

ORIGINAL ARTICLE

Hereditary breast/ovarian and colorectal cancer genetics knowledge in a national sample of US physicians

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Background: Clinically relevant genetics knowledge is essential for appropriate assessment and management of inherited cancer risk, and for effective communication with patients. This national physician survey assessed knowledge regarding basic cancer genetics concepts early in the process of introduction of predictive genetic testing for breast/ovarian and hereditary non-polyposis colorectal cancer (HNPCC) syndromes.

Methods: A stratified random sample was selected from the American Medical Association Masterfile of all licensed physicians. In total, 1251 physicians (820 in primary care, 431 in selected subspecialties) responded to a 15 minute questionnaire (response rate 71%) in 1999–2000. Multivariate logistic regression analyses were conducted to identify demographic and practice characteristics associated with accurate response to three knowledge questions.

Results: Of the study population, 37.5% was aware of paternal inheritance of *BRCA1/2* mutations, and 33.8% recognised that these mutations occur in <10% of breast cancer patients. Only 13.1% accurately identified HNPCC gene penetrance as $\geq 50\%$. Obstetrics/gynaecology physicians, oncologists, and general surgeons were significantly more likely than general and family practitioners to respond accurately to the breast/ovarian questions, as were gastroenterologists to the HNPCC question.

Conclusions: These nationally representative data indicate limited physician knowledge about key cancer genetics concepts in 1999–2000, particularly among general primary care physicians. Specialists were more knowledgeable about syndromes they might treat or refer elsewhere. Recent dissemination of practice guidelines and continued expansion of relevant clinical literature may enhance knowledge over time. In addition to educational efforts to assist physicians with the growing knowledge base, more research is needed to characterise the organisational changes required within the healthcare system to provide effective cancer genetics services.

The past 10 years have seen a substantial increase in clinical research to develop appropriate risk assessment and management practices for patients at high risk of breast, ovarian, and colorectal malignancy.^{1–3} The continued expansion and dissemination of an evidence base may significantly reduce the physician knowledge gaps that were first identified during the early period of cancer susceptibility gene characterisation.⁴ Competent knowledge of cancer genetics is essential for effectively assessing and managing risk, deciding when to refer for specialty follow up, and communicating with patients and families. The manner in which physicians frame the discussion of inherited risk and options for screening or risk reducing treatment may strongly influence patient decision making.⁵ In one study, newly diagnosed breast cancer patients with suspected hereditary disease were five times more likely to undergo bilateral mastectomy compared with other or no surgery) if they reported receiving physician recommendations for the procedure, independent of *BRCA1/2* genetic test results.⁶

In 1999–2000, a national survey that examined use of and attitudes towards predictive tests for cancer risk, and the state of knowledge about key cancer genetics concepts was conducted with US physicians in primary care and selected specialties^{7,8}. This study provides nationally representative baseline data about responses to three knowledge questions ascertained at an early period in the diffusion of predictive testing into clinical practice, and evaluates physician and practice characteristics associated with accurate responses. This report also describes awareness regarding commercial availability of predictive tests for germline mutations in the *BRCA1/2*, *MLH1/MSH2*, and *APC* genes, which were developed

in 1991–95⁹ and marketed in the mid to late 1990s, prior to questionnaire administration.^{10,11}

METHODS

Survey methods

Following IRB approval, a nationally representative, stratified random sample of 2079 physicians was selected from the American Medical Association (AMA) Physician Masterfile, a database of all licensed physicians, independent of AMA membership. Practising physicians whose primary professional activity was patient care, and who were licensed to practice medicine in the state of their preferred mailing address, were stratified by specialty and systematically sampled by a fractional sampling interval after sorting by census region, urban/rural location, and sex. The physicians were selected from four primary care specialties (general internal medicine, general practice, family practice, and obstetrics/gynaecology), and four other specialties likely to provide care for cancer patients or patients at high cancer risk (oncology, general surgery, urology, and gastroenterology). They were sampled in proportion to the representation of their specialty in the US physician population, except oncologists, who were oversampled.

Recruitment methods have been described in detail elsewhere.⁷ Data collection commenced on 27 September 1999, and ended 31 March 2000. Consent was indicated by return of a self administered questionnaire by mail, fax, or a

Abbreviations: AMA, American Medical Association; HMO, health maintenance organisation; HNPCC, hereditary non-polyposis colorectal cancer

Table 1 Physician responses to questions about *BRCA1* and 2 mutations, by specialty and practice characteristics

Characteristics	Suppose you had a patient whose aunt or grandmother on her father's side carries the <i>BRCA1</i> gene mutation for breast/ovarian cancer syndrome. In your opinion, could your patient also be a carrier of this mutation?*					In your opinion, what percentage of female breast cancer patients have a <i>BRCA1</i> or <i>BRCA2</i> gene mutation?*				
	Yes (%)	No (%)	Not sure (%)	OR†	95% CI	<10 (%)	10–100 (%)	Not sure (%)	OR‡	95% CI
Total	37.5	10.6	49.0			33.8	27.4	36.7		
Medical specialty										
Family/general practice	28.1	10.8	58.0	1.0	–	21.8	26.7	49.1	1.0	–
Internal medicine	37.3	11.3	47.7	1.3	0.9 to 1.8	29.5	30.8	36.6	1.4	0.9 to 2.0
Obstetricians/gynaecologists	51.9	11.9	34.4	2.0	1.3 to 3.0	53.6	29.3	16.5	3.0	1.9 to 4.6
Oncologists	66.8	7.6	21.8	3.4	2.2 to 5.3	71.0	21.5	4.2	5.7	3.6 to 9.0
General surgeons	45.0	13.7	38.8	1.7	1.1 to 2.7	57.8	20.5	20.9	4.6	2.9 to 7.4
Gastroenterologists	24.8	6.7	68.5	0.6	0.3 to 1.4	22.4	19.9	57.9	0.9	0.4 to 2.2
Age										
≥60	37.3	5.8	53.4	1.0	–	28.7	19.7	49.2	1.0	–
40–59	36.7	11.6	48.5	0.9	0.6 to 1.3	34.7	27.5	35.6	1.4	0.9 to 2.0
<40	40.2	11.0	46.6	1.1	0.7 to 1.8	34.8	33.7	29.8	1.6	0.9 to 2.6
Cancer genetics services provided in past 12 months										
None	33.3	9.2	54.5	1.0	–	27.6	28.3	41.8	1.0	–
Did not order breast/ovarian cancer genetics tests, but did order other cancer genetics tests or referred patients elsewhere for testing or risk assessment	45.3	12.6	40.6	1.2	0.8 to 1.6	45.2	27.5	26.4	1.4	1.0 to 1.9
Ordered breast/ovarian tests but did not refer patients elsewhere	54.6	17.0	25.0	1.6	0.8 to 3.3	55.8	21.3	19.5	2.3	1.1 to 4.7
Both ordered a breast/ovarian test and referred patients elsewhere	49.0	16.6	24.3	1.4	0.6 to 3.6	58.5	18.8	17.7	2.1	0.9 to 5.4
Local facilities for genetic counselling and testing for inherited cancer risk										
No	43.2	13.0	40.5	1.0	–	33.6	37.0	28.8	1.0	–
Yes	41.6	9.5	48.3	1.0	0.6 to 1.4	43.9	28.1	26.2	1.2	0.8 to 1.9
Not sure	28.6	7.7	61.4	0.7	0.4 to 1.0	20.6	24.4	52.7	0.6	0.4 to 1.0
Clear guidelines or strategies are not available for managing patients with inherited cancer susceptibility mutations										
Agreed with statement, somewhat or strongly	40.8	12.4	45.9	1.0	–	37.1	31.1	31.6	1.0	–
Disagreed, somewhat or strongly	42.1	6.5	47.5	1.1	0.7 to 1.7	39.9	26.4	33.7	1.0	0.6 to 1.6
Not sure	22.7	5.4	72.0	0.5	0.3 to 0.8	17.1	13.1	69.1	0.5	0.3 to 0.8
Received cancer genetic test advertising										
No or not sure				1.0	–	29.3	26.8	41.8	1.0	–
Yes				1.3	0.9 to 1.8	45.7	29.8	23.7	1.2	0.8 to 1.6
Academic affiliation										
No	36.6	9.8	51.0	1.0	–	31.8	26.3	40.0	1.0	–
Yes	39.8	11.9	45.3	1.0	0.8 to 1.3	37.4	30.0	31.1	1.0	0.7 to 1.3
Specialties in the practice										
Single specialty	36.9	10.9	49.3	1.0	–	33.9	27.0	37.2	1.0	–
Multispecialty	40.8	9.9	47.6	1.1	0.8 to 1.6	34.8	29.4	34.9	0.9	0.6 to 1.4
Practice arrangement										
Full or part owner	37.6	10.1	49.6	1.0	–	33.7	26.6	37.4	1.0	–
Employee of physician practice, HMO, hospital, university, or clinic	38.0	11.0	48.5	1.0	0.8 to 1.4	33.9	28.4	36.5	1.1	0.8 to 1.6

*Unadjusted percentages representing physician responses are weighted to the U.S. population of physicians in the selected specialties. Row percentages may not add to 100% due to nonresponse to some items. †The dependent variable in the logistic regression model is awareness that a mutation can be inherited from father (referent category = no or not sure). Weighted odds ratios (OR) and 95% confidence intervals (CI) are adjusted for all variables in the table. ‡The dependent variable in the logistic regression model is understanding that <10% of female breast cancer patients carry a mutation (referent category = 10–100% or not sure). Weighted ORs and 95% CI are adjusted for all variables in the table. HMO, health maintenance organisation.

password protected Internet site, or by verbal agreement to participate in a telephone interview. The questionnaire (available at the Internet site <http://riskfactor.cancer.gov/studies/physician/status.html>) took an average of 15 minutes to complete. The final sample size was 1251, which included 820 primary care physicians and 431 other specialists. The overall response rate was 71.0%.

Statistical analysis

The first cancer genetics knowledge question assessed awareness that *BRCA1* and *BRCA2* mutations, which are associated with hereditary breast and ovarian cancers, can be transmitted through paternal inheritance. The second

question asked what percentage of female breast cancer patients will have *BRCA* mutations (<10% was considered accurate), and the third question asked about penetrance of mutations in the DNA mismatch repair genes *MLH1* and *MSH2*, which are associated with hereditary non-polyposis colorectal cancer (HNPCC) (≥50% penetrance was considered accurate). It was hypothesised that physicians would be more likely to respond accurately if they: (a) were in medical specialties involving frequent management of high risk patients (that is, oncologists, obstetricians/gynaecologists, and gastroenterologists); (b) could interact readily with cancer genetics specialists or seek access to cancer genetics information (that is, they knew of local facilities for genetic

testing and counselling, believed that relevant practice guidelines were available, had previous exposure to genetic test advertisements, had an academic affiliation, practised in a multispecialty setting, or were employees in a health maintenance organisation, university, or other setting (rather than being full or part owners of a practice)); (c) had provided a full range of cancer genetics services within the past 12 months (that is, both ordered genetic tests and referred patients elsewhere for testing or risk assessment) or, to a lesser extent, provided at least some type of service (that is, either ordered or referred); and (d) had more recent medical training (that is, younger age at the time of survey response).

Following bivariate analyses to assess response distributions by physician and practice characteristics, multivariate analyses were conducted to test these hypotheses. Independent variables were entered into full logistic regression models, in which the dependent variable was accurate response (*versus* inaccurate or unsure). Odds ratios (OR) and 95% confidence intervals (CI) were computed to assess associations adjusting for covariates. Non-significant variables were eliminated from the regression models in backwards fashion. All analyses were weighted using SUDAAN software.¹² The weight for each respondent consisted of the total number of US physicians in each physician's specialty, divided by the number of physicians in the specialty that had been sampled for the survey. The weight was multiplied by a non-response factor. Urologists (n = 45) were excluded, owing to small numbers and limited relevance of the research questions to their practice.

RESULTS

BRCA1/2 paternal inheritance

As shown in table 1, slightly over one third of respondents accurately recognised that patients could inherit *BRCA1/2* mutations through their fathers. Approximately 10% did not respond accurately, and one half were uncertain. Statistically significant differences were observed between medical specialties ($p < 0.0005$), with awareness of paternal inheritance highest among oncologists and obstetricians/gynaecologists, and lowest among gastroenterologists and family/general practitioners.

In multivariate analysis (table 1), awareness remained significantly higher among oncologists, followed by obstetricians/gynaecologists and general surgeons, relative to family or general practitioners. Physicians who were uncertain about the availability of clear guidelines or strategies for managing high risk patients were less likely to be aware of paternal inheritance (referent group "believed guidelines were unavailable"). A marginal inverse association was also observed for uncertainty about availability of local genetic testing and counselling facilities (referent group "had no facilities"). ORs suggested a somewhat higher likelihood of accurate response among physicians who had provided some type of cancer genetics services or received genetic test advertisements during the past 12 months compared with those who had not.

Percentage of breast cancer patients with BRCA1/2 mutations

Overall, one third of physicians accurately responded that <10% of female breast cancer patients carry *BRCA1/2* mutations (table 1). This percentage varied by specialty ($p < 0.0005$), ranging from 21.8% of family/general practitioners to 53.6% of obstetricians/gynaecologists and 71.0% of oncologists. Approximately a quarter of respondents overestimated the percentage of carriers, and one third were not sure. The percentage of unsure responses was markedly low among oncologists (4.2%).

In multivariate analysis, the likelihood of an accurate response was significantly higher among oncologists, obstetricians/gynaecologists, and general surgeons, relative to general or family practitioners. Response accuracy was also significantly associated with having directly ordered a breast/ovarian genetic test. ORs for having provided other types of cancer genetics services (that is, "both ordered a breast/ovarian genetic test and referred patients elsewhere", "only made referrals", or "only ordered other cancer genetic tests") were also higher. Accuracy was inversely associated with uncertainty about the availability of guidelines for testing, and marginally with uncertainty about local genetic testing and counselling facilities. Accuracy increased somewhat with decreasing age; however, the test for trend was not statistically significant ($p = 0.08$).

Penetrance of HNPCC mutations

As shown in table 2, one third of physicians underestimated the penetrance of HNPCC associated mutations, responding that colorectal cancer developed in <50% of carriers. An additional 13.1% accurately responded that penetrance was $\geq 50\%$, while half (50.9%) were not sure. Differences in accuracy were statistically significant across specialties ($p < 0.0005$). Gastroenterologists had the highest percentage of accurate responses (38.9%), although half of this specialty group (49.4%) still underestimated penetrance. Oncologists had the second highest percentage of accurate responses (25.1%), although this was markedly lower than the percentage that had responded accurately to the breast/ovarian knowledge questions.

In multivariate analysis, gastroenterologists were six times more likely than family/general physicians to correctly recognise the high penetrance of HNPCC associated mutations, and the likelihood of accurate response was also significantly elevated for oncologists and internists. As with the breast cancer knowledge questions, accuracy was associated with decreasing age (test for trend: $p = 0.01$), particularly for physicians <40 years old relative to those >60 years old. Otherwise, knowledge of penetrance was marginally associated with being an employee as opposed to an owner of the practice.

Most ORs in the breast/ovarian and colorectal models were unaltered when variables not significantly associated with response accuracy were eliminated in backwards logistic regression analysis (data not shown). One exception was that the inverse associations of younger age with accurate response became statistically significant in the most parsimonious model (1.7 (95% CI 1.1 to 2.4) for 40–59 years of age and 2.6 (1.6 to 4.2) for <40 years *v* 60+ years).

Commercial availability of tests

Table 3 shows the percentages of physicians who responded "yes", "no", or "not sure" to the question about commercial availability of predictive tests for mutations in genes associated with four hereditary cancer syndromes. For all specialties except gastroenterology, uncertainty about commercial availability was lowest for *BRCA1/2* tests. Among gastroenterologists, only 21.2% were uncertain about commercial availability of tests for the *APC* gene (for familial adenomatous polyposis), in contrast to 52.2% who were uncertain about tests for the *MLH1* and *MSH2* genes.

DISCUSSION

In this study, practising physicians displayed limited knowledge about the three key cancer genetics concepts. Only 37.5% of all physicians surveyed were aware that patients could inherit *BRCA1/2* mutations from either parent, and one third understood that these mutations occurred in <10% of breast cancers. Most notably, the percentage of "not sure"

Table 2 Physician responses to question about penetrance of HNPCC associated mutations, by specialty, practice characteristics, and age

Characteristics	In your opinion, what percentage of patients who carry a gene for hereditary non-polyposis colorectal cancer will actually go on to develop colorectal cancer?*				
	<50 (%)	≥50 (%)	Not sure (%)	OR†	95% CI
Total	33.6	13.1	50.9		
Medical specialty					
Family/general practice	30.0	9.3	58.1	1.0	–
Internal medicine	32.4	17.5	46.7	1.9	1.1–3.0
Obstetricians/gynaecologists	35.9	5.2	57.6	0.5	0.2–1.1
Oncologists	44.1	25.1	27.1	2.7	1.5–4.8
General surgeons	38.0	11.2	50.1	1.2	0.6–2.4
Gastroenterologists	49.4	38.9	11.7	6.1	2.8–13.4
Age					
≥60	34.2	5.9	57.6	1.0	–
40–59	33.8	13.1	50.5	1.9	1.0–3.8
<40	32.2	19.0	46.6	2.7	1.3–5.9
Cancer genetics services provided in past 12 months					
None	30.9	12.4	54.3	1.0	–
Did not order colon cancer genetics tests, but did order other cancer genetics tests or referred patients elsewhere for testing or risk assessment	37.9	15.0	45.5	1.3	0.8–2.1
Ordered colon cancer tests but did not refer patients elsewhere	40.8	18.5	35.2	0.9	0.3–2.8
Both ordered a colon test and referred patients elsewhere	67.8	13.7	18.5	0.9	0.3–3.2
Local facilities for genetic counselling and testing for inherited cancer risk					
No	42.1	13.8	42.7	1.0	–
Yes	37.1	14.5	46.6	1.0	0.5–1.8
Not sure	26.3	11.1	60.0	0.8	0.4–1.6
Clear guidelines or strategies are not available for managing patients with inherited cancer susceptibility mutations					
Agreed with statement, somewhat or strongly	38.6	13.8	47.0	1.0	–
Disagreed, somewhat or strongly	30.9	19.2	49.9	1.2	0.7–2.1
Not sure	13.9	7.2	78.1	0.6	0.3–1.2
Received cancer genetic test advertising					
No or not sure	30.9	12.8	54.0	1.0	–
Yes	40.7	14.1	43.6	1.1	0.7–1.7
Academic affiliation					
No	31.9	11.4	54.3	1.0	–
Yes	36.3	16.3	45.6	1.3	0.9–2.0
Practice arrangement					
Full or part owner	33.8	10.3	53.0	1.0	–
Employee of physician practice, HMO, hospital, university, or clinic	33.1	16.9	48.7	1.6	1.0–2.4
Specialties in the practice					
Single specialty	33.9	11.8	51.9	1.0	–
Multi specialty	32.9	17.6	48.6	1.1	0.7–1.6

*Unadjusted percentages representing physician responses are weighted to the U.S. population of physicians in the selected specialties. Row percentages may not add to 100% due to item nonresponse. The dependent variable in the logistic regression model is understanding that ≥50% of carriers of HNPCC associated germline mutations develop colorectal cancer (versus <50% or not sure as the referent category). Weighted ORs and 95% CI are adjusted for all variables in the table. HMO, health maintenance organisation.

respondents was 49.0% for the paternal inheritance question, and 36.7% for the mutation prevalence question, indicating considerable uncertainty about basic breast/ovarian cancer genetics concepts. Similarly, half the physicians were uncertain about the penetrance of HNPCC associated mutations, while only 13.1% accurately identified penetrance as ≥50%. In contrast to greater awareness about *BRCA1/2* test availability, two thirds were unsure about *APC* and *MLH1/MSH2* tests.

However, genetics knowledge was not uniform across medical specialties, and specialty was a stronger and more consistent determinant of response accuracy than other hypothesised factors, including age or having provided cancer genetics services during the past year. Higher response accuracy among obstetricians/gynaecologists, oncologists, and general surgeons for the breast/ovarian questions, and among gastroenterologists for the HNPCC question, may

reflect selective information seeking by specialists who had to meet the needs of their specific patient populations and who, thereby, became early providers of state of the art cancer genetics services. Direct to consumer marketing of genetic tests¹³ and family history assessment tools¹⁴ may indirectly promote information seeking by primary care providers faced with increasing patient inquiries about inherited risk.

Our findings of uncertainty and limited accuracy related to clinical genetics knowledge are consistent with reported knowledge levels in several regional,^{13 15–17} national,¹⁸ and international^{19–23} surveys conducted at a comparable time-point. In the aggregate, these findings are not unexpected given the relatively recent identification of major breast/ovarian and colorectal cancer susceptibility genes^{24 25} and the evolving understanding of their clinical implications. Continued expansion of the clinical literature, provider education programmes, and the recent dissemination of new

Table 3 Weighted percentages* (and 95% CI) of physician responses to the question about commercial availability of predictive cancer genetic tests, by medical specialty

Based on your current knowledge, are tests for the following inherited cancer susceptibility genes commercially available?								
Genes	Medical specialty							
	All specialties combined	Family or general practice	Internal medicine	Obstetrics/gynaecology	Oncologists	General surgeons	Gastroenterologists	
<i>BRCA1</i> and 2 genes for hereditary breast/ovarian cancer								
Yes	60.7 (58.0 to 63.4)	44.9 (39.6 to 50.2)	60.8 (55.5 to 66.1)	91.2 (86.7 to 95.7)	90.9 (87.0 to 94.8)	75.6 (68.0 to 83.2)	35.3 (20.6 to 50.0)	
No	4.0 (2.8 to 5.1)	4.2 (2.0 to 6.4)	4.6 (2.2 to 7.0)	2.6 (0.1 to 5.1)	1.9 (0.1 to 3.7)	5.0 (1.1 to 8.9)	2.5 (0.0 to 7.4)	
Not sure	33.2 (30.4 to 35.9)	48.6 (43.3 to 53.9)	31.6 (26.5 to 36.7)	5.7 (2.2 to 9.2)	4.0 (1.5 to 6.5)	17.7 (10.8 to 24.6)	62.2 (47.3 to 77.1)	
<i>MLH1</i> and <i>MSH2</i> genes for hereditary non-polyposis colorectal cancer								
Yes	23.1 (20.6 to 25.6)	16.8 (12.9 to 20.7)	22.7 (18.0 to 27.4)	22.4 (15.7 to 29.1)	42.8 (36.1 to 49.5)	35.7 (27.1 to 44.3)	43.8 (28.5 to 59.1)	
No	4.0 (2.4 to 5.6)	7.1 (4.4 to 9.8)	7.2 (4.5 to 9.9)	4.5 (1.2 to 7.8)	12.4 (8.1 to 16.7)	7.2 (2.7 to 11.7)	4.0 (0.0 to 9.7)	
Not sure	67.8 (65.1 to 70.5)	73.2 (68.5 to 77.9)	67.1 (62.0 to 72.2)	72.4 (65.1 to 79.7)	41.5 (35.0 to 48.0)	55.4 (46.6 to 64.2)	52.2 (36.9 to 67.5)	
APC gene for familial adenomatous polyposis								
Yes	25.7 (23.2 to 28.2)	19.6 (15.5 to 23.7)	26.2 (21.3 to 31.1)	17.5 (11.2 to 23.8)	44.0 (37.3 to 50.7)	33.0 (24.6 to 41.4)	76.4 (63.3 to 89.5)	
No	5.6 (4.2 to 7.0)	5.0 (2.6 to 7.4)	6.2 (3.5 to 8.9)	5.8 (2.1 to 9.5)	7.7 (4.2 to 11.2)	6.3 (2.0 to 10.6)	2.5 (0.0 to 7.4)	
Not sure	66.5 (63.8 to 69.2)	72.8 (68.1 to 77.5)	64.5 (59.2 to 69.8)	76.0 (69.1 to 82.9)	44.6 (37.9 to 51.3)	59.0 (50.2 to 67.8)	21.2 (8.7 to 33.7)	

*Unadjusted percentages (and 95% CI) representing physician responses are weighted to the U.S. population of physicians in the selected specialties. "Yes", "no", and "not sure" percentages within a specialty may not add to 100% due to non-response for some items.

or updated practice guidelines,^{26–29} should increase cancer genetics knowledge among a broader spectrum of physicians. However, differences in guideline recommendations between various professional organisations can result in practice variability, particularly across medical specialties.³⁰

In practice settings where genetic counselling and testing, heightened surveillance, and risk reduction interventions are relevant, physician uncertainty or inaccurate understanding of clinically significant genetics concepts can adversely affect quality of care, resulting in underutilisation of services by high risk groups and overutilisation by low to moderate risk groups. Therefore, accurate knowledge of modes of inheritance, penetrance, mutation prevalence, and management options is essential to properly informed risk assessment and decision making for both the physician and the patient.

For example, consideration of *BRCA1/2* testing and referral for genetic counselling may be appropriate for an asymptomatic 55 year old woman whose two paternal aunts had premenopausal breast or ovarian cancers. A physician who is unaware of the autosomal dominant transmission of *BRCA1/2* mutations may not obtain sufficient information about, nor give adequate consideration to, a paternal family history of these cancers. Consequently, they may not discuss indicated risk assessment or management options with patients and their families, or may fail to make appropriate referrals that could lead to better understanding of risk reducing interventions, such as tamoxifen, mastectomy, or oophorectomy. In contrast, recommendations for *BRCA1/2* testing would be inappropriate for an asymptomatic 55 year old woman whose only family history was a mother diagnosed with ductal carcinoma *in situ* at the age of 82 years. In this scenario, knowledge of inheritance patterns enables physicians to provide immediate reassurance to patients who harbour anxiety about inherited cancer based on inaccurate risk perceptions. Correction of such misperceptions may also reduce the anxiety that low to moderate risk patients convey to their family members.

Accurate recognition of the low prevalence of *BRCA* mutations in unselected breast cancer patients is critical to informed use of complex and costly risk assessment options. Physician knowledge about HNPCC gene prevalence is important for similar reasons, although this study did not specifically evaluate this. HNPCC is the most common familial colorectal cancer syndrome,³¹ and, as a disorder of both men and women, the absolute number of affected patients is larger relative to hereditary breast/ovarian cancer. Underestimation of HNPCC prevalence may result in failure

to place this condition high enough on the list of diagnostic or aetiological considerations, or to learn about or consider proper syndrome specific evaluation of patients (such as when to test appropriate tumours for microsatellite instability and *MLH1/MSH2* protein expression by immunohistochemistry or when to consider predictive genetic testing). Underestimation may also result in failure to recommend adequate frequency of colonoscopic surveillance, and to understand the practical implications of the fact that five or six different genes cause this syndrome.

If physicians underestimate HNPCC associated gene penetrance, as our data suggest, they may be less inclined to encourage patients to alert family members about inherited risk, or refer patients to a clinical setting that can provide optimum care. Consequently, the patient may not take the problem seriously enough to implement recommended management guidelines, to consider aggressive approaches to their management, or to alert at risk family members. Asymptomatic carriers may also make erroneous assumptions regarding whether the trait can be passed on to their children, as the concept of being mutation positive but phenotypically normal is confusing.

On the other hand, physician overestimation of penetrance could cause unnecessary alarm for patients, who may fail to appreciate that a substantial number (15–20%) of HNPCC related gene mutation carriers never develop colorectal cancer. It may also lead to recommendations for inappropriately aggressive management (such as more frequent colonoscopies or more serious consideration of risk reducing colectomy, hysterectomy, or oophorectomy than needed), particularly in the clinical care of families with a history suggestive of HNPCC, in which a deleterious mutation in one of the mismatch repair genes has not been identified. The complexity of HNPCC associated gene penetrance is amplified by the diversity of cancers implicated as part of the syndrome. The managing physician must not only be aware of colorectal cancer penetrance but also penetrance of endometrial (which may reach 60% among female carriers of HNPCC related mutations), ovarian, gastric, renal, brain, and small bowel cancers. Recognising that other cancers (most notably, endometrial carcinoma) are part of the HNPCC syndrome will have a substantial impact on how a physician interprets family history information and, thus, on the seriousness with which they consider HNPCC as a diagnostic possibility. Finally, it may alter their surveillance recommendations, which may need to take into account patients' susceptibility to a broader range of cancers.

A major strength of this study is that it provides a nationally representative cross sectional sample of physician knowledge regarding several clinically relevant cancer genetics concepts. The period 1999–2000 represents an early point in the diffusion of commercial tests for inherited cancer susceptibility mutations and the dissemination of clinical recommendations for risk assessment, counselling, and management of carriers. Therefore, these data can serve as a unique national benchmark for studying time trends in knowledge gaps or for comparisons with local estimates. An additional strength is the 71% response rate, which is unusually high for a physician survey. However, the specialty specific estimates were less stable for small subgroups such as general surgeons and gastroenterologists, and the data on availability of genetic tests should be interpreted cautiously, because “commercial availability” may have had different meanings for different respondents.

In conclusion, this survey confirms the continuing need to raise provider knowledge levels in cancer genetics, especially among primary care physicians. Research suggests that physicians are receptive to educational interventions to strengthen their understanding of cancer genetics,^{32–34} and that they are able to recommend risk reduction options tailored to individual patients’ risk levels.³⁵ However, lessons drawn from many other areas of medicine indicate that education alone does not necessarily translate into effective adoption of innovative practices.^{36–37} Additional research is needed to further characterise contextual factors (such as continuity and quality of care, reimbursement, literacy, and cultural competence) influencing the incorporation of cancer risk assessment and management into clinical practice,^{38–40} and the organisational changes needed within the healthcare system to provide cancer genetics services effectively.^{41–42}

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