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The development and first results of a health-related outcomes set in familial hypercholesterolemia (FH) patients: Knowledge is health

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HIGHLIGHTS

- A health-related outcomes set has been developed for familial hypercholesterolemia (FH) patients.
- This set contained both outcomes defined by health care professionals as patient-related outcomes (PROMS).
- The response rate of the PROMS was 81.4%, implicating high acceptance.
- Sufficient knowledge of a patient was associated with better health-outcomes.

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ABSTRACT

Background and aims: Familial hypercholesterolemia (FH) is the most common hereditary lipid disorder requiring life-long treatment to prevent cardiovascular disease. A recent concept in healthcare is not only to focus on outcomes defined by healthcare professionals, but also take Patient-Reported Outcomes Measures (PROMs) into account. The aim of this study is (1) to describe the development and first results of a health-related outcomes set including PROMs for FH patients and (2) investigate the influence of patient knowledge on health-related outcomes.

Methods: A multidisciplinary group of FH experts, in collaboration with a sounding board of FH patients (n = 166), developed a health-related outcomes set containing the domains: medication adherence (MARS-5), smoking, self-efficacy and self-management, quality of life (QOL) (EQ-5D-5L), reported adverse drug reactions, lipid outcome measures, and FH and cardiovascular risk factor knowledge. Knowledge scores ranged from 0 to 10. Two groups were created: Insufficient knowledge (INSUF) (< 7.5), and Sufficient knowledge (SUF) (≥7.5).

Results: The response rate of the questionnaires was 81.4% (n = 429), implicating acceptance of PROMs. In general, FH patients showed good knowledge, high QOL and were adherent to medication. However, the INSUF group had higher triglycerides levels (1.0 *vs* 0.9, $p < 0.05$), lower QOL (0.89 [0.79, 1.00] *vs* 0.89 [0.85, 1.00], $p < 0.05$), were more often smokers (14% *vs* 7%, $p < 0.05$) and reported more adverse drug reactions (62% *vs.* 49%, $p < 0.05$).

Conclusions: A health-related outcomes set for FH patients, including PROMs, has been developed, which shows that insufficient knowledge of FH is negatively related to health outcomes. Improving patients' knowledge of FH may lead to better health.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in the world [1]. Its burden on society is still increasing in terms of costs and years of life lost [1,2]. The most common hereditary cause of early-onset CVD is familial hypercholesterolemia (FH) [3]. Recent evidence, e.g. from the Netherlands and Denmark, showed that FH is prevalent in approximately 1: 250 in the general population [4,5]. FH patients have elevated low-density lipoprotein cholesterol (LDL-C) levels from birth onwards due to a genetic defect influencing the LDL metabolism predominantly in the *LDLR*, *APOB*, or *PCSK9* gene [6,7]. Inheritance of the mutation generally occurs in an autosomal dominant pattern. Extensive

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years of untreated elevated LDL-C levels lead to an increased risk of accelerated atherosclerosis and premature CVDs [6,8]. Hence, starting treatment early on in life is critical. The main treatment of FH consists of the combination of a healthy lifestyle and lipid-lowering medication (e.g. statins, ezetimibe, or PCSK9 inhibitors). It is important not only to focus on clinical outcomes such as LDL-C levels, but also on health-related outcomes such as quality of life. As the majority of patients does not notice any physical symptoms, it is essential that FH patients understand why it is worthwhile to lower their LDL-C levels to optimize adherence [8–10]. Therefore, their understanding of FH as well as cardiovascular risk factors and how to maintain a healthy lifestyle is imperative. To evaluate the value of FH care, relevant health-related outcomes need to be identified and measured. This approach fits with the principle of value-based healthcare (VBHC), which defines value for the patient by outcomes that matter to the patient over the costs necessary to achieve these outcomes [11]. To our knowledge, currently no health-related outcome set, nor patient-reported outcome measurements (PROMs) have been defined for FH patients. Hence the aims of this study are (1) to develop a set of outcome measures including PROMs for FH patients as basis for a future VBHC framework (2) to analyse the influence of the FH patient's knowledge on the measures of the health-related outcome set.

2. Materials and methods

2.1. Objectives

The purpose of developing an outcome measurement set for FH patients is to identify outcomes that matter to them. To measure these outcomes systematically, adequate instruments need to be identified. Data can then be collected and used in clinical practice and for analysis to determine possible improvements. This could lead to more value for the patient.

2.2. Design and cohort definition

The present study has a descriptive design and complies with the Declaration of Helsinki. We submitted our protocol to the Medical Ethics Committee of Erasmus MC (METC) and received a waiver for METC evaluation (MEC20190555). The following inclusion criteria for participation were defined: (1) FH patients with a confirmed heterozygous pathogenic mutation in the *LDLR, APOB* or *PCSK9* gene and (2) above the age of 18 years. Homozygous FH patients, having a more severe disease and different treatment modalities, were excluded. Clinically diagnosed FH patients with a score of ≥6 based on the Dutch Lipid Clinic Network [12] without a pathogenic mutation in the aforementioned genes were also excluded.

2.3. Working group

At Erasmus University Medical Center (Erasmus MC), Rotterdam, the Netherlands, a working group of FH experts was established consisting of: an internist vascular medicine specialized in lipid disorders, nurse practitioner, 2 specialized FH nurses, and an FH patient representing the Dutch national FH patient support group “Harteraad”. The VBHC expert team of Erasmus MC, including a health psychologist, guided the working group through an institutional, standardized process [13].

2.4. Development of the outcome set

The development of FH specific patient outcome measures was structured according the blueprint previously described [13]. The working group convened for 5 sessions between November 2015 and March 2016. After discussing the FH patient journey in detail, possible outcomes were brainstormed, taking into account pre-existing knowledge and personal expertise, guidelines from literature, and dimensions of the disease such as the effect on the patient's direct environment and (in)visible burdens of FH. Also, possible relevant initial patient conditions were discussed for risk stratification. Having identified potential outcomes and patient conditions, group members individually scored and ranked them on a scale from 0 to 5 (with 5 being most important).

Outcomes were scored on (1) relevance, (2) impact on patient, and (3) frequency. For initial patient conditions, relevance for risk adjustment and frequency were scored. Also, an online survey was sent out to patients (N = 372) between the 24th of December, 2015 and 5th of January, 2016 with questions regarding the same possible outcomes to get the patients’ opinions on what matters to them. This resulted in 166 (44,6%) responses. Results of the survey were discussed in the working group in relation to the prioritized outcomes. After reaching consensus on both the outcomes and initial patient conditions, possible measuring instruments were discussed and agreed upon. In March 2017, the standard set was implemented in the FH clinic at Erasmus MC. FH patients received a link by email containing the FH outcomes questionnaires. If the questionnaires were not completed, they were re-sent twice. The healthcare professional discussed the answers of the questionnaires with the patients during the out-patient clinic visit and used this to customize the recommendations and treatment plan of the patients.

2.5. FH patient outcome measures

The final FH patient outcome set contains the following domains: medication adherence, smoking, self-efficacy and self-management, quality of life, FH and cardiovascular risk factor knowledge, reported adverse drug reactions and lipid outcome measures (Fig. 1).

2.5.1. Medication adherence

The Medication Adherence Report Scale (MARS-5) was selected for medication adherence. The MARS-5 questionnaire has been employed before in FH research and validity as well as reliability of MARS-5 has

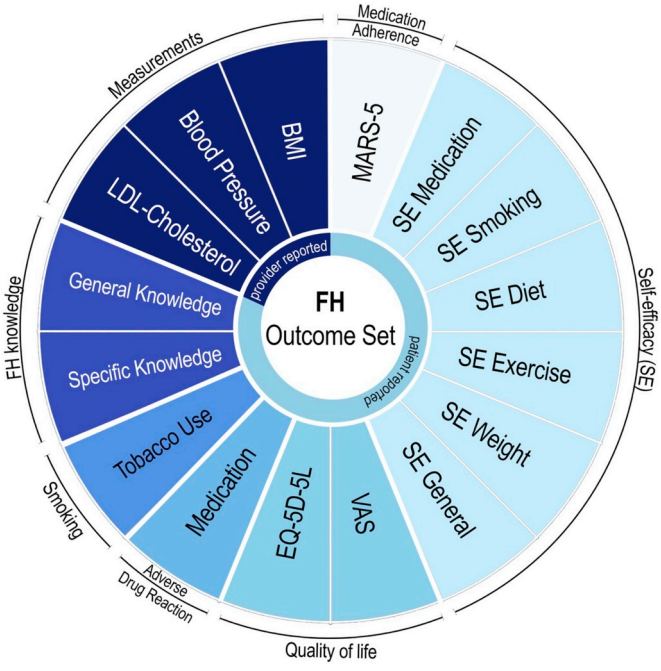

Fig. 1. Health-related outcome set for patients with familial hypercholesterolemia.
FH: Familial hypercholesterolemia, SE: self-efficacy, VAS: Visual Analogue Scale, EQ-5D-5L: EuroQol 5D with 5-point Likert scale, BMI: Body Mass Index.

been found acceptable [14,15]. MARS-5 contains questions about e.g. forgetting medication, changing dosage of the medication, and decision to disregard an intake.

2.5.2. Smoking

Regarding smoking, the clinical building block tobacco use questionnaire was used, which was developed by the Dutch Centre of expertise for eHealth [16]. Besides being a case-mix variable, smoking was selected as an outcome parameter, since smoking prevention and guidance in smoking cessation is regarded as part of FH care [17].

2.5.3. Self-efficacy and self-management

The self-efficacy questionnaire covers aspects such as motivation and self-management regarding medication, smoking, diet, exercise, weight, and overall general self-management. A pre-existing validated self-efficacy questionnaire was not available for FH patients. The questionnaire used in the current outcome set is based on the self-efficacy questionnaire implemented in the research by Sol et al. [18] investigating self-efficacy in vascular patients, which was derived from the Diabetes Management Self-Efficacy Scale (DMSES) for diabetic patients, and was revised for FH patients, including motivation questions.

2.5.4. Quality of life (EQ5D)

The EuroQol 5D (EQ5D) measurement, which is widely used in cardiovascular research [19], was selected to measure QOL along with the visual analogue scale (VAS). The 5-point Likert scale was preferred above the 3-point version since it has better discriminatory power [20]. Validity and reliability of this measurement has proven to be high in the cardiovascular field [19].

2.5.5. Knowledge survey FH

The working group developed questions for the knowledge survey on FH. This survey contains questions regarding various cardiovascular risk factors important for FH patients. In total, patients are asked 10 questions concerning knowledge about the cause and inheritance pattern of FH, meaning and interpretation of lipid levels, medication use, body mass index (BMI), blood pressure, and exercise. Patients could score full or half points, resulting in an end score between 0 and 10 points in total.

2.5.6. Reported adverse drug reactions

Reported adverse drug reactions of medication were determined per patient by questioning whether patients experienced physical or mental symptoms which they attributed to the use of medication.

2.5.7. Other relevant outcomes

Other relevant outcomes included are measurements such as LDL-C and ApoB concentrations as well as BMI and blood pressure, which were assessed during routine check-up.

2.5.8. Initial patient conditions

Important initial patient conditions (IPCs) for defining the case mix were: sex, age, date of FH diagnosis, starting date lipid-lowering treatment, socioeconomic status (SES), untreated LDL-C levels, self-reported adverse drug reactions, BMI, DNA-mutation, diabetes, hypertension, status CVD, smoking, and family history of premature CVD. For on-going patient conditions (OPCs) the following variables are updated every year after IPC (t_0): LDL-C level, adverse drug reactions, BMI, diabetes, hypertension, CVD, and family history of premature CVD. SES scores based on postal codes for 2017 are available online and are provided by the Netherlands Institute for Social Research [21]. SES scores are calculated per neighbourhood using: mean annual income per household, percentage of persons with a low income, percentage of lower-educated people, and the percentage of unemployed people in a neighbourhood. Average SES score in the Netherlands is 0 with a standard deviation (SD) of 1.

2.6. Statistical analyses

All analyses were performed in SPSS version 24 for Windows. Baseline characteristics of the respondents were compared to the non-respondents as well as for the different knowledge groups. Because all data distributions were abnormal, analyses were done using Mann-Whitney and Chi-squared tests. Results were therefore mentioned in terms of medians with interquartile ranges [IQR] or in the case of categories in numbers and percentages. Statistical significance threshold was set at $p < 0.05$. Looking at the distribution of the knowledge scores, knowledge was deemed sufficient at the median knowledge score of ≥7.5. Consequently, patients with a score of ≥7.5 were placed in the sufficient knowledge group and patients with a score < 7.5 in the insufficient knowledge group. Further sub-analyses were performed using aforementioned statistical tests or Spearman's rho correlation.

3. Results

3.1. Study population

Between March 2017 and early October 2018, 540 FH patients received the questionnaires of which 13 did not meet the inclusion criteria and were excluded (Fig. 2). Of the 527 eligible patients, 429 filled in the questionnaire, resulting in a response rate of 81.4%. Supplemental Table 1 shows the baseline characteristics of responders and non-responders (Appendix A). Respondents were significantly older than the non-responders (49 years *vs.* 41 years, $p = 0.001$), had higher SES scores (0.2894 *vs* 0.1164, $p = 0.036$), and had higher HDL-C and lower LDL-C and ApoB levels.

Median age of respondents was 49 years [35, 59] and 48% were male. Median SES score was 0.2894 [-0.3228, 0.9151], which is slightly above the Dutch average. Baseline characteristics were compared for the different knowledge groups (Table 1). The sufficient knowledge group (SUF) had a significantly lower median age compared to the insufficient knowledge group (INSUF) (51 *vs* 48 years, $p = 0.022$). In general, no significant differences were found between the groups regarding medication use.

A closer look at the results of the knowledge questionnaire showed that all respondents scored best on questions about FH specifically (Appendix B). With 97.2% of the patients knowing what the cause is of FH (question 7) and 91.6% knowing about FH's heritability (question 1). Respondents scored worst on questions 3 and 5, which concerned

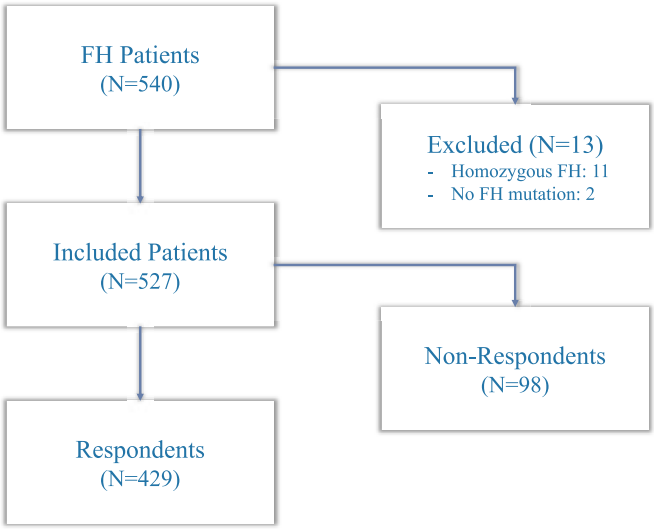

Fig. 2. Flowchart of inclusion process of the study.
FH: familial hypercholesterolemia.

Table 1
Baseline characteristics of familial hypercholesterolemia patients per knowledge group.

	Respondents	Insufficient knowledge (n = 184)	Sufficient knowledge (n = 245)	*p*-value[a]
Male, n (%)	**206 (48.0)**	**94 (51.1)**	**112 (45.7)**	**0.27**
Age (years), median [IQR]	**49 [35, 59]**	**51 [37, 63]**	**48 [35, 57]**	**0.022***[b]
SES, median [IQR]	0.2894 [-0.3228, 0.9151]	0.3249 [-0.4083, 0.9009]	0.2609 [-0.3230, 0.9187]	0.71[b]
Current smoking, n (%)	42 (9.8)	25 (13,6)	17 (6.9)	0.022*
Diabetes mellitus II, n (%)	17 (4.0)	8 (4.3)	9 (3.7)	0.072
Hypertension, n (%)	65 (15.2)	31 (16.8)	34 (13.9)	0.39
CVD, n (%)	79 (18.5)	38 (20.7)	41 (16.8)	0.31
CVD in family members, n (%)	226 (56.1)	104 (60.8)	122 (52.6)	0.10
Years of statin use, median [IQR]	7 [4.5, 10]	7 [4, 10]	7 [5, 10]	0.34[b]
On lipid-lowering medication, n (%)	418 (97.4)	97.8%	97.1%	0.65
Atorvastatin	132 (30.8)	57 (31.0)	75 (30.6)	0.87
Rosuvastatin	216 (50.3)	93 (50.5)	123 (50.2)	0.38
Simvastatin	31 (7.2)	14 (7.6)	17 (6.9)	0.80
Pravastatin	5 (1.2)	4 (2.2)	1 (0.4)	0.25
Fluvastatin	2 (0.5)	2 (1.1)	0 (0.0)	0.10
Ezetimibe	320 (74.6)	135 (73.4)	185 (75.5)	0.61
Alirocumab	51 (11.9)	26 (14.1)	25 (10.2)	0.05
Evolocumab	51 (11.9)	24 (13.0)	27 (11.0)	0.52
Lab, median [IQR]				
Tot-C	4.30 [3.80, 5.00]	4.4 [3.8, 5.2]	4.3 [3.7, 4.8]	0.24[b]
HDL	1.37 [1.13, 1.60]	1.36 [1.09,1.63]	1.39 [1.14, 1.59]	0.33[b]
ApoB	0.91 [0.77, 1.08]	0.92 [0.78, 1.14]	0.90 [0.77, 1.06]	0.20[b]
TG	0.95 [0.73, 1.30]	1.00 [0.77, 1.46]	0.90 [0.70, 1.24]	0.003*[b]

Socioeconomic status (SES): Mean (SD) Dutch population is 0 (−1,1).
CVD: cardiovascular disease; Lah: laboratorium serum levels of; Tot-C: total cholesterol, HDL: HDL-cholesterol, ApoB: apolipoprotein B, TG: triglycerides.
* Significant ($p < 0.05$).
[a] Chi-squared test was used for all variables unless indicated otherwise (b).
[b] Mann-Whitney test was performed.

knowledge about “bad” cholesterol measures and frequency of forgetting medication respectively.

Comparing the outcomes, several domains differed significantly between the SUF and INSUF. BMI was significantly lower in the SUF compared to the INSUF (25.28 kg/m^2 *vs.* 26.33 kg/m^2, $p = 0.022$). For all three domains of self-management (diet, exercise and weight) the SUF had lower, thus better, scores (Table 2). Regarding lipid levels, only triglycerides were lower in the SUF (0.90 mmol/L *vs.* 1.00 mmol/L, $p = 0.003$). In the INSUF significantly more patients reported to have experienced adverse drug reactions from statins in comparison with the SUF (62.3% *vs* 48.8%, $p = 0.005$) and were more often smokers (13.6% *vs.* 6.9%, $p = 0.022$). QOL represented by the EQ-5D-5L index score, was higher in the SUF than in the INSUF (0.8872 [0.7877,1.000] *vs.* 0.8872 [0.8499, 1.0000], $p = 0.048$).

A sub-analysis for the EQ-5D subdomains showed that mobility was good in 88% of the SUF *versus* 74% of the INSUF (1.0 [1.0–1.0] *vs* 1.0 [1.0–2.0], $p = 0.002$).

A correlation analysis indicated a moderate strength of association between general self-efficacy with self-efficacy regarding medication use, smoking habits, healthy food intake, exercise, and healthy weight (respectively: 0.333, 0.413, 0.398, 0.381, 0.452; $p = 0.000$ for all correlations). Besides, significant associations were found between whether the patient's BMI < 25 kg/m^2 and self-efficacy of weight (0.444, $p < 0.001$) as well as between whether the patient smoked and self-efficacy of smoking (0.678, $p < 0.001$).

4. Discussion

This is the first study to identify and describe the development of a health-related outcome set for FH patients according to a predefined method involving both health-care professionals as patients. The result was a health-related outcome set containing the domains: medication adherence, smoking, self-efficacy and self-management, quality of life, reported adverse drug reactions and lipid outcome measures, and FH and cardiovascular risk factor knowledge. The acceptance of this outcome set was high with a response rate of 81%. Moreover, we showed that a patients’ knowledge on FH and cardiovascular risk factors is associated with better health outcomes.

4.1. Health-related outcome set

The importance of VBHC is that health-related outcome sets are being developed to measure all outcomes relevant for the patient. The data of these outcome sets not only give insights in the current care delivered, but also will lead to improvements for the future, and more personalized care. In this study, all relevant outcomes for FH patients were developed by a multidisciplinary team including patients. Patient behaviours such as adherence and smoking were designated by both the multidisciplinary team and the sounding board of FH patients as health-related outcomes. These factors are of great importance as they have an adverse effect on their current health situation. FH healthcare professionals could then use the patient's outcome scores to customize recommendations and treatment. The scores can be used to compare the scores within one patient over the years, or to compare between patients in one or even multiple centres. A study in Finnish statin users found that a 10% increase in statin use was associated with a 5% decrease of the risk of coronary heart disease mortality [22]. In the Danish population, people with definite or probable FH had a higher odds ratio of developing coronary artery disease when they are not receiving lipid-lowering medication in comparison to when they are on lipid-lowering medication [23]. Moreover, recently we showed that in FH patients using maximum statin therapy the risk of CVD was in particular related to smoking underlying the importance of smoking as CVD risk factor in FH patients [24].

Systematic (inter)national implementation of the FH outcome set will also stimulate benchmarking. All in all, having a clearly defined outcome set for FH could help healthcare professionals in taking better care of FH patients.

Table 2
Outcome scores of familial hypercholesterolemia patients per knowledge group.

	Insufficient knowledge (n = 184)	Sufficient knowledge (n = 245)	*p*-value[b]
Medication adherence, median [IQR]			
MARS-5 value	24.0 [23, 25]	24.0 [23, 25]	0.34
Self-efficacy, median [IQR]			
Medication	1.00 [1.00, 1.50]	1.00 [1.00, 1.50]	0.94
Smoking	1.50 [1.00, 2.50]	1.50 [1.00, 2.00]	0.15
Diet	1.67 [1.33, 2.33]	1.67 [1.00, 2.00]	0.011*
Exercise	1.33 [1.00, 2.00]	1.00 [1.00, 1.67]	< 0.001*
Weight	1.67 [1.00, 2.33]	1.33 [1.00, 2.00]	0.018*
General	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	0.32
Quality of Life, median [IQR]			
EQ5D Index value	0.8872 [0.7877, 1.0000]	0.8872 [0.8499, 1.0000]	0.048*
VAS value	80 [70, 90]	81 [74, 90]	0.44
Adverse drug reactions, n (%)			
Side-effects lipid-lowering medication	114 (62.3)	119 (48.8)	0.005*[a]
Smoking, n (%)			
Current smoker	25 (13.6)	17 (6.9)	0.022*[a]
FH Knowledge, median [IQR]			
Overall knowledge	6.5 [5.5, 7.0]	8.0 [7.5, 8.5]	< 0.001*
FH specific knowledge	6.7 [5.8, 7.5]	8.3 [7.5, 9.2]	< 0.001*
General knowledge	5.0 [5.0, 7.5]	7.5 [5.0, 7.5]	< 0.001*
Measurements, median [IQR]			
Lab			
LDL-cholesterol	2.75 [2.31, 3.52]	2.69 [2.21, 3.32]	0.29
Blood pressure (mmHg)			
Systolic pressure	126 [115, 135]	127 [117, 136]	0.51
Diastolic pressure	78 [70, 84]	76 [70, 82]	0.84
BMI (kg/m^2) [IQR]			
BMI	26.33 [23.51, 29.34]	25.28 [22.81, 22.78]	0.022*

MARS-5: Medication Adherence Report Scale.
Self-efficacy: scale from 1 to 5, 1 being the best result.
EQ-5D-5L index-value: EuroQol 5D: scale from -0.028 to 1.
Visual Analogue Scale (VAS): from 0 to 100.
FH knowledge: scale from 0 to 10.
BMI: Body Mass Index.
* Significant ($p < 0.05$).
[a] Chi-squared test was used.
[b] Mann-Whitney test was performed unless stated otherwise ([a]).

4.2. Importance of knowledge

In previous studies it was concluded that the knowledge of FH in health care professionals was suboptimal [25–28]. A study in Saudi-Arabia found that 67% of healthcare professionals was not aware of FH heritability and that also other knowledge aspects, such as LDL-C target levels, were lacking [25]. Another study with data from ten countries in the Asia-Pacific, also found several areas of knowledge to be insufficient, in particular recognition of FH's heritability differed per country with lowest percentage being 26% till highest 61% [26]. To be able to educate FH patients and their families it is essential that healthcare professionals have basic knowledge on the subject.

Previous research showed that patient activation, including a patient's disease knowledge, is associated with better outcomes [29]. In studies with CVD patients, patient education led to better self-care behaviours [30,31]. As FH is a predominantly autosomal dominant condition, patients' knowledge that the risk of having FH is 50% in first degree family members is important to mobilize family members to attend an FH clinic to be tested on FH. In our study, almost all patients (91.6%) were aware of the inheritance pattern which is higher than in the previously mentioned studies on knowledge in health-care professionals. The high awareness in our patients is likely because our clinic is a specialized FH clinic and patient education is one of our priorities. This underlies the importance of FH patients attending specialized FH clinics.

4.3. FH patients vs general populations

The mean VAS score for QOL in the Dutch population is 80.6 and the EQ-5D index value 0.869 for the 5L version [32]. The median scores in the FH respondent population are respectively 80 and 0.8872, indicating that the QOL of FH patients in our clinic seems to not be negatively affected. The same applies for the measured self-efficacy, which are all between the highest score, being 1 and 2. We found that the EQ-5D index level was significantly lower in the INSUF group compared to the SUF group (0.8872 [0.7877, 0.1.000] *vs* 0.8872 [0.8499, 1.0000], $p = 0.048$). The mean EQ-5D index value of the INSUF group (0.8497) is much lower than the median and below the Dutch population average, indicating potential room for improvement. Compared to the Dutch population BMI, overweight and obese percentages were slightly higher in our patients (42.1% and 16.3%) compared to the Dutch population age 40–50 years (38.5% and 14.9%)

[33]. On the other hand, the percentage smokers in our study population was much lower than in the general Dutch population ≥18 years (9.8% *vs* 23.1%) [33]. In our clinic, education about smoking prevention and cessation is explicitly part of the care provided to FH patients. These results indicate that this active approach is effective.

As most of FH patients are asymptomatic it is a challenge to optimize preventive treatment and it essential that the individual patient sees the necessity of investing in their health. EHealth could play an important role in improving cardiovascular prevention by continuously offering patients information and reminding the importance of treatment [34].

4.4. Strengths and weaknesses

Strengths of this study are the large sample size and high response rate. However, ideally all patients would fill in the questionnaires. Questionnaires were sent by email which might be a hurdle for patients lacking digital skills. To further increase the response rate, we now offer FH patients visiting the FH clinic the option to fill in the questionnaires on a tablet assisted by nurses while waiting.

Another limitation of this study is that it has been developed and executed in a single FH centre. Implementation in other FH centres could support or differentiate the results leading to generalizable findings. Furthermore, the average SES score of the patients attending our clinic proved to be above the national average indicating that we miss FH patients with lower SES. This implies inequity in the care of FH patients and should lead to a more active policy for attracting specifically patients with low SES, especially as low SES is associated with having more modifiable and behavioural risk factors for CVD [35].

4.5. Conclusions

Relevant to the concept of value-based healthcare, a health-related outcomes set, including PROMs, has been developed for heterozygous FH patients. First results of this set have been measured in 429 FH patients from the Netherlands and show valuable insights for FH care and how to improve this. We found that a patient's knowledge of FH has an influence on outcomes and therefore on a patient's health. Therefore, this study concludes that stimulating patients' FH knowledge may improve value for the FH patient.

Supporting patients and improving insufficient knowledge of patients as a part of clinical practice, may lead to better outcomes. To optimize the outcome set, further research into its use over a longer period of time and in more FH centres is needed. Further investigation is needed in non-respondents and the inequity with respect to FH patients not attending the clinic. Also, more work is needed on the effects of knowledge interventions and the role eHealth could play.

The outcome set developed can be used as a tool in FH management to capture useful data on the patient in an organized way. In addition, implementation of the outcome set is important for future benchmarking with other FH centres to improve FH care.

Author contributions

JM, JH and JRVL designed the study and wrote the manuscript. JH and JRVL supervised the study. JM, JGB and LJV performed the analyses. All authors critically revised the manuscript and approved the final manuscript.

Declaration of competing interest

Prof. Dr. Hazelzet received a personal fee from Bayer for an educational lecture. The other authors report no conflicts.

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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.2019.11.030.

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