Identifying Patients at Increased Disease Risk: Comparing Clinical Judgment and a Clinical Risk Assessment Tool

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Abstract

Introduction: There are several barriers to the appropriate use of Family Health History (FHH) for risk management within primary care. Among these is a lack of physician confidence in their ability to identify high risk individuals and determine guideline concordant care. In this study, we compared Primary Care Providers’ (PCP) clinical assessment of appropriate risk-management for patients to guideline based recommendations generated by an IT platform, MeTree. In addition, we compared MeTree with clinical assessments of Genetic Counselors (GC).

Methods: Pedigrees from 100 consecutive patients who entered their FHH into MeTree were evaluated by a PCP and a GC. Recommendations from MeTree were compared to those selected by the PCP and GC.

Results: PCPs and GCs were discordant with MeTree 13.7% (N=49/356) and 13.5% (N=48/356) of the time respectively. In instances of discordance, PCPs were more likely to underestimate risk (77.5%, N=38/49) while GCs underestimated (45.8%, N=22/48) and overestimated (54.2%, N=26/48) risk almost equally in instances of discordance. PCPs most commonly underestimated risk regarding need for genetic counseling and early colonoscopy. PCPs overestimated the need for breast MRI, chemoprophylaxis, and ovarian cancer screening.

Conclusion: In this study we have demonstrated that provider knowledge of risk stratification and identification of appropriate risk-management strategies is in fact a significant barrier to guideline concordant care for patients. Our findings support the need to embed a clinical tool such as MeTree, into primary care to act as an intermediary between the PCP and GC.

ABBREVIATIONS

FHH: Family Health History; PCP: Primary Care Provider; GMM: Genomic Medicine Model; CDS: Clinical Decision Support; USPSTF: US Preventive Services Task Force; GC: Genetic Counselor; CRC: Colorectal Cancer

INTRODUCTION

Family Health History (FHH) remains an important component of risk stratification for numerous diseases, including cancer. Clinical guidelines recommend collection of FHH for disease risk stratification and surveillance [1,2]. Unfortunately collection of
adequate FHH in primary care settings is challenging. This is due to a variety of barriers including inadequate patient knowledge concerning FHH, clinical encounter time constraints, and competing clinical demands [3-5]. Even when FHH is adequately collected, current guidelines delineating early screening and identification of high-risk individuals are complex. Primary Care Providers (PCP) have been found to lack confidence in their ability to identify high-risk individuals or create actionable risk-management plans based on FHH [6-8].

To address these issues, the Genomedical Connection, collaboration among Duke University, the University of North Carolina at Greensboro, and the Cone Health System, developed the Genomic Medicine Model (GMM) for primary care. This model was designed to improve utilization of FHH for risk stratification and risk management within primary care. The GMM includes education for patients and providers concerning the importance of FHH and how to collect and use FHH for risk stratification. At the core of the GMM is MeTree, a patient-facing information technology platform for collection of FHH with integrated risk stratification and Clinical Decision Support (CDS). MeTree collects FHH on 48 conditions and provides risk stratification and risk tailored guideline-directed CDS for 5 conditions (breast cancer, ovarian cancer, colorectal cancer (CRC), hereditary cancer syndromes, and thrombosis). MeTree CDS is entirely based on well recognized clinical guideline recommendations (e.g., US Preventive Services Task Force (USPSTF), American Cancer Society). Use of MeTree prior to a primary care visit facilitates collection of FHH data prior to the PCP encounter, thus allowing the clinical encounter to be focused on discussing a personalized risk management healthcare plan.

We desired a better understanding of the potential influence of provider knowledge on clinical care, specifically those related to risk assessment and synthesis of risk information into actionable risk management plans. Therefore, we compared providers’ clinical assessment of appropriate risk-management for patients with complete FHHs to MeTree’s guideline based recommendations. In addition, we compared recommendations made by MeTree, which uses the guidelines most widely accepted and most familiar to PCPs (e.g., USPSTF) with clinical assessments of genetic counselors, who may use a variety of guidelines to inform their recommendations.

MATERIALS AND METHODS

De-identified 3-generation pedigrees from the first 100 consecutive patients enrolled in the larger Genomedical Connection study (i.e., probands) [9] were given to 7 PCPs and 4 genetic counselors (GCs). Pedigrees were consecutively sorted with 5 PCPs reviewing 14 each and 2 reviewing 8 each, while the GCs reviewed 25 each. Physicians were academic primary care physicians in Durham, NC; GCs were 4 hereditary cancer specialists with clinical practices in the southeastern U.S. None were associated with the Genomedical Connection. Details of the Genomedical Connection study are previously published [9,10]. In brief, all adult patients with upcoming primary care appointments in 2 Greensboro, NC community-based primary care clinics were invited to participate in this study of FHH collection and risk assessment.

PCPs and GCs were asked to evaluate risk and possible risk-management actions for each of the following conditions: breast cancer, colorectal cancer, ovarian cancer and thrombosis, based on complete FHHs for each proband. A complete FHH included the following elements necessary for risk stratification: 1) pedigree with relatives’ disease status, age of disease onset, and current age or age and cause of death if deceased, 2) probands’ disease status, age of disease onset, and current age, and 3) risk calculation results (Gail score [11] and BRCAPRO score [12] for breast cancer risk). Guideline-based options for disease surveillance and/or risk management, consistent with possible recommendations made by MeTree, were presented in multiple choice format for each condition (Table 1). PCPs and GCs were instructed to choose which action or actions were appropriate for the patient (i.e. they needed to decide if the patient was at average risk, above average risk, or hereditary risk and choose the appropriate risk management option for their level of risk for each condition). The study was approved by the IRBs of Duke University, University of North Carolina at Greensboro, Cone Health System, and the funding agency, the Department of Defense.

Measures and analysis

We collected specialty, year of medical school graduation, and gender for PCPs and collected years in practice and gender for GCs. Descriptive statistics of the probands, probands’ FHHs (e.g., number of relatives and number of relatives with cancer), and participating physicians were tabulated with calculations of median or mean and range when appropriate. Two by two tables were created to compare recommendations made by GCs and PCPs to recommendations made by MeTree. For those cases where PCPs and/or GCs were discordant with MeTree, we evaluated whether GCs and/or PCPs had a tendency to recommend actions reflecting perceived higher or lower risk than assigned by MeTree. Instances in which there were disagreements between MeTree and PCPs and/or GCs concerning recommendations for genetic counseling referrals for cancer risk (breast cancer, ovarian cancer, and colon cancer) were also tabulated.

RESULTS AND DISCUSSION

Participant characteristics

Of the seven PCPs who participated in this study, all were Internists, five were male and two female, and the average number of years since medical school graduation was 21 (range 11-36 years). Of the four GCs, all were female, and all had been in practice 5-10 years.

Of the 100 probands whose pedigrees were used in this study, 43 were male and 57 female, with a mean age of 54.8 years (SD 12.61, range 21-86) and a mean Gail score of 1.64% (range 0.26% - 7.92%). The mean number of probands’ relatives was 21.32 (SD 12.61, range 21-86) and a mean Gail score of 1.64% (range 0.26% - 60%).

Overall agreement and disagreement

Agreement and disagreement between PCPs and MeTree, and GCs and MeTree is summarized in Table 2. Overall PCPs and MeTree were discordant on 49 recommendations out of total of 356 possible recommendations (100 probands getting
Disease Options for Disease Surveillance

Breast Cancer
1. Patient already has breast cancer
2. Routine screening with mammography
3. Breast MRI as an adjunct to mammography for early breast cancer detection
4. Chemoprevention for breast cancer prevention
5. Refer to genetic counselor for risk of hereditary cancer syndrome.

Ovarian Cancer
1. Patient already has ovarian cancer
2. No surveillance
3. Refer to gynecology for discussion of the pros and cons of ovarian cancer surveillance
4. Refer to genetic counselor for risk of hereditary cancer syndrome

Colorectal Cancer
1. Patient already has colorectal cancer
2. Routine screening
3. Begin colorectal cancer screening early
4. Begin colonoscopy screening early and perform more frequently
5. Colon polyps on prior colonoscopy, repeat based on number, size, and histology
6. Refer to genetic counselor for risk of hereditary cancer syndrome

Thrombosis
1. No action required
2. Refer to genetic counselor
3. Genetic testing for inherited thrombophilia

Table 1: Guideline-based disease Surveillance options.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Options for Disease Surveillance</th>
</tr>
</thead>
</table>
| Breast Cancer          | 1. Patient already has breast cancer  
2. Routine screening with mammography  
3. Breast MRI as an adjunct to mammography for early breast cancer detection  
4. Chemoprevention for breast cancer prevention  
5. Refer to genetic counselor for risk of hereditary cancer syndrome. |
| Ovarian Cancer         | 1. Patient already has ovarian cancer  
2. No surveillance  
3. Refer to gynecology for discussion of the pros and cons of ovarian cancer surveillance  
4. Refer to genetic counselor for risk of hereditary cancer syndrome |
| Colorectal Cancer      | 1. Patient already has colorectal cancer  
2. Routine screening  
3. Begin colorectal cancer screening early  
4. Begin colonoscopy screening early and perform more frequently  
5. Colon polyps on prior colonoscopy, repeat based on number, size, and histology  
6. Refer to genetic counselor for risk of hereditary cancer syndrome |
| Thrombosis             | 1. No action required  
2. Refer to genetic counselor  
3. Genetic testing for inherited thrombophilia |

Table 2: Agreement and disagreement between PCPs and MeTree and GCs and MeTree.

<table>
<thead>
<tr>
<th>Disease</th>
<th>PCP % (N)</th>
<th>GC % (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>88% (88)</td>
<td>90% (90)</td>
</tr>
<tr>
<td>• Agreement</td>
<td>88% (88)</td>
<td>90% (90)</td>
</tr>
<tr>
<td>• Disagreement</td>
<td>12% (12)</td>
<td>10% (10)</td>
</tr>
<tr>
<td>o Underestimate risk</td>
<td>66.6% (8/12)</td>
<td>40% (4)</td>
</tr>
<tr>
<td>o Overestimate risk</td>
<td>33.3% (4/12)</td>
<td>60% (6)</td>
</tr>
<tr>
<td>Ovarian cancer*</td>
<td>93% (52/56)</td>
<td>91% (51/56)</td>
</tr>
<tr>
<td>• Agreement</td>
<td>93% (52/56)</td>
<td>91% (51/56)</td>
</tr>
<tr>
<td>• Disagreement</td>
<td>7% (4/56)</td>
<td>9% (5/56)</td>
</tr>
<tr>
<td>o Underestimate risk</td>
<td>25% (1/4)</td>
<td>20% (1/5)</td>
</tr>
<tr>
<td>o Overestimate risk</td>
<td>75% (3/4)</td>
<td>80% (4/5)</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>70% (70)</td>
<td>77% (77)</td>
</tr>
<tr>
<td>• Agreement</td>
<td>70% (70)</td>
<td>77% (77)</td>
</tr>
<tr>
<td>• Disagreement</td>
<td>30% (30)</td>
<td>23% (23)</td>
</tr>
<tr>
<td>o Underestimate risk</td>
<td>93.3% (28/30)</td>
<td>60.9% (14/23)</td>
</tr>
<tr>
<td>o Overestimate risk</td>
<td>6.6% (2/30)</td>
<td>39.1% (9/23)</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>97% (97)</td>
<td>90% (90)</td>
</tr>
<tr>
<td>• Agreement</td>
<td>97% (97)</td>
<td>90% (90)</td>
</tr>
<tr>
<td>• Disagreement</td>
<td>3% (3)</td>
<td>10% (10)</td>
</tr>
<tr>
<td>o Underestimate risk</td>
<td>33.3% (1/3)</td>
<td>30% (3/10)</td>
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<tr>
<td>o Overestimate risk</td>
<td>66.6% (2/3)</td>
<td>70% (7/10)</td>
</tr>
<tr>
<td>Total</td>
<td>86.2% (307/356)</td>
<td>86.5% (308/356)</td>
</tr>
<tr>
<td>• Agreement</td>
<td>86.2% (307/356)</td>
<td>86.5% (308/356)</td>
</tr>
<tr>
<td>• Disagreement</td>
<td>13.8% (49/356)</td>
<td>13.5% (48/356)</td>
</tr>
<tr>
<td>o Underestimate risk</td>
<td>77.5% (38/49)</td>
<td>54.2% (26/48)</td>
</tr>
<tr>
<td>o Overestimate Risk</td>
<td>22.4% (11/49)</td>
<td>45.8% (22/48)</td>
</tr>
</tbody>
</table>

\* Denominator is 100 unless otherwise specified.

Genetic Counseling referrals

MeTree made 23 recommendations for genetic counseling for hereditary cancer risk (breast, ovarian, and colon cancer genetic counseling recommendations combined). PCP recommendations for genetic counseling were concordant with MeTree in 35% of cases (N=8/23); GC recommendations were concordant in 96% of cases (N=22/23). Underestimating risk of hereditary cancer was most common when considering colon cancer (n=14/23, 60.9%) and breast cancer (N=6/23, 26.1%). Even when PCPs did recommend referral for genetic counseling, there was discordance with MeTree regarding which condition to refer for in 11/22 (50%) cases. GCs more commonly agreed on when to refer patients for genetic counseling but there was still discordance regarding for which condition the patient was being referred (N=13/22, 59.1%).

Genetic Counseling referrals

MeTree made no recommendation for genetic counseling in 77 probands. In those instances PCP recommendations were concordant with MeTree recommendations in 96% of cases (N=74/77); GC recommendations were concordant in 90% of cases (N=69/77). In the 8 probands for whom GCs recommended genetic counseling but MeTree did not, all were referrals for colon cancer risk. One proband was also referred for breast cancer and one proband was referred for breast and ovarian cancer in addition to colon cancer.

Chemoprevention, Breast MRI, and Gynecology Referral

MeTree did not recommend anyone for chemoprevention or breast MRI, while PCPs recommended 4 for chemoprevention and
1 for breast MRI, and GCs recommended 6 for chemoprevention and 1 for breast MRI (different proband than the PCP). MeTree made one recommendation for referral to gynecologist for discussion of ovarian cancer risk. The PCP did not consider this patient to be at elevated risk, but the genetic counselor did. For the other 99 patients, MeTree did not recommend referral to a gynecologist. Of those patients, PCPs recommended 4 for gynecology referral and GCs recommended 5. For the 8 women that PCPs recommended chemoprevention, breast MRI, and/or gynecology referral, MeTree identified 7/8 (87.5%) as being at average risk based on guidelines. The eighth patient was referred to genetic counseling, but did not receive a recommendation for chemoprevention, breast MRI, or gynecology referral. For the 9 women that GCs recommended chemoprevention, breast MRI, and/or gynecology referral, MeTree identified 6/9 (66.7%) as being at average risk and the remaining 3/9 (33.3%) as needing genetic counseling referral only.

**Colonoscopy**

When MeTree recommended early and more frequent colonoscopy (N=9), PCPs only recommended it 3/9 times (33.3%) and GCs recommended it 7/9 times (77.8%). When MeTree did not recommend early and more frequent colonoscopy (N=91), PCPs did not recommend it 90/91 times (98.9%) and GCs did not recommend it 88/91 times (96.7%). When MeTree recommended early colonoscopy (N=8), PCPs recommended it 0/8 times and GCs recommended it 7/8 times (87.5%). When MeTree did not recommend early colonoscopy (N=92), PCPs also did not recommend early colonoscopy 92/92 times (100%) and GC did not recommend early colonoscopy 90/92 times (97.8%).

**CONCLUSION**

Risk stratification is well supported in clinical guidelines [1,2]. Two key requirements for implementation of risk stratification within clinical practice is full and complete FHH data and providers’ knowledge and familiarity with risk-based guidelines. Even when full pedigrees are provided, if medical providers are not confident in their ability to identify those at high risk or are unsure of appropriate next steps for high risk patients, that information cannot be utilized to its full potential. In this study we have demonstrated that provider knowledge of risk stratification and implementation of risk-management strategies is in fact a significant barrier to creation of appropriate actionable risk-management plans for patients.

PCPs frequently did not identify patients as being the same risk level as the risk-based guidelines used by MeTree, primarily the USPSTF [1,13-19]. PCPs primarily underestimated risk (N=38/49, 77.5%), mostly in regards to hereditary cancer risk (genetic counseling referrals) and colon cancer risk (use of colonoscopy). In particular regarding colonoscopy, providers appeared unaware of the indications for early (vs. early and more frequent) colonoscopy (i.e. individuals with first degree relatives with CRC or polyps after age 60, ≥ 2 second degree relatives with CRC or polyps[11] as they misidentified 7/8 such patients as being at average risk. Our findings are supported by a similar study among gastroenterologists [20].

In contrast PCPs tended to overestimate need for utilization of more aggressive screening methods for breast and ovarian cancer, identifying 8 women in need of breast MRI, chemoprevention and/or gynecology referral that MeTree did not identify as such. In some instances this was a case of misclassification of risk (i.e. identifying women as being at increased risk who were at normal risk based on guidelines). In other instances, PCPs correctly identified increased risk but did not select appropriate guideline-concordant risk management recommendations (e.g. recommending breast MRI or chemoprophylaxis when only genetic counseling was indicated.) This is consistent with other results reported in the literature showing that primary care providers tend to overestimate risk of ovarian and breast cancer [21,22].

Genetic counselors also had significant disagreement with MeTree recommendations but there was a more equal balance of underestimation (45.8%) and overestimation (54.2%) of risk. Specifically in regards to the need for genetic counseling referrals, where GCs would be expected to have the most expertise (versus use of breast MRI or colonoscopy for example), GCs identified most of the patients that MeTree identified as needing genetic counseling (N=22/23). But GCs also identified 8 additional patients for genetic counseling related to colon cancer that MeTree did not. This discrepancy is due primarily to the GC’s reliance upon the NCCN guidelines [23] for decision making, rather than the USPSTF, which is more conservative [19] (unpublished data from Genomedical Connection study).

Limitations of our study that must be considered include its sample size, limited geographic diversity, and differences in guidelines upon which providers may rely for their risk assessment decisions. First, our patient sample size and geographic representation were small. Only a small number of PCPs and GCs from one region of the country participated in the study, both of which limit generalizability. However, our findings are consistent with other studies performed in different populations and different geographic areas [20-22]. Secondly, MeTree is based on guidelines most commonly accepted in primary care. Other guidelines, particularly the NCCN, can vary widely from the USPSTF regarding when referrals should be made and therefore, risk assessments can be guideline-based but differ from what MeTree recommends. However, where PCPs differed from MeTree their risk assessments were not consistent with the other risk-based guidelines (such as NCCN), while discrepancies between MeTree and GCs were largely explained by this difference.

Our findings raise concerns that primary care providers may inaccurately estimate risk for a significant proportion of patients, which results in both 1) recommending unnecessary screening and referrals for those at average risk and 2) missing opportunities to provide appropriate more intensive risk management and disease surveillance for those at high risk. Given the complexity of current clinical guidelines, along with the many other barriers to utilization of FHH for risk assessment, our findings support the need to embed a clinical tool for FHH collection, risk calculation, and clinical decision support, such as MeTree, into primary care. Importantly, MeTree may act as an intermediary between the PCP and GC by initiating risk discussions between patient and provider, generating pedigrees to facilitate communication with GCs, and by recommending efficient [24] and guideline consistent actionable risk-management strategies for PCPs to consider [19].
As new findings demonstrate the role of genomics to predict risk and guidelines become even more complex, the need for such a decision aid will only continue to grow.

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REFERENCES


