JCVI statement on

Rotavirus vaccines

This statement reflects the opinion of the Joint Committee on Vaccination and Immunisation (JCVI, the committee) on rotavirus vaccines. The statement reviews the considerations made by JCVI, the evidence examined, and the conclusions and recommendations of JCVI.

Contents

Executive summary

Rotavirus infection is the most common cause of [gastroenteritis](#) in children under five years of age worldwide.[1] It is estimated that globally, rotavirus is responsible for causing approximately 111 million episodes of gastroenteritis requiring care at home, 25 million clinic visits, two million hospitalisations and around 611,000 deaths annually in children under five years of age.[2,3] Although the burden of disease of rotavirus gastroenteritis is greatest in developing countries, it accounts for a large number of hospitalisations, and a few deaths in developed countries.[4]

In England and Wales, an estimated 130,000 episodes of rotavirus-induced gastroenteritis occur each year in children under five years of age and approximately 12,700 of these children are hospitalised.[5-7] In the UK, deaths caused by rotavirus are extremely rare and difficult to quantify accurately, but in England and Wales there are approximately three to four a year.[8]

There are two licensed rotavirus vaccines - Rotarix® (manufactured by GlaxoSmithKline) and RotaTeq® (manufactured by Sanofi Pasteur MSD) - they are both highly effective in preventing severe disease. The strength of evidence for protection against milder disease differs between them. Both vaccines are given orally. Rotarix® vaccine requires two doses; RotaTeq® vaccine requires three doses.

JCVI considered that the licensed rotavirus vaccines provided good protection in infants against rotavirus infection, and that the vaccines have good safety profiles. Rotavirus vaccination would reduce the incidence of gastroenteritis in the population. However, the cost-effectiveness analysis[7] showed that, based on current vaccine prices, universal vaccination of young children significantly exceeded the commonly accepted threshold for cost-effective healthcare interventions. Introduction of rotavirus vaccines may become cost-effective if the vaccine price is reduced significantly.

The role of JCVI

 JCVI is a statutory expert Standing Advisory Committee. Its purpose is to provide expert, impartial advice to the Secretaries of State for Health for England, Scotland, Wales and Northern Ireland on matters relating to communicable diseases, preventable and potentially preventable through immunisation.

JCVI has submitted its advice to ministers on the use of rotavirus vaccines and their potential benefit based on the best evidence reflecting current good practice and/or expert opinion. The process involved a robust, transparent, and systematic appraisal of all the available evidence from a wide range of sources.
JCVI processes: www.advisorybodies.doh.gov.uk/jcvi/processes.htm

JCVI was notified of new rotavirus vaccines that were in development in a horizon scanning paper in October 2004: www.advisorybodies.doh.gov.uk/jcvi/mins011004.htm

JCVI then considered rotavirus vaccines on eight separate occasions and the minutes of these meetings can be found at the following links:

Feb 2006: www.advisorybodies.doh.gov.uk/jcvi/mins150206.htm
June 2006: www.advisorybodies.doh.gov.uk/jcvi/mins210606.htm
October 2006: www.advisorybodies.doh.gov.uk/jcvi/mins181006draft.htm
June 2007: www.advisorybodies.doh.gov.uk/jcvi/mins20jun07.htm
October 2007: www.advisorybodies.doh.gov.uk/jcvi/mins17Oct07.htm
June 2008: www.advisorybodies.doh.gov.uk/jcvi/mins20jun07.htm
June 2007: www.advisorybodies.doh.gov.uk/jcvi/mins20jun07.htm
March 2008:
www.advisorybodies.doh.gov.uk/jcvi/Rotavirus_Subgroup_Minutes_17_March_2008.pdf

Evidence examined by JCVI

JCVI examined both published and unpublished research and reviewed the available evidence. This section details the work that JCVI considered before deciding not to recommend rotavirus vaccines at the vaccine prices considered:

The areas of work included:

- epidemiology and burden of rotavirus disease in the UK
- vaccine composition, efficacy and safety studies
- expected impact of rotavirus vaccination programme including:

  - impact on herd immunity
  - cost-effectiveness of rotavirus vaccination
  - whether any specific risk groups should be targeted

Appendix B lists the evidence considered by JCVI in making their decision.

Epidemiology and burden of rotavirus disease in the UK

Epidemiology of rotavirus disease

Rotavirus infections in humans are caused by three groups of rotaviruses (Groups A, B and C); Group A is the commonest cause of severe gastroenteritis. Rotavirus infection in the UK is seasonal (see figure 1), occurring mostly in winter and early spring (January to February/March). Although deaths from rotavirus in the UK are rare and therefore difficult to quantify accurately, in England and Wales they are likely to be approximately three to four a year.[8] In England and Wales, an estimated 130,000 episodes of rotavirus-induced gastroenteritis occur each year in children under five years of age and approximately 12,700 of these children are hospitalised. [5,6,7]

People of any age can be infected by rotavirus but most infections occur in children between one month and four years of age (see figure 2). Infections are often recurrent, and many children experience infection on more than one occasion by three years of age.[9] Recurrent symptomatic infections are usually associated with another genotype although asymptomatic infections can be the result of infection with a strain previously encountered. Infection in newborns is common but tends to be either mild or asymptomatic because of protection by circulating maternal antibodies.[10,11] Once someone has had a rotavirus infection they usually develop immunity although it may be short lived.[11] Infections in adults are rarely reported although not uncommon in individuals caring for, or in contact with, children who have rotavirus gastroenteritis. Older children and adults can also develop asymptomatic infection, which may be important in maintaining rotavirus infection in the community.[12] Rotavirus is highly contagious and is mainly transmitted by the faecal-oral route, although respiratory transmission may also occur.[1]

Gastroenteritis caused by rotavirus leads to severe diarrhoea, vomiting, stomach cramps, dehydration and mild fever; in developing countries, severe diarrhoea can lead to deaths. Dehydration that results from gastroenteritis is the main cause of rotavirus-deaths in developing countries. Gastroenteritis usually lasts from three to eight days.[13]
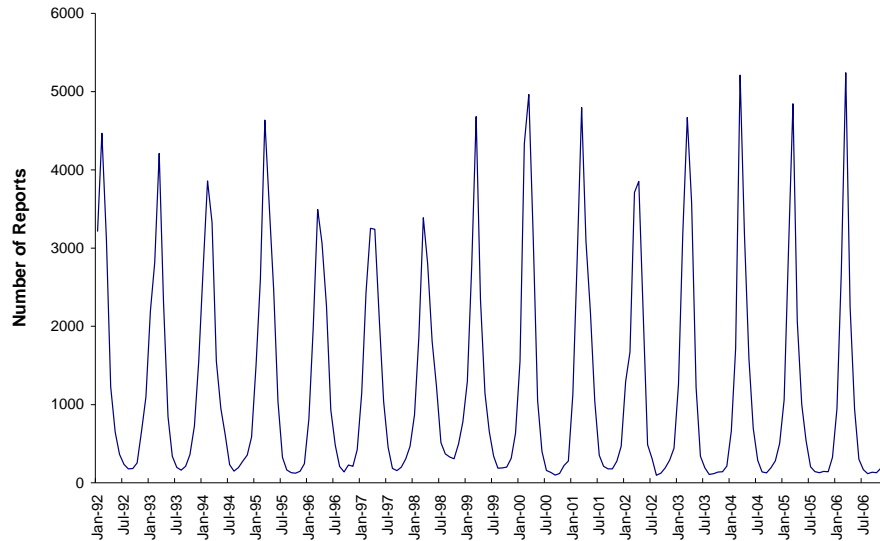
Figure 1: Seasonal distribution of rotavirus infections - laboratory reports of all identifications by month England and Wales, 1992-2006. This graph illustrates that rotavirus infections occur mainly in the late winter and early
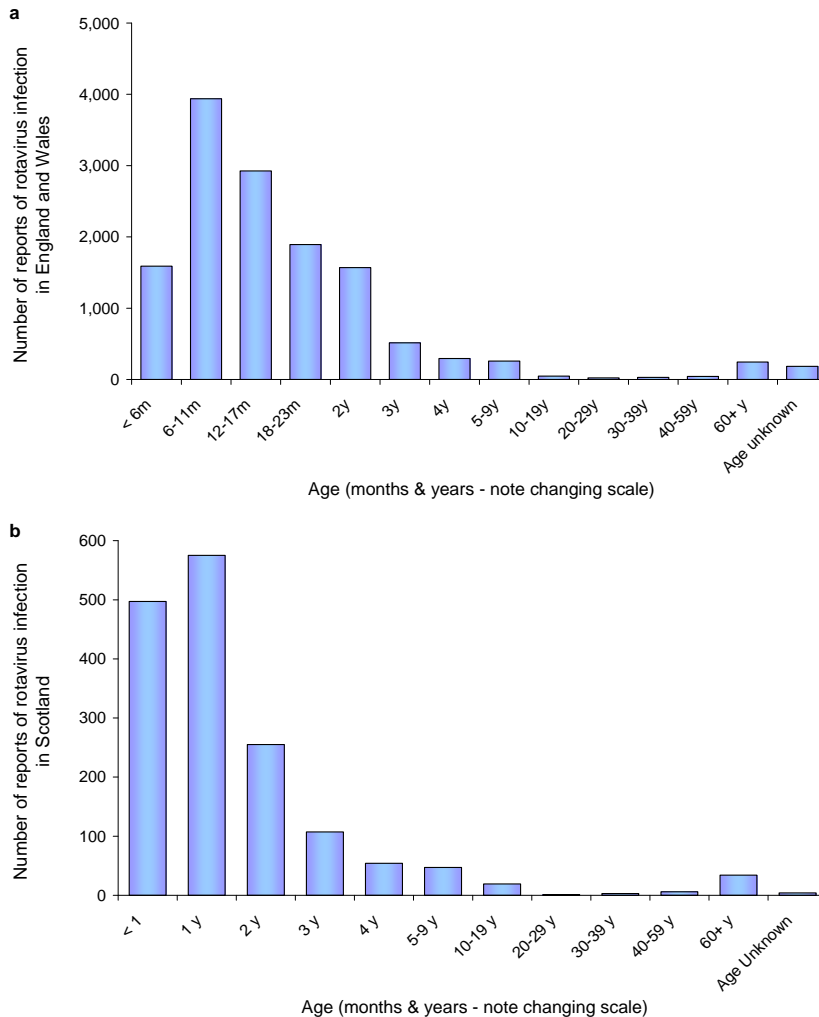

Figure 2: Age distribution of rotavirus infections reported, (a) England and Wales, 2005 (n = 13,549) *Source: Rotavirus LabBase, Health Protection Agency* (b) Scotland, 2005 (n = 1,602) *Source: Health Protection Scotland.*

Virology and burden of disease

Rotavirus is the most significant cause of gastroenteritis in young children under five years of age. The group agreed that the data on disease burden was sufficiently robust and further efforts to obtain further morbidity data were not needed. Although there were differences in the absolute number of cases between the studies presented, the percentage of gastroenteritis cases that were attributable to rotavirus remained similar. This was reflected in the cost effectiveness work. A critical issue in determining cost effectiveness is the number of deaths caused by rotavirus in the UK but, as this is so rare, it is difficult to quantify accurately. However, it is likely to be approximately three to four deaths a year.[8] Furthermore, it is unclear to what extent other illnesses that these individuals have (co-morbidities) may contribute to these rare events.

Appendix A gives a more detailed explanation supporting this conclusion.

Vaccine composition, efficacy and safety studies

JCVI has considered vaccine efficacy data presented from published papers and data provided by the vaccine manufacturers. The findings are summarised below.

Vaccine composition

There are two rotavirus vaccines licensed for use in the UK; the two vaccines are not interchangeable:

- Rotarix® (manufactured by GlaxoSmithKline); and
- RotaTeq® (manufactured by Sanofi Pasteur MSD).

Both are live vaccines. Rotarix® was attenuated through serial cell culture passage and RotaTeq® was the result of reassortment between a naturally attenuated bovine strain (G6P[5]) and human rotavirus strains. This attenuation means they cause no disease in humans. The reassortant strains carry the major antigenic properties of the common co-circulating human rotavirus strains (i.e. they produce an immune response by generating antibodies that are effective against the naturally circulating human strains that cause disease).

The RotaTeq® vaccine contains five live human-bovine reassortants (HBRV):

- the bovine strain [14] used to make the reassortants was of G6P[5] type
- the four human strains comprised G1P[8], G2P[6], G3P[8] and G4P[8].

From these parent strains, the five reassortants in the vaccine are as follows:

- four each express one VP7 glycoprotein from the four human rotavirus strains (i.e. one of G1-G4) plus the VP4 protein (P7) from the bovine strain
- one expresses the VP4 protein from the G1P[8] human rotavirus strain plus the VP7 protein (G6) from the bovine strain.

It is the reassortment step that limits replication in the human gut so that it can be described as abortive; in other words, the virus cannot reproduce itself very well, so does not cause rotavirus infection. Nevertheless, some replication in the gut does occur. This small amount of replication that does occur could theoretically irritate the gut lining, causing diarrhoea in some patients.

The strain in Rotarix® is a live, attenuated derivative of a virus isolated from the stool sample of a 15-month-old infant and then passaged 26 times in cultured cells.

Both Rotarix® and RotaTeq® are administered orally.

The Rotarix® vaccination course consists of two doses given from the age of six weeks and an interval of at least four weeks between doses.[15] The RotaTeq® vaccination course consists of three doses given from the age of six weeks and an interval of at least four weeks between the doses.[16]

Vaccine efficacy and safety

JCVI looked at the evidence of vaccine efficacy from published clinical trials.[14,17,18] Both Rotarix® and RotaTeq® have been shown to protect against gastroenteritis due to rotavirus of serotypes G1P[8], G2P[4], G3P[8], G4P[8], G9P[8], which account for around 88% of the rotavirus strains that are in circulation in the UK.[7]

In the past, there had been safety concerns with Rotashield® - a rotavirus vaccine that was originally introduced in the United States in 1998 and is now no longer available. Rotashield® was withdrawn from use in the United States in 1999 because of evidence of an increased but small risk of an adverse event called intussusception following vaccination.

Pre-licensing studies for Rotarix® and Rotateq® were designed to identify any increased risk of intussusception. The results of these studies did not show a statistically significant increase in risk.

To date, there is no evidence suggesting a causal association between RotaTeq® or Rotarix® and the development of intussusception. The Centers for Disease Control and Prevention (CDC) are also examining data from 90,000 vaccinations but the results are not yet available. In addition, the company that manufactures RotaTeq® has also received 241 passive reports of intussusception. Analysis of this data shows that there is no link between the vaccine and intussusception, there is no clustering with time after vaccination and the observed rates are lower than the expected rate for this disease in the general population.

There was a suggestion of an increased risk (signal) of Kawasaki disease from pre-licensing trials with RotaTeq® - five cases of Kawasaki disease in the RotaTeq® treated individuals versus one case in the placebo treated individuals. Reports following an announcement by the FDA and consequent regulatory action have been lower than expected. Although 16 cases of Kawasaki disease (15 in the US) have been spontaneously reported within the last year they are likely to be a result of stimulated reporting and no causal link has been shown. The observed rates were lower than the expected rate for this disease in the general population. In the post-marketing study, no cases of Kawasaki disease had been identified at the time of last reporting[19] in the RotaTeq® group compared with one case in the historical controls for the same period at risk.

For Rotarix®, a post-marketing surveillance study using spontaneous reporting is ongoing in Mexico. Over the last three years, 61 cases of intussusception have occurred within 30 days of vaccination and no cases of Kawasaki disease have been reported. The Group noted that the two vaccines have been used in countries that are likely to have very different reporting requirements for suspected adverse reactions (see Appendix C).

Conclusions

Both rotavirus vaccines are broadly similar in their efficacy at preventing severe disease but they may not be equally effective at preventing milder disease. However, this is difficult to assess as vaccine trials for both vaccines use different outcome measures. The Rotarix® vaccination course (two doses) can be completed as early as ten weeks and should be completed by around six months (24 weeks). The RotaTeq® vaccine course (three doses) can be completed as early as fourteen weeks and should be completed by around six months (26 weeks). The vaccines are not interchangeable.

JCVI noted that because of possible links with Kawasaki disease and intussusception, detailed evaluation of the vaccines against these adverse reactions has been undertaken. Within 30 days of vaccination, Kawasaki disease and intussusception is lower in those who have been vaccinated than in the population as a whole. Therefore, there is no evidence of a causal association between RotaTeq® or Rotarix® and the development of Kawasaki disease or intussusception.

Risk groups for rotavirus

The committee noted that published papers have been provided on risk groups that are particularly vulnerable to rotavirus infection. There was no indication for a recommendation for vaccination of specific risk groups as opposed to universal immunisation of infants. As rotavirus infection is endemic in the population, immunocompromised individuals are certain to be infected naturally. However, there is no evidence that natural rotavirus infection in an immunocompromised host is life threatening or results in unusual illness. However, as both rotavirus vaccines are live, people who are immunocompromised should not receive the vaccine on a precautionary basis.

Expected impact of rotavirus vaccination programme

The committee examined work carried out on the cost-effectiveness of rotavirus vaccines. This work considered the cost of introducing rotavirus vaccines against the potential benefits of preventing rotavirus illness.

The Health Protection Agency (HPA) presented their model on the benefit of introducing a rotavirus immunisation programme in the UK.[7] The model assessed the effectiveness of the vaccine in children up to five years of age.

The assumed price of RotaTeq® used for the base case was £25 per dose. The assumed price of Rotarix® used for the base case was £35 per dose.

Apart from the protection offered against the strains in the vaccine, the vaccines offer cross protection against additional rotavirus strains. This was taken into account in the modelling. There is no evidence of differences between the severities of disease caused by the different strains. In the model, vaccine efficacy was adjusted for the genotype distribution in the UK. These data were estimated from 315 samples from patients affected by rotavirus-induced gastroenteritis. Samples were obtained from specimens sent to the Health Protection Agency's Centre for Infections from several UK surveillance centres from January to June 2006.

Impact of herd immunity

In addition to the vaccine impact estimated in the published model, the extra possible benefit of vaccination due to herd immunity was estimated in three groups:

- infants four months old and under who have not yet received a full course of vaccination
- individuals over five years old who were not included in the model as being directly protected. Constant vaccine efficacy was assumed between the ages of birth to five years. The model assumed that after five years of age, individuals were no longer protected from the vaccine because protection is not likely to persist to adulthood
- the five per cent of the eligible cohort who missed the vaccination (assuming 95% vaccine coverage).

It was estimated that if these groups were fully protected from the first year of vaccination, the number of rotavirus disease cases prevented by vaccination would increase by an additional 15% at the most.

Cost-effectiveness of rotavirus vaccination

The committee considered the differences in two cost-effective modelling papers by Lorgelly *et al.*, 2008 [20] and Jit *et al.*, 2007. [7] The ranges of estimates of disease burden overlapped in the Jit *et al* and the Lorgelly *et al* papers except in their estimates of cases in the community, which were higher in the Lorgelly paper. These additional cases do not present to health services so do not impose a cost to the health service but do suffer a loss in terms of, for example, quality of life, parents/carers taking time off work.

The Jit *et al.*, 2007 paper[7] was considered in the main by the committee because it presented results in terms of costs per quality adjusted life years (QALYs) gained. The source of data for QALY losses for an episode of rotavirus were based on those obtained in a Canadian physician-clinic based survey of the effects on both the child and the carer.[21] The study estimated that the quality of life detriment per rotavirus episode to a carer is almost as great as the detriment to a child. The survey did not sample children infected by rotavirus who were treated at home and not brought to the physician clinic, so it is not known whether these cases (and their carers) would suffer the same quality of life detriment. It was noted that other studies using the Canadian data, for example studies in Australia [22] and Belgium,[23] assumed that QALY losses to caregivers in such cases were substantially lower than for cases presenting to primary care.

The committee was presented with a number of cost-effectiveness estimates using alternative scenarios to that in the Jit *et al* model.[7] These included using alternative estimates of rotavirus cases not presenting to the health service reported in other studies,[24,25] estimates of hospital acquired infection reported by a hospital-based study,[26] and including quality of life impact for zero, one, and two carers. The scenario with the most favourable cost-effectiveness results was one which used the additional rotavirus cases from the Lorgelly *et al.*, 2008 paper [20] and which assumed full quality of life impact on two caregivers even for cases not presenting to the health service (GP clinics, A&E or NHS Direct). None of the other estimates were even marginally cost-effective based on the current vaccines list prices.

Conclusion

Using the cost-effective analysis and assumptions, the cost of both the vaccines would need to be much less than their current list prices before either could be considered to be cost-effective using currently accepted thresholds in the majority of scenarios considered.

Recommendation

Rotavirus vaccines would reduce the incidence of gastroenteritis in the population. However, at the vaccine prices considered they do not meet the current economic criteria for the introduction of a new vaccine.

Introduction of rotavirus vaccines would only become cost-effective if the vaccine prices are much less than those at which they are currently being offered.

Appendix A

Virology

Rotaviruses consist of a [genome](#) with 11 segments of double-stranded (ds)[RNA](#) contained within a [protein](#) core (VP2), a middle protein layer (VP6) and an outer layer made up of two proteins, VP7 and VP4, on which a dual classification is based (G type and P type, respectively). Although there are at least 15 G type and 28 P type rotaviruses, only 10 G and 11 P types have been identified in humans (see figure 3).[27] Rotavirus strains co-circulate in any one region and during a rotavirus season and the most common types globally contain either G1, G2, G3, G4 or G9 in conjunction with P[4] or P[8] proteins. In the UK, between 1995 and 2007, a total of 28 different strains were identified, the strain VP6 is the most abundant type. Among other types, G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8] account for 88.1 per cent of genotypes identified from European surveillance data from 16 countries over three years. Distribution changes over time, for example, in 2005 and 2006, G9P[8] strains were the second most common rotavirus strains (42.28 per cent and 23.18 per cent respectively) detected in the UK. Diversity among rotaviruses is maintained through the accumulation of point mutations resulting in the selection, driven by short-term herd immunity, of antibody escape mutants and the introduction, through reassortment, of animal/human hybrid strains to which herd immunity associated with antibodies to the outer proteins does not exist. Since 1990, two novel rotavirus strains have had a major impact on public health worldwide. A variant of G2P[4], resulting from the accumulation of point mutations and G9P[8] an animal/human reassortant strain.
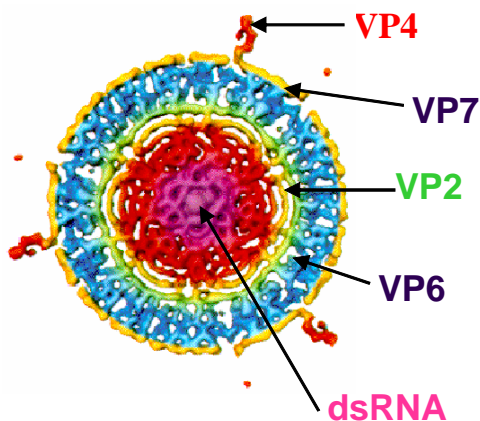

Figure 3: Graphical representation of rotavirus and table showing how groups, subgroups and types are classified.
Picture from B.V. Venkataram Prasad.

Classification	Diversity	Determined by
Groups	A to E	VP6
Sub-groups	I, II, I + II non I and non II	VP6
G-type	G1 to G15	VP7
P-type	P1 to P25	VP4
NSP4 genotype	A to E	NSP4

Burden of rotavirus disease

The main obstacle to calculating the burden of rotavirus disease is that the symptoms caused by rotavirus infection are similar to those caused by a number of other viruses. In addition, most cases of rotavirus gastroenteritis presenting to the health service do not involve laboratory confirmation of the causal organism. In order to get a robust calculation of the number of infections cause by rotavirus in the UK, JCVI considered different studies using various techniques. The committee considered the differences in surveillance (passive versus structured), diagnostic methods (classical versus molecular), and changes in disease burden over time.

In a number of studies, the burden of rotavirus disease was measured in the number of children under five years of age admitted to hospital suffering from rotavirus-like symptoms (hospitalisation rates) and those going to a general practitioner (GP consultation data).

One structured surveillance study carried out in the mid 1990s looked at the burden of rotavirus in both GP consultation and community specimen data from patients suffering from gastroenteritis using classical diagnostic techniques (for example, electron microscopy).[28] This study identified a diagnostic gap of 45.1 per cent (in other words, in 45.1 per cent of the gastroenteritis cases, no cause could be identified) in the community cohort, and 63.1 per cent in cases attending a GP consultation. In an attempt to reduce the diagnostic gap, these samples were reanalysed using molecular amplification techniques - RT-PCR.[29]

Using RT-PCR reduced the diagnostic gap considerably to 25 per cent. Rotavirus was detected in 51.1 per cent of the cases of gastroenteritis in children under five years and in 23.3 per cent of children under five years in the absence of any symptoms. Even when there were no symptoms, the rates of rotavirus detection were 20 to 29 per cent in young people aged up to 19 years and 4 to 13 per cent in adults aged twenty years and over. These asymptomatic carriers may represent a large reservoir of virus - a source of potential infection for non-immune individuals or those in whom immunity has waned.

The committee noted that conducting structured surveillance also has a large impact on estimating the incidence of infection by rotaviruses, and in reducing the diagnostic gap. A structured surveillance in East Anglia[4] analysed the stool samples from children under five years of age who either attended a GP involved in the surveillance study or from samples collected from GPs, and hospitals in the same area who were not participating. Rotavirus infection was identified in 47.5 per cent of samples from children going to GPs that participated in the structured surveillance programme, a higher percentage than that found in children attending GPs in the same region but not participating in the structured surveillance (29.6 per cent). The committee noted that the reason why rotavirus was found in a higher percentage of samples from GPs participating in the structured surveillance might be due to better case definition in the structured surveillance study.

The committee also considered a structured surveillance study of infectious intestinal disease in pre-school children in the community 'The Nappy Study'.[30] Reports indicate a fall in the number of cases of gastroenteritis seen in primary care in recent years, possibly as a result of better hygiene control, but other factors such as the introduction of NHS Direct and changes to the out of hours primary care service provision may also have had an influence in the number of cases reported.

The study also indicated that, compared with the study carried out in the 1990s,[28,29] there has been a significant reduction in the number of cases of gastroenteritis caused by bacteria and parasites in young children. However, the proportion of gastroenteritis cases due to viruses, and to rotavirus has remained comparable. There were differences from year to year, associated with the natural seasonal variability characteristic of enteric viruses. For instance, compared with previous seasons, the 2006/7 rotavirus winter season started later and fewer cases were seen. Questions were raised about whether rotavirus caused all the cases of intestinal disease. The committee noted that detection of rotavirus RNA using an RT-PCR test is less sensitive than the PCR tests for bacterial DNA. For example, PCR can identify as few as ten copies of bacterial DNA whereas 100 to 1000 copies are required for viral RNA detection.

A further approach considered by the committee is to estimate the proportion of health care burden for gastrointestinal disease attributable to different organisms by using the seasonal trend in laboratory diagnoses for those organisms.[31] The advantage of this method is that it takes into account that not all episodes of rotavirus disease presenting to the health service necessarily lead to a laboratory diagnosis. Using this method, an estimated 45 per cent of hospitalisations for acute gastroenteritis in the zero to five years age range are attributable to rotavirus.

The committee also considered the burden of hospital acquired rotavirus infection and several published papers were reviewed. One early paper indicated that a third of rotavirus infections among patients in hospitals in the US had been acquired in hospital.[32] Several other studies and reviews of the subject had also documented the importance of hospital-acquired rotavirus infection, although wide variation in study methodologies rendered comparison between studies difficult.[33,34] The committee noted that a study to determine the disease burden of community-acquired and healthcare-associated rotavirus gastroenteritis at Alder Hey hospital, Liverpool, was ongoing. Subject enrolment had recently been completed and laboratory analyses and data cleaning were under way. Preliminary, unpublished observations indicated that of the 356 community-acquired gastroenteritis cases examined, rotavirus was detected by RT-PCR in 42 per cent of cases. In the 220 healthcare-acquired cases, rotavirus was detected in 31 per cent of cases. Co-infections with other enteric viruses were recognised but few bacterial infections were seen.

The committee noted that the treatment of rotavirus infection in hospitals usually involved oral rehydration and there was no need to give fluids intravenously.

Glossary

Antibodies are proteins, naturally present in the body or produced in response to the introduction of an antigen, which react with specific antigens (foreign bodies).

Asymptomatic infection is an infection where the infected individual does not show symptoms.

Attenuated means to weaken the effect, in this case to weaken the ability of rotavirus to cause disease.

Electron microscopy is the use of the electron microscope in scientific investigation. An electron microscope magnifies objects using electrons rather than light. Electron microscopes can obtain a much higher magnification than light microscopes.

Enteric virus is a virus that inhabits the intestinal tract.

Gastroenteritis is an inflammation of the stomach and intestines, causing diarrhoea, vomiting, stomach cramps, dehydration and mild fever.

Genome refers to the total genetic content contained in a living cell, or in the DNA or RNA of a virus.

Genotype is the genetic constitution of an organism.

Immunity is the condition that permits either natural or acquired resistance to disease.

Immunocompromised refers to an individual who has impaired immune function.

Intussusception is a potentially life-threatening condition that occurs when part of the intestine infolds (telescopes) into a nearby portion. It is age-dependent, occurring most commonly between the ages of four and 11 months and peaking in those between seven and 11 months. The cause of intussusception is not identified in more than 90 per cent of infants.

Kawasaki disease, otherwise known as 'mucocutaneous lymph node syndrome', is a serious illness in children that is characterised by fever of at least five days duration together with conjunctivitis, redness or swelling of the hands or feet or generalised skin peeling, rash, cervical lymphadenopathy and gingivitis. Progression to vasculitis, coronary artery aneurysm and resultant myocardial infarction makes it a leading cause of acquired heart disease among children in developed countries.

Maternal antibodies are transferred to the baby in the womb by its mother so that when it is born it may have some immunity (protection) against diseases that its mother has immunity against.

Passive surveillance of rotavirus is the most common form of surveillance and relies on standardised reporting to the Health Protection Agency/Scotland when cases of disease are detected.

PCR, short for polymerase chain reaction, is a technique used to amplify DNA (in other words to increase the amount of DNA in a sample to make analysis easier).

Protein is one of the essential constituents of living organisms. The significance in terms of vaccination, is that the particular protein combinations of a virus are recognised by the individuals immune system as 'foreign' and the body develops antibodies that target these proteins.

Reassortment is the swapping of genetic material between two rotavirus strains to produce a new virus strain.

RNA (ribonucleic acid) is a constituent of all living cells and many viruses. The structure and base sequence of RNA are determinants of protein synthesis and the transmission of genetic information.

RT-PCR, short for reverse transcription polymerase chain reaction, is a technique used to amplify RNA (in other words to increase the amount of RNA in a sample to make analysis easier).

Structured surveillance is a form of surveillance that actively stimulates reporting of specific diseases. This includes surveillance of a disease with a well-defined case definition within a well-characterised population of known denominator.

Symptomatic infection is an infection where the infected individual shows symptoms (signs) of the infection for example, vomiting, diarrhoea, stomach cramps etc.

Appendix B
Published papers considered by JCVI

Vaccine efficacy and safety

Reference numbers:

1, 14-19

Rotavirus epidemiology

Reference numbers:

2-4, 9-12, 25-30, 32-55

Modelling

Reference numbers:

5-8, 20-24, 31

Appendix C

List of countries that have implemented rotavirus vaccination according to the World Health Organization, updated 19 December 2008

Country	Schedule (months)	Comments
Brazil	2, 4	
Colombia	2, 4, 6	For risk groups
Costa Rica		Some private sectors
Ecuador	2, 4	
El Salvador	2, 4	
Honduras		
Mexico	2, 4	
Nicaragua	2, 4, 6	
Panama	2, 4	
Peru	2, 4, 6	Part of country
United States of America (the)	2, 4, 6	
Venezuela (Bolivarian Republic of)	2, 4	
Bahrain		
Qatar	2, 6	
Belgium	2, 3, (4)	Two or three doses are recommended depending on which vaccine is used
Cyprus		Given only by the private sector
Finland		From May 2009
Luxembourg	2-3, 3-4	
Australia	2, 4, 6	Part of country third dose is dependent on vaccine brand used (chosen by state or Territory)
Micronesia (Federated States of)		

Adapted from: *WHO vaccine-preventable diseases: monitoring system 2008 global summary*

www.who.int/vaccines/globalsummary/immunization/scheduleselect.cfm

Go back to vaccine efficacy and safety

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