

Supplement C

Search Strategy

A search strategy was developed that aimed to identify UK studies reporting epidemiological and economic data associated with cCMV. The strategy was designed for MEDLINE (OvidSP).

The strategy comprised the following concepts:

1. cCMV (search lines 1 – 7)
2. Prevalence/risks of cCMV infection (lines 8-14)
3. Intervention (therapy screening etc.) (lines 15 -24)
4. Long term impairments /sequelae of cCMV (lines 25 – 90)
5. Economic costs (search lines 94- 115)
6. Epidemiology studies (search lines 118 - 123)

The search concepts were combined as follows:

Congenital CMV AND ((prevalence OR risk)

OR

Congenital CMV AND (hearing loss OR speech and language rehabilitation)

OR

Congenital CMV AND [(screening OR treatment OR drug therapy) AND cost]

OR

cCMV AND etiological or epidemiological studies

The strategy was devised using a combination of subject indexing terms and free text search terms in the title, abstract and keyword heading word fields. The search terms for cCMV and its sequelae (Table C1) were identified through scanning background literature, browsing database thesauri and suggestions from KOL. The terms include synonyms / alternative terms / associated terms.

Table C1: Search Terms

Criterion	Text word	Subject headings/MESH
Population	congenital AND (CMV or cytomegalovirus)	congenital AND Cytomegalovirus [Mesh] OR Cytomegalovirus Infections [Mesh]

Criterion	Text word	Subject headings/MESH
Interventions	valganciclovir valaciclovir valacyclovir ganciclovir ganciclovir early diagnos* hearing screen* hearing test* newborn hearing screen* neonatal screen*	Valganciclovir [Supplementary Concept] Ganciclovir [Mesh] Hearing Tests [Mesh] Neonatal Screening [Mesh]
Outcomes: economic	economic\$ cost* price or prices or pricing pharmoeconomic* value for money budget* charges fees (note: terms from YHEC economics search filter will be used)	Economics [Mesh] Costs and Cost Analysis [Mesh] Budgets [Mesh] Models, economic [Mesh] Fees and Charges [Mesh]
Outcomes: prevalence	prevalence risk incidence	Prevalence [Mesh] Risk Factors [Mesh] Incidence [Mesh]
Outcomes: Sequelae	sequelae or symptom* or abnormal* or impair* or defect* or outcome* or prognosis hearing adj1 loss. speech language auditory ocular or ophthalmolog* or ophthalmic or eye* or optic or vision or visual optic nerve cochlea* cerebral palsy neurobehaviour* or brain or neurologic* or neurodevelopment* or intellectual or cognitive or development* impair* or disorder* or delay* or complication* or manifest* or disability or disabilities or retard* or disease* or abnormal* or defect* or damage* ADHD or "attention deficit hyperactivity disorder" or "attention deficit disorder" or "hyperkinetic syndrome autism or autistic autistic spectrum autism adj spectrum intellectual adj disabilit* intellectual development disorder* mental adj (retard* or defficienc*) vestibular adj disorder* vestibular adj disease* vestibular adj damage* vestibular adj function* vestibulocochlear nerve disease* motor skills	Symptom Assessment [Mesh] Prognosis [Mesh] Deafness/cn [Congenital] hearing loss, mixed conductive- sensorineural [Mesh] hearing loss, sensorineural [Mesh] rehabilitation [Mesh] correction of hearing impairment [Mesh] neurological rehabilitation [Mesh] rehabilitation of speech and language disorders [Mesh] rehabilitation, vocational [Mesh] Optic Nerve [Mesh] Eye Diseases/cn [Congenital] Cochlea [Mesh] Neurologic Manifestations[Mesh] Neurodevelopmental Disorders [Mesh] Epilepsy[Mesh] Seizures [Mesh] Cerebral Palsy [Mesh] Intellectual Disability [Mesh] Language Development Disorders [Mesh] Attention Deficit Disorder with Hyperactivity [Mesh] Autism Spectrum Disorder [Mesh] Autistic Disorder [Mesh] Vestibular Diseases [Mesh] Vestibulocochlear Nerve Diseases Postural Balance [Mesh] developmental disabilities [Mesh] motor skills disorders[Mesh]

Criterion	Text word	Subject headings/MESH
	balance and (body or walk* or gait) walk* or ambulation or ambulatory or mobility "special education* need* ". "special healthcare need* ". (child* and (disable* or disability or disabilities) precocious puberty (intelligence quotient or IQ) and (score* or test* or assess*)	Child Development[Mesh] Child Development Disorders, Pervasive [Mesh] mobility limitation Needs Assessment [Mesh] Disabled Children [Mesh] Puberty, Precocious [Mesh] Intelligence Tests [Mesh]
Study designs	Reviews Burden of illness studies Cost studies Cohort studies Epidemiologic epidemiology	Epidemiology [Mesh] Epidemiologic Studies"
Limits	English Language Economics and UK studies filters as appropriate	

The filter used for economics terms in search lines 94 - 115 is based on the search filter developed by the University of York Centre for Reviews and Dissemination (CRD) for retrieval of economic evaluations for inclusion in the NHS EED database¹. Given that the context for this project is retrieval of all studies reporting costs (not just economic evaluations) the CRD filter has been enriched by the inclusion of additional economics terms. This filter will be applied as appropriate in the final search strategy. The strategy will filter to exclude animal studies using a standard algorithm. The strategy has not been restricted by date but has been restricted to studies published in English.

Search strategy for: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

1. (CMV or cytomegalovirus).ab,ti.
2. exp Cytomegalovirus Infections/ or exp Cytomegalovirus/
3. 1 or 2
4. congenital.fs.
5. congenital.mp.
6. 4 or 5
7. 3 and 6
8. risk factors/
9. risk.ab,ti.
10. prevalence.ab,ti.
11. prevalence/
12. incidence.ab,ti.
13. Incidence/
14. 8 or 9 or 10 or 11 or 12 or 13
15. (valganciclovir or valaciclovir or valacyclovir).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
16. Ganciclovir/ or ganciclovir.mp.
17. "early diagnos*".ab,ti.
18. "hearing screen*".ab,ti.
19. "hearing test*".ab,ti.
20. "newborn hearing screen* ".ab,ti.
21. exp Hearing Tests/

¹ <http://www.crd.york.ac.uk/crdweb/searchstrategies.asp#nhseedmedline>

22. exp Neonatal Screening/
 23. neonatal screen*.mp.
 24. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
 25. (sequelae or symptom* or abnormal* or impair* or defect* or outcome* or prognosis).ab,kf,ti.
 26. exp Symptom Assessment/
 27. exp Prognosis/
 28. (hearing adj1 loss).ab,kf,ti.
 29. speech.ab,kf,ti.
 30. language.ab,kf,ti.
 31. auditory.ab,kf,ti.
 32. Deafness/cn [Congenital]
 33. exp hearing loss, mixed conductive-sensorineural/ or exp hearing loss, sensorineural/
 34. rehabilitation/ or exp "correction of hearing impairment"/ or exp neurological rehabilitation/ or
 "rehabilitation of speech and language disorders"/ or exp rehabilitation, vocational/
 35. (ocular or ophthalmalog* or ophthalmic or eye* or optic or vision or visual).ab,kf,ti.
 36. optic nerve.ab,kf,ti.
 37. exp Optic Nerve/
 38. exp Eye Diseases/cn [Congenital]
 39. exp Cochlea/
 40. "cochlea*".ab,kf,ti.
 41. exp Neurologic Manifestations/
 42. exp Neurodevelopmental Disorders/
 43. exp Epilepsy/
 44. Seizures/
 45. cerebral palsy.mp. or exp Cerebral Palsy/
 46. exp Intellectual Disability/
 47. Language Development Disorders/
 48. (neurobehaviour* or brain or neurologic* or neurodevelopment* or intellectual or cognitive or
 development*).ab,ti.
 49. (impair* or disorder* or delay* or complication* or manifest* or disability or disabilities or retard* or
 disease* or abnormal* or defect* or damage*).ab,ti.
 50. 48 and 49
 51. 25 or 26 or 27 or 49
 52. 29 or 30 or 31 or 35
 53. 36 or 37 or 39 or 40 or 48
 54. 52 or 53
 55. 51 and 54
 56. 28 or 32 or 33 or 38 or 41 or 42 or 43 or 44 or 45 or 46 or 47
 57. 55 or 56
 58. (ADHD or "attention deficit hyperactivity disorder" or "attention deficit disorder" or "hyperkinetic
 syndrome").mp. [mp=title, abstract, original title, name of substance word, subject heading word,
 keyword heading word, protocol supplementary concept word, rare disease supplementary concept
 word, unique identifier, synonyms]
 59. exp Attention Deficit Disorder with Hyperactivity/
 60. (autism or autistic).ab,ti.
 61. "autistic spectrum".ab,ti.
 62. (autism adj spectrum).ab,ti.
 63. exp Autism Spectrum Disorder/ or exp Autistic Disorder/
 64. exp Intellectual Disability/
 65. ((intellectual adj disabilit*) or "intellectual development disorder").mp. or (mental adj (retard* or
 defficienc*)).ab,ti. [mp=title, abstract, original title, name of substance word, subject heading word,
 keyword heading word, protocol supplementary concept word, rare disease supplementary concept
 word, unique identifier, synonyms]
 66. (vestibular adj disorder*).ab,ti.
 67. (vestibular adj disease*).ab,ti.
 68. (vestibular adj damage*).ab,ti.
 69. (vestibular adj function*).ab,ti.
 70. exp Vestibular Diseases/
 71. exp Vestibulocochlear Nerve Diseases/ or vestibulocochlear nerve disease*.mp.
 72. exp Postural Balance/

73. developmental disabilities/ or motor skills disorders/
74. exp Child Development/
75. exp Child Development Disorders, Pervasive/
76. motor skills.ab,ti.
77. (balance and (body or walk* or gait)).ab,ti.
78. (walk* or ambulation or ambulatory or mobility).mp. and (difficult* or limit* or impair*).ab,ti. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
79. (walk* or ambulation or ambulatory or mobility).mp. and (difficult* or limit* or impair*).ab,ti. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

80. mobility limitation/
81. Needs Assessment/
82. "special education* need* ".ab,ti.
83. "special healthcare need* ".ab,ti.
84. exp Disabled Children/
85. (child* and (disable* or disability or disabilities)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
86. precocious puberty.mp. or exp Puberty, Precocious/
87. exp Intelligence Tests/
88. (intelligence quotient or IQ).mp. and (score* or test* or assess*).ab,ti. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
89. 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88
90. 57 or 89
91. 7 and 14
92. 7 and 90
93. 7 and 24
94. Economics/
95. exp "Costs and Cost Analysis"/
96. Economics, Nursing/ or Economics, Dental/ or exp Economics, Hospital/ or Economics, Pharmaceutical/ or Economics, Medical/
97. (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic\$).ab,kf,ti.
98. (expenditure\$ not energy).ab,kf,ti.
99. value for money.ab,kf,ti.
100. budget\$.ab,kf,ti.
101. 94 or 95 or 96 or 97 or 98 or 99 or 100
102. ((energy or oxygen) adj cost).ab,kf,ti.
103. (metabolic adj cost).ab,kf,ti.
104. ((energy or oxygen) adj expenditure).ab,kf,ti.
105. 102 or 103 or 104
106. ((Economics or "Costs and Cost Analysis" or (Economics, Nursing or Economics, Dental or Economics, Hospital or Economics, Pharmaceutical or Economics, Medical) or (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic\$) or (expenditure\$ not energy) or value for money or budget\$) not (((energy or oxygen) adj cost) or (metabolic adj cost) or ((energy or oxygen) adj expenditure))).ab,kf,ti.
107. exp Budgets/
108. exp models, economic/
109. ec.fs.
110. Income/
111. Remuneration/
112. "Salaries and Fringe Benefits"/
113. exp "Fees and Charges"/
114. (expens\$ or earning\$ or salar\$ or wage\$1 or pay or pays or paid or paying or payment\$1 or income\$1 or remunerat\$ or financ\$ or money or monetary or fee or fees or charg\$).ab,kf,ti.

- 115. 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114
- 116. exp Epidemiology/
- 117. exp Epidemiologic Methods/
- 118. exp epidemiologic factors/
- 119. exp epidemiologic studies/
- 120. (epidemiology or epidemiologic\$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 121. 116 or 117 or 118 or 119 or 120
- 122. 7 and 121
- 123. 93 and 115
- 124. 91 or 92 or 122 or 123
- 125. 115 and 124

Key to Ovid symbols and commands

\$	Unlimited right-hand truncation symbol
*	Unlimited right-hand truncation symbol
\$N	Limited right-hand truncation - restricts the number of characters following the word to N
?	Wildcard symbol wild card character stands for zero or one characters within a word or at the end of a word
ti,ab,kf.	Searches are restricted to the Title, Abstract, or Keyword Heading Word fields
adjN	Retrieves records that contain terms (in any order) within a specified number (N) of words of each other
/	Searches are restricted to the Subject Heading field
exp	The subject heading is exploded
pt.	Search is restricted to the publication type field
or/1-4	Combines sets 1 to 4 using OR

The MEDLINE search strategy was adapted suitably to perform efficiently in the other databases listed in Table C2.

Table C2: Databases searched

Database / information source	Interface / URL
PubMed	
MEDLINE, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily	OvidSP
Embase	OvidSP
EconLit	Cochrane Library / Wiley
NHS Economic Evaluation Database (NHS EED)	Cochrane Library / Wiley
Cochrane Database of Systematic Reviews (CDSR)	Cochrane Library / Wiley
Cochrane Central Register of Controlled Trials (CENTRAL)	Cochrane Library / Wiley
Database of Abstracts of Reviews of Effects (DARE)	Cochrane Library / Wiley

Database / information source	Interface / URL
Health Technology Assessment Database (HTA)	Cochrane Library / Wiley
Health Management Information Consortium Database (HMIC)	OvidSP

Selection of eligible studies

The results of the database searches were transferred to an EndNote library. They were de-duplicated using several algorithms. An experienced reviewer rapidly removed obviously irrelevant records (e.g. non-human studies), before identifying records that met the inclusion criteria (Table C3) for selection on the basis of title and abstract. Copies of potentially relevant full papers were obtained and assessed in detail for relevance to the inclusion criteria. Only papers that are accessible free of charge through the University of York subscription services were included.

Table C3: Eligibility criteria

Population	Studies will be eligible for inclusion in this review if they report on individuals with congenital CMV. Other forms of CMV will not be eligible for inclusion.
Intervention	Study selection will not be limited by the intervention assessed. Studies reporting on any intervention used for treating congenital CMV including; valganciclovir, ganciclovir, screening and treatment of sequelae, will be eligible.
Outcome	<p>Studies will be eligible for inclusion in this review if they report on:</p> <ul style="list-style-type: none"> • Prevalence or incidence of cCMV or related sequelae • Costs/resource use associated with cCMV or related sequelae <p>Cost and resource use will be separated into direct medical costs (including diagnostics, acute treatment, long-term primary or community care, medication or therapy) and indirect societal costs (including productivity loss for those who work, social care costs, educational support costs) incurred through congenital CMV infection and subsequent sequelae.</p>
Study design	Any study design that meets other eligibility criteria will be eligible for inclusion in the review. This includes reviews, cost studies, burden of illness studies, cohort studies, prospective, retrospective and follow-up studies, and epidemiological studies. Studies published as abstracts or conference presentations will be considered though rarely provide adequate data.
Limits	The search will be restricted to English-language studies only. Studies from all years will be considered. We will conduct the searches with a UK filter.

Search results

The study selection process is shown in figure 1. The literature searches were undertaken on 10 and 11 August 2017 and retrieved 619 records. 3 records were retrieved through other sources. After deduplication, the title and abstract of 467 records were screened by one reviewer and 415 records were rejected. The full texts for 52 records were retrieved and were assessed for relevance. 9 documents were excluded and 43 studies were included that were used to inform model development.

Figure C1: Flow diagram of the study selection process

