32 ILI per 10,000). This applied especially to patients with cardiovascular disease (a discrepancy of an average of 0.26 contacts) and diabetic patients (a discrepancy of an average of 0.29 contacts). Per 1000 patients listed at a GP, this implied a reduction of 10.4 contacts by cardiovascular patients or 6.1 contacts by diabetics during the epidemic period (9 weeks in 1999–2000) (see Appendix A for the calculation). The effect we found for cardiovascular patients has been shown before when hospitalisation and morbidity rates were the main outcomes of the vaccination programme [26,27]. In general, the effects found in our study were not strong. Vaccination only seemed to reduce the contact rate in cardiovascular and diabetic patients. However, when the epidemic was less severe (like in 2001–2002, maximum of 13 ILI per 10,000), there was no reduction in the number of contacts even in these patients. A possible explanation for the disappointing effect of vaccination is the fact that influenza vaccination rates have been high in The Netherlands for several years [28].

A major source of bias in our study may be the fact that the presence of risk factors is higher among vaccinated than unvaccinated persons. We attempted to minimise this so-called ‘confounding by indication’ using the propensity score technique. Probably we were not able to correct for all bias factors.

Our study was carried out within the LINH. Former research showed that the LINH vaccination rate of the total population is comparable to the national vaccination rate based on data about the vaccine delivery (available from the National Program Influenza Prevention Foundation (SNPG) [8]. Besides this, GP based data were very suitable to find answers to our research question, because the GP staff keep automated medical records in order to document and ensure the quality and continuity of the health care they provide [29]. Furthermore, in The Netherlands, influenza vaccination is carried out by GPs and there is great likelihood that patients who develop influenza or influenza related problems consult their GP.

One might argue that we did not have more specific information on the reason of the contact. Hence, efficacy of the vaccine could not be addressed. However, our primary aim was to assess the effects of vaccination on the total workload including all contacts by GPs. Similarly, we did not obtain virological information to more accurately estimate the presence of influenza in the population. Influenza itself has no specific symptoms and is not clearly distinguishable from other acute infections by its clinical profile [9]. Therefore, it is difficult to link contacts on virus isolates. Furthermore, Thompson et al. [30] found that many influenza-associated deaths occur from secondary complications when influenza viruses are no longer detectable. We think this is not only the case with mortality, but also with morbidity underlying consultations in GP. Monto describes that it is difficult to detect whether influenza was the cause of the illness by the time the contact occurred, because in the GP setting it is not common to confirm influenza illness by a laboratory test [31], so the question arises if it is possible to get reliable information. On the other hand, Govaert et al. found that the predictive value of the diagnostics of GP amounted to 35% [32].

In our study, we did not encounter any diagnostic problems when we compared all contacts by vaccinated and unvaccinated high-risk patients during the epidemic periods, i.e. not only influenza-related contacts. A sub-analysis on reasons for the contact may have given different results, but less interesting for our research question. After correction for confounding by indication, the number of non-influenza related contacts are comparable for vaccinated and unvaccinated high-risk patients. The more complicated way of data gathering (with detailed information on the reason for the contacts or a selection of contacts linked to virological diagnoses of influenza) would add little to the picture of the workload in GP.

To our knowledge, this is the first study on the effect of vaccinating high-risk patients on the number of contacts with GP. In general, we did not find any effect of vaccination on the utilisation of primary care during a mild influenza epidemic. Contrastingly, we did find an effect in patients with cardiovascular diseases or diabetes during a more severe epidemic. It is known that family physicians are reluctant to increase their workload by taking on preventive care activities [33,34]. However, the preventive care activity itself (i.e. vaccination) can be considered as an investment of time, it can easily be organised and it is paid for. If a severe epidemic period follows, the earlier investment would lead to a reduction in workload during the busy winter season. Influenza epidemics severe enough to affect the workload in primary care as a result of vaccination occur fairly often: in the past 30 years, a comparable or more serious epidemic than that in 1999–2000 (a highest weekly incidence per season of 32 ILI per 10,000 or more) occurred in approximately 6 out of 10 years [21,35,36]. Thus, about every other year, family physicians would really benefit from vaccinating their high-risk patients. Obviously, the most important benefits of preventive care are improved patient-related outcomes (morbidity and mortality reduction) [11–14]. Nonetheless, any reduction in utilisation is a welcome side-effect given the rising workload in primary care. Greater investment in preventive care would mean that family physicians have less work for the same capitation paid.

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TABLES AND APPENDIX

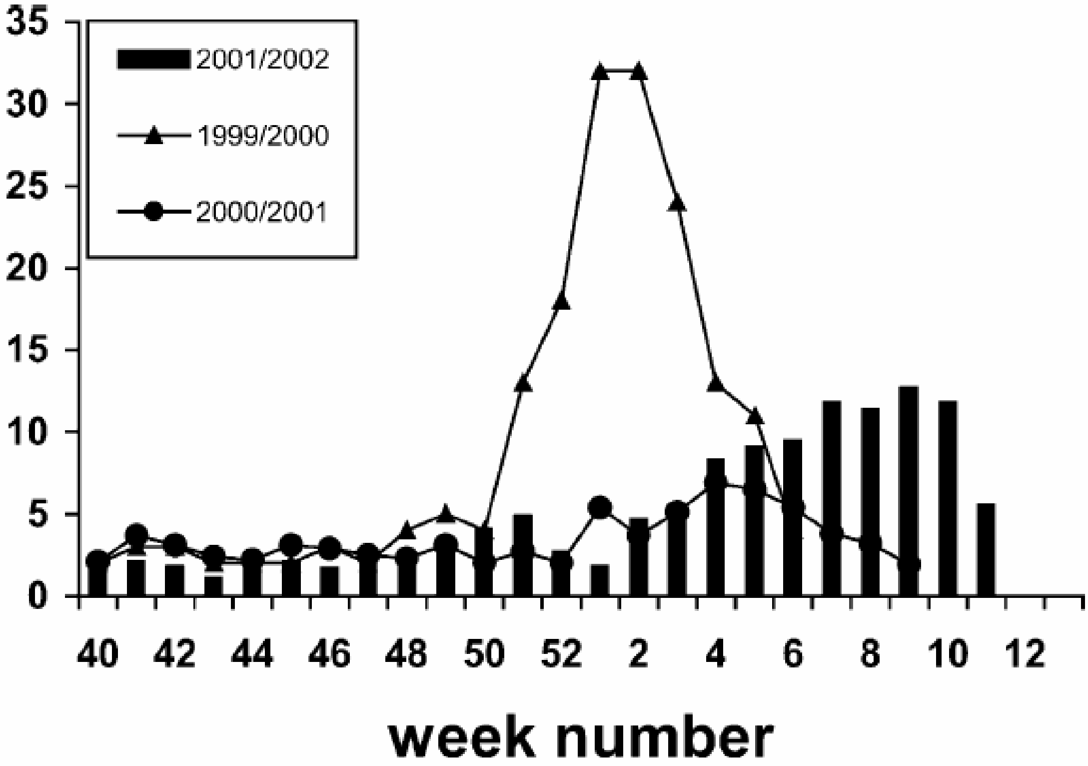

Fig. 1. Influenza activity in The Netherlands, number of influenza-like illnesses per week, per 10,000 inhabitants (1999–2002). *Source*: http://www.nivel.nl/influenza/images/grafiek10208.gif. Annual influenza surveillance monitoring is carried out by the National Influenza Centre in collaboration with the Sentinel Stations The Netherlands.

Table 1
Patient characteristics of the patients listed at the 30 or 40 practices in comparison with the Dutch population

	1999		2001	
	Listed at 30 practices, $n = 125,226$ (%)	Dutch population[a], $N = 15,760,225$ (%)	Listed at 40 practices, $n = 174,458$ (%)	Dutch population[b], $N = 15,987,075$ (%)
Age (years)				
<15	19	19	19	19
15–44	43	44	44	43
45–64	25	24	25	25
65+	13	14	13	14
Gender				
Female	51	51	50	51
Male	49	49	50	49
Health insurance				
Social health insurance	60	64	64	65
Private insurance	40	36	36	35

Source: CBS (in 2001, the data for insurance type are from July instead of January).
[a] In 01-01-1999.
[b] In 01-01-2001.

Table 2
Association (separate) of vaccination with the variables included in the propensity model (odds ratios and 95% confidence intervals)

Characteristics	1999–2000 OR (95% CI)	2001–2002 OR (95% CI)
Type of health insurance		
Private insurance	1.0	1.0
Social health insurance	1.47 (1.38–1.57)	1.42 (1.35–1.49)
Pulmonary disease		
No	1.0	1.0
Yes	0.84 (0.79–0.90)	0.97 (0.86–0.96)
Cardiovascular disease		
No	1.0	1.0
Yes	2.17 (2.00–2.36)	2.29 (2.14–2.45)
Diabetes mellitus		
No	1.0	1.0
Yes	1.99 (1.78–2.23)	2.00 (1.85–2.17)
Age (years)		
<65	1.0	1.0
65+	2.03 (1.90–2.16)	1.97 (1.88–2.07)
Number of contacts[a]		
Less than mean (0–4)	1.0	1.0
More than mean (5 or more)	2.11 (1.97–2.26)	2.30 (2.18–2.43)

[a] Number of contacts in 6 months before vaccination (mean number of contacts in 6 months before vaccination by all high-risk patients was 4.69 in 1999 and 4.12 in 2001).

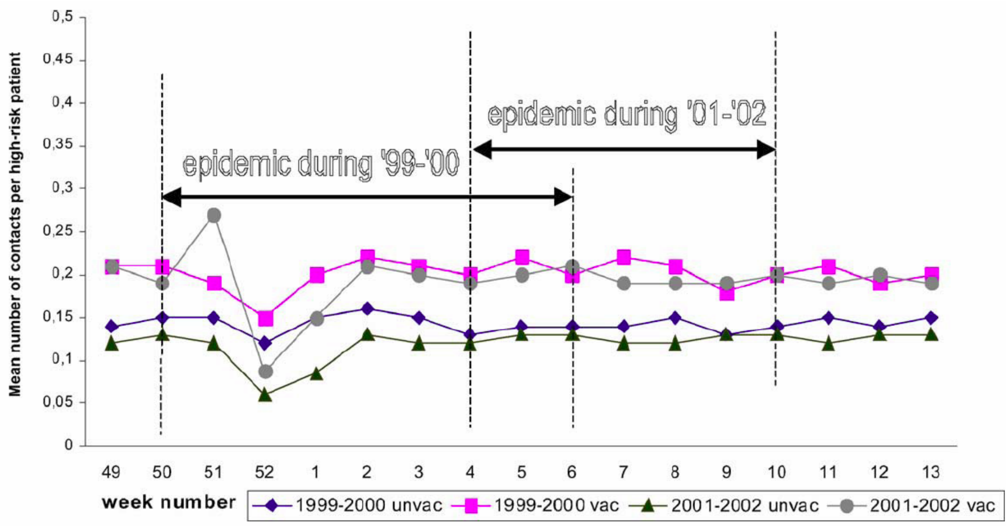

Fig. 2. Mean number of contacts per week by the high-risk patients (vaccinated and unvaccinated patients).

Table 3
Mean number of contacts in the epidemic period of season 1999–2000 (week 50–week 6) comparison between vaccinated and unvaccinated high-risk patients

	N	Mean number of contacts (unadjusted) during the epidemic period (*N*)		Adjusted difference in number of contacts		*P* levels
		Vaccinated		Vaccinated − unvaccinated	95% CI	
		No	Yes			
Total high-risk population[a]	24236	1.30 (5313)	1.81 (19051)	−0.06	−0.13 to 0.00	<0.1
Cardiovascular disease[b]	5705	1.88 (742)	2.35 (4963)	−0.26	−0.44 to −0.08	<0.05
Pulmonary disease[c]	7877	1.25 (1874)	1.97 (6003)	−0.05	−0.16 to 0.06	ns
Diabetes mellitus[d]	2944	2.23 (384)	2.56 (2560)	−0.29	−0.55 to −0.03	<0.05
Age 65+ (years)[a]	13474	1.40 (2211)	1.99 (11263)	−0.05	−0.15 to 0.05	ns
Age <65 (years)[a]	10890	1.22 (3102)	1.55 (7788)	−0.06	−0.14 to 0.02	ns

Note: Due to co-morbidity, patients may belong to more than one high-risk group.
[a] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication pulmonary condition, indication cardiovascular condition, indication diabetes mellitus (propensity model: AUC = 0.699).
[b] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication pulmonary condition, indication diabetes mellitus (AUC = 0.672).
[c] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication cardiovascular condition, indication diabetes mellitus (AUC = 0.675).
[d] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication pulmonary condition, indication cardiovascular condition (AUC = 0.676).

Table 4
Mean number of contacts in the epidemic period of season 2001–2002 (week 4–week 10 in 2002) comparison between vaccinated and unvaccinated high-risk patients

	N	Mean number of contacts (unadjusted) during the epidemic period (*N*) (vaccinated)		Adjusted difference in number of contacts		*P* levels[a]
		No	Yes	Vaccnated − unvaccinated	95% CI	
Total high-risk population[b]	38398	0.86 (9739)	1.36 (28659)	0.08	0.04 to 0.12	–
Cardiovascular disease[c]	7940	1.27 (1162)	1.74 (6778)	−0.02	−0.14 to 0.11	ns
Pulmonary disease [d]	10329	0.86 (2760)	1.44 (7569)	0.00	−0.08 to 0.07	–
Diabetes mellitus [e]	5035	1.39 (780)	1.98 (4255)	0.11	−0.05 to 0.27	–
Age 65+ (years)[b]	20967	0.93 (4097)	1.50 (16870)	0.10	0.03 to 0.16	–
Age <65 (years)[b]	17431	0.81 (5642)	1.16 (11789)	0.05	−0.01 to 0.09	–

Note: Due to co-morbidity, patients may belong to more than one high-risk group.
[a] Only reductions due to vaccination were tested.
[b] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication pulmonary condition, indication cardiovascular condition, indication diabetes mellitus (propensity model: AUC = 0.688).
[c] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication pulmonary condition, indication diabetes mellitus (AUC = 0.681).
[d] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication cardiovascular condition, indication diabetes mellitus (AUC = 0.684).
[e] Adjusted for age (continuous), type of insurance, number of contacts 6 months before vaccination, indication pulmonary condition, indication cardiovascular condition (AUC = 0.685).

Appendix A

Calculation of utilisation of primary care during the epidemic period in 1999–2000

1999	CV[a]	DM[b]
Number of high-risk patients at 30 practices	5797	2969
'Prevalence' (total number of patients at 30 practices = 125,226)	4.6%	2.4%
Per 1000 patients listed	4.6% of 1000 patients = 46	2.4% of 1000 patients = 24
Vaccination rate in 1999	86.7%	87.1%
Number of vaccinated patients per 1000 patients	86.7% of 46 = 40	87.1% of 24 = 21
Mean contact reduction per patient during epidemic period 1999–2000 (9 weeks)	0.26	0.29
Total contact reduction during epidemic period 1999–2000 (9 weeks) per 1000 patients	40 × 0.26 = 10.4	21 × 0.29 = 6.1

Due to co-morbidity patients may belong to both high-risk groups.
[a] CV: patients with cardiovascular diseases.
[b] DM: patients with diabetes mellitus.

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