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THE ROLE OF PRIMARY CARE PHYSICIANS IN THE CO-MANAGEMENT OF PATIENTS WITH GENETIC CONDITIONS

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ABSTRACT

Primary care physicians (PCPs) care for patients from cradle to grave, across multiple disciplines and within the context of the family. They are thus well-placed to provide genomic education and clinical services to their patients in partnership with Genetics Healthcare Professionals (GHPs). However, the specific role of PCPs to support genomic medicine is unclear, and hence a review was conducted to understand the ways PCPs can integrate genomic medicine practices. Materials and Methods: Relevant publications were retrieved from Google Scholar and PubMed using the keywords of "Genomics", "Primary Care Physicians", and "Role". Main results: Thirty-seven retrieved articles provided information that is included in this review. PCPs need to increase their knowledge and understanding of genomics; develop competency in the collection of family histories; have knowledge of the genetic screening tests available; know when to refer their patients for genetic screening; and be able to manage ethical, legal, and social issues that may arise. Conclusion: PCPs play an essential role in the provision of appropriate genomics services, in improving access, in co-managing patients with GHPs, and in providing scientific understanding of genomics to the community.

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Key words: Genomics, Primary Care physicians (PCPs), Hereditary conditions

INTRODUCTION

As the emphasis of precision and genomic medicine continues to take centre stage, the integration of genomic medicine practices are expected to happen at the primary care level. However, a systematic review of primary care providers' (PCPs) perceived barriers to the integration of genetics services within primary care revealed several concerns.[1] First, PCPs generally lacked awareness regarding the presence and utility of genetic testing, which led to the perception that genetic testing is of low clinical utility and low referrals to genetic services.[2-5] The review also highlighted ethical, legal, and social issues (ELSI) associated with genetic testing. Concerns for PCPs include the potential for patient anxiety, distress, or the possibility of insurance discrimination after genetic testing. This highlights that low genetic literacy amongst PCPs and the lack of time, training, and access to geneticists may be factors inhibiting the uptake of genetic services in the primary care setting.

"Roadmaps" for incorporating genomic results into clinical care include engaging stakeholders, identifying early adopters, securing funding, selecting a pilot project, education, and collecting outcome data. Another noteworthy area to highlight is the importance of improved linkages between PCPs and GHPs.[6-9]

Haga et al[3] noted that as genetic testing becomes more prevalent in multiple disciplines, including primary care, PCPs are in a good position to assume a valuable role in the delivery of genomic medicine. This is in view of their focus on disease prevention and screening, like how PCPs routinely offer screening mammograms and colonoscopies to individuals who may be at inherited risk of breast or colon cancer respectively. PCPs will however, need ready access to genetics experts, and the best practice standards will come from a collaboration between medical genetics and other clinical specialties.

In Singapore, we have Genomic centres[9,10] led by multidisciplinary teams that are staffed by genetic counsellors, pharmacists, and research staff who can link up with PCPs to help integrate genomics care in their practices.

Family history has traditionally been an integral part of clinical care to assess health risks. However, declining sequencing costs may precipitate a shift towards genomics-first approaches in some population screening programmes. However, this remains to be seen in view of the controversies and limited data in this novel area.[11]

PCPs have described their various roles in genomics management such as taking a complete family history, identifying individuals at increased risk for genetic conditions and referring appropriately, discussing the benefits and limitations of genetic testing, and providing post-test care for patients, which include psychosocial support, coordination of screening, and management.[5,12,13]

Many patients want to know their genomic findings, regardless of available treatment. The aggressive direct-to-consumer marketing of increasingly cheaper DNA tests without medical consultation has resulted in many PCPs being in a dilemma when patients consult them to advise on choice of tests and interpreting results. Studies have shown that curricula in medical schools have limited content and PCPs are ill-prepared to deal with genomics issues.[14]

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MATERIALS AND METHODS

Relevant publications were retrieved from Google Scholar and PubMed using keywords of "Primary Care Physicians", "Genomics", and "Role". Thirty-seven retrieved publications provided information included in this review.

MAIN RESULTS

Knowledge, Attitudes, and Communication Behaviours

A systematic review was done to identify PCPs' knowledge, attitudes, and communication-related behaviours regarding genetic testing in USA.[15] Many studies documented limited knowledge among PCPs, many of whom were uncertain about guidelines and felt unqualified to provide counsel regarding the pros and cons of testing for specific conditions. Across studies, PCPs expressed some concerns about the ethical, legal, and social implications of testing. Attitudes about the utility of clinical genetic testing for targeted cancer screening, were generally favourable. PCPs were more sceptical of direct-to-consumer testing. Barriers to implementation of genomic medicine within primary care include lack of confidence in genomic medicine skills, particularly in the emerging areas.[16]

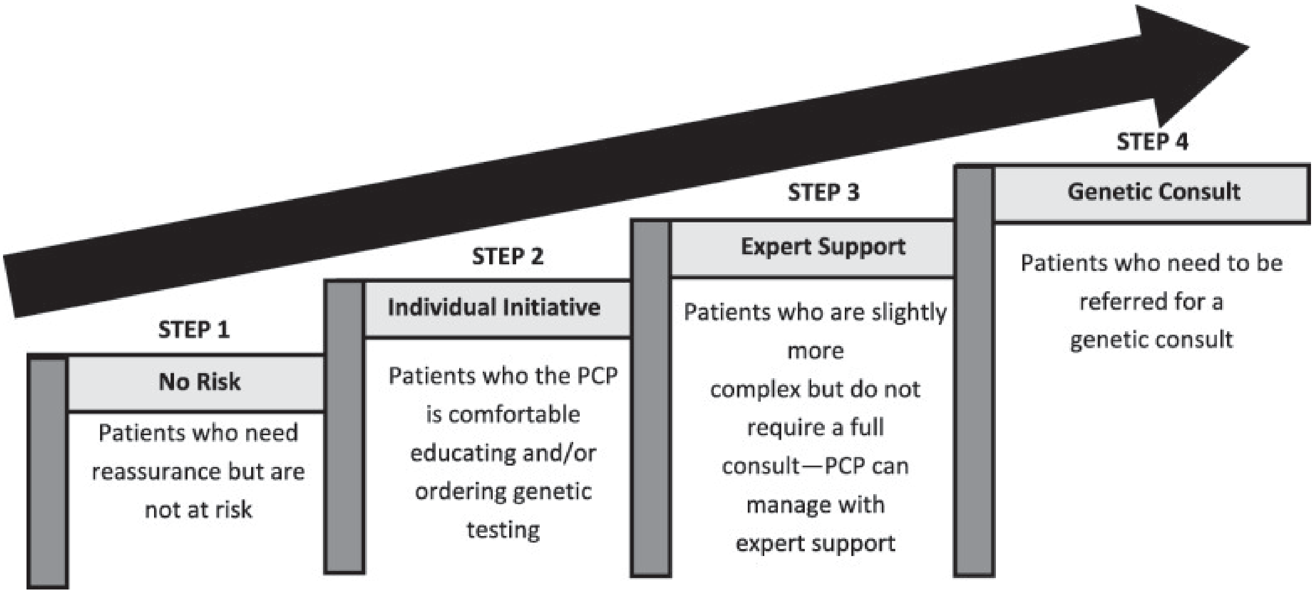
A focus group study in Ontario, Canada consisting of five focus groups to explore the expectations of genetic health professionals (GHPs) of PCPs' role in genomic medicine presently and in the future was published in 2021.[17] The findings were that PCPs play a vital role in addressing the genomic service needs of patients. GHPs participating in the focus groups were also "very clear" about the need for PCPs and GHPs to work together more effectively in making the best use of existing care GHPs.

To help address gaps in PCP confidence in providing genetic care, proposals directed at accessible just-in-time support and consultation have been mooted; such implementations can empower PCPs to manage their patients' genetic conditions. A progressive framework through a "stepped model" for bridging primary to specialty care was developed to assess risk, complexity, and competency to guide delivery of educational and clinical interventions.[18]

A study of PCPs' use of genetic services in Southeast United States based on 11 interviews noted that PCPs face barriers at three different levels when engaging with genetic services: systems, providers, and patients. At the system level, there are logistic challenges and a lack of genetic providers. At the provider level, there might be lack of knowledge. At the patient level, there is a lack of genetic appointment knowledge. Solutions lie in seeking help and in educating users (refer to **Figure 2**). Health system change is needed to create new service delivery models, building the relationship between GHPs and PCPs, improve communication with a common electronic medical record, and developing educational materials and decision support for PCPs.[19]

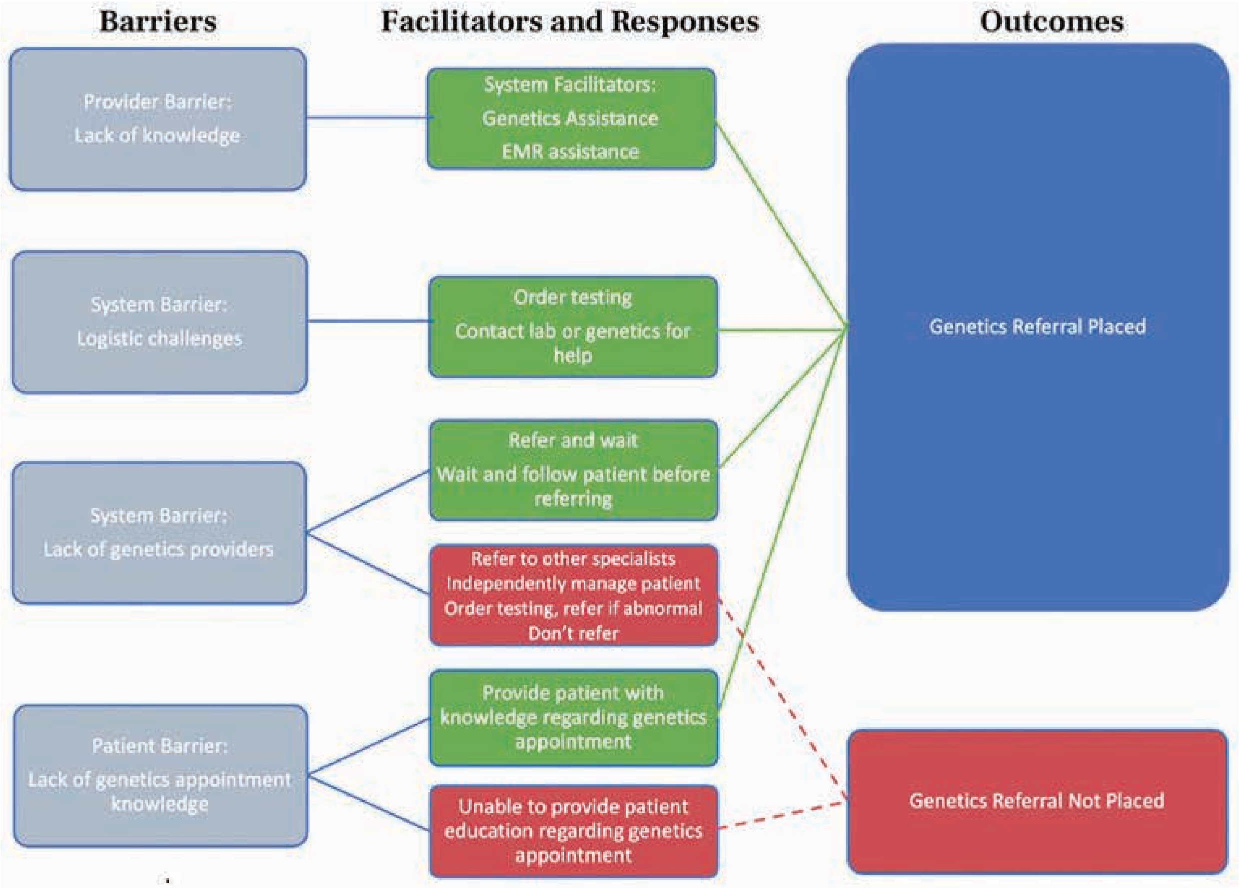
The rapid expansion of genetic knowledge and the implications for healthcare has resulted in an increased need for PCPs to include genomics in their clinical practice.[20] Targeted training is needed and the ideal timing for education intervention appears to be in Residency and/or Fellowship rather than in medical school.[21] To empower PCPs to gain confidence in genomics, the Royal Australian College of General Practitioners (RACGP) incorporated genomics as a distinct education module in their curriculum.[22] In 2018, the RACGP also published a document titled "Genomics in general practice"[24].

Figure 1. Bridging the Gap in Genetics: A Progressive Model for Primary to Specialist Care



Source: Harding B, Webber C, Rühland L, et al, 2019[18].

Figure 2. Barriers and Facilitators in the Use of Genetic Services in Southeast USA



Source: Siebel E et al, 2021[19]

Role of PCPs in Co-Management of Patients with Genetic Conditions

The primary care physician has six tasks in the co-management of patients with genetic conditions with the multidisciplinary team. These are:

1. Family History Screening and Early Detection of Medical Conditions

Screening with a family history is an important role of PCPs in view of the long-term relationship with the patient and the family. A focused, "just-in-time" family history will often meet the needs of PCP, although a multigenerational family history is an important tool.[24]

Certain types of cancer, such as hereditary breast cancer and colon cancer, may appear more frequently in multiple family members in the pedigree. Medical conditions like coronary artery disease, familial hyperlipidaemia, and chronic kidney disease may also have familial tendencies.[25,26]

Computer-based tools have been utilised as collection of family history is a time-consuming process. This is now made easier and possible through the availability of access to electronic datasets shared amongst relatives and stored in electronic health records or personal files, enabling portability of family history information.[27]

2. Risk Assessment and Timely Referral

Genetic testing for patients at risk for hereditary cancer susceptibility genes, e.g., *BRCA 1/2*, is an important component of preventive medicine.[28] Results can inform risk stratification and personalised cancer risk management strategies, including the use of appropriate cancer screening tests with the greatest benefit and least harm.[15]

PCPs play an important role in primary cancer prevention (e.g., assessment and timely referral to specialists for risk management), and secondary cancer prevention (e.g., use and timing of screening tests) In this context, the 2023 NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic focus "primarily on assessment of pathogenic/ likely pathogenic (P/LP) variants associated with increased risk of breast, ovarian, pancreatic, and prostate cancer, including *BRCA1*, *BRCA2*, *CDH1*, *PALB2*, *PTEN*, and *TP53*, and recommended approaches to genetic counselling/testing and care strategies in individuals with these P/LP variants" is very useful.[29]

Its NCCN Guidelines Insights summarise "important updates regarding: (1) a new section for transgender, nonbinary, and gender-diverse people who have a hereditary predisposition to cancer focused on risk reduction strategies for ovarian cancer, uterine cancer, prostate cancer, and breast cancer; and (2) testing criteria and management associated with *TP53* P/LP variants and Li-Fraumeni syndrome".[29]

3. Safe Prescribing

There is increasing evidence that pharmacogenomics can improve the safety and/or efficacy of several medications commonly prescribed in primary care. Barriers to implementation include a perceived lack of evidence for clinical utility, unclear cost effectiveness, and unclear roles and responsibilities, particularly between PCPs and pharmacists. However, certain drugs like allopurinol have been associated with severe cutaneous adverse reactions in patients with HLA-B*58:01. Tramadol and codeine have variable clinical efficacy and toxicity in patients with variations in CYP2D6 genotype. Alternative drugs are recommended in such scenarios. Education, protocols and incorporating point-of-care clinical decision support systems will empower PCPs in appropriate prescription.[30,31]

4. Preventive Care

Polygenic risk testing examines variation across multiple genes to estimate a risk score for a particular disease or chronic health conditions like diabetes or heart disease. PCPs can then recommend appropriate preventive care to optimise health outcomes. However, this has to be balanced with patient preferences and medication adherence.[32]

5. Care of Comorbidities and Continuity of Care

Co-morbidities. PCPs have a critically important role in counselling patients and their families to adopt healthy lifestyle to reduce the risk of chronic non-communicable diseases, namely, overweight and obesity, hyperlipidaemia, high blood pressure, and type 2 diabetes mellitus. These adverse lifestyle factors also predispose at risk individuals to cancers, e.g., breast, colorectal, and endometrial cancers.

Continuity of care of high-risk hyperlipidaemia. In a qualitative study in Singapore that explored the facilitators and barriers of PCPs towards optimisation of statin therapy in high-risk patients with high-risk hyperlipidaemia, using in-depth interviews conducted in four polyclinics, many PCPs felt that seeing the same patient repeatedly over time helps build good doctor-patient relationship which in turn helps to facilitate statin therapy optimisation.[33]

Continuity of follow-up of low-risk breast cancer recurrence survivors. Another qualitative study in Singapore conducted explored the role of PCPs participating in a community-based shared care breast cancer survivorship model with breast cancer specialists. Seventy PCPs participated (55 from polyclinics, 15 from private GPs). Eleven focus groups (each with 3-8 PCPs) and six in-depth interviews were conducted. In the discussions, it was felt that breast cancer survivors suitable for this type of follow-up were those with low risk of breast cancer recurrence. This model of shared care survivorship follow-up was perceived favourably by the participating PCPs as it "echoed principles of primary care to provide holistic and well-coordinated care".[34]

6. Managing Secondary Genomic Findings

A secondary genomic finding is defined as "a genomic variant if potential medical value that is unrelated to the primary reason for testing". An approach consisting of a framework of five domains of evaluation has been proposed, namely: (1) medical history; (2) physical examination; (3) family history; (4) diagnostic phenotypic testing; and (5) variant correlation. With this approach, both geneticist healthcare providers (GHPs) and PCPs can maximise their ability to detect and manage the risks of genomic disease and avoid the risk of overdiagnosis.[35]

Facilitators and Barriers in Co-Managing Patients with Genetic Conditions

Facilitators. Strategies, such as tele-genetics, promotion of evidence-based guidelines, point-of-care risk assessment tools, tailored education in genetics-related topics, and other system-level strategies will facilitate better genetics and primary care integration, which in turn might improve genetic service delivery.[35]

Barriers. In co-managing patients with GHPs, PCPs can leverage on the collaborative relationship with GHPs to overcome barriers that might occur at the system, provider, or patient levels, as has been discussed earlier.[19]

Although it is ideal for PCPs to have a prominent role in genomics, research suggests that PCPs may be unprepared for this task in view of limitations in their knowledge about basic genetics and confidence in collecting and interpreting family history data, along with attitudes and concerns about patient distress.[1,37] (Scheuner et al., 2008; Mikat-Stevens et al., 2015). Continuing improvement and partnership with GHPs is the way forward.

CONCLUSION

PCPs play an essential role in the provision of appropriate genomics services, in improving access, in co-managing patients with GHPs, and in providing scientific understanding of genomics to the community.

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- **Figure 1:** Harding B, Webber C, Rühland L, et al. Bridging the gap in genetics: a progressive model for primary to specialist care. BMC Med Educ. 2019 Jun 11;19(1):195. doi: 10.1186/s12909-019-1622-y. PMID: 31185964; PMCID: PMC6558677.
- **Figure 2:** Seibel E, Gunn G, Ali N, Jordan E, Kenneson A. Primary Care Providers' Use of Genetic Services in the Southeast United States: Barriers, Facilitators, and Strategies. J Prim Care Community Health. 2022 Jan-Dec;13:21501319221134752. doi: 10.1177/21501319221134752. PMID: 36345220; PMCID: PMC9647281.

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LEARNING POINTS

- **Primary care physicians (PCPs) are well-placed to provide genomic education and clinical services to their patients in partnership with Genetics Healthcare Professionals (GHPs).**
- **The role of PCPs covers the following six tasks: Screening and early detection; risk assessment & timely referral; safe prescribing; preventive care; care of co-morbidities & continuity of care; and managing secondary genomic findings.**
- **Continuing improvement and partnership with GHPs is the way forward.**
