Independent report

JCVI statement on a childhood varicella (chickenpox) vaccination programme

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Recommendation

The Joint Committee on Vaccination and Immunisation (JCVI) recommends a universal varicella (chickenpox) vaccination programme should be introduced as part of the routine childhood schedule. This should be a 2-dose programme offering vaccination at 12 and 18 months of age using the combined MMRV (measles, mumps, rubella and varicella) vaccine.

As has been shown in other countries which include varicella in their routine vaccination schedule, a 2-dose schedule is predicted to decrease the number of cases of varicella seen in childhood rapidly and dramatically. The programme will prevent severe cases of varicella, and other serious complications of varicella, which while rare may have otherwise resulted in hospitalisation or other serious outcomes.

A catch-up programme should also be initiated following implementation of a programme to prevent a gap in immunity.

Background and epidemiology

The JCVI is an expert scientific advisory committee which advises the UK government on vaccination and immunisation matters.

Varicella (commonly known as chickenpox) is a highly contagious infectious disease caused by the varicella zoster virus. Infection is characterised by the presence of an itchy, spotty rash with spots appearing then blistering and scabbing over. Other typical symptoms of varicella that may appear one or two days before the rash develops, may include a fever, muscle aches and pains and generally feeling unwell.

Varicella is very common and affects most children during childhood, although it can be caught for the first time at any age. It’s transmitted through direct contact between people, or indirectly through airborne droplets. Most varicella cases in children are relatively mild and the illness resolves without any need for treatment from a medical professional, though most children are unwell for several days and will miss 5 or more days from school or nursery. Parents may have to take time off work to care for them. However, some children will go on to develop complications from varicella including bacterial infection of skin lesions (including group A streptococcus) and in rare cases, encephalitis, pneumonitis and stroke. These complications can result in hospitalisation and very rarely may result in death.

Varicella is often more serious in very young infants (under 4 weeks) and adults, in particular in pregnancy when it may cause complications in both the mother and the foetus, and in adults who are immunosuppressed.
Recent sero-epidemiology data from the UK Health Security Agency (UKHSA) indicates that approximately half of children have had varicella by the time they are 4 years old, rising to 90% by the time they are 10 years old (UKHSA, unpublished). During the COVID-19 pandemic, restrictions on social mixing led to fewer cases of varicella in younger age groups compared with before the pandemic, therefore leaving a larger pool of children susceptible to varicella.

Herpes zoster (commonly known as shingles) is caused by reactivation of the varicella zoster virus in a previously infected person, a risk because the virus remains dormant in the body following an initial varicella infection. People with herpes zoster can transmit the virus to susceptible people to cause chickenpox, but herpes zoster is not acquired from coming into contact with someone who has varicella. Herpes zoster is characterised by a blistered rash and pain. In some cases, this pain persists for more than 3 months, known as post-herpetic neuralgia. The severity of herpes zoster increases with age, with post-herpetic neuralgia rare under 55 years of age in otherwise healthy individuals.

The UK has had a universal shingles vaccination programme in place since 2013 in older adults. This programme was updated in September 2023 to use Shingrix® recombinant zoster vaccine, which is considered to be more effective than the live zoster vaccine (Zostavax®) previously used. The programme has also been expanded to include:

- adults turning 65 years of age (from 1 September 2023)
- those aged 70 (from their 70th birthday)
- those aged over 50 years with a severely weakened immune system

As this programme rolls out over the next 10 years, the recombinant zoster vaccine eventually will become part of a routine programme offered to all adults aged 60 years.

Previous considerations

In 2009, the JCVI considered vaccination strategies for protection against varicella and herpes zoster and made recommendations based on the evidence at the time. The committee considered both the possibility of a combined varicella and herpes zoster vaccination programme, or a herpes zoster only programme.

The committee did not recommend that varicella vaccination should be implemented (JCVI meeting minutes, October 2009). Cost-effectiveness modelling (Van Hoek and others) at the time indicated that a varicella vaccination programme could be cost-effective but only after a long period of time (80 to 100 years), and in the medium term (30 to 50 years) was not likely to be cost-effective. This was driven mainly by a predicted increase in cases of
herpes zoster in middle-aged adults, who are not old enough to be vaccinated and rely on exposure to circulating varicella to maintain immunity (exogenous boosting).

The exogenous boosting hypothesis postulates that those who have previously had varicella have their immunity boosted by exposure to circulating varicella zoster virus, thereby inhibiting reactivation of the varicella virus and the development of herpes zoster. It was theorised that a varicella vaccine programme would prevent exogenous boosting by preventing cases of varicella, and that this would therefore lead to a significant increase in cases of herpes zoster in middle-aged adults as immunity would not be boosted. At the time of this analysis, it was thought that this effect on exogenous boosting could last for as much as 20 years.

At the time, the JCVI did recommend a herpes zoster vaccination programme should be implemented in older adults aged 70 to 79 years to prevent cases of shingles and its complications in this population.

It was agreed at the time that this recommendation should be reviewed when further information relating to varicella epidemiology, vaccination and exogenous boosting were available.

Updated evidence reviewed

The varicella zoster JCVI sub-committee met multiple times during 2022 and 2023 to review the updated evidence including:

- varicella disease burden
- potential impact on exogenous boosting
- updated seroprevalence data
- modelling cost-effectiveness and real world data from countries who have already implemented a programme

This was then discussed by the main JCVI committee in their October 2023 meeting.

Disease burden

A study was carried out by the University of Bristol to better capture the impact on quality of life for children hospitalised with varicella. This study also considered cases within the community and the impact on children and their caregivers (Marlow and others).
The true extent of hospitalisations caused by varicella is underestimated through routine data sources due to errors in coding. This is because hospitalisations are frequently due to secondary complications of varicella infection including cellulitis, invasive group A streptococcal infection or childhood stroke, and therefore are not always recorded as a hospital admission related to varicella. It was also thought that there may be other secondary complications from varicella infection which are not currently well understood or captured.

The community arm of the study estimated the quality adjusted life year (QALY) loss in cases which would not be captured in any medical datasets. Primary care datasets will capture those cases where medical attention has been sought (moderate cases). This study aimed to assess the impact of mild varicella on quality of life, healthcare use and the financial and health impact on the family unit.

Results from both the hospitalisation and community arms of the study were presented to the JCVI sub-committee and these findings were used to parameterise the model. The results from the community study estimated the mean QALY loss per case of varicella, as well as the average time off work for both primary and secondary caregivers and the days at nursery missed.

The hospital surveillance study identified all paediatric admissions over a given time period to assess the relative contribution of varicella among paediatric hospital admissions. The study concluded that complications from severe varicella were common, costly and placed a burden on health services. Uncomplicated varicella can also cause hospitalisation in very young children and those with underlying medical conditions (unpublished data, University of Bristol).

**Real world experience**

Varicella vaccination is included in the routine vaccine schedules of several countries either as a 2-dose or single-dose strategy including the USA, Canada, Australia and Germany. Countries that have introduced programmes have observed significant impact on cases of varicella and resulting hospitalisations. In countries introducing a 2-dose schedule, indirect effects on the younger cohort not eligible for vaccination have also been observed (Marin, Leung and others, Marin, Lopez and others, Wormsbecker and others, Waye and others, Sheel and others), with no evidence of a rebound in rates of infection among those missing out on vaccination following introduction of a programme.

A varicella vaccination programme was first introduced as a single-dose strategy in the USA in 1995 with a second dose added in 2007. In 2022, the Centers for Disease Control and Prevention (CDC) published data from the first 25 years of experience from this programme including the impact on herpes
zoster cases (Journal of Infectious Diseases). Herpes zoster cases had been increasing in the USA prior to the implementation of a varicella vaccination programme and continued at the same rate once the programme was introduced but have now levelled off - the reason for this increasing trend was unclear. CDC has concluded that this data does not support predictions that the varicella vaccination programme would increase herpes zoster incidence (Leung and others).

The data from the USA was reviewed by the sub-committee and it was agreed that this should be incorporated into the modelling work, fitting the model to the USA data to investigate further the true extent of the potential effect of vaccination on exogenous boosting.

**Cost-effectiveness modelling**

The JCVI sub-committee reviewed and provided the input parameters for the modelling work carried out by the University of Cambridge (currently unpublished). Real world data from the USA had been applied to the transmission dynamic model. The updated model was then refitted to UK data including updated data on seroprevalence, quality of life impact and data on primary care consultations for chickenpox.

It was agreed that based on the updated real world data and study data on exogenous boosting, the previous assumptions on the duration of protection from herpes zoster though exogenous boosting (20 years) was too long. From reviewing the model which had been fitted to the new data, it was agreed that the duration was likely to be around 3 years, with sensitivity analysis using durations of 1 and 5 years included to account for uncertainty.

Unlike the previous model used in 2009, the updated model did not show a rebound of varicella cases following the initial sharp decline. This was considered to be due in part to the short period of time between the first and second dose, but also was consistent with data seen in countries which have implemented vaccination already.

Cost-effectiveness analysis showed that a routine childhood programme would be cost effective, and may be cost saving depending on the vaccine price obtained. The main driver of the cost-effectiveness analysis was the price of the vaccine, followed by the estimated QALY loss from varicella.

**Vaccination programme**
**Vaccine to be used**

Varicella vaccination is available as a varicella-only product, or as a combination with measles, mumps and rubella (MMR, as MMRV). The proposed schedule is to give a dose at 12 and 18 months. As per the planned upcoming changes to the routine infant schedule (https://www.gov.uk/government/publications/changes-to-the-childhood-immunisation-schedule-jcvi-statement), this would be at times already reserved for the MMR vaccine doses.

Using the combined MMRV vaccine as a first dose has been associated with a slightly increased rate of febrile seizures when compared with using separate MMR and varicella vaccines at the same visit. This increased rate has not been observed when using the combined MMRV vaccine as a second dose.

Using a combined vaccine for both the first and second dose would mean that fewer injections would need to be given in a single immunisation visit. Previous attitudinal work has suggested that having fewer injections is preferred among parents, and a recent study (Sherman and others) among UK parents indicated that a combined varicella vaccine was preferred to separate vaccines.

Febrile seizures are usually benign and self limiting, and are unlikely to cause long-term effects or harm. Febrile seizures usually affect children aged between 6 months and 6 years old. Febrile seizures can occur as a result of infection including varicella but are also an established side effect of both the MMR and varicella vaccines.

Although there is an increased risk of febrile seizures occurring when using the MMRV as the first dose, the absolute risk is very low. The CDC estimates that one additional febrile seizure is seen for every 2,300 doses given compared with using separate vaccines. The combined MMRV vaccine is offered as a first dose in other countries including the USA and Canada. The JCVI considered that this very small increased risk was not of clinical concern and that there was a considerable benefit from giving fewer injections across all eligible children.

It is the view of the committee that both doses given in the varicella programme should be as the combined MMRV vaccine.

**Catch-up programme**

The JCVI discussed the potential for a catch-up vaccination programme. Most countries following the implementation of a routine programme have offered some form of catch up.

Real world data from other countries has shown that implementation of a universal routine varicella vaccination programme leads to a significant and
dramatic decrease in the number of cases seen. Due to the larger pool of varicella-susceptible children following the pandemic restrictions and, as vaccination is predicted to significantly decrease circulation of varicella, susceptible people may continue to be vulnerable to catching varicella as they head into adulthood. Therefore, the committee considered that it would be beneficial to ensure that a catch-up programme is implemented to prevent a gap in immunity.

Analysis of the cost-effectiveness of potential catch-up vaccination scenarios are underway. Initial findings suggest that a universal catch-up vaccination programme using a single dose of vaccine is likely to be cost-effective for children aged up to and including 5 years. Further work is needed to understand whether a targeted catch-up programme could be cost-effective for children aged 6 to 11 years.

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