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Postpartum women's attitudes to disclosure of adult-onset conditions in pregnancy

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Abstract

Background: Advanced prenatal genomic technologies can identify risks for adult-onset (AO) conditions in the fetus, challenging the traditional purpose of prenatal testing. Professional guidelines commonly support disclosure of high-penetrance AO actionable conditions, yet attitudes of women/parents to these findings and factors affecting their attitudes are understudied.

Methods: We explored 941 (77% response rate) postpartum women's attitudes towards receiving prenatal genetic information, and associations of sociodemographic, medical and psychological characteristics with their choices, focusing on AO conditions.

Results: Women largely support the disclosure of actionable AO findings (58.4%), in line with professional guidelines. A third of the women also supported the disclosure of non-actionable AO conditions. Stronger religious observance ($p < 0.001$) and higher psychological distress ($p = 0.024$) were associated with decreased interest in receiving actionable AO conditions, whereas higher concern for fetal health yielded increased interest ($p = 0.032$). Attitudes towards disclosure were strongly associated with women's perceived benefit of such information for their own, partner's, and future child's health. Termination of pregnancy based on such information received very little support.

Conclusion: In-light of the demonstrated understanding of nuanced genetic information and the observed diversity in attitudes, a culturally competent opt-in/out policy could be considered. If full-disclosure is practiced, support should be provided to those expressing higher levels of distress.

Authors Shiri Shkedi-Rafid and Hagit Hochner have contributed equally to this work

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Key points

What is known

- Advanced prenatal genomic technologies can identify risks for adult-onset (AO) conditions.
- Professional guidelines support disclosure of high-penetrance AO actionable conditions in pregnancy, yet attitudes of women/parents towards receiving this information are understudied.

What this study adds

- Investigating the attitudes of nearly 1000 postpartum women demonstrates that women largely support the disclosure of actionable AO findings in pregnancy.
- Stronger religious observance and higher psychological distress predict decreased interest in receiving this information.

1 | INTRODUCTION

Advanced genomic technologies (AGT), such as chromosomal-microarray-analysis (CMA) and whole-exome-sequencing (WES) have become an integral part of prenatal care, especially in cases of fetal malformations,[1–7] yet growingly also in uneventful pregnancies.[1,8–10] Alongside the increased capacity of AGT to detect childhood-onset pathogenic findings, they can also identify risks for adult-onset (AO) conditions in the fetus. Detection of such findings challenges the traditional purpose of prenatal testing[11,12] and raises dilemmas typically related to predictive genetic testing in adults.

WES is commonly done in parent-fetus trios, and thus allows the identification of risks in the parents, irrespective of fetal genotype.[13] In CMA however, only the fetus is tested, yet parents may be tested subsequently to determine if the finding is de novo or inherited. Therefore, disclosing variations associated with risks for actionable AO conditions identified in the fetus enables to recognize at-risk individuals in the family and to provide them with medically actionable and even life-saving information. Consequently, most guidelines support disclosure of high-penetrance AO actionable conditions identified in pregnancy.[4,5,14–16] Actionability, as referred to by the American College of Medical Genetics and Genomics (ACMG), takes into consideration the severity, penetrance, and impact and/or burden of available treatment modalities or screening recommendations.[13] In WES a set list of genes associated with actionable conditions that merit disclosure has been defined by the ACMG. However, it is almost impossible to similarly pre-determine a set list of copy number variants that encompass more than a single gene. Therefore, decisions are left to the individual lab scientists/clinicians. In addition, actionability may be perceived differently by various people, which makes disclosure in pregnancy challenging to both clinicians and women/parents.

Overall, several studies demonstrate that when given choice, women are more likely to request extended genetic information about their fetus, beyond clearly pathogenic childhood-onset conditions.[6,7,17–20] Empirical data on disclosure of AO conditions in pregnancy is scarce[17,20,21] and the characteristics of women who choose to receive/avoid AO information in pregnancy are largely unknown.

Using a diverse population of women, this study set out to explore women's attitudes towards receiving different types of genetic information in pregnancy, and the associations between multiple socioeconomic, medical and psychological characteristics and their choices, focusing mainly on AO conditions. We recruited women immediately after giving birth to facilitate participant recruitment. Although these women have not necessarily experienced disclosure of AO information in their pregnancies, their theoretical choices can indicate trends and understanding, which can in turn prepare clinicians for women's actual choices if such are granted.

2 | METHODS

2.1 | Participants and data collection

The study included women hospitalized after delivery (24–72 h) in the maternity wards of Hadassah Medical Center and Rabin Medical Center, between May 2017 and April 2019. These two centers, covering different geographical areas in Israel, were selected because the populations giving birth there represent women of child bearing age from diverse socioeconomic, ethnic and cultural backgrounds. Parturients of all ethnicities who gave birth to a healthy newborn were approached by a research assistant, who conducted a 15-minute computer-assisted anonymous interview in Hebrew, using a structured questionnaire.

2.2 | The questionnaire

A multiple-choice questionnaire was constructed for this study by the research team, which includes experts in medical genetics, epidemiology, and sociology. The questionnaire was designed to collect

information on 5 major components: (1) women's willingness to receive genetic information on three types of conditions in their fetus (referred hereafter as choice-related outcomes): severe congenital diseases leading to death in childhood; actionable AO conditions ("severe diseases that do not manifest in childhood/teens and have treatment and/or prevention at older ages, such as breast cancer"); and non-actionable AO conditions ("severe diseases that do not manifest in childhood/teens and currently have no treatment and/or prevention, such as Alzheimer's disease); (2) women's level of agreement with various reasons for and against disclosure of information on AO conditions in pregnancy; (3) socioeconomic information; (4) obstetric and medical characteristics; and (5) information related to the women's psychological well-being, including the Kessler Psychological Distress Scale (K6).[22] The use of the K6 allowed us to tap into the broader construct of "psychological distress" which encompasses both anxiety and depression that are common in pregnancy and postpartum and often occur together.[23] We also chose the K6 because its time frame of reference includes the 30 days prior to the interview, rather than the past 7 days (as in the Edinburgh Postnatal Depression Scale (EPDS)) or current/general anxiety (as in the STAI), and because its measure of psychological distress is more closely aligned with DSM-5 definitions of depression and anxiety disorders than either of those in the EPDS or STAI.

2.3 | Study variables

Level for all three choice-related outcomes was measured using a five-level Likert scale, between 1 - strongly agree with disclosure of genetic information, and 5 - strongly disagree. The five-level scale was then dichotomized by merging values 1 and 2 (i.e., reflecting agreement) and values 4 and 5 (i.e., reflecting disagreement). The few women (up to 5.8%) responding as not having an opinion (value 3) were excluded from the primary analyses, as done in other similar studies.[18,24,25] An additional choice variable was constructed reflecting the various combinations of choices women were interested in receiving (e.g. all three conditions, congential disease only, etc.).

Explanatory variables were divided into three domains: (1) sociodemographic; (2) obstetric and medical; and (3) psychological. The following variables were assessed for the corresponding domains: (1) sociodemographic domain: age (i.e. ≤ 29, 30–34, and ≥35), education (i.e. no academic degree, bachelor's, master's or doctoral) and religiosity (i.e. secular, traditional, orthodox, and ultraorthodox); 2) obstetric and medical domain: number of children, recurrent miscarriages (i.e. 3 or above (yes/no)), family history of medical or developmental problems in first degree relatives (yes/no), prenatal diagnosis performed in current pregnancy (yes/no), and self-assessment of the number of performed tests during their just completed pregnancy (i.e. similar, more than others, less than others, and don't know); and 3) psychological domain: level of concern about fetal health (i.e. not concerned, concerned, very concerned) and level of psychological distress (based on the K6 scale, responses to each of the six questions were coded between 0 and 4, with a sum of 0–24 to all questions and applying the standard categorization of the score into 3 levels (non-distress (score≤4), moderate distress (5–12), severe distress (score≥13)) or dichotomous (moderate or severe vs. low).

Women's level of agreement with 5 statements proposing possible reasons for or against disclosure of AO conditions in pregnancy was also explored: (1) expected to cause anxiety; (2) useful for the woman/her partner; (3) useful for preparing the child for future risks; (4) useless if non-treatable; and (5) allows to consider termination of pregnancy. A five-level Likert scale was used and dichotomized to reflect agreement versus no agreement.

The questionnaire was pre-tested on 16 women who gave birth within the last couple of years and revised accordingly, and then re-tested a month later to assess reliability. Kappa estimates for questions on self-assessment of number of tests performed during pregnancy, level of concern for fetus' health and reported willingness to receive genetic information about various types of genetic conditions were 0.88, 0.67 and 0.8, respectively.

2.4 | Statistical analysis

Univariable associations between each of the explanatory variables and the choice-related outcomes were tested using Chi square ($\chi 2$) test. Multivariable logistic regression models were carried-out to assess the independent associations of the socioeconomic, obstetric and medical, and psychological domains with each of the choice-related dependent variables. Using hierarchical modelling we first evaluated the contribution of each one of the domains. We began with a saturated model, which includes all variables from the three domains, and then continued by examining more condensed models by removing domains one after the other, starting with the psychological followed by the obstetric and medical and ending with the socioeconomic. This nested design allowed to compare each condensed model with the previous model by using a likelihood ratio test. Comparisons of this set of nested models demonstrated that all domains contributed significantly to at least one of the three outcomes examined (Appendix 1). Thus, for comparability, reported results from the multivariable regressions are based on the saturated models.

Since the K6 scale was added to the questionnaire approximately two months after the initiation of the study, there were 120 women for which these data were missing. Missing values were imputed using the mean K6 values by educational attainment and level of religious observance. Comparisons of the results of logistic regression models with or without imputed data yielded nearly identical estimates and standard errors, thus reported findings include the imputed K6 values. Analyses were carried out using SPSS 25.0. All tests were two-tailed with alpha level set at 0.05. Results are reported as odds ratios with 95% CIs and p values.

Ethical approval for this study was obtained from the medical ethics committees of Hadassah Medical Center (0377-15-HMO) and Rabin Medical Center (0808-16-RMC).

3 | RESULTS

The study sample included 941 post-partum women, aged 18–50 (mean = 30.8; SD = 5.6 years), who have completed the survey (77% response rate) (Table 1). Approximately half of the women reported having an academic degree (N = 478, 50.8%). More than half of the women were self-identified as religious orthodox (N = 261, 28.2%) or ultraorthodox (N = 267, 28.8%). The majority of women reported being concerned (42.0%) or very concerned (42.2%) about their fetus health during pregnancy and based on the K6 scale, moderate and severe distress was observed in 35.1% and 2.1% of the women, respectively.

3.1 | Women's attitudes to receiving genomic information in pregnancy

Women's responses clearly differed based on age at onset and actionability of the genetic conditions. As shown in Figure 1, more than two-thirds of the women (N = 670, 71.5%) agreed with

TABLE 1 Characteristics of the study population[a]

Domain	Characteristic	Category	N	%
Sociodemographic	Age (years)	<30	381	40.9
		30–34	297	31.9
		35+	253	27.2
	Religious affiliation	Secular	236	25.5
		Traditional	163	17.6
		Orthodox	261	28.2
		Ultraorthodox	267	28.8
	Academic degree	Without degree	463	49.2
		Bachelor's	337	35.8
		Master's and doctoral	141	15.0
Medical and obstetric	Number of children	1	246	26.1
		2	224	23.8
		3	199	21.1
		4	115	12.2
		5+	157	16.7
	Prenatal diagnosis (amniocentesis\CVS)	Performed	131	13.9
	Recurrent miscarriages (≥3)	Yes	43	4.6
	Positive family history[b]	Yes	109	11.8
	Number of performed tests during the last pregnancy compared to other women (self-assessment)	Similar	505	53.7
		Higher	214	22.7
		Lower	194	20.6
		Unknown	28	3.0
Psychological	Level of concern about fetal health	Not concerned	149	15.8
		Concerned	395	42.0
		Very concerned	397	42.2
	Psychological distress K6	Non-distressed (≤4)	591	62.8
		Moderate distressed (5–12)	330	35.1
		Severe distressed (≥13)	20	2.1

[a]The total number of women included in the analysis of nearly all characteristics was 941. The total for age, religiosity and positive family history was 931, 927 and 924, respectively, owing to missing data.

[b]Self-report of first degree relatives with congenital anomalies, neurodevelopmental disorders or autism spectrum disorder.

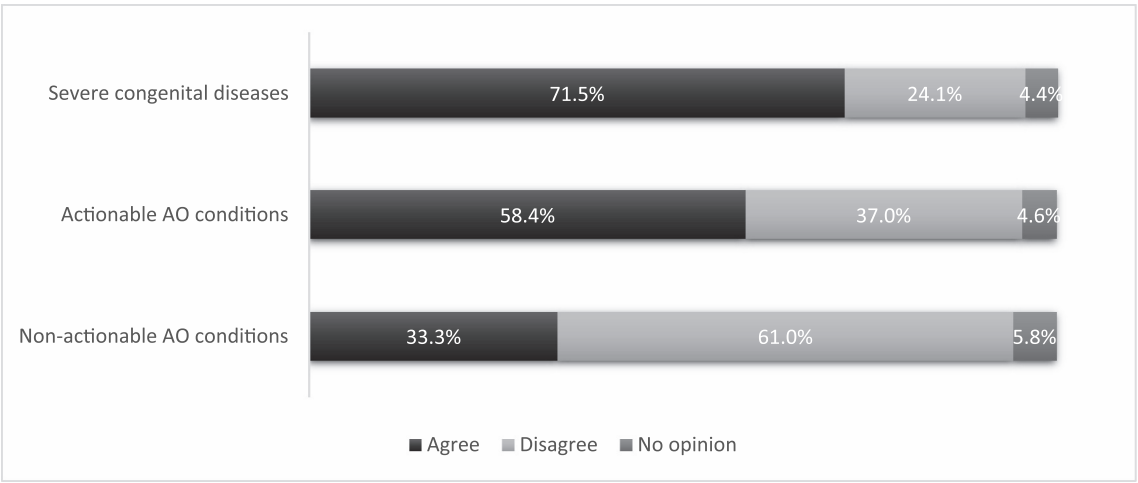

FIGURE 1 Women's agreement with disclosure of various types of genetic information in pregnancy. Level of agreement was measured using a five-level Likert scale. Values 1 and 2 were merged to reflect agreement, value 3 reflects no opinion, and values 4 and 5 were merged to reflect disagreement

disclosure of information on severe and lethal congenital diseases in their fetus, 58.4% (N = 546) were interested in information on actionable AO conditions and only 33.3% (N = 311) on non-actionable AO conditions. Examining the distribution of combination of choices (Table 2), we found that in approximately 50% of women, preferences were other than simply being interested in information on either all (29.1%) or none (19.2%) of the three types of genetic conditions, but rather 20.2% were interested in severe congenital diseases only and 19.6% were interested in severe congenital and actionable AO condition.

3.2 | Associations of women's characteristics with their attitudes towards receiving genomic information

3.2.1 | Sociodemographic domain

The univariable associations between each of the sociodemographic factors (i.e., age, level of religiosity and education) were significant for nearly all choice-related outcomes examined (Appendix 2). It is noteworthy that religiosity, and especially being ultraorthodox, demonstrated a strong impact on preferences, flipping the picture from the majority of women wishing to receive information on all three types of outcomes in secular and traditional women to the minority of women in the ultra-orthodox group (Figure 2). Interestingly, 44.1% of ultraorthodox women wished to receive information on actionable AO conditions compared to severe congenital disease (35.2%) or non-actionable AO conditions (9.3%). Next, we ran multivariable logistic regression adjusting simultaneously for all factors across domains (Table 3). Both level of religiosity and education showed significant independent associations with the agreement to receive information on the genetic conditions examined and these associations differed by the condition under investigation.

TABLE 2 Women's agreement with disclosure of genetic information on fetus by combinations of the three types of genetic conditions[a]

Condition combinations	Expressed agreement with disclosure	
	n	%
All three types of conditions	274	29.1
Severe congenital diseases only	190	20.2
Severe congenital and AO actionable conditions	184	19.6
None of the three types of conditions	181	19.2
AO actionable conditions only	75	8.0
Severe congenital and AO non-actionable conditions	22	2.3
AO actionable and AO non-actionable conditions	13	1.4
AO non-actionable conditions only	2	0.2
Total	941	100

[a]Genetic conditions include severe congenital diseases and actionable and non-actionable adult-onset (AO) conditions.

With regards to AO conditions, orthodox women differed significantly from secular women in that they had lower willingness to receive information only on non-actionable AO conditions (adjusted odds ratio (aOR) = 0.52, $p = 0.004$). Ultraorthodox women, compared to secular women, showed even stronger negative attitudes towards receiving information on actionable (aOR = 0.37, $p < 0.001$) and even more so towards non-actionable (aOR = 0.13, $p < 0.001$) AO conditions, but these effects were attenuated compared to their objection towards receiving information on congenital conditions in fetus (aOR = 0.03, $p < 0.001$). Educational

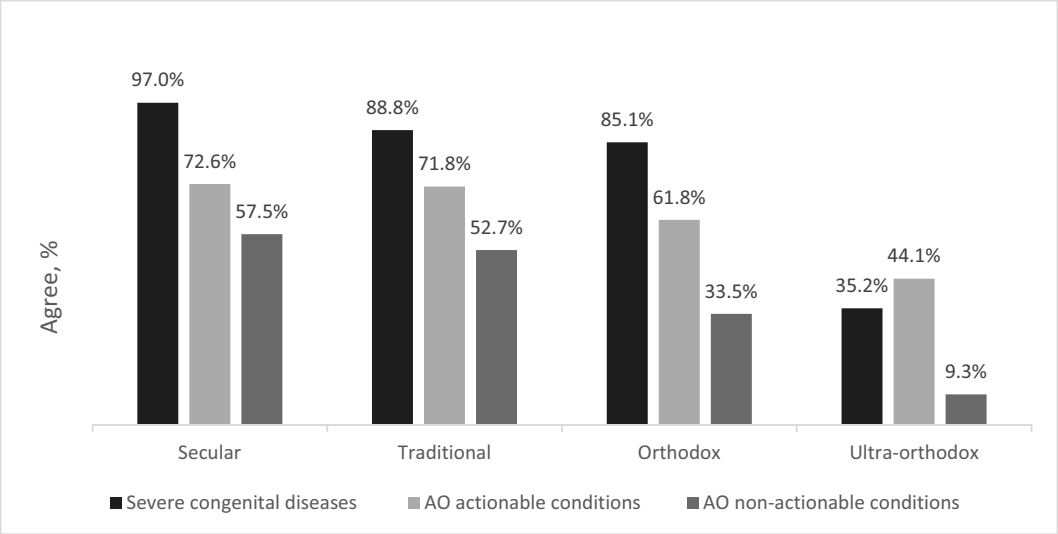

FIGURE 2 Women's agreement with disclosure of various type of genetic information in pregnancy, by level of religiosity. Percent agreement reflects proportion of women who responded one or two in the five-level Likert scale. Bars represent agreement with disclosure of severe congenital disease (dark grey) and adult-onset actionable (light grey) or non-actionable (grey) conditions within each of the four religiosity categories (secular, traditional, orthodox and ultraorthodox)

TABLE 3 Multivariable associations of sociodemographic and psychological characteristics with women's agreement with disclosure of genetic information on three types of genetic conditions in fetus[a]

		Actionable AO conditions			Non-actionable AO conditions			Severe congenital diseases		
Characteristic	**Category**	**aOR**	**95% CI**	***p***	**aOR**	**95% CI**	***p***	**aOR**	**95% CI**	***p***
Sociodemographic domain										
Age	<30	Ref.			Ref.			Ref.		
	30–34	0.98	0.65–1.49	0.939	1.35	0.88–2.09	0.17	0.75	0.42–1.33	0.33
	35+	0.95	0.58–1.53	0.821	1.41	0.84–2.35	0.191	0.65	0.33–1.27	0.21
Religious affiliation	Secular	Ref.			Ref.			Ref.		
	Traditional	1.22	0.74–1.99	0.438	1.02	0.64–1.63	0.922	0.35	0.14–0.89	**0.027**
	Orthodox	0.74	0.47–1.18	0.212	0.52	0.33–0.82	**0.004**	0.21	0.09–0.53	**0.001**
	Ultraorthodox	0.37	0.21–0.63	< **0.001**	0.13	0.07–0.24	< **0.001**	0.03	0.01–0.07	< **0.001**
Academic degree	Without degree	Ref.			Ref.			Ref.		
	Bachelor's	1.05	0.75–1.47	0.782	0.71	0.49–1.04	0.075	1.92	1.23–2.99	**0.004**
	Master's and doctoral	1.44	0.88–2.36	0.143	1.16	0.71–1.90	0.55	4.05	1.66–9.89	**0.002**
Psychological domain										
Level of concern about fetal health	Not concerned	Ref.			Ref.			Ref.		
	Concerned	1.59	1.04–2.42	**0.032**	1.66	0.99–2.77	0.052	1.14	0.65–1.99	0.654
	Very concerned	2.48	1.61–3.82	< **0.001**	2.07	1.24–3.45	**0.006**	1.84	1.03–3.29	**0.041**
Psychological distress K6	Non-distressed (≤4)	Ref.			Ref.			Ref.		
	Distressed (≥5)	0.70	0.52–0.96	**0.024**	0.87	0.62–1.20	0.387	0.71	0.46–1.08	0.111

Abbreviations: AO, adult-onset; aOR, adjusted odds ratio; CVS, Chorionic villus sampling; K6, Kessler Psychological Distress Scale; Ref, reference.

[a]Variables from the three domains (sociodemographic, obstetric and medical and psychological) were introduced together as covariates into the logistic regression models. Associations of covariates were assessed for each one of the three dependent variables separately, dichotomized to reflect agreement with disclosing information on actionable AO conditions, non-actionable AO conditions or severe congenital diseases versus disagreement.

level was only associated with willingness to receive genetic information on congenital conditions. Adjusted associations between age and examined outcomes were not significant (Table 3).

3.2.2 | Obstetric and medical domain

Although some of the obstetric and medical factors were significantly associated with AO conditions in the univariable analysis (Appendix 2), no significant associations were observed in the multivariable regression models (Appendix 3).

3.2.3 | Psychological domain

The level of concern about fetal health was a significant factor for willingness to receive genetic information about all types of genetic conditions in both the univariable analysis (Appendix 2) and multivariable logistic regressions (Table 3). Compared with women who were not concerned about fetal health, very concerned women were nearly twice as likely to support the disclosure of severe congenital diseases (aOR = 1.84, $p = 0.04$), as well as actionable (aOR = 2.48, $p < 0.001$) and non-actionable (aOR = 2.07, $p = 0.006$) AO conditions. A smaller, yet significant difference, was also identified between women who were concerned (but not very concerned) about their fetus, compared with those not concerned, towards the disclosure of AO actionable (aOR = 1.59, $p = 0.032$) and non-actionable (aOR = 1.66, $p = 0.052$) conditions. Interestingly, an opposite picture was seen for psychological distress. Compared with non-distressed women, women with moderate or severe distress (K6 score≥5) were in fact less likely to choose to receive information on actionable AO conditions (aOR = 0.7, $p = 0.024$) (Table 3). Similar trends were seen for the other genetic conditions, but the associations were non-significant.

3.3 | Arguments for/against disclosure of adult-onset conditions

Women were asked to rate their agreement with statements proposing reasons for or against disclosure of AO conditions. When asked about AO condition in general (i.e. without specifying whether the condition is actionable or not), the majority of the women ($N = 503$, 56.5%), expressed their agreement with the argument describing the availability to prepare a child in advance as an advantage of disclosing AO conditions. Additionally, 141 women (15.3%) responded that knowing that their child may develop an AO condition later in life is not expected to cause them any anxiety, 316 (34.0%) reported low to moderate anxiety and 464 (50.4%) reported high anxiety. When asked specifically about reasons for and against disclosure of either actionable or non-actionable conditions, women's level of agreement differed between those that supported disclosure of such findings in pregnancy and those who did not (Figure 3A and B). Women who were in favor of disclosure tended to more frequently agree with the importance of this information to themselves or their partner, compared to women who disagreed with disclosure: 90.5% ($N = 487$) and 61.6% ($N = 202$) for actionable conditions, and 80.3% ($N = 241$) and 31.6% ($N = 172$) for non-actionable conditions, respectively. Remarkably, the vast majority of both supporters and objectors of the disclosure of AO conditions in pregnancy would not consider termination of pregnancy because of an actionable AO condition: 94.6% ($N = 491$) and 98.5% ($N = 331$), respectively. With regards to non-actionable AO conditions, there was slightly higher support in considering termination, yet still only about 20% ($N = 55$) of women who supported disclosure would consider termination, compared with 2.2% ($N = 12$) of women who objected.

4 | DISCUSSION

This study demonstrates that women differentiate between nuanced types of genetic information and that most of them support the disclosure of actionable AO conditions. Three major independent predictors of interest in actionable AO diseases were identified: lower level of religiosity, greater concern for fetal health and less personal distress.

Previous studies showed significant negative associations between level of religiosity and uptake of various prenatal genetic tests.[26–29] A possible explanation is that religious women are less prepared to terminate their pregnancies in case of genetic abnormalities. Yet, most studies were conducted before the implementation of AGT, when genetic testing in pregnancy mainly identified risks for congenital/early-onset disorders. Interestingly, nearly 45% of the ultraorthodox women in our study showed interest in receiving information on actionable AO conditions. This may reflect the realization of the importance of such information for parents' and child's future health, irrespective of their stance towards pregnancy termination. This is further supported by the disinterest reported by the vast majority of ultraorthodox women (over 90%) in receiving non-actionable AO conditions.

With respect to psychological factors, some studies have demonstrated associations between higher levels of anxiety during pregnancy with choosing extended genetic information from prenatal CMA[30] and uptake of invasive prenatal diagnosis.[7,31,32] The fact that in our study psychologically distressed women, in contrast with those who are merely 'concerned', prefer to avoid information on actionable AO conditions, can be supported by work suggesting that anxiety is linked to risk-avoidant decision-making, possibly because it promotes psychological responses that help reduce vulnerability to threat or because it endorses pessimistic appraisals of future events.[33] Particularly in light of increased vulnerability to anxiety and depressive disorders during pregnancy,[34–37] it may be postulated that women who know that specific genetic information would likely have a negative impact on their psychological wellbeing will be less likely to request such knowledge. Millo et al. indeed showed that

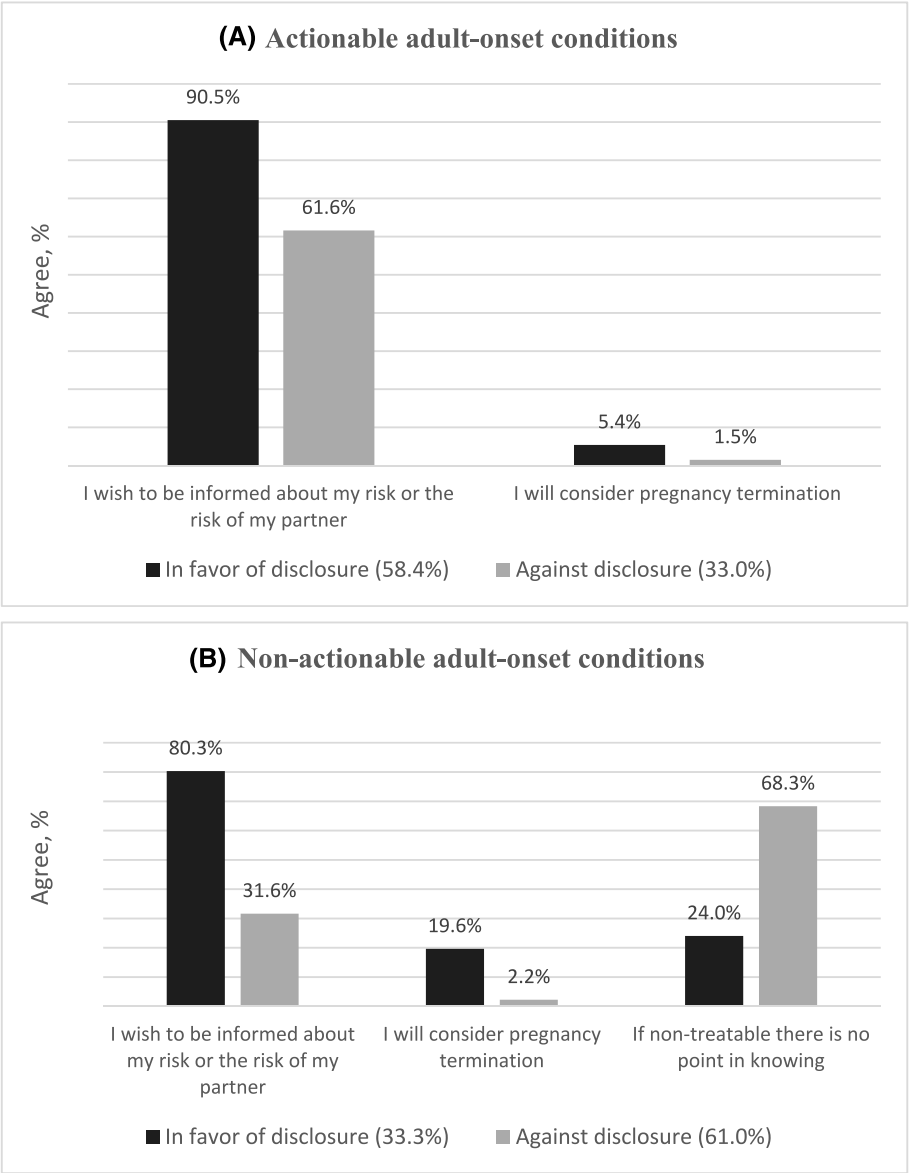

FIGURE 3 Women's agreement with statements in favor or against disclosure of genetic information about adult-onset conditions in pregnancy, by attitudes towards disclosure. Women's percent agreement with statements proposing reasons for or against disclosure of information about actionable (Panel A) or non-actionable (Panel B) adult-onset (AO) conditions. Responses were evaluated separately for supporters (dark grey bars) and objectors (light grey bars) of disclosure. Figures in parentheses correspond to the figures provided in Figure 1

women and their partners asked not to be informed of certain types of CMA findings that they perceived as anxiety-provoking.[21] Furthermore, although in a different setting, it has been demonstrated that high levels of distress may prevent women from opting for BRCA1/2 predictive testing,[38] lending support to the notion that distress may be associated with avoiding genetic knowledge.

None of the other factors examined in our study contributed substantially to women's attitudes towards disclosure of AO conditions in pregnancy, in-line with previous studies that did not identify other major contributors to women's interest in receiving extended information from prenatal CMA.[7,30] The lack of association with age in our study, that somewhat contradicts previous results,[30] may be explained by the strong associations between religiosity, education and other obstetric factors adjusted for in our multivariable models.

Women's responses to the arguments for/against disclosure of AO conditions indicate that there is little support in termination of pregnancy based on increased risks for AO conditions, in both supporters of disclosure and objectors. A similar observation was reported by Millo et al.[21]

The major strength of our work is the large sample of women who are likely representative of Israeli Hebrew-speaking postpartum women. Although the Israeli population has its unique characteristics, the sociodemographic, cultural and religious diversity of the women included in our study add to accumulated work focusing on underserved ethnic minority groups[39,40] and make the findings relevant to other countries, where culturally competent genetic counseling should also be considered.

In this study we chose to interview women just after pregnancy, rather than during it, to facilitate participant recruitment and data collection. Yet, the views of these women are highly relevant as they all recently faced decisions related to tests conducted in pregnancy. Moreover, they were potentially more open-minded to deliberate about AO conditions as they all gave birth to healthy newborns. Nevertheless, women's theoretical responses may not accurately

reflect their actual choices should such choices been made during pregnancy. Additionally, it is reasonable to assume that giving birth to a healthy baby may have immediate effects on mood or other aspects of psychological state, which were not measured in this study, and these may have affected mothers' responses. Notwithstanding, collecting data on actual choices of 1070 women showed that 74% of the women chose in favor of receiving genomic information on AO conditions in pregnancy. The higher support demonstrated in 'real-life' compared to theoretical choices might be explained by the somewhat different demographics of women actually opting for invasive prenatal testing. If genomic prenatal testing will become non-invasive,[41] a more diverse population may opt for testing, which may better resemble this study's population. Two other groups of women, not represented in this study, are women whose fetus had a problem of some kind, or women whose newborn were diagnosed with medical problems. We previously found that women who performed prenatal CMA based on abnormal ultrasound findings were less interested in findings not associated with the indication for testing, compared to women who underwent testing because of advanced maternal age or personal wish.[20]

To conclude, secondary findings, that is, risks for actionable conditions not related to the clinical indication for testing, some of which only manifest in adulthood, are a unique and new potential component of AGT. In the pediatric setting, the newborn/child's future autonomy to decide for herself if and when to be tested for AO conditions is highly emphasized.[42] Consequently, a shift has been made in the pediatric and adult populations from recommending mandatory disclosure of actionable secondary findings, to practicing either opt-in or opt-out policy.[43–45] In the prenatal setting, however, somewhat surprisingly, most guidelines either leave the disclosure decision open to lab/clinicians' discretion,[15,46] or support disclosure.[4,14,16] Although filtering out such information respects the future child's autonomy, it may prevent life-saving information from parents in cases where such findings are inherited.

Given the complexity of receiving results on AO conditions during pregnancy, which is undoubtedly not the primary goal of prenatal testing and may have substantial consequences on the immediate health of parents, clinicians have a major responsibility to discuss, prior to testing, the implications of such knowledge on the health of both the child and parents. To accommodate women's/parents' cultural background, beliefs and coping mechanisms, we strongly support pre-test parental choice with regards to information on actionable AO conditions, to allow personalized disclosure. Current and previous empirical data show that with adequate preparation, women/parents are able to understand complex and nuanced genetic information, and they widely support parental choice.[21,30] Prenatal parental choice concerning secondary findings is in-line with opt-in/out policy commonly practiced in advanced genomic testing done in children/adult.[43–45,47] In countries where full disclosure is practiced, we suggest that women's cultural background as well as anxiety levels should be addressed during pre-test counseling. If pre- and postnatal screening for maternal depression is practiced, as recommended by US national guidelines,[48,49] it could be useful to conduct the prenatal assessment shortly before pre-CMA genetic counselling. In countries where such assessments are not being conducted, genetic counselors' inquiry into women's depression and anxiety levels may be important. Any women who reported excess levels of depression and anxiety should be referred for follow-up with mental healthcare providers.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise, in the writing of this manuscript.

DATA AVAILABILITY STATEMENT

The database generated and analyzed during the current study are available from the corresponding author on request.

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