
Executive summary

New vaccine can help to prevent cervical cancer

The Netherlands has had a successful cervical cancer screening programme for several decades. Women between the ages of thirty and sixty are checked for the disease or its precursors, with a view to providing treatment as early as possible in appropriate cases. Recently, however, vaccines have come onto the market, which can be used to prevent cervical cancer – one of the more common forms of cancer in women.

It has been known for some time that persistent infection by human papilloma virus (HPV) is responsible for cervical cancer. HPV is transmitted by sexual contact; most women acquire HPV infections, most of them without any untoward consequences. However, a small percentage of women who become infected go on to develop pre-cancerous conditions and in a small proportion of these women, the pre-cancerous conditions lead to cervical cancer. The vaccines now available prevent the development of the precursors of cervical cancer, and thus are likely to prevent the cancer itself. The use of such vaccines would therefore enable primary prevention, to complement the existing early detection and early treatment activities.

Vaccines require careful assessment before they can be included in the National Immunisation Programme

Now that vaccination against HPV is possible, it is necessary to consider whether such vaccination should be included in the National Immunisation Programme (NIP). The NIP is the vehicle for the provision of large-scale public vaccination in the Netherlands. If inclusion in the programme is considered appropriate, it is also necessary to decide which population groups should undergo vaccination. The Minister of Health, Welfare and Sport accordingly asked the Health Council to address these questions.

New forms of vaccination are not included lightly in the National Immunisation Programme. Inclusion in the NIP implies administration to large numbers of healthy people, which is justifiable only where there is convincing scientific evidence that the vaccination is both effective and safe. Various other criteria must also be met before a vaccination can be added to the NIP list. However, it is important to recognise that absolute satisfaction of any individual criterion is not possible: almost no vaccine is totally effective or entirely without adverse events.

It is not possible to say definitively whether a new form of vaccination should or should not be included in the NIP until it has been carefully assessed against the relevant criteria. Such assessment is required for HPV vaccination just as for any other form of vaccination. Indeed, assessment is all the more important where a new vaccine, such as HPV vaccine, is concerned, since relatively little experience of its use has been gained and little long-term research has been conducted.

The currently available data on efficacy and safety is favourable

The first criterion for admission to the NIP is that the condition addressed by the vaccine must be a serious public health problem. This is self-evidently the case where HPV vaccination is concerned: cervical cancer is a relatively common form of cancer in women between thirty and sixty years old. Despite the existence of an effective screening programme, there are roughly six hundred cases of the disease a year in the Netherlands, leading to the death of between 200 and 250 women.

Whether HPV vaccination satisfies the second criterion – that the vaccination should be an effective means of preventing the relevant disease – is harder to say. The vaccines have been developed only recently and, because the interval between HPV infection and the development of cervical cancer averages about twenty years, there are as yet no data to show whether vaccination leads to a fall

in the incidence of cervical cancer. At present, the only information available relates to the vaccine's effectiveness as a means of preventing HPV infection and the precursors of cervical cancer. Nevertheless, it is reasonable to assume that a lower infection rate and a lower incidence of pre-cancerous conditions – phenomena which *are* demonstrably associated with vaccination – will lead to less cervical cancer. The basis for this assumption is the proven correlation between prolonged HPV infection and the development of cancer of the cervix.

Certainty regarding the effectiveness of vaccination as a means of preventing cervical cancer can be obtained only through clinical use of the vaccine and by following up vaccinated girls and women over an extended period. Further research and conscientious monitoring are therefore essential.

Research has shown that vaccination is useful only if a woman has yet to be infected by HPV. It would therefore seem rational to make the vaccine available to girls at an age when most have yet to become sexually active. The Committee regards twelve years old as appropriate in this regard. The question arises, however: if girls are vaccinated at that age, does the vaccine provide lifelong protection against HPV infection? Unfortunately, this question cannot yet be answered with confidence. Here again, long-term research is required to establish whether booster vaccinations are needed in order to provide proper protection.

It is also worth noting that, even if vaccination were fully efficacious, it could not prevent more than 70 per cent of cervical cancer cases in the Netherlands. The reason being that the available vaccines are designed to protect against two particular cancer-triggering HPV types, which together account for 70 per cent of cases of the disease.

With regard to safety, the third assessment criterion, there is currently no reason to suppose that the vaccine has any adverse events that might preclude its inclusion in the NIP. Nevertheless, the possibility cannot be excluded that, if it were administered to large numbers of people, relatively uncommon adverse events might come to light in due course. This underlines the importance of careful monitoring following the introduction of this form of vaccination.

The cost is relatively high

The fourth and fifth assessment criteria relate to the acceptability of the vaccination in its own right and as an element of the vaccination programme as a whole. The Committee sees no problem on either count: if vaccination against HPV were included in the NIP, it would not represent a disproportionate burden on the target group. Nevertheless, the particular nature of this vaccination does warrant consideration. Given that what is at issue is the vaccination of twelve-year-old

girls against a sexually transmitted infection that can lead to cancer, proper education is very important.

Assessment of HPV vaccination against the sixth criterion – that the vaccination should be an efficient means of preventing the target disease – is more difficult. Because the Netherlands already has a successful cervical cancer screening programme, the benefit attainable by HPV vaccination is less than it would be in a country without such a well organized programme. Consequently, the cost-benefit ratio is less favourable in the Netherlands than in most countries. It should be recognised that the inclusion of HPV vaccination in the NIP would not do away with the need for screening, partly because vaccination does not provide universal protection and partly because unvaccinated women would still need screening.

Given that screening will continue to be necessary even if HPV vaccination is provided through the NIP, the cost of operating the combined programme will be quite high, relative to the attainable health benefit. This is apparent from modelling undertaken specifically to support this report. Furthermore, uncertainty exists regarding a number of factors relevant for modelling, such as the long-term efficacy of the vaccine, the possible need for booster vaccinations, and the price of the vaccine. It is only by monitoring prolonged use that the relationship between the cost of vaccination and the benefits will become clear.

Nevertheless, the Committee believes the capital cost apparent at the present time to be justified by the attainable benefits. It is reasonable to suppose that the provision of HPV vaccination to twelve-year-old girls, in combination with screening, will in due time prevent several hundred more cases of cervical cancer a year, and about a hundred deaths.

Hence, the introduction of this vaccination may be regarded as urgently needed – the seventh and final assessment criterion. No other form of vaccination currently under consideration for inclusion in the NIP is capable of having such a marked effect on mortality. Equally urgent is a catch-up programme of vaccination for girls aged thirteen to sixteen at the time that HPV vaccination is introduced. Considerable health benefit could be obtained by vaccinating females in this age range, since most of them will not yet have been infected by the virus.

Where older girls and women are concerned, consideration should be given to funding vaccination through the Reimbursement System for Pharmaceutical Products (Geneesmiddelenvergoedingssysteem). This would imply communally-funded vaccination outside the context of the NIP.

Inclusion in the NIP requires flanking policy

Assessment against the seven criteria suggests that the admission of HPV vaccination to the NIP would be justified. A particularly attractive feature of such a move is that a certain amount of cervical cancer could be prevented altogether, rather than merely caught early and treated. The Committee accordingly recommends the introduction of HPV vaccination for twelve-year-old girls through the NIP. The Committee further recommends that girls aged thirteen to sixteen at the time that HPV vaccination is introduced be vaccinated in the context of a catch-up programme. Finally, it is also recommended that consideration should be given to asking the Health Care Insurance Board to look at the possibility of funding the vaccination of girls and women aged seventeen or older through the Reimbursement System for Pharmaceutical Products.

The Committee qualifies its recommendations by emphasising that the introduction of HPV vaccination to the NIP should be accompanied by establishment of an ongoing programme for studying and monitoring the effectiveness and safety of this form of vaccination and the longevity of the protection afforded. Other relevant factors, such as public acceptance and the effectiveness of the accompanying education activities (which are very important in this case), require careful evaluation as well. Such steps are necessary in order to obtain the knowledge that is currently lacking, and to ensure that the vaccination programme remains effective and safe.

Following the introduction of HPV vaccination, participation in the cervical cancer screening programme will continue to be very important, even for vaccinated women. It is vital that this message is effectively communicated to the public.