

ORIGINAL ARTICLE

Views of patients and parents of children with genetic disorders on population-based expanded carrier screening

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Abstract

Objective: Faster and cheaper next generation sequencing technologies have enabled expansion of carrier screening for recessive disorders, potentially facilitating population-based implementation regardless of ancestry or family history. Little is known, however, about the attitudes regarding population-based carrier screening among families with genetic disorders. This study assessed views among parents and patients with a recessive disorder and parents of children with Down syndrome (DS) on expanded carrier screening (ECS).

Method: In total, 85 patients with various recessive disorders, 110 parents of a child with a recessive disorder and 89 parents of a child with DS participated in an online survey in the Netherlands. Severity of recessive disorders was classified as mild/moderate or severe/profound.

Results: The majority of the (parents of) patients with a recessive disorder had a positive attitude towards population-based ECS, including screening for their own or their child's disorder. DS parents were significantly less positive towards ECS. Subgroup analyses showed that the severity of the disorder, rather than being a patient or parent, influences the attitudes, beliefs and intention to participate in ECS.

Conclusion: Our findings have important implications for future implementation initiatives as they demonstrate the different perspectives from people with experiential knowledge with genetic disorders.

Key points

What's already known about this topic?

- Carrier screening panels for recessive disorders are rapidly expanding.
- Concerns have been raised about the possible impact of expanded carrier screening (ECS) on people affected by genetic disorders.

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What does this study add?

- The majority of Dutch (parents of) patients with a recessive disorder had a positive attitude towards ECS. Parents of children with Down syndrome are less positive.
- Severity of the disorder, rather than being a patient or parent, influenced the attitudes, beliefs and intention to participate in ECS.

1 | INTRODUCTION

Carrier screening aims to identify couples who have an increased risk of having a child with a recessive disorder to facilitate informed reproductive decision making and is performed preferably prior to pregnancy. Couples with an increased risk have multiple reproductive options available, including refraining from having biological children, pre-implantation genetic testing for monogenic disorders (PGT-M), prenatal diagnosis (PND) followed by pregnancy termination or preparation for the birth of a child with a disorder.¹

Until recently, carrier screening was used to detect one or few relatively frequent, severe childhood-onset disorders within specific population groups, based on ethnicity and/or geographic background. Faster and cheaper next-generation sequencing technologies have enabled expanded carrier screening (ECS) panels that include multiple recessive disorders, which can be applied regardless of ancestry, thus allowing a population-based (universal) approach.²

While most attitudinal research concerning ECS to date has focused on the general population,³⁻⁵ socially responsible implementation of ECS warrants considering the views of “experiential experts”. These are people with personal experience of a subject, in this case, primarily patients with a genetic disorder and their families. Little is known about the attitudes towards population-based ECS among families with genetic disorders.⁶ So far, studies mostly addressed the perspectives on screening for a single disorder, such as cystic fibrosis (CF)⁷ or Spinal Muscular Atrophy (SMA).⁸ The perspectives on population-based ECS among parents of children with mucopolysaccharidosis type III (MPSIII) have also been studied.⁴ However, MPSIII is considered a very severe disorder and the findings cannot be generalised. Overall, attitudinal studies suggest that affected families are predominantly positive towards population-based screening for single disorders.^{7,8} Offering preconception ECS to the whole population can increase awareness and lead to better understanding of genetics on a societal level. Concerns, however, have been raised about possible negative impacts of population-based ECS for people affected by genetic disorders, including stigmatisation and a reduction of societal support, medical expertise and research funding due to potentially declining numbers of people born with genetic disorders.^{6,9} Given the (continuing) expansion of carrier screening panels,¹⁰ it has become increasingly urgent to gain deeper insights into the perceptions towards ECS among (parents of) patients with a broad range of mild to severe recessive disorders.

As ECS becomes increasingly available to people who do not have an a priori higher risk of being a carrier couple based on their personal or family history, couples will more likely make reproductive

decisions without having experiential knowledge of living with (a child with) a genetic disorder. The expected higher use of medical information, as opposed to experiential knowledge, is seen as a problematic development by the disability rights community. They fear that this may both lead to discrimination of people living with the conditions screened for and poorly informed reproductive decision making by those to whom screening for those conditions is offered.⁹ From this perspective, experiential knowledge is essential for responsible implementation of population-based ECS, including for decision making about which conditions should and should not be included in screening programs, and for what reasons.

Research on attitudes towards prenatal screening for Down syndrome (DS) has shown that many parents of a child with DS are concerned that expanded prenatal testing may cause an increase in pressure to test and social stigma.^{11,12} Even though prenatal screening for DS is different from ECS, and ECS is preferably offered before pregnancy and does not include DS, the experiential knowledge of parents of a child with DS can, in our view, contribute to the discussion on responsible implementation of ECS as well, as there has been a long tradition of prenatal screening for this disorder. ECS and screening for DS resemble each other in the sense that they are both forms of reproductive screening and are generally offered to people who have a low a priori risk of having an affected child and who have no prior experience with the disorder to be screened.

Hence, in this survey study, we aimed to assess attitudes towards population-based ECS among parents and patients with a broad range of recessive disorders and parents of children with DS.

2 | METHODS

2.1 | Participants and procedure

A cross-sectional survey using an online questionnaire was conducted among parents and patients with recessive disorders (December 2020–January 2021) and among parents of a child with DS (February–March 2021) in the Netherlands. Recruitment of (parents of) patients with a recessive disorder (aged ≥ 18 years) was carried out in collaboration with the Patient Alliance for rare and genetic diseases (VSOP),¹³ representing over 100 patient and parent organisations in the Netherlands with a wide range of rare and genetic disorders. In addition, two clinical geneticists (PL and IvL) from two Dutch academic medical centres personally invited (parents of) patients with recessive disorders to participate via email.

Recruitment of parents of a child with DS was carried out in collaboration with two Dutch organisations for people with DS and their parents.^{14,15} Calls for participants were also placed in the organisations' newsletters and social media pages; hence, we were unable to calculate the response rate.

In the Netherlands, population-based carrier screening is not standard practice. ECS is available to interested couples through two academic centres; there are no commercial offers allowed by law. Basic information about ECS and reproductive options, including the purpose of our research, was given in the recruitment calls (Appendix 1). The Medical Ethical Committee of VU University Medical Center Amsterdam approved the study protocol (no. 2020.464). All participants provided informed consent online.

2.2 | Survey and measures

A questionnaire was developed by a multidisciplinary research team (clinical geneticists, health scientists, psychologist, an ethicist and three representatives from patient organisations) based on the literature.^{4–6,8} Attitudes towards ECS were assessed with four items using five-point semantical differential scales (negative–positive; undesirable–desirable; frightening–not frightening; and obvious–not obvious).⁴ Respondents' opinion on an ECS offer was measured by the question: "Do you think ECS should be offered to all couples who are considering a (future) pregnancy?" (yes/no/don't know). Beliefs about ECS, including perceived benefits, barriers and expectations regarding stigmatisation/discrimination, were measured by 11 statements.⁴ Perceived proportionality of ECS was measured by the question: "Do you think the benefits of ECS outweigh its harms?" (yes/no). Intentions towards participating in ECS was measured by the question: "Would you want to participate in ECS?" (yes/no/don't know/does not apply). This question was presented to respondents considering a pregnancy. They were also asked which reproductive options they would prefer (PGT-M/PND/accepting the risk of having a child with a disorder/donation/sperm or oocyte donation/other/don't know). Parents of a child with a recessive disorder were asked if they would have made a different reproductive decision if they had been aware of their risk prior to pregnancy (PGT-M/PND/no child/no/other/don't know/don't want to say). Respondents were asked which type of disorders should be included in an ECS test panel (physical disorders/conditions that cause intellectual disability/severe disorders/mild disorders/all disorders/own disorder/child's disorder. Multiple options possible). Preferences were enquired regarding which group ECS should target (newborns/all couples with a desire to have children/all couples with a positive family history/high risk groups/people at reproductive age (defined as 15–45 years) who visit the physician for other reasons. Multiple options possible).

The autosomal and X-linked recessive disorders reported by respondents were classified as mild/moderate or severe/profound according to existing criteria of disease characteristics, including shortened life span, impaired mobility, sensory impairment and reduced fertility^{16–19} (see Supplementary Table S1 for disorders and

severity classification). For disorders that had not been previously classified in literature, two clinical geneticists (PL and IvL) determined which classification was appropriate based on their medical knowledge.

Sociodemographic and clinical variables included were: age, sex, education, marital status, considering a future pregnancy and perceived disorder severity.

2.3 | Statistical analyses

Descriptive analyses were used to summarise characteristics. Subgroup comparisons (patients vs. parents of a child with a recessive disorder vs. parents of a child with DS and mild/moderate vs. severe/profound) were made using Chi-Square tests for categorical variables and Independent Sample T-tests for continuous variables.

To separate negative or non-attitudes from positive responses, the opinion on whether ECS should be offered to all prospective parents in the general population was dichotomised into score 0 (negative/don't know) and score 1 (positive). Proportionality was dichotomised into score 0 (harms of ECS outweigh benefits/don't know) and score 1 (benefits of ECS outweigh harms). Multiple logistic regression analyses investigated whether being a parent of a child with a recessive disorder or a patient, age, sex, educational level (low/middle vs. high), relationship status, member of religion, perceived severity (high vs. low) and classified severity (mild/moderate vs. severe/profound) were associated with 'opinion on ECS offer' and 'proportionality of ECS'. All analyses were completed using SPSS 26.

3 | RESULTS

Of the 284 participants, 85 (29.9%) were patients with an autosomal ($n = 47$) or X-linked ($n = 38$) recessive disorder (AR-XL patients), 110 (38.7%) were parents of a child with an autosomal ($n = 80$) or X-linked recessive disorder ($n = 30$) (AR-XL parents), and 89 (31.3%) were parents of a child with DS (DS parents). The majority of respondents were women with high educational level. Of the 110 AR-XL parents, 40 (36.4%) and 70 (63.6%) had a child with a mild/moderate or severe/profound disorder, respectively. Of the 85 AR-XL patients, 42 (49.4%) had a mild/moderate disorder and 43 (50.6%) had a severe/profound disorder (Table 1).

3.1 | Attitudes towards expanded carrier screening

Of the 85 AR-XL patients, 62 (72.9%) believed that ECS should be offered to all couples who are considering a (future) pregnancy. This was slightly lower for AR-XL parents (66.4%) and significantly lower for DS parents (27%; $p < 0.001$). There were no significant differences in overall mean attitude scores between AR-XL patients ($M = 3.7$; $p = 0.288$) and AR-XL parents ($M = 3.5$, scale 1–5). The DS parents had a significantly lower mean attitude score ($M = 2.3$; $p < 0.001$) compared

TABLE 1 Characteristics of study population

| | Patients with recessive disorder (n = 85) (AR-XL patients) | Parents of a child with recessive disorder (n = 110) (AR-XL parents) | Parents of a child with Down syndrome (n = 89) (DS parents) |
|---|---|---|--|
| Age in years, mean (SD) | 41.30 (14.02) | 43.50 (11.58) | 46.40 (7.96) |
| 18–30 | 20 (23.5) | 8 (7.3) | 2 (2.2) |
| 31–45 | 38 (44.7) | 62 (56.4) | 41 (46.1) |
| 46–>60 | 27 (31.8) | 40 (36.4) | 46 (51.7) |
| Sex, n (%) | | | |
| Male | 13 (15.3) | 9 (8.2) | 2 (2.2) |
| Female | 70 (82.4) | 100 (90.9) | 87 (97.8) |
| Other | 2 (2.4) | 1 (0.9) | 0 |
| Education^a, n (%) | | | |
| Low | 3 (3.5) | 6 (5.5) | 0 |
| Middle | 31 (36.2) | 28 (25.5) | 29 (32.6) |
| High | 51 (60.0) | 74 (67.3) | 60 (67.4) |
| Decline to answer | 0 | 2 (1.8) | 0 |
| Religious beliefs, n (%) | | | |
| No | 57 (67.1) | 80 (72.3) | 52 (58.4) |
| Yes | 28 (32.9) | 30 (27.5) | 37 (41.6) |
| Marital status, n (%) | | | |
| Single | 20 (23.5) | 11 (10.3) | 6 (6.7) |
| Relationship/married | 65 (76.5) | 96 (87.3) | 83 (93.3) |
| Declined to answer | 0 | 1 (0.9) | 0 |
| Missing | 0 | 2 (1.8) | 0 |
| Considering a (future) pregnancy, n (%) | | | |
| Yes | 26 (30.6) | 19 (17.3) | 9 (10.1) |
| No/not possible | 49 (57.6) | 83 (75.5) | 80 (89.8) |
| Do not know (yet) | 10 (11.7) | 8 (7.3) | 0 |
| My (child's) disorder is severe, n (%) | | | |
| (Completely) agree | 61 (71.8) | 97 (82.7) | 13 (14.6) |
| Neutral | 13 (15.3) | 8 (7.3) | 12 (13.5) |
| (Completely) disagree | 11 (12.9) | 5 (4.5) | 64 (71.9) |
| Classification of disorder severity^b, n (%) | | | |
| Mild/Moderate | 42 (49.4) | 40 (36.4) | n.a. |
| Severe/Profound | 43 (50.6) | 70 (63.3) | n.a. |

Abbreviations: AR, Autosomal recessive; DS, Down syndrome; n.a., not applicable; SD, Standard deviation; XL, X-linked.

^aEducational level was categorised into low (primary school, lower level of secondary school, lower vocational training), middle (higher level of secondary school, intermediate vocational training) and high (high vocational training, university).

^bAutosomal and X-linked recessive disorders were classified into mild/moderate or severe/profound severity by clinical geneticists (PL and IvL), according to existing criteria of disease characteristics, including shortened life span, impaired mobility, sensory impairment and reduced fertility (based on 16–19).

to AR-XL parents and AR-XL patients (Figure 1). AR-XL patients and parents with severe/profound disorders were significantly more likely to have positive attitudes towards a population-based ECS offer

($M = 3.8$) compared to those with mild/moderate disorders ($M = 3.4$; $p < 0.013$). AR-XL patients and parents with severe/profound disorders viewed ECS as more desirable ($M = 3.9$) and not frightening

($M = 3.8$) compared to those with mild/moderate disorders ($M = 3.5$, $p = 0.028$; $M = 3.2$, $p = 0.002$, respectively).

3.2 | Beliefs about expanded carrier screening

AR-XL patients and parents held generally positive beliefs regarding ECS (no significant differences between these two groups). For instance, a majority of AR-XL patients (70.0%) and AR-XL parents (78.8%) disagreed with the statement 'ECS ensures that less money goes to research for treatments of disorders that are being tested for'. In addition, a minority of 20% of AR-XL patients and parents agreed with the ECS statements concerning pressure to participate, discrimination and lesser acceptance of people with a disorder that was included in the test. In contrast, DS parents held more negative views towards a population-based ECS offer. For example, DS parents were significantly more likely to agree with the statement 'ECS leads to discrimination against people with conditions that are included in the test,' compared to AR-XL parents (55.1% vs. 19.1%) (Table 2). Patients affected by a severe/profound disorder were more likely to believe that ECS prevents grief for future parents compared to those affected by mild/moderate disorders (74.3% vs. 54.9%, $p = 0.006$). In contrast, those affected by a mild/moderate disorder, compared to those affected by a severe/profound disorder, were more likely to believe that ECS may lead to discrimination (24.4% vs. 12.4%, $p = 0.036$), may devalue the lives of people with disorders that can be tested for (31.7% vs. 17.7%, $p = 0.027$), and may cause people to feel obligated to participate due to external pressure (34.1% vs. 10.6%, $p < 0.001$), although the majority disagreed on these items.

3.3 | Perceived proportionality of expanded carrier screening

With regard to the perceived proportionality of population-based ECS, 48 (56.5%) AR-XL patients, 72 (65.5%) AR-XL parents and 20 (22.5%) DS parents believed that the benefits of ECS outweigh the harms. Of the respondents affected by a mild/moderate or severe/profound recessive disorder, 44 (53.7%) and 76 (67.3%), respectively, believed that the benefits of ECS outweigh the harms ($p = 0.054$).

3.4 | Intention to participate in expanded carrier screening

Of the 63 (parents of) AR-XL patients considering a (future) pregnancy, 34 (54.0%) intended to participate themselves in ECS if available for the general population, 13 (20.6%) were unsure and 16 (25.4%) had no intention of participating. There were no significant differences for intention to participate between AR-XL patients (52.8%) and AR-XL parents (55.6%, $p = 0.195$) nor between the mild/moderate subgroup (53.8%) and the severe/profound subgroup (54.1%, $p = 0.196$).

3.5 | Intended reproductive choices

We asked AR-XL patients who were considering a (future) pregnancy ($n = 63$) which reproductive option they would prefer. Among these,

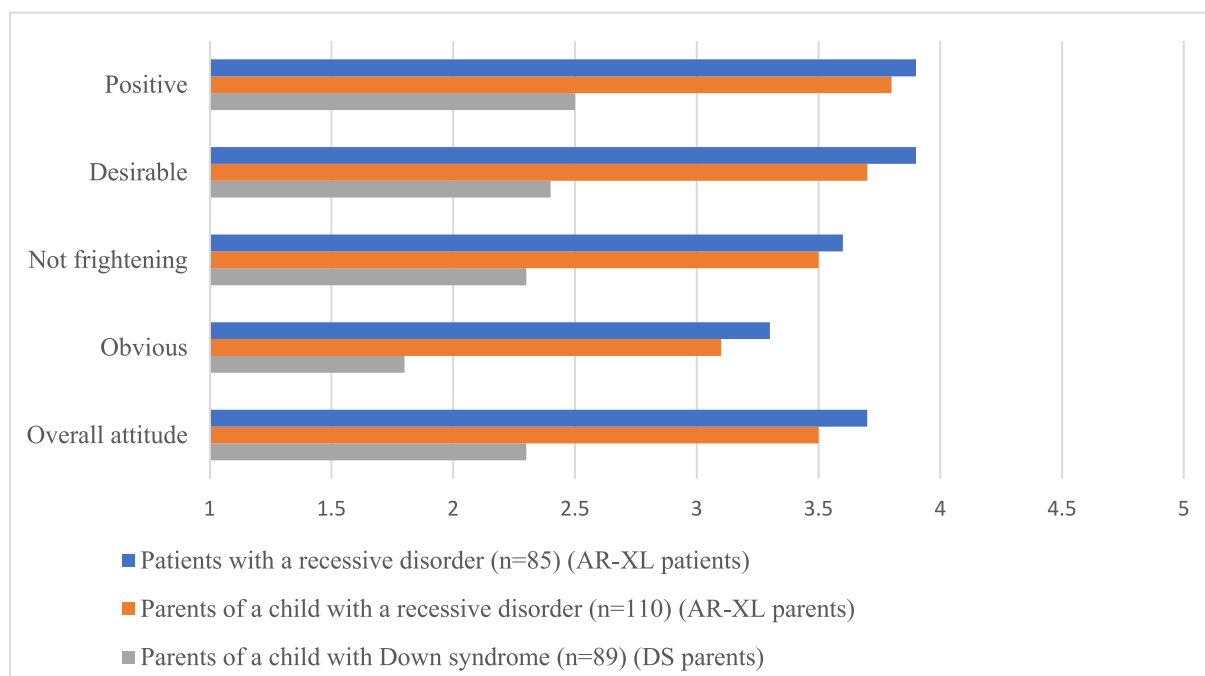


FIGURE 1 Attitudes towards expanded carrier screening. Mean scores on attitude scale. Significant differences were found between patients with recessive disorder (AR-XL) versus parents of a child with Down syndrome (DS parents) ($p < 0.01$) and parents of a child with recessive disorder (AR-XL parents) versus parents of a child with Down syndrome (DS parents) ($p < 0.01$) [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Beliefs towards expanded carrier screening (ECS)

| | Patients with a recessive disorder (n = 85) (AR-XL patients) | Parents of a child with a recessive disorder (n = 110) (AR-XL parents) | Parents of a child with Down syndrome (n = 89) (DS parents) |
|---|--|--|---|
| % Agreement with following beliefs: | N (%) | N (%) | N (%) |
| ECS ensures that (future) parents can better prepare for a child with a genetic disorder | 69 (81.2) | 89 (80.9) | 71 (79.8) |
| ECS ensures that fewer children suffer from a serious genetic disorder | 57 (67.1) ^a | 85 (77.3) ^b | 45 (50.6) ^{a,b} |
| ECS prevents much grief for future parents | 52 (61.2) ^a | 77 (70.0) ^b | 30 (33.7) ^{a,b} |
| ECS prevents many costs for the society | 39 (45.9) ^a | 57 (51.8) ^b | 22 (24.7) ^{a,b} |
| ECS causes having children to become less of a given | 26 (30.6) ^a | 46 (41.8) ^b | 55 (61.8) ^{a,b} |
| ECS leads to anxiety in people who want to become pregnant | 29 (34.1) ^a | 42 (38.2) ^b | 49 (55.1) ^{a,b} |
| ECS ensures that less money goes to research for treatments of disorders that are being tested for | 18 (21.2) ^a | 33 (30.0) ^b | 48 (53.9) ^{a,b} |
| ECS devalues the lives of people with disorders that can be tested for | 21 (24.7) ^a | 25 (22.7) ^b | 65 (73.0) ^{a,b} |
| ECS causes people to feel obligated to participate due to external pressure | 19 (22.4) ^a | 21 (19.1) ^b | 58 (65.2) ^{a,b} |
| ECS leads to discrimination against people with conditions that are tested for | 13 (15.3) ^a | 21 (19.1) ^b | 49 (55.1) ^{a,b} |
| ECS leads to lesser acceptance of people with disorders being tested for | 19 (22.4) ^a | 20 (18.2) ^b | 67 (75.3) ^{a,b} |

Abbreviations: AR, Autosomal recessive; DS, Down syndrome; XL, X-linked.

^aSignificant differences between patients with a recessive disorder (AR-XL patients) versus parents of a child with Down syndrome (DS parents) ($p < 0.01$).

^bSignificant differences between parents of a child with a recessive disorder (AR-XL parents) versus parents of a child with Down syndrome (DS parents) ($p < 0.01$).

the most preferred option was PGT-M (62; 41.3%) (see Supplementary Table S2). We asked AR-XL parents ($n = 102$; missing $n = 7$) which reproduction option they would have chosen had they been aware of their carrier status prior to having a child. Among these, again PGT-M was the most preferred option (42; 38.5%) (see Supplementary Table S3).

3.6 | Preferences for possible offer of ECS

With regard to which disorders should be included in a population-based ECS test panel, 'severe life-threatening disorders for which there is no treatment available' was the most preferred option (Figure 2). Furthermore, 73% of AR-XL parents and 72% of AR-XL patients agreed on including their own or familial disorder in the ECS test panel. Moreover, 58% of the AR-XL (parents of) patients, and only 21% of DS parents, preferred to offer ECS to all couples considering a future pregnancy (Figure 3).

3.7 | Multiple regression analyses

When characteristics of AR-XL parents and patients were analysed in a multiple logistic regression model, the variable 'own/child's disorder severity' was the only one that remained significantly associated with having a positive view on ECS ($p = 0.016$). None of the variables were significantly associated with perceived proportionality of benefits and harms of ECS (Supplementary Table S4).

4 | DISCUSSION

This study assessed the views of patients and parents of children with genetic disorders on population-based expanded carrier screening (ECS). In general, the AR-XL parents and patients included in our study had similar positive attitudes and intentions towards ECS. Subgroup analyses showed that the severity of the disorder, rather than being an AR-XL patient or parent, mostly influenced the

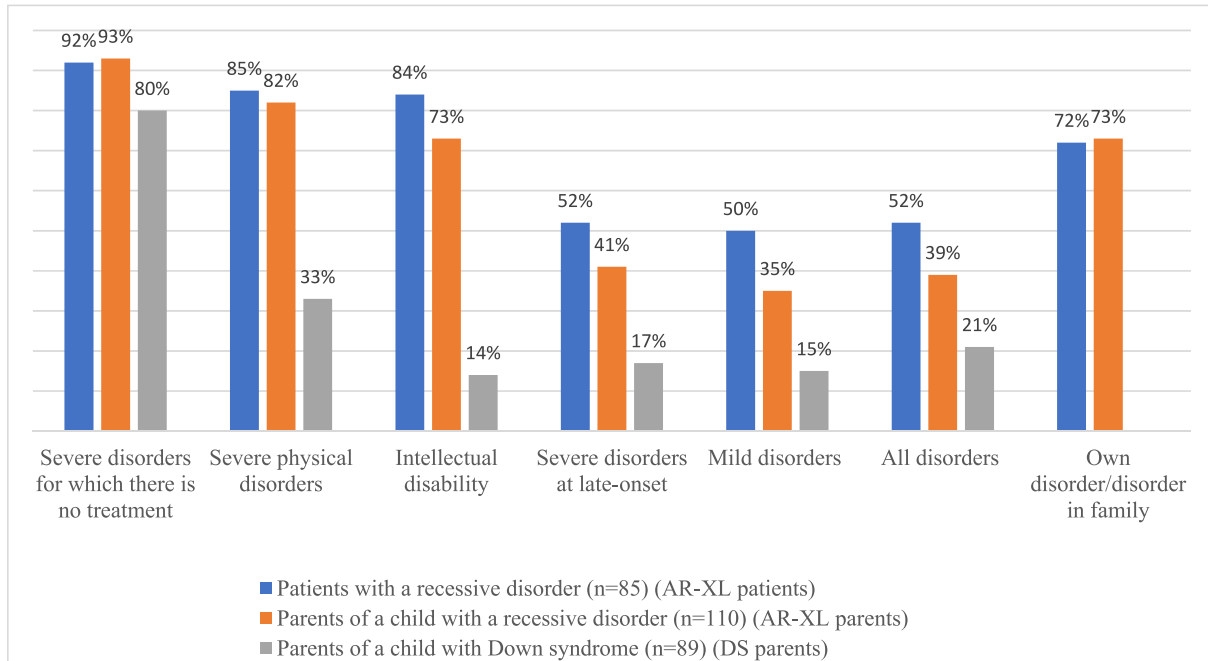


FIGURE 2 Preferences for disorders in expanded carrier screening test panel [Colour figure can be viewed at wileyonlinelibrary.com]

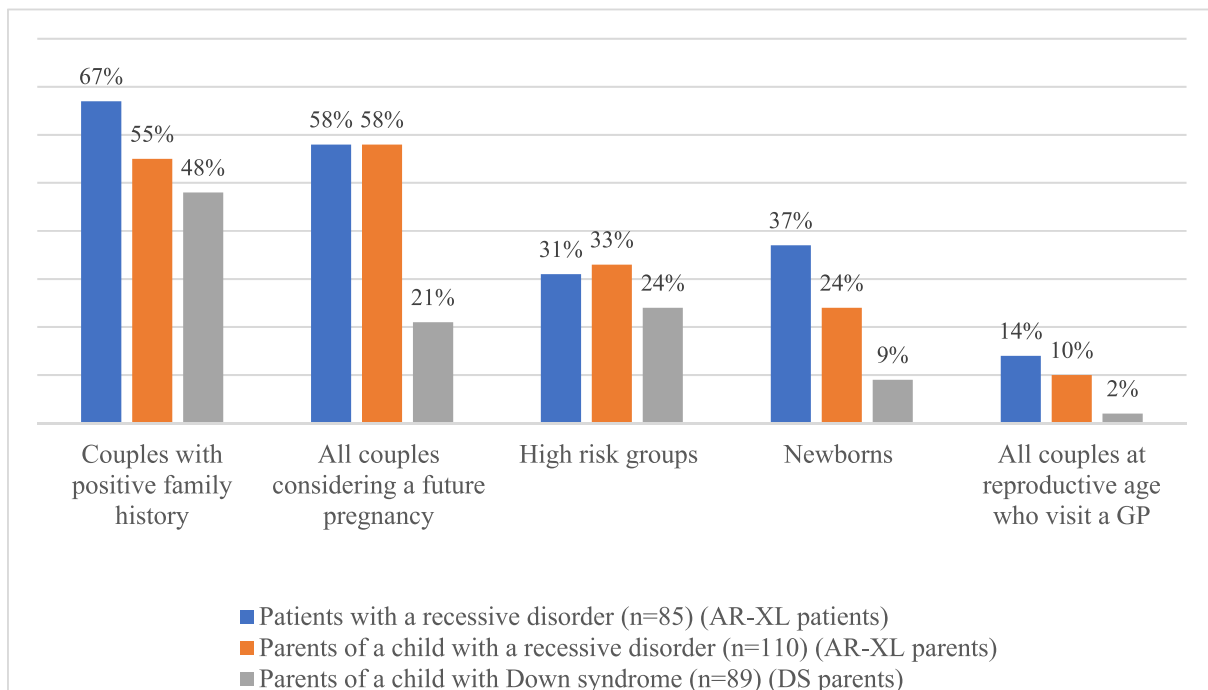


FIGURE 3 Preferences for target population for expanded carrier screening. Reproductive age was defined as 15–45 years old. GP, General practitioner [Colour figure can be viewed at wileyonlinelibrary.com]

attitudes, beliefs and intentions. Of the AR-XL respondents who were considering a (future) pregnancy, 55.6% had the intention to participate in ECS. This is lower than that found in a study involving family members of patients with the severe disorder MPSIII (84.3%).⁴ This difference might be explained by the broader range of disorder severity (mild to profound) included in our study.

There were significant differences between parents and patients with mild/moderate disorders and those with severe/profound disorders. The severe/profound subgroup was significantly more likely to consider population-based ECS as desirable and not frightening compared to the mild/moderate subgroup. Those affected by severe/profound disorders were significantly more likely to believe that ECS

can prevent grief for future parents as well. Accordingly, they were less likely to believe that population-based ECS can lead to discrimination, devalues the lives of people with disorders or causes people to feel obliged to participate, compared to those affected by mild/moderate disorders. These findings support previous UK research on attitudes towards population-based screening among SMA-affected families.⁸ Those perceiving the lowest SMA-related quality of life were most likely to support screening.⁸

Despite the differences in beliefs between those affected by mild/moderate disorders and those affected by severe/profound disorders, more than half of the AR-XL parents and patients agreed that the benefits of ECS outweigh the potential harms. This finding is in line with previous research in Belgium that found that (parents of) patients with CF had concerns regarding possible negative implications of ECS yet still believed that ECS had more benefits than harms.⁷

An interview study showed that, despite support for population-based screening for haemophilia among adults with haemophilia and their family members, 90% of the respondents did not agree with pregnancy terminations for haemophilia.²⁰ Notably, in our study, the statement: 'ECS ensures that (future) parents can better prepare for a child with a genetic disorder' was highly endorsed by all subgroups. In order to responsibly implement population-based ECS, it is essential to further understand the motivations behind parents and patients' positive attitudes towards ECS, as this does not naturally imply support for all possible reproductive options, such as prenatal diagnosis followed by termination of pregnancy.

Our findings show that more than 70% of the AR-XL parents and patients supported the inclusion of their child's/own disorder in an ECS panel. This was slightly lower, yet still substantial, for (parents of) patients with mild/moderate disorders (63.4%). This finding is in line with previous research, which found that support for the inclusion for milder disorders was lower (yet still over 50%) than that for more severe disorders among AR-XL parents.²¹

Previous recommendations state that ECS panels should be limited to severe childhood-onset disorders.¹ This discussion on responsible implementation may be extended to the question of whether to include milder disorders in ECS panels. Screening mild disorders may not primarily facilitate reproductive autonomy; however, this genetic information may prepare parents for affected children or realise health benefits by initiating treatment as soon as possible after birth. Offering parents ECS with different types of disorders, and with different aims, in one panel may, however, be challenging with regard to pretest counselling and gaining valid consent.

Even though the regression analysis showed that disorder severity was the only variable associated with a positive opinion towards a population-based ECS offer, it is important to realise that understanding ECS attitudes among those affected by a genetic disorder remains complex. Previous qualitative research found that patients with negative attitudes towards population-based ECS viewed their impairment or disorder (whether mild or severe) as integral to their identity.⁶ As that study highlights, disorder severity

should not be the only consideration in the discussion on responsible implementation of ECS and the inclusion of disorders in ECS panels, as the nature of one's experiences with a certain disorder is of great value in this discussion.

Our study showed that DS parents had significantly less positive attitudes towards population-based ECS compared to (parents of) AR-XL patients. The experiential knowledge of having a child with Down syndrome might be a contributing factor, as the majority of the DS parents disagreed with the statement 'Down syndrome is a severe disorder'. In addition, the overall mean attitude score of DS parents regarding prenatal testing ($M = 2.4$) was similar to their overall mean attitude score regarding ECS ($M = 2.3$). In contrast to the experts' views,⁹ DS parents do not find preconceptional ECS less ethically contentious than prenatal testing. DS parents raised concerns about discrimination, lesser acceptance and a loss of diversity in society in both screening contexts.¹² A previous study among DS parents underlined the positive impact that their children have on their lives and how they would not want to "cure" their child's condition.²² Future research could compare the perspectives on ECS of people with different types of disorders in relation to their perceptions of quality of life and degree of suffering from this condition (e.g. comparing conditions that cause intellectual disability vs. physical and sensory disabilities and combinations thereof), as this may influence how parents view their child's disorder and hence, influence their attitudes towards preconception and prenatal screening.²³

5 | STRENGTHS AND LIMITATIONS

This study included parents and patients with a wide range of genetic disorders. There are a number of limitations. Even though existing criteria were used to classify the disorders into mild/moderate or severe/profound, there is a subjective nature to the classification. The data that we had on respondents' disorders were provided by the respondents themselves, and respondents did not always describe their disorder type; some types may be more severe than others. Furthermore, most respondents were highly educated and female and were recruited via patient organisations or personally invited, which may have introduced bias, as people who are more interested in the topic might have participated. Moreover, parents of individuals with recessive disorders were most likely unfamiliar with carrier screening and unexpectedly confronted with the disorder of their child after birth, whereas this was probably less true for parents of a child with DS due to their awareness and/or use of prior prenatal screening. This may have also introduced bias, as the latter group may have explicitly chosen not to have prenatal DS screening and may therefore have held more negative attitudes towards genetic screening prior to the start of our study. The responses of parents of DS children may thus not be representative of the views that would be held by DS parents in a population that did not have access to prenatal screening. Finally, we did not include parents of children with de novo pathogenic variants or other types of inheritance, who may have other views on reproductive genetic screening.

6 | CONCLUSION

Understanding the perspectives from 'experiential experts' is essential for responsible implementation of ECS in the general population. Our findings suggest that the severity of the disorder, rather than being a patient or parent, predominantly shapes the views towards ECS. Overall, AR-XL parents and patients were positive towards the offer of population-based ECS, as well as population-based ECS for their own or child's disorder, regardless of severity. Future discussions should consider including disorders with varying severity in ECS panels too, for which health benefits can be achieved by treatment as soon as possible after birth. Contrasting the perspectives of AR-XL parents and patients, most parents of a child with DS in our study were reluctant about population-based ECS and raised concerns about discrimination, lesser acceptance and a loss of diversity in society. Our findings have important implications for future implementation initiatives, as they underline the complexity of arguments in decision making on the severity of disorders and different options for reproductive choices from different perspectives. Nevertheless, despite concerns regarding discrimination and stigmatisation, most of the parents and patients with autosomal and X-linked recessive disorders believed that the benefits of a population-based ECS offer outweigh the harms.

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CONFLICT OF INTEREST

Anke J. Woudstra, Lieke M. van den Heuvel, Phillis Lakeman, Irene M. van Langen, Lotte Haverman and Lidewij Henneman are affiliated with a hospital that offers expanded carrier screening in a noncommercial setting. The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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