



To the Minister of Health, Welfare and Sport

Subject : Presentation of advisory letter *Vaccination against seasonal influenza 2010-2011*
Your reference : PG-CI 2.995.461
Our reference : I-488/10/HH/db/824-S Publication no. 2010/05E
Enclosure(s) : 1
Date : April 8, 2010

Dear Minister,

The Health Council of the Netherlands and the Centre for Infectious Disease Control (CIb) at the National Institute for Public Health and the Environment (RIVM) jointly monitor national and international developments relating to the pandemic of influenza A/H1N1 2009. Within the scope of this, on 29 March 2010 you requested an advisory report on vaccination against seasonal influenza 2010-2011. The World Health Organisation (WHO) expects influenza A/H1N1 2009 to be the dominant influenza virus in the coming season in the Northern Hemisphere; and also thinks influenza A/H3N2 and B may continue to cause influenza. The vaccine for the 2010-2011 season therefore includes influenza A/H1N1 2009, influenza A/H3N2 and influenza B.

In the 2009-2010 season, on the recommendation of the Health Council and CIb/RIVM, pregnant women, children and members of households with very young children were indicated for vaccination against the pandemic influenza A/H1N1 virus, in addition to the usual target groups for vaccination against seasonal influenza. The question now arises as to whether pregnant women, children and household members should also be offered vaccination against influenza A/H1N1 2009 in the 2010-2011 season.

In view of the short period within which you requested the advisory report, we have presented your questions and our recommendations in writing to the same experts we consulted last year. Moreover, we consulted a number of them by telephone on 1 April 2010. In providing answers we limited ourselves to your questions that are of immediate importance for policy.



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Do you see any reason to again indicate for vaccination against the same virus the groups that were specifically indicated last year for vaccination against pandemic influenza A/H1N1 2009, namely pregnant women as of the 2nd trimester, children aged from 6 months up to and including 4 years and members of households that include children younger than 6 months old?

Previous advisory reports on seasonal influenza

In 2007 the Health Council of the Netherlands advised against vaccinating these groups against seasonal influenza, insofar as the people concerned did not have a medical condition which constituted an indication for vaccination. The reason for this in the case of pregnant women and children older than two years was that no clear increase had been demonstrated in the burden of the disease and likelihood of death. However, in the case of children between the age of 6 months and 2 years, it had been demonstrated that there was an increased risk of influenza and the associated complications but that there was no clear excess mortality and that there was a lack of data on the efficacy of the available vaccines in this age category. No studies have been conducted on the use of influenza vaccines in children younger than 6 months old, nor are the vaccines authorised for any such use.

Children and household members

Previous analysis of data on the course of the A/H1N1 2009 influenza pandemic in other countries indicated a high proportion of children in the age group up to five years were affected; there was a high number of hospital admissions for this age group and some of these children had to be placed in an intensive care ward and on a respirator. There is a risk of long-term damage to the lungs of young children who are given artificial respiration. Consequently, the Health Council's advice last autumn was for vaccination against influenza A/H1N1 2009 for children from 6 months up to and including four years and for members of households which included babies younger than six months. Another reason for this advice was to avoid any excessive burden being placed on intensive care wards for children in the event of the course of the pandemic being severe. Unpublished analyses conducted by the National Institute for Public Health and the Environment (RIVM) now show that complications and disease resulting from influenza A/H1N1 2009 did not occur more frequently during the 2009-2010 season than normally with seasonal influenza. The mild course of the pandemic meant that there was no excessive burden on the health services. Studies conducted in other countries produced a similar picture.^{1,2}



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In the light of these considerations, we are of the opinion that vaccination of healthy young children (or members of their household) is not indicated for the 2010-2011 season.

Pregnant women

Healthy pregnant women were indicated for vaccination against influenza A/H1N1 in 2009 because the limited data available at the time suggested an increased risk of complications with this pandemic virus in particular.

A recent as yet unpublished analysis by RIVM of data in the Netherlands shows that the proportion of pregnant women among patients admitted to hospital was clearly higher than the proportion of pregnant women in the general population. However, it is not known how much this differs from other years. All admissions of pregnant women to an intensive care ward in the Netherlands involved an underlying medical condition. There were no deaths of pregnant women in the Netherlands who had been diagnosed as having influenza A/H1N1 2009.

It emerged from international scientific publications that pregnant women infected with influenza A/H1N1 2009 had an increased risk of complications developing.³⁻⁷ However, it is difficult to assess on the basis of the available data to what extent pregnancy itself is a risk factor for the development of complications, as the aforementioned analyses had not been systematically corrected for other factors that may have affected the course of the illness. Examples of such factors include medical risk factors in the case of infection by influenza, and the accessibility and organisation of health services.

Making such a thorough assessment of the available data would require more detailed discussions with experts than has thus far been possible. We hope to be able to provide you with a more specific advisory report this summer, on the basis of such discussions. At the moment, we recommend you to assume that pregnant women should be offered vaccination against influenza A/H1N1 2009 in the 2010-2011 season. *Vis-à-vis* the number of vaccine doses provided annually to people in the known target groups for influenza vaccination, which is around five million, vaccinating pregnant women as of the second trimester in the period concerned will only involve a small number of doses, estimated to be no more than 100,000.



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The Netherlands still has a stock of adjuvanted vaccine against pandemic influenza A/H1N1 2009. These vaccines will still be suitable for use in the coming influenza season. The influenza vaccines that manufacturers are producing for the 2010-2011 influenza season also provide protection against influenza A/H1N1 2009. Are the two vaccines sufficiently safe and efficacious to use for vaccinating the various target groups or is one preferable?

Only adjuvanted vaccine was available last autumn for the vaccination campaign against influenza A/H1N1 2009 in the Netherlands. There are now strong indications that also the non-adjuvanted vaccines against A/H1N1 2009 are efficacious.^{8,9} We are of the opinion that the same vaccine should be used for all target groups, namely the one given against seasonal influenza.

Will one dose of the vaccine be sufficient for the medical risk groups that will be vaccinated in the coming influenza season, as they are every year, within the scope of the National Influenza Prevention Programme?

To provide optimum protection for people with a medical condition that warrants placing them in risk groups for influenza, the aim should be for vaccination to provide the highest possible level of efficacy. With this consideration in mind and in view of the threat of a pandemic, we maintained the primary dose recommendation of the European registration authorities for vaccination against influenza A/H1N1 2009, namely a vaccination schedule comprising two doses. This advice was based on research conducted using model vaccines. However, various studies have now revealed that the available vaccines against influenza A/H1N1 2009, including the non-adjuvanted, lead to a relatively high antibody response.⁸⁻¹³ However, no data have thus far been published on the actual protection against disease. Nevertheless, in the case of vaccines against seasonal influenza it is normal practice to work on the basis of antibody levels and considerable experience has been accumulated on this over years. On the basis of these considerations and the mild course of the pandemic in 2009-2010, our starting point for the 2010-2011 season is a single dose of vaccine, as is usual for vaccination against seasonal influenza outside the context of a pandemic; children older than 6 months who have not previously been vaccinated against influenza A/H1N1 2009 will require two doses.



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As mentioned, the Health Council of the Netherlands and the CIb/RIVM will make further recommendations this summer on the vaccination of pregnant women. We will also continue to monitor more general developments concerning influenza.

Yours sincerely,

(signed)

Professor J.A. Knottnerus MD PhD
President, Health Council of the
Netherlands

(signed)

Professor R.A. Coutinho MD PhD
Director, RIVM Centre for
Infectious Disease Control



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The request for advice

Date of request: March 29,2010; reference: PG/CI-2.955.461

I received five advisory reports in 2009 on vaccination against pandemic influenza A (H1N1). On 8 May 2009 the Health Council of the Netherlands presented its initial advisory letter: 'Vaccination against Mexican flu'. The Health Council and the National Institute for Public Health and the Environment (RIVM) jointly presented further advisory reports on this subject in 2009, on 17 August, 17 September, 9 and 25 November. These advisory reports formed the basis for a large-scale vaccination campaign in the Netherlands in the autumn of 2009 against pandemic influenza A (H1N1).

Besides the risk groups that qualify every year for vaccination against seasonal influenza, you designated two new groups in 2009 that would qualify for the vaccination on medical grounds. The groups were pregnant women as of the 2nd trimester and children from 6 months up to and including 4 years. You also recommended vaccinating members of households which included children younger than 6 months old in view of the envisaged additional indirect protection it would provide the young children concerned. I adopted your recommendations and the people in the aforementioned risk groups were invited last year to have the pandemic vaccination.

The pandemic influenza virus A (H1N1) is still circulating. Consequently, on the advice of the WHO, this strain has been included in the influenza vaccines manufacturers are producing this year for the 2010-2011 influenza season. This brings me to the question of whether the target groups that were added to the list of those qualifying for vaccination against pandemic Influenza A (H1N1) in 2009

should also be offered the influenza vaccination this year. I request you to produce an advisory report on this. I have the following specific questions:

- 1 Do you see any reason to again indicate for vaccination against the same virus the groups that were specifically indicated last year for vaccination against pandemic influenza A (H1N1), namely pregnant women as of the 2nd trimester, children aged from 6 months up to and including 4 years and members of households that include children younger than 6 months old?

If yes,

- a Is there an indication for vaccination again this year in the case of people in the aforementioned groups who were vaccinated (once or twice) last year against pandemic influenza A (H1N1)?
 - b The Netherlands still has a stock of adjuvanted vaccine against pandemic influenza A (H1N1). These vaccines will still be suitable for use in the coming influenza season. The influenza vaccines that manufacturers are producing for the 2010-2011 influenza season will also provide protection against pandemic influenza A (H1N1). Are the two vaccines sufficiently safe and effective to use for vaccinating the various target groups or is one of these vaccines preferable?
 - c Will one efficacious dose of the vaccine be sufficient for these target groups?
 - d What is the optimum period within which vaccination should be offered to provide sufficient protection and would you be able to state the latest possible date?
- 2 Following on from the above, I also request you to answer questions 1c and 1d for the medical groups that are vaccinated every year within the scope of the National Influenza Prevention Programme.

It will be necessary to make preparations for organising the vaccination of extra groups, if I decide to do so on your advice. Any such decision will have to be communicated to those concerned in good time and it may be necessary to start a new time-consuming tendering procedure. I therefore request you to send me your recommendations by no later than 2 April 2010.

The Minister of Health, Welfare and Sport,
(signed)
dr. A. Klink

The experts

This advisory letter is the result of cooperation between the Health Council of the Netherlands and the Centre for Infectious Disease Control (CIb) at the National Institute for Public Health and the Environment (RIVM) on the basis of written consultations and consultations conducted on 1 April 2010 by telephone with experts.

The following persons participated in the telephone consultations or were consulted prior to that in writing:

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 - Dr. M.A.E. Conyn-van Spaendonck
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 - Professor R.A. Coutinho
Epidemiologist/ virologist, Director of the RIVM Centre for Infectious Disease Control, Bilthoven
 - Professor J.T. van Dissel
Internist-infectiologist, University Medical Center, Leiden
 - G.D. van Dijk, *observer*
Ministry of Health, Welfare and Sport, The Hague
 - Professor W. van Eden
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- G. A. van Essen PhD
Research Fellow in General Practice, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht
 - Professor R. de Groot
Professor of paediatrics, St Radboud University Medical Centre, Nijmegen
 - Dr. E. Hak
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 - Professor E.K. van de Velden
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The Health Council and interests

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