

H1N1 influenza vaccination and the risk of childhood narcolepsy

IN MARCH, 2012 A SIGNIFICANT INCREASE in the rate of childhood narcolepsy associated with the influenza vaccine Pandemrix (GlaxoSmithKline) was reported in Finland.¹ This vaccine was administered to over 30 million people in Europe to provide protection during the 2009 H1N1 pandemic. Following the observation in Finland, the European Centre for Disease Prevention and Control commissioned two reports to investigate the rates of narcolepsy in Sweden, Finland, Denmark, Italy, France, the Netherlands, Norway and the United Kingdom. The report concluded that:²

1. There was no increase in the rates of narcolepsy due to the 2009 pandemic itself
2. An increase in the rate of childhood narcolepsy in Finland and Sweden had occurred with Pandemrix vaccination
3. There was no detectable association between influenza vaccination and childhood or adult narcolepsy in the Netherlands, Italy, the United Kingdom, Norway* and Denmark**
4. A significantly increased risk of narcolepsy in adults, associated with Pandemrix vaccination did occur in France, although the risk of selection bias could not be excluded. This result should be interpreted with caution and is being investigated further.

* The data from Norway is problematic as individuals presenting with narcolepsy prior to 2008 could not be clearly identified

** An increase in the rates of narcolepsy was detected in Denmark, however, this trend started before the introduction of the vaccination campaign.

In February, 2013, a study from the United Kingdom also reported an increase in childhood narcolepsy associated with Pandemrix vaccination. This study retrospectively reviewed the medical records of 245 young people aged four – 18 years, who had been identified by an expert panel as being likely to have narcolepsy.³ In April, 2013, a Swedish study of 37 children with narcolepsy, found that nine of the children had onset of narcolepsy symptoms before vaccination with Pandemrix, and 28 had onset post-vaccination.⁴ The authors calculated the incidence of narcolepsy to be 25 times higher after vaccination compared with the period before vaccination.⁴

Within the literature, estimates of the number of children who need to be vaccinated with Pandemrix for one instance of childhood narcolepsy to develop ranges from 13 000 to 57 500 children.^{1,3}

Influenza vaccination guidelines remain unchanged in New Zealand

Any association between influenza vaccination and narcolepsy does not appear to be a worldwide phenomenon.⁵ There have been no reports linking influenza vaccination to narcolepsy in New Zealand. In Canada, a vaccine similar to Pandemrix was used and no increases in narcolepsy have been reported.⁵ The United States Centres for Disease Control and Prevention continues to recommend influenza vaccination to protect individuals from influenza and its complications, and there have been no reports of narcolepsy associated with vaccination.⁶

The following points should also be considered when placing the results of European studies on narcolepsy risk and influenza vaccination into a New Zealand context:

- Pandemrix is the only vaccine, for any disease, that has ever been associated with an increased risk of narcolepsy
- Pandemrix has never been used in New Zealand
- The use of Pandemrix is now restricted in people aged under 20 years⁵
- The strain of inactivated virus contained in the 2013 New Zealand influenza vaccines Fluarix (GlaxoSmithKline) and Fluvax (CSL) is different to Pandemrix (Table 1)
- Pandemrix uses an oil-in-water adjuvant to boost the individual's immune response. Fluarix and Fluvax both use a phosphate-buffered saline adjuvant
- Pandemrix was specifically created for the 2009 H1N1 influenza pandemic whereas Fluarix and Fluvax also provide protection against three seasonal influenza strains: A/California (N1N1pdm09), A/Victoria (H3N2) and B/Winsconsin
- The influenza vaccines used in New Zealand in 2009 were also different to Pandemrix and provided protection against seasonal A(H1N1), A(H3N2) and B/Florida strains of influenza

Table 1: H1N1 vaccines and the strains of virus used to generate the 2009 Pandemrix and 2013 Fluarix and Fluvax vaccines^{2, 7, 8}

Vaccine	H1N1 strain used in vaccine production
Pandemrix	X-179A
Fluarix	NIB-74xp
Fluvax	NYMC X-181

How could Pandemrix cause an increase in childhood narcolepsy?

Narcolepsy is a rare condition caused by the selective loss of cells in the hypothalamus that regulate arousal. An autoimmune mechanism for narcolepsy has been proposed that includes both genetic and environmental factors.⁴ Most children with narcolepsy share the same leukocyte antigen and in the Swedish study it was reported that all the children who developed narcolepsy following vaccination with Pandemrix had this antigen. Therefore it is possible that rather than increasing the prevalence of narcolepsy, Pandemrix may have caused earlier onset of narcolepsy in young people who may have been predisposed to develop the condition later in life.

Reports of an increased risk of narcolepsy may also have heightened awareness of narcolepsy causing an increase in the number of people presenting with the condition. Long-term follow-up and a subsequent decrease in the rates of narcolepsy diagnosis would be needed to confirm if either of these possibilities had occurred.

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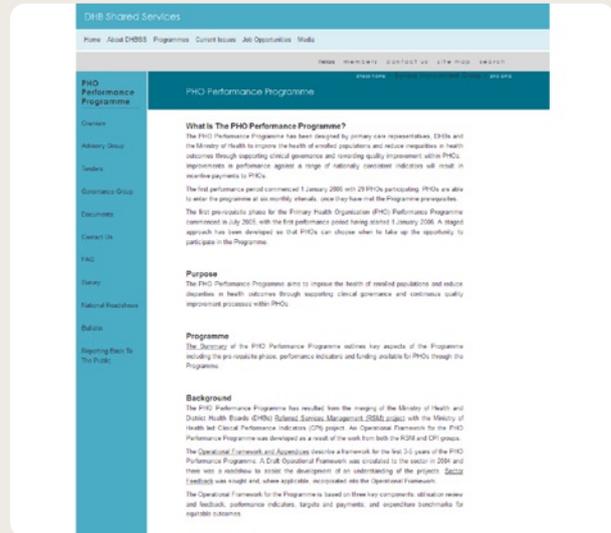
Influenza vaccination is a PHO Performance Programme indicator

Influenza vaccination in people aged 65 years and over accounts for 9% of the PHO Performance Programme funding; 3% for the total population and 6% for the high need population. High need populations include Māori and Pacific Peoples and people living in Quintile 5 (most deprived) socioeconomic areas. The target is assessed by counting the enrolled patients aged 65 years and over who have received an influenza vaccination during the most recent campaign (the numerator). This number is then divided by the number of enrolled patients aged 65 years and over at the beginning of the most recent campaign period (the denominator).

The programme goal is for at least 75% of people aged 65 years and over at the end of the annual influenza vaccination season to have received the influenza vaccine during the most recent campaign.



 Further information about the PHO Performance Programme, including a summary of all performance indicators is available from: www.dhbsharredservices.health.nz/Site/SIG/pho/Default.aspx



Funding for influenza vaccination now extended

PHARMAC have announced that from 1 April, 2013 children aged from six months to four years (i.e. until their fifth birthday) with a significant respiratory illness are now eligible for fully subsidised influenza vaccination. In Canterbury DHB all children aged under 18 years are also eligible for free influenza vaccination.

This is in addition to pregnant women, people aged over 65 years and people with specific long-term health conditions, for whom influenza vaccination is already subsidised.

People eligible for subsidised vaccination must receive their influenza vaccination before 31 July, 2013.

 For further information on influenza subsidy, see: www.pharmac.health.nz

