

Varicella zoster virus

Occupational
aspects of
management

A national guideline

2010



Royal College
of Physicians
Setting higher medical standards

fom
Faculty of Occupational Medicine

NHS
Plus

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NHS Plus

The NHS Plus Project aims to improve the quality and delivery of occupational health services to NHS staff and in turn increase the availability of NHS Plus services to small and medium employers. In addition to commissioning the Health and Work Development Unit to produce evidence-based guidelines and conduct national audits, the Project has work strands to improve the delivery of services, provide an improved trading model and improve the strategic leadership of occupational health services in the NHS.

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The Health and Work Development Unit is a partnership between the Royal College of Physicians and the Faculty of Occupational Medicine. The unit's work focuses on improving the health of the working population by improving the quality of clinical occupational healthcare and supporting the implementation of evidence-based standards in the workplace.

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Conflicts of Interest: No conflicts of interest were declared at the first Guideline Development Group meeting. Any conflicts raised during the production of the guideline were discussed on a question by question basis. Where the Guideline Development Group members authored any of the reviewed papers, their papers were allocated to other members of the Group for appraisal.

Executive summary

The purpose of this guideline is to offer evidence-based advice on the management of chickenpox and shingles in the workplace. The document is intended to be of use to employers, employees, occupational health (OH) professionals and other interested parties involved in the workplace management of chickenpox and shingles. The recommendations cover immunisation against chickenpox, management of employees with chickenpox or shingles and the prevention of transmission of these infections to colleagues/patients.

A steering group oversaw the production of the guideline. A separate multidisciplinary Guideline Development Group (GDG) undertook the key stages of critical appraisal and synthesis of a body of published evidence.

Four key questions were identified by the GDG at the outset, and defined according to a standard format that made explicit the target population, intervention, comparison groups and outcomes of interest. The evidence was identified by a systematic literature search and a series of recommendations was drafted. The standard methodology of the Scottish Intercollegiate Guideline Network (SIGN) was applied in the critical appraisal phase of the guideline development process.

Good practice points (GPPs) have been produced where there is no robust evidence but guidance is needed. The GPPs are based on consensus amongst the GDG. Recommendations for future research have been made where there are important gaps in the evidence.

Prevention and management of chickenpox infection is more complex in healthcare settings than non-healthcare settings. To reflect this we have produced a set of recommendations for healthcare workers (HCWs) and separate recommendations for non-healthcare settings.

For HCWs, much of the evidence assessed by the GDG supports the recommendations in the published national guidance, *Immunisation against infectious disease* ('the Green Book').¹ These recommendations have been summarised in green text. To avoid confusion or duplication the reader is referred to the Green Book for the full details. Where the GDG believed that the evidence review supports additional recommendations, or where the GDG wished to make GPPs in areas not covered by existing guidance, the text is in black print.

The majority of the recommendations for healthcare workers are aimed at those responsible for staff infection control. In most National Health Service (NHS) trusts this is the occupational health team with support from the infection control team.

Four key questions were used as the basis for the systematic review:

- 1 What is the appropriate occupational health management of HCWs at the pre-employment stage of recruitment, with particular reference to indications for screening of varicella zoster virus (VZV) status and the methodology to be employed?
- 2 What is the appropriate occupational health management of HCWs in relation to the administration of VZV vaccination?
- 3 What is the appropriate occupational health management of workers who present with chickenpox or shingles and what is the optimal management of their work colleagues? (Also, in healthcare, what is the appropriate management of workers exposed to infected colleagues or patients?)
- 4 What is the likely economic consequence of the implementation of such policies?

Key findings and recommendations

A reasonable amount of high-quality research was found to answer questions about the reliability of a history of chickenpox for predicting likelihood of natural immunity, and effectiveness of the vaccine. There was far less evidence to inform recommendations on the management of staff with, or exposed to, VZV infection. The recommendations for question 3 are labelled as GPPs to reflect this lack of evidence. Below we summarise the key findings and recommendations of this review. Please refer to section 4 for the full recommendations.

Healthcare settings

- A history of chickenpox has a high positive predictive value (95–98%) in HCWs from temperate climates. In this group, history alone is sufficient to determine immunity to chickenpox. Those with a negative or uncertain history should be serologically tested.
- A history of chickenpox has a lower positive predictive value in HCWs born or raised in tropical or subtropical climates. This group should have serological screening regardless of a history of chickenpox.
- VZV vaccine is effective in providing adults with long-term protection from serious VZV disease, and VZV-susceptible HCWs should be offered vaccination using two doses of vaccine.
- Where an HCW declines vaccination, the occupational health (OH) professional should explore their reasons for declining, explain the benefits of vaccination and the individual's professional duty to protect their patients from infection, and encourage them to take up vaccination.
- Where HCWs have a contraindication to vaccination, eg they are immunocompromised through illness or treatment, the OH professional should assess the risk of varicella infection to the HCW and the risk of onward transmission of infection to their patients.
- When considering whether restrictions are necessary for HCWs who cannot or will not be vaccinated, the OH professional should take into account the level of infection risk to the HCW and their patients, and the effect of redeployment on staffing levels, skill mix and therefore patient safety.
- Decisions about restrictions will need to be taken in conjunction with the HCW, their manager and infection control, while respecting the HCW's right to medical confidentiality.
- HCWs diagnosed with chickenpox should be excluded from the workplace until there are no new lesions and all lesions have crusted over.
- HCWs diagnosed with localised herpes zoster on a part of the body that can be covered with a bandage and/or clothing should be allowed to work if they are clinically well. If they work with high-risk patients, an individual risk assessment should be carried out, to determine the appropriate action.
- HCWs with localised herpes zoster lesions that cannot be covered or who are immunocompromised, and HCWs with disseminated herpes zoster, should be excluded from the workplace until there are no new lesions and all lesions have crusted over.
- Susceptible HCWs who have a significant exposure to VZV should either be excluded from contact with high-risk patients or inform their occupational health department if they feel unwell or develop a rash or fever during the incubation period.
- In the majority of situations a high level of vigilance for malaise, rash or fever (including taking temperature daily) throughout the incubation period will be adequate.

- Pregnant HCWs exposed to chickenpox or shingles should be assessed by an OH or other appropriate health professional for varicella zoster immunoglobulin (VZIG).

Prisons and immigration removal centres

- Staff in prisons and immigration removal centres should follow their sector's guidance. A summary of this guidance is included in the recommendations section.

General workplaces (outside the healthcare and prison sector)

- Chickenpox vaccination and antibody testing is not routinely recommended for workers in employment sectors outside healthcare or the prison service.
- A worker diagnosed with chickenpox should remain away from the workplace until there are no new lesions and all lesions have crusted over.
- A worker with localised herpes zoster on a part of the body that can be covered with a bandage and/or clothing should be allowed to continue working. Workers with disseminated zoster, localised zoster that cannot be covered (eg facial), and those who are immunocompromised, regardless of the site and extent of the lesions, should remain away from the workplace until the lesions have crusted over.
- Employers should ask pregnant or immunosuppressed workers who have been exposed to an infected colleague at work to contact their GP or relevant specialist immediately for advice.

Definitions

Healthcare workers (HCWs): workers who have direct contact with patients. This includes both clinical and non-clinical healthcare workers as defined below:

Clinical healthcare workers have regular clinical contact with patients and are directly involved in patient care. This includes doctors, dentists, midwives, nurses, healthcare assistants, paramedics, ambulance drivers, occupational therapists, physiotherapists and radiographers. Students and trainees in these disciplines and volunteers who are working with patients must also be included.

Non-clinical healthcare workers are staff in healthcare settings who may have social contact with patients but are not directly involved in patient care. This group includes receptionists, ward clerks, porters and cleaners, whether employed directly or through contract.

Occupational health professional: A person who has received formal training and a recognised qualification in either occupational medicine or occupational health. For the purposes of this guideline this will be an occupational health doctor or nurse.

Susceptible to VZV: at risk of developing VZV infection as no antibodies to VZV. This is usually because the individual has not had chickenpox and has not been vaccinated.

Immunocompromised: weakened immunity because of disease, eg HIV disease and some cancers, or treatment with immunosuppressant drugs or radiation. For full details see the Green Book, Chapter 34, Varicella page 430. www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_063665.pdf

High-risk patients: people who are at high risk of developing complications if infected with VZV, in particular pregnant women, fetuses, neonates and immunocompromised individuals.

Significant exposure: three aspects of the exposure are relevant:

Type of varicella-zoster infection in index case: chickenpox, or the following: disseminated zoster, immunocompetent individuals with exposed lesions (eg ophthalmic zoster) or immunosuppressed patients with localised zoster on any part of the body (in whom viral shedding may be greater).

The timing of the exposure in relation to onset of rash in index case: exposure to a case of chickenpox or disseminated zoster between 48 hours before onset of rash until crusting has ceased and crusting of all lesions, or day of onset of rash until crusting for those exposed to localised zoster.

Closeness and duration of contact: The following should be used as a guide to the type of exposure (other than maternal):

- contact in the same room (eg in a house or classroom or a 2–4 bed hospital bay) for a significant period of time (15 minutes or more)
- face-to-face contact, for example while having a conversation
- in the case of large open wards, air-borne transmission at a distance has occasionally been reported.

1 Introduction

Varicella zoster virus

Varicella zoster virus (VZV) is one of the human herpes viruses. Primary infection causes varicella (chickenpox). The virus is not cleared from the body but persists in a dormant state in the dorsal root and/or cranial nerve ganglia. Subsequent reactivation of the latent virus, typically occurring years later, causes zoster (shingles).

Chickenpox (varicella)

Chickenpox (varicella) is characterised by a generalised vesiculopustular rash. Symptoms usually begin with 1 or 2 days of fever, flu-like symptoms and generalised malaise, although this may be absent. The classic sign of chickenpox is the appearance of blisters (vesicles) on the face and scalp, which spread to the trunk and eventually limbs. After around 7 days the blisters dry out and scab over, at which stage they are no longer considered to be infectious. Healing can be slower in people who are immunocompromised, who may remain infectious for several weeks.

Typically a benign and self-limiting illness in healthy children, chickenpox in adults may be severe, leading to hospital admission (rate 180 per 10,000 cases) and even death (rate 5 per 10,000 cases). The illness poses a particular threat for pregnant women, fetuses, neonates and immunocompromised individuals.

Shingles (zoster)

Shingles (zoster) is due to reactivation of the virus in someone who has previously been infected with VZV. It is a self-limiting, localised vesicular rash occurring over one to three contiguous unilateral dermatomes. Pain is a frequent complication and may persist after the rash resolves (post-herpetic neuralgia).

Recent developments

There have been significant changes in the understanding of the implications of VZV in the workplace in recent years. More options are available for managing the risk of chickenpox and shingles, and the prevention of VZV infection itself: antiviral therapy can modify disease;² varicella zoster immune globulin (VZIG) is available for prophylactic use in appropriate situations; and a vaccine was licensed in the UK in 2003 for use in susceptible individuals. Department of Health (DH) guidance on the use of the vaccine in the healthcare environment is designed to reduce the risk of exposure of vulnerable patients to staff with varicella and to reduce the impact that an exposure to VZV may cause.³ Healthcare workers (HCWs) themselves also benefit from the protection vaccination affords.

The Guideline Development Group (GDG) identified a need to:

- examine the evidence base for management of chickenpox in the healthcare setting
- provide further guidance on the practical implementation of recommendations in the healthcare setting where the evidence base or consensus allows

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- produce evidence-based, practical advice to other employers about how to manage infected staff and any exposed work colleagues.

This document is based on a systematic literature review of the evidence for the prevention and management of chickenpox in the workplace. Most of the published research is based in the healthcare setting. However, where appropriate, it can be applied to other work environments.

2 Background

Epidemiology

In the UK, chickenpox most commonly occurs during childhood. At least 90% of adults in England and Wales are VZV IgG seropositive,⁴ confirming prior infection. In tropical and sub-tropical climates, the mean age of chickenpox infection may be older. A significant proportion of individuals raised in those regions remain VZV IgG seronegative and may be susceptible to primary infection in adulthood.⁵

Varicella is a notifiable disease in Northern Ireland but not in Scotland, England or Wales. The Royal College of General Practitioners (RCGP) research and surveillance centre collects and monitors data on chickenpox and shingles infections from a network of approximately 100 participating GPs throughout England and Wales. Analysis of their data shows that approximately 80% of chickenpox consultations are with children aged 0–14 years. The majority of cases are managed within primary care. A minority will attend hospital accident and emergency departments and a small proportion of these will require hospital care. There are no national data on chickenpox incidence by occupation.

A national voluntary surveillance scheme for occupational diseases and work-related ill health run by the occupational and environmental health research group at Manchester University⁶ collects data from over 2,000 specialist physicians. Four cases of chickenpox were reported under this scheme between 2002 and 2008. Two of these were care staff working in a nursing home and two were NHS HCWs – one of whom was reported to have contracted chickenpox from the vaccine. These figures are unlikely to represent the true burden of chickenpox amongst workers. The scheme requires reporting of cases where infection is contracted through work, whereas the majority of infections in adults are likely to be acquired in the community, particularly from infected children in a home setting. Also reporters to the scheme are doctors, whereas some cases of chickenpox in the workplace are dealt with by occupational health (OH) nurses without involvement of the OH doctor.

Transmission

Chickenpox is highly infectious and can be transmitted by the respiratory route from 48 hours before onset of the rash. The skin lesions of varicella and zoster are considered to be infectious until crusted over. This usually takes around 7 days.

Following exposure to chickenpox or shingles, susceptible contacts may develop chickenpox rash after an incubation period of 10 to 21 days. Infectivity, and early symptoms such as malaise and fever, may begin up to 2 days before the rash appears.

Complications and high-risk groups

Varicella is usually a mild illness and most healthy children recover with no complications.^{7,8}

Some individuals may experience serious complications such as viral pneumonia, secondary bacterial infections and encephalitis.⁹ Groups at risk of complications from varicella infection

include neonates, adults, smokers, pregnant women and their fetuses, and those who are immunocompromised.

Varicella infection in pregnant women can cause severe chickenpox with increased risk to the mother from varicella pneumonia and other complications. Maternal varicella also carries the risk of congenital varicella syndrome to the fetus. Congenital varicella syndrome can cause a range of problems including shortened limbs, skin scarring, cataracts and growth retardation. The risk of this occurring is highest if the pregnant woman is infected with VZV within the first 20 weeks of pregnancy.

Infection with varicella in the later stages of pregnancy can cause premature delivery or neonatal chickenpox infection. This is particularly serious if the mother develops chickenpox in the period 7 days before, to 7 days after, giving birth.^{10,11}

Treatment

Treatment of chickenpox in children is normally based on reducing symptoms such as fever and itchiness. Adults and those at an increased risk of developing serious complications from chickenpox should receive antiviral drugs such as aciclovir early in the course of illness. Shingles may be treated with oral antiviral drugs such as high dose aciclovir which, if given within 72 hours of onset of symptoms in appropriate doses, may reduce the duration of viral shedding and post-herpetic neuralgia.

Vaccination

Two varicella vaccines are licensed in the UK (Varilrix® (Glaxo SmithKline) and Varivax® (Aventis Pasteur MSD)). Both vaccines contain live attenuated VZV propagated in human diploid cells. At present, varicella vaccine is not given routinely to children but it may be given to children aged 1 to 12 years, and to adults, who are close contacts of those people considered to be at high risk of complications from chickenpox or shingles. It is also licensed for healthy adults and children over 13 years old who are not immune to varicella (indicated by VZV seronegative blood test).

In immunocompetent adults, two doses of varicella vaccine, given 4 to 8 weeks apart, provide 75% protection against varicella and over 95% protection against severe disease.² Immunity may wane over time, manifested as mild breakthrough infections with wild-type virus. Vaccinated healthcare workers followed for up to 8 years after vaccination have an attack rate of 10%.¹²

Up to 10% of immunocompetent adults develop a vaccine-associated rash, localised at the site of injection or generalised, within 1 month of immunisation.^{13,14} Transmission of vaccine virus from vaccines has been documented only rarely, and only from individuals with vaccine-associated rashes.

The vaccine can establish latent infection in some individuals and could potentially reactivate to cause zoster. When this vaccine-associated zoster occurs, there may be a history of rash at the time of vaccination, but this is not always the case.¹⁵

Seropositivity

The presence of VZV antibody in an unvaccinated individual indicates naturally acquired protection against varicella. However, because many tests are insensitive, some patients who test negative by commercial assays will in fact be found to be antibody positive in more sensitive in-house assays. Subjects who have grown up in tropical and subtropical countries may test antibody negative despite a positive history of chickenpox. It is not clear why this is so, but in current practice these individuals are considered to be susceptible to chickenpox.

Over 90% of healthcare workers will seroconvert when vaccinated with two doses of Oka strain VZV vaccine. Those who do not seroconvert have an increased risk of developing breakthrough varicella compared with those who do (60% (3/5) versus 8% (9/115)). Of those who are seronegative following two doses of vaccine, 79% (11/14) will seroconvert if given a third dose.¹⁶

In subjects who do develop breakthrough varicella despite mounting a post-vaccination antibody response, the risk seems to be associated with loss of antibody, which can occur in up to 35% of adults within 5 years of vaccination.

Current guidance in the Green Book is that post-vaccination serological testing is not routinely recommended but is advisable for healthcare workers in units dealing with highly vulnerable patients (eg transplant units).¹ However, the scientific evidence to support this advice is not clear.

Post-vaccination testing may not reflect who is protected as there is no nationally agreed standardised VZV antibody test, and false-positive and false-negative results are common. Also serology testing does not predict who will lose antibody.

Another factor to consider is that most vaccinated staff with breakthrough infection will be from the group who seroconverted initially (because this is the larger group) and who were cleared to work with high-risk groups. Breakthrough infection in this group should be milder, however, than in the smaller group who did not seroconvert.

In summary, post-immunisation antibody testing may not achieve its aim of identifying healthcare workers who present a risk to patients. We acknowledge this in our recommendations section.

Post-exposure prophylaxis

VZV vaccine

VZV vaccine is a rapid inducer of immune responses. It might have a role in the prevention or amelioration of primary VZV infection if administered shortly after exposure.

Although limited, the evidence available suggests that varicella vaccine administered to children within 3 days of household contact with a varicella case reduces infection rates and the severity of cases. However, infection may still occur in those who received vaccine. The Cochrane review identifies that 13 out of 56 vaccine recipients (18%) developed varicella compared with 42 out of 54 placebo (or no vaccine) recipients (78%).¹⁷ Varivax, but not Varilrix, is licensed for post-exposure prophylaxis in susceptible healthy individuals exposed to VZV if administered within 3 days of exposure. The manufacturers of Varivax quote limited data supporting its use up to 5 days post-exposure.¹⁸

Varicella zoster immunoglobulin

Varicella zoster immunoglobulin (VZIG) is made from pooled plasma of non-UK donors with suitably high titres of VZV antibody. After a significant exposure to VZV, pregnant staff who do not give a positive history of chickenpox, and immunocompromised staff, should have their VZV IgG status checked. VZIG prophylaxis is recommended for those who test seronegative within 10 days, and ideally within 7 days, of exposure. The duration of protection is 3 weeks. In the event of a second exposure after 3 weeks, repeat administration of VZIG prophylaxis is recommended.²

Antiviral therapy

Limited data indicate that chickenpox in healthy children may be prevented, or attenuated, by administration of aciclovir starting between 7 and 10 days after exposure, for a total of 7 days.^{19,20} The equivalent dose of aciclovir in adults is 800 mg four times daily. There are no published controlled trials comparing aciclovir prophylaxis directly with VZIG.

Existing published national guidance

Healthcare workers

The Green Book has a comprehensive chapter on chickenpox.¹ This includes advice on immunisation of HCWs including laboratory staff, and management of HCWs who have developed, or been exposed to, chickenpox or shingles. This guideline indicates where the systematic literature review supports the Green Book recommendations (see section 4). Readers should consult the Green Book for full details on management and refer to the recommendations in black text within this guideline (section 4) for areas that the Green Book does not cover.

Prisons, places of detention and immigration removal centres

Non-immune staff are at risk of both contracting and transmitting infection in environments such as prisons or immigration removal centres. The heightened risk in these environments is due to the close working environment of the population and the fact that, particularly in immigration removal centres, there are likely to be many individuals who have not previously been exposed to varicella.

There have been several instances of outbreaks of chickenpox in immigration removal centres, where detainee characteristics may make them particularly vulnerable to chickenpox. Outbreaks have involved transmission by staff and have resulted in disruption, with closure of units.

In 2008 the Health Protection Agency (HPA) and the DH published *Guidance on chickenpox and shingles infection control in prisons, places of detention and immigration removal centres*.²¹ This is adapted from the Department of Health 2006 Green Book, *Immunisation against infectious disease; varicella*.¹ Our literature review and evidence statements support the recommendations in this document and readers should refer to the original guidance when managing staff in these employment sectors.

Schools and other childcare settings

There is no national guidance recommending chickenpox immunisation for teachers or others working in childcare settings. Guidance from the HPA on infection control in schools and other childcare settings, issued in 2006, makes a general statement that ‘all staff should undergo a full occupational health check prior to employment; this includes ensuring they are up to date with immunizations’. It does not mention specific immunisations.²²

The guidance has a section on female staff and pregnancy, which states:

In general, if a pregnant woman develops a rash or is in direct contact with someone with a potentially infectious rash this should be investigated by a doctor. The greatest risk to pregnant women from such infections comes from their own child/children rather than the workplace.... If exposed to chickenpox the GP and anti-natal carer should be informed.

Readers should refer to the original guidance when managing staff in these employment sectors.

Other employment sectors

For most workers the risk of contracting chickenpox is no greater than for adults who do not go to work. As 90% of adults in the UK are immune to chickenpox it is not commonly seen amongst the workforce. When a case of chickenpox does arise within a workforce there are some simple things that the employer can do and these are included in the guideline section.

3 Methodology

Aim

The aim of this guideline is to offer evidence-based advice on the management of chickenpox and shingles in the workplace.

Scope

The guideline scope was agreed by the Guideline Development Group (GDG) who then formulated four key questions. Although key questions 1 and 2 are about healthcare workers, the literature review search strategy included all types of workers. This has allowed the recommendations to be extended beyond the healthcare setting.

Audience

The guidance is intended for anyone who might give advice to workers who present with chickenpox, including OH professionals, GPs, and other healthcare professionals. It is also aimed at employees themselves, their representatives and their managers, whether or not they have access to professional occupational health advice.

We have defined HCWs as workers who have direct contact (both clinical and non-clinical) with patients. We have used the Green Book definitions described below.¹

Clinical HCWs have regular clinical contact with patients and are directly involved in patient care. This includes doctors, dentists, midwives, nurses, healthcare assistants, paramedics, ambulance drivers, occupational therapists, physiotherapists and radiographers. Students and trainees in these disciplines and volunteers who are working with patients must also be included.

Non-clinical HCWs are staff in healthcare settings who may have social contact with patients but are not directly involved in patient care. This group includes receptionists, ward clerks, porters and cleaners, whether employed directly or through contract.

The process of guideline development

The process of guideline development included overall direction from a Steering Group and the Health and Work Development Unit (HWDU) (formerly the Occupational Health Clinical Effectiveness Unit) team. Most of the detailed work was undertaken by a multidisciplinary Guideline Development Group (GDG). The roles of the various contributors to the guideline are summarised in Appendix 1.

The key steps in the process of guideline development were:

- formulating clinical evidence-based questions
- systematically searching for the evidence in the published literature
- critically appraising the evidence
- distilling and synthesising the evidence and writing the recommendations
- grading a series of evidence statements and recommendations

- agreeing the recommendations
- structuring and writing the guideline
- disseminating and publishing the guideline.

Developing evidence-based questions

The approach to developing the questions for this review aimed to be inclusive, but it also aimed to prioritise the most important areas for occupational health practice. An initial literature search was carried out in order to identify any existing reviews or guidelines on varicella zoster (scoping search). A series of questions that would affect practical aspects of the care pathway was generated from the scoping search. It was agreed that, given the limitations of time and resource, a maximum of four questions could be addressed. As a result, the GDG discussed and prioritised the inclusive list, and reduced it to an agreed shortlist of four key questions. It was acknowledged that some important questions could not be included on the final list, and that these would be a priority for future revisions or extensions of the VZV guideline work.

Searching for the evidence – search strategy

The literature search strategy was developed after identifying the four key questions. This iterative process involved input from the group and the HWDU information scientist. The databases searched were Medline, Embase, HSE Line, FOM library, Cochrane Library, Health Periodicals Database, Evidence Based Periodicals and CINAHL.

The key terms for the literature search were derived directly from the key questions. The full search strategy is shown in Appendix 2. The guideline leader sifted the output from the initial literature search on the basis of title and abstract. Papers that were obviously not relevant to each question and foreign language papers were excluded (first sift). We retrieved papers that might be relevant and hand-searched the full manuscript. Papers that were not relevant or did not meet very basic quality criteria (eg having an appropriate control group) were rejected (second sift). The reference lists of all relevant papers were hand-searched, and any useful papers that had not been identified previously were also retrieved. In particular, all relevant original studies that were referenced in retrieved reviews were also retrieved and assessed. According to the SIGN methodology, we did not search for grey literature, instead confining the search to papers that had been published in peer-reviewed journals.

Appraising the evidence

All relevant papers that met the inclusion criteria were put forward for full appraisal. Appraisal was undertaken by members of the GDG according to the Scottish Intercollegiate Guideline Network (SIGN) methodology.²³ SIGN was chosen because the method suited the level of funding available and is a validated, widely used method for developing clinical guidelines in the UK. An adapted SIGN method is used for all guidelines produced by NHS Plus.

All GDG members undertook specific training in critical appraisal using the SIGN method. Each paper was scored independently by the guideline leader and one other GDG member, using standardised SIGN checklists. The scores were compared, and any discordant scores were discussed initially by the appraisers, and allocated a mutually agreed score. Any cases where

discordant scores were not resolved by this process were brought to the GDG for discussion and agreement of a final score.

The results of the literature searches, both titles and abstracts, were reviewed by the guideline leader. Those studies (randomised controlled trials, cohort studies or systematic reviews) that appeared to address the disorder of interest, workplace interventions and occupational outcomes were selected for full text review. In addition, those articles with no abstract or where the titles did not provide sufficient information to assess their relevance were obtained for full text review. The full text of selected papers was then reviewed by the guideline leader and those papers that addressed the workplace management of that disorder were selected for data extraction by two reviewers, one of whom was the guideline leader. The reference lists of the papers chosen were reviewed to identify any additional papers. These literature searches were repeated in May 2009 to identify any additional studies published during the period of the guideline's development: the final search date for all questions was 10 May 2009.

According to the SIGN methodology, papers are given a single quality rating (++ , + or –) based on a combination of the risk of bias and confounding. One limitation of this method is that the allocation of the quality score is not structured explicitly, making it difficult to demonstrate consistency of scoring between appraisers. However, it was beyond the scope of our resources to develop a new detailed scoring system for appraisal. Therefore, we handled the problem by raising awareness among appraisers, asking them to consider bias and confounding separately and to comment on each specifically in their recorded assessment form. Training was given to appraisers on the assessment of bias, including whether the effect of bias was inflationary or to the null and what the size of the effect might be. Appraisers were also asked to consider not just whether confounders were addressed in the study method, but (if not) whether this omission was likely have an important effect on the findings. The lack of consideration of a confounding factor in a study was considered to be a serious methodological flaw if the association of health outcomes with the potential confounder was strong and the factor was likely to be common in the study population. These studies were allocated a score of minus (–) for quality, and were rejected. The remaining studies, with quality scores of + or ++, were summarised in evidence tables (see Appendix 5).

Distilling and synthesising the evidence

Having compiled summary tables of the relevant studies, the GDG considered the body of evidence for each question separately. A number of factors were considered, with the overall aim of deriving evidence-based statements from these tables. This formulation took account of both the volume and quality of the evidence. The consistency of the findings was also considered. Well-conducted studies with negative findings (no significant associations) and studies that reported significant associations were given equal weight. We considered the likelihood that results might have arisen by chance, preferentially by looking at confidence intervals (CI), but if CIs were not available, tests of statistical significance (for example a 'p' value) were examined. We aimed to look at the size of the effect, based on a risk estimate wherever possible. We also considered the applicability of the study to our target population. In the synthesis, more weight was given to large well-conducted studies in workplace settings.

Grading the evidence statements

The SIGN guidelines²³ employ a grading system for evidence from peer reviewed publications. This system ranks evidence on a 4-point scale based on the study design and its potential for bias where a high-quality meta-analysis or a randomised controlled trial with a very low risk of bias is graded as 1++, case reports are graded as 3 and expert opinion is graded as 4. A detailed account of this system is given in Appendix 4.

Agreeing the recommendations

The final stage of the SIGN process comprises the discussion and agreement of recommendations based on the evidence-based statements. This process occurred within the setting of a GDG meeting. In formulating recommendations about interventions for workers with chickenpox, we have taken into account existing legal requirements, the evidence synthesis and the likelihood that any of the interventions might actually cause harm to workers or their patients. For this particular guideline it was not possible to make evidence-based recommendations for OH practice on some of the key questions due to a lack of evidence. However, the GDG made recommendations for consensus-based good practice points and for research based on addressing the identified gaps in the evidence base. Where the evidence base supported recommendations published in existing guidance, we have indicated this and directed the reader to the existing guidance to avoid duplication.

Guideline limitations

Limitations of the SIGN methodology

The main limitation of the SIGN methodology is the lack of transparency in quality assessment, as discussed above. Another specific problem arose from the historical development of the SIGN method for the assessment of clinical interventions. The resulting emphasis on randomised controlled trials (RCTs) as a gold standard is not particularly well suited to the occupational health literature, which typically has few RCTs and comprises mostly observational studies (including non-randomised intervention studies with a comparison group). Therefore it is difficult to achieve recommendations with a SIGN rating above 3 from research in occupational health. Moreover, there was no specific SIGN assessment pro forma for assessing either non-randomised trials or cross-sectional studies. Therefore appraisers were instructed to use the SIGN RCT pro forma for non-randomised intervention studies and the cohort study pro forma for cross-sectional surveys.

Limitations of the literature/database searches

The search was confined to papers and documents published in English and in learned and peer-reviewed journals and documents. They included only those relating to humans and human disease.

Other limitations

Publication bias is recognised as being a problem in guideline development that is based on published literature. Positive studies are much more likely to achieve publication than negative

studies, tending to give a biased view of the consistency of evidence at the synthesis stage. This is out of the control of the GDG, and it is difficult to assess the impact of publication bias. A further problem was the paucity of any focused research for some of the key questions. Problems that were specific to particular questions are covered under each question in section 4.

Writing the guideline

The first draft of the guideline was drawn up by the guideline leader and revised after full discussion with the GDG. This draft was submitted for external review. The second draft was presented to the GDG and Steering Group for further comments. The third draft was put out for public consultation, prior to revision and publication.

Updating the guideline

Literature searches were repeated for all evidence-based questions at the end of the GDG development process, allowing any relevant papers published and indexed up until 10 May 2009 to be considered. Future guideline updates will consider published evidence indexed after this cut-off date.

Use of the guideline

Healthcare providers, employers and employees need to use their judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited in this guideline are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the healthcare professional, employer and employee in the light of individual circumstances, the wishes of the patient, clinical expertise and resources.

4 The guideline

Most of the recommendations in this section are aimed at OH professionals. There may be circumstances where recommendations will be followed by other health professionals involved in the management of staff exposed to, or infected with, VZV. As arrangements within organisations vary, we have not listed alternatives to OH professionals within the guideline.

The GDG assumes that in the healthcare sector, employers have implemented the 2003 Chief Medical Officer's letter 'Chickenpox (varicella) immunization for health care workers PL/CMO/2003/'. This letter recommended a 'catch-up' exercise of vaccination for non-immune HCWs already in post (www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4065217.pdf [accessed 1 April 2009]).

Box 1 Recommendations from the Green Book¹

For HCWs, much of the evidence assessed by the GDG supports the recommendations in the published national guidance, *Immunisation against infectious disease* ('the Green Book').¹ These recommendations have been summarised in green text. To avoid confusion or duplication the reader is referred to the Green Book for the full details.

Where the GDG believes that the evidence review supports additional recommendations, or where the GDG wishes to make good practice points in areas not covered by existing guidance, the text is in black.

Question 1

What is the appropriate occupational health management of healthcare workers at the pre-employment stage of recruitment, with particular reference to indications for screening of VZV status and the methodology to be employed?

Statement	Evidence
<i>Temperate zones</i>	
A systematic literature review, looking at the predictive value of a history of varicella infection, reported studies in HCWs which found that a history of chickenpox has high positive predictive value (PPV), as high as 95–98% in HCWs from temperate climates, but has a low negative predictive value (NPV) (6–27%).	Holmes 2005 ²⁴
Of 119 house officers (junior doctors) in the USA reporting a history of varicella, only 2 had non-protective titres, and 4 of 15 who reported no history of VZV had non-protective titres. The seroprevalence was 96%, PPV 95% and NPV 27%.	Alagappan 1999 ²⁵
In another study involving HCWs in Ireland, 970 were tested for antibodies, of whom 206 were asked for VZV history. PPV was 95% and NPV 11%.	Gallagher 1996 ²⁶
In Belgium, 4,293 hospital employees had a 98.5% VZV seroprevalence, and a history of past VZV infection had a PPV of 98.9% and NPV 3.4%.	Vandersmissen 2000 ²⁷
In the UK, 356 nursing applicants in 1998 had 96% VZV seroprevalence. A history of past VZV infection had a PPV of 98% and NPV 14%.	Waclawski 2002 ²⁸

continued

Statement	Evidence
<i>Temperate zones – continued</i>	
In Italy, in a study of 333 HCWs, 97.9% were seropositive for VZV and a study of 616 paramedical students in Italy showed that a history of past VZV infection gave a positive predictive value of 98.3% for VZV antibody seroprevalence.	Fedeli 2002 ²⁹ Trevisan 2007 ³⁰
In the USA, 1,331 hospital workers had 98.4% VZV seroprevalence. Of the 1.6% who were seronegative, 8.7% had given a negative history of past VZV infection and 0.5% had given a positive history.	Brunell 1999 ³¹
<i>Mixed climate zones</i>	
When HCWs have been studied in other parts of the world, seroprevalence of VZV has been lower. For example, in a study of 4,006 new HCW recruits (local and international), in Saudi Arabia, only 86% were seropositive. However, there was regional variation, ranging from 91% for those originating in western countries, to 81% for those from the Far East.	Almuneef 2006 ³²
In a UK hospital, in a cohort of 747 HCWs (431 from temperate and 192 from tropical regions) at pre-employment, the seroprevalence of VZV was 91.7% in the temperate group, as opposed to 84.4% in the tropical group.	MacMahon 2004 ³³
Other studies support the lower seroprevalence in those from the tropical regions, such as the one below.	
In 335 Israeli medical personnel, there was a 94.8% seroprevalence overall, but this was significantly lower if the medical personnel were from Asian tropical regions or Africa (77%).	Chodick 2006 ³⁴
In Saudi Arabia, 450 soldiers were screened by serology testing, and seropositivity for VZV was 88.5%.	Memish 2001 ³⁵
When the cost effectiveness of different approaches is also taken into account from the economic evaluation studies, the conclusion is that it is most cost effective to screen with history first. The results are described under Key Question 4.	Skull 2001 ³⁶ Thiry 2003 ³⁷ Gray 1997 ³⁸

On the basis of the studies listed in this section, and the economic evaluation ones, the following is recommended.

Recommendation*	Grade
OH professionals should ask the HCW, on employment, if they have ever had chickenpox and/or shingles. For employees who grew up in temperate climates, a positive history should be taken as evidence of immunity to VZV.	B
OH professionals should arrange for HCWs who give a negative or uncertain history of chickenpox and shingles to have serological testing for VZV antibodies.	B
OH professionals should ensure that on employment HCWs born or raised in tropical or subtropical climates have serological screening regardless of a positive history of past VZV infection (see Appendix 6 for a map of tropical and subtropical zones).	C
(This recommendation clarifies and strengthens the advice in Green Book which states that routine testing should be considered in individuals 'born and raised overseas'.)	

*Recommendations in green are similar to those in the Green Book¹ which should be referred to for consistency of actions.

Question 2

What is the appropriate occupational health management of healthcare workers in relation to the administration of vaccination?

Statement	Evidence
VZV vaccine gives adults long-term protection from serious VZV disease, with only 9% of vaccinated adults developing breakthrough chickenpox when followed up for nearly 12 years post vaccination. Moreover, this breakthrough infection was mild even amongst vaccinated adults who did not seroconvert or who had lost detectable antibody.	Ampofo 2002 ¹⁶
In the USA, of 263 seronegative HCWs who were tested post vaccination, 57.1% who had received one dose of vaccine seroconverted, and 81.6% of those who received two doses seroconverted.	Weinstock 1999 ³⁹
100 Australian HCWs non-immune to VZV were vaccinated with two doses and 94.9% had detectable antibodies after the first and 100% after the second vaccine.	Burgess 1999 ⁴⁰

On the basis of the studies listed in this section the following is recommended.

Recommendation*	Grade
OH professionals should offer the VZV vaccination, using two doses of vaccine, to all VZV susceptible HCWs (HCWs who test seronegative to VZV).	C

*Recommendations in green are similar to those in the Green Book¹ which should be referred to for consistency of actions.

The GDG was also interested in considering the question of what actions and/or advice should be followed if HCWs decline vaccination, or have temporary or permanent contraindications. There was no direct evidence from the papers to answer this question; however, the following suggestions have been made in the form of 'good practice points'.

Recommendation	Grade
Where immunocompetent HCWs decline vaccination, the OH professional should assess the risk of varicella infection to the HCW and the risk of onward transmission of infection to their patients.	GPP
The OH professional should explore with the HCW their reasons for declining vaccination, explain the benefits of vaccination and the individual's professional duty to protect their patients from infection, and encourage them to take up vaccination. Doctors should be reminded of the relevant General Medical Council guidance (<i>Good medical practice</i>) which states that 'you should protect your patients, your colleagues, and yourself by being immunised against common serious communicable diseases where vaccines are available' (www.gmc-uk.org/guidance/good_medical_practice/health.asp). Other HCWs should be reminded of any relevant professional guidance.	GPP
Where vaccination is still declined, the OH professional should recommend that the HCW should preferably avoid work with high-risk patients, eg immunocompromised patients, pregnant women and neonates.	GPP

continued

Recommendation	Grade
Where HCWs have a contraindication to vaccination, eg immunocompromised through illness or treatment, the OH professional should assess the risk of varicella infection to the HCW and the risk of onward transmission of infection to their patients. Where appropriate the HCW should be advised to avoid work with high-risk patients.	GPP
Where a contraindication to vaccination is temporary, eg pregnancy, the OH professional should advise the HCW to be vaccinated once the contraindication ceases.	GPP
For all the groups above, avoiding high-risk patients is the ideal for susceptible staff who remain unvaccinated. However, where particular skills or numbers of staff will be compromised by excluding such staff, the risk assessment needs to acknowledge the additional risk, and staff must be made aware of the need to be vigilant to symptoms and signs of infection.	GPP
Decisions about placement will need to be taken in conjunction with the HCW, their manager and infection control, while respecting the HCWs right to medical confidentiality.	GPP
OH professionals should advise non-immunised HCWs to avoid patient contact immediately and take advice from their OH department or GP if they develop signs or symptoms suggestive of chickenpox or zoster.	GPP

Question 3

What is the appropriate occupational health management of workers who present with chickenpox or shingles and what is the optimal management of their work colleagues? (And in healthcare, what is the appropriate management of workers exposed to infected colleagues or patients?)

Statement	Evidence
In a study of 158 patients and 93 HCWs exposed to 14 index cases with chickenpox, VZV transmission only occurred when the index case and contacts were in the same room and not in a multiple room setting. Attack rates were 11.8% and 0% respectively. There was a low observed risk of nosocomial transmission (in a setting with high seroprevalence of VZV antibody (97%) in HCWs).	Langley 2000 ⁴¹
There is weak evidence that if exposure is sufficient to produce infection the source is more likely to be a patient, not a HCW. In a study of transmission in a hospital setting, 6.8% (8/118) of HCWs developed VZV when a patient was the source, as opposed to 1.4% (1/72) of HCWs when another HCW was the source. This difference was not statistically significant; however, there were small numbers in the study and if the trend were to continue a sample size double the one used here would have given statistically significant difference. These findings may reflect a difference between HCW–patient exposure and HCW–HCW exposure.	Josephson 1990 ⁴²

There was no direct evidence from the papers to answer this question; however, the following suggestions have been made in the form of good practice points.

Recommendation*	Grade
OH professionals should advise a HCW diagnosed with chickenpox to remain away from the workplace until there are no new lesions and all lesions have crusted over.	GPP

continued

Recommendation*	Grade
OH professionals should recommend that a HCW diagnosed with localised herpes zoster on a part of the body that can be covered with a bandage and/or clothing, and who does not work with high-risk patients, should be allowed to continue working. If the HCW is in contact with high-risk patients, then an individual risk assessment should be carried out.	GPP
The risk assessment should consider the vulnerability of the patients and whether skill and staffing levels will be compromised by redeploying the infected staff member. Decisions about redeployment will need to be taken in conjunction with the HCW, their manager and infection control, while respecting the HCW's right to medical confidentiality.	GPP
OH professionals should recommend that HCWs with localised herpes zoster lesions that cannot be covered with a bandage and/or clothing, or who are immunocompromised, and HCWs with disseminated herpes zoster, should be excluded from the workplace until there are no new lesions and all lesions have crusted over.	GPP
OH professionals should recommend that unvaccinated HCWs without a definite history of chickenpox or zoster and having a significant exposure to VZV should either be excluded from contact with high-risk patients from 8 to 21 days after exposure, or should be advised to inform their OH department before having patient contact if they feel unwell or develop a fever or rash.	GPP
In the majority of situations a high level of vigilance for malaise, rash or fever (including taking temperature daily) throughout the incubation period will be adequate. Decisions about redeployment away from high-risk patients need to take into account the vulnerability of the patients and whether skill and staffing levels will be compromised by redeploying the exposed staff member. Decisions about redeployment will need to be taken in conjunction with the HCW, their manager and infection control.	GPP
OH professionals should offer VZV vaccine to unvaccinated HCWs without a definite history of chickenpox or zoster and having a significant exposure to VZV. Where vaccine is given within 3 days of exposure, the OH professional should explain to the HCW that the vaccine may offer some protection from the recent exposure but it cannot be relied upon to interrupt transmission.	GPP
Irrespective of the interval since exposure, OH professionals should offer vaccine to reduce the risk of the HCW exposing patients to VZV in the future.	GPP
OH professionals should inform vaccinated HCWs exposed to VZV that the vaccination does not give 100% protection and they must report any symptoms to OH.	GPP
Where pregnant and immunocompromised HCWs are exposed to VZV, an OH or other appropriate health professional must assess them for VZIG. Pregnant HCWs with a positive history of chickenpox do not require VZIG.	GPP
Pregnant HCWs <i>without</i> a positive history of chickenpox or shingles and HCWs who are immunocompromised regardless of their history of VZV infection, should be tested promptly for VZ antibodies. Those who are antibody negative require VZIG.	GPP

*Recommendations in green are similar to those in the Green Book¹ which should be referred to for consistency of actions.

Question 4

What is the likely economic consequence of the implementation of such policies?

Statement	Evidence
A simulation model was constructed to assess the relative costs and cost-effectiveness of different screening and vaccination strategies. Screening HCWs by history, testing those with uncertain or negative history, and vaccinating those who test negative for VZV antibodies reduces the mean number of incidents per hospital year of chickenpox from 3.9 to 2.2 and gives net savings of £440 per incident averted (data on an average hospital with 1,450 staff involved in the programme and 255,000 patient bed-days/year).	Gray 1997 ³⁸
Two systematic reviews of economic models quote three papers that consider HCWs. Of these, the Gray paper is the only UK-based one. They both agreed with the conclusions from the Gray paper, which is that serotesting of HCWs with a negative history of VZV is the most cost-effective approach to vaccination.	Skull 2001 ³⁶ Thiry 2003 ³⁷
A third and more recent systematic review again demonstrated that serotesting of HCWs with a negative history of VZV is the most cost-effective approach to vaccination.	Rozenbaum 2008 ⁴³

No studies were found that examined the cost effectiveness of universal serology testing to determine need for vaccine in HCWs from tropical and subtropical climates.

The healthcare setting

On the basis of the studies listed in this section the following is recommended.

Recommendation	Grade
In the healthcare setting, a programme which consists of taking a history of previous chickenpox infection and/or shingles, testing those with uncertain or negative history, and vaccinating those who test negative for VZV antibodies is the most cost-effective approach.	B

Staff in prisons and immigration removal centres

The recommendations from the referenced guidance²¹ are reproduced below. The wording is taken directly from the guidance and is not that of the GDG. Readers should refer to the full guidance document for background and further detail.

Where the GDG believes that findings from their literature review can be generalised to the prison setting, the recommendation has been given the appropriate grade.

Recommendation	Grade
All prison/centre staff without a history of chickenpox should ideally have their varicella immune status tested.	B
In immigration removal centres those who are non-immune should ideally be offered vaccine, as an occupational health measure.	C
Staff who develop symptoms of chickenpox infection must inform their employer of their illness and stay away from work until crusting over of lesions.	GPP

continued

Recommendation	Grade
Staff with localised herpes zoster on a part of the body that can be covered with a bandage and/or clothing should be allowed to continue working unless they are in contact with vulnerable detainees, in which case an individual risk assessment should be carried out.	GPP
Vulnerable non-immune contacts with significant exposure to chickenpox-infected staff in the prison or centre should be identified and offered VZIG prophylaxis.	GPP

Other employment sectors

Recommendation	Grade
Chickenpox vaccination and antibody testing is not routinely recommended for workers in employment sectors outside healthcare or the prison service.	GPP
A worker diagnosed with chickenpox should remain away from the workplace until there are no new lesions and all lesions have crusted over.	GPP
A worker with localised herpes zoster on a part of the body that can be covered with a bandage and/or clothing should be allowed to work if they are well enough. Workers with disseminated zoster, localised zoster that cannot be covered (eg facial), and those who are immunocompromised, regardless of the site and extent of the lesions, should remain away from the workplace until all the lesions have crusted over.	GPP
Employers should ask pregnant or immunosuppressed workers who have been exposed to an infected colleague at work to contact their GP or specialist immediately for advice.	GPP

5 Future research and audit criteria

Future research

Future research should include the following studies:

- Studies of immunity in non-immunised populations of different ethnic groups growing up in temperate and non-temperate climates to ascertain the contribution of climate and ethnicity to epidemiology of chickenpox infection and immunity.
- Studies of effectiveness and cost-effectiveness of different approaches to managing control of nosocomial infection.
- Longitudinal studies of healthcare workers measuring vaccine uptake, breakthrough infection rates and transmission of infection in the workplace amongst staff and patients.
- Management of vaccinated healthcare workers: no testing post vaccine, test at exposure and if negative give a booster, versus administration of a single booster to all healthcare workers at time of exposure.
- Studies of the relationship between post vaccination antibody titres and breakthrough infection.
- Evaluation of reference testing for antibody in relation to protection.

Suggested audit criteria

Recommendation	Audit criteria
VZV vaccine is effective in providing adults with long-term protection from serious VZV disease and VZV-susceptible HCWs should be offered vaccination using two doses of vaccine.	Proportion of VZV-susceptible HCWs offered two doses of vaccine. Proportion of those offered vaccine who complete the full course of two doses of vaccine.
Where HCWs are born or raised in temperate climates, occupational health professionals should arrange for those who give a negative or uncertain history of chickenpox and shingles to have serological testing for VZV antibodies.	Proportion of HCWs born or raised in temperate climates where history of chickenpox or shingles is recorded. Proportion of healthcare workers with negative or uncertain history of chickenpox and shingles who have serological testing for VZV antibodies.
Occupational health professionals should ensure that on employment HCWs born or raised in tropical or subtropical climates have serological screening regardless of a positive history of past VZV infection (see Appendix 6 for map of tropical and subtropical zones).	Proportion of healthcare workers born or raised in tropical or subtropical climates who have serological testing for VZV antibodies.

Appendix 1 Role and remit of the guideline developers

The Guideline Development Group (GDG) was established for the duration of the project, to comprise representation of key stakeholder groups and to undertake development of the guideline.

The team delivering the project was made up of:

- guideline development group leader
- guideline development group
- project manager
- information scientist
- clinical director of OHCEU (now Health and Work Development Unit (HWDU)).

Membership of the project team is listed on page v of the guideline. Declarations of interest were required from all individuals involved in development of the guideline.

The governance framework within which HWDU operates ensures that the development and delivery of projects is overseen by the Steering Group and Executive Committee of the HWDU. Respectively these are an external and internal stakeholder group responsible for the strategic direction of the HWDU, advising on the relevance of the work programme to those delivering occupational health services in the UK, and responsible for the delivery to NHS Plus of high-quality deliverables.

Appendix 2 Electronic searches

Deriving search terms and concepts from the key questions led to the search terms as detailed below. They comprised a core of MeSH terms relating to VZV, and were supplemented by a list of additional terms which were then combined in the actual search using Boolean Operators.

Sources

The published literature was sought via the following databases:

Medline	Cochrane Library
Embase	Health Periodicals Database
HSE Line	Evidence Based Periodicals
FOM library	CINAHL

Search dates

The search strategy limited papers to those published between 1 January 1995 and 1 January 2005.

Literature searches were repeated for all evidence-based questions at the end of the GDG development process, allowing any relevant papers published and indexed up until 10 May 2009 to be considered. Future guideline updates will consider published evidence indexed after this cut-off date. We recommend that this guideline is reviewed in five year's time.

MeSH terms

Varicella-Zoster virus	Human herpes virus 3
Herpesvirus 3, human	Ocular Herpeszoster virus
Chickenpox virus	VZ virus
Herpeszoster virus	HHV 3
Herpesvirus varicella	Varicella Zoster

Search terms

Population/Environment:

Healthcare worker	Occupation
Worker	Occupational
Employee	Work
Carer	Workplace
Patient	Hospital
Pregnancy	Community
Maternity	Institution
Immunosuppressed	Prison
Immunocompromised	School
Infection	
Infectious	

Core terms:

(MeSH Terms – as above)

Shingles

Occupational Health

Actions/Interventions:

Vaccination

Inoculation

Immunity

Contra-indication

Screening

Antiviral

VZIG

Preventative

Risk

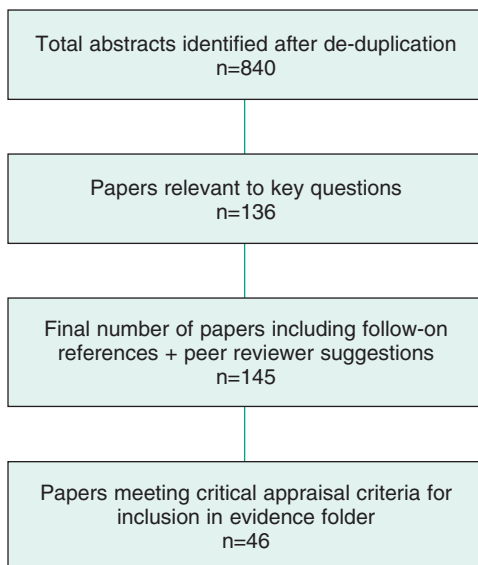
Exclusion

Isolation

Redeployment

Appendix 3 Summary of literature search (all questions)

Fig 1 Flow chart for study selection



Appendix 4 SIGN grading system for evidence statements

SIGN guidelines (SIGN 2000) employ a grading system for evidence from peer-reviewed publications. This system ranks evidence on a 4-point scale, based on the study design and its potential for bias. A high-quality meta-analysis or a randomised controlled trial (RCT) with a very low risk of bias is graded as 1++, case reports are graded as 3 and expert opinion is graded as 4.

Levels of evidence	
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs) or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2–	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Case reports, case series
4	Expert opinion

Thus, the level of evidence indicates both the type of study from which the evidence is derived and the quality of the study as graded by the reviewers. This guideline includes study types that SIGN 2000 does not categorise (eg cross-sectional studies and economic evaluations).

The evidence statements are used to generate recommendations, with grades indicating the quality and weight of evidence behind each recommendation. The grades employed are shown below.

Grades of recommendation	
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

Good practice points

Good practice points (GPPs) are practical points that the GDG wished to emphasise but for which there is no research evidence and nor is there likely to be any. These points would include, for example, some aspect of management or treatment that is regarded as such sound clinical practice that nobody is likely to question it. These are not alternatives to evidence-based recommendations, and are only used where there is no other way of highlighting the issue.

Appendix 5 Evidence tables

Summary of papers included as evidence

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Alagappan (1999) ²⁵	Cross sectional	+	1	154 new house officers from April to July 1997	Pre-employment screening for VZV by questioning and serology testing	Of 119 house officers who reported a history of varicella, only 2 had non-protective titres, and 4 of 15 who reported no history of VZV had non-protective titres. The authors conclude that a reported history of VZV infection or vaccination did not ensure presence of protective titres. House officers should be tested for immunity.
Almuneef (2003) ⁴⁴	Cohort	2+	1, 4	2,047 multi-national HCWs in a Saudi Arabian hospital including doctors, nurses, medical technicians and clerical staff who responded to a questionnaire	Identification of VZV IgG sero-negatives for vaccination among subgroup with negative or unknown history of VZV	217 (29%) of those with a negative or unknown history were tested. 83% tested seropositive. There was no difference in seroprevalence among different nationalities or occupational groups.
Almuneef (2004) ⁴⁵	Cohort	2+	1	1,058 new HCW recruits of different nationalities	Self-administered questionnaire and serology	Positive predictive value of history of chickenpox for seropositivity was 89%; negative predictive value was 22%. Authors conclude history of varicella was an unreliable indicator of susceptibility in HCWs of different nationalities.
Almuneef (2006) ³²	Cohort	2+	1	4,006 new HCW recruits, international and local, in Saudi Arabia	Serology for VZV antibodies	86% were seropositive, which is lower than in other studies. However, there was regional variation, ranging from 91% for those originating from western countries, to 81% for those from the Far East.

continued

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Alter (1986) ⁴⁶	Cohort	2+	1, 2	2,730 HCWs in a children's hospital USA working in 1984	Screening by questionnaire, and serology offered to those with negative or uncertain past history of VZV infection; monitoring of VZV susceptible for 12 months	19% had no or uncertain history of VZV infection and of these, 28% were found to be susceptible, representing 5% of the total population. Six of the potential 135 VZV susceptible HCWs acquired varicella during the 12 months of the study.
Ampofo (2002) ¹⁶	Cohort	2+	1, 2	461 adults enrolled in VZV vaccine trials in 1979–99	Various doses of vaccine produced by different companies	9% developed breakthrough chickenpox 8 weeks to 11.8 years post vaccination, but this was mild even amongst vaccinees who did not seroconvert or who had lost detectable antibody.
Apisarnthanarak (2007) ⁴⁷	Cohort and cost-benefit analysis	2+	1, 4	110 HCW and 8 ICU patients in Thailand exposed to 1 index case of VZV	Prospective follow-up of exposed group and implementation of policy	Reported history of VZV was reliable predictor of immunity. Self-reported history of VZV correlates well with seroprevalence (PPV 100%). A report of no prior history was unreliable (NPV 61%). VZV surveillance and immunisation appears to be a cost-saving strategy to thwart anticipated future outbreaks of VZV. Cost model calculations: routine screening and vaccination for 30 new HCWs in this facility, annual cost \$1,600, as opposed to treatment etc costs of \$3412.50 on the basis of the outbreak data.
Banz (2004) ⁴⁸	Retrospective cross-sectional epidemiological survey	+	4	1,344 unvaccinated cases from 278 paediatricians, GPs and internists in Germany	Review of available German health statistics, retrospective survey, and economic evaluation	Average total cost for society – €188 million. 82% (€154 million) due to work loss, but this is a general population study, and not limited to HCWs.
Behrman (2003) ⁴⁹	Case series	3	1	5 HCWs with VZV infection	Serology testing by latex bead agglutination assay (LA)	All 5 HCWs had documented positive VZV titres by LA. Follow-up investigation of 53 LA samples was tested against IgG enzyme-linked immunosorbent assay (ELISA), and 9 were judged to be falsely positive by LA. LA may be prone to false positives and may be inappropriate for screening HCWs.

continued

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Brunell (1999) ³¹	Cohort	2+	1	1,331 HCWs	Serological testing versus history of chickenpox	Only 1.6% seronegative for VZV, including 8.7% of those with a negative history, and 0.5% of those with a positive history.
Burgess (1999) ⁴⁰	Cohort	2+	2	100 Australian HCWs non-immune to VZV	Vaccination with 2 doses of live attenuated varicella vaccine given 2 months apart	94.9% had detectable antibodies after the first and 100% after the second vaccine. 81% were re-tested 12 months after the second dose, and 3 had become seronegative.
Burken (1997) ⁵⁰	Economic model	+	4	HCWs with doubtful or negative history of VZV at medical centre	Economic evaluation	Depending on the economic model used and based on Hep B vaccination as a comparative outcome – may or may not be effective.
Celikbas (2006) ⁵¹	Cross sectional	+	1, 4	363 HCWs (in Turkey)	Serology for VZV and cost comparison between screening and vaccinating and vaccinating alone	98% had antibodies to VZV, and economic evaluation suggested that it was more cost effective to screen before vaccination.
Chodick (2005) ⁵²	Economic evaluation	+	4	63,353 HCWs (in Israel)	Cost- effectiveness analysis	Based on numerous assumed models, concludes routine vaccination of HCWs, with or without selection of susceptible people, is not cost effective.
Chodick (2006) ³⁴	Cross sectional	+	1	335 Israeli medical personnel	Serological testing	94.8% seroprevalence overall, but significantly lower if from Asian tropical regions (77%).
Chong (2004) ⁵³	Cohort	2+	1	HCWs in children's hospital in Singapore. Phase 1 had 278, and Phase 2 had 2,006 HCWs	Screening by questionnaire, those with negative or uncertain history of VZV were serologically tested, and those who lacked VZV antibodies were offered vaccination	14.7% and 26.9% in Phases 1 and 2 respectively had no previous history of varicella. Of these, 55.3% in Phase 1 and 26.9% in Phase 2 tested negative for antibodies.
Faoagali (1995) ⁵⁴	Case series	3	4	HCWs in Australia	Cost of monitoring and control of outbreak	20 cases in a large metropolitan hospital from an outbreak. A total of 165.6 person days were lost, at an estimated cost of \$18,000.

continued

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Fedeli (2002) ²⁹	Cohort	2+	1	333 HCWs in Italy	Testing for VZV antibodies	97.9% were seropositive for VZV. Attempted to analyse age-specific seroprevalence but numbers very small.
Gallagher (1996) ²⁶	Cohort	2+	1	970 HCWs in Ireland tested for antibodies, of which 206 were asked for VZV history	Testing for antibodies, compared with history of VZV	History is a good predictor of immunity (PPV=95%) but not of non immunity (NPV=11%).
Gayman (1998) ⁵⁵	Economic evaluation	+	4	All employees of a single hospital	Comparison of 2 vaccine strategies: screen or screen and vaccinate	Screen and vaccinate more cost effective. This strategy generated cost savings of about \$50 per employee.
Gray (1997) ³⁸	Economic evaluation	+	4	Simulation model based on published data and replies to a 1994 postal survey questionnaire from 39 UK hospitals	The relative costs and cost-effectiveness of different screening and vaccination strategies for dealing with hospital incidents of varicella (index case in staff member or patient)	Screening all staff for previous VZV, testing those with uncertain or negative history, and vaccinating those who test negative for VZV antibodies, reduces annual incidents to 2.3 (from 3.9), with a net saving of £440 per incident averted.
Gurevich (1990) ⁵⁶	Cross sectional	++	1	1,001 employees tested by employee health service	Serology testing	94% were seropositive for VZV.
Hatakeyama (2004) ⁵⁷	Cross sectional	++	1, 2	877 HCW population of University of Tokyo Hospital Sept–Oct 2002	Pre-vaccination Screening	Out of 854 HCW tested for varicella 2.8% (24/854) were susceptible.
Holmes (2005) ²⁴	Systematic review	2++	1, 2	12 articles identified from 2,103 articles from January 1996 to May 2002	Predictive value of a history of varicella infection	A positive history of varicella is reliable, but a negative history is not. Most studies also conclude that for those with a negative or uncertain history of varicella, serologic testing is advisable, rather than presumptive vaccination, because most of this group will be immune.

continued

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Josephson (1990) ⁴²	Comparative study of management post exposure strategies	2+	3, 4	Susceptible HCWs in a hospital following exposure to VZV	3 trial protocols: (1) standard – susceptible HCW kept off work. (2) Trial I – HCW screened post-exposure and kept off work. (3) Trial II – as (2) but separate off duty for those with home exposure.	Trial II was safe and the most cost effective of the strategies – though more lost days prevented additional HCW exposure.
Kanra (2003) ⁵⁸	Cross sectional	+	1	Medical students	Comparison of history versus serological testing	History has a good PPV for seropositivity and a poor NPV.
Katial (1999) ⁵⁹	Case report	3	1, 2	1 case of an immunocompetent HCW with negative history and serology for VZV working in a paediatric unit	Vaccination with 3 doses of VZV and serology testing	HCW was removed from clinical duties because she continued to remain seronegative by ELISA testing. She had 3 direct contacts with infectious children and did not develop chickenpox. Using more sensitive assays, she was found to have VZV specific IgG at a titre of 1:8. ELISA testing post vaccination may not be sensitive, and in cases of non seroconversion, more sensitive assays may need to be considered before removal from work.
Knaggs (1998) ⁶⁰	Case report	3	1, 3	1 ambulance driver	Occupational exposure to VZV pneumonia	Ambulance driver contracted chickenpox acute respiratory distress syndrome, and required 13 days of ventilatory support before making a full recovery. He had had no VZV screening or vaccination prior to, or after, exposure.

continued

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Langley (2000) ⁴¹	Prospective cohort	2+	1–3	158 patients and 93 HCW exposed to 14 index cases chickenpox in a paediatric hospital in Canada over 3 years	Exposure to one of 14 index cases of chickenpox	97% (90/93) staff and 44% (69/158) patients were 'immune'. Overall attack rate for all exposed susceptibles was 4.5% (4/89, 95% CI 1.2–11.1%). Transmission only occurred when the index case and susceptible contacts were in the same room and not in a multiple room setting (Fisher exact test $p=0.02$). Attack rates were 11.8% (4/34, 95% CI 3.3–27.5) and 0 (0/55, 95% CI 0–6.5%) respectively. Low observed risk of nosocomial t/m (in setting with high seroprevalence of VZV (97%) in HCW).
Lerman (2004) ⁶¹	Cross-sectional prevalence study	+	1	335 hospital and community HCWs, 117 day-care centre workers and 121 blue collar workers as controls in Israel	Serology testing for VZV antibodies	Total VZV seropositivity was 94.4%, with no significant difference between the study groups. High seroprevalence suggests that no special occupational precautions are necessary.
Levy (2003) ⁶²	Cohort	2+	3	Over 300 prison inmates and staff in Australia	VZV exposure from contact with 1 index case	5 cases of chickenpox were identified. There were 23 contacts of the index case during transport, and 2 of these contacts developed chickenpox despite having given a prior history of infection. No cases of chickenpox were notified among staff during the course of the investigation.
MacMahon (2004) ³³	Cohort	2+	1	747 HCWs (431 from temperate and 192 from tropical regions) at pre-employment (Guy's and Thomas') between Sept 2001 and July 2002 in the UK	Questionnaire and serology	Seroprevalence of VZV was 91.7% in temperate group, as opposed to 84.4% in tropical group. Authors suggest that a significantly higher proportion of seronegative HCWs will be fail to be detected if history alone is used to decide whether to vaccinate, in those born, and/or raised in tropical climates.

continued

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Memish (2001) ³⁵	Cross sectional	+	1, 4	450 soldiers in Saudi Arabia	Screening by serology testing	Seropositivity for VZV was 88.5%. Calculations in this paper indicate that to achieve cost savings through pre-vaccination antibody tests (as opposed to universal vaccination), the minimum seroprevalence rate for VZV would be 57.1%. Therefore, in this scenario, pre-vaccine screening is cost effective for VZV rather than universal vaccination.
Ng (1996) ⁶³	Case report	3	3	57 patients 129 staff in a neonatal unit in Hong Kong	Management of potential outbreak following exposure to VZV	No cases of VZV from this exposure. Measures included rapid identification of VZV status of all neonates and staff with uncertain history of VZV infection.
O'Neill (2003) ⁶⁴	Telephone survey/audit and vaccine economic evaluation	+	4	Audit: OH VZV policy in 22 hospitals in major UK cities treating paediatric inpatients and neonatal unit staff at John Radcliffe Hospital	Audit of policies and economic evaluation	21 of 22 hospitals had varying OH VZV screening policies. Cost of VZV cases in neonatal unit staff in prior 5 years £2,474. £1,601 estimated cost of necessary screening and vaccination of current staff complement.
Qureshi (1999) ⁶⁵	Cross sectional	+	2, 3	70 of 90 VZV seronegative HCWs at Cleveland Clinic, USA	Uptake and attitudes to vaccination among VZV seronegative HCWs	19 (27%) gave pre-employment history of chickenpox. 24% did not recollect initial notification letter re VZV status and offer of VZV vaccine at no cost. Significantly ($p<0.05$) higher uptake of VZV vaccine among HCW with (27/38, 71%) versus without (6/15, 40%) direct patient care.

continued

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Rozenbaum (2008) ⁴³	Economic evaluation, systematic review	++	4	Cost effectiveness of varicella vaccination programmes: 21 studies in all, 2 relating to HCWs	Study One (UK) focused on HCWs in paediatric units, vaccinating staff without a clear history of varicella and serological testing of those. Study Two (Israel) focused on HCWs in general, using cost of vaccination only as the cost. Three strategies were used: 1. Vaccination after screening for history of VZV followed by serology test 2. Vaccination after serological test 3. Mass vaccination of all eligible subjects	Study One: Introduction of vaccination of susceptible staff would involve a relatively small incremental cost and was likely to be cost effective. However, various aspects of study unclear, including discounted rates and perspective, limiting validity of model. Study Two: Cost of avoided cases between \$25,000 and \$89 million per life year, and using the first strategy was the most favourable. Costing had a limited perspective, calculating incremental cost per avoided case but the incremental cost of the vaccination campaign was not accurately taken into account.
Ryan (2003) ⁶⁶	Cohort	2+	1	192,335 navy recruits in USA	All recruits screened by serological testing and those who were seronegative were vaccinated (2 doses of vaccine)	7.2% were seronegative to VZV. Overall incidence of chickenpox in navy has reduced by over 80% since introduction of programme.
Saiman (2001) ¹²	Cohort (Follow-up of subjects in different vaccine trial cohorts)	2+	1, 2	120 healthy USA HCWs with no history of chickenpox, seronegative for VZV by the gold standard fluorescent antibody to membrane antigen (FAMA) VZV antibody test	1, 2 or 3 doses of the Merck or Smith Kline and Beecham VZV vaccines with variable duration of follow-up	10% (12/120) crude chickenpox attack rate 0.5–8.4 years after vaccination in 91 (76%) vaccine recipients following one or more exposures. Cases occurred in 4/22 (18%) following household and 6/72 (8%) with hospital exposure. No case was severe, with on average 40 vesicles.
Santos (2004) ⁶⁷	Cross sectional	2+	1, 4	215 (97%) HCW in 2 neonatal units in Sao Paulo University hospitals	Questionnaire, serological testing using in-house VZV ELISA, and vaccination of seronegatives. Cost comparison of various possible strategies	100% (150/150) of HCWs with history of varicella tested VZV seropositive and 92% (60/65) without a history also tested positive. Following vaccination, 2 out of 5 had high avidity antibodies after the first dose suggesting prior infection.

continued

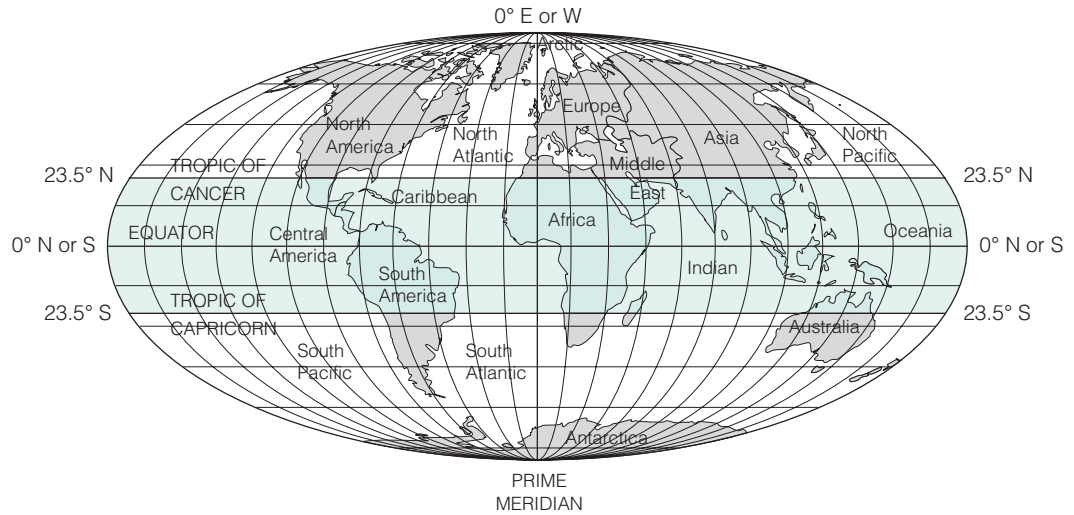
First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Skull (2001) ³⁶	Systematic review	2++	4	High-quality studies from 1966 to 2000, all age groups	VZV administered	Review of cost-effectiveness data: study by Gray ³⁸ found serotesting of adult HCW with a negative or uncertain history of varicella was the most cost-effective approach to vaccination. This approach is supported by mathematical modelling.
Tennenberg (1997) ⁶⁸	Economic evaluations	+	4	224 HCW susceptible to VZV in New York	40 exposures to VZV in 1994	31% of exposed susceptibles became VZV immune following exposure. 59% had multiple exposures and special paid absences while employed by the hospital. Varicella vaccination for susceptible employees would result in financial savings.
Thiry (2003) ³⁷	Economic evaluations	++	4	17 relevant papers to November 2000, of which 3 relate to HCW	Economic evaluations of VZV vaccination programmes	All 3 studies reported that vaccination of susceptible HCWs generated savings from an employer's viewpoint.
Trevisan (2007) ³⁰	Cross sectional	+	1	616 para-medical students in Italy between 2003–2005	Determination of seroprevalence and predictive value of self-reported questionnaire	High PPV (98.3%) of history of varicella for seroprevalence.
Vandersmissen (2000) ²⁷	Cross sectional	+	1	4,293 hospital employees in 22 hospitals in Belgium	History of varicella and VZV serological status	98.5% VZV seroprevalence. History of chickenpox was 83% sensitive, 38.9% specific, with PPV 98.9% and NPV 3.4%. Seronegativity was significantly associated with age and job, increasing with both older and younger age.
Waclawski (2002) ²⁸	Cohort study	2+	1	356 nursing applicants b/w June 1998 and August 1998	Pre-vaccination serology testing and history	96% were seropositive for VZV. PPV of a history of VZV for seropositivity was 98%, and the NPV was 14%. The authors comment that screening using past history alone would have missed 40% of those possibly susceptible to VZV, and therefore advocate pre-vaccine serology testing of HCWs regardless of history.

continued

Varicella zoster virus: occupational aspects of management

First author	Study design	Research quality (SIGN grading)	Key question(s)	Study population	Intervention or exposure	Main results
Weinstock (1999) ³⁹	Cohort	2+	2, 4	263 sero-negative HCWs in tertiary cancer centre in New York	Latex agglutination testing for VZV antibodies post vaccination	Of those tested, 57.1% who had received one dose of vaccine seroconverted, and 81.6% of those who received 2 doses seroconverted. Total cost of vaccination was compared with cost of absence through VZV infection, and projected savings exceeded \$53,000 in the first year of vaccination.
Wurtz (1999) ⁶⁹	Case study	3	2	1 case of a nurse	VZV vaccination	VZV antibodies following vaccination with one dose of vaccine. This was milder than primary VZV, in keeping with other similar reports.

Appendix 6 World map showing tropical and temperate zones



Tropical zones are shown within the Tropic of Cancer and the Tropic of Capricorn. Tropical climates have high temperatures throughout the year. Subtropical climates are found adjacent to the tropics. Temperate climates have mild to warm summers and cool winters (most European countries). Some countries have a mixture of climates. Map reproduced with kind permission of: www.worldatlas.com

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