

Family planning decisions for parents of children with a rare genetic condition: a scoping review

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Published version

GEE, Melanie, PIERCY, Hilary and MACHACZEK, Katarzyna (2017). Family planning decisions for parents of children with a rare genetic condition: a scoping review. *Sexual & Reproductive Healthcare*, 14, 1-6.

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1 **Family planning decisions for parents of children with a rare genetic condition: a**
2 **scoping review**

3 **Abstract**

4 Expansion of newborn screening programmes increases the complexity around reproductive
5 choices, both in terms of the increased number of parents faced with making reproductive
6 decisions from the earliest days of their affected child's life, and the number of conditions for
7 which such decisions have to be made.

8 We conducted a scoping review to explore: (i) reproductive decision-making among parents
9 of children with recessive genetic conditions; and, (ii) the involvement of healthcare services
10 in facilitating and supporting those decisions. Systematic search processes involved seven
11 bibliographic databases, citation, and grey literature searches. From an initial total of 311
12 identified articles, seven met the inclusion criteria and were included in the review.

13 The extracted data were organised around three themes: factors influencing reproductive
14 decisions taken by parents, how those factors changed over time, and the involvement of
15 healthcare services in supporting and facilitating reproductive decisions.

16 Most studies focused on attitudes towards, and uptake of, pre-natal diagnosis (PND) and
17 termination. None of the studies considered the wider range of reproductive choices facing all
18 parents, including those of children with conditions for whom PND and termination is not
19 available or where good health outcomes make these options less justifiable. The literature
20 provided little insight into the role of healthcare staff in providing family planning support for
21 these parents. There is a need to better understand the support parents need in their decision-
22 making, and who is best placed to provide that support.

23 **Key words**

24 Scoping review; recessive genetic conditions; family planning; reproductive decisions;
25 reproductive services

26 **Abbreviations**

27 CF: Cystic Fibrosis; MCADD: Medium Chain Acyl-CoA dehydrogenase deficiency; NBS:
28 Newborn bloodspot screening; PIHM: pre-implantation genetic diagnosis; PND: pre-natal
29 diagnosis; SCD: Sickle Cell Disease; SMA: Spinal Muscular Atrophy

30 Introduction

31 ~~Developments in newborn screening technologies, with T~~the expansion of newborn
32 bloodspot screening programmes (NBS); ~~has have~~ brought a substantial increase in the early
33 detection of rare inherited disorders (1). In the USA, the NBS routinely tests for over thirty
34 conditions (2), and a similar expansion has occurred in other countries including the
35 Netherlands, Denmark and Germany (3). In the United Kingdom (UK), more modest
36 expansions have resulted in the inclusion of six inherited metabolic conditions (Box 1) (4).

37

Box 1: Conditions currently screened by the newborn bloodspot screening (NBS) programme in the UK

(Conditions in **bold** were included in the database search strategy.)

sickle cell disease (SCD)

cystic fibrosis (CF)

congenital hypothyroidism (CHT)

inherited metabolic diseases (IMDs):

phenylketonuria (PKU)

medium-chain acyl-CoA dehydrogenase deficiency (MCADD)

maple syrup urine disease (MSUD)

isovaleric acidaemia (IVA)

glutaric aciduria type 1 (GA1)

homocystinuria (HCU)

38

39 Screening and early detection of rare conditions enable treatment to be initiated before
40 significant morbidity has occurred, and can result in substantially improved health outcomes
41 and reduced likelihood of mortality (5). For example, the benefits of early detection and
42 active management for phenylketonuria are well established (6), and more recent evidence
43 indicates the benefits for medium chain Acyl-CoA dehydrogenase deficiency (MCADD) (7-
44 11). The responsibility for managing these conditions, however, rests primarily with parents.
45 The associated family burden may be substantial (12), although there is some evidence that
46 this can be mediated by adequate support (13,14).

47 When a child is diagnosed with a recessive genetic condition, parents need to decide whether
48 or not to have subsequent children. Their reproductive choices are made within a highly
49 complex and changing healthcare, social, and technological contexts. ~~Their decisions are~~
50 ~~informed by various factors, such as the severity of the condition, and its impact on the child~~

51 ~~and the family. Furthermore, technological developments make the decision-making process~~
52 ~~even more complex. The severity of the condition, and its effect on the child and the family,~~
53 ~~are likely to play a key role in parents' decisions.~~

54 ~~Another set of factors that may affect the parents' decision are concerned~~ Their decisions
55 may also be affected by ~~with~~ the genetic risk (1 in 4) of another affected pregnancy; ~~and~~ the
56 availability ~~and acceptability~~ of reproductive technologies including prenatal diagnosis
57 (PND), or pre-implantation genetic diagnosis (PIGM), to manage that risk; and willingness to
58 use those technologies. Advances in non-invasive PND increase the acceptability of these
59 techniques to parents (15,16), although ethical concerns about their availability and use have
60 been identified (17). Expansion of the NBS has increased the number of parents faced with
61 making more complicated reproductive decisions from the earliest days of their affected
62 child's life, and the number of conditions for which such decisions have to be made. This
63 indicates the need to understand how parents make decisions about subsequent pregnancies
64 and the involvement of healthcare services in facilitating and supporting those decisions.

65 Previous reviews (18,19) have focused on reproductive outcomes in this population but have
66 not considered reproductive decision-making. In this scoping review we identified and
67 mapped all studies that explored reproductive decision-making amongst parents of children
68 with recessive genetic conditions, with respect to the following questions:

- 69
- 70 1. What factors influence these decisions?
 - 71
 - 72 2. How do these factors change over time?
 - 73
 - 74 3. What is the involvement of healthcare services in supporting and facilitating these
 - 75 decisions?
 - 76

77 **Methods**

78 We used scoping review methodology (20,21), with robust literature searching and study
79 selection, coupled with data charting and a thematic narrative summary. We did not formally
80 assess the quality of included studies.

81

82 *Search strategy*

83 Searches in the following databases were carried out in April 2014 and updated in January
84 2017: ASSIA (ProQuest), CINAHL Complete (EBSCOHost), HMIC (NICE Evidence
85 Search), Medline (EBSCOHost), PsycINFO (ProQuest), Scopus (Elsevier), and Web of
86 Science (Thomson Reuters).

87 We combined search words/phrases and indexing terms related to autosomal recessive
88 conditions (named disorders with synonyms, and generic terms) with search words/phrases
89 and indexing terms related to reproductive decision-making. The named disorders searched
90 are shown in bold in Box 1. A sensitivity search in Scopus established that none of the
91 disorders additionally screened for in the US (2) were worth searching for explicitly.

92 Results were restricted to items published from 2000 onwards, as we were interested in
93 family planning decision-making within the modern context of an availability of genetic
94 testing procedures. No language or study design restrictions were applied to the searches, but
95 non-human studies were removed from the results. An indicative search strategy is provided
96 in supplementary file 1.

97 Social Care Online (SCIE) was searched for each disorder of interest separately, screening
98 the results for relevance to reproductive decision-making. ~~Other websites~~ Grey literature
99 sources known to the review team were also searched: see Box 2. searched are shown in Box
100 2. Reference and citation searches were carried out in respect of included studies.

Box 2: Websites Grey literature searched

NHS Evidence search (<https://www.evidence.nhs.uk/>) - search terms: "family planning rare genetic disorder". The first 100 results (ordered by relevance) were checked

The Genetic Alliance UK Website (<http://www.geneticalliance.org.uk/>) - browsed for relevant publications

The Ottawa Hospital Research Institute Website (<http://204.187.39.28/index.html>) - browsed for relevant decision aids

101

102 *Study selection*

103 Inclusion and exclusion criteria were independently applied by two reviewers, with any
104 disagreements resolved through discussion within the review team. -Papers were included if

105 they related to reproductive decision-making by couples who had a child with a recessive
106 genetic condition and were considering having more children. We excluded papers relating to
107 couples who did not have an affected child, or papers focusing on: (i) women with a genetic
108 condition; (ii) the uptake of genetic technologies without exploring the decision-making
109 process; or (iii) attitudes towards parental screening or (hypothetical) non-invasive prenatal
110 diagnosis. Included conditions of interest were those shown in bold in Box 1. We excluded
111 studies relating to autosomal dominant conditions (e.g. Huntington's), or other non-genetic
112 conditions (e.g. hypothyroidism).

113 We only included studies set in countries whose reproductive health services included well-
114 developed early detection technologies, i.e. Europe, USA, Canada, Australia, and New
115 Zealand. We included papers that reported any original empirical study, but the reference lists
116 of retrieved reviews were consulted.

117 *Data extraction and synthesis*

118 ~~We developed a data extraction form for We charted charting~~ the key study characteristics of
119 the included studies and findings of relevance to our review, which were further thematically
120 analysed according to our review questions.

121 **Results**

122 **Characteristics of included studies**

123 From 311 unique records from the original database searches, plus two further records from
124 the search update, seven records were included in this review (see Figure 1).

125 All were peer-reviewed journal articles apart from one conference abstract (22). The main
126 characteristics of the included studies are provided in Table 1.

127 Four studies related to reproductive decision-making for parents of children with Cystic
128 Fibrosis (CF) (23-26), and one each to Sickle Cell Disease (SCD) (22), Spinal Muscular
129 Atrophy (SMA) (27), and rare metabolic disorders (28). In most of the studies the participants
130 were recruited from populations using, or known to, health services (22-26,28); one study
131 recruited predominantly via an advocacy group for the condition (SMA) (27). Four studies
132 used quantitative (23,24,26,28), and three qualitative research methods (22,25,27).

133 Most of the studies explored decisions concerning whether to have more children following
134 the birth of an affected child (22-27), and focused almost exclusively on parental attitudes

135 towards use of reproductive technologies to avoid having further affected children. Six of the
136 studies (22-26,28) focussed on parental attitudes towards PND and termination of affected
137 pregnancies, with two of these (22,26) also exploring the use of assisted reproductive
138 technologies such as donor-In Vitro Fertilisation (IVF), and preimplantation genetic
139 diagnosis (PGD), but provided minimal information about this to inform our review.

140 In just one study the separate opinions of mothers and fathers in participating couples were
141 explicitly sought (25). Most studies recruited predominantly mothers (over 87% in three
142 (22,27,28) and 100% in one (24). One study (23) reported a 'poor response' from fathers in
143 the baseline survey and only surveyed mothers in the follow-up. The genders of the parent
144 participants were not reported in one study using data from a national survey (26).

145 Ethnicity was reported in four of the seven studies. Three included all or mainly white/
146 Caucasian participants (24,25,28) and the fourth which focused on SCD included parents of
147 black or African American origin (22).

148

149 **Findings: reproductive decision-making**

150 *What factors influence the reproductive decisions taken by parents of a child with a recessive*
151 *genetic condition?*

152 In most studies, parental perceptions of coping with their affected child were key to decisions
153 about having any further children, and decisions about the use of reproductive technologies to
154 avoid having further affected children. Decisions were based on factors centred both on the
155 child, and on the parent and their wider family and social network, which-They included
156 perceptions around their current and future situation, which shifted over time as the parents
157 adapted to caring for their affected child.

158 Factors centred on the child included the perceived severity (or otherwise) of the condition
159 (23,26), concerns about the child's current health (23), worry about the child's future and their
160 future health (23,28), the (poor) quality of life of the child and the family (23), the potential
161 impact of another affected child on the existing child and family life, including concern for
162 increased infection risk (25), and having experienced suffering and death of previous
163 children(27). In one study, some parents considered their existing child as a role model or
164 support system for a hypothetical future child having the same condition (22), and in another

165 study (23) one mother believed that termination of an affected pregnancy would devalue the
166 life of their existing child with CF.

167 Factors centred on the parents included parental stress (28), the impact of caring for the child
168 on the parents' daily activities (26), the perceived difficulty of meeting the child's care needs
169 (28), the size of the parents' social support network (28), and the physical strain of caring for
170 a child with a condition involving a physical disability (27). In one study, the parents'
171 experience caring for their affected child gave them confidence in their abilities to look after
172 another child with the same condition (25); indeed, one father was quoted as saying they had
173 considered adopting another child with CF because of their experiences (25).

174 Some parents did plan future pregnancies but were prepared to take the risk of having a
175 further affected child, trusting to chance. In one study (23), some parents believed that the
176 odds were more likely to be in favour of having a healthy child in the next pregnancy. One
177 study found that some parents appeared not to make active reproductive choices, but rather
178 were 'overtaken by events' (25) p.409, which the authors described as a 'decision *not to*
179 *decide*'. Conversely, in another study (26) some parents of children with CF had decided not
180 to have more children as this was 'easier to decide', obviating potential engagement with
181 reproductive technologies.

182 Moral issues were of lesser importance in decision-making: lack of religious conviction was
183 found to correlate with intention to use PND and consideration of termination (26), and 2/16
184 mothers cited 'religious reasons' for not terminating a hypothetical affected pregnancy in one
185 study (23). One study found that for some parents the decision not to have any further
186 children was driven by a desire not to have any more affected children and unwillingness to
187 terminate an affected pregnancy (24).

188 The studies highlight much ambivalence around the use of PND to make decisions about
189 continuation of pregnancy. Three studies (23,26,28) explored parents' decision making and
190 reasoning in relation to hypothetical future pregnancies. In one study (26), 13/97 and 26/97
191 parents of children with CF who were planning more children did not know whether they
192 would *consider* terminating or *decide to* terminate a hypothetical subsequent affected
193 pregnancy respectively. Two studies (23, 28) found a disjoint between parents wanting to
194 undergo prenatal diagnosis and their intention to terminate a pregnancy on the basis of that
195 diagnosis. Among parents of children with CF who had embarked on subsequent pregnancies,

196 uptake of PND was largely justified in terms of enabling them to adjust to a positive result,
197 although all five CF-affected pregnancies had resulted in termination (23).

198

199 *How do those factors change over time?*

200 Reproductive decisions may change as the situation of caring for a child with a rare genetic
201 condition unfolds. ~~This has been explored only with respect to parents of children with CF. In~~
202 ~~one study, participants describing their evolving response to having a child with CF (25)~~
203 ~~reported that One of the studies invited participants to describe their evolving response to~~
204 ~~having a child with CF (25). Participants reported that~~ after the initial shock of diagnosis,
205 they took some time to adapt and learn how to manage the condition, but once they had
206 adapted, they felt able to cope and could consider having another child.

207 ~~As decisions can change over time, hypothetical decisions may not necessarily translate to~~
208 ~~actual behaviour.~~ Only one study followed up participants over time to explore this how
209 hypothetical decisions translated to actual behaviour (23). They found that 16 of the 27
210 mothers of young children with CF who had at baseline reported not wanting any more
211 children, had changed their mind at a five-year follow-up. Again, coping was cited as a main
212 reason for this, along with the child's good health and being more comfortable with the
213 diagnosis. Conversely, four of the six mothers who originally wanted more children had
214 changed their mind due to concerns over the child's health. Overall, the study found that in
215 67% of mothers, the hypothetically reported behaviour regarding the use of PND was the
216 same as the actual behaviour, but 'mothers not uncommonly changed their minds, and in both
217 directions' (23) (pe654).

218 *What is the involvement of healthcare services in supporting and facilitating these decisions?*

219 Four studies (23-25, 28) considered the role of healthcare services and all confined their
220 attention to genetic counselling services and their availability, uptake and acceptability. Some
221 of the studies reported that some or all the participants had received genetic counselling,
222 mostly by specialist genetic counselling services (23-25); in the study of reproductive
223 decisions of parents of children with metabolic disorders (28), the author provided a
224 breakdown of professional groups which provided genetic counselling, and less than 4% of
225 genetic counselling was provided by a specialist genetic counsellor either within or outside
226 the metabolic centre. One study (23) reported that 72% of mothers had rated consultations

227 with genetic counsellors as 'extremely useful' or 'very useful'. Other than reporting the
228 availability and uptake of genetic counselling services, however, the studies did not explore
229 the role of these or other services in supporting and facilitating reproductive decisions.

230 Discussion

231 We found a dearth of recent studies exploring reproductive decision-making of parents of
232 children with recessive genetic conditions, as previously highlighted (29); the collective
233 scope of the studies was narrow. Only a small number of conditions were considered, with
234 the majority focusing on CF, whose findings will have limited applicability to other
235 conditions. Most studies focused on attitudes towards, and uptake of, PND and termination.
236 None of the studies considered the wider range of reproductive choices facing all parents
237 (including those of children with conditions for whom PND and termination is not available
238 or where good health outcomes make these options less justifiable), and the extent to which
239 those choices are facilitated. With regard to familial relationships, only one of our included
240 studies (25) explored the role of both mothers and fathers in couples' reproductive decision-
241 making; for most of the others, mothers were the focus. More generally, this literature base
242 failed to recognise that reproductive decisions take place in a wider social arena that extends
243 beyond the confines of PND (30)., ~~and outside the confines of consideration of, and~~
244 ~~engagement with, PND.~~

245 The reviewed literature did reveal a number of factors which seem to affect reproductive
246 decisions for this particular population and their relative importance. Many of those revolved
247 around parental perceptions of coping, now and in the future, with some parents using
248 scenario-based thinking as a decision-making strategy (25). Moral and religious
249 considerations seemed to be less significant which is consistent with findings from Atkin et al.
250 (30).

251 In presenting factors which may be important in reproductive decision-making, it is important
252 to recognise the complex interplay between them (25), and the ways in which parents manage
253 the complexity of decisions related to use of reproductive technologies. In some cases, this is
254 done using simplifying heuristics (25). Some who find reproductive decisions too
255 overwhelming choose *not* to choose, leaving future children to chance, rejecting PND and
256 therefore any subsequent, potentially stressful decisions (32). Others elect to eliminate the
257 possibility of future pregnancies altogether, as Kelly (29) found in her qualitative study of
258 parents of children affected with various genetic conditions.

259

260 The literature provided little insight into the role of healthcare staff in providing family
261 | planning support for these parents. In those studies where it was considered (23-25, 28), it
262 | was confined to the role of metabolic physicians or genetic counsellors in offering genetic
263 | technologies and explaining them, if appropriate. There is a lack of consideration of specialist
264 | reproductive services in the published literature.

265

266 A lack of access to acceptable contraception, and inconsistent or incorrect use of
267 | contraceptives, are major contributors to unplanned pregnancies (323,334). Early initiation of
268 | effective postpartum contraception including long-acting reversible methods substantially
269 | improves the odds of an inter-pregnancy interval of greater than 18 months (354,356). Access
270 | to high-quality reproductive healthcare from the point of diagnosis of the affected child is
271 | therefore particularly important. As our review has highlighted, reproductive decisions may
272 | alter over time, as parents adjust to their role or in response to the changing health status of
273 | their child (23,25). It is therefore important to recognise that decisions about whether or not
274 | to have children are not isolated events; they take place over time and need to be underpinned
275 | by a deliberative approach to contraceptive decision-making and access to effective
276 | contraceptive methods including long-acting reversible contraceptives, in order to both
277 | prevent unplanned pregnancy, and to enable planned pregnancy. The parents of younger
278 | children with genetic conditions are vulnerable to stress associated with caring and treatment
279 | management (14). However, there is a lack of literature to indicate the situation regarding
280 | contraceptive related decisions and the ways in which they impact on and contribute to wider
281 | reproductive decision-making processes.

282

283

284 *Limitations*

285

286 Our review has benefited from rigorous database searches and study selection processes. The
287 | grey literature searches, however, were not exhaustive, ~~therefore some potentially relevant~~
288 | ~~materials may have been missed. It could be argued that o~~One limitation was a decision not
289 | to quality assess the included studies. However the role of quality assessment in scoping
290 | reviews has been debated (36,37), and in our review we were not synthesising the evidence

291 on the basis of its strength and quality, but rather identifying emergent themes and identifying
292 gaps where research is lacking (387).

293

294 **Conclusion**

295 We found an overall paucity of research evidence on reproductive decision-making and the
296 role of reproductive health services. The evidence base was confined to a limited number of
297 conditions (predominantly CF). Although the studies were largely concerned with decisions
298 about the use of reproductive technologies, these decisions were secondary to fundamental
299 decisions about whether to have a further child. These decisions, which changed over time,
300 centred on the reality of caring for the affected child and its implications on the family unit.
301 There is a need to better understand what support parents need in their decision-making, how
302 and when best to provide it, and by whom. Mothers' voices dominated the current literature,
303 therefore subsequent research should focus more on the whole family unit.

304 **Funding statement**

305 This research was funded by the NIHR Collaboration for Leadership in Applied Health
306 Research and Care Yorkshire and Humber (NIHR CLAHRC YH). [www.clahrc-](http://www.clahrc-yh.nihr.ac.uk)
307 [yh.nihr.ac.uk](http://www.clahrc-yh.nihr.ac.uk). The views and opinions expressed are those of the author(s), and not
308 necessarily those of the NHS, the NIHR or the Department of Health.

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411 | **Figure 1. Document flow diagram**

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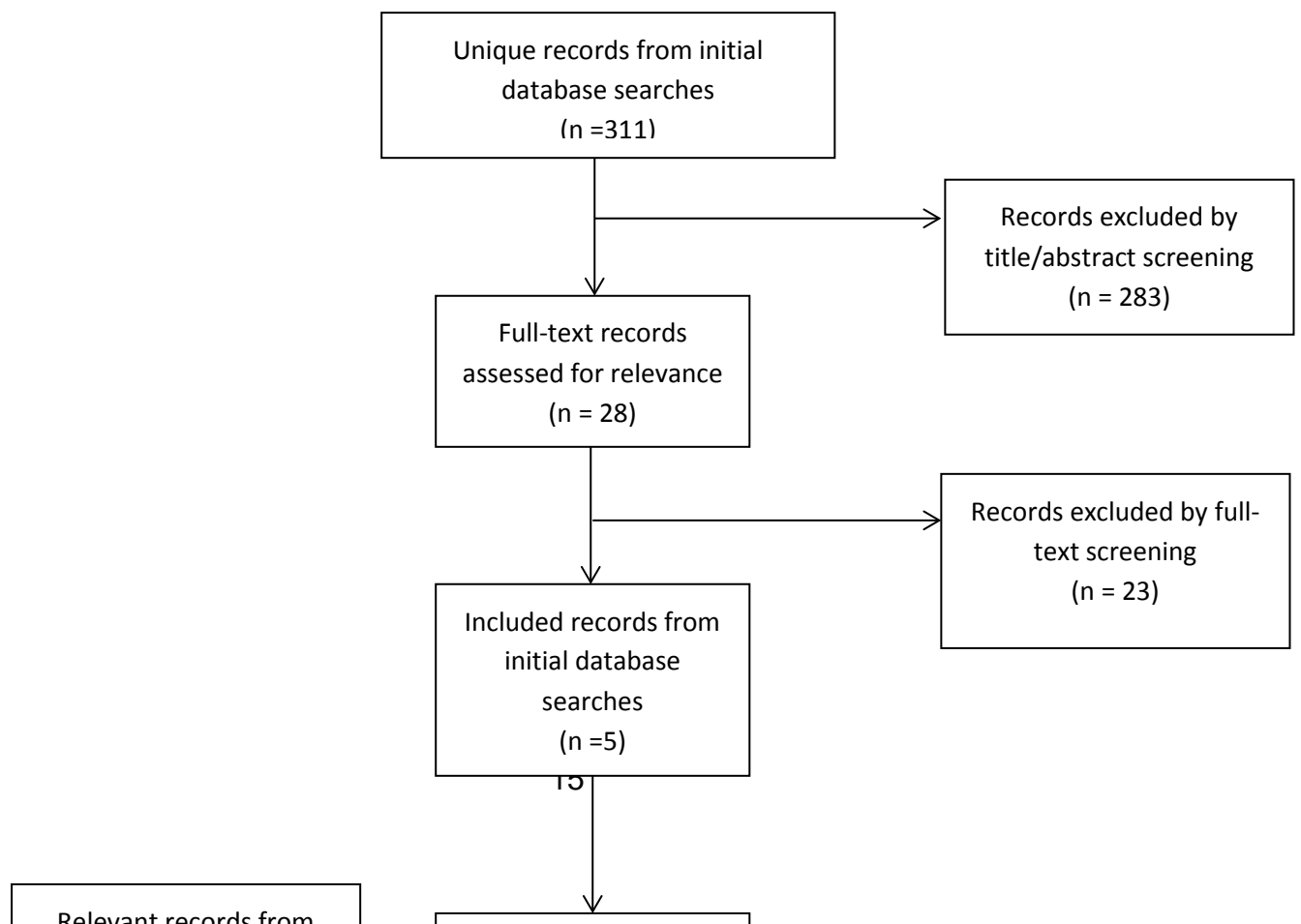
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Supplementary file 1: Search strategy in Medline and CINAHL Complete (EBSCOHost)

TI = title words

AB = abstract words

MH = database subject headings

n4 = proximity operator

<u>#</u>	<u>Query</u>	<u>Results</u>
<u>S1</u>	<u>TI "family planning" OR AB "family planning"</u>	<u>14,206</u>
<u>S2</u>	<u>TI ((decid* OR decision* OR choos* OR choice* OR plan* OR inten* OR options) n4 reproduct*) OR AB ((decid* OR decision* OR choos* OR choice* OR plan* OR inten* OR options) n4 reproduct*)</u>	<u>5,387</u>
<u>S3</u>	<u>TI ((decid* OR decision OR choos* OR choice* OR plan* OR inten* OR options) n4 (contracept* OR "birth control")) OR AB ((decid* OR decision OR choos* OR choice* OR plan* OR inten* OR options) n4 (contracept* OR "birth control"))</u>	<u>3,778</u>
<u>S4</u>	<u>TI ((decid* OR decision OR choos* OR choice* OR plan* OR inten* OR options) AND (pregnan* n4 (further OR subsequent OR later))) OR AB ((decid* OR decision OR choos* OR choice* OR plan* OR inten* OR options) AND (pregnan* n4 (further OR subsequent OR later)))</u>	<u>1,381</u>
<u>S5</u>	<u>TI ((decid* OR decision OR choos* OR choice* OR plan* OR inten* OR options) AND (preconceptual OR "pre fertili?ation" OR prefertili?ation OR PIGM OR CVS OR "antenatal diagnosis" OR FTS OR "first trimester screening" OR "noninvasive genetic testing" OR "prenatal screening" OR "antenatal screening")) OR AB ((decid* OR decision OR choos* OR choice* OR plan* OR inten* OR options) AND (preconceptual OR "pre fertili?ation" OR prefertili?ation OR PIGM OR CVS OR "antenatal diagnosis" OR FTS OR "first trimester screening" OR "noninvasive genetic testing" OR "prenatal screening" OR "antenatal screening"))</u>	<u>1,852</u>
<u>S6</u>	<u>(MH "Family Planning+")</u>	<u>6,614</u>
<u>S7</u>	<u>(MH "Contraception+")</u>	<u>27,895</u>
<u>S8</u>	<u>S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7</u>	<u>51,665</u>
<u>S9</u>	<u>TI (Huntingdon* OR HD) OR AB (Huntingdon* OR HD)</u>	<u>28,847</u>
<u>S10</u>	<u>(MH "Huntington's Disease")</u>	<u>1,071</u>
<u>S11</u>	<u>(MH "Huntington Disease")</u>	<u>9,032</u>
<u>S12</u>	<u>S9 OR S10 OR S11</u>	<u>34,882</u>
<u>S13</u>	<u>S8 AND S12</u>	<u>110</u>

S14	TI (PKU OR phenylketonuria OR hyperphenylalaninemia OR "PAH deficiency" OR "phenylalanine hydroxylase deficiency" OR H-PHE) OR AB (PKU OR phenylketonuria OR hyperphenylalaninemia OR "PAH deficiency" OR "phenylalanine hydroxylase deficiency" OR H-PHE)	6,379
S15	(MH "Phenylketonuria+")	518
S16	(MH "Phenylketonurias+")	6,102
S17	S14 OR S15 OR S16	8,193
S18	S8 AND S17	40
S19	TI "congenital hypothyroidism" OR AB "congenital hypothyroidism"	2,767
S20	(MH "Congenital Hypothyroidism")	3,728
S21	S19 OR S20	4,610
S22	S8 AND S21	3
S23	TI sickle OR AB sickle	21,310
S24	(MH "Anemia, Sickle Cell+")	20,605
S25	TI "cystic fibrosis" OR AB "cystic fibrosis"	36,723
S26	(MH "Cystic Fibrosis")	32,496
S27	TI (MCAD OR MCADD OR ("medium chain" AND "dehydrogenase deficiency")) OR AB (MCAD OR MCADD OR ("medium chain" AND "dehydrogenase deficiency"))	869
S28	TI (MSUD OR "maple syrup urine disease" OR "BCKD deficiency" OR "branched-chain ketoaciduria" OR ketoacidemia) OR AB (MSUD OR "maple syrup urine disease" OR "BCKD deficiency" OR "branched-chain ketoaciduria" OR ketoacidemia)	957
S29	TI (IVA OR IVE OR "isovaleric acidemia" OR "IVD deficiency" OR (isovaleric n3 deficiency) OR (isovaleryl n3 deficiency)) OR AB (IVA OR IVE OR "isovaleric acidemia" OR "IVD deficiency" OR (isovaleric n3 deficiency) OR (isovaleryl n3 deficiency))	5,250
S30	TI (GA-1 OR GA1 OR GA-2 OR GA2 OR "glutaric acidemia" OR "glutaric aciduria" OR (glutaryl n4 deficiency) OR (glutarate n4 defect) OR "dicarboxylic aminoaciduria") OR AB (GA-1 OR GA1 OR GA-2 OR GA2 OR "glutaric acidemia" OR "glutaric aciduria" OR (glutaryl n4 deficiency) OR (glutarate n4 defect) OR "dicarboxylic aminoaciduria")	2,980
S31	TI (HCU OR HCY OR homocystinemia OR homocystinuria OR "CBS deficiency" OR (cystathionine n3 deficiency)) OR AB (HCU OR HCY OR homocystinemia OR homocystinuria OR "CBS deficiency" OR (cystathionine n3 deficiency))	4,314
S32	TI (LCHAD OR LCHADD OR "trifunctional protein deficiency") OR AB (LCHAD OR LCHADD OR "trifunctional protein deficiency")	184
S33	TI ("phenotype-genotype correlation" OR "genotype-phenotype correlation") OR AB ("phenotype-genotype correlation" OR "genotype-phenotype correlation")	2,709

<u>S34</u>	<u>TI "rare genetic disorder*" OR AB "rare genetic disorder*"</u>	<u>1.037</u>
<u>S35</u>	<u>TI "rare genetic condition*" OR AB "rare genetic condition*"</u>	<u>155</u>
<u>S36</u>	<u>TI "rare metabolic disorder*" OR AB "rare metabolic disorder*"</u>	<u>209</u>
<u>S37</u>	<u>TI "autosomal recessive disorder*" OR AB "autosomal recessive disorder*"</u>	<u>5.635</u>
<u>S38</u>	<u>TI "autosomal recessive condition*" OR AB "autosomal recessive condition*"</u>	<u>672</u>
<u>S39</u>	<u>TI "cinderella condition*" OR AB "cinderella condition*"</u>	<u>1</u>
<u>S40</u>	<u>(MH "Maple Syrup Urine Disease")</u>	<u>981</u>
<u>S41</u>	<u>S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40</u>	<u>92.357</u>
<u>S42</u>	<u>S8 AND S41</u>	<u>484</u>

Table 1: Characteristics of included studies

Citation	Country	Study aim* and design	Study population* and sample size*
Schultz et al. 2014 (22)	US	To explore how having a child with SCD affects parents' future reproductive decisions or acceptability of alternative family planning options Qualitative/Semi-structured Interview and grounded theory informed analysis	Parents of children < 6 years diagnosed with SCD n=20
Sawyer et al. 2006 (23)	Australia	To assess the attitudes of parents of children with CF to PND and abortion, and to explore how attitudes and behaviours change over time Quantitative/Interview, repeated after 5 years	Mothers of children 2-7 years diagnosed with CF n=56 at baseline n=43 at follow-up
Dudding et al. 2000 (24)	Australia	To document the reproductive choices made in a subsequent pregnancy after the birth of a child with CF identified by neonatal screening; and to determine which factors influence these decisions Quantitative/Interview and Statistical Analysis	Mothers of children diagnosed with CF by neonatal screening between 1981-1996 n=124
Myring et al. 2011 (25)	UK	To explore the reproductive decision making in a sample of CF carriers with partners who are also CF carriers, and the views of male and female participants about the decision-making process Qualitative/Semi- structured Interview and grounded theory informed analysis	Parents of children diagnosed with CF n=19
Henneman et al. 2001 (26)	Netherlands	To investigate attitudes of parents of children with CF to use of PND and abortion, and their family planning and reproductive behaviours Quantitative/Postal Survey (part of a national study)	Parents of children <16 years diagnosed with CF n=288
Boardman 2014 (27)	UK	To present an analysis of the ways in which 'experiences with disability', 'embodied experiences of impairment' and 'embodied experiences of illness, death and bereavement' emerged in families' accounts of living with, and making reproductive decisions around, SMA Qualitative/In-depth Interview and grounded theory informed analysis	Parents of children diagnosed with SMA n=24
Read et al. 2002 (28)	US	To quantify and identify correlates of receptivity to PND, likelihood of terminating a future affected pregnancy, and whether measures had been taken to prevent a future affected pregnancy in parents of children with rare metabolic disorders Quantitative/Interview and Statistical Modelling	Parents of children aged 6 months-18 years diagnosed with a rare metabolic disorder n=230
<p>*Study aim, Study population, Sample size: Some studies addressed several research questions; only those pertinent to this review have been included in the table. The table only includes population and sample size data pertinent to the parents of affected children. SCD = Sickle Cell Disease; CF = Cystic Fibrosis; SMA = Spinal Muscular Atrophy; PND = pre-</p>			

