



Real-world family planning and pregnancy practices in women with homozygous familial hypercholesterolemia

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ABSTRACT

Background and aims: Homozygous familial hypercholesterolemia (HoFH) is characterized by extremely high plasma low-density lipoprotein cholesterol (LDL-C) levels and high premature atherosclerotic cardiovascular disease risk. During pregnancy LDL-C levels increase, while limited therapeutic options are available. This international study documented current approaches of healthcare professionals (HCPs) to family planning, pregnancy, and breastfeeding in HoFH.

Methods: An online HCP survey was distributed among the HoFH International Clinical Collaborators (HICC, NCT04815005). Responses were analyzed according to HCPs' gender, medical specialty, country income status, and world region.

Results: In total, 87 HCPs (39.1 % women) from 48 countries participated (64.4 % practicing in high-income countries). Most HCPs (79.3 %) always discuss family planning with patients with HoFH. Most (72.4 %) recommend contraception, with intrauterine devices (50.8 %) and oral contraceptives (49.2 %) being most commonly recommended. One in three HCPs would advise against pregnancy if ASCVD risks were deemed too high. Except for lipoprotein apheresis and colesevelam, most HCPs would recommend discontinuing LLT during the conception, pregnancy, and breastfeeding periods. However, approximately 30 % advise continuation or reinitiation of statins and/or ezetimibe during pregnancy and breastfeeding despite labelled restrictions on use during pregnancy and breastfeeding. Nearly half (48.3 %) of HCPs would recommend that women with HoFH shorten the breastfeeding period to resume LLT earlier, with HCPs from high-income countries significantly more likely to do so (51.8 % vs. 41.9 %; $p = 0.008$).

Conclusions: This study highlights significant variability in the management of HoFH in women of childbearing age, especially concerning LLT use during conception, pregnancy, and breastfeeding. The findings underscore the need for further research to establish global evidence-based guidelines tailored to individual needs, to improve cardiovascular risk management and reproductive health outcomes for women with HoFH worldwide.

1. Introduction

Homozygous familial hypercholesterolemia (HoFH) is a rare genetic disorder characterized by extremely elevated low-density lipoprotein cholesterol (LDL-C) levels from birth, leading to a significantly increased

risk of early-onset atherosclerotic cardiovascular disease (ASCVD) [1–3]. Clinical data show a median death age of 28 (17–45) years in both women and men with HoFH globally [4]. Recent advances in treatments, including novel lipid-lowering agents such as proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, and LDL-receptor

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independent drugs like microsomal triglyceride transfer protein (MTTP) and angiotensin-like protein 3 (ANGPTL3) inhibitors, are likely to improve life expectancy in HoFH patients [5–7]. However, the majority of patients with HoFH do not achieve guideline-recommended LDL-C goals, even when receiving combination lipid-lowering therapy (LLT) [8,9].

Pregnancy is a particularly challenging period for women with HoFH. Although LDL-C levels physiologically increase by 30–40 % in all women, the absolute increase is much greater in women with FH due to their significantly higher baseline LDL-C levels [10]. Combined with the limited therapeutic options which are deemed safe for both the mother and fetus, this poses a significant clinical challenge [1]. Following pregnancy, LLT options remain restricted during breastfeeding due to concerns regarding exposure of the infant to LLT via breastmilk [1,11].

Given that the lifetime cumulative LDL-C burden is directly related to ASCVD risk [12], these pregnancy-related periods of elevated LDL-C may adversely impact women with HoFH [13,14]. Recent sex-specific analyses in the largest global HoFH registry showed no differences in age of ASCVD onset between women and men with HoFH [8]. This contrasts with the general population, where women typically develop ASCVD 7–10 years later than men [15–18].

The 2023 EAS clinical guidance on HoFH recommends discussing family planning with patients. In addition, cardiovascular assessment prior to pregnancy is advised for women who wish to conceive [1]. The HoFH consensus paper also emphasizes the importance of a multidisciplinary approach to care before, during, and after pregnancy [1]. Currently, little is known about family planning advice and pregnancy care for women with HoFH globally. The primary objective of this study is to provide a comprehensive overview of how HCPs manage family planning, pregnancy, and breastfeeding in women with HoFH.

2. Methods

2.1. Participating centers and healthcare professionals

The HoFH International Clinical Collaborators (HICC, NCT04815005) is a global consortium of clinicians and researchers dedicated to the care of patients with HoFH [4]. This consortium enabled the inclusion of a diverse and representative sample of HCPs from various geographical and healthcare settings. HCPs directly involved in HoFH patient care were eligible to participate and identified through their affiliation with the HICC registry. In addition, HICC collaborators were asked to distribute the survey to colleagues outside of the HICC consortium who treat patients with HoFH. To be included, HCPs needed to have experience in treating HoFH patients, see these patients regularly, and be currently involved in the care of ≥ 1 patient(s) with HoFH. This study complied with the Declaration of Helsinki and was approved by the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Cape Town (329/2024).

2.2. Study design and data collection

The authors constructed an online survey on the management of women with HoFH during family planning, pregnancy and breastfeeding (Supplemental Methods). Potential participants received a survey link to collect data on the advice provided and factors potentially associated with practice differences, including HCP's self-reported gender, medical specialty, and healthcare system variables (Supplemental Methods). Additionally, this survey collected data on other aspects, including the registration, reimbursement, and availability of LLTs across countries. The open survey link was emailed on May 25, 2024, and disseminated at a HICC collaborators meeting on May 28, 2024. HCPs could choose to participate anonymously or to provide contact details at the survey start. Answers were captured using Cas-terEDC version 2024.2.4.1 between May 25 and August 20, 2024.

2.3. Survey outcomes

The study aimed to assess what information and advice HCPs provide regarding contraception, pregnancy, and breastfeeding. HCPs who indicated a specific LLT as unavailable or not used by them were grouped and categorized based on issues with registration status, reimbursement, or patient access to the LLT, which was reported earlier in the survey. Our survey asked about the use of statins, ezetimibe, PCSK9 monoclonal antibodies (alirocumab and evolocumab), PCSK9 small interfering RNA (siRNA) (inclisiran), MTTP inhibitor (lomitapide), ANGPTL3 inhibitor (evinacumab), bile acid sequestrant (colesevelam), ATP-citrate lyase (ACL) inhibitor (bempedoic acid), and lipoprotein apheresis in women who were either trying to conceive, pregnant or breastfeeding.

2.4. Data analysis

Data was stratified by HCP characteristics: self-reported gender, medical specialty, country income status, and world region. For the comparison between high-income and non-high-income regions of the world, countries were categorized according to the 2024 World Bank definition of income categories: high income, upper-middle income, lower-middle income, and low-income [19]. The upper-middle income, lower-middle income, and low-income countries were combined into a single "non-high-income" category. The countries were also grouped into continental regions according to the United Nations geoscheme [20].

2.5. Statistical analysis

Only data from HCPs who completed more than 95 % of the survey were included in the analyses. Continuous data are reported as mean (standard deviation) or as median [interquartile range], for normally and non-normally distributed data, respectively. Categorical data are presented as frequencies and percentages. Differences in categorical data between HCP characteristics were analyzed with a Chi-squared test or Fischer's exact test. All statistical analyses were performed using R, version 4.3.2 (R Foundation, Vienna, Austria). Statistical significance was set at 0.05 (2-sided).

3. Results

3.1. Demographic characteristics

In total, 87 HCPs from 48 countries (Fig. 1 and Supplemental Table 1) completed the survey (Table 1). Thirty-four (39.1 %) were women and 29 (33.3 %) were lipidologists, followed by cardiologists (26 (29.9 %)), internists (12 (13.8 %)), pediatricians (9 (10.3 %)), endocrinologists (5 (5.8 %)), and other specialties (6 (6.9 %)). Generally, HCPs treated a median of 6 [3–10] HoFH patients annually, with a median of 3 [2–6] female patients. Nearly two-thirds of the HCPs (56 (64.4 %)) were from high-income countries. Of the non-high-income countries, the majority were from upper or lower middle-income countries (54.8 % and 32.3 % respectively) (Supplemental Table 1). Five (5.8 %) HCPs practiced in Africa, 24 (27.6 %) in Asia, 41 (47.1 %) in Europe, 16 (18.4 %) in the Americas, and one (1.2 %) in Oceania (Supplemental Tables 2-3).

3.2. Family planning

Sixty-nine HCPs (79.3 %) always discuss family planning, 10 (11.5 %) address family planning only if the patient raises the topic, and 8 (9.2 %) never discuss family planning (Table 2). HCP responses were comparable across HCP characteristics (Supplemental Table 4).

Of the HCPs who discuss family planning with their patients, most ($n = 40$, 50.6 %) would discuss family planning-related aspects with both female and male patients and their partners. No significant differences

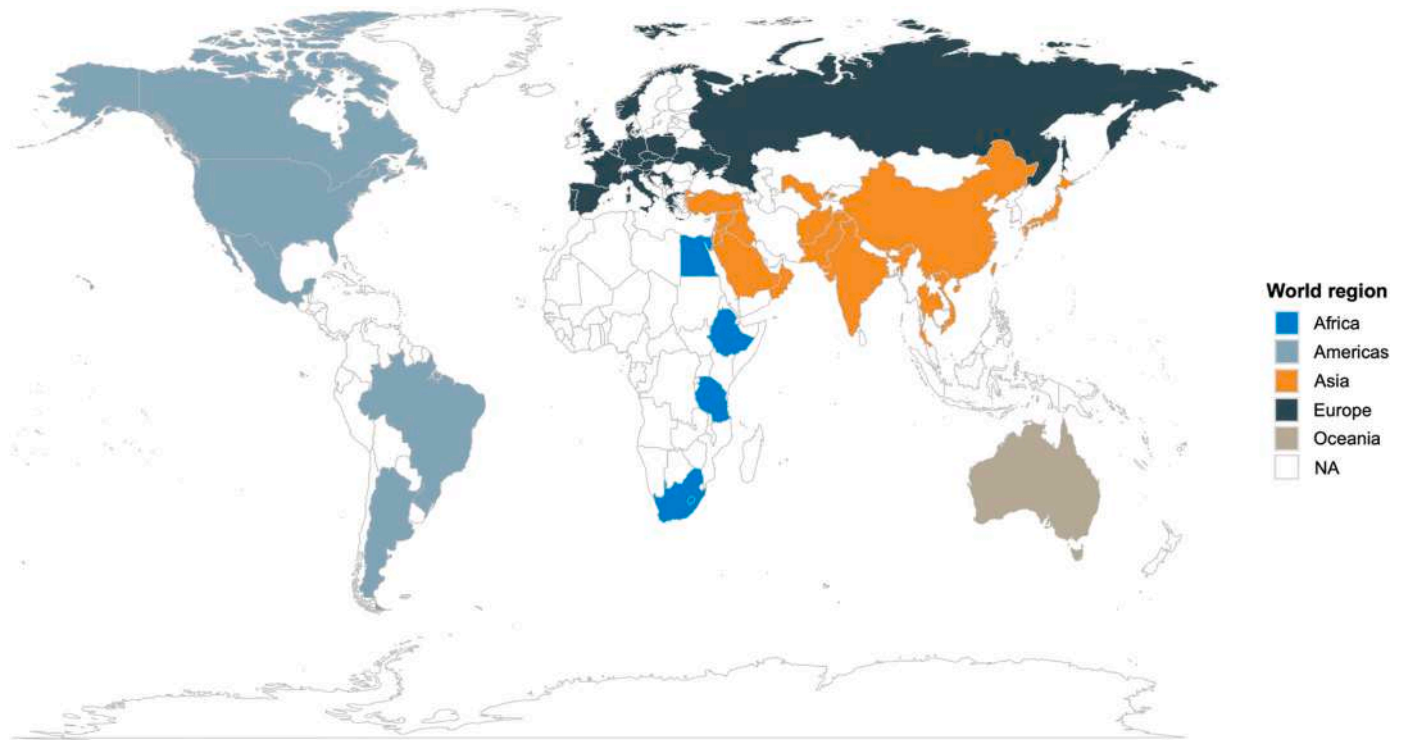


Fig. 1. Map of countries of the participating healthcare professionals
This figure illustrates the countries that participated in this survey, classified by world region.

Table 1
Characteristics of the participating healthcare professionals.

Characteristic	HCPs
Total number of HCPs	87
Total number of participating countries	48
Gender, women, N (%)	34 (39.1 %)
Demographic region, N (%)	
Africa	5 (5.8 %)
Asia	24 (27.6 %)
Europe	41 (47.1 %)
Americas	16 (18.4 %)
Oceania	1 (1.2 %)
Specialty, N (%)	
Cardiologist	26 (29.9 %)
Internist	12 (13.8 %)
Lipidologist	29 (33.3 %)
Pediatrician	9 (10.3 %)
Endocrinologist	5 (5.8 %)
Other ^a	6 (6.9 %)
Number of total annual HoFH patients, median [IQR]	6 [3–10]
Female patients	3 [2–6]
Male patients	3 [1–5]
Number of responders by country income status, N (%)	
High-income countries	56 (64.4 %)
Non-high-income countries	31 (35.6 %)

Values are N (%) and median [IQR]. HoFH, homozygous familial hypercholesterolemia; HCPs, Healthcare Professionals.

^a Other medical specialties were hematology, medical biochemistry, cardiometabolic medicine, translational medicine. Gender was self-reported by the healthcare professional.

were observed based on HCP characteristics (Supplemental Table 5). The majority (51.9 %) initiate the conversation in patients aged 18–25 years (Fig. 2A and Supplemental Table 6). Family planning was discussed significantly more frequently with patients <18 years in high-

Table 2
Overview of the main survey findings regarding recommendations on contraceptive methods, family planning conversations, pregnancy advice, and breastfeeding recommendations.

	HCPs
	N = 87
Recommend contraceptive methods in women	
Yes	63 (72.4 %)
Family planning conversations with patients	
Yes, always	69 (79.3 %)
Yes, if the topic is raised by the patient	10 (11.5 %)
No	8 (9.2 %)
Advice against pregnancy	
Would consider advising against pregnancy if risks are high	30 (34.5 %)
No	29 (33.3 %)
Would discuss risks and benefits of pregnancy	28 (32.2 %)
Delivery recommendations	
Depends on the individual female patient	31 (35.6 %)
Refer to maternal-fetal medicine specialist	31 (35.6 %)
No preferred method	11 (12.6 %)
Other	9 (10.3 %)
Patients prefer a scheduled C-section	5 (5.7 %)
Recommend shortening the breastfeeding period	
Yes	42 (48.3 %)
Depends on the individual female patient	24 (27.6 %)
No	13 (14.9 %)
Other	9 (10.3 %)

Values are N (%). HCPs, Healthcare Professionals.

income countries compared to non-high-income countries (42.3 % vs 18.5 %; $p = 0.046$), with significant differences by world region (Africa 0 %; Americas 46.7 %; Asia 10.5 %; Europe 43.6 %; Oceania 100 %; $p = 0.011$).

Family planning consultations were initiated for various reasons, including a patient reaching reproductive age (89.9 %), expressing a

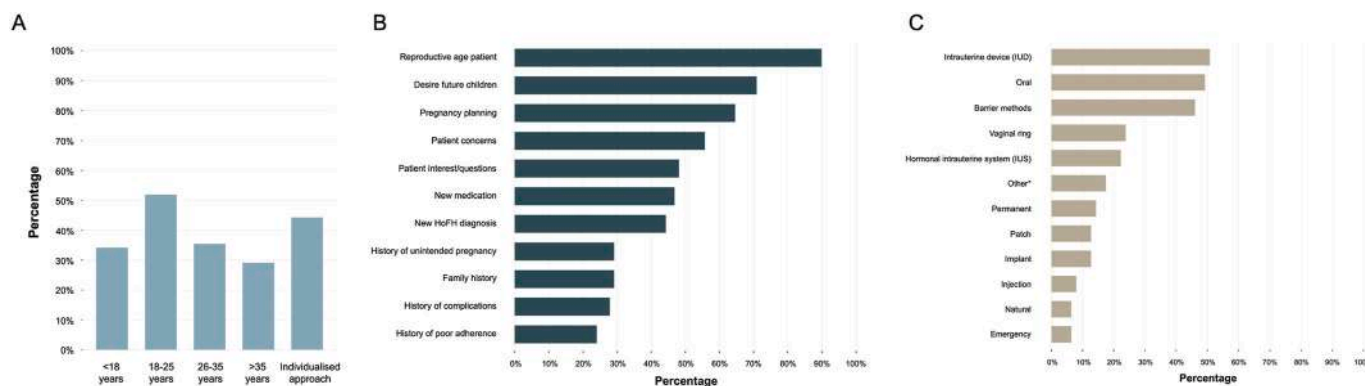


Fig. 2. (A) Age at which family planning conversation is initiated, (B) Prompts for family planning conversations, and (C) recommended types of contraceptives. This figure illustrates the ages at which healthcare providers initiate family planning conversations with patients with HoFH, the prompts for healthcare professionals to start a conversation about family planning with their patients with HoFH, and the types of contraceptives recommended by healthcare professionals for their patients with HoFH, arranged from most to least common. * includes: communication with/referral to gynecologist (7x) and/or depending on patient preferences (5x).

future desire to have children (70.9 %), actively planning a pregnancy (64.6 %), voicing concerns about the impact of HoFH on family planning decisions (55.7 %), asking questions about pregnancy-related risks and benefits (48.1 %), starting new medication (46.8 %), and receiving a new diagnosis of HoFH (44.3 %) (Fig. 2B and Supplemental Table 7). HCPs from high-income countries selected the initiation of new medication (57.7 % vs 25.9 %; $p = 0.009$), patient concerns (65.4 % vs 37.0 %; $p = 0.019$), and a patient's history of unintended pregnancies (38.5 % vs 11.1 %; $p = 0.017$) significantly more often as prompt compared to HCPs from non-high-income countries.

Main family planning-related topics that are addressed by HCPs include the hereditary risk of HoFH (98.7 %), medication use during pregnancy and breastfeeding (93.7 %), and ASCVD risks associated with pregnancy (87.3 %). Pregnancy-related ASCVD risks were significantly more often addressed by HCPs from non-high-income countries than those from high-income countries (100 % vs 80.8 %, $p = 0.013$) (Supplemental Table 8).

3.3. Recommendations on the use of contraceptives

The majority of HCPs 63 (72.4 %) provide contraceptive recommendations (Supplemental Table 9). Most commonly, HCPs discuss contraceptive strategies in women <18 years (33.3 %) and/or women 18–25 years old (29.9 %; Supplemental Table 10). The most recommended contraceptive methods were intrauterine devices (IUDs; 50.8 %), oral contraceptives (49.2 %), and barrier methods (46.0 %) (Fig. 2C and Supplemental Table 11). Female HCPs were significantly more likely than male HCPs to recommend barrier methods (63.0 % vs 33.3 %, $p = 0.024$) and the vaginal ring (37.0 % vs 13.9 %, $p = 0.041$) (Supplemental Table 11).

Over half (41 (65.1 %)) consider thrombotic risk before recommending systemic estrogen contraceptives, with no significant differences across HCP characteristics (Supplemental Table 12).

3.4. Recommendations regarding pregnancy and breastfeeding

Over a third of HCPs (30 (34.5 %)) would consider advising a woman with HoFH against pregnancy if the overall ASCVD risk, including the risk associated with LLT discontinuation, was deemed too high (Supplemental Tables 13–14). This was more often the case for male HCPs than female HCPs (41.5 % vs 23.5 %, $p = 0.021$), while female HCPs were more likely to discuss risks and benefits with the patient (50.0 % vs 20.8 %; $p = 0.021$).

Most HCPs (76 (87.3 %)) did or would consider performing additional diagnostic tests (e.g. cardiovascular imaging) to assess ASCVD risk before pregnancy planning and use this information for shared decision-

making. Cardiologists (69.2 %) and HCPs from Asia (70.8 %) and Europe (46.3 %) were more likely to perform additional diagnostic tests to assess ASCVD risk compared with other specialists ($p = 0.034$) and HCPs from other world regions ($p = 0.047$) (Supplemental Table 15). Seventy-six (87.3 %) HCPs discuss lipid testing of the partner with patients in the context of family planning, with 53 (60.9 %) HCPs discussing this routinely (Supplemental Table 16).

In women actively wishing to conceive, most HCPs recommend discontinuation of LLT, except for lipoprotein apheresis and colesevelam (Fig. 3). However, approximately one-third of HCPs recommend the continuation of statins (28.7 %) and ezetimibe (39.1 %) despite the contraindication to use these medications during pregnancy.

In pregnancy, similar LLT recommendations were observed, with most HCPs advising discontinuation of LLT (Supplemental Table 17). Interestingly, some HCPs would recommend restarting statins (20.6 %) and/or ezetimibe (16.1 %) at the start of the second or third trimester, and a smaller proportion would recommend continuing statins (9.2 %) and/or ezetimibe (13.8 %) throughout pregnancy (Supplemental Table 17).

Thirty-one (35.6 %) HCPs stated that the preferred delivery method depends on the individual patient and 31 (35.6 %) HCPs refer women with HoFH to a maternal-fetal medicine specialist for delivery planning.

Most HCPs advise women with HoFH to discontinue the majority of LLTs, except for lipoprotein apheresis or colesevelam when breastfeeding (Fig. 3). A substantial number of HCPs recommend the use of statins (29.9 %), ezetimibe (29.9 %), PCSK9 monoclonal antibodies (24.1 %), evinacumab (10.3 %), or PCSK9 siRNA (9.2 %) during breastfeeding contrary to the drug labels (Supplemental Table 17).

Approximately half (48.3 %) of HCPs recommend shortening the duration of the breastfeeding period to resume LLTs (Supplemental Table 19), which was more common in HCPs from high-income countries than those from non-high-income countries (51.8 % vs 41.9 %, $p = 0.008$).

4. Discussion

Our findings show that most HCPs discuss family planning and inform women with HoFH of the increased ASCVD risks of pregnancy. One in three HCPs consider advising against pregnancy if ASCVD risks are deemed too high for the individual patient. During conception, pregnancy, and breastfeeding, a substantial proportion of HCPs recommend continuation of LLT, including LLTs that are contraindicated during these periods. Almost half of the HCPs advise shortening the breastfeeding duration to resume LLT.

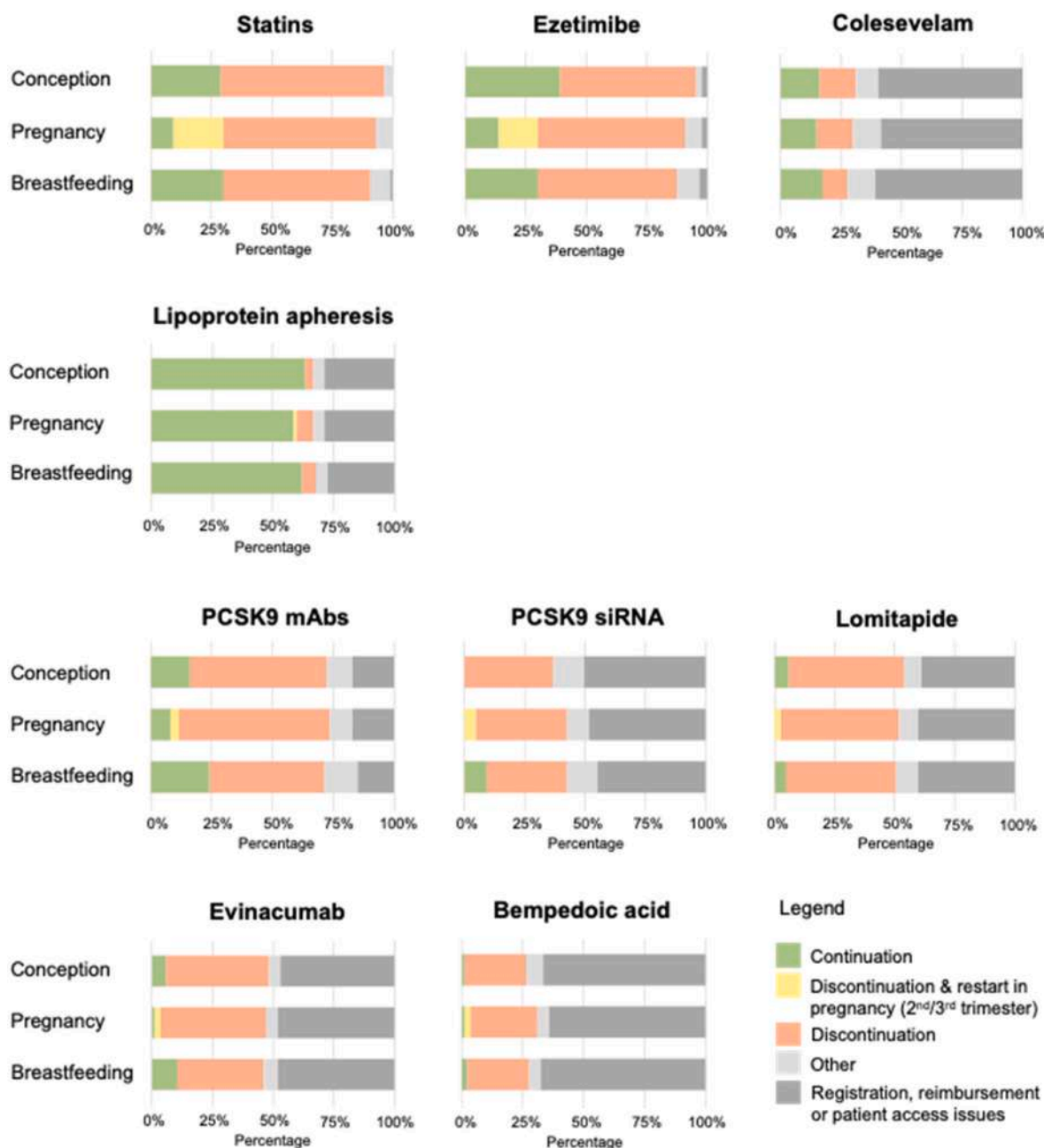


Fig. 3. Lipid-lowering treatments during conception, pregnancy, and breastfeeding in women with HoFH. This figure illustrates the recommendations for each lipid-lowering treatment by healthcare professionals for patients with HoFH during conception, pregnancy, and breastfeeding. PCSK9 mAbs = proprotein convertase subtilisin/kexin type 9 monoclonal antibodies; PCSK9 siRNA = proprotein convertase subtilisin/kexin type 9 small interfering RNA.

4.1. Pre-pregnancy counseling

The majority of HCPs (79.3 %) addressing family planning differs to findings from the general population and other conditions [21–24]. For example, a U.S. study in 107 young women aged 14–21 years with congenital heart disease found that reproductive topics, including pregnancy risks and possible transmission to the child, were discussed in only 21–46 % of women [22].

The 2023 EAS clinical guidance on HoFH recommends comprehensive cardiovascular evaluations before pregnancy, including echocardiographic assessments and, when feasible, CT coronary angiography to evaluate coronary artery disease [1]. Our findings show that the majority of HCPs consider or perform additional diagnostic tests (e.g. cardiovascular imaging) to assess ASCVD risk prior to planned pregnancy.

The higher proportion of HCPs in Asia (70.8 %) and Europe (46.3 %) who perform additional diagnostic tests compared to other regions, may reflect better access to diagnostic resources in these regions, enabling more comprehensive risk assessments to guide decision-making processes.

One third of HCPs (34.5 %) consider advising against pregnancy due to increased ASCVD risk heightened by LLT interruption. Several case reports and case series have shown that women with HoFH have a considerable risk of ASCVD during pregnancy - a period which is considered a physiological stress test for women. This may be particularly concerning for women with established ASCVD. Over the past decade, 6 cases of women with HoFH experiencing cardiovascular events or maternal death have been reported in the literature to our knowledge [25–28]. Besides the cases highlighting the potential

detrimental impact of HoFH during pregnancy, safe pregnancy outcomes for the mother have also been reported [27,29–33]. A retrospective review of 39 pregnancies in 20 women with HoFH revealed no cardiovascular complications or deaths during pregnancy and within the first year after delivery [29]. In 14 of these pregnancies, women used no LLT. Future research should investigate the longer-term prognostic impact of this period of elevated LDL-C levels on ASCVD outcomes in women with HoFH.

These findings reflect the delicate balance HCPs navigate between supporting reproductive autonomy and ensuring patient safety, underscoring the importance for women with HoFH and their partners to make informed reproductive decisions. This also illustrates why HoFH has a greater impact on family planning for women than men, consistent with a Dutch qualitative study in patients with HoFH, where approximately 50 % of patients expressed family planning concerns, with women being more affected than men [34].

Additionally, the observed gender disparity in counseling, with male HCPs more likely to advise against pregnancy, warrants further investigation to understand underlying differences in risk tolerance or counseling approaches between HCPs' genders.

4.2. Pregnancy

Given the extreme ASCVD risk in HoFH driven by cumulative LDL-C exposure, it is essential to reduce LDL-C levels as early and aggressively as possible. Pregnancy poses challenges for LLT management in women with HoFH, as the exclusion of pregnant women from clinical trials and consequently limited real-world data leaves a significant gap in data on the safety of many LLTs [35]. Consequently, the use of LLT during pregnancy and breastfeeding remains contraindicated based on the “do no harm” principle [3,13]. Regulatory frameworks like the FDA's Pregnancy and Lactation Labeling Rule (PLLR) and the ESC guidelines for cardiovascular disease management during pregnancy advocate for avoiding LLTs during pregnancy planning, pregnancy, and breastfeeding in general [36]. In 2021, the FDA removed its strongest warning against statin use during pregnancy, allowing for an individualized assessment of the benefits and risks of statin use for very high-risk women [37]. Because of the very high cardiovascular risk of women with HoFH, the 2023 EAS clinical guidance on HoFH recommends minimizing LDL-C burden by offering lipoprotein apheresis and colesvelam during pregnancy, and restarting statins and other LLTs from the second trimester onwards [1]. In the aforementioned case series describing 39 pregnancies of 20 women with HoFH, in 46.2 % of the pregnancies, women were using statins sometime during their pregnancy. There was no increase in adverse outcomes for babies who had been exposed to statins during pregnancy compared to those not exposed [29]. Similar findings have been reported in a limited number of cases of pregnant women with HoFH with some exposure to other contraindicated LLT (e.g. lomitapide and PCSK9 inhibitor) [30,31].

Our findings show that while some HCPs continue to recommend discontinuation of these treatments during conception, pregnancy, and breastfeeding, others recommend their continuation. This variability likely reflects the limited evidence and uncertainty surrounding the optimal management of women with HoFH and its potential impact on their offspring. Physicians may also be influenced by whether they can offer patients therapeutic options considered safe during pregnancy such as lipoprotein apheresis. Further research is essential to develop clear, evidence-based international guidelines to ensure consistent and optimal pregnancy care for women with HoFH worldwide.

4.3. Breastfeeding

Data on the safety of breastfeeding is limited, particularly regarding the transfer of lipid-lowering drugs into breast milk and their potential effects on the infant. Therefore, all lipid-lowering drugs are contraindicated during breastfeeding [38,39]. Although breastfeeding offers

metabolic benefits, such as lowering maternal LDL-C levels and reducing the risk of metabolic syndrome [40–42], this must be weighed against the need to resume LLTs postpartum and the potential adverse effects for the child [43].

In many non-high-income countries, refraining from breastfeeding may be unsafe due to limited access to high-quality formula milk, compounded by challenges related to hygiene and the risk of contamination. Additionally, cultural norms in certain regions may strongly promote breastfeeding, making it a difficult option for women to decide not to breastfeed. These factors must be considered when recommending breastfeeding practices in these countries.

We showed that approximately half (48.3 %) recommend shortening the breastfeeding period for women with HoFH. HCPs from high-income countries were significantly more likely to recommend a shorter breastfeeding period than those from non-high-income countries (51.8 % vs 41.9 %, $p = 0.008$). This variation may be explained by the urgency to resume LLTs, which are more readily available in high-income countries. On the other hand, in non-high-income countries, where access to these treatments is often limited, the perceived need to shorten breastfeeding may be less urgent and good alternatives for breast milk may be less available. These findings suggest that healthcare resources may play a role in shaping clinical recommendations.

4.4. Strengths and limitations

A strength of this study is that it is the first study focused on global practices in family planning, contraceptive counseling, and pregnancy management for women with HoFH. A limitation is that 87 HCPs from 48 countries were included and the findings might not be generalizable to non-participating countries. The survey findings may predominantly reflect practices from Europe, Asia, and the Americas, due to the underrepresentation of HCPs from Africa and Oceania. However, given the rarity and thus limited number of HCPs treating HoFH, the inclusion of 87 HCPs from 48 countries represents the largest global study to date. Especially since the inclusion criteria required HCPs to actively treat at least one patient with HoFH annually, providing valuable insights into current HoFH care. Also, the cross-sectional survey design does not allow for the assessment of changes in family planning and pregnancy practices over time, but it provides a contemporary baseline for understanding current practices and identifying areas for future research and guideline development.

Additionally, as with any survey-based study, we had to rely on self-reported data which introduces potential biases, including participation, response, recall, and social desirability biases. HCPs from all but one country from those participating in HICC completed the survey, which minimizes the risk of participation bias. In addition, HCPs from 6 non-HICC countries completed the survey. To address potential reporting biases, the survey was carefully designed with the option to participate anonymously to mitigate these biases and encourage honest responses. The HCPs' specialized expertise in HoFH plus professional responsibility likely contributed to more accurate and reflective responses, even in self-reported data. The survey's specific questions focused on current practices to minimize recall bias.

5. Conclusions

This study reveals significant worldwide variability in the management of reproductive health in women with HoFH. The differences between HCPs' characteristics and the limited data available in the literature underscore the urgent need for more research to come to clear evidence-based guidelines. Those should be tailored to the unique needs of women with HoFH, to improve cardiovascular risk management, reproductive health outcomes, and patient outcomes for all women with HoFH worldwide.

CRedit authorship contribution statement

Janneke W.C.M. Mulder: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Willemijn A.M. Schonck:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Tycho R. Tromp:** Conceptualization, Investigation, Methodology, Writing – review & editing. **M. Doortje Reijman:** Conceptualization, Investigation, Methodology, Writing – review & editing. **Laurens F. Reeskamp:** Conceptualization, Investigation, Methodology, Writing – review & editing. **G. Kees Hovingh:** Conceptualization, Investigation, Methodology, Writing – review & editing. **Dirk J. Blom:** Conceptualization, Formal analysis, Investigation, Methodology, Writing – review & editing. **Jeanine E. Roeters van Lennep:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – review & editing. All authors had full access to the data and had the final responsibility to submit for publication.

Data sharing statement

The full aggregated results of the survey can be obtained from the corresponding author upon reasonable request.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr Reeskamp is co-founder of Lipid Tools and reports lecture fees from Novartis, Ultragenyx, and Daiichi Sankyo. Dr Hovingh reports research grants from the Netherlands Organization for Scientific Research (vidi 016.156.445), CardioVascular Research Initiative, European Union and the Klinkerpad fonds, institutional research support from Aegerion, Amgen, AstraZeneca, Eli Lilly, Genzyme, Ionis, Kowa, Pfizer, Regeneron, Roche, Sanofi, and The Medicines Company; speaker's bureau and consulting fees from Amgen, Aegerion, Sanofi, and Regeneron until April 2019 (fees paid to the academic institution); GKH is part-time employment at Novo Nordisk and has stock in Novo Nordisk, Denmark. Dr Blom reports research grants from Amgen, Amryt, AstraZeneca, Sanofi, and Regeneron; lecture fees and personal fees from Amgen, Amryt, MSD, Sanofi-Aventis and Novartis; participation in advisory board for Amryt (Chair of the LOWER study steering committee); and being a member of the executive committee of the Lipid and Atherosclerosis Society of South Africa and the International Atherosclerosis Society. Dr Roeters van Lennep reports that a research grant from Novartis was received by the department. The other authors JM, WAMS, TT, and MDR do not have disclosures for this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.atherosclerosis.2025.119187>.

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