



Psychological determinants and evidence-based behavior change interventions in adherence to therapy for familial hypercholesterolemia

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Purpose of review

Patients with familial hypercholesterolemia have an elevated risk of premature atherosclerotic cardiovascular disease. Risks can be minimized through pharmacological and 'lifestyle' behavioral (low fat diet, physical activity) therapies, although therapeutic adherence is sub-optimal. Behavioral interventions to promote familial hypercholesterolemia therapy adherence should be informed by theory-based psychological determinants for maximal efficacy. The current review summarizes research on determinants of familial hypercholesterolemia therapy adherence and behavior change interventions, identifies limitations of the extant research, and sets future research agenda.

Recent findings

A recent meta-analysis identified attitudes, subjective norms, self-efficacy, and risk perceptions as key determinants of familial hypercholesterolemia therapy adherence intentions, with intentions identified as a key correlate of concurrent behavior. Studies have specified techniques targeting key theory-based determinants that may be efficacious in interventions. Research is limited by overuse of cross-sectional correlational study designs, use of self-report behavioral measures, few theory-based intervention tests, and limited consideration of nonconscious processes and effects of socio-structural variables.

Summary

Researchers should adopt study designs permitting better directional and causal inferences in determinant effects, provide tests of interventions targeting determinants and their mechanisms of action, consider determinants representing nonconscious processes (habits, implicit attitudes), and test determinants as mediators of socio-structural variables on familial hypercholesterolemia therapy adherence.

Keywords

behavior change, cardiovascular disease risk, familial hypercholesterolemia, psychological determinants, social cognition theory

INTRODUCTION

Familial hypercholesterolemia is an inherited disorder that elevates low-density lipoprotein-cholesterol leading to markedly increased risk of early-onset atherosclerotic cardiovascular disease (ASCVD) [1[•]]. Familial hypercholesterolemia can be effectively managed by pharmacological treatment (e.g., statin therapy) and regular participation in 'lifestyle' behaviors (i.e., a diet low in saturated fats, physical activity) [2–4,5^{••},6^{••}]. However, therapy adherence frequently falls short of guideline levels required for maximum efficacy [4,5^{••},7,8]. Clinicians and health-care providers have, therefore, prioritized development of behavioral interventions purposed to promote therapy adherence [5^{••},6^{••},7]. Such interventions should have a basis in behavioral theory for

optimal efficacy [9[•],10]. Theory guides identification of modifiable psychological determinants reliably related to therapy adherence in familial hypercholesterolemia patients. Accordingly, techniques used

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KEY POINTS

- Behavior change interventions promoting adherence to pharmacological and 'lifestyle' behavioral therapies are at the forefront of means to minimize atherosclerotic cardiovascular disease risk in individuals with familial hypercholesterolemia.
- Identification of psychological theory-based determinants of adherence to familial hypercholesterolemia therapeutic behaviors may signal salient techniques for adoption in behavior change interventions.
- Primary and meta-analytic research has identified belief-based determinants of adherence to familial hypercholesterolemia therapeutic behaviors, with attitudes, subjective norms, self-efficacy, and risk perceptions featuring prominently.
- Limitations of current determinants and intervention research on familial hypercholesterolemia therapy adherence include a preponderance of correlational study designs and use of self-report behavioral measures, and research on interventions is sparse and typically does not focus on determinants or test how the interventions work to change behavior through mechanisms of action.
- Future research needs to adopt study designs that enable better causal and directional inferences in determinant effects on familial hypercholesterolemia therapeutic behavior, including randomized controlled and cross-lagged panel designs, consider effects of determinants representing nonconscious processes to action (e.g., habit, implicit attitudes), and evaluate the role of determinants as mediators of socio-structural variables on behavior.

in behavioral interventions targeting change in, or activation of, determinants may increase the likelihood of behavior change [11,12²²]. In the current review we summarize and critically evaluate research on theory-based psychological determinants of therapy adherence in familial hypercholesterolemia patients and theory-based behavioral interventions purposed to promote adherence. We also review key challenges, outstanding questions, and evidence gaps in determinants and behavioral intervention research in familial hypercholesterolemia therapy adherence, and suggest important avenues for future research and practice [4,7].

THEORY-BASED RESEARCH ON FAMILIAL HYPERCHOLESTEROLEMIA THERAPY ADHERENCE: DETERMINANTS AND INTERVENTIONS

In this section, we critically review current determinants and intervention research.

Identifying determinants

Mirroring research on other health behaviors [9¹³], researchers have applied social cognition and motivational theories to identify the psychological determinants of familial hypercholesterolemia patients' intentions to adopt and adhere to familial hypercholesterolemia therapies [14–16]. The theories assume individuals' beliefs with respect to future participation in a target behavior inform their intentions to perform the behavior. The beliefs represent the psychological processes implicated in behavioral decision-making and are assessed using validated psychometric scales. Reviews of observational research applying theories of this class in health behavior contexts, such as social cognitive theory [10,17] and protection motivation theory [18], have identified utility beliefs (referred to as attitudes), social norms (injunctive and descriptive norms), risk appraisals (risk perceptions), and capacity beliefs (self-efficacy) as reliable determinants of intentions. Intention, representing individuals' level of motivation, is the most proximal behavioral determinant and mediates effects of beliefs on health behavior participation. Effects of these determinants, and their mediation by intention, on familial hypercholesterolemia therapy adherence are represented in Fig. 1.

Studies adopting correlational designs have supported theory-stipulated effects of these determinants on familial hypercholesterolemia therapy intentions [14,19,20²⁴]. Specifically, familial hypercholesterolemia patients' attitudes, subjective norms, self-efficacy, and risk perceptions are determinants of familial hypercholesterolemia patients' intentions to engage in statin therapy and 'lifestyle' behaviors [14,19] and behavior-related indices such as BMI [15]. Intentions are a consistent correlate of concurrent behavioral measures [14]. A recent meta-analysis of observational studies corroborated findings of primary research. Specifically, the analysis identified small-to-medium sized averaged effects of attitudes, subjective norms, and self-efficacy on with smaller effects for risk perceptions [20²⁴]. The latter finding indicated that patients' risk perceptions were less salient to intention formation than personal, social, or capacity beliefs, likely due to samples that tended to skew younger, were asymptomatic, and did not have ACVD. However, there were insufficient data to estimate effects of intentions on follow-up measures of therapy adherence. Taken together current evidence identifies personal, social, and capacity beliefs, as reliable, consistent correlates of intentions to participate in key familial hypercholesterolemia therapeutic behaviors, statin use and 'lifestyle' behaviors, and intentions as correlates of past therapy behavior.

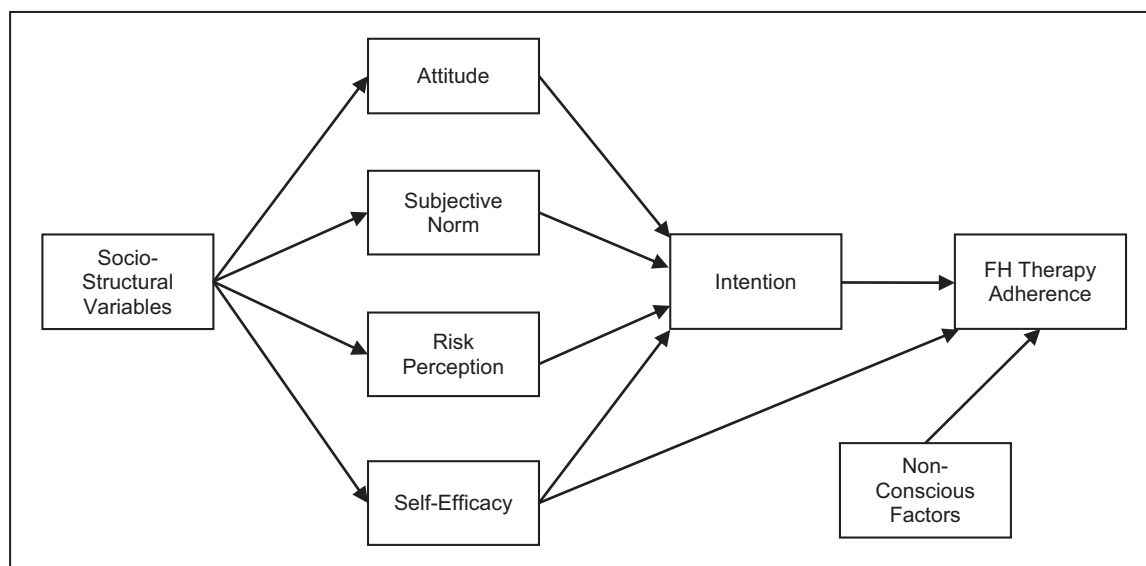


FIGURE 1. Diagrammatic representation of the theory-based psychological determinants of adherence to familial hypercholesterolemia therapy behaviors.

Behavior change interventions

Theory-based determinants represent potential mediators of behavior change interventions and indicate candidate mechanisms by which intervention techniques operate to change behavior [12²²,21]. Studies have applied systematic means to map behavior change techniques used in interventions on to these determinants in familial hypercholesterolemia therapy interventions [22,23²²]. For example, Kinnear *et al.* [23²²] matched theory-based determinants with techniques to inform interventions to promote ‘lifestyle’ behavior adherence in familial hypercholesterolemia. They identified skill development (e.g., learning to prepare healthy meals), behavioral regulation strategies (e.g., self-monitoring, goal setting, planning), modeling, and seeking social support as key techniques, but did not report a follow-up trial based on these findings. In addition, randomized controlled trials (RCTs) testing theory-based intervention effects have reported changes in familial hypercholesterolemia self-management behaviors [24]. However, RCTs are comparatively rare and have tended not to be based on previously conducted determinants research [25,26] and no study to date has examined adherence over time. Overall, while evidence indicates that theory-based behavioral interventions may have efficacy in promoting familial hypercholesterolemia therapy adherence, few report a basis in theoretical determinants research or examine long-term adherence.

Practically, researchers have made tentative suggestions of potentially effective techniques that may promote familial hypercholesterolemia therapy

adherence based on current determinants research, RCTs, and clinician experience [24,25,27,28]. Examples of advocated techniques include provision of messages highlighting advantages and dispelling negative beliefs, emphasizing and recruiting support from significant others, prompting self-efficacy experiences and use of cues to action, and offering practical ‘how-to’ advice. These techniques can be delivered by print or online messages or via practitioner-mediated counseling. Although this represents ‘best available’ advice for clinicians seeking to promote behavior change in familial hypercholesterolemia patients, it is not based on robust evidence.

LIMITATIONS, EVIDENCE GAPS, AND A FUTURE RESEARCH AGENDA

Next, we review some limitations of the extant research on determinants of familial hypercholesterolemia therapy adherence and theory-based interventions, and suggest agenda for future research.

Alternative study designs and measurement

Despite proliferation of research on theory-based determinants of familial hypercholesterolemia therapy adherence, studies have tended to fixate on cross-sectional correlational designs. Such designs do not permit inference of cause or direction in determinant effects, and do not model temporal change in determinants [29]. Determinants research enabling such inferences has a greater value as a basis for intervention [9²⁹]. Resolution lies in the adoption of research designs that permit better

directional and causal inferences. For example, longitudinal designs provide a basis for directional and reciprocal effects between determinants and behavioral outcomes while controlling for temporal and, in some implementations, intra-individual stability [30]. RCTs permit better causal inferences and a better basis for intervention development as the manipulations or intervention content used point to potentially efficacious behavior change techniques [9]. If the techniques used in RCTs target determinants proposed to be activated or changed consistent with theory, they also afford opportunity for mediation analyses to evaluate how the intervention works in changing behavior, known as mechanisms of action [12²²,31,32]. However, there is a dearth of RCTs testing behavioral intervention effects on familial hypercholesterolemia therapy adherence and existing trials tend not to include measures of determinants precluding mechanism tests. This remains a priority for future research.

Another notable methodological concern in familial hypercholesterolemia therapy adherence research is an overreliance on self-report behavior measures [20]. Bias associated with self-report measures can inflate error variance in effect size estimates [33,34]. Researchers should be encouraged to consider nonself-report measures of therapy adherence in future studies. One approach may be to infer behavior change from change in familial hypercholesterolemia relevant outcomes such as BMI or blood lipid profiles. More direct approaches include use of devices such as accelerometers to measure physical activity or MEMS dispensers to measure medication adherence. Furthermore, use of networked devices such as smartphones or watches to measure physical activity offer promise as they permit accurate tracking and frequent sampling and data access. To date, researchers have not capitalized on such nonself-report methods to measure familial hypercholesterolemia therapy adherence and this represents an important future research direction.

Additional determinants and processes

Research on familial hypercholesterolemia therapy adherence has tended to focus on psychological determinants from a narrow set of social cognition and motivational theories. These theories assume behavioral decisions are a function of reasoned, deliberative processing of social information regarding the behavior [9,17]. Behavioral intentions, therefore, arise from an evaluative ‘weighing up’ of salient information relating to outcomes, social influences, capacity estimates, and risk information as represented by the attitude, subjective norm, self-efficacy, and risk perception determinants,

respectively, that feature prominently in these theories. The exclusive focus on reasoned processes has been criticized as it provides only a limited description of the processes related to behavioral engagement and neglects other processes that lead to behavior engagement, such as nonconscious or automatic processes [9²,35]. This has led to renewed interest in dual process theories of behavior [36], which propose two processes or ‘routes’ to behavior, a reasoned, conscious, intention-mediated route represented by effects of social cognition or motivational determinants on behavior and an automatic, nonconscious route represented by direct effects of determinants such as habits or implicit attitudes on behavior. The nonconscious ‘route’ to behavior is represented in Fig. 1 by direct effects of the nonconscious factor on familial hypercholesterolemia therapy adherence.

A central question with respect to dual process models that underscores their value in providing comprehensive descriptions of behavior is which of the two ‘routes’ prevails in determining behavior. Identifying the predominant route provides important information on the mechanisms driving behavior and the behavior change techniques that could be potentially efficacious in changing behavior. Observational research applying these theories in health behavior contexts have included measures of habit and implicit attitudes as behavioral determinants alongside belief-based determinants, such as attitudes and self-efficacy [35²,37]. Habits reflect the extent to which a given behavior is enacted efficiently and ‘automatically’ without need for extensive deliberation. Habits arise through learned contingencies between the behavior and environmental conditions or ‘cues’. Implicit attitudes reflect behavioral judgments that instigate behavior beyond individuals’ awareness. They can be ‘activated’ on presentation of contextual or other conditions (e.g., another performing the behavior) that are also associated behavioral performance.

Studies indicate consistent, direct effects of these determinants on health behavior participation, independent of the intention-mediated effects of the belief-based determinants, implicating nonconscious processes in behavioral enactment [35²,37,38]. Importantly, research has indicated that the effects of these nonconscious determinants predominate under certain conditions, such as when the behavior has high propensity to be formed as a habit (i.e., performed regularly in the presence of stable conditions or cues) or the behavior is likely to be highly rewarding or consistently evaluated positively [35²]. This has inspired researchers and interventionists to identify behavior change techniques that could promote health behaviors as habits

obviating the need for ongoing intervention [39,40]. Studies have indicated that strategies such as environmental restructuring (prompting individuals to identify and link relevant cues or 'reminders' to the behavior) and plan formation (prompting 'if-then' plans to repeat behavioral performance under similar contexts or conditions) are effective in promoting habits [41].

Based on research in other health behavior contexts, researchers have acknowledged the potential value of promoting habit formation [42] and inducing positive implicit attitudes as potentially useful strategies in promoting familial hypercholesterolemia therapy adherence [43]. However, there are no data to date on the role of these processes or techniques in the familial hypercholesterolemia context, and it remains a key avenue for future research.

Socio-structural variables: mechanisms

There is good evidence linking social demographic (e.g., sex, age) and structural variables (e.g., ethnicity, socio-economic status, health literacy) and health behavior participation [44,45]. Findings indicate substantive disparities in health behavior participation such that individuals from traditionally underserved groups or with on lower incomes have lower adherence to health-related behaviors. Further, deficits in health behavior participation accounts for nontrivial variance in disparities in health outcomes such as cardiovascular disease risk [46]. Such associations have also been reported in familial hypercholesterolemia patients, for example, patients from traditionally underserved groups or with inadequate health literacy report lower adherence to familial hypercholesterolemia therapy [47,48]. There is also research reporting lower participation in health behaviors in certain demographic groups; for example, women and older adults tend to be less physically active [49,50].

Researchers have suggested that psychological determinants of health behavior play a key mechanistic role for links between socio-structural variables indicating disparities and health behavior [51]. Specifically, socio-structural variable effects on health behavior participation are mediated by the belief-based determinants from social cognition theories [52]. For example, meta-analyses have observed indirect effects of SES indices such as education level and health literacy on health behavior such as physical activity participation and healthy eating [52,53]. Interpreting these findings, individuals with lower education and inadequate health literacy are less likely to value outcomes associated with health behavior (e.g., they may have insufficient knowledge of the behavior-health outcome

link), which ultimately leads to lower behavioral engagement. In another example, research has shown that the association between membership of traditionally underserved ethnic minority groups and lower colorectal cancer screening participation is mediated by perceived costs of the behavior and self-efficacy [54]. This may be attributed to experiences of disenfranchisement through discrimination in healthcare affecting patients' confidence in screening efficacy and its perceived negative impact on their everyday life.

To date, this approach has not been applied to explain disparities in familial hypercholesterolemia therapy adherence. For example, low therapy adherence among familial hypercholesterolemia patients with inadequate health literacy may be attributable to a lack of understanding of familial hypercholesterolemia cause and treatment, likely captured by their attitudes [15]. Similarly, observed age effects on deficits in therapy adherence in younger familial hypercholesterolemia patients may be mediated by attitudes or risk perceptions, indicating that younger patients attach less value to therapy or do not perceive familial hypercholesterolemia to be a significant health threat. Such research is valuable, as it indicates the kinds of beliefs that could be targeted in behavioral interventions. Importantly, these interventions may be more accessible and less costly than efforts targeting socio-structural change, such as education programs that aim to improve health literacy or financial packages aimed at reducing socio-economic disparities. Such research is strongly advocated in future.

CONCLUSION

Given that reduction in ACVD risk in familial hypercholesterolemia patients is associated with adherence to pharmacological treatment and 'lifestyle' behaviors, researchers have sought to identify modifiable determinants of therapy adherence derived from behavioral theory that could signal targets in behavior change interventions. We set out to summarize current research identifying determinants of familial hypercholesterolemia therapy adherence based on psychological theory and the extent to which they have been utilized in behavior change interventions. We also aimed to outline the key challenges and evidence gaps in determinant and intervention research, and identify emergent research questions and future research directions on determinants and interventions to promote greater familial hypercholesterolemia therapy adherence.

Observational studies have indicated that belief-based psychological determinants from social cognition theories, particularly attitudes, subjective

norms, self-efficacy, and risk perceptions are associated with familial hypercholesterolemia therapeutic behaviors [20[■]]. There has also been research outlining how such determinants may be targeted to change behavior and outlining the types of techniques that could be used in behavior change interventions aimed at promoting therapy adherence [16,23[■]]. However, research on determinants is relatively sparse and dominated by correlational cross-sectional observational designs with an over-reliance on self-report behavioral measures. Studies adopting longitudinal or randomized controlled designs and using nonself-report behavioral measures are needed to permit better causal inference and greater precision in determinant effects. There also few theory-based interventions targeting determinants to promote therapy adherence, which represents a clear evidence gap that needs to be addressed to provide practitioners with better data on which to base therapy adherence efforts. Finally, researchers should consider broadening the theoretical approaches applied to therapy adherence in familial hypercholesterolemia to provide more comprehensive descriptions of these behaviors, such as the potential role of nonconscious or 'automatic' processes, and to explain effects of socio-structural variables such as SES and health literacy on adherence.

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Conflicts of interest

The authors declare no competing interests.

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- of outstanding interest

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