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Establishing a Cancer Genetics Programme in Asia – the Singapore Experience

Wei-Shieng Chieng, Soo-Chin Lee

Department of Haematology-Oncology, National University Hospital, Singapore

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Corresponding author: Soo-Chin Lee, MD, Department of Haematology-Oncology, National University Hospital, 5 Lower Kent Ridge Road, Main Building Level 2, Singapore 119074, tel.: 6772-4621, e-mail: Soo_Chin_Lee@nuh.com.sg

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Abstract

Cancer genetics is now an established oncology subspecialty with the primary prevention role of identifying high-risk individuals through genetic information for enrolment into screening and preventive programmes. Integrated into major Western centres since the late 1990s, such a programme has been established in Singapore since 2001. Our programme has evaluated 367 index patients comprising mainly breast and colorectal cancer cases. Cancer patients were receptive to genetic counselling, but cost posed a major barrier to genetic testing. However, when the cost barrier was removed through government subsidy plans, more than half of high-risk patients still declined testing. The major barriers were reluctance to involve family members, perception that the information would not change management, and fears of negative feelings. Confirmed mutation carriers were compliant to screening and receptive to prophylactic surgery. Uptake of predictive testing among cancer-free family members has been low, possibly arising from the stigma associated with cancer in our Asian culture. These potential barriers are being addressed through government subsidy plans, continuing education to increase awareness, and being culturally sensitive when dealing with the Asian family.

Introduction

About five to ten percent of all cancers are hereditary and due to germline mutations in cancer predisposition genes [1]. Advancements in molecular biology and genetics in the last 1-2 decades have enabled the cloning of key cancer predisposition genes, resulting in better characterization of major hereditary cancer syndromes. These include hereditary breast and ovarian cancer syndrome due to the *BRCA1/2* genes [2, 3], hereditary non-polyposis colorectal cancer syndrome due to the mismatch repair genes [4-6], and familial adenomatous polyposis due to mutations in the *APC* gene [7]. The recognition of these syndromes and the establishment of management guidelines have led to the development of cancer genetics as a subspecialty in oncology [8-13]. Cancer genetics services have been incorporated into routine cancer services in major oncology centres in the West since the late 1990s. Such services represent an important primary prevention arm of oncology in its role of identifying high-risk individuals through family history assessment or genetic testing, and to enrol them into early cancer detection and prevention programmes, with the ultimate goal of reducing cancer burden and mortality.

Singapore is a small country of 699 km^2 in South East Asia and home to 4 million people. Cancer is one of the major causes of mortality, and about 7800 cancer cases are diagnosed every year, with the leading

cancers being lung, colorectal and breast cancers [14]. Health care in Singapore is provided through 9 public hospitals, 7 private hospitals, 16 government outpatient polyclinics, and some 1900 private medical clinics. Of the 9 public hospitals, two are tertiary hospitals that offer comprehensive cancer services, encompassing surgical, medical, and radiation oncology specialties. Cancer genetics services have been formally incorporated into the cancer services of both tertiary hospitals since 2001.

Singapore is a multi-ethnic country comprising three major Asian ethnic populations: Chinese (77%), Malay (14%), and Indian (8%). The Chinese and Indians are largely first- or second-generation migrants from China and Southern India, while the Malays are indigenous to the regions including Malaya, Sumatra, Java, and the other islands of the Indonesian archipelago. English is the official language, but Mandarin and Chinese dialects are the preferred languages used at home among 35% and 24% of Singaporeans respectively, followed by English (23%), Malay (14%) and Tamil (3%). The average monthly household income in Singapore is S$4,943 (US$2,907), with 27% earning less than S$1,999 (US$1,176) [15].

Health cost is made affordable to the Singaporean public through government subsidized medical services at the public hospitals and outpatient government polyclinics through a co-payment system, where citizens pay a percentage of the medical bill, with the remainder subsidized by the government. This is aided by compulsory medical savings for every working adult, who contributes 6-8% of his or her monthly salary to a personal Medisave account that can be utilized to pay inpatient medical costs and outpatient cancer treatment.

Cancer Genetics Programme at the National University Hospital, Singapore

The cancer genetics programme at the National University Hospital, Singapore, is directed by a medical oncologist (SCL), who trained in cancer genetics at the John Hopkins University School of Medicine, USA, and was credentialed in 'Familial cancer risk assessment and management' by the Institute for Clinical Evaluation in the USA. The programme is assisted by a full-time cancer genetics counsellor (WSC), who is a graduate in Biomedical Science and who trained on the job.

The clinic receives patient referrals from specialists within the hospital and from other government hospitals, specialists practising in the private sector, as well as primary care physicians. The National University Hospital cancer service sees about 1500 new cancer cases every year, including approximately 600 new breast and colorectal cancers. Three-generation family cancer history forms are given routinely to all cancer patients at the hospital Cancer Centre. These forms are screened by the genetics counsellor to identify high-risk patients, such as those with young onset cancer, familial cancer clustering, and multiple primary cancers, who would warrant genetics risk assessment. High-risk cases are flagged to the primary cancer physician for referral to the cancer genetics programme.

The programme currently runs a weekly clinic, evaluating 1-5 patients per session. Patients who are referred from the government hospitals and polyclinics pay the subsidized rate of S$21 (US$12) for both first and follow-up visits. Patients who are self-referred, or referred by private hospitals and general practitioners, pay the full consultation fee of S$75 (US$44) and S$50 (US$29) for first and follow-up visits respectively.

The duration of each new case consultation is 45-60 minutes, while a typical follow-up visit lasts 15-20 minutes. Patients are evaluated and counselled individually or with their family members. During each new consultation, the patient's cancer and family histories are evaluated and an assessment made. Patients are classified as low, modest, moderate, or high risk of having a hereditary cancer syndrome, and are counselled accordingly. Patients assessed to be at low risk are given cancer screening recommendations pertaining to themselves and their family members based on their cancer and family history. Those assessed to have at least 10% chance of having a hereditary cancer syndrome are given genetic counselling for the particular syndrome [16], including the mode of inheritance, projected lifetime cancer risks, genetic testing including test interpretation and potential benefits and disadvantages of testing, and screening and preventive options [1]. The counselling session is conducted using picture aids, in English, Mandarin, a Chinese dialect, or Malay through an interpreter, according to the patient's preference. At the end of the session, a pamphlet in English or Mandarin summarizing the pertinent features of the hereditary cancer syndrome discussed is given to patients to facilitate retention of information. Pamphlets in Malay and Tamil are currently not available but may be developed in the future. Patients are given 1-2 weeks to assimilate and share the information with their family members. They are then followed up by a phone call or a separate clinic visit to address queries that may arise.

Genetic testing that is offered through the programme includes *BRCA1/2* comprehensive sequencing and single site mutation analysis for hereditary breast and ovarian cancer syndrome, *MLH1/MSH2* comprehensive sequencing and single site mutation analysis and tumour microsatellite instability testing for hereditary non-polyposis colorectal cancer, *APC* protein truncation test for familial adenomatous polyposis, and sequencing of exons 10, 11, 13-16 of the *RET* proto-oncogene for multiple endocrine neoplasias 2A and 2B [17, 18]. The latter three tests are offered by local laboratories, and cost S$260-370 (US$153-218) per test. *BRCA1/2* and *MLH1/MSH2* comprehensive sequencing and respective single site mutation analysis are performed at Myriad Genetics Laboratories (Salt Lake City, Utah, USA) at the cost of S$5,058 (US$2,975), S$3,315 (US$1,950), and S$595 (US$350) respectively. Karyotyping for chromosomal abnormalities is offered locally, while genetic testing for rare conditions such as von Hippel Lindau syndrome and E-cadherin gene analysis for hereditary diffuse gastric cancer syndrome [19] is performed in overseas laboratories. Costs for genetic testing are all out-of-pocket expenses as they are not subsidized by the Singapore government nor payable using Medisave. Since the initiation of the programme, colorectal cancer patients fulfilling eligibility criteria may opt to be tested for germline *MLH1/MSH2* mutations free of charge as part of a research protocol. Since September 2003, patients assessed to have at least 30% chance of carrying a *BRCA1/2* mutation are eligible to receive a 100% subsidy for *BRCA1/2* sequencing, while their family members are eligible to a 50% subsidy for predictive testing through a special government subsidy programme.

Demographic information, cancer history, family history, genetic risk assessment information, screening recommendations, and genetic test results of patients evaluated in the cancer genetics programme are collected and stored in a user-defined and password-protected database.

Results

As cancer genetics is a new field in Singapore, we conducted a questionnaire survey in 2002, shortly after we started the programme, to assess the level of knowledge on breast cancer risk factors and hereditary breast cancer syndrome. Among 284 health professionals and 221 medical students surveyed, less than a quarter recognized that paternal family history of cancer is as important as maternal family history in evaluating for hereditary breast cancer syndrome, and less than half were aware that genetic testing for hereditary breast cancer is clinically available, or that prophylactic mastectomy is a preventive option for women at high risk for breast cancer (Table 1) [20]. This general lack of awareness on emerging diagnostic and preventive options for hereditary breast cancer syndrome was identified as an important potential barrier to optimal utilization of the cancer genetics service, and active steps were taken to promote awareness through continuing medical education.

We next conducted a questionnaire survey to evaluate the acceptance and potential motivators and barriers of breast cancer genetic counselling among breast cancer patients and cancer-free women. About 70% of the 313 respondents indicated interest in attending genetic counselling when medically indicated and perceived the potential benefits. Higher education level among respondents was associated with greater acceptance of genetic counselling. Important motivators were learning about cancer risk and cancer detection,

Table 1. Awareness of breast cancer risk factors and genetics among health professionals and medical students (n=505)

Questionnaire items	Percentage of correct response			
	doctors (n=124)	nurses (n=124)	paramedical staff (n=36)	medical students (n=221)
to determine if a patient is at risk for hereditary breast cancer, the maternal family history is more important than paternal family history[a]	22	19	27	20
preventive mastectomy may reduce breast cancer risk and may be recommended for women at high risk for breast cancer[a]	55	31	35	44
genetic testing for hereditary breast cancer through a blood test is now clinically available[a]	62	41	40	56
genetic breast cancer makes up **5-10%** of all breast cancer[b]	45	15	24	59

[a]respondents were given the options 'true', 'false', or 'don't know'; [b]respondents were given the options '<1%', '5-10%', '20-30%', '50-60%', or 'don't know'

Table 2. Acceptance, potential motivators and barriers of breast cancer genetic counselling among breast cancer patients and cancer-free women (n=313)

	Percentage
Education level	**willing to attend genetic counselling**
<10 years formal education	73
10-12 years formal education	82
university/post-graduate	92
	p=0.024
important motivators	**% citing motivator as important**
I can learn what to do to reduce my cancer risk	91
I want to know my cancer risk	89
I can learn what to do to detect cancer early	89
information may help my family understand their cancer risk	86
information may help my family make better health decisions	85
the doctor asked me to	81
important barriers	**% citing barrier as important**
I already have cancer and it does not make a difference	63[a]
I am concerned about the cost	58
I do not like to hear bad news	43
I will not know what to do with the information	42

[a]responses of breast cancer patients only

helping the family, and the doctor's recommendation. Important barriers were the misperception that cancer patients could not gain personally, cost issues, fears of bad news, and concerns of inability to make use of the information (Table 2) [21].

From January 2001 to March 2006, 367 new patients were evaluated at the cancer genetics clinic. 72% of referrals were from within the institution, while 28% were from other hospitals or clinics outside the institution. Patients with suspected hereditary breast cancer (60%) and colorectal cancer syndromes (31%) formed the majority of cases (Table 3). 87% of patients were assessed to have at least 10% chance of having a hereditary cancer syndrome and therefore offered genetic counselling and testing. Of these, 40% underwent genetic testing, and 23% of those tested were found to carry deleterious germline mutations (Table 4).

From July 2003, cancer patients and their accompanying family members were surveyed after the genetic counselling session (Table 5). The age distribution of the 110 cancer patients (median 37, range 23-77) and 95 cancer-free family members (median 39, range 16-65) surveyed were similar. Cancer-free family members who attended genetic counselling were more educated and more likely to express interest in genetic testing than cancer patients, with 81% indicating that they would definitely or probably take up genetic testing if medically indicated compared to 61% of cancer patients. For both groups, the most common motivators for genetic testing were to help their children and family members. Concerns about the cost of testing and belief that the information could not prevent another cancer were the most common reasons cited for not undertaking genetic testing. More than 80% of respondents indicated willingness to share genetic information with siblings and spouses, but only about 70% were willing to share the information with their parents. After the counselling session, 30% and 22% of all respondents felt 'interested' and 'empowered or informed' respectively. Cancer patients were more likely to experience negative feelings after the session compared to cancer-free family members.

A total of 182 index patients were evaluated to have at least 10% chance of carrying a *BRCA1/2* mutation and offered genetic testing. 48% were young onset breast cancer patients without significant family history, 38% were from breast cancer families, 12% were from breast-ovarian cancer families, and 2% were patients with male or bilateral breast cancers. 53/182 (29%) eventually underwent *BRCA1/2* comprehensive sequencing. There was no significant difference in ethnic group, age, and marital status between the acceptors and decliners. 28% of young breast cancer patients and 17% of patients from breast cancer families underwent testing, while 62% of index patients from breast-ovarian cancer families were tested. Seventeen patients (17/53, 32%) were found to carry deleterious germline *BRCA1/2* mutations. Family histories of breast or breast-ovarian cancer were the strongest predictors of finding a

Table 3. Characteristics of patients reviewed in the cancer genetics clinic (n=367)

age	
median (range)	39 (17-80)
ethnic group	
Chinese	78%
Malay	11%
Indian	4%
others	7%
index patient has cancer	74%
risk categories	
breast cancer-related cases (n=219)	
low risk (<10%) for hereditary breast cancer (HBC) syndrome	12%
modest risk (10-20%) for HBC syndrome	65%
moderate risk (20-40%) for HBC syndrome	11%
high risk (>40%) for HBC syndrome[a]	12%
colorectal cancer-related cases (n=114)	
low risk (<10%) for hereditary colorectal cancer (HCRC) syndrome	4%
modest risk (10-20%) for HCRC syndrome	61%
moderate risk (20-40%) for HCRC syndrome	24%
high risk (>40%) for HCRC syndrome[b]	11%
others (n=34)[c]	
familial clustering of stomach cancers/young stomach cancers	35%
familial cancer clustering in a pattern not distinctive of known hereditary cancer syndromes	30%
others[d]	35%

[a]include 10 patients counselled for predictive testing for a familial mutation; [b]include 1 patient counselled for predictive testing for a familial mutation; [c]18 patients were deemed to have at least 10% chance of having a known hereditary cancer syndrome and offered genetic counselling and testing; [d]familial clustering of or young nasopharyngeal cancers (9%), familial clustering of renal cancers (9%), suspected Li Fraumeni syndrome (6%), familial clustering of paragangliomas suspicious of *SDHD* mutations (3%), multiple endocrine neoplasia IIA (3%), suspected neurofibromatosis (3%), Turner's syndrome with young endometrial cancer (3%)

deleterious mutation (Table 6). Of the 17 index patients found to carry *BRCA1/2* mutations, five had bilateral mastectomy for breast cancers, and three had bilateral oophorectomy for ovarian cancer. Among the 12 carriers with intact breast(s), two (17%) opted for prophylactic mastectomy, and two (17%) are considering the option. Among the 14 carriers with intact ovaries, three (21%) opted for prophylactic oophorectomy and three (21%) are considering the option. Compliance to breast cancer screening with mammography among the high-risk breast cancer patients evaluated at the cancer genetics programme is 84%, while that of *BRCA1/2* mutation carriers is 94%.

Twenty cancer-free family members were counselled for *BRCA1/2* predictive testing. Of these, 55% were siblings and 25% adult children of the index patient, while the remaining were second- or third-degree relatives (15% nieces, 5% cousins). 67% of cancer-free family members who attended counselling for predictive testing were married, and 50% had more than 10 years of formal education. Seven eventually underwent testing, of whom six (86%) were found to carry deleterious mutations and are now on surveillance programmes. Two cancer-free mutation carriers are considering prophylactic surgery.

Sixty-six high-risk colorectal cancer patients were tested for *MLH1/MSH2* mutations, predominantly as part of a research protocol free of charge. Nine mutation carriers (14%) were identified. Fourteen family members had undergone predictive testing, and 6 were

found to carry deleterious mutations and are on surveillance. None of the carriers had undergone prophylactic surgery. Factors that were associated with deleterious germline mutations include family history fulfilling Amsterdam I/II criteria (60%), proband with early onset colorectal cancer and family history of colorectal cancer or extracolonic cancers (46%), proband with colorectal cancer and family history of stomach cancer (40%), and proband with colorectal cancer demonstrating high microsatellite instability (36%) [22]. In contrast to what was reported in the West [23], family history of endometrial cancer predicted poorly for a deleterious mutation [22]. Compliance to screening colonoscopy among mutation carriers is 77%.

Among the potential barriers uncovered through our previous hypothetical questionnaire survey, we found cost to be a major practical barrier to genetic testing. Prior to the initiation of the government subsidy programme for *BRCA1/2* testing in 2003, 67/70 (96%) breast cancer patients offered genetic testing declined the test, with the majority citing cost as a major barrier. After the initiation of the subsidy programme, 47/106 (44%) eligible patients underwent *BRCA1/2* testing at 100% government subsidy. However, 59/106 patients (56%) still declined genetic testing despite removal of the cost barrier. A telephone survey of 39/59 (66%) patients who declined testing revealed the following major reasons: siblings/family members were not keen to know of such information or to be tested (41%), perception that testing would not prevent cancer recurrence or alter medical management (39%), and concerns about negative feelings associated with genetic test results (31%) (Table 7).

Table 4. Genetic testing in Cancer Genetics Programme, National University Hospital, Singapore

patients who underwent genetic testing (n=127)	
test category	%
BRCA1/2 comprehensive sequencing	42
MLH1/MSH2 sequencing	52
APC protein truncation test	2
others[a]	4
patients with germline deleterious mutation identified (n=29)	%
BRCA1/2 mutation	59
MLH1/MSH2 mutation	31
APC mutation	3
others[b]	7

[a]others: comprehensive sequencing and rearrangement analysis for von Hippel Lindau (2), karyotyping for Turner's syndrome (1), sequencing for E-cadherin gene mutation (1), sequencing for *SDHD* gene mutation (1); [b]others: Turner's syndrome (1), *SDHD* deleterious mutation (1)

Discussion

Cancer is a leading cause of morbidity and mortality in Singapore [14], and cancer genetics and risk assessment programmes represent the primary prevention arm of oncology. As a new programme in a mature comprehensive cancer centre, our current workload of approximately 75 new cases annually is close to the target 60-120 new referrals that are expected to arise from our institution. This has in part been attributed to our standard procedure to obtain family cancer history from each new cancer patient to identify high-risk patients for referral into the programme. In addition, the success of continuing medical education to increase awareness among physicians has been reflected by increasing referrals from outside the institution, now accounting for about 30% of our new cases.

In contrast to developed nations in the West, where lay press and lay media routinely report new medical advances and provide patients and community physicians easy access to new medical knowledge, health providers in Singapore generally rely on medical journals and seminars for information on medical advances, while patients rely on their health providers for pertinent medical information. Consequently it comes as no surprise to find only a handful of health providers in Singapore who are aware of *BRCA1/2* genetic testing or prophylactic surgery for high-risk individuals. More importantly, lack of awareness of the mode of inheritance of the *BRCA1/2* gene has led many health providers to have the mistaken notion that paternal family history is not as important as maternal family history in evaluating for hereditary breast cancer syndrome [20]. Such information has been critical for us to focus continuing medical education efforts on filling important knowledge gaps.

Cost has been cited as an important barrier to genetic counselling and testing in many prior studies, including our own [21, 24, 25]. While genetic counselling is available to Singaporeans at a subsidized and affordable rate, genetic testing is not. In fact, although a significant proportion of index patients expressed interest in *BRCA1/2* testing, the uptake rate was a dismal 4% prior to 2003 when the cost of testing was not subsidized. This posed a significant barrier to downstream work of risk

Table 5. Survey on genetic testing (n=205)

Category	Percentage		
	cancer patients (n=110)	cancer-free family members (n=95)	p-value[a]
breast cancer-related cases	74	42	0.000
colorectal cancer-related cases	23	57	
others	3	1	
education level			
≤6 years formal education	11	5	0.036
6-10 years formal education	36	25	
>10 years formal education/diploma	24	22	
university/ post-graduate degree	29	48	
perception of likelihood of carrying genetic mutation			
very certain of carrying mutation	6	2	0.020
quite certain of carrying mutation	36	19	
not sure	39	52	
quite certain of not carrying mutation	16	21	
very certain of not carrying mutation	3	6	
taking genetic test if medically indicated?			
yes definitely	33	53	0.004
yes probably	28	28	
not sure	20	15	
no probably	8	1	
no, not at all	11	3	
reasons for undergoing genetic testing[b]			
beneficial to children	60	58	0.777
beneficial to family members	51	43	0.326
understand my cancer risk	16	38	0.000
motivates me to go for cancer screening	18	34	0.015
reasons against genetic testing[b]			
cost	21	8	0.018
can't prevent another cancer	12	11	0.827
may feel depressed/angry/upset/stressed	9	7	0.801
worried about feelings of family	8	5	0.580
worried about insurability	5	7	0.553
will share information with			
parents	68	76	0.278
siblings	87	95	0.090
children	66	72	0.447
spouse	82	82	1.000
feelings after genetic counselling[c]			
negative feelings[d]	40[e]	24[f]	0.018
indifferent	29	14	0.011
interested	26	35	0.169
empowered/informed	19	24	0.398
relieved/satisfied	12	23	0.040

[a]statistical analysis was performed using Chi-square test for categorical variables, and Student's t-test for age; [b]respondents were allowed to cite more than one reason; [c]respondents may describe more than one kind of feelings; [d]respondents may describe more than one kind of negative feelings; [e]negative feelings: anxious (19%), burdensome (8%), upset (8%), confused (7%), distracted (4%), afraid (4%), numb (3%), shocked (3%), angry (2%), stressed (2%), depressed (1%); [f]negative feelings: anxious (13%), afraid (5%), confused (4%), upset (4%), stressed (4%), burdensome (3%), depressed (3%), distracted (3%), numb (1%)

segregating individuals and tailoring screening and preventive recommendations using genetic testing. Under the special government subsidy programme that provided free *BRCA1/2* testing for index patients, we observed an eleven-fold increase in genetic testing uptake rate to 44%, allowing mutation carriers to be identified and facilitating predictive testing in cancer-free family members. This highlights the importance of overcoming cost as a barrier to allow the full realization of the potential of a cancer genetics programme.

Despite removing the cost barrier, we found more than half of eligible patients to still decline genetic testing, suggesting that other barriers exist. A survey on the decliners revealed a striking reluctance to involve family members. The central role of the family in Asian culture is underscored by the fact that more than 80% of respondents in a hypothetical situation [21], and more than 50% of high-risk patients who underwent genetic counselling in our population, cited 'helping the family' to be an important motivator to attend genetic counselling and undertake genetic testing respectively. Yet, when it comes to actual genetic testing and the real possibility of involving family members for predictive testing, two-fifths of decliners cited 'siblings/family members not keen' to be the reason. Even among families with deleterious *BRCA1/2* mutations, fewer than 2 family members per index patient have attended genetic counselling, and less than 1 family member per index patient has opted for predictive testing, highlighting the complexity of involving cancer-free family members in cancer predisposition testing. This low uptake in predictive testing has similarly been reported both in the West and in Asia [26, 27]. It was also noteworthy that while over 80% of patients counselled were willing to share genetic information with spouses and siblings, only about 70% were willing to involve the older generation such as their parents. These behaviours may stem from traditional Asian beliefs that cancer is a curse that is associated with a stigma and therefore shameful to discuss, causing some cancer patients to be unwilling to broach the subject with cancer-free family members. Cancer is also viewed as a taboo in traditional Chinese beliefs, and many may feel that discussing it freely in the family or testing for cancer predisposition constitutes bad luck [28-31]. Indeed, one-third of patients described 'negative feelings' after receiving genetic counselling, and about 30% of high-risk breast cancer patients who declined genetic testing were worried about 'negative feelings' that the test results may incite. These concerns may be amplified in our traditional Asian society [32].

Table 6. Nature of *BRCA1/2* deleterious mutations and factors associated with deleterious *BRCA1/2* mutation (n=17)

	Percentage
nature of deleterious mutation	
frameshift	59
nonsense	23
large deletions/rearrangements	18
probability of identifying deleterious *BRCA1/2* mutation based on risk profile	
cancer patient with family history of breast and ovarian cancer (n=13)	54
cancer patient with family history of breast cancer (n=12)	50
young onset breast cancer without family history of cancer (n=25)	16
male breast cancer/bilateral breast cancer (n=3)	0

Table 7. Demographic characteristics of index patients who declined *BRCA1/2* testing despite test cost subsidies and reasons for declining (n=39)

age	
median (range)	36 (23-77)
married	80%
educational level	
≤6 years formal education	20%
6-10 years formal education	23%
>10 years formal education/diploma	30%
university/post-graduate degree	27%
reasons for declining genetic testing[a]	
siblings/family members not keen	41%
doing this test would not prevent recurrence/change anything much	39%
fear of negative feelings associated with knowing genetic test results	31%
worried about feelings of family	13%
worried about insurance/employability	10%
50% subsidy for predictive testing is still a barrier[b]	8%
sceptical about modern medicine such as genetic testing	3%

[a]patients were allowed to indicate more than one reason for declining test; [b]cost of single site mutation analysis in predictive testing is S$595 (US$350) and the Singapore government provides 50% reimbursement

The low uptake of predictive testing is contrary to our survey finding of high interest in genetic testing among cancer-free family members who attended genetic counselling. One reason could be that family members needed more time to decide on predictive testing, since many index patients had only been confirmed to carry mutations in the last 2-3 years [24]. Another reason for this discrepancy is the possibility that cancer-free family members who attended genetic counselling represent a select and more health-conscious population, but who may ultimately not have access to genetic testing because the index patient opted not to be tested or was not found to carry a mutation. In addition, while many family members may express interest in the hypothetical situation, when faced with the real prospect of genetic testing, they may ultimately decline testing because of the fear of being labelled a gene carrier in a traditional society that views cancer as a stigma [32].

We found encouragingly high cancer screening compliance rates among the high-risk breast and colorectal cancer patients in our programme, while the uptake rate for prophylactic surgery among *BRCA1/2* mutation carriers is comparable to those reported in other centres [33, 34], with 47% of carriers undergoing or contemplating prophylactic mastectomy and/or oophorectomy in our programme.

Conclusion

Singapore is a developed nation with a comprehensive public healthcare system, and we have successfully initiated a cancer genetics programme in the context of a tertiary hospital. By increasing awareness and level of knowledge among health providers in Singapore, we hope to extend the programme to the community in the future. Certain elements unique to Singapore could enhance the success of our programme, including easy access to medical records and family members, affordable health screening services, and good doctor-patient relationships. At the same time, we have identified potential barriers that are actively being addressed. These include overcoming the cost issue of genetic testing through government assistance plans or health policy changes, continuing medical and public education to increase awareness and knowledge, and being culturally sensitive when dealing with the subject of cancer and cancer predisposition testing with the Asian family. Complex medical, social, ethical and legal aspects surround genetic testing, and we hope in the future to integrate other specialists, such as surgeons, psychiatrists, and social workers into a more comprehensive programme.

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