

# Pregnant women and measles: we need to be vigilant during outbreaks



Asma Khalil,<sup>a,b,c</sup> Athina Samara,<sup>d,e,f,\*</sup> Colin Campbell,<sup>g</sup> and Shamez N. Ladhani<sup>g,h</sup>

<sup>a</sup>Fetal Medicine Unit, St George's Hospital, St George's University of London, UK

<sup>b</sup>Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, UK

<sup>c</sup>The Royal College of Obstetricians and Gynaecologists, London, UK

<sup>d</sup>Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

<sup>e</sup>Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden

<sup>f</sup>FUTURE, Center for Functional Tissue Reconstruction, University of Oslo, Oslo, Norway

<sup>g</sup>Immunisation and Countermeasures Division, UK Health Security Agency, UK

<sup>h</sup>Paediatric Infectious Diseases Research Group and Vaccine Institute, Institute of Infection and Immunity, St George's University of London, London, UK



## Summary

A number of countries including the UK are currently experiencing large outbreaks of measles affecting mainly young children but also adolescents and young adults. Women of childbearing age are a particular group of concern because the 1988 Wakefield Lancet paper, which falsely asserted a connection between the MMR vaccine and autism, was associated with a large and sharp decline in childhood MMR uptake over several years. This has left large cohorts of non-immune adolescents and young adults (born between 1998 and 2004), including young women who are now of childbearing age and remain susceptible to measles as well as rubella. Pregnant mothers are at higher risk of serious complications, such as pneumonia, with adverse pregnancy complications including fetal loss, premature birth, and neonatal death. Measles infection may also result in subacute sclerosing panencephalitis (SSPE), a very rare but very severe and invariably fatal neurodegenerative complication that typically manifests many years after acute measles infection but can have a short-onset latency with a fulminant course in pregnant women. Here, we summarise the epidemiology of measles infection, factors associated with the current measles outbreaks, as well as the risks and outcomes of measles, including SSPE, in pregnancy. We propose an algorithm for clinical management of measles infection in pregnancy. We also highlight the importance of early liaison with local health protection teams for risk assessment, diagnosis and management of suspected measles in pregnancy and close contacts as well as susceptible pregnant women exposed to a person with measles in the community.

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## Introduction

A number of countries have reported a large increase in measles cases and outbreaks recently.<sup>1</sup> According to a World Health Organization (WHO) report released in November 2023, the number of measles cases worldwide increased by 18% between 2021 and 2022, and deaths from measles increased by 43%.<sup>1</sup> More recently, the WHO reported a nearly 50-fold increase in measles cases among its 40 European Region member states, from fewer than 1000 in 2022 to 42,200 measles cases in 2023.<sup>2</sup> On 19th January 2024, the UK Health Security Agency (UKHSA) declared a national incident over the rise in measles cases in the UK, signalling a growing public health risk.<sup>3</sup> Given that most measles cases in the

community are not confirmed through laboratory testing, the reported number of laboratory-confirmed cases is likely to be only the tip of the iceberg, with true case numbers being much higher in the community.

In England, most measles cases have been confirmed in children,<sup>4</sup> and consequently, local and national campaigns have been implemented to improve the uptake of the measles–mumps–rubella (MMR) vaccine in this age group.<sup>1</sup> A substantial proportion of measles cases, however, occur in adults (25% in England),<sup>5</sup> which has important implications for high-risk populations, including pregnant individuals. Women of childbearing age are a particular group of concern in the current measles outbreak because the 1988 Wakefield Lancet paper,<sup>6</sup> which falsely asserted a connection between the MMR vaccine and autism, was associated with a large and sharp decline in childhood

\*Corresponding author. Department of Women's and Children's Health, Karolinska Institutet, 17177 Stockholm, Sweden.

E-mail address: [athina.samara@ki.se](mailto:athina.samara@ki.se) (A. Samara).

MMR uptake over several years. This has left large cohorts of non-immune adolescents and young adults (born between 1998 and 2004),<sup>5</sup> including young women who are now of childbearing age (Fig. 1) and remain susceptible to measles, despite multiple catch-campaigns targeted for these cohorts over the years.<sup>7</sup>

Additionally, whilst childhood MMR vaccine uptake had mostly recovered after many years of campaigning to pre-Wakefield MMR vaccine uptake rates, there has been a slow and consistent year-on-year decline in childhood immunisation rates generally, including MMR, for more than the past decade (Fig. 2).<sup>8</sup> In the UK, London remains the most vulnerable region with the lowest MMR vaccine uptake over many years, as well as some under-vaccinated communities such as the Charedi Orthodox Jewish community, the traveller community, Steiner (Anthroposophic) community and recent migrants.<sup>5</sup> Notably, too, the recent COVID-19 pandemic was associated with large declines in routine childhood immunisation uptake, including MMR, in most parts of the world, including the UK<sup>9</sup> In 2022. The WHO and the United Nations Children's Fund (UNICEF) reported<sup>10</sup> that global vaccination coverage continued to decline in 2021, with 25 million infants missing out on lifesaving vaccines. Compared to 2019, there were 6.7 million more children who missed the third dose of the polio vaccine and 3.5 million who missed the first dose of the HPV vaccine, which protects against cervical cancer later in life. Additionally, the CDC recently reported that,<sup>11</sup> between 2020 and 2022, over 61 million doses of measles-containing vaccine were postponed or missed due to COVID-19-related delays, elevating the risk of larger outbreaks globally.

A consequence of the erratic MMR vaccine uptake over the past two decades is that many countries are now failing to achieve the high population immunity required to interrupt transmission of the highly infectious measles virus<sup>12</sup> The risk of large outbreaks associated with low vaccine uptake is further compounded by growing anti-vaccine sentiments and “vaccine fatigue”<sup>13</sup> after the COVID-19 pandemic and the growth of displaced populations through wars and famine in many parts of the world.

### Measles in pregnancy

Measles is a highly contagious disease, whose basic reproduction number (R0, the average number of secondary cases arising from an infectious individual in a susceptible population) ranges from 9 to 18, much higher than smallpox (R0, 5–7) or influenza (R0, 2–3).<sup>14,15</sup> Although measles virus is not teratogenic and the disease is usually mild and self-limiting in most children and adults, it can cause serious and potentially fatal complications, especially in high-risk populations, including immunocompromised and pregnant individuals. Contracting measles during pregnancy poses risks to both the mother and the fetus.<sup>16</sup> The highest burden of measles is however among children under five years old, and infants born susceptible to measles remain so until they receive their first routine dose of vaccination. Pregnant mothers are at higher risk of hospitalization, and severe complications, such as pneumonia and death compared to non-pregnant women.<sup>17–19</sup> Additionally, pregnancy complications consistent with serious infections may arise, including

## MMR1 coverage at two and five years of age, England 1997/98 to 2022/23 MMR2 coverage at five years of age, England 1997/98 to 2022/23

Source: Childhood Vaccination Coverage Statistics - 2022-23 Annual National Official Statistics, NHS Digital, UKHSA

**Aim: achieve 95% coverage with 2 doses of MMR in the routine childhood programme (by age 5 years)**

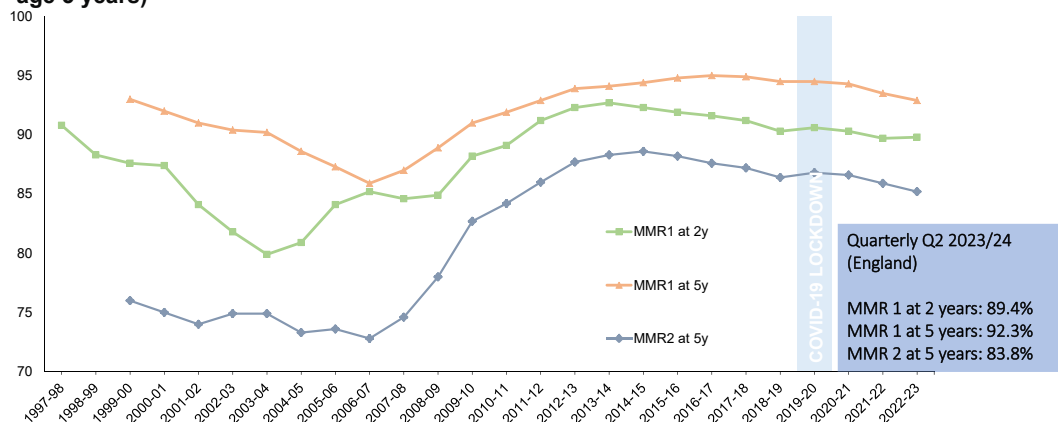
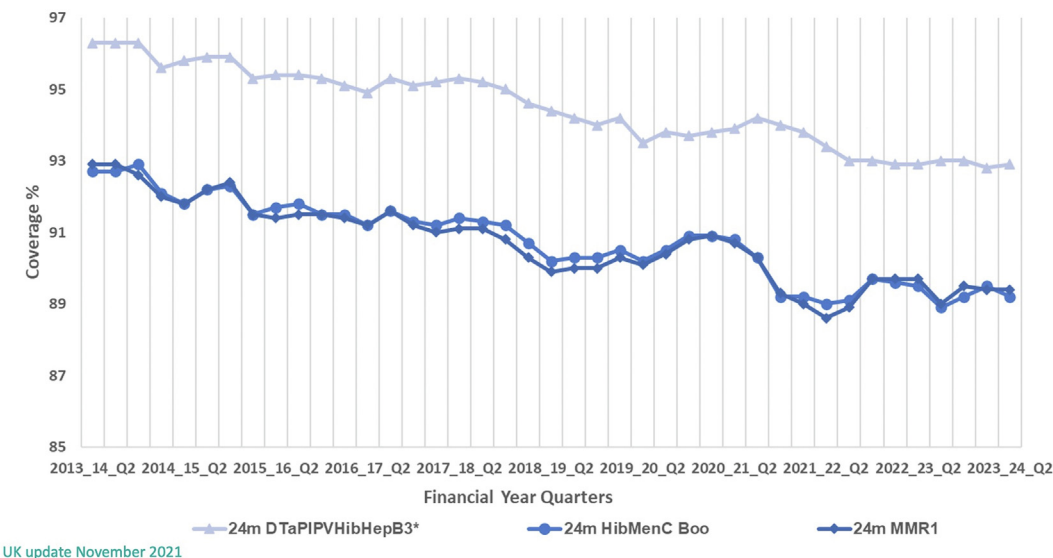


Fig. 1: MMR (measles, mumps and rubella) vaccine uptake in England.

## MMR1, HibMenC and Hexavalent vaccine coverage in 2 year olds by quarter from 2013 to July-Sep 2023



**Fig. 2:** Decline in MMR (measles, mumps and rubella) vaccine uptake is similar to the decline in *Haemophilus influenzae* type b/Meningococcal group C (Hib/MenC) vaccine uptake.

fetal loss, intrauterine growth retardation, premature birth, and neonatal death.<sup>15,16,19–21</sup> A systematic review of clinical outcomes of measles in pregnant women identified 420 cases of measles in pregnant individuals from 1941 to 2012.<sup>15</sup> Among them, there were 18 deaths (case fatality rate, 4.3%), with pneumonia being the most common complication (75 of 420 cases, 17.9%). Prematurity was identified as the most significant fetal complication, affecting 55 of the 410 cases with available information (13.4%). More recently, during a measles outbreak in Catania, Italy from May 2017 to June 2018, 24 pregnant patients aged 17 to 40 contracted measles. Adverse pregnancy outcomes included 2 miscarriages, 1 abortion, 1 fetal death, and 6 preterm deliveries. Respiratory complications were more common in pregnant women (21%) than non-pregnant women (9%) with measles. Fourteen health-care workers (1.7%) were also infected, none of whom had been vaccinated.<sup>21</sup> In addition to the risks of severe disease in the pregnant woman, infection around the time of delivery may give rise to perinatal infection of the infant, which, albeit rare, has been associated with subacute sclerosing panencephalitis (SSPE) characterized by a short onset latency and fulminant course in the infant.<sup>16</sup>

### Recent measles seroprevalence studies

Given that measles infections, especially mild cases in the community, are not routinely confirmed through

laboratory diagnosis, seroprevalence studies provide useful information about immunity in the population. In a recent global meta-analysis of measles antibody seroprevalence studies published until June 2018, the random-effects pooled seroprevalence of measles among 20,546 pregnant women worldwide, albeit with high heterogeneity, was 89.3% (95% CI: 87.3–91.1%), ranging from 86% (95% CI, 82–89%) in both Asia and America to 93% (95% CI, 88–97%) in Europe.<sup>15</sup> Additionally, there was a decline in measles antibody seroprevalence over time, although this was not statistically significant.<sup>15</sup> This is important because antibody seroprevalence among pregnant women in many parts of the world remains below the herd immunity threshold for measles (which is estimated to be around 95%), thus putting pregnant women and their infants at risk of measles during their most vulnerable period. More recently, In Mersin, Turkey, a smaller cohort study investigated measles seroprevalence in women aged 15–49 years between Oct 2019 and Jun 2021 and found a 25.7% measles antibody seropositivity, suggesting that three out of every four babies born in the region were not adequately immunoprotected against measles.<sup>22</sup> Similarly, following a measles outbreak affecting several European countries including Greece during 2016–2018, two Greek seroprevalence studies found that around 13% of pregnant women were seronegative for measles antibodies.<sup>23,24</sup> Elsewhere, an African study conducted in Zambia during 2015–2017 among adult women of

childbearing age found that 25% of women were seronegative.<sup>25</sup>

## SSPE: a rare measles complication

An often-undervalued benefit of MMR vaccination is the prevention of subacute sclerosing panencephalitis (SSPE), a very rare but very severe and invariably fatal neurodegenerative complication of measles that typically presents many years after acute measles infection.<sup>26</sup> The symptoms typically progress to general convulsions, coma, and death over a period of 1–3 years. SSPE, usually seen in childhood, can be challenging to diagnose due to its long latency. Rare cases occur in adults, including pregnant women, sometimes mistaken for eclampsia. Infants born to mothers with perinatal measles infection progressing rapidly to SSPE, were not subsequently diagnosed with SSPE themselves.<sup>16</sup> A recent review analyzing outcomes in 21 pregnant women with SSPE found that most ( $n = 14$ ) experienced symptoms during pregnancy, with nine reporting vision loss.<sup>27</sup> Tragically, 13 women with SSPE died soon after delivery or subsequent follow up, with the duration of illness spanning from a few weeks to 10 months. Fifteen fetuses survived, usually after premature birth, and 5 were either stillborn or died shortly after birth. Although rare, the rapid progression of SSPE in pregnancy highlights the critical need for universal childhood measles vaccination, providing direct and herd protection.

## The importance of high MMR vaccination rates

Another important reason for maintaining high MMR vaccination rates in the population is for protection against mumps and rubella. The latter is particularly important for pregnant women because of congenital rubella syndrome which is now extremely rare because of widespread MMR vaccination worldwide.<sup>27</sup> It has been however previously associated with high rates of congenital defects, miscarriage and fetal death in the pre-vaccine era, especially if infection occurred in the first trimester of pregnancy.<sup>28</sup> In England, 0–3 cases of congenital rubella syndrome were reported annually before the COVID-19 pandemic.<sup>29,30</sup>

Much of the national and international effort is rightly targeted towards improving vaccine uptake in young children eligible for MMR vaccination through the national immunisation programme, alongside mass immunisation campaigns, catch-up programmes and opportunistic vaccination of unvaccinated older children and young adults. However, little attention is focussed on the risks and complications of measles infection in pregnancy. In the current environment of high measles transmission in many countries, healthcare professionals in the community and hospitals should take every opportunity to ascertain a clear and detailed immunisation history, establish a dialogue, address

concerns, and offer vaccination to those who remain unimmunised, especially against measles and rubella among adolescents and women of childbearing age, with the aim of reducing their risk of acquiring measles infection during pregnancy.

## Management of suspected measles infection in pregnancy

Obstetricians and midwives need to actively enquire about and document MMR vaccine status of pregnant individuals, raise awareness of the pregnancy-associated risks and complications of measles (and rubella) in unvaccinated pregnant individuals and establish clear pathways for MMR vaccination after delivery to reduce the postnatal risk of measles in the mother and infant as well as protect the mother in future pregnancies. Given the limited published literature on the management of pregnant individuals with suspected measles, we propose an algorithm for the clinical management pathway for pregnant individuals with suspected measles infection in the hospital setting (Fig. 3).

Measles is a notifiable disease in most countries. In the UK, national guidelines for the clinical and public health management of suspected measles cases and close contacts have been published by the UKHSA and were recently updated in January 2024.<sup>5</sup> Clinicians are required to notify all suspected measles cases as soon as possible to their local health protection team (HPT), both as part of surveillance and so that timely public health management can be undertaken.<sup>5</sup> In the hospital setting, especially for vulnerable patients, acute measles infection should be confirmed according to local hospital protocols. The diagnosis can be confirmed by PCR of a mouth swab or, alternatively, throat swab. A history of MMR vaccination or prior measles infection are usually reliable markers of prior immunity. Alternatively, immunity can be assessed by measurement of serum measles IgM and IgG antibodies through a blood test. In some countries, such as the UK, measles PCR can also be performed on oral fluid samples, in regional public health laboratory or the national virus reference laboratory. The oral fluid test has several advantages, including ease of use, option for self-testing and posting the sample to the laboratory and measurement of measles IgM and IgG antibodies in the oral fluid to aid diagnosis and assess prior immunity (although measles IgM antibodies may be negative in early infection) but the results of the oral fluid test, which was implemented primarily to aid national surveillance of measles, can take several days to report.

Pregnant women with laboratory-confirmed measles infection should be assessed for the need for passive immunisation with intramuscular, subcutaneous or intravenous immunoglobulin (if available) based on

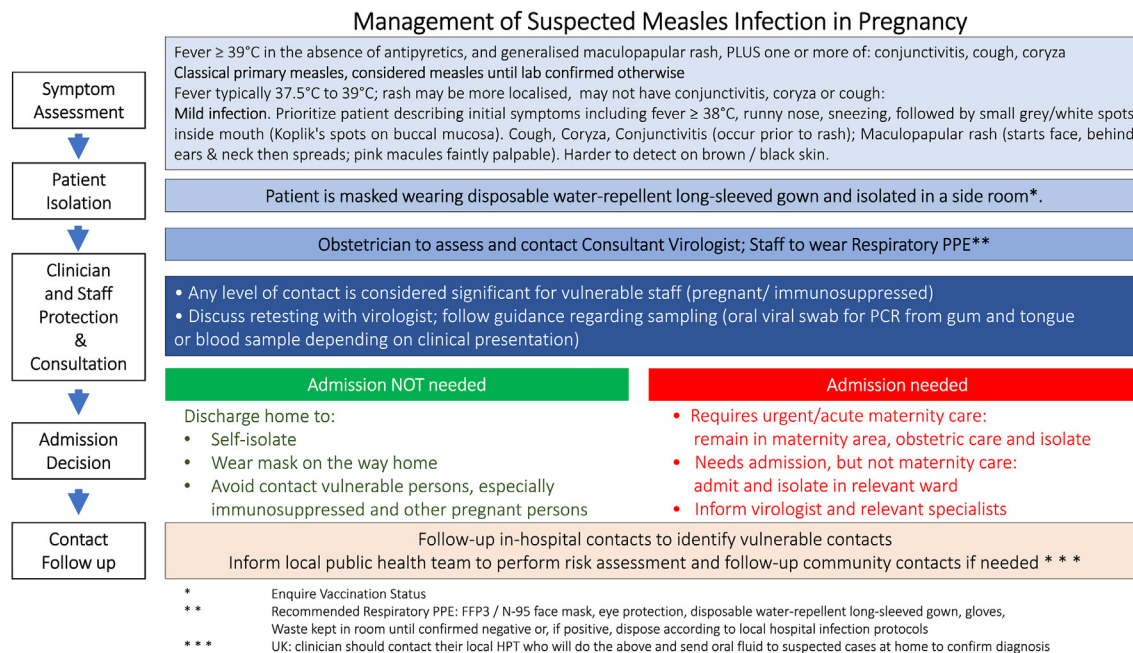


Fig. 3: Management algorithm of suspected measles infection in pregnancy.

prior immunity status through infection and/or vaccination. We additionally recommend assessment of fetal wellbeing with an ultrasound scan or cardiocograph according to the gestation. Hospital staff should also work closely with their local health protection teams to identify vulnerable close contacts of the confirmed case and offer MMR vaccination if necessary.

Furthermore, obstetricians and midwives should be aware of national guidance on the risks, investigations and management of susceptible pregnant individuals exposed to a case of measles during pregnancy. In the UK, the national UKHSA guidelines<sup>5</sup> emphasise the role of health protection teams in identifying high-risk close contacts of index cases. For immunocompetent vulnerable individuals (infants, pregnant women), health protection teams are advised to prioritise contact tracing efforts to those exposed to a primary measles infection, but not breakthrough (reinfection) infection in the index case. Pregnant women born before 1990 with no history of measles infection should be tested for measles antibodies and, if negative, offered Human Normal Immunoglobulin (HNIG) within 6 days of exposure. Pregnant women born since 1990 are assumed to be immune if they have received two measles vaccine doses or, if unvaccinated or only had a single measles vaccine dose, should be tested for measles antibodies and offered HNIG if negative. The guidelines also emphasise the importance of offering MMR vaccination after birth to susceptible pregnant women to protect them in subsequent pregnancies. At the same time, the guidance recommends that

pregnant women who are inadvertently administered MMR do not require post-exposure prophylaxis and is not associated with adverse outcomes in the pregnant woman or the infant. In addition to pregnant women, the UKHSA also guides the management of contacts who are infants younger than 12 months of age, using HNIG (for infants aged  $< 6$  months and following household exposure to infants aged 6–8 months) or MMR vaccination (following exposure outside the household in infants aged 6–8 months and for infants aged 9 months and older).

### Conclusion

Many parts of the world are currently facing large increases in measles infections and outbreaks, mainly in children, because of reduced childhood MMR vaccine uptake in previous years, perpetuated by more recent drops in the uptake of routine childhood immunisations since the COVID-19 pandemic. Much of the clinical, public health, and political drive has been targeted at improving childhood MMR vaccine uptake. Pregnant women, however, should not be neglected during the current resurgence, especially because a large cohort of older adolescent and younger adult women remain unvaccinated following the Wakefield saga after 1998. Obstetricians and midwives need to have a high index of suspicion for measles in pregnant women presenting with an infection-related illness, especially in the presence of a rash, and be aware of local and national guidelines on infection control, isolation, diagnosis, and

## Search strategy and selection criteria

References for this review were identified through searches of PubMed for articles published until January 31, 2024, by combining “measles” or “mmr” or “sspe” with “Pregnan\*” to identify publications in English language on the risks, assessment, management, outcomes and prevention of measles in pregnancy. We also conducted an online search for national public health (including those published by UK Health Security Agency, UKHSA) and international agencies (including the World Health Organization, the US Center for Disease Control and Prevention, the European Centre Disease Prevention and Control, and the United Nations Children’s Fund) for recent communications relating to measles epidemiology including outbreaks, MMR vaccine uptake and trends, as well as guidelines on the prevention, assessment and management of suspected and confirmed cases and contacts.

management of women with suspected measles. Additionally, some countries such as the UK have national guidelines on active management of susceptible pregnant women who are exposed to a confirmed measles case, including the offer of HNIG to prevent or at least attenuate the severity of the disease. For all suspected cases and contacts, close liaison between clinical staff and local health protection teams is critical for containing the infection, reducing the spread, and protecting vulnerable contacts.

## Contributors

Manuscript conceptualization, literature search, figures, study design, and writing were led and coordinated by AK, AS, CC, and SL. All authors contributed to the development and refinement of the manuscript and endorsed the decision to submit it for publication.

## Declaration of interests

AK is Vice President of the RCOG. We declare no competing interests. All other authors declare no competing interests.

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