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Effectiveness of the Family Heart Talk Communication Tool in Improving Family Member Screening for Dilated Cardiomyopathy: Results of a Randomized Trial

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Citation

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Circulation

ORIGINAL RESEARCH ARTICLE

Effectiveness of the *Family Heart Talk* Communication Tool in Improving Family Member Screening for Dilated Cardiomyopathy: Results of a Randomized Trial

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BACKGROUND: Managing disease risk among first-degree relatives of probands diagnosed with a heritable disease is central to precision medicine. A critical component is often clinical screening, which is particularly important for conditions like dilated cardiomyopathy (DCM) that remain asymptomatic until severe disease develops. Nonetheless, probands are frequently ill-equipped to disseminate genetic risk information that motivates at-risk relatives to complete recommended clinical screening. An easily implemented remedy for this key issue has been elusive.

METHODS: The DCM Precision Medicine Study developed *Family Heart Talk*, a booklet designed to help probands with DCM communicate genetic risk and the need for cardiovascular screening to their relatives. The effectiveness of the *Family Heart Talk* booklet in increasing cardiovascular clinical screening uptake among first-degree relatives was assessed in a multicenter, open-label, cluster-randomized, controlled trial. The primary outcome measured in eligible first-degree relatives was completion of screening initiated within 12 months after proband enrollment. Because probands randomized to the intervention received the booklet at the enrollment visit, eligible first-degree relatives were limited to those who were alive the day after proband enrollment and not enrolled on the same day as the proband.

RESULTS: Between June 2016 and March 2020, 1241 probands were randomized (1:1) to receive *Family Heart Talk* (n=621) or not (n=620) within strata defined by site and self-identified race/ethnicity (non-Hispanic Black, non-Hispanic White, or Hispanic). Final analyses included 550 families (n=2230 eligible first-degree relatives) in the *Family Heart Talk* arm and 561 (n=2416) in the control arm. A higher percentage of eligible first-degree relatives completed screening in the *Family Heart Talk* arm (19.5% versus 16.0%), and the odds of screening completion among these first-degree relatives were higher in the *Family Heart Talk* arm after adjustment for proband randomization stratum, sex, and age quartile (odds ratio, 1.30 [1-sided 95% CI, 1.08–∞]). A prespecified subgroup analysis did not find evidence of heterogeneity in the adjusted intervention odds ratio across race/ethnicity strata (P=0.90).

CONCLUSIONS: *Family Heart Talk,* a booklet that can be provided to patients with DCM by clinicians with minimal additional time investment, was effective in increasing cardiovascular clinical screening among first-degree relatives of these patients.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03037632.

Key Words: cardiomyopathy, dilated ■ health communication ■ randomized controlled trial

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ORIGINAL RESEARCH ARTICLE

Clinical Perspective

What Is New?

- A booklet to facilitate family communication about shared genetic risk for dilated cardiomyopathy, *Family Heart Talk*, was developed and tested in a randomized trial in the multisite DCM Precision Medicine Study.
- For families in whom the proband was randomized to receive the booklet, first-degree relatives had greater odds of obtaining the recommended clinical screening.
- A prespecified subgroup analysis did not find evidence that this effect varied across self-identified race/ethnicity strata.

What Are the Clinical Implications?

- *Family Heart Talk* is an effective tool for increasing the uptake of clinical screening among at-risk relatives in families affected by dilated cardiomyopathy.
- This intervention is low-cost and requires minimal time investment to implement into clinical care.

Nonstandard Abbreviations and Acronyms

COVID-19	coronavirus disease 2019
DCM	dilated cardiomyopathy

Dilated cardiomyopathy (DCM) underlies a substantial proportion of heart failure and is the leading cause of cardiac transplant. Because of its genetic background[1–3] and substantial risk to family members,[4] a diagnosis of idiopathic DCM should trigger a clinical evaluation of at-risk family members to mitigate DCM risk.[3] Clinical cardiovascular screening, including cardiovascular imaging to assess left ventricular size and function, is essential because DCM can be asymptomatic for months or years before it presents as late-phase disease with heart failure.[5] Traditional care models rely on the proband, the first in the family diagnosed with DCM, to share screening recommendations with their at-risk first-degree relatives, who include parents, full siblings, and children. However, studies of family communication of genetic risk have shown that information transmission is selective and incomplete.[6–8] Probands frequently are ill-equipped to communicate genetic risk effectively, which contributes to inadequate family member clinical screening.[9,10] A family-centric care model, in which providers interact directly with family members, may be a solution. However, this model presents formidable implementation challenges[11] because of the constraint against directly contacting at-risk family members arising from the need to keep the proband's medical information confidential.

Family communication research in hereditary breast and colorectal cancer syndromes found that communication about risk does not flow seamlessly among family members[8,12,13] and often does not motivate clinical screening or genetic testing.[14,15] In hereditary cardiovascular disease, retrospective single-center studies have also demonstrated incomplete uptake of cardiovascular screening among first-degree relatives for whom these interventions are indicated.[9,10,16–18] Additional disparities in uptake of recommendations for genetic risk mitigation have been observed in Black women at risk for hereditary breast cancer syndromes.[19,20] Methods for addressing such family communication challenges in DCM have not been studied.

A communication tool in booklet format, *Family Heart Talk* (Supplemental Material), was developed by clinicians with cardiovascular and genetic expertise and vetted by patients with DCM[21] to help probands communicate DCM genetic risk information and clinical screening recommendations to at-risk first-degree relatives. We conducted a randomized controlled trial to evaluate the effectiveness of *Family Heart Talk* in improving clinical cardiovascular screening completion among first-degree relatives.[21] The study hypothesized that first-degree relatives of probands with DCM randomized to receive the *Family Heart Talk* booklet would have a higher probability of completing clinical cardiovascular screening compared with the control group.

METHODS

Trial Design and Oversight

This open-label, cluster-randomized, controlled trial was conducted at 25 heart failure and cardiac transplant programs in the United States (Figure S1) as part of the multisite, consortium-based DCM Precision Medicine Study.[21] The overall study aimed to test the hypothesis that DCM has substantial genetic basis and to evaluate the effectiveness of providing probands with the *Family Heart Talk* booklet in improving uptake of recommended preventive behaviors among their first-degree relatives.[21] The trial was designed and overseen by investigators at the Ohio State University Coordinating Center, who also analyzed the data; site investigators collected the data and contributed to their interpretation. Detailed methods, research materials, and additional data from this study can be made available by the corresponding author on reasonable request.

Participants

Eligible participants were patients with DCM (probands) of any age identified by physicians and clinical research personnel at the participating sites and their first-degree relatives (parents, full siblings, and children)[4] of any age who were alive the day after proband enrollment and not previously enrolled. All probands met criteria for idiopathic DCM,[22] defined as left ventricular systolic dysfunction (left ventricular ejection fraction <50%) and left ventricular enlargement without other clinical causes, as previously described.[21] In addition, probands needed

to be willing to invite family members to participate in the study. Proband recruitment was managed to achieve geographic diversity, sex balance, and inclusion of historically underrepresented groups (protocol, Table S1, or Reference 21). Probands were asked at enrollment to inform first-degree relatives about the study and to seek their permission for contact by study personnel. Study staff approached first-degree relatives who provided permission for contact to invite them to participate. The institutional review boards at the Ohio State University and all clinical sites approved the initial period of the study followed by single institutional review board oversight at the University of Pennsylvania. Written informed consent was obtained from all participants.

Randomization and Intervention

Probands were randomized (1:1) at the time of enrollment within strata defined by site and self-identified race/ethnicity (non-Hispanic Black, non-Hispanic White, Hispanic; Supplemental Methods) to receive the *Family Heart Talk* booklet (*Family Heart Talk* arm) or not (control arm). There were 28 recruitment sites used for defining these strata (Figure S2): 26 of them were advanced heart failure programs (1 operated only briefly and was inactivated); 1 was a geographically remote satellite site of a program; and 1 was a virtual site at the Ohio State University Coordinating Center. For each stratum, the statistician at the Ohio State University Coordinating Center generated an independent sequence of randomization assignments with a computer program using randomly permuted blocks with equal treatment allocations and an equiprobable random block size of 2, 4, or 6. The assignment for each proband was revealed to recruiting staff at enrollment on opening the next sealed opaque envelope in sequence for the proband's self-identified race/ethnicity stratum at that site (see protocol or Reference 21 for details). Probands in both arms received a study brochure with information for family members, a Dear Family Member letter, and a letter to physicians of family members.

The *Family Heart Talk* intervention was designed to help probands communicate about DCM risk and to stimulate clinical screening of their at-risk family members. It is based on the Leventhal's Self-Regulation Model of Health Behavior[23] and is modeled after a previously developed web-based family communication intervention for melanoma survivors that resulted in increased family communication about shared risk.[24] *Family Heart Talk* was vetted by a focus group of cardiovascular and genetics experts and in structured interviews with patients with DCM.[21] The intervention consisted of a guide to family communication about DCM provided in print booklet format. The booklet included visuals and lay language explanations of the evaluation and care of individuals with DCM, emphasizing the necessity of a clinical cardiac evaluation in asymptomatic family members to detect DCM at the earliest possible stage. It also provided guidance on how to talk with family members about DCM risk and included samples of emails and letters to aid in this process.

Primary Outcome

The primary outcome for this analysis was completion of clinical cardiovascular screening initiated within 12 months after proband enrollment among eligible first-degree relatives as defined previously. Enrolled first-degree relatives obtained study-sponsored cardiovascular screening by echocardiogram and ECG at the time of their enrollment unless they were able to provide reports of screening studies completed within the previous 3 years or to arrange for clinical screening through their own physicians. A positive outcome required both enrollment in the DCM Precision Medicine Study within 12 months (365 days) after proband enrollment and provision of information sufficient to determine the presence or absence of DCM by the time of analysis. The definition of eligible first-degree relatives used in evaluating the primary outcome was modified from the original protocol because of difficulty obtaining reliable data on DCM status of unenrolled relatives and a change in study operations to emphasize enrollment of first-degree relatives on the same day as the proband (see Supplemental Methods for details).

Statistical Analyses

Simulations with the planned enrollment of 1300 probands estimated >99% power to detect an odds ratio of 1.5 with a screening completion rate of 20% in the control arm at a typical site (ie, one at the mean or mode of the random-effects distribution),[25,26] which would correspond to a screening completion rate of 27% in the *Family Heart Talk* arm at that site (see protocol or Reference 21). Although the accrual period was extended for non-Hispanic Black probands to attain the planned enrollment target of 600, the executive committee closed proband enrollment on March 15, 2020, before achieving this target because enrollment activities were curtailed at all clinical sites as a result of the coronavirus disease 2019 (COVID-19) pandemic. Updated simulations using the same model and parameter values showed that power to detect the effect above remained high (98.5%) with the attained sample size (see Supplemental Methods for details).

Because the intervention was administered at the family level through the proband and the primary outcome was measured among eligible first-degree relatives, this trial was cluster randomized,[27] with each family defining a cluster. To estimate the effect of *Family Heart Talk* on the odds of screening completion in a first-degree relative of a proband with particular characteristics, a moments-based[28] or generalized estimating equation–type[29] generalized linear mixed model with the logit link was fit to binary outcome data from eligible first-degree relatives (enrolled and unenrolled) using residual subject-specific pseudolikelihood. The linear predictor included a 2-level normal random effects structure (proband site and self-identified race/ethnicity stratum within site) and fixed effects for self-identified race/ethnicity stratum to account for stratified randomization. Fixed effects for proband sex and enrollment age quartile, which were expected a priori to affect the outcome, were also prespecified in the statistical analysis plan to improve power.[30] Residual correlation between outcomes of first-degree relatives of each proband was addressed by assuming a compound symmetric conditional variance matrix for the outcomes among first-degree relatives of the same proband and no conditional correlation between the outcomes of first-degree relatives of different probands. To facilitate valid inferences even if this conditional variance structure was misspecified, inference on fixed effects used the Morel-Bokossa-Neerchal bias-corrected empirical covariance estimator, with sites as independent

units.[29,31] Additional motivation for and technical details on this analytic approach are provided in the Supplemental Methods.

Because the recommendation would be not to implement the *Family Heart Talk* intervention with either no effect or a negative effect of any magnitude, a 1-sided inferential posture was appropriate[32,33] and specified a priori in the statistical analysis plan (see protocol and Reference 21). The null hypothesis that the odds ratio between the *Family Heart Talk* and control arms was ≤1 was tested against the alternative that it was >1 at an α of 0.05 with a Wald test using the standard normal distribution; a 1-sided Wald 95% CI for the odds ratio was also produced.

To determine whether the overall *Family Heart Talk* odds ratio could reasonably describe the intervention effect in all proband race/ethnicity strata, a single secondary subgroup analysis prespecified in the statistical analysis plan was performed (see protocol). In this analysis, an interaction between the self-identified race/ethnicity stratum and receipt of *Family Heart Talk* fixed effects was added to the model, and the null hypothesis of no interaction was tested at an α of 0.05 with the 2-sided *P* from a Wald test using the χ^2 distribution with 2 *df*, as recommended.[34,35] Because this was a secondary analysis, the study was not explicitly powered to detect a particular degree of heterogeneity or to perform a formal test of equivalence of the intervention effect across subgroups. Thus, although failing to reject this null hypothesis implies that there is not enough evidence of heterogeneity in the intervention effect to warrant using less precise subgroup-specific estimates rather than the overall estimate to describe the likely intervention effect in each subgroup,[34] it does not provide evidence that the intervention effect is equivalent across the subgroups.[35]

Our approach was identical to the original statistical analysis plan (see protocol or Reference 21) with 2 exceptions. First, a fixed effect for self-identified race/ethnicity stratum was added to the random effects structure originally proposed to account for stratified randomization because of systematic differences in the rates of first-degree relative enrollment across these groups[4] that were unanticipated at the design stage. Second, an originally proposed fixed effect for proband-reported family history of DCM, which was included only for its potential to increase power, was removed because of difficulty in obtaining reliable data. Additional details are provided in the Supplemental Methods.

Because statewide stay-at-home orders resulting from the COVID-19 pandemic could have modified the intervention effect, a sensitivity analysis was also performed using only families who completed the 12-month follow-up period before the earliest such order (see Supplemental Methods for details). All analyses were performed with SAS/STAT 15.2 software, version 9.4 (TS1M7) of the SAS System for 64-bit Windows (SAS Institute Inc, Cary, NC) and R version 4.0.2 (R Foundation, Vienna, Austria).

RESULTS

Participants

Between June 2016 and March 2020, 1265 probands with DCM provided written informed consent. Of these, 1241 probands were randomly assigned to the *Family Heart Talk* arm (n=621) or control arm (n=620; Figure 1). Follow-up for the primary outcome for this analysis was completed 12 months after the last proband enrollment. Final analysis excluded families of probands who: (1) did not meet study inclusion criteria on central review of medical records received after enrollment (n=25); (2) subsequently withdrew consent for participation and data collection (n=10); (3) were unable to complete study assessments (n=5); (4) were assigned to the incorrect randomization stratum (n=6); (5) were subsequently identified as third-degree or closer relatives of another DCM Research Project proband (n=8); (6) provided incomplete vital status information on first-degree relatives (n=1); or (7) had no eligible first-degree relatives (n=75). This resulted in a total of 550 families (n=2230 eligible first-degree relatives) in the *Family Heart Talk* arm and 561 (n=2416) in the control arm (Figure 1).

Treatment assignments were nearly balanced within the strata in the final analysis sample (Figure S2). In this sample, probands in the *Family Heart Talk* and control arms were comparable in terms of baseline demographic characteristics (Table 1) such as median enrollment age (51.7 years versus 53.3 years), sex (44.0% versus 43.3% female), race (41.8% versus 44.2% Black), and Hispanic ethnicity (7.8% versus 8.4%). The arms were also comparable in terms of education and employment status among those who responded. The median number of eligible first-degree relatives was 4 in both arms. DCM duration was similar between arms (median time since first diagnosis, 5.0 years versus 5.6 years), as were various measures of severity, including median left ventricular ejection fraction (20% in both), median left ventricular internal diameter end diastole *z* score (4.2 versus 4.1), and percentages with previous implantable cardioverter defibrillator implant, ventricular assist device implant, and heart transplant. Completion of formal cardiovascular genetic evaluation or genetic testing either before or within 12 months after proband enrollment was also similar between arms (13.7% versus 11.8%).

Full siblings were the most common type of eligible first-degree relative in both arms (42.9% versus 44.6%), followed by adult and minor children (37.7% versus 38.0%) and parents (19.4% versus 17.3%; Table 2). Enrollment within 12 months of proband enrollment was the most important determinant of screening completion; among eligible first-degree relatives who satisfied this criterion, >96% had completed screening by the time of data analysis.

Primary Outcome

The percentage of first-degree relatives who completed clinical screening was 19.5% in the *Family Heart Talk* arm and 16.0% in the control arm. For probands with the same site–race/ethnicity randomization stratum, sex, and enrollment age quartile, first-degree

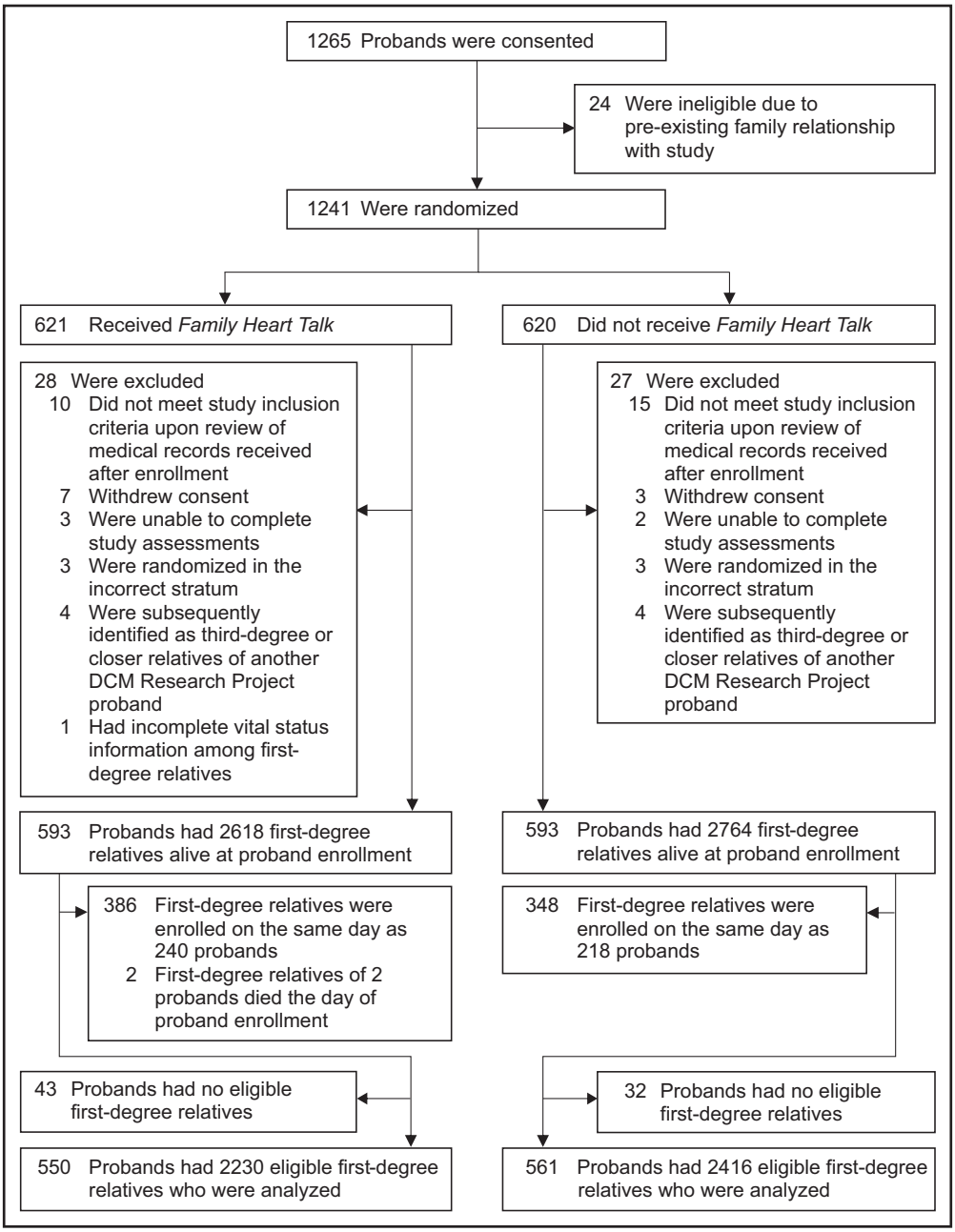

Figure 1. Study flow diagram.

relatives had higher odds of completing clinical screening in the *Family Heart Talk* arm compared with the control arm (odds ratio,1.30 [1-sided 95% CI, 1.08–∞]; 1-sided *P*=0.01; Figure 2). A prespecified subgroup analysis did not find evidence that the effect of *Family Heart Talk* differed between first-degree relatives of non-Hispanic Black, non-Hispanic White, and Hispanic probands (*P*=0.90; Figure 2). A sensitivity analysis including only families who had completed follow-up before the first statewide stay-at-home order resulting from the COVID-19 pandemic yielded similar inferences for the effect of *Family Heart Talk* (odds ratio, 1.39 [1-sided 95% CI, 1.08–∞]; 1-sided *P*=0.02) and its heterogeneity across race/ethnicity subgroups (*P*=0.70; Figure 2).

DISCUSSION

This multicenter, open-label, cluster-randomized, controlled trial demonstrated that providing the *Family Heart Talk* booklet to a proband with DCM was effective in increasing clinical cardiovascular screening completion among first-degree relatives.

The effectiveness of *Family Heart Talk* in increasing screening among first-degree relatives of patients with DCM is highly relevant given the elevated DCM risk in

Table 1. Baseline Characteristics of Study Probands With at Least 1 Eligible First-Degree Relative Contributing to the Analysis

Characteristic	*Family Heart Talk* (n=550)	Control (n=561)	Overall (N=1111)
Enrollment age, y, median (IQR)	51.7 (40.6–61.4)	53.3 (43.4–61.8)	52.6 (42.3–61.6)
Female, n (%)	242 (44.0)	243 (43.3)	485 (43.7)
Race, n (%)			
White	317 (57.6)	313 (55.8)	630 (56.7)
Black	230 (41.8)	248 (44.2)	478 (43.0)
Other	3 (0.5)	0 (0.0)	3 (0.3)
Hispanic n, (%)	43 (7.8)	47 (8.4)	90 (8.1)
Race/ethnicity stratum, n (%)			
Non-Hispanic Black	228 (41.5)	244 (43.5)	472 (42.5)
Non-Hispanic White	279 (50.7)	270 (48.1)	549 (49.4)
Hispanic	43 (7.8)	47 (8.4)	90 (8.1)
Years of schooling, n/N respondents (%)			
0–13	237/520 (45.6)	232/527 (44.0)	469/1047 (44.8)
14–17	204/520 (39.2)	208/527 (39.5)	412/1047 (39.4)
≥18	79/520 (15.2)	87/527 (16.5)	166/1047 (15.9)
Employment status, n/N respondents (%)			
Working or studying	246/525 (46.9)	240/532 (45.1)	486/1057 (46.0)
Not working by choice	180/525 (34.3)	184/532 (34.6)	364/1057 (34.4)
Involuntarily not working	99/525 (18.9)	108/532 (20.3)	207/1057 (19.6)
No. of first-degree relatives alive at proband enrollment, median (IQR)	4 (3–6)	4 (3–6)	4 (3–6)
No. of eligible first-degree relatives, median (IQR)	4 (2–5)	4 (2–6)	4 (2–6)
Years since first DCM diagnosis, median (IQR), No. available	5.0 (1.2–12.6), 549	5.6 (1.4–12.2)	5.3 (1.3–12.5), 1110
LVEF, %, median (IQR), No. available	20 (15–29), 548	20 (15–28), 558	20 (15–28), 1106
LVIDd			
LVIDd, mm, median (IQR), No. available	65 (60–70), 547	64 (60–70), 558	65 (60–70), 1105
Z Score,* median (IQR), No. available	4.2 (3.0–5.6), 546	4.1 (3.0–5.5), 557	4.1 (3.0–5.5), 1103
ICD, n/N available (%)	371/548 (67.7)	374/558 (67.0)	745/1106 (67.4)
VAD, n (%)	123 (22.4)	118 (21.0)	241 (21.7)
Heart transplantation, n (%)	78 (14.2)	89 (15.9)	167 (15.0)
Completion of a formal cardiovascular genetic evaluation or genetic testing before or during study,† n/N available (%)	75/549 (13.7)	66/560 (11.8)	141/1109 (12.7)

DCM indicates dilated cardiomyopathy; ICD, implantable cardioverter defibrillator; IQR, interquartile range; LVEF, left ventricular ejection fraction; LVIDd, left ventricular internal diameter end diastole; and VAD, ventricular assist device.

*Calculated from sex and height[36] for all study participants with heights of at least 152 cm (men) or 137 cm (women).

†Defined as completion of a formal cardiovascular genetic evaluation or genetic testing substantiated by review of medical records that occurred either before or within 12 months after proband enrollment. Because the study protocol did not explicitly require providing updated medical records with postenrollment clinical cardiovascular genetic evaluation and testing data, some probands who received these services within 12 months after enrollment may not have been identified.

this group; another analysis of the families in this study estimated that 29.7% of probands overall had at least 1 living first-degree relative with DCM.[4] Furthermore, the estimated cumulative risk of DCM in first-degree relatives was 19% by 80 years of age, rising to 33% when those with left ventricular systolic dysfunction or left ventricular enlargement alone were also considered. Demonstrating overall effectiveness in a study including 42.5% non-Hispanic Black families is highly relevant. Although the estimated proportion of Black probands having at least 1 first-degree relative with DCM was 11.3% higher than for White probands in this cohort,[4] lower trust of the medical enterprise among Black patients[19,20,37,38] and social and economic factors may present substantial obstacles to screening uptake.

Risk information sharing within families must occur for at-risk family members to have the opportunity to obtain the recommended risk-mitigating clinical screening. Barriers to dissemination of genetic risk information among family members include emotional or geographic distance between relatives, low health literacy, lack of confidence to explain genetic information, and reluctance to share

Table 2. Relationship to Proband and Screening Completion Outcome Determination for Eligible First-Degree Relatives Contributing to the Analysis

Characteristic/outcome	*Family Heart Talk* (n=2230)	Control (n=2416)	Overall (N=4646)
Relationship to proband, n (%)			
Parent	433 (19.4)	419 (17.3)	852 (18.3)
Full sibling*	956 (42.9)	1078 (44.6)	2034 (43.8)
Child (adult or minor)	841 (37.7)	919 (38.0)	1760 (37.9)
Screening completion outcome, n (%)			
No: did not enroll within 12 mo of proband enrollment	1787 (80.1)	2006 (83.0)	3793 (81.6)
No: enrolled within 12 mo of proband enrollment but did not complete screening by time of analysis	9 (0.4)	24 (1.0)	33 (0.7)
Yes: enrolled within 12 mo of proband enrollment and completed screening by time of analysis	434 (19.5)	386 (16.0)	820 (17.7)

*Siblings sharing both parents with the proband who were not also monozygotic twins of the proband.

personal information, among other concerns.[8] Because current care models inhibit direct contact of the provider with at-risk family members because of confidentiality and Health Insurance Portability and Accountability Act mandates, genetics providers have attempted to disseminate genetic risk information by preparing letters for the proband to distribute to family members[39,40] with limited success.[41] In addition, a randomized controlled trial of a tailored approach, including direct contact with relatives by a genetic counselor to inform them of their cardiovascular risk, did not result in a significant difference in uptake of counseling compared with usual practice.[42]

The results of this trial are comparable to those of randomized studies evaluating the effects of communication interventions on screening behaviors for heritable cancer. A study of a communication tool using a web-based format demonstrated an increase in preventive actions for family members at risk for melanoma relative to controls.[43] In another trial, a 20-minute provider-led intervention for probands that included a personalized review of familial cancer risk was successful relative to the control and not substantially different from the outcomes for web- and paper-based tools.[44]

Provider-driven strategies require substantial clinician time for counseling patients with risk of familial disease. This can diminish productivity and may be less cost-effective, particularly when no genetic counselor or other support is available in the clinical setting. In contrast, provision of the *Family Heart Talk* booklet entailed minimal production cost and required minimal time and effort for the clinical research coordinators at the DCM Consortium sites. Site personnel were instructed that they were free to explain the purpose of the *Family Heart Talk* tool and address any questions from probands, but such activities were not expected or required. Moreover, provision of the booklet did not require specialized training. Site clinical research coordinators had no specific genetics background or training on the tool aside from a 20-minute slide presentation shown by a study genetic counselor at the study initiation event of each research site. As a result, the effectiveness of the *Family Heart Talk* booklet observed in this study is likely to generalize to most care settings, in which this tool could be provided to probands with DCM by any member of the care team with minimal cost or effort.

Although there were small imbalances in some baseline characteristics between treatment arms among analyzable probands, they are unlikely to affect the validity of the results. First, these imbalances are likely attributable to chance because treatment assignment was randomized and the reasons for exclusion among 114 of the 130 randomized probands not analyzed were related to baseline characteristics necessarily independent of the treatment assignment (Figure 1), such as absence of eligible first-degree relatives. Furthermore, adjustments for site–race/ethnicity stratum, sex, and enrollment age quartile prespecified in the statistical analysis plan should also have protected against bias arising from chance imbalances in any of these variables.

This study has limitations. First, the probands with DCM in this study were enrolled at advanced heart failure programs, and patients with DCM without advanced disease in community programs may not be as responsive to the *Family Heart Talk* booklet. However, the proband clinical demographics showed that the study enrolled a clinically diverse group of patients, including those with only mild DCM, and nearly half of the probands were still working or studying. Second, probands needed to indicate willingness to assist with the enrollment of their family members, so this intervention was unable to evaluate whether the provision of *Family Heart Talk* could spur probands unwilling to interact with their families to do so. Third, it is possible that the effectiveness of *Family Heart Talk* differs across time points in the disease progression of DCM. However, enrolled probands represented a wide spectrum of disease duration and severity, providing reassurance that the intervention may be generally applicable regardless of disease stage.

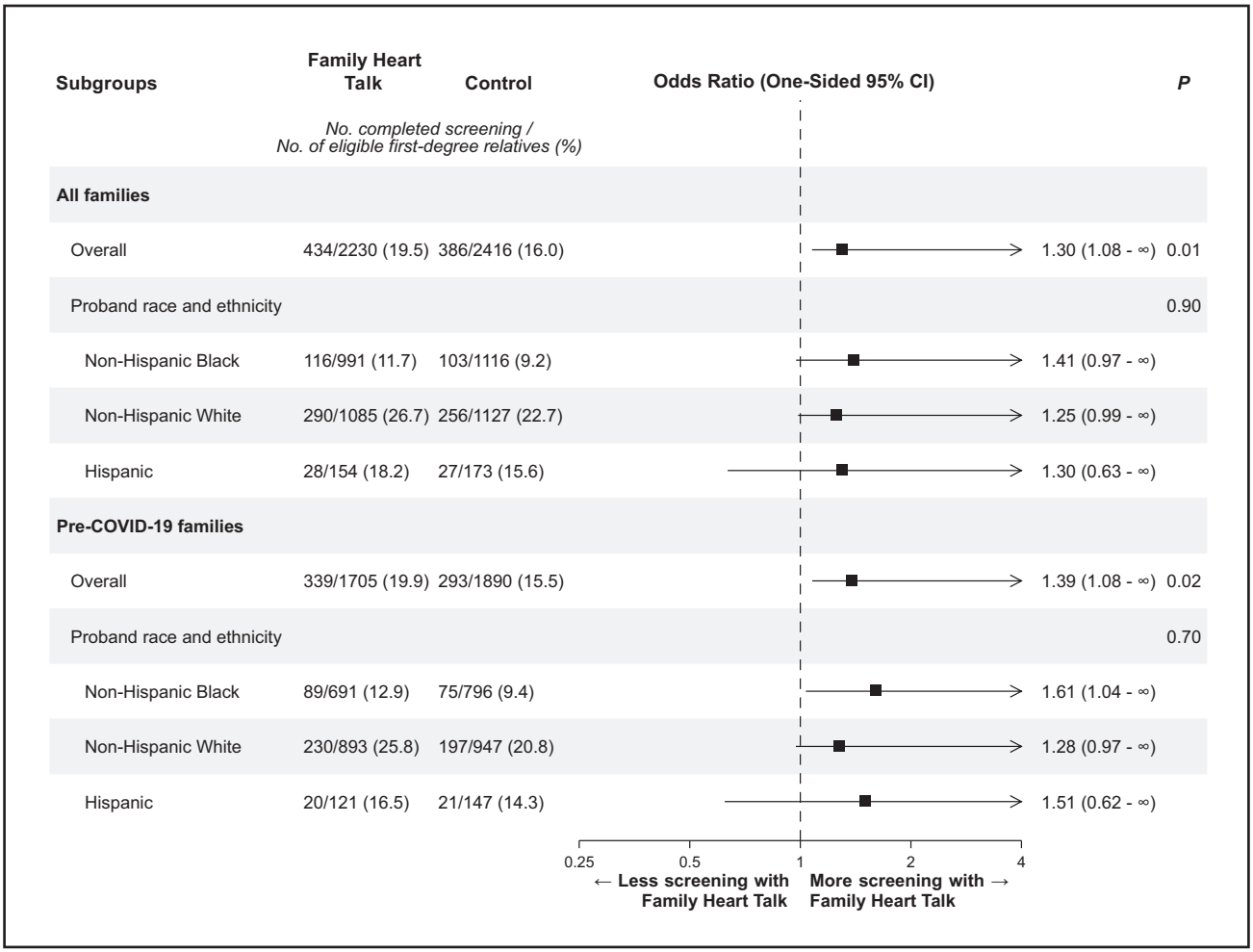

Figure 2. Effectiveness of *Family Heart Talk* overall and by race/ethnicity group.
Odds ratios comparing the *Family Heart Talk* arm with the control arm given proband site–race/ethnicity randomization stratum, sex, and enrollment age quartile were obtained from a generalized estimating equation–type generalized linear mixed model with the logit link fit to binary outcome data from eligible first-degree relatives (enrolled and unenrolled) using residual subject-specific pseudolikelihood. The linear predictor included a 2-level normal random effects structure (proband site and self-identified race/ethnicity stratum within site) and fixed effects for self-identified race/ethnicity stratum to account for stratified randomization. Fixed effects for proband sex and enrollment age quartile, which were expected a priori to affect the outcome, were also prespecified in the statistical analysis plan to improve power. Residual correlation between outcomes of first-degree relatives of each proband was addressed by assuming a compound symmetric conditional variance matrix for the outcomes among first-degree relatives of the same proband and no conditional correlation between the outcomes of first-degree relatives of different probands. Bias-corrected robust standard errors were obtained with the Morel-Bokossa-Neerchal correction with sites as independent units, and 1-sided Wald 95% CIs were calculated with the standard normal distribution. Except for the overall effects, CIs have not been adjusted for multiplicity and should not be used to infer statistical significance. *P* values calculated from this model included a 1-sided Wald test for the null hypothesis that the odds ratio between the *Family Heart Talk* and control arms was ≤1 and a 2-sided Wald *P* value for the null hypothesis of no interaction between race/ethnicity stratum and the intervention effect. Detailed information on the model fits contributing to this figure is provided in Tables S2 through S5. COVID-19 indicates coronavirus disease 2019; and pre-COVID-19 families, those who had completed the 12-month follow-up period before the first statewide stay-at-home order resulting from the COVID-19 pandemic.

In conclusion, in a multicenter, open-label, cluster-randomized, controlled trial, providing the *Family Heart Talk* booklet to probands with DCM was effective in increasing clinical cardiovascular screening completion among first-degree relatives.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Supplemental Methods

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Protocols and Statistical Analysis Plans

Family Heart Talk booklet

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