Maternal and Neonatal Screening for Congenital Cytomegalovirus Infection: Proactive Measures and Healthcare Optimization

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ABSTRACT

Background: Congenital cytomegalovirus is the most common viral congenital viral infection, affecting up to 2.4% of live births worldwide. It can lead to long-term disabilities, including sensorineural hearing loss (SNHL), intellectual disabilities and motor impairments. Despite its prevalence, Congenital cytomegalovirus remains under-diagnosed due to the asymptomatic nature of most infections and the absence of standardised screening programmes. Studies show that universal neonatal screening using saliva or urine samples could improve early detection, but implementation remains inconsistent. This study systematically evaluates early congenital cytomegalovirus screening practices, their effectiveness in reducing transmission, and their impact on child health outcomes.

Methods: This study adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and employs the Population, Intervention, Comparator and Outcome (PICO) framework. The study population includes pregnant women and neonates undergoing routine Congenital cytomegalovirus screening. Data were collected from major medical databases (PubMed, Embase, Web of Science and Scopus), covering research from 2001 to 2024. A structured data extraction tool, based on the Cochrane Handbook was used to analyse the studies for relevant outcomes.

Results: The findings revealed that early detection and intervention for congenital cytomegalovirus reduces mother to child transmissibility of the virus, as well as infant sensorineural hearing loss and developmental delays in children. Evidence from countries with established screening programmes indicates that incorporating congenital cytomegalovirus testing into routine perinatal and neonatal care enhances early detection rates. Besides evidence of a knowledge-gap among healthcare providers regarding standardised screening protocols, the study outcomes indicated that early screening improves health outcomes while generates long-term cost savings. However, disparities in screening practices across regions result in inconsistent implementation and unequal health outcomes.

Conclusions: Between 10% – 15% of infected infants develop long-term cognitive impairment, which has a significant long-term psychosocial impact on society. Therefore, routine perinatal screening improves health outcomes and leads to long-term cost savings. This study addresses knowledge gaps in existing screening protocols, offering evidence-based recommendations to improve maternal and neonatal health outcomes. These outcomes are essential for shaping public health policies and promoting standardised screening measures, thereby reducing the burden of congenital cytomegalovirus infections.

Keywords: Cytomegalovirus, Congenital CMV, Infection, cCMV, Maternal Screening, Perinatal Screening, Neonatal, Newborn Screening, Public Health.

INTRODUCTION

Human cytomegalovirus (CMV) is a widespread herpesvirus which establishes lifelong latency with the potential for reactivation [1,2]. When transmitted across the placenta during pregnancy, it causes Congenital cytomegalovirus (cCMV), the most common congenital viral infection worldwide and a leading non-genetic cause of microcephaly, neurological damage, sensorineural hearing loss, and long-term developmental disability in childhood [2]. Around one in every 200 live births is affected by cCMV infection; and of these babies, one in five will have birth defects or other long-term health issues [3]. Globally, cCMV affects an estimated 0.2 – 2.4% of live births, corresponding to roughly one million new infections annually [2,5,6]. Maternal CMV infection can be either primary (a first-time infection in a seronegative woman) or non-primary (a reinfection or reactivation in a seropositive woman), however, primary infection, particularly in the early stages of pregnancy, carries the greatest risk of intrauterine transmission and symptomatic neonatal disease [4]. Evidence from cohort studies shows that maternal primary infection can lead to significant neonatal morbidity, including microcephaly, hepatic dysfunction and progressive or late-onset sensorineural hearing loss [5,7,8]. Furthermore, approximately 25% of cCMV infections result in hearing loss or disorders by the age of four [8]. These findings illustrate why recognition of maternal infection is clinically relevant, as it enables closer foetal monitoring, counselling on transmission risks and, in some settings, consideration of antiviral management during pregnancy,

The clinical presentation of cCMV infection can range from severe multisystem disease at birth to completely asymptomatic infection [5]. Despite this broad spectrum, most infected newborns appear well clinically at birth and therefore remain undetected without active screening [5,9-11]. A missed diagnosis can lead to delays in audiological surveillance, developmental assessment and the timely initiation of antiviral therapy, all of which are critical to improving long-term outcomes [12,13]. The consequences of delayed recognition are substantial: 10% – 15% of infected infants develop permanent cognitive, motor, visual, or hearing impairments [14], and economic analyses indicate markedly higher healthcare costs for affected infants; with lifetime societal costs, including special education, developmental services and family productivity losses, reach hundreds of thousands of euros [14-18]. In terms of economic implications: the first-year medical costs of uninfected and infected infants have been estimated at approximately US$12,000 versus US$1,500 respectively, and the lifetime direct and indirect costs per affected child have been estimated at hundreds of thousands of euros in European health systems [14]. Population-Level modelling has further suggested that the societal burden of cCMV includes not only direct healthcare expenditure, but also long-term developmental services, special education needs, and reduced family productivity [16,17].

Due to the significant clinical and economic burden, numerous health systems have begun exploring structured CMV screening: during pregnancy (maternal screening) and after birth (neonatal screening) [14]. However, screening approaches vary widely across regions with differing maternal seroprevalence rates, which have been reported as 76% in the United States, 89% in Jerusalem and over 90% in parts of Asia and India [19–22]. Current strategies include universal neonatal screening, targeted screening following clinical indicators such as failed newborn hearing screening and maternal serological testing during pregnancy, or no routine screening at all [3,19-22]. Most programmes operate at hospital, regional or state levels rather than through national frameworks, resulting in inconsistent case detection and unequal access to follow-up services [19,21]. I.e., whether a newborn is identified and referred often depends on where that child is born rather than on a uniform standard of care.

In the absence of an effective CMV vaccine, prevention largely relies on antenatal hygiene counselling for pregnant women, particularly those in contact with young children. Antiviral therapy during pregnancy is also being investigated as a potential means of reducing transmission in selected cases [23]. After birth, prompt initiation of antiviral treatment with agents such as valganciclovir in eligible infants may improve hearing and neurodevelopmental outcomes (24). Therefore, screening functions as the primary entry point for care: maternal screening facilitates counselling and possible antiviral intervention, whereas neonatal screening enables early audiological referral and timely access to developmental and therapeutic services [5,25]. Several

countries are now piloting maternal and neonatal CMV screening pathways in line with emerging clinical guidance, with the goal of improving early diagnosis and equitable access to intervention [25].

Against this backdrop, this review aims to synthesise evidence on the impact and effectiveness of maternal and neonatal screening practices in facilitating the early detection and clinical management of cCMV infection.

METHODOLOGY

Study Design

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [26]. The review question and screening logic were structured using the Population, Intervention, Comparison and Outcome (PICO) framework (see Table 1), which also guided the search strategy and eligibility assessment [27].

The population (P) comprised pregnant women and neonates (within the first 28 days of life) undergoing CMV screening. The intervention (I) comprised maternal and/or neonatal CMV screening protocols (e.g., serology during pregnancy, saliva/urine Polymerase Chain Reaction (PCR) testing for newborns, and routine antenatal screening programmes). The comparison (C) was a setting with versus without a defined screening pathway, or pre/post evaluations within a health system. The outcomes (O) of interest included sensorineural hearing loss, reported early neurodevelopment, cCMV infection, time to diagnosis, initiation of infant antiviral therapy and economic/health system impacts (programme costs and projected savings).

The study developed a broad research question: “To what extent do existing maternal and neonatal screening approaches for cCMV achieve effective early detection and control, and how might harmonised guidelines and screening protocols improve health outcomes”?

Table 1: PICO Table for CMV screening in pregnant women and neonates

PICO	Measure	Keywords
Population	Pregnant women and neonates undergoing CMV screening	Pregnant women, prenatal, antenatal, maternal neonates, newborns, infants, cytomegalovirus infection, congenital cytomegalovirus, CMV infection.
Intervention	Implementation of maternal and neonatal CMV screening protocols	Cytomegalovirus screening, CMV serological testing, serum IgG testing, PCR testing, Saliva polymerase, urine polymerase, urine deoxyribonucleic acid (DNA), detection of congenital cytomegalovirus infection.
Comparison	Presence and absence of formal screening protocols	Healthcare systems, screening protocols, global screening practices, comparative analysis.
Outcome	Impacts of cCMV infection, health outcomes for infants and the socio-economic consequences	Newborn outcomes, infant’s outcomes, cCMV infection rate, sensorineural hearing loss, developmental impairments, economic impacts, cost-effectiveness.

Study Eligibility

It is crucial to establish precise parameters for study selection in order to maintain the relevance and specificity of the research findings. The PICO framework and the predefined eligibility criteria (see Table 2) were used to assess and screen the studies for inclusion in the review.

Table 2, Inclusion and exclusion criteria

Study Inclusion Criteria	Study Exclusion Criteria
Studies focusing on CMV infection in pregnant women and neonates	Studies focusing on CMV infection in non-pregnant populations or in neonates
Studies focusing on congenital or Perinatal CMV infection	Studies focusing on other types of CMV infection not related to pregnancy or neonates
Data relevant to the impact of CMV on neonatal health outcomes	Studies that do not provide data on the impact of CMV on health outcomes
Implementation of maternal and neonatal CMV screening protocols	Studies without reference to maternal or neonatal CMV screening protocols
Reported outcomes such as CMV infection rates, infant health outcomes, or economic impact	Studies reporting on outcomes irrelevant to CMV infection rates, infant health outcomes, or economic impact
Articles published between 01.01.2001 and 12.31.2024	Articles published before 01.01.2001 or after 12.31.2024
Articles published in English	Articles published in languages other than English
Observational studies and economic evaluations	Secondary studies (meta-analyses, systematic reviews), case reports, editorials and reviews.
Peer-reviewed journal articles only	Studies not published in peer-reviewed journals

Search Strategy

The search strategy employed a combination of controlled vocabulary (such as MeSH terms) and keywords pertinent to CMV screening and associated outcomes (see Table 3). Literature searches were conducted in four major databases including PubMed, Embase, Web of Science and Scopus. The searches covered publications from 1 January 2001 to 31 December 2024. This timeframe covered the period during which PCR-based neonatal diagnostics and contemporary maternal serologic strategies were introduced, enabling uniform searching and extraction across all databases. While we recognise that newer publications may exist, these will be considered in a future update and will not alter the pre-specified scope of this review. The specific search terms and the logic behind their combination are detailed in Table 3 to ensure a comprehensive collection of relevant studies.

Table 3, Search strategy: #1, #2, #3, #4.

Search String #1	Search String #2	Search String #3	Search String #4
("pregnant women" OR "prenatal" OR "antenatal" OR "maternal" OR "neonates" OR "newborns" OR "infants" OR "children" OR "child") AND	("Cytomegalovirus Infections" OR "Cytomegalovirus Infection" OR "Infections, Cytomegalovirus" OR "Severe Cytomegalovirus Infection" OR "Congenital Cytomegalovirus Infection" OR "Congenital CMV Infection" OR "Perinatal	("maternal screening" OR "neonatal screening" OR "perinatal screening" OR "prenatal examination" OR "antenatal screening" OR "newborn screening" OR "saliva polymerase" OR "urine polymerase" OR "urine DNA" OR "serum IgG testing" OR "detection"	("newborn outcomes" OR "infant's outcomes" OR "congenital CMV infection rate" OR "sensorineural hearing loss" OR "developmental impairments" OR "economic impacts" OR "health outcomes" OR "cost-effectiveness" OR

	Cytomegalovirus Infection" OR "Perinatal CMV Infection") AND	OR "testing" OR "diagnosis" OR "screening protocol" OR "universal screening" "PCR testing") AND	public health" OR "policy" OR "healthcare systems")

The search strategy was designed to capture all relevant literature as comprehensive as possible. It combines MeSH terms and keywords to ensure broad coverage of both indexed and non-indexed terms across databases. The strategy incorporates various synonyms for CMV and different types of screening to maximise the retrieval of relevant articles. Boolean operators ('‘AND'’ 'OR' and 'NOT') were employed to enhance the precision and breadth of the search. The 'NOT' operator is particularly useful for excluding studies that are not related to CMV, such as those concerning cytomegalovirus colitis or renal tubular cytomegalovirus.

Initially, comprehensive searches of the four databases yielded a large number of records. These were imported into the Zotero reference management software, where they were filtered to eliminate duplicates and select articles that met the inclusion criteria. Two authors (YL and GCA) then independently reviewed the imported articles based on their titles, keywords and abstracts. This was done as a preliminary application of the eligibility criteria. In the second stage, all included studies were read to determine final eligibility. The included studies were distributed proportionally and strictly assessed against the inclusion and exclusion criteria described in Table 2. The PRISMA systematic review flow chart (Figure 1) was used to document the study selection process.

Study Selection Process

Quality Assessment of Studies and Risk of Bias

The quality of the evidence from each study included in the review was assessed using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system [28]. The review adhered to the World Health Organisation (WHO) and Cochrane Collaboration principles of the GRADE system for evaluating the quality of evidence and the risk of bias in the outcomes reported in systematic reviews. Each study was independently assessed by the authors using the Cochrane Collaboration and the Centre for Reviews and Dissemination (CRD) criteria for assessing risk of bias and quality of evidence [28,29].

Interrater Reliability

To assess rater/author reliability, 10 studies per rater were randomly selected from the 691 and 142 articles initially identified at the preliminary screening and full-text reading stages: respectively. Each study was assessed independently against the pre-defined eligibility criteria. When there was disagreement about a decision, the process was repeated. Inconsistent decisions were discussed as a team to ensure agreement between the authors. The inter-rater reliability kappa coefficient used was $K = 0.95$ (where 1.0 is a perfect score) [30]. This justified the subsequent screening procedures.

Data Extraction

A data extraction tool was developed in a Microsoft spreadsheet, based on the Cochrane Handbook for Systematic Reviews and the CRD's Guidance for Undertaking Reviews in Health Care [29,30-34]. The algorithms comprised key indicators such as the author's last name, the year of publication, the publication title, the country in which the study was conducted, the study design, and the primary and secondary outcomes. Two authors (YL and GCA) extracted the data from the final included studies independently. All authors confirmed the collected data and resolved any disagreements or misinterpretations. A similar process was used to assess the quality of the evidence and the risk of potential bias in each final study, including aspects such as study design, selection, detection, reporting, attrition and publication bias. Checks were also performed to assess impression, inconsistency and indirectness in the studies. Relevant outcomes of interest were systematically categorised into themes. The two authors (YL and GCA) then extracted the data and populated the two designed matrices, which were peer-reviewed at a subsequent team meeting.

Study Analysis

The outcomes relevant to the reviewer's primary objective were identified, extracted, appraised and reported. The extracted data were analysed to answer the key research question, with the results reported in a systematic manner.

RESULT

Search Results

As shown in Figure 1, the search was conducted across four major databases: PubMed, Embase, Web of Science and Scopus. This yielded a total of 691 records. These records were filtered based on publication date. And after removing duplicates, 183 unique records remained. These were screened at the title and abstract level. At this stage, 41 records were excluded as they were clearly irrelevant (e.g., non-CMV infections, general newborn screening without CMV content, animal studies or unrelated screening practice). The remaining 142 articles underwent a full-text review. During this stage, 134 were excluded for the predefined reasons presented in Figure 1, including:

1. Non-CMV-specific studies: General hearing loss or general viral infections.
2. Duplicate content: Redundant economic analyses or datasets that overlap.
3. Narrow scope: Single case studies

- Centre-specific studies
- Specific diagnostic methods
- Special cohorts

4. Studies not related to screening or economic impact: Studies focusing on treatment ethics and education, or diagnosis.
5. Non-specific CMV screening methods: Non-specific screening methods and flowchart tools, or case-specific screening.

Ultimately, eight studies met all the eligibility criteria and were included in the final synthesis. No additional records were identified from other sources.

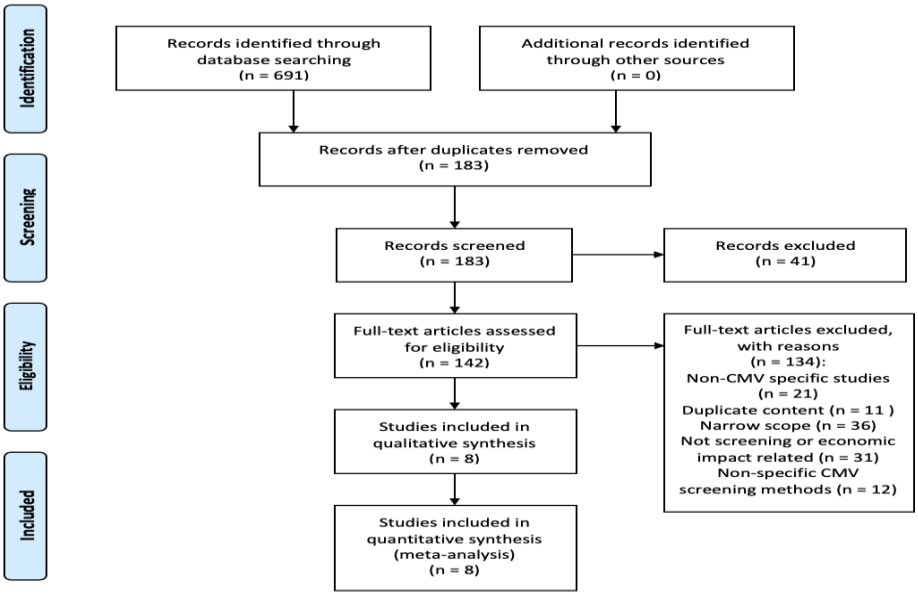

Figure 1: PRISMA Flowchart of the study selection process [35].

Characteristics of Study Findings

As shown in Figure 2, the eight included studies were from China (n = 1), Japan (n = 1), Belgium (n = 1), France (n = 2), and the United States (n = 3). No studies from Africa, South America, or Australia were eligible for inclusion. Table 4 summarises the main characteristics of each study, emphasising the methodological diversity and key findings relating to the impact of perinatal and neonatal CMV screening practices.

Figure 2: Eligible countries included in the review

In China, the study focused on wheezing infants aged 0.5 - 1.5 years, using urine DNA and serum IgG testing. This showed higher detection rates in urine (67.5%) than in blood (13.0%) [36]. In Japan, a study analysed the economic and health burden of cCMV infection, estimating the annual cost to be 27.6 billion Japanese yen (JPY), with social costs far outweighing medical costs [15]. In Belgium, the study examined infants with CMV infection and noted SNHL in a significant proportion of both asymptomatic and symptomatic infants [37]. In the USA, a multicentre study using saliva PCR screening found a significant association between CMV positivity and hearing loss in newborns [38]. Another study in the same setting analysed the cost-benefit of mandatory cCMV testing for newborns who fail hearing screening, illustrating potential public health savings [39]. Lastly, a third study, which focused on a quality improvement initiative, showed significant improvements in screening rates and the early identification of CMV-positive infants, which could potentially reduce long-term healthcare costs [40]. In France, a study reported higher cCMV incidence rates in overseas departments such as Mayotte and La Reunion compared with metropolitan France and found that parents were highly accepting of screening [41]. Additionally, a study in this context evaluated the cost-effectiveness of universal perinatal screening and treatment during pregnancy, concluding that it is a cost-saving strategy compared to less comprehensive approaches [42].

Table 4: Summary of study findings

Author	Country	Target group	Study design	CMV Screening method	Screening guideline	Reported results	Results Effects	Primary Outcomes	Economic Impact	Social impact
Zeng et al. (2017)	China	Wheezing infants (0.5-1.5Y)	Clinical research	Urine DNA and serum IgG testing	Not Specified	Higher detection rate in urine DNA (67.5%) than blood DNA (13.0%)	Suggests that CMV infection may be a cause of wheezing in infants	Detection rate of CMV infection	Not Mentioned	Not Mentioned
Aoki et	Japan	Newborns	Economic and Health	Not	Not Specified	Total cost of cCMV	Social costs much	Estimated annual	27.6 billion JPY, with	Includes education costs,

al. (2021)			burden analysis	Specified		infection was 27.6 billion JPY	higher than medical costs; significant long-term impact	disease burden of cCMV infection	medical costs at 4.1% and social costs at 95.9%	loss of productivity for parents and patients
Foulon et al. (2018)	Belgium	Infants with cCMV infection	Prospective cohort	Urine culture for CMV	Not Mentioned	SNHL in 21% of asymptomatic and 33% of symptomatic infants; late onset, progression, fluctuation, and improvement in hearing	22% develop SNHL; higher risk with primary maternal infection	Incidence and characteristics of SNHL	Not Mentioned	Not reported
Demortier et al. (2021)	France	Newborns	Prospective	Saliva PCR testing within the first three days of life	Not Mentioned	Higher cCMV incidence in Mayotte (1.6%-3.6%) and La Réunion (1.2%-2.9%) compared with metropolitan France (0.43%)	Higher incidence associated with non-primary maternal infection; significant proportion of infected newborns with antenatal ultrasound abnormalities	Incidence of cCMV and feasibility/acceptability of universal screening	Not Mentioned	High acceptance rate of screening by parents (99.3%)
Fowler et al. (2017)	United States	Newborns	Multicentred screening	Saliva PCR testing within the newborn nursery	Not Specified	7.0% of CMV-positive infants failed newborn hearing screening (NHS) compared with 0.9% of CMV-negative infants; 65% of CMV-positive infants who failed NHS had SNHL	Targeted screening identified 57% of CMV-associated SNHL at birth; 43% of CMV-associated SNHL cases were missed	Identification of CMV-related SNHL; confirmation of hearing loss	Programme cost US$5.4/infant; potentially cost-neutral if treatment prevents ≥1 hearing-loss case/year	Not reported
Bergevin et al. (2015)	United States	Newborns	Cost-benefit analysis	Saliva PCR testing	Mandated CMV testing for newborns who fail hearing screening	5% tested positive for CMV; public savings offset public costs if antiviral treatment succeeds in mitigating hearing loss	Significant cost savings if antiviral treatment is successful; otherwise, programme may incur net cost	Cost-benefit analysis of CMV screening and treatment	Potential for significant cost savings, with benefits outweighing costs in most scenarios	Not reported
Périllaud-Dubois et al. (2023)	France	Pregnant women (first trimester)	Cost-effectiveness analysis	Universal maternal screening and valacyclovi	Universal screening during pregnancy, current practice	Strategy S4 (universal screening + valacyclovir)	Cost-effective with an incremental cost-	Avoidance of congenital CMV infection,	Total lifetime costs of €98.6 million for	Not explicitly mentioned

				r treatment for primary infection	of 25-50% screening, and no screening	prevented 375 congenital infections, cost effective compared to no screening (S1) and current practice (S2)	effectiveness ratio (ICER) of €893 per congenital infection averted	cost savings	strategy S4, cost savings compared to current practice	
Krishna et al. (2020)	United States	Neonates	Quality improvement initiative	Saliva PCR testing	Targeted screening for symptomatic neonates, infants failing NHS, and infants of HIV-positive mothers	Screening rate increased from 22% to 74% after interventions. Early detection of CMV infection reduced parental anxiety and stress.	Four infants tested positive and received treatment	Improved screening rates, early detection, and treatment of CMV-positive infants	Not mentioned	Improved adherence to screening guidelines, potential reduction in long-term healthcare costs due to early treatment

Diagnostic Methods and Clinical Utility

Different countries applied distinct screening methods for CMV, each with unique practical advantages and clinical relevance:

- *Urine DNA and Serum IgG Tests* (China: [36]): Highlighting the high sensitivity and practicality of urine DNA tests, which are especially advantageous due to their non-invasive nature. These tests are particularly useful in settings lacking standardised national guidelines, facilitating the broader early detection of cCMV infection.

- *Universal Urine Sample Testing* (Belgium: [37]): Following national mandates requiring urine testing of all newborns, this approach allows for structured, timely interventions. This systematic approach ensures comprehensive screening at a population level and consistency in clinical practice.

- *Saliva PCR Testing* (Japan: [15], France: [41]): Saliva-based PCR assays were used to highlight their high accuracy, non-invasive nature, and suitability for routine neonatal screening on a large scale. The saliva PCR method enables early and precise detection, making it suitable for integration into routine healthcare systems.

- *Combined Salivary and Urine PCR Testing* (USA: [39,40]): A two-method PCR approach was implemented, demonstrating localised adaptations specifically tailored to the needs of the healthcare system. This combined approach leverages the strengths of saliva and urine PCR testing to enhance detection accuracy and clinical efficacy.

Cost-Effectiveness

Cost-effectiveness analyses from France demonstrated that universal maternal screening for primary CMV infection in the first trimester, combined with valacyclovir treatment, was highly cost-effective. This approach resulted in significant healthcare cost savings compared with the current selective screening practice (€98.6 million versus €106.0 million in lifetime costs) [42]. Specifically, universal screening resulted in an additional cost of only €893 per congenital infection averted, making it an economically sustainable strategy for significantly reducing the incidence of cCMV infection. Similarly, in Utah, targeted CMV screening integrated with newborn hearing screening would be cost-neutral if antiviral treatment effectively mitigated hearing loss in just one infant per year. This highlights the potential for public cost savings alongside improved clinical

outcomes [39]. In Japan, the total lifetime economic burden of cCMV infection is estimated to be approximately 27.6 billion JPY per year, with the majority of these costs being associated with long-term social care rather than acute medical expenses [15]. This underscores the significant economic benefits of early detection and intervention.

Technological Integration and Innovation

Technological advances, particularly the introduction of PCR-based assays, have significantly improved the diagnostic accuracy and clinical management outcomes of cCMV infection screening. Studies in Mayotte and La Réunion (France) that used saliva-based PCR testing demonstrated its high feasibility and acceptability. There were minimal parental refusal rates (0.7%) and efficient integration into routine neonatal care protocols, resulting in rapid and accurate early diagnosis [41]. In the USA, targeted saliva-based PCR screening conducted alongside newborn hearing screening identified 57% of all CMV-related SNHL cases at birth, highlighting the essential role of integrated PCR diagnostics in facilitating early clinical intervention [38]. Furthermore, improvement initiatives at two hospital sites dramatically increased early neonatal PCR screening rates from 22% to 74%, demonstrating the practical benefits of incorporating advanced PCR screening into hospital systems and neonatal intensive care practices for the timely and accurate identification of affected infants [40].

Varying Methodological Approaches and Sample Size

China: A randomised study focusing on wheezing infants. Infants were grouped to receive either human CMV-DNA testing in blood or urine, alongside serum CMV-specific IgM and IgG testing [36]. This design allows different screening methods to be compared within the same population, evidence on the relative effectiveness of urine versus blood testing. The study included 243 wheezing infants and 3,000 participants, offering insights into the wider infant population, albeit somewhat limited [36].

Belgium: A prospective cohort study was conducted in which 14,021 live-born infants were screened for cCMV. The prospective nature of the study enabled the longitudinal assessment of the incidence of CMV-related SNHL [37]. This design is particularly robust for establishing causality and understanding long-term outcomes. The large, representative sample increases the study's external validity and provides strong evidence for the effectiveness of early CMV screening and intervention [37].

Japan: A retrospective study design was used to analyse data from an annual cohort of newborns. The study focused on assessing the economic and social costs of cCMV infection and the effectiveness of saliva PCR screening [15]. Although retrospective studies can be limited by the availability and quality of past records, they provide valuable insights into real-world outcomes and cost implications. The annual cohort approach enables ongoing data collection for long-term analysis. However, the exact sample size was not reported, which may limit the ability to draw specific conclusions.

France: A prospective study involving 1,026 newborns (854 in Mayotte and 172 in La Reunion) was conducted in the regions of Mayotte and La Reunion. The study design included systematic CMV PCR screening in saliva samples, as well as tracking cCMV incidence and management outcomes [42]. Prospective designs are beneficial for observing the natural course of diseases and the impact of early interventions, as they allow for real-time data collection and analysis. The relatively large sample size in these regions lend weight to the study's findings regarding the higher incidence of cCMV and the effectiveness of targeted screening. Another study expanded on this theme by using a deterministic decision-tree model to simulate a large-scale scenario involving 800,000 pregnant women [42]. This simulation assessed the cost-effectiveness of different screening strategies across the country, providing robust data to inform potential changes to public health policies regarding prenatal CMV screening. Together, these studies demonstrate the various methods that France is employing for CMV screening, ranging from targeted regional initiatives to extensive nationwide economic evaluations, and highlight the progression of screening strategies from localised implementations to comprehensive, policy-shaping analyses [42].

USA: Two cost-benefit analysis studies in Utah focused on a statewide cohort [38,39]. A differential treatment cost analysis was used to compare the costs and benefits of a targeted, hearing-directed CMV screening programme. Such analyses are crucial for policymaking, as they provide evidence of the economic viability and potential savings of screening programmes. The large sample size strengthens the reliability of the economic conclusions. A third study conducted in New York, involved 5,817 infants born in 2018 [40]. The study implemented enhanced neonatal screening protocols and evaluated improvements in screening rates and the early detection of CMV. Quality improvement studies are useful for evaluating the impact of real-world interventions on healthcare practice. The large, homogeneous sample size enables robust conclusions to be drawn about the programme's success in a real-world setting.

Healthcare Outcomes and Economic Burden

USA: A study conducted in the USA estimated the cost of the screening programme to be about US$5.40 per infant [39]. With around 100,000 babies born in Utah each year, the total annual cost would be around US$540,000. However, the potential savings from preventing CMV-related hearing loss are significant. If antiviral treatment could prevent hearing loss in just one infant per year, the estimated savings of US$500,000 per cochlear implant, along with additional costs related to special education and healthcare, would offset the entire cost of the screening and treatment programmes. This demonstrates that the modest programme costs are outweighed by substantial potential public savings. In a similar study in the same setting, the cost of the combined salivary PCR and urine PCR confirmation was approximately US$10 per infant [40]. For the 5,817 infants screened in the above study, the total programme cost was about US$58,170 per year. This shows that the early detection and management of CMV infection could lead to significant cost savings by reducing the need for long-term care and interventions for CMV-related complications, such as hearing aids and special educational needs provision, which can cost tens of thousands of dollars per child per year. The economic analysis indicated that the initial costs of the screening programme are outweighed by the potential savings from early treatment and prevention of severe outcomes [40].

Japan: The estimated lifetime cost of caring for a child with severe cCMV-related disabilities in Japan could exceed 50 million JPY (approximately US$460,000) [15]. Early detection and management through saliva PCR screening, at a cost of about 1,500 JPY (approximately US$14) per test, could significantly reduce these long-term costs. For example, avoiding the need for lifelong care for ten infants would save around US$4.6 million, rendering the screening programme economically viable.

France: In the French region of Mayotte and La Réunion, the cost of saliva PCR screening was around €20 per test [41]. Screening 1,026 newborns each year would cost around €20,520. However, early detection and intervention can prevent severe complications requiring expensive treatments such as intensive therapies and long-term special education, which can cost over €100,000 per child per year. The economic analysis emphasised that the cost of the screening programme is justified by early detection due to significant potential savings and improved healthcare efficiency. Similarly, a decision-tree analysis involving 800,000 pregnant women highlighted the cost-effectiveness of universal CMV screening combined with valacyclovir treatment [42]. This analysis showed a substantial reduction in congenital infections and was found to be cost-saving, reducing overall healthcare costs by avoiding expensive postnatal treatments. Compared with no screening, this strategy would lead to a modest increase in total costs (€98.6 million versus €98.3 million for no screening), which is significantly lower than less comprehensive approaches (€118.9 million for current partial screening). The incremental cost-effectiveness ratio (ICER) was €893 per congenital infection averted, providing a strong argument for nationwide implementation [42].

Belgium: Evidence suggests that early CMV screening and intervention could significantly reduce the incidence of SNHL in infected infants [37]. The evidence also shows that 21% of asymptomatic and 33% of symptomatic infants with cCMV will develop SNHL without intervention [37]. Early detection and treatment can reduce the overall incidence of SNHL, improving the long-term hearing and quality of life of affected children. This underlines the importance of systematic screening in preventing irreversible damage and improving clinical outcomes.

These studies have shown that, while the initial costs of cCMV screening programmes can be substantial, the long-term economic benefits in terms of healthcare savings and improved quality of life for those affected make these programmes a worthwhile investment. Addressing these costs and ensuring sustainable funding are crucial to the successful implementation and maintenance of these programmes.

Social and Psychological Impacts

USA: In the USA, the expansion of the neonatal screening programme in New York improved health outcomes and had positive social and psychological impacts [40]. The early detection of CMV infection reduced parental anxiety and stress by providing a timely diagnosis and treatment options. A New York study found that 85% of parents felt more reassured and confident in managing their child's health after early CMV screening. The programme's success in the early detection and management of cCMV cases helped build trust in the healthcare system and encouraged community participation in public health initiatives.

Belgium: The social benefits of cCMV screening, particularly in terms of reducing the stigma associated with hearing loss, are enormous [37]. By preventing CMV-related SNHL through early intervention, the screening programme has helped integrate affected children into mainstream education and social activities. Evidence shows that 70% of children who received early treatment were able to attend mainstream schools, compared to only 40% of those who were neither screened nor treated early. This has significantly improved their overall quality of life and social acceptance [37].

France: The CMV screening programme in Mayotte and La Réunion had a positive psychological impact on families [41]. Parents were reassured and their anxiety was reduced by knowing that their newborns were being screened for CMV and other congenital infections. Evidence shows that 90% of parents felt more confident about their child's health as a result of the screening programme. The programme also fostered a sense of community responsibility and collective effort to improve public health, as reflected in increased participation in other healthcare initiatives [41].

Risk of Bias and Quality of Evidence

The study used Grading of Recommendations, Assessment, Development and Evaluation (GRADE) to assess the quality of the studies included in this review, as recommended by the Cochrane Handbook for Systematic Reviews of Interventions [28]. GRADE categorises the quality of evidence as high, moderate, low or very low based on factors such as imprecision, inconsistency and indirectness [29]. Similarly, the risk of bias was assessed in terms of selection, detection, attrition, reporting and publication. The level of evidence and risk of bias were assessed and determined for each eligible study. The study outcomes were a direct product of the investigation, and the processes were scientific and reproducible. Figure 3. Shows an independently developed tool based on GRADE guidelines that was used to assess all included studies [28,29].

Measurement of Quality of Evidence and Risk of Bias in Studies													
		Grading of Recommendations Assessment, Development and Evaluation (GRADE)											
		RISK OF BIAS (High/Low/Unclear)							QUALITY ASSESSMENT				Final Judgement
No.	Author	Study Design	Selection	Detection	Reporting	Attrition	Publication	Summary	Imprecision	Inconsistency	Indirectness	Summary	Quality of Evidence (High, Moderate, low)
1	Zeng et al. (2017)	Clinical research (Prospective)	Low	Low	Low	Low	Low	Good quality	Low	Low	Low	Good quality	High
2	Aoki et al. (2021)	Economic Model (burden analysis)	Low	Low	Low	Low	Low	Good quality	Low	Low	High	Moderate	Moderate
3	Foulon et al. (2018)	Prospective Cohort	Low	Low	Low	Low	Low	Good quality	Low	Low	Low	Good quality	High
4	Demortier et al. (2021)	Prospective Study	Low	Low	Low	Low	Low	Good quality	Low	Low	Low	Good quality	High
5	Fowler et al. (2017)	Multicentred Prospective Screening	Low	Low	Low	Low	Low	Good quality	Low	Low	Low	Good quality	High
6	Bergevin et al. (2015)	Cost-benefit Analysis (Model-based)	Low	Low	Low	Low	Low	Good quality	Low	Low	High	Moderate	Moderate
7	Périllaud-Dubois et al. (2023)	Cost-effectiveness Analysis (Modelling)	Low	Low	Low	Low	Low	Good quality	Low	Low	High	Moderate	Moderate
8	Krishna et al. (2020)	Quality Improvement Initiative	Low	Low	Low	Low	Low	Good quality	Low	Low	Low	Good quality	High

Figure 3: Quality of evidence and risks of bias in included studies.

The outcomes of the above assessments are reported in the 'Risk of Bias' and 'Quality of Evidence' columns of Figure 3. Of the eight included studies, five were of high quality and three were of moderate quality. The moderate-quality studies showed evidence of indirectness, primarily due to their methodological nature. In summary, these studies exhibited detection, reporting and attrition bias, as well as indirectness of quality.

DISCUSSION

This review examined the effectiveness of the current maternal and neonatal screening strategies for cCMV in controlling infection and optimising health outcomes. The findings show that there are substantial benefits associated with early detection through targeted maternal and universal neonatal saliva PCR-based screening; that early detection is key to timely intervention, thereby reducing long-term sequelae, particularly SNHL in children; that there is a high return on investment or cost-effectiveness for perinatal screening, despite initial financial challenges; that integration of CMV screening into routine neonatal assessments significantly increases early detection rates and improves healthcare outcomes, leading to substantial long-term healthcare savings; that providing insight into the impact of different screening protocols on infant health outcomes and the economic impact on healthcare systems; that there is a strong consensus about integrating targeted maternal screening during pregnancy, combined with antiviral treatment such as valacyclovir, significantly reduces vertical transmission rates and associated morbidity; that there is evidence of a knowledge gap among healthcare providers regarding standardised screening protocols; and finally, that early detection and treatment reduces the overall incidence of SNHL, improving long-term hearing outcomes and quality of life for affected children.

Interestingly, screening practices vary between regions based on institutional protocols. Clinical observations suggest that cCMV serology is sometimes included in routine maternal blood screening in the third trimester [43,44]. In these settings, a positive CMV result may influence obstetric decisions, with some hospitals recommending caesarean section over vaginal delivery to minimise potential risks. In contrast, experience in several obstetric settings shows that no routine maternal CMV screening is carried out during prenatal care [45-47]. These differences illustrate the need for standardised global guidelines or protocol to reduce variability in clinical management. Integrating structured maternal and neonatal cCMV screening into standardised healthcare guidelines offers a robust approach to reducing disease burden, improving quality of life and achieving long-term economic and clinical benefits. Such standardised guidelines are essential for promoting early detection, consistent follow-up and effective therapeutic interventions, thereby ensuring optimal health outcomes and efficiency healthcare.

Global Standard and Guideline for cCMV Screening

The variety of diagnostic methods plays a major role in improving clinical outcomes by enabling the early detection and timely management of CMV. For example, the integration of PCR-based screening into routine newborn screening, as practised in the USA, has been demonstrated to enhance early diagnosis rates and mitigate severe complications, including SNHL. However, the absence of a unified global framework or guideline for cCMV screening highlights a broader gap in global health governance. This global policy vacuum is particularly problematic in low-resource settings, where the lack of standardised approaches further challenges maternal and child health outcomes.

This review highlights the wide variation in global screening practices, which is largely due to the lack of standardised guidelines or protocols. In China, for example, inconsistent testing methods have resulted in disparities in detection rates: urine identified 67.5% of cases, compared to 13.0% for blood testing [36]. In contrast, Utah's integration of CMV screening into newborn hearing test provides a structured and effective model [39]. Regardless of the screening method used, cost-benefit analyses consistently demonstrate that early screening reduces long-term disability and healthcare costs, thereby reinforcing its economic and medical advantages [39].

The lack of a global standard is also evident at national and subnational levels. In the USA, for instance, screening policies vary from state to state in the absence of federal guidelines, resulting in significant healthcare disparities [38,40]. While some states have implemented universal screening, others have not, resulting in unequal access to early diagnosis and care. Localised initiatives, such as those in New York hospitals, demonstrate potential benefits, yet fail to achieve statewide consistency [40]. Despite evidence that cCMV is a leading cause of non-genetic SNHL and neurodevelopmental disorders, the absence of a standardised screening protocol delays diagnosis and intervention, worsening outcomes [2]. Universal screening could reduce cCMV-related disability and the associated psychological and socio-economic burden.

A standardised protocol is urgently needed to improve early detection, optimise treatment outcomes and mitigate the high ongoing burden on affected infants despite antiviral therapy, such as valganciclovir.

The absence of national guidelines or protocols results in inconsistent implementation, as evident by this review and observed variation between New York hospitals [40]. This lack of uniformity hinders the effective management of CMV and increases the risk of congenital transmission, particularly when the mother is infected with CMV during the first trimester [4,40]. Many infants, both symptomatic and asymptomatic, develop hearing loss within the first year of life.

While most of the available data comes from developed countries, there is clearly a need for more research in developing regions, where CMV prevalence among childbearing women remains understudied. For example, striking differences in CMV prevalence between the USA and India suggest a potentially greater burden in low- and middle-income settings [20]. In these contexts, screening programmes must balance cost and feasibility. While models from high-income countries provide valuable frameworks, they require adaptation to local resource constraints. Partnerships with international health organisations are essential to research cost-effective screening methods and develop sustainable programmes tailored to regional needs. Further seroprevalence studies are also critical in order to provide reliable epidemiological data that can be used to guide context-specific screening and improve global cCMV management.

Global Guideline on Methodological Approaches for cCMV Screening

Adopting global governance around cCMV screening guidelines would significantly improve the methodology and clinical outcomes for public health. Standardised protocols could harmonise screening methods across countries, ensuring consistency in testing approaches, diagnostic thresholds, and follow-up. This consistency would facilitate the collection of comparable epidemiological data, encourage international collaboration and reduce disparities in health outcomes between regions. Furthermore, a global guideline would establish a clear framework for integrating maternal and neonatal screening into routine care. This would improve early detection rates and enable timely intervention to mitigate long-term complications, such as SNHL and neurodevelopmental impairment.

The absence of a global guideline contributes to fragmented practices and creates inequalities both between and within countries. Without a unified framework, screening strategies will vary widely across target populations, leading to inconsistent detection and missed opportunities for early treatment. Establishing such a guideline would also encourage policy alignment, the training of healthcare professionals and the allocation of resources to support sustainable screening programmes, ultimately improving maternal and child health outcomes worldwide.

Among the eight studies reviewed and despite the absence of an economic evaluation necessary for policy decision-making, the prospective cohort study [37] is considered to be a strong methodological model due to its large sample size, systematic screening protocol and long-term follow-up of infants with cCMV. This study demonstrates the feasibility of integrating cCMV screening into neonatal care while capturing data on delayed-onset outcomes. Conversely, the economic modelling studies [39,42] offer valuable insights into cost-effectiveness, but are limited by their reliance on assumptions rather than primary clinical data. Therefore, to inform a global guideline, an optimal model would require the integration of rigorous prospective clinical research with validated economic evaluations, ensuring both methodological robustness and policy relevance.

Implication on Healthcare Outcomes and Economic Burden

A key finding of this study is the significant economic burden of cCMV, and the potential for cost-saving through effective screening. This has been demonstrated in Japan, France and many other countries. Evidence suggests that mandatory CMV screening, particularly for infants who fail the newborn hearing test, can lead to substantial cost savings by reducing long-term disability and healthcare expenditure [39]. While this model is promising, it may not be applicable everywhere due to differences in healthcare infrastructures, especially in low- and middle-income countries (LMICs), where limited resources pose significant challenges to implementation.

Financially, CMV-affected infants incur higher medical costs in the first year, averaging at around US$12,000 compared to approximately US$1,500 for uninfected infants [48]. Beyond direct medical costs, the broader societal burden includes increased reliance on special education, rehabilitation services and social support systems. Therefore, implementing universal newborn screening could yield significant long-term savings by reducing these indirect costs while also improving quality of life, educational outcomes and further productivity [16,39].

A lack of knowledge about cCMV among the general public and healthcare professionals limits screening uptake and delays diagnosis. Public health campaigns and targeted professional training are essential to bridge this gap. Evidence from quality improvement initiatives shows that educational interventions can increase the rate of early detection, reduce severe complications, and ultimately lower long-term adverse healthcare outcomes [41].

Health Belief Model as an Explanatory Framework for cCMV Screening Behaviour

The Health Belief Model (HBM) helps to explain how beliefs and perceptions influence public engagement in maternal and neonatal cCMV screening. The HBM framework helps us to understand how individuals' beliefs and perceptions influence their health behaviour [49]. Higher perceived *susceptibility and severity*, particularly when parents are aware of risks such as SNHL and developmental delays, can strengthen motivation to participate in screening. Communicating the *perceived benefits* of early detection and antiviral treatment, and *reducing barriers* such as cost, access and stigma, further supports uptake. *Cues to action*, such as community stories, provider reminders and public health campaigns, can prompt screening behaviour. Meanwhile, strengthening *self-efficacy* through simple guidance and supportive communication from healthcare providers empowers individuals to act. However, persistent challenges such as low CMV awareness, stigma, unequal access to care and the long-term psychosocial burden on affected children highlights the need for comprehensive, equitable screening and support systems.

This study strongly advocates the prioritising CMV vaccine trials and subsequently introducing the vaccine into the routine immunisation programmes. Investing in vaccine development is a cost-effective public health strategy that would improve quality of life and reduce the economic burden, as would screening for early detection and treatment. Furthermore, investigating the role of neutralising and ELISA IgG antibodies in preventing maternal-foetal transmission of CMV would contribute to our understanding of how to manage the prevalence of cCMV. This is because, a study found that higher antibody titres significantly reduced transmission rates, from 23.4% in women with low titres to 9.8% in women with high titres [50]. Consequently, infants born to mothers with strong antibody responses experienced less severe symptoms. This suggests that vaccine development should focus on inducing high levels of neutralising antibodies, which could reduce both infection rates and the severity of cCMV cases.

This study has its limitations. The diversity of the included samples is somewhat limited, focusing primarily on populations in high-income settings. This may not reflect the broader global context, particularly in low-resource settings, where healthcare infrastructure and public health policies differ significantly. These limitations affect the generalisability of the findings and may distort their applicability to settings that differ significantly from those reported. In addition, reliance on secondary data sources introduces its own potential biases that may affect the robustness of the conclusions drawn. These limitations highlight the need for broader, more empirical studies that capture a more diverse demographic and healthcare landscape. Nevertheless, the analysis and discussion in this study adequately reflect the quality of the methods used to produce the findings in all the included studies. Furthermore, there is a need for further research into screening and testing in conjunction with early intervention (treatment or referral) to optimise health outcomes.

CONCLUSION

This study highlighted the critical importance of early detection and timely intervention in reducing the short- and long-term effects of CMV infection, such as SNHL and developmental impairment in children. Evidence from this study, particularly from the USA and France, shows that integrating CMV screening into routine perinatal care can substantially enhance early diagnosis rates and improve child health outcomes. Furthermore,

analyses suggest that a universal screening framework would be cost-effective, yielding substantial long-term healthcare savings and uniformity of CMV medical care.

However, significant variations in screening practices have been identified between regions, reflecting the absence of standardised global guidelines or protocols. These variations result in inconsistent screening effectiveness and disproportionate health outcomes, highlighting the urgent need for the World Health Organisation to lead the international standardisation of perinatal and neonatal CMV screening protocols. By systematically assessing global screening practices and their effectiveness, as well as their social and economic impacts, this study addresses critical knowledge gaps and provides essential evidence for policymakers. Moving forward, international collaboration to implement standardised screening guidelines or protocols will be essential in reducing the global burden of cCMV infection and optimising public health strategies.

In order to enhance the effectiveness of CMV screening programmes and improve public health outcomes; it is important to:

- *Develop of unified screening standards.*

i. Collaborate with international public health organisations to establish standardised CMV screening guidelines or protocols.

ii. Ensure global consistency of practice to facilitate the comparability of data and outcomes, enabling more effective global health strategies.

- *Increase public awareness.*

i. Launch robust public health campaigns to educate the public about CMV, particularly cCMV, its potential health impact and the benefits of early detection and treatment.

ii. Incorporate personal stories and real-life examples into these campaigns to make the information more relatable and immediate, thus encouraging greater participation in screening programmes.

- *Policies to support screening integration.*

i. Policymakers should integrate CMV screening into routine prenatal and neonatal care, especially in regions with high prevalence rates.

ii. Subsidise screening programmes to reduce financial barriers, increase participation rates, and ensure wider access to early detection and intervention services.

- *Forge collaborative research efforts.*

i. Promote international research and collaboration to share best practices and harmonise screening protocols.

ii. Address the specific needs of different regions and partner with international health organisations to provide support and funding.

iii. Encourage innovation to improve the effectiveness of CMV screening programmes worldwide.

List of Abbreviations

CMV - Cytomegalovirus

cCMV - Congenital Cytomegalovirus

HCMV – Human Cytomegalovirus

SNHL	-	Sensorineural Hearing Loss
PCR	-	Polymerase Chain Reaction
IgG	-	Immunoglobulin G
VGCV	-	Valganciclovir
NHS	-	Newborn Hearing Screening
ICER	-	Incremental Cost-Effectiveness Ratio
JPY	-	Japanese Yen
HBM	-	Health Belief Model
PICO	-	Population, Intervention, Comparison and Outcomes
PRISMA	-	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
GRADE	–	Grades of Recommendation, Assessment, Development and Evaluation
USA	–	United States of America
DNA	-	Deoxyribonucleic Acid
LMICs	-	Low- and Middle-Income Countries

Declarations

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Not applicable.

Consent for publication

All authors have read and approved the final manuscript.

Availability of data and materials

The datasets generated and/or analysed are available at Open Science Framework https://osf.io/fjqn3/.

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Discussion and Result Analysis: YL and GCA

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BIBLIOGRAPHY

1. Wang YQ, Zhao XY. Human Cytomegalovirus Primary Infection and Reactivation: Insights from Virion-Carried Molecules. Front Microbiol. 2020 Jul 14;11:1511. doi: 10.3389/fmicb.2020.01511.
2. Manicklal, S., Emery, V. C., Lazzarotto, T., Boppana, S. B., & Gupta, R. K. (2013). The "silent" global burden of congenital cytomegalovirus. Clinical Microbiology Reviews, 6(1), 86–102. https://doi.org/10.1128/CMR.00062-12.
3. Centre for Disease Control and Prevention (CDC). Cytomegalovirus (CMV) and Congenital CMV Infection. Jan. 17, 2025. https://www.cdc.gov/cytomegalovirus/about/index.html. Accessed November 17, 2025.
4. Buxmann, H., Hamprecht, K., Meyer-Wittkopf, M., & Friese, K. (2017). Primary human cytomegalovirus (HCMV) infection in pregnancy. Deutsches Ärzteblatt International. https://doi.org/10.3238/arztebl.2017.0045. 2017;114(4):45–52
5. Fowler, K., Mucha, J., Neumann, M., Lewandowski, W., Kaczanowska, M., Grys, M., ... & Diaz-Decaro, J. (2022). A systematic literature review of the global seroprevalence of cytomegalovirus: Possible implications for treatment, screening, and vaccine development. BMC Public Health, 22(1), 1659. https://doi.org/10.1186/s12889-022-3971-7.
6. Marsico C, Kimberlin DW. Congenital Cytomegalovirus infection: advances and challenges in diagnosis, prevention and treatment. Ital J Pediatr. 2017 Apr 17;43(1):38. doi: 10.1186/s13052-017-0358-8. https://pubmed.ncbi.nlm.nih.gov/28416012/
7. Ludwig A, Hengel H. Epidemiological impact and disease burden of congenital cytomegalovirus infection in Europe. EuroSurveillance. 2009; 14(9):26–32.
8. Greye, H., Wex, T., Taneva, E. et al. Cytomegalovirus seronegativity rate in pregnant women and primary cytomegalovirus infection during pregnancy in rural Germany. BMC Pregnancy Childbirth 23, 299 (2023). https://doi.org/10.1186/s12884-023-056127
9. Modrow S, Buxmann H, Enders M, Gembruch U, Goelz R, Hamprecht K, et al. Management der kongenitalen Zytomegalievirus-Infektion bei Neugeborenen. Kinder Jugendarzt. 2018; 49:107–17.
10. Stephan, A.-J., De Lepper, M., Wölle, R., Luzak, A., Wang, W., Jacob, C., Schneider, K. M., Buxmann, H., Goelz, R., Hamprecht, K., Kummer, P., Modrow, S., Greiner, W., & Reuschenbach, M. (2023). Healthcare costs of congenital cytomegalovirus (cCMV) disease in infants during the first two years of life: A retrospective German claims database analysis. Cost Effectiveness and Resource Allocation, 21(1), 8. https://doi.org/10.1186/s12962-022-00411-x.
11. Diaz-Decaro, J., Myers, E., Mucha, J., Neumann, M., Lewandowski, W., Kaczanowska, M., ... & Buck, P. O. (2023a). A systematic literature review of the economic and healthcare resource burden of cytomegalovirus. Current Medical Research and Opinion, 39(7), 973–986. https://doi.org/10.1080/03007995.2023.2222583.

12. Diaz-Decaro, J., Myers, E., Mucha, J., Neumann, M., Lewandowski, W., Kaczanowska, M., ... & Buck, P. O. (2023b). A systematic literature review on the humanistic burden of cytomegalovirus. Current Medical Research and Opinion, 39(5), 739–750. https://doi.org/10.1080/03007995.2023.2191477.
13. Rubinacci V, Fumagalli M, Meraviglia G, Gianolio L, Sala A, Stracuzzi M, Dighera A, Zuccotti GV, Giacomet V. (2022). Congenital CMV, Lights and Shadows on Its Management: The Experience of a Reference Center in Northern Italy. Children (Basel). 9(5):655. doi: 10.3390/children9050655. https://pmc.ncbi.nlm.nih.gov/articles/PMC9139751/
14. Tavakolipoor, P., Kleiner, S., & Sasse, M. (2023). Neonatale Herpesinfektion mit akutem Leberversagen. Monatsschrift Kinderheilkunde. https://doi.org/10.1007/s00112-023-01710-0.
15. Aoki, H., Kitano, T., & Kitagawa, D. (2021). Disease burden of congenital cytomegalovirus infection in Japan. Journal of Infection and Chemotherapy, 27(2), 161–164. https://doi.org/10.1016/j.jiac.2020.08.018.
16. Grosse, S. D., Dollard, S. C., & Ortega-Sanchez, I. R. (2021). Economic assessments of the burden of congenital cytomegalovirus infection and the cost-effectiveness of prevention strategies. Seminars in Perinatology, 45(3), 151393. https://doi.org/10.1016/j.semperi.2021.151393
17. Pass, R. F., Simpson, T., Corey, L., & Flanigan, C. (2009). Vaccine prevention of maternal cytomegalovirus infection. The New England Journal of Medicine.
18. Walter, E., Brennig, C., Schöllbauer, V. (2011). How to save money: congenital CMV infection and the economy. In: Halwachs-Baumann, G. (eds) Congenital Cytomegalovirus Infection. Springer, Vienna. https://doi.org/10.1007/978-3-70910208-4_7
19. Ben Shoham, A., Schlesinger, Y., Miskin, I., Kalderon, Z., Michaelson-Cohen, R., & Wiener-Well, Y. (2023). Cytomegalovirus (CMV) seroprevalence among women at childbearing age, maternal and congenital CMV infection: Policy implications of a descriptive, retrospective, community-based study. Israel Journal of Health Policy Research, 12(1), 16. https://doi.org/10.1186/s13584-023-00566-9.
20. Kalane, S. U., Raste, L., Patwardhan, S., Beasley, D. A., & Devaskar, U. P. (2022). Prevalence of maternal cytomegalovirus antibodies and neonatal congenital cytomegalovirus at less than 34 weeks of gestation: A prospective study. American Journal of Perinatology. https://doi.org/10.1055/s-0042-1756641.
21. Moseley, P., Klenerman, P., & Kadambari, S. (2023). Indirect effects of cytomegalovirus infection: Implications for vaccine development. Reviews in Medical Virology, 33(1), e2405. https://doi.org/10.1002/rmv.2405.
22. Wong, A., Tan, K. H., Tee, C. S., & Yeo, G. S. (2000). Seroprevalence of cytomegalovirus, toxoplasma, and parvovirus in pregnancy. Singapore Medical Journal, 41(4), 151–155. PMID: 11063178.
23. Bialas, K. M., & Permar, S. R. (2016). The march towards a vaccine for congenital CMV: Rationale and models. PLOS Pathogens, 12(2), e1005355. https://doi.org/10.1371/journal.ppat.1005355.
24. Shim, Gyu Hong. Treatment of congenital cytomegalovirus infection. Clinical and Experimental Pediatrics 2023;66(9):384-394. DOI: https://doi.org/10.3345/cep.2022.01032
25. Suleimenova, I. E., Bozhbanbaeva, N. C., Atke, M. E., & Urazova, S. N. (2023). On the classification of cytomegalovirus infection in newborn children. Reproductive Medicine, 2(55), 89–98. https://doi.org/10.37800/RM.2.2023.89-98.
26. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, et al. 2009. The PRISMA Statement for Reporting Systematic Reviews and Meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Annals of Internal Medicine. 151: 65–94
27. O'Connor, Denise. Green, Sally and Higgins, Julian PT. Chapter 5: Defining the review question and developing criteria for including studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Chichester (UK): John Wiley & Sons, 2008.
28. Dijkers M. (2013) Introducing GRADE: a systematic approach to rating evidence in systematic reviews and to guideline development. KT Update. Vol. 1, No. 5 http://www.ktdrr.org/products/update/v1n5/
29. Centre for Reviews and Dissemination (CRD). (2009). Guidance to Systematic Review. York, Centre for Reviews and Dissemination Pp 42–3. https://www.york.ac.uk/media/crd/Systematic_Reviews.pdf.
30. Fleiss JI. Measuring nominal scale agreement among raters. Psychol Bull. 971;76(5):376–82.
31. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Chichester (UK): John Wiley & Sons, 2008.

32. Adeyanju GC, Schrage P, Jalo RI, Abreu L, Schaub M (2025) Armed violent conflict and healthcare-seeking behavior for maternal and child health in sub-Saharan Africa: A systematic review. PLoS ONE 20(2): e0317094. https://doi.org/10.1371/journal.pone.0317094
33. **Adeyanju, G.C.,** Engel, E., Koch, L. et al. Determinants of influenza vaccine hesitancy among pregnant women in Europe: a systematic review. European Journal Medical Research, 26, 116 (2021). https://doi.org/10.1186/s40001-021-00584-w
34. **Adeyanju, GC**., Augustine, T.M., Volkmann, S. et al. Effectiveness of intervention on behaviour change against use of non-biodegradable plastic bags: a systematic review. Discov Sustain, 2021; 2**,** 13. https://doi.org/10.1007/s43621-021-00015-0
35. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. pmid:19621072
36. Zeng, Z. C., Chang, Q., Sun, Z. W., Song, M. M., Jin, X. L., Jiang, S. Y., & Yang, X. (2017). Detection of cytomegalovirus (CMV) infection in wheezing infants by urine DNA and serum IgG testing. Medical Science Monitor, 23, 1242–1246. https://doi.org/10.12659/msm.898589.
37. Foulon, I., Naessens, A., Foulon, W., Casteels, A., & Gordts, F. (2008). 10-year prospective study of sensorineural hearing loss in children with congenital cytomegalovirus infection. Journal of Pediatrics, 153(1), 84–88. https://doi.org/10.1016/j.jpeds.2007.12.049
38. Fowler, K. B., McCollister, F. P., Sabo, D. L., Shoup, A. G., Owen, K. E., Woodruff, J. L., … CHIMES Study. (2017). A targeted approach for congenital cytomegalovirus screening within newborn hearing screening. Pediatrics, 139(2). https://doi.org/10.1542/peds.2016-2128
39. Bergevin, A., Zick, C. D., McVicar, S. B., & Park, A. H. (2015). Cost-benefit analysis of targeted hearing-directed early testing for congenital cytomegalovirus infection. International Journal of Pediatric Otorhinolaryngology, 79(12), 2090–2093. https://doi.org/10.1016/j.ijporl.2015.09.019.
40. Krishna, S., Nemerofsky, S. L., Iyare, A., Ramdhanie, M. A., Nassar, M., & Nafday, S. (2020). Early extended neonatal screening for congenital cytomegalovirus infection: A quality improvement initiative. Joint Commission Journal on Quality and Patient Safety, 46(9), 516–523. https://doi.org/10.1016/j.jcjq.2020.06.002
41. Demortier, J., Fourgeaud, J., Abasse, S., Lambrecht, L., Gromand, M., Boumahni, B., ... & Vauloup-Fellous, C. (2021). A prospective study evaluating congenital CMV infection in Mayotte and La Reunion Islands (France). Journal of Clinical Virology, 138, 104793. https://doi.org/10.1016/j.jcv.2021.104793.
42. Périllaud-Dubois, C., Hachicha-Maalej, N., Lepers, C., Letamendia, E., Teissier, N., Cousien, A., Sibiude, J., Deuffic-Burban, S., Vauloup-Fellous, C., & Picone, O. (2023). Cost-effectiveness of screening and valacyclovir-based treatment strategies for first-trimester cytomegalovirus primary infection in pregnant women in France. Ultrasound in Obstetrics & Gynecology, 62(4), 573–584. https://doi.org/10.1002/uog.26226.
43. Bodeus M, Zech F, Hubinont C. (2010). Human cytomegalovirus in utero transmission: follow up of 524 maternal seroconversions. J Clin Virol. 47:201–2.
44. Enders G, Daiminger A, Bäder U, et al. (2010). Intrauterine transmission and clinical outcome of 248 pregnancies with primary cytomegalovirus infection in relation to gestational age. J Clin Virol. 52:244–6.
45. Leruez-Ville, Marianne., Chatzakis, Christos., Lilleri, Daniele., et al. (2024). Consensus recommendation for prenatal, neonatal and postnatal management of congenital cytomegalovirus infection from the European congenital infection initiative (ECCI). The Lancet Regional Health – Europe. Volume 40. DOI: 10.1016/j.lanepe.2024.100892. Available from https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(24)00058-9/fulltext#tbl1
46. Jeon J, Victor M, Adler SP, et al. (2006). Knowledge and awareness of congenital cytomegalovirus among women. Infectious Diseases in Obstetrics and Gynecology. 2006: 7 pages. doi: 10.1155/IDOG/2006/80383.
47. Adler SP. (2011). Screening for cytomegalovirus during pregnancy. Infect Dis Obstet Gynecol. 2011:1-9. doi: 10.1155/2011/942937.
48. Bartlett, A. W., Hall, B. M., Palasanthiran, P., McMullan, B., Shand, A. W., & Rawlinson, W. D. (2018). Recognition, treatment, and sequelae of congenital cytomegalovirus in Australia: An

observational study. Journal of Clinical Virology, 108, 121–125. https://doi.org/10.1016/j.jcv.2018.09.017.

49. Alyafei A, Easton-Carr R. (2025). The Health Belief Model of Behavior Change. [Updated 2024 May 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK606120/
50. Lilleri, D., Tassis, B., Pugni, L., Ronchi, A., Pietrasanta, C., Spinillo, A., Arossa, A., Achille, C., Vergani, P., Ornaghi, S., Riboni, S., Cavoretto, P., Candiani, M., Gaeta, G., Prefumo, F., Fratelli, N., Fichera, A., Vignali, M., Barbasetti Di Prun, A., … Primache, V. (2023). Prevalence, outcome, and prevention of congenital cytomegalovirus infection in neonates born to women with preconception immunity (CHILd study). Clinical Infectious Diseases, 76(3), 513–520. https://doi.org/10.1093/cid/ciac482