A Pilot Study into the Comparative Effectiveness and Safety in the Elderly of a Homeopathic Flu Prophylaxis and the Regular Flu Vaccination in the Netherlands

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Abstract

A prospective observational pilot study was conducted in the Netherlands between October 12, 2013 and February 21, 2014 to measure the effectiveness and safety of three immunisation options against influenza, as well as changes in participants' well-being. It appears that vaccination against influenza may not be the most effective and safest option and that the use of homeoprophylaxis against influenza should be studied in larger cohorts.

Keywords

- influenza
- immunisation
- vaccination
- homeoprophylaxis
- effectiveness
- safety

Introduction

Influenza is an annual seasonal problem in most countries. It is common for different strains of influenza to be active in successive years. In most Western countries the onset of cooler weather is accompanied by calls by public health officials for people who may be badly affected by the flu to be vaccinated.

The effectiveness of the flu vaccination ranges between 10 and 60% according to the Centers for Disease Control in the United States,[1] and may cause influenza-like symptoms in some people.[2] Homeopathic prophylaxis against influenza has been used for decades around the world. While stand-alone studies exist measuring the effectiveness of homeopathic influenza prophylaxis,[3] no studies measuring its comparative effectiveness to vaccination have been undertaken.

This paper describes the findings of a prospective observational pilot study which took place in the Netherlands between October 12, 2013 and February 21, 2014 comparing the effectiveness and safety of three influenza immunisation options in 150 patients aged between 60 and 85 years, of a family physician, including (1) regular flu vaccination (Vaxigrip, 2013–2014), (2) a homeopathic flu prophylaxis (HgP)[a] (Poly Influenzinum combi C200 Influvac, Vaxigrip, 2013–2014), and (3) no immunisation.

Method

Formal ethics approval was not sought for the in-house pilot study, although standard protocols were followed. In this study posters and a covering letter describing the study were prepared in advance. The posters in both Dutch and English were displayed in the practice of the family doctor located in the South of the Netherlands a few days before influenza vaccinations scheduled on October 22 and 24, 2013. Recruitment into the study occurred in the following way.

Cohort 1: Patients Who Chose Vaccination

Cohort 1A was vaccinated on October 22, 2013. Cohort 1B was vaccinated on October 24, 2013. Patients' permission was sought to cooperate in the investigation while waiting in line for the vaccination. Personal data and a well-being score were also requested from patients who gave permission before they were vaccinated. After this brief interview they received

[a] HgP as Dutch for influenza is 'griep'.

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a covering letter which explained exactly what was expected of them. Accompanying this letter were two questionnaires with the date on which the researcher (Gerrie Hasselaar) would call.

Cohort 2: Patients Who Chose Homeopathic Immunisation

Patients in cohort 2 were recruited by GH following advice by the doctor of patients who requested (and usually received) homeopathic flu immunisation. These participants were sent a covering letter and three questionnaires. GH then contacted the participants by telephone, during which consent was requested. In this first interview the consenting participants graded their feeling of well-being at that time, and were advised about the scheduled dates for taking the HgP. The dosing schedule consisted of taking 3 gr of the HgP weekly for the first 3 weeks, and then 4 gr every 3 weeks until March 2014.

It was agreed that 2 months after this phone interview, they would be contacted again by GH in December 2013 for the middle interview, and then again in February 2014 for the final interview. The data from this cohort were collected between October 24, 2013 and February 21, 2014.

Cohort 3: Patients Who Chose to Use No Method of Immunisation against Influenza

Cohort 3 patients were recruited by GH following advice by the doctor of patients who had not requested either vaccination or homeopathic flu immunisation. In the week before November 1, 2013, this cohort was sent a covering letter with three questionnaires. The premeasurement of cohort 3 was undertaken by GH by telephone on November 1, 2013 during which consent to participate was obtained. The second interview by telephone by GH followed on December 27, 2013, and the final interview was held via telephone February 21, 2014.

In all 152 persons were invited to participate and 2 declined. The relevant numbers and dates are shown in ►**Table 1**.

An outline of the questionnaires used in the survey is shown in ►**Fig. 1**. Participants were first asked to confirm their immunisation status. Then they were asked whether or not they had contracted an influenza-like illness. If 'yes', the date of the first symptoms was recorded, whether these were confirmed by a doctor and whether the symptoms were mild, moderate or severe. The next two questions for cohorts 1 and 2 participants concerned any residual effects from the immunisation, and if so, how many days before the symptoms started, whether recovery had occurred, and a description of the symptoms. The fifth question asked participants to rank their well-being by recording a number between 1 and 10, where 1 was very poor and 10 very good. The final question asked respondents to assess whether or not their health had changed after the immunisation (or after November 1, 2013 for cohort 3 respondents), and if so, whether it had decreased or increased.

Table 1 Timing of questionnaires

Cohort	Recruited	Number	Follow-up	
			Q2	Q3
1A	22.10.13	47	17.12.13	11.2.14
1B	24.10.13	36	19.12.13	13.2.14
2	12.10.13	19	12.12.13	21.2.14
3	1.11.13	48	27.12.13	21.2.14
	Total	150		

Results

►**Table 2** shows the average age and the number of males and females in each cohort within the study population.
►**Table 3** shows the incidence of an influenza-like illness at the 2nd and 3rd interview, and whether it was confirmed by the GP (*Diag GP*). The intensity of the symptoms is classified as being mild, moderate or severe.
►**Table 4** compares the attack rates for each option. Note that it was not possible to determine whether participants were exposed to the influenza virus.
►**Table 5** shows Odds ratio and Chi Squared calculations for the three immunization options.
►**Table 6** compares the relative risk associated with each of the three immunization options at both the 2nd and the 3rd interviews.
►**Fig. 2** shows comparisons between the three immunisation options and three rankings of the severity of influenza.
►**Table 7** reports the timing of adverse reactions to vaccination and HgP. It is impossible to know if a reaction that occurred weeks after an immunization was or was not directly related to the procedure.
►**Table 8** shows a summary of the type and timing of reactions to vaccination. Both of the reported reactions to HgP related to cold/flu like symptoms.
►**Table 9** shows the percentage of participants in each wellbeing score at each of the three interviews.
►**Table 10** shows the reported changes in health at the 2nd and 3rd interviews.

The health changes are described graphically in ►**Fig. 3**.

Discussion

The findings of the pilot study will be considered under three subheadings: effectiveness, reactions/safety and well-being.

Effectiveness

The attack rates shown in ►**Table 4** and the calculations presented in ►**Tables 5** and **6** suggest that the vaccinated cohort were clearly the most likely to acquire an influenza-like illness. The small numbers in the study, uncertainty regarding exposure, plus the lack of demographic analysis mean that this result may not transfer to the wider community, but if it did, it would have significant ramifications for public health policy regarding influenza vaccination.

QUESTIONNAIRE 1:
Date: ..... Personal details: .....

Do you give permission to use your information for research? Y/N
IF Yes

Q1. Immunisation-status for Influenza in 2013 (please tick the appropriate box) :
- O Orthodox vaccination (date .....)
- O Homeopathic flu prophylaxis (date .....)
- O No immunization against the flu

Q2. How are you feeling right now?
Give a number between 1- 10, with 1 being very poor and 10 being very well .....

QUESTIONNAIRE 2: and QUESTIONNAIRE 3:
Date: ..... Personal details: .....

Q1. Immunisation status for Influenza in 2013 (please tick the appropriate box):
- [ ] Orthodox vaccination (date .....)
- [ ] Homeopathic flu prophylaxis (date .....)
- [ ] No immunization against the flu

Q2. Did you get the flu? Yes/No
If Yes, date symptoms first began: .....
If Yes, was this flu confirmed by a doctor? Yes / No
If Yes, please circle whether the symptoms were mild / moderate / severe

Q3. If you were vaccinated, did you suffer any adverse reactions following the vaccination? Yes/No
If Yes, how many days following the vaccine did the symptoms begin? ... .
If Yes, have you now fully recovered from your adverse reaction? Yes/No
If Yes, please describe your symptoms:
.....

Q4. If you used homeopathic prophylaxis, did you suffer any adverse reactions following the homeopathic prophylaxis? Yes / No
If Yes, how many days following the medicine did the symptoms begin? .....
If Yes, have you now fully recovered from your adverse reaction? Yes/No
If Yes, please describe your symptoms:
Q5. How are you feeling right now?
Give a number between 1-10, with 1 being very poor and 10 very well. .....

Q6. If you were vaccinated or used homeopathic prophylaxis, has your health changed after: Yes/No
If Yes, from the procedure until todays date, please circle whether your health and overall wellbeing has: increased/decreased

NOTE: Cohort 3 respondents were asked to assess changes from 1/11/13

Fig. 1 Outline of the questionnaires.

However, the three cohorts were patients of a single-family physician, which should increase the chances of demographic homogeneity.

Table 2 Composition of study population; sex/age

Cohorts	Total	Male	Female	Av. age
Vaccinated	83	32	51	70
%	55.3	38.6	61.4	
HgP	19	6	13	72
%	12.7	31.6	68.4	
Nothing	48	28	20	67
%	32.0	58.3	41.7	
Total	**150**	**66**	**84**	**69**
%		44.0	56.0	

Abbreviation: HgP, homeopathic flu prophylaxis.
Note: This table shows the average age and the number of males and females in each cohort within the study population.

The comparison between the HgP and the no-immunisation cohort is less clear. The HgP attack rate was 0% after 2 months and 5.5% after 4 months. The no-immunisation cohort showed 6.3 and 2.1%, respectively. The smaller numbers clearly limited the generalisability of the comparison. The larger incidence after 4 months for the HgP cohort may suggest that use of a different remedy for HgP should be considered in future research (e.g., *Nosodes* or *Genus Epidemicus* remedies instead of vaccine potencies), or a different potency or dosing regimen.

Reactions/Safety

►**Table 7** reports the number and timing of adverse reactions to vaccination and HgP. There were five times more reactions within the first week in the vaccinated cohort compared with the HgP cohort. Over a quarter of vaccinated respondents reported, a reaction within the first week was compared with 5.3% in the HgP cohort.

The type and timing of reactions to vaccination are shown in ►**Table 8**. A quarter of reactions related to pain and soreness at the injection site. Over one-third of all reactions to vaccination were cold and flu like symptoms, 13.9% were

Table 3 The incidence and severity of influenza

2nd interview	Total	Influenza-like illness		Severity (% of 'yes')			
		Yes	Diag GP	Mild	Mod.	Severe	ND
Vaccinated	83	11	2	3	6	2	0
%	55.3	13.3	18.2	27.3	54.5	18.2	0.0
HgP	19	0					
%	12.7	0					
Nothing	48	3	0	1	1	0	1
%	32.0	6.3	0.0	33.3	33.3	0.0	33.3
Total	**150**	**14**	**2**	**4**	**7**	**2**	**1**
%		9.3	14.3	28.6	50.0	14.3	7.1
3rd interview							
Vaccinated	83	15	2	7	6	2	0
%	55.3	18.1	13.3	46.7	40.0	13.3	0.0
HgP	19	1		1			
%	12.7	5.5		100.0			
Nothing	48	1	0	1	0	0	0
%	32.0	2.1	0.0	100.0	0.0	0.0	0.0
Total	**150**	**17**	**2**	**9**	**6**	**2**	**0**
%		11.3	11.8	52.9	35.3	11.8	0.0

Abbreviations: GP, general practitioner; HgP, homeopathic flu prophylaxis; ND, no details.
Note: This table shows the incidence of an influenza-like illness at the second and third interviews, and whether it was confirmed by the GP (*diag GP*). The intensity of the symptoms is classified as being mild, moderate or severe.

gastrointestinal reactions, and the remainder were reports of muscle aches, weakness, and from one respondent who lost consciousness and collapsed following the vaccination.

The two respondents reporting a reaction to HgP described cold and flu-like symptoms.

Well-Being

The measures of well-being and health changes shown in ►**Tables 9** and **10** respectively give somewhat conflicting indications. The exception is that overall health and well-being declined from October 2013 to February 2014. The most obvious explanation is that the effects of winter impacted all cohorts.

The well-being measures in ►**Table 9** show that the HgP cohort reported the lowest initial measure of well-being, but that their well-being declined less over the 4 months of

Table 4 Attack rates of influenza-like illness in three cohorts at two measurement periods

Immunisation option	Interview		Both periods
	2nd	3rd	
	Attack rate (%)		
Vaccinated	13.3	18.1	31.3
HgP	0.0	5.5	5.3
Nothing	6.3	2.1	8.3

Abbreviation: HgP, homeopathic flu prophylaxis.
Note: This table compares the attack rates for each option. Note that it was not possible to determine whether participants were exposed to the influenza virus.

Table 5 Odd ratios[b] and Chi Squared probability[c] in three immunisation options

Cohorts	OR	Chi sq
Vaccinated: not Vaccinated	5.66	0.000
HgP: not HgP	0.19	0.076
No-immunisation: immunised	0.25	0.010

Abbreviations: HgP, homeopathic flu prophylaxis; OR, odds ratio.
Note: This table shows OR and chi-squared calculations for the three immunisation options.

[b] "the **odds ratio** (usually abbreviated "OR") is one of three main ways to quantify how strongly the presence or absence of property A is associated with the presence or absence of property B in a given population."

[c] "Chi-square is a statistical test commonly used to compare observed data with data we would expect to obtain according to a specific hypothesis. The chi-square test is always testing what scientists call the **null hypothesis,** which states that there is no significant difference between the expected and observed result."

Table 6 Comparison of relative risks at second and third interviews

	2nd interview	3rd interview
Vaccination	2.96	6.05
HgP	0.00	0.43
Nothing	0.57	0.13

Abbreviation: HgP, homeopathic flu prophylaxis.
Note: This table compares the relative risk associated with each of the three immunisation options at both the 2nd and the 3rd interviews.

the study than in the other cohorts. Well-being in the no-immunisation cohort declined the most. However, this was reversed in ►**Table 10** showing changes in health where the vaccinated cohort reported the greatest net decline in health with the no-immunisation cohort the least.

The apparent inconsistency in these findings suggests that participants in future studies may need a clearer explanation of what is meant by health and well-being, and/or that additional information may need to be collected in any subsequent studies. In particular, the use of standard and validated questionnaires for quality of life should be considered.

Conclusion

The purpose of this pilot study was to compare the safety and effectiveness against influenza of vaccination, HgP and no-immunisation. If the results could be taken without qualification, it could be concluded that vaccinated people are much more likely to acquire influenza-like symptoms than people using HgP or doing nothing, and that vaccination causes significantly more adverse reactions than HgP. None of the three immunisation options produced unambiguously greater or lower health or well-being effects

However, the findings must be qualified due to the small size of each cohort. It was impossible to know whether influenza exposure rates were similar for each cohort, although the fact that participants were all patients at the one medical clinic suggests that demographic bias would be low. There was some difference in the male/female ratio in the three groups. Other demographic data encompassing possible confounders were not collected.

Questions concerning the choice of and dosing with the HgP remedy should be addressed before a larger study is undertaken, as should be the methodology to measure well-being and health changes in participants.

Further research involving large cohorts is warranted, as there is an indication from this pilot study that public health officials may not be promoting the most beneficial method of

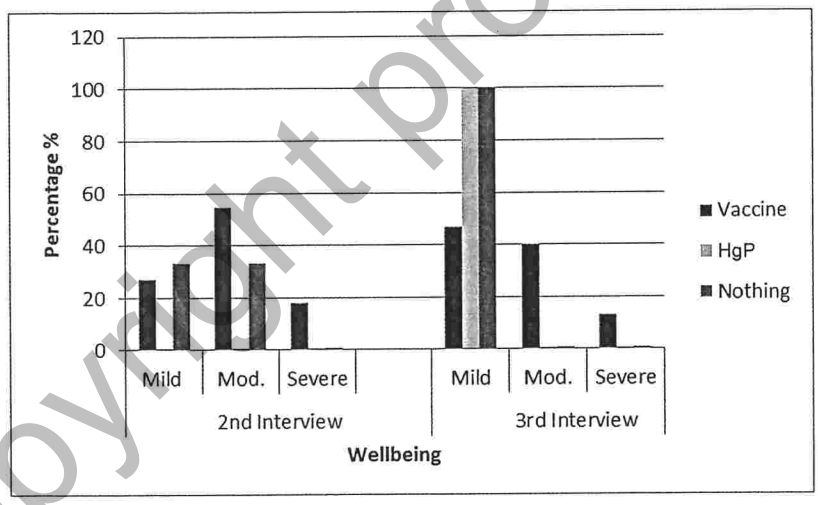

Fig. 2 Severity of influenza-like illness by immunisation option. HgP, homeopathic flu prophylaxis.

Table 7 Number and timing of adverse reactions to vaccination and HgP

	Total	Reacted—days following				
		Yes	1–7	8–14	15–28	ND[a]
Vaccinated	83	33	22	2	2	7
%		39.7	26.5	2.4	2.4	8.4
HgP	19	3	1	0	0	2
%		15.8	5.3	0.0	0.0	10.5

Abbreviations: HgP, homeopathic flu prophylaxis; ND, no details.
[a]ND given for timing of reaction, or reaction more than 28 days after immunisation.
Note: This table reports the timing of adverse reactions to vaccination and HgP. It is impossible to know if a reaction that occurred weeks after an immunisation was or directly related to the procedure or not.

Table 8 Type and timing (days following vaccination) of reactions to vaccination

Type of Reaction	#[a]	%	1–7[a]	8–14	15–28	ND[a]
Site of injection	10	26.3	10	0	0	0
Gastrointestinal	4	10.5	2	0	0	2
Cold/flu-type symptoms	15	39.5	8	2	2	3
Muscle aches	3	7.9	2	0	0	1
Weakness/heaviness	4	10.5	4	0	0	0
Collapse	1	2.6	0	0	0	1
Unclear	1	2.6	0	0	0	1
Totals	**38**	**100.0**	**26**	**2**	**2**	**8**

Abbreviation: ND, no details.
[a]Includes multiple responses.
Note: This table shows a summary of the type and timing of reactions to vaccination. Both of the reported reactions to HgP were related to cold/flu-like symptoms.

Table 9 Figures for well-being (%)

Cohort	Interview	Well-being (%)								
		4	5	6	7	8	9	10	NR	Av.
Vaccinated	1st	1.2	6.0	12.0	27.7	34.9	14.5	3.6	0.0	7.5
	2nd	0.0	9.6	7.2	36.1	33.7	12.0	1.2	0.0	7.4
	3rd	2.4	4.8	16.9	27.7	34.9	7.2	4.8	1.2	7.3
HgP	1st	0.0	15.8	15.8	26.3	31.6	10.5	0.0	0.0	7.1
	2nd	0.0	10.5	26.3	36.8	15.8	10.5	0.0	0.0	6.9
	3rd	5.3	5.3	21.1	31.6	26.3	10.5	0.0	0.0	7.0
Nothing	1st	0.0	2.1	6.3	18.8	39.6	18.8	14.6	0.0	8.1
	2nd	0.0	4.2	6.3	25.0	33.3	14.6	14.6	2.1	7.8
	3rd	0.0	4.2	6.3	29.2	35.4	10.4	10.4	4.2	7.4
Total	1st	0.7	6.0	10.7	24.7	36.0	15.3	6.7	0.0	7.6
	2nd	0.0	8.0	9.3	32.7	31.3	12.7	5.3	0.7	7.5
	3rd	2.0	4.7	14.0	28.7	34.0	8.7	6.0	2.0	7.3

HgP, homeopathic flu prophylaxis; NR, no response
Note: This table shows the percentage of participants in each well-being score at each of the three interviews.

Table 10 Changes in health reported at 2nd and 3rd interviews

Cohorts	Total	Health changed					
		2nd interview			3rd interview		
		Yes	Increased	Decreased	Yes	Increased	Decreased
Vaccinated	83	13	3	10	21	0	21
%	55.3	15.7	3.6	12.0	25.3	0.0	25.3
HgP	19	2	0	2	6	1	5
%	12.7	10.5	0.0	10.5	31.6	5.3	26.3
Nothing	48	12	6	6	8	3	5
%	32	25	12.5	12.5	16.7	6.3	10.4
Total	**150**	**27**	**9**	**18**	**35**	**4**	**31**
%		18.0	6.0	12.0	23.3	2.7	20.7

Abbreviation: HgP, homeopathic flu prophylaxis.
Note: This table shows the reported changes in health at the second and third interviews.

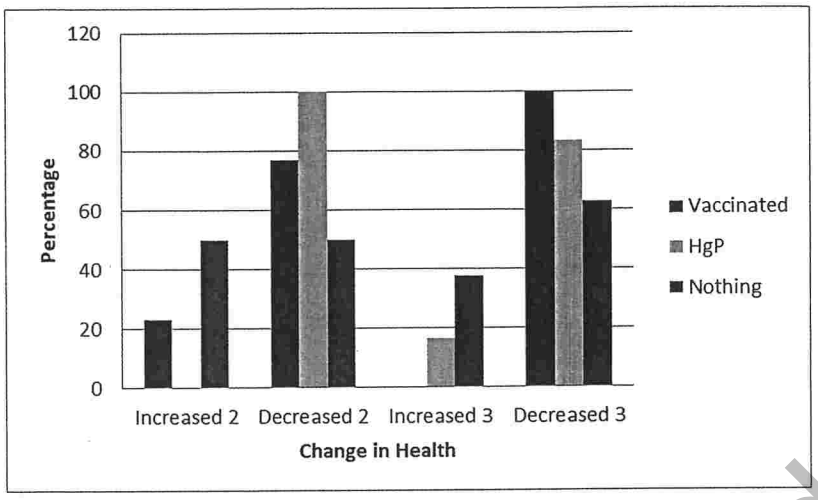

Fig. 3 Comparison health changes at second and third Interviews. HgP, homeopathic flu prophylaxis.

influenza prevention when assessed by means of measurements of effectiveness and safety.

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