

# Delivery of Genomic Medicine for Common Chronic Adult Diseases

## A Systematic Review

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**T**HE GREATEST PUBLIC HEALTH BENEFIT of advances in understanding the human genome will likely occur as genomic medicine expands its focus from rare genetic disorders to inclusion of more common chronic diseases, such as coronary heart disease, stroke, diabetes mellitus, and cancer. These diseases are generally due to complex interactions between variations in multiple genes and the environment and only rarely are due to single-gene forms of the disease. With genomics discoveries relating to common chronic diseases, numerous genetic tests may emerge that hold promise for significant changes in the delivery of health care, particularly in preventive medicine and in tailoring drug treatment.

Attempts to integrate genetic/genomic knowledge of common chronic conditions into clinical practice are in the early stages, and as a result, many questions surround the current state of this translation. These questions include, what are the outcomes of genomic medicine? What is the current level of consumer understanding about genomic medicine, and what information do consumers need before they seek services? How is genomic medicine best delivered? What are the challenges and barriers to integrating genomic medicine

**Context** The greatest public health benefit of advances in understanding the human genome may be realized for common chronic diseases such as cardiovascular disease, diabetes mellitus, and cancer. Attempts to integrate such knowledge into clinical practice are still in the early stages, and as a result, many questions surround the current state of this translation.

**Objective** To synthesize current information on genetic health services for common adult-onset conditions by examining studies that have addressed the outcomes, consumer information needs, delivery, and challenges in integrating these services.

**Data Sources** MEDLINE articles published between January 2000 and February 2008.

**Study Selection** Original research articles and systematic reviews dealing with common chronic adult-onset conditions were reviewed. A total of 3371 citations were reviewed, 170 articles retrieved, and 68 articles included in the analysis.

**Data Extraction** Data were independently extracted by one reviewer and checked by another with disagreement resolved by consensus. Variables assessed included study design and 4 key areas: outcomes of genomic medicine, consumer information needs, delivery of genomic medicine, and challenges and barriers to integration of genomic medicine.

**Data Synthesis** Sixty-eight articles contributed data to the synthesis: 5 systematic reviews, 8 experimental studies, 35 surveys, 7 pre/post studies, 3 observational studies, and 10 qualitative reports. Three systematic reviews, 4 experimental studies, and 9 additional studies reported on outcomes of genetic services. Generally there were modest positive effects on psychological outcomes such as worry and anxiety, behavioral outcomes have shown mixed results, and clinical outcomes were less well studied. One systematic review, 1 randomized controlled trial, and 14 other studies assessed consumer information needs and found in general that genetics knowledge was reported to be low but that attitudes were generally positive. Three randomized controlled trials and 13 other studies assessed how genomic medicine is delivered and newer models of delivery. One systematic review and 19 other studies assessed barriers; the most consistent finding was the self-assessed inadequacy of the primary care workforce to deliver genetic services. Additional identified barriers included lack of oversight of genetic testing and concerns about privacy and discrimination.

**Conclusion** Many gaps in knowledge about organization, clinician, and patient needs must be filled to translate basic and clinical science advances in genomics of common chronic diseases into practice.

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into clinical practice? By examining studies relevant to these questions, this systematic review attempts to synthesize available information on the delivery of genomic medicine for common adult-onset conditions.

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## METHODS

### Data Sources and Study Selection

A review of articles published in peer-reviewed journals between January 2000 and February 2008 was conducted using MEDLINE. Searches were conducted independently by 1 of us (M.T.S.) and a professional librarian using the following Medical Subject Headings: *genetics/genomics AND, outcomes, patient information needs/willingness to participate, delivery of services, workforce manpower issues, role of primary care, privacy issues, including insurance and employment issues*. Reference mining of retrieved articles from these searches was used to identify additional articles.

Only original research articles and systematic review articles were reviewed. Systematic reviews were defined by having described a search for literature using computerized databases (eg, MEDLINE) and the presentation of findings in a systematic way. If we identified an article as already summarized in an accepted systematic review, we excluded it to avoid double-counting data. Commentaries, essays, legal analyses, consensus statements, and editorials were excluded. Delivery of genetic services and the associated issues were different in developed as compared with developing countries; therefore, we excluded articles about developing countries.

Because we were interested in genetic services for adults who have or who are at risk for common chronic diseases, such as cancer, diabetes, and coronary heart disease, we only included articles concerning these types of conditions, including multifactorial forms of common chronic diseases, and single-gene disorders that typically present in adulthood and feature common chronic diseases, such as breast and ovarian cancer due to *BRCA1* and *BRCA2* gene mutations or iron overload due to *HFE* gene mutations. This means we excluded articles that dealt with children or adolescents; genetic disorders that generally manifest in childhood (eg, neurofibromatosis or sickle cell anemia); rare genetic disor-

ders that manifest in adulthood (eg, Huntington disease); reproductive issues; animal studies; genetically modified foods; research that did not pertain to clinical genetic services (eg, genetic association studies or studies describing participation in basic genetics research); and genetics educational resources, materials, curricula, or educational interventions for health professionals or the public.

### Data Extraction and Synthesis

Data were extracted (M.T.S.) and checked (P.G.S.) with disagreement resolved by consensus. Variables assessed included study design and topics within 4 key areas based on the key questions. We encountered 2 instances of potential overlap between topic categories and elected to resolve them as follows: we considered studies describing consumer educational needs as information needs rather than a barrier to integration of genetic services, and articles assessing use of family history in practice were classified as barriers to integration of genetic services rather than a model of integration into primary care, since these articles uniformly described inadequacies of most physicians in collecting and assessing familial risk.

Frequencies of data were tabulated and articles were grouped into topic categories. Evidence tables were created for each key area, and a narrative synthesis was performed. Because of the heterogeneous nature of the studies, we could not justify statistical pooling.

## RESULTS

The literature searches and reference mining yielded 10 866 titles. After removal of duplicates and clearly irrelevant titles, 3371 citations were reviewed, and from these, 68 articles were selected and retrieved (FIGURE).

The number of articles in each category and topic according to type of study are presented in TABLE 1. The most common study designs were cross-sectional surveys and qualitative or descriptive studies. There were 5 systematic reviews and 8 experimental studies.

### Outcomes of Genomic Medicine

We identified 16 articles that described outcomes resulting from genomic medicine. These studies were further categorized as relating to psychological, affective, and cognitive outcomes; behavioral outcomes; or clinical outcomes (TABLE 2).

**Psychological, Affective, or Cognitive Outcomes.** We identified 7 articles that assessed psychological, affective, or cognitive outcomes, including 2 systematic reviews, 2 randomized controlled trials (RCTs), 1 survey, and 2 pre/post studies. One systematic review addressed the perceived risks and psychological and behavioral impacts of genetic testing in adults with a family history of disease.<sup>1</sup> A total of 35 articles involving 30 studies met criteria for this review. Only 1 RCT was included, 2 were cross-sectional studies, and the remainder had prospective designs.

Sixteen studies described outcomes for hereditary breast and ovarian cancer, 11 for hereditary nonpolyposis colorectal cancer, 1 for both hereditary breast and ovarian cancer and hereditary nonpolyposis colorectal cancer, and 2 for Alzheimer disease. The majority of the studies reported negative effects on affective outcomes for individuals found to carry genetic susceptibility mutations—but these effects were generally short-lived, and there were generally no differences between carriers and noncarriers with respect to perceived risk 12 months after genetic testing. An increase in screening behavior was observed in carriers, but the change was less than expected.

We identified another systematic review that addressed the effects of genetic counseling and testing for breast cancer susceptibility.<sup>2</sup> This review identified 15 studies, which were mostly observational in design, and concluded that, in general, counseling and testing was not associated with increased psychological distress and was associated with some improvements in decreased worry, anxiety, and depression.

One RCT involving obese individuals found that consultation that included genetics content did not have

negative effects on self-efficacy, self-control, or increase in body weight after 6 months. In addition, the individuals with a family history of obesity who received consultation with genetics content reported significant improvement of negative mood after 6 months.<sup>3</sup> Another RCT reported that education and personalized prevention recommendations increased the accuracy of risk perception without increasing worry in adult nondiabetic offspring of diabetic parents.<sup>4</sup>

The importance of risk perception associated with family history was described in a survey of patients with and without a family history of colorectal cancer. Being screened appropriately was significantly associated with a high perception of risk for colorectal cancer among those with a family history.<sup>5</sup> The remaining identified studies were pre/post in design, assessing psychological or affective outcomes in pa-

tients before and after genetic counseling, and reported improvements in satisfaction, knowledge, and reductions in worry.<sup>6,7</sup>

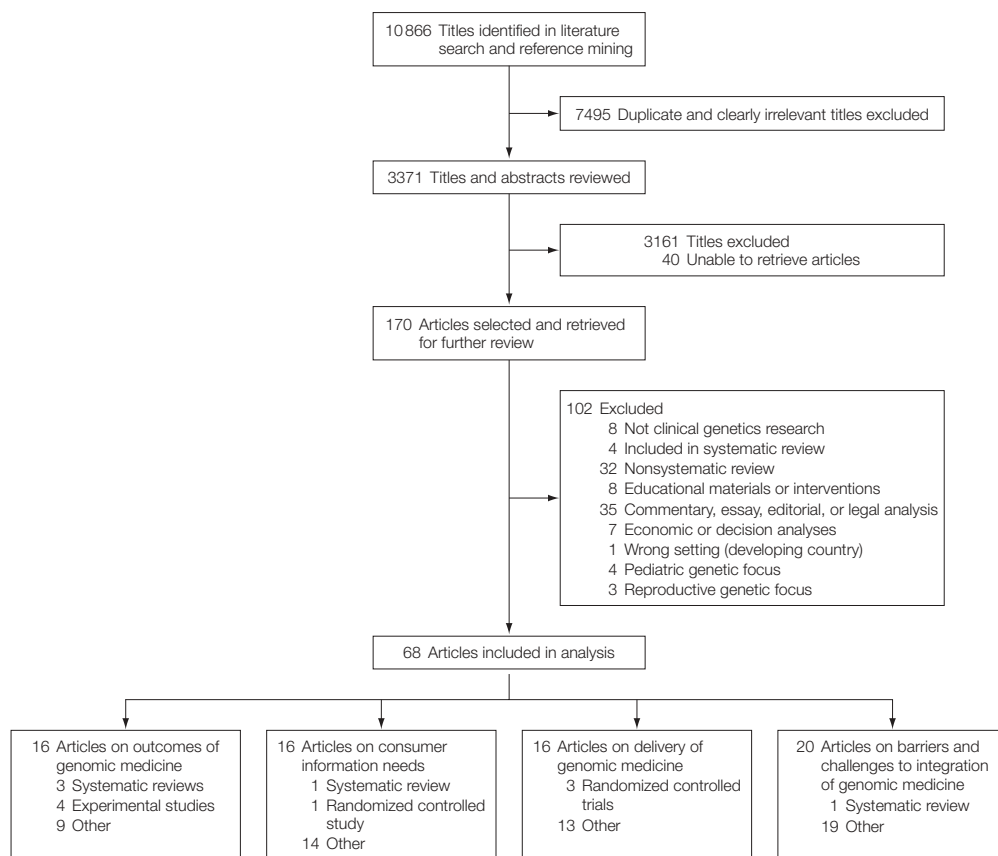
**Behavioral Outcomes.** We identified 5 articles relating to patient or clinician behavioral outcomes resulting from genetic services. A systematic review of 11 studies assessing patients' behavioral responses to genetic risk information relating to cancer and heart disease concluded that results were mixed, with some studies showing no change in behavioral outcomes, whereas other studies reported increased motivation to participate in cancer screening.<sup>8</sup>

Results from a survey of US physicians about exposure to and attitudes toward advertisements for genetic tests for inherited cancer susceptibility found that 27% had received advertising for genetic susceptibility tests and 25% felt that such advertising would be important in

their decision-making to recommend testing.<sup>9</sup> Another survey of primary care clinicians in the United States assessed factors influencing whether these physicians would order a genetic test to individually tailor smoking-cessation treatment. The study found that the most important factors for ordering such a test included the ability to more precisely target smoking-cessation treatment and to encourage patients with the knowledge that their treatment was tailored. However, concerns about genetic discrimination were an important barrier.<sup>10</sup>

A survey of Massachusetts family physicians found that physicians expected their patients to be more likely to get screened for cancer and make lifestyle and behavioral changes if genetic testing identified them as at increased risk.<sup>11</sup> Survey data from 65 patients with history of depression found that depressed patients reported that they were

**Figure.** Literature Flow



willing to pay for improvements in treatment response to antidepressant medication, and their stated willingness to pay for a 5% improvement in treatment response exceeded the price of a pharmacogenetic test.<sup>12</sup>

**Clinical Outcomes.** We identified 4 studies that assessed clinical outcomes. A pre/post study assessed women with *BRCA* mutations and reported that after counseling, 15% and 50% underwent risk-reducing surgery for breast and ovarian cancer, respectively, and 4 early stage cancers were identified. Among women who did not undergo prophylactic surgery, recommended cancer screening increased.<sup>13</sup>

A nonrandomized comparison of Greek patients who had at least 2 unsuccessful attempts at weight loss compared conventional diet and nutrition counseling with nutrition counseling informed by a nutrigenomics test result. For the first 300 days, weight loss between groups was not statistically different, but among the 50% of patients with more than 300 days of follow-up, there was a statistically significant difference of about 5 kg, with the test group weighing less on average.<sup>14</sup>

We identified only 1 RCT of a genetic testing intervention for a common condition that measured a clinical outcome.<sup>15</sup> In this trial, 200 adults requiring warfarin anticoagulation were randomized to standard dosing vs a dosing schedule determined from a formula that takes into account *CYP2C9* and *VKORC1* genotypes. During the time to achieve a stable maintenance dose, there was no difference between groups in the primary outcome of the percentage of international normalized ratios outside the therapeutic range (31% in the pharmacogenetic group and 33% in the standard dosing group). Patients in the pharmacogenetic group did have significantly fewer dose adjustments and fewer blood samples drawn for testing international normalized ratios.

One study reported possible harms from genetic testing. Among 24 patients who had *BRCA* testing and were found to have an unclassified variant (meaning the result of the test was uninformative), semistructured interviews revealed that 19 interpreted this information as “pathogenic” and 10 went on to undergo preventive surgery. None of the 5 patients who inter-

preted this test result as uninformative had preventive surgery.<sup>16</sup>

**Consumer Information Needs**

We identified 16 articles describing consumer information needs, including 1 systematic review, 1 RCT, 10 surveys, 2 pre/post studies, and 2 qualitative studies. Five articles addressed consumers’ knowledge, attitudes, and beliefs about genetics and the other 11 addressed the intention to seek or participate in genetic services, including uptake of genetic testing (TABLE 3).

Five surveys from the United States and the Netherlands assessed consumers’ knowledge, attitudes, and beliefs, and generally they all found that genetic knowledge was low, but attitudes about genetics were positive. However, there were concerns about genetic discrimination.<sup>17-21</sup> Two surveys from the United States investigated knowledge and attitudes of Hispanic participants regarding cancer genetic services, found interest in such services,<sup>20</sup> and found that acculturation factors related to language may affect awareness.<sup>21</sup>

Six articles focused on the intention to seek genetic services, including

**Table 1.** Characteristics of 68 Genomics Health Services Articles Included for Review

Category/Topic	Type of Study					
	Systematic Review	Experimental	Survey	Pre/Post	Observational	Qualitative/Descriptive
Outcomes						
Psychological, affective, cognitive	2 <sup>a</sup>	2	1	2		
Behavioral	1		4			
Clinical		2		1		1
Consumer information needs						
Knowledge, attitudes, and beliefs			5			
Intention to seek genetic services		1	4	1		
Participate in genetic services	1		1	1		2
Delivery of genetic services						
Existing genetics services and the genetics workforce			4 <sup>b</sup>			1 <sup>c</sup>
Integrating genetics into primary care practice		1	1	2		2
New models of genetic services		2	2		1	
Barriers to integration of genetic services						
Health professionals’ knowledge, attitudes, beliefs, and abilities	1		10		2	2 <sup>d</sup>
Lack of oversight of genetic testing			1			
Privacy and discrimination concerns			2			2 <sup>e</sup>
Total	5	8	35	7	3	10

<sup>a</sup>One review also included behavioral outcomes.  
<sup>b</sup>Qualitative technique was also used (interviews) in 1 study.  
<sup>c</sup>Descriptive study.  
<sup>d</sup>Included 1 medical record review.  
<sup>e</sup>Qualitative comparative studies.

**Table 2.** Evidence Table of Studies of Outcomes of Genetic/Genomic Health Services

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
<b>Psychological or Cognitive Outcomes</b>				
Heshka et al, <sup>1</sup> 2008	Systematic literature review (2000-2006)	Adults with family history of any multifactorial adult-onset disorder who had undergone genetic testing	Review perceived risks and psychological and behavioral effects of genetic testing for common chronic diseases	1 RCT, 2 cross-sectional studies, 27 prospective studies: short-lived negative psychological effects and modest increases in screening for carriers, no differences in perceived risk after testing for carriers or noncarriers
Butow et al, <sup>2</sup> 2003	Systematic literature review (1980-2001)	Women with family history of breast cancer who had genetic counseling or testing	Review the perceived risks and psychological effects of genetic counseling and testing	1 RCT, no differences in outcomes; 1 RCT, significantly less breast cancer-specific stress at 3 mo; 13 pre/post studies, mostly no changes or some improvements in perceived risk, worry, anxiety, or depression
Rief et al, <sup>3</sup> 2007	RCT (Marburg, Germany) <sup>a</sup>	410 Obese (BMI ≥30) patients; intervention groups, 145 and 146; controls, 116	Patients received consultation with or without genetic information; controls, no intervention	Patients who received consultation with genetic information rated it as superior, showed no negative psychological effects or increase in weight after 6 mo; those with family history had lasting psychological benefits
Pierce et al, <sup>4</sup> 2000	RCT (south London, England, 2000)	152 Adult, nondiabetic offspring of diabetic patients, 105 enrolled; intervention, 43; controls, 62	Patients received interviews with genetic counseling or interviews only	Genetic counseling and personalized prevention recommendations improved accuracy of risk perception with no increase in worry, anxiety, or depression
Palmer et al, <sup>5</sup> 2007	Cross-sectional survey (Boston, Massachusetts, 2004)	1065 Adults aged 35-55 y enrolled in a multispecialty practice surveyed by mail, 355 with family history of colon cancer and 710 without; 833 respondents	Assess health beliefs and attitudes about colon cancer and their effects on colon cancer screening	Patients with greatest familial risk and with strong perceived risk nearly 3 times more likely to have been appropriately screened
Collins et al, <sup>6</sup> 2000	Pre/post (Australia, 1998-1999)	193 Adult patients with family history of colorectal cancer; 157 completed preclinic, 127 postclinic questionnaires	Assess colorectal cancer-related worries, risk perceptions, their effects on interest in genetic testing, overall satisfaction with clinic	Worry positively associated with younger age, higher education, higher perceived risk; colon cancer worry significantly reduced after genetic consultation
Pieterse et al, <sup>7</sup> 2007	Pre/post (Utrecht, the Netherlands, March 2001 to August 2003)	622 Adult patients with family history of cancer; 200 completed previsit, 171 postvisit questionnaires	Assess associations between counselor-patient communication and patient satisfaction, cognitions, anxiety, and perceived control after a genetic consultation	Receiving medical information increases patient satisfaction, does not increase level of anxiety
<b>Behavioral Outcomes</b>				
Marteau and Lerman, <sup>8</sup> 2001	Systematic literature review <sup>a</sup>	Evidence about behavioral responses to genetic risk information	Review evidence, literature on behavior; consider how it might be changed in response to genetic information	11 Studies described effects on behavior: genetic risk can increase or have no effect on motivation to screen for cancer; little known about effect of genetic test results on lifestyles
Vadaparampil et al, <sup>9</sup> 2005	Cross-sectional survey (United States, 1999-2000)	2079 Physicians; 1251 respondents	Assess physicians' exposure, attitudes toward advertisements for genetic tests for cancer susceptibility	27% Received advertisements; 25% considered them important in their recommendations for cancer genetic susceptibility testing
Levy et al, <sup>10</sup> 2007	Cross-sectional survey (United States, 2002)	2000 Primary care physicians; 562 respondents	Assess training and experience with genetics, attitudes and concerns about use of genetic testing	75% Had training in genetics, 5% confident in their ability to interpret test results; most important factors in offering test: ability to target cessation treatment, ability to encourage patients with tailored messages
Gramling et al, <sup>11</sup> 2003	Cross-sectional survey (Massachusetts, 2002)	691 Family physicians; 300 respondents	Assess opinions about patients' motivation to change behavior based on genetic test results indicating high risk for cancer	Expected that their patients would be more likely to screen (89.9%), improve their diet and exercise (92.5%), or quit smoking (93.6%)
Herbild et al, <sup>12</sup> 2008	Cross-sectional survey (Denmark, 2002)	89 Patients treated with antidepressant medications; 65 respondents	Assess willingness to pay for improvements in treatment response to antidepressant medication	Willing to pay for 5% probability of improvement, which exceeded price of genetic test that could predict these benefits
<b>Clinical Outcomes</b>				
Scheuer et al, <sup>13</sup> 2002	Pre/post (Boston, Massachusetts, 1995-2000)	251 Women with deleterious <i>BRCA1/2</i> gene mutations and tissue at risk for breast or ovarian cancer	Assess participation in screening for early detection, chemoprevention, and risk-reducing surgery after receiving cancer prevention recommendations	14.9% and 50.3% underwent risk-reducing surgery for breast cancer and ovarian cancer, respectively; 4 cancers identified; screening behavior increased in women who did not undergo risk-reducing surgery
Arkadianos et al, <sup>14</sup> 2007	Nonrandomized comparison (Greece) <sup>a</sup>	43 Attendees at weight management clinic matched to 43 controls on clinical characteristics	Intervention patients received dietary instructions informed by results of a nutrigenetic test; control patients received standard diet and exercise	Weight loss not statistically different between groups up to 300 d; then 22 control patients gained an average 2.74 kg while intervention patients lost an average 2.54 kg

(continued)

**Table 2.** Evidence Table of Studies of Outcomes of Genetic/Genomic Health Services (cont)

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
			<b>Clinical Outcomes</b>	
Anderson et al, <sup>15</sup> 2007	RCT (Salt Lake City, Utah) <sup>a</sup>	200 Adults requiring warfarin therapy, about 50% male, and more than half preoperatively for orthopedic procedures	Patients were randomized to conventional warfarin dosing vs a formula that takes into account <i>CYP2C9</i> and <i>VKORC1</i> genotypes	No statistically significant difference between groups in the primary study end point, 30.7% INR in intervention group, 33.1% INR in standard group
Vos et al, <sup>16</sup> 2007	Semistructured interviews (the Netherlands, 1998-2006)	24 Patients who received <i>BRCA1/2</i> genetic test results classified as a variant of uncertain clinical significance	Assess recall and interpretation of result and effects on life domains	Little change reported to most lives in general; a third reported large changes in preventive behaviors; 10 of 19 who had interpreted their results as pathogenic had preventive surgery; 0 of 5 who interpreted their results as uninformative did so

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); INR, international normalized ratio; RCT, randomized controlled trial.  
<sup>a</sup>Year not stated.

motivations for genetic testing. An RCT randomized 2165 primary care patients into 2 groups—one offered a DNA-based test for hemochromatosis and the other a phenotypic test—and then assessed the willingness to have the testing. The authors found that acceptance of testing was about the same for both groups (56% for genotypic and 58% for phenotypic testing) and that reasons for refusal included a need to talk with a physician (44%), concern about privacy (32%), and dislike of blood drawing (29%).<sup>22</sup>

Two surveys of patients with colorectal cancer assessed factors contributing to decision making about genetic testing for hereditary nonpolyposis colorectal cancer, including germline testing<sup>23</sup> and tumor microsatellite instability testing.<sup>24</sup> Among 314 patients, motivations for germline testing included learning of increased risk to children and finding out whether additional screening was needed. For 125 patients eligible for tumor microsatellite instability testing, the majority had positive attitudes about the potential benefits and perceived few barriers to undergoing the test, despite having little knowledge about the test. A pre/post study used interviews and questionnaires to assess barriers to participating in genetic counseling and *BRCA* gene testing for patients newly diagnosed with breast cancer.<sup>25</sup> Participation was not influenced by distress, knowledge about hereditary breast cancer, previous genetic testing in relatives, or perceived risk and barriers.

A survey of 187 mothers undergoing *BRCA* gene testing who had children

aged 8 to 21 years found that most of these women were motivated to have testing for the information it provided to their children, and they believed that having such information could be used to prevent or control cancer in their children. The 2 most common informational resource needs of these mothers for discussing their *BRCA* test results with their children included reading educational literature (93%) and speaking with a family counselor (86%).<sup>26</sup>

Another survey of 139 women previously treated for early stage breast cancer found that the majority (76%) would have been interested in genetic testing to determine risk of recurrence with most (84%) wanting to include information from test results in decision making about treatment.<sup>27</sup>

Five articles addressed patients' information needs related to participation in genetic services. Two articles underscored the importance of eliciting the patient's perspective when discussing risk of chronic disease, particularly in the context of the family history. A systematic literature review that included 11 qualitative research studies found that for individuals with a family history of cancer, coronary heart disease, or diabetes, the salience of their family history was determined by acknowledging that a disease runs in the family, and this was strongly influenced by the personal experiences of that illness in relatives. Some of these factors were the same as the medical factors used to assess familial risk (ie, the number of affected relatives and age at onset), but others were more per-

sonal, such as emotional or physical closeness of a family member.<sup>28</sup> A qualitative study published the following year delved further into patients' perceived familial risk and found that a sense of vulnerability to common chronic disease depended on the emotional impact of experiencing the illness in the family, especially if the illness was sudden, premature, or fatal, and the nature of personal relationships within the family.<sup>29</sup>

A pre/post study from the United States of women eligible for referral to cancer genetics consultation found that after 6 months those who had attended the consultation were significantly more knowledgeable, but clinical history, perceived risk, family history, psychological state, and anxiety were not associated with attendance.<sup>30</sup>

Two articles addressed the genetic counselor-patient interaction. A cross-sectional study of observed behavior from the Netherlands found that adults referred for cancer genetics consultation had a strong psychosocial focus, which was important to their agenda for the consult; however, these needs only minimally influenced the interaction during the visit because patients did not communicate their previsit needs.<sup>31</sup> A qualitative study from the United States that interviewed genetic counselors and their patients found that the goals of genetic counseling were often unclear to both. Although counselors objected to stating goals because doing so implied a preset agenda, patients were uncertain about the role of the counselor and the boundaries of what would be discussed.

**Table 3.** Evidence Table of Studies of Knowledge, Attitudes, and Beliefs About Genetic Services and Informational Needs of Consumers

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
<b>Knowledge, Attitudes, and Beliefs About Genetic Services</b>				
Morren et al, <sup>17</sup> 2007	Cross-sectional survey (the Netherlands, 2001)	1916 Patients aged ≥15 y with chronic disease; 1496 respondents	Assess perceived knowledge and attitudes about genetics	10% Reported sufficient genetics knowledge; DNA testing frightened about 25%; two-thirds wanted to know if their disease was genetic; 40% would want to know if they were at risk; about half concerned about genetic discrimination by employers and insurers; primary care clinician preferred source of genetics information
de Vries et al, <sup>18</sup> 2005	Cross-sectional survey (the Netherlands) <sup>a</sup>	4000 Adults (aged 18-50 y) who were not undergoing cancer treatment; 478 respondents	Assess knowledge, risk perception, attitudes, and beliefs about hereditary cancer	25% Correctly indicated hereditary types of cancer; two-thirds to three-quarters wanted to know types with hereditary aspects, how to recognize them, personal risks, and steps to take; preferred sources for information were leaflets, general practitioner, Internet
Peters et al, <sup>19</sup> 2004	Cross-sectional survey (Philadelphia, Pennsylvania, December 2001 to January 2002)	430 African American and white prospective jurors; 75% response rate, 90% completion rate	Assess awareness of and attitudes about genetic testing for cancer risk	61% Had heard about genetic testing; positive attitudes were prevalent (>80%); lower awareness, less belief in potential benefits, more concern about racial discrimination among African American compared with white participants
Ricker et al, <sup>20</sup> 2007	Cross-sectional survey (Los Angeles County, 2000)	235 Adult Latino attendees of outpatient clinics, about 98% of eligible participants	Assess personal and family history of cancer, beliefs about cancer, screening behaviors, access to screening information, interest in genetic services	More than 85% expressed interest in information about risk and motivation to participate in cancer genetics services; heredity perceived as most frequent cause of cancer after smoking
Vadaparampil et al, <sup>21</sup> 2006	Cross-sectional survey (United States, 2000)	4313 US Hispanic respondents aged >25 y to National Health Interview Survey	Assess knowledge, attitudes, and practices related to cancer prevention and control	21% Had heard of genetic testing for cancer risk (highest rates: 27% of Puerto Rican and 14% of Mexican respondents); completing the interview in Spanish, having an intermediate or low level of English-language preference inversely and significantly associated with test awareness
<b>Intention to Seek Genetic Services</b>				
Anderson et al, <sup>22</sup> 2005	RCT (United States) <sup>a</sup>	2165 primary care patients; genotype vs phenotype test randomization intervention, 559 and 538 white, 538 and 530 African American	Assess willingness, knowledge, attitudes, and beliefs about phenotypic or genotypic testing for hereditary hemochromatosis	Test acceptance associated with interest in knowing more about health (81%), helping family members (71%); refusal reasons included need to talk with physician (44%), concern about privacy (32%), dislike of blood drawing (29%); African American respondents in deep South less likely to accept either test than white or African American respondents in mid-Atlantic
Esplen et al, <sup>23</sup> 2007	Cross-sectional survey (Ontario, Canada) <sup>a</sup>	483 Adult colorectal cancer patients from population-based cancer registry; 314 respondents	Assess motivational factors, expectations, psychosocial functioning related to genetic testing	More than 80% motivated to find out about risk in children; women significantly more likely to test to find out if more screening was needed (84% vs 67%) and in response to recommendations from a health professional (67% vs 45%); women and younger patients had higher levels of distress
Manne et al, <sup>24</sup> 2007	Cross-sectional survey (United States) <sup>a</sup>	173 Adults with colorectal cancer meeting the Revised Bethesda criteria for tumor MSI testing; 125 respondents	Assess knowledge, exposure, perceived benefits, and barriers to MSI testing	Average percentage of correct answers, 17.5% (median, 6%); highest rated benefit, to learn if children or other relatives were at risk (98.3%); most frequent barriers, possible insurance discrimination (32%), uncertainty of test result (37%); more distressed patients, those who perceive higher risk for recurrence, those with metastatic disease less motivated to have MSI testing
Schlich-Bakker et al, <sup>25</sup> 2007	Pre/post (the Netherlands, 2002-2004)	102 Adults with newly diagnosed breast cancer	Assess participation in genetic counseling and BRCA testing	57% Had genetic counseling and BRCA testing; no differences in psychological distress or knowledge between patient groups; patients who declined testing had lower perceived risks; motivation for testing, information for children, information for prevention
Tercyak et al, <sup>26</sup> 2007	Cross-sectional survey (United States) <sup>a</sup>	187 Women with children aged 8-21 y who had not yet received BRCA test results; consent rate of 81%	Assess informational resource needs, BRCA testing motivations, decision making, vigilance, decisional conflict regarding communicating test results to children	80% Reported that learning about their children's risks of inheriting mutation "very important" motivation for testing; 44% believed results could be used to prevent or control cancer in children; mothers with greater interest in testing to learn about their children's risks, those with more vigilant decision-making styles, those with higher decisional conflict had greatest information needs for communicating results to children
O'Neill et al, <sup>27</sup> 2007	Cross-sectional survey (North Carolina, 2005)	231 Women with early stage breast cancer; 166 participants, 139 with complete data	Assess interest in genomic testing for risk of breast cancer recurrence and preferences for incorporating results into treatment decisions	Majority would definitely want genetic recurrence risk testing (76%) and were willing to pay on average \$997; participants significantly more willing to have chemotherapy if results indicated high recurrence risk and if physicians advised them to do so; participants' worry increased as function of recurrence risk results

(continued)

**Table 3.** Evidence Table of Studies of Knowledge, Attitudes, and Beliefs About Genetic Services and Informational Needs of Consumers (cont)

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
<b>Information Needs Related to Participation in Genetic Services</b>				
Walter et al, <sup>28</sup> 2004	Systematic literature review and meta-analysis (1993-2001)	Qualitative studies describing familial risk for cancer, coronary heart disease, and diabetes mellitus for at-risk individuals	Explore understanding about familial risk	11 Qualitative studies; features recognized as contributing to familial risk: number of affected relatives, age at diagnosis, severity of illness; premature death or severe disability increased salience of family history; risk perception influenced by personal experience with relative's disease; ambivalence and uncertainty may be exacerbated by difficulty in obtaining accurate information
Walter and Emery, <sup>29</sup> 2005	Qualitative (United Kingdom, 2002-2003)	180 Adult patients with family history of cancer, heart disease, or diabetes	Assess how patients understand family history and its influence on consultations about disease risk and management	Sense of vulnerability depended on number or sex of affected family members, age at onset, and emotional impact of witnessing illness; beliefs about contributions of nature and nurture can affect patients' views on control they can exert over risk
O'Neill et al, <sup>30</sup> 2006	Pre/post (Pennsylvania) <sup>a</sup>	43 Women with breast cancer and at least 10% probability of having <i>BRCA</i> mutation	Assess referral uptake for clinical cancer genetic counseling	Awareness about genetics overall significantly associated with referral uptake; acceptors and decliners had significantly better knowledge scores than intenders; perceived benefits did not influence referral uptake; most important barriers were potential for insurance discrimination (77%) and cost (69%)
Pieterse et al, <sup>31</sup> 2005	Cross-sectional study of observed behavior (the Netherlands, 2001-2003)	130 Adults aged ≥18 y who were first in their family referred for cancer genetic consultation	Describe counselor-patient interaction and examine whether communication reflects patients' previsit needs	Patients had strong psychosocial focus; previsit needs minimally influenced interaction and patients did not appear to tailor verbal communication to needs
Bernhardt et al, <sup>32</sup> 2000	Qualitative (United States) <sup>a</sup>	Genetic counselors and clients in focus groups (10 counselors, 19 clients) and telephone interviews (8 counselors)	Assess quality of providing genetic counseling services	Many counselors objected to stating goals since it implied preset agenda; clients had few expectations about how counseling would be delivered, role of counselor, boundaries of discussion not clear; most clients believed physicians could not provide the services

Abbreviations: MSI, microsatellite instability; RCT, randomized controlled trial.  
<sup>a</sup>Year not stated.

Most patients appreciated the time spent by genetic counselors and believed that their physicians could not provide the service.<sup>32</sup>

**Delivery of Genomic Medicine**

We identified 16 articles that described the delivery of genomic medicine. These studies were further classified as relating to existing genetic services and the genetics workforce, integration of genetics into primary care, and new models of genetic services delivery (TABLE 4).

Five articles described genetic services and the current genetics workforce: 4 surveys of the genetics workforce in the United States and 1 descriptive study of regional genetic health centers in the United Kingdom. Two surveys used data from a mailed questionnaire to the 1576 active physician and PhD members of the American Board of Medical Genetics and found that 60% of respondents perceived that there were inadequate numbers of geneticists<sup>33</sup> and that geneticists provid-

ing services for adult-onset diseases represented the smallest proportion of geneticists (7%).<sup>34</sup> Another survey obtained data from active members of the American Academy of Pediatrics Section of Genetics and Birth Defects and physicians certified by the American Board of Medical Genetics and found that 5% had training in internal medicine, and adult patients seen for reasons other than prenatal services represented only 12% of patients seen by geneticists.<sup>35</sup> The fourth survey described characteristics and professional roles of 211 nurse genetics specialists in the United States and found that most (57%) provided direct patient care and worked in genetics (26%) or oncology (22%) settings.<sup>36</sup> The descriptive study from the United Kingdom found that half of referrals come from primary care, genetic counselors were key to providing genetic services, and genetic testing was primarily for single-gene disorders.<sup>37</sup>

Six articles described the integration of genetics into primary care. This included 1 qualitative study from Canada

that found family physicians anticipate providing more genetic services, but they were uncertain and had concerns about their abilities to do so.<sup>38</sup> The remaining 5 articles were from the United Kingdom and described a range of approaches to integrating clinical genetic services into primary care, including 2 pre/post studies, 1 survey, 1 qualitative study, and 1 cluster RCT.

Three studies (the RCT, the survey, and a pre/post study) addressed the use of a nurse genetics specialist within the primary care setting. Both the RCT and the survey found that patient satisfaction with the service provided by the nurse genetics specialist was high and costs with the new model were less.<sup>39,40</sup> The pre/post study found that physicians believed that contact with a nurse genetics specialist helped in identifying patients in need of a genetics referral and that nurse genetics specialists provided current genetics information to them.<sup>41</sup>

The other 2 studies examined the effect of referral guidelines for cancer genetics services among general

**Table 4.** Evidence Table of Studies Assessing How Genetic/Genomic Medicine Is Delivered

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
<b>Medical Genetics Workforce</b>				
Cooksey et al, <sup>33</sup> 2005	Survey (United States, 2003)	1567 US resident, active medical geneticists certified by ABMG; 861 respondents	Describe current models of providing clinical genetic services and roles of health professionals; identify measures to monitor changes in demand; establish description of genetic services	Medical geneticists providing patient care spend 50% of their time on patient care activities; about 70% report their practice is full or nearly full; about 60% report supply of geneticists in community not adequate for demand
Cooksey et al, <sup>34</sup> 2006	Survey and qualitative study (United States, 2003)	1567 US resident, active medical geneticists certified by ABMG; 861 respondents	Identify clinically relevant subgroups of geneticists and assess their genetics practices, patient care, other characteristics	Geneticist subgroups included general (36%), pediatric (28%), reproductive (15%), metabolic (14%), adult (7%); adult geneticists practice almost exclusively in academic medical centers, spend substantial time in laboratories, spend fewest hours in patient care
Pletcher et al, <sup>35</sup> 2002	Survey (United States, 1997-1998)	735 Active members of American Academy of Pediatrics Section of Genetics and Birth Defects and physicians certified by ABMG; 506 respondents	Gather practice information from practicing geneticists	Most clinical geneticists have training in another specialty, but only 5% in internal medicine; 81% practice in urban setting, almost two-thirds at a medical school; adults comprise 12% of patients seen; respondents spend 3.1 h with new patients, 1.4 h for follow-up visit; "suboptimal" reimbursement for services
Lea et al, <sup>36</sup> 2006	Cross-sectional survey (United States, 2004)	293 Members of ISONG; 211 respondents	Describe current models of providing clinical genetics services and demand for genetic services	One-third held doctoral degrees, one-third held academic positions, 57% provided direct patient care, with most working in genetics (26%) or oncology (22%)
Donnai and Elles, <sup>37</sup> 2001	Descriptive (United Kingdom) <sup>a</sup>	12 Regional genetic health centers	Describe genetics services and workforce	Regional genetic centers provide diagnosis, risk assessment, counseling, surveillance, support; about half of referrals come from specialists, other half from primary care; genetic counselors have key role in delivery
<b>Integrating Genetics into Primary Care</b>				
Carroll et al, <sup>38</sup> 2003	Qualitative (Ontario, Canada) <sup>a</sup>	40 Urban and rural family physicians in 4 focus groups	Explore physicians' experiences in dealing with genetic susceptibility to cancer	Escalating expectations for genetic testing met with uncertainty, concern, and anxiety as participants acknowledged inadequacies in current role; about 14% had patients who inquired about inherited cancers, but only a few had patients who had been referred for counseling or testing
Holloway et al, <sup>39</sup> 2004	Cluster RCT (United Kingdom, 1998-1999)	374 Women without breast or ovarian cancer referred for genetic risk assessment; 189 novel service, 185 standard service	Assess satisfaction with the new community-based service model; baseline and follow-up data compared between the groups	Satisfaction with both models was high; women with low familial risk less satisfied; community-based cancer genetic service about 30% less expensive in staff and patient costs
Westwood et al, <sup>40</sup> 2006	Survey (United Kingdom, 2002-2003)	64 Patients in primary care referred to clinical genetics; 45 attended appointments, 34 returned survey	Assess feasibility and patient satisfaction with genetic nurse counselor service	Almost half (48%) of patients seen did not need to attend further appointments; patients were satisfied with travel time, distance to clinic; patient costs perceived as low
Drury et al, <sup>41</sup> 2007	Pre/post (United Kingdom, 2003)	17 General practices in central England; 10 randomly selected, 7 urban, 3 rural	Assess genetic nurse counselor clinic that acted as liaison between regional clinical genetics service	Physicians reported limitations and gaps in current knowledge; referral guidelines provided by the nurse gave them more confidence; most felt contact with genetic nurse helped significantly in identifying patients whose risk warranted referral
Elwyn et al, <sup>42</sup> 2002	Qualitative (United Kingdom) <sup>a</sup>	19 General practitioners in Wales; 14 attended	Examine physicians' reactions to referral guidelines and telephone triage system for cancer genetics services	Participants had few objections to triage system to regulate access to scarce specialist service, thought referral guidelines would help them refer patients appropriately
Lucassen et al, <sup>43</sup> 2001	Pre/post (United Kingdom) <sup>a</sup>	12 General practitioners in Oxfordshire County, England	Assess genetics referrals and risk assessment in primary care clinicians before and after dissemination of guidelines	After guidelines, more referrals from primary care correctly met criteria, fewer low-risk referrals, and more informative letters sent to specialists; no change in referrals from counties that did not receive guidelines
<b>New Models of Genetic Services</b>				
Jenkins et al, <sup>44</sup> 2007	RCT (United States) <sup>a</sup>	136 English-speaking people who had consented to <i>BRCA1/2</i> gene mutation analysis; 111 enrolled, 102 completed	Compare psychological sequelae, knowledge, satisfaction, preferences, and cost of telephone vs in-person disclosure of results	No significant differences in anxiety and general well-being, similar rates of satisfaction; among those who did not receive their preferred method of disclosure (n = 22), statistically significant tendency to prefer phone results; greater costs associated with in-person result disclosure
Lea et al, <sup>45</sup> 2005	Survey (Maine) <sup>a</sup>	Rural physician practices and public health nurses: 650 participants in educational presentations, 85% response rate; 24 clinics and 125 patients eligible for satisfaction surveys, 18% and 25% response rates	Describe 3-y telegenetics pilot project that provided educational and clinical services	Survey evaluations overall very positive; provider and patient responses regarding satisfaction low but mean satisfaction scores high; consulting physicians very satisfied overall and confident in evaluating and managing patients seen via telemedicine

(continued)

**Table 4.** Evidence Table of Studies Assessing How Genetic/Genomic Medicine Is Delivered (cont)

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
<b>New Models of Genetic Services</b>				
Emery et al, <sup>46</sup> 2007	Cluster RCT (England) <sup>a</sup>	170 General practice teams in eastern England using the health service intranet; intervention group 23, comparison 22	Evaluate effect of genetic risk assessment strategy for familial breast, ovarian, and colorectal cancer using computer decision support system	Significantly more referrals from intervention practices than comparison practices (6.2 and 3.2 referrals per 10 000 registered patients per year); referrals from intervention practices more than 5 times more likely to be consistent with referral guidelines; patients referred from intervention practices had lower cancer worry scores
Kutz, <sup>47</sup> 2006	Observational (United States, 2006)	Direct-to-consumer marketers of nutrigenomic tests available from 4 Web sites; 14 fictitious consumers created	Investigate whether nutrigenomic tests provide consumers with information needed to tailor diet and exercise according to risks	Results from 2 of 4 Web sites included recommendations for consumer to purchase costly dietary supplements; lifestyle information influenced recommendations more than genetic test result
Goddard et al, <sup>48</sup> 2007	Cross-sectional survey (United States, 2006)	Consumers participating in HealthStyles 2006 survey (5250 respondents, 80% response rate) and physicians participating in DocStyles 2006 survey (1250 respondents, 52% response rate)	Assess consumers' awareness and use of nutrigenomic tests and practicing primary care physicians' and pediatricians' awareness of nutrigenomic tests	14% of consumers were aware of nutrigenomic testing; 0.6% report using such tests; of these, 10% discussed result with physicians; 44% of physicians were aware of nutrigenomics testing; media are major source of information about nutrigenomics testing for both consumers and physicians

Abbreviation: ABMG, American Board of Medical Genetics; ISONG, International Society of Nurses in Genetics; RCT, randomized controlled trial.  
<sup>a</sup>Year not stated.

practitioners. The qualitative study found that physicians appreciated that referral guidelines would improve their referral patterns,<sup>42</sup> and the pre/post study found that guidelines were associated with improved referral patterns.<sup>43</sup>

Five articles described new models of genetic services. One experimental study evaluated telephone disclosure of *BRCA* genetic test results compared with traditional genetic services and found there were no significant differences in anxiety and general well-being between the 2 groups, and both groups reported similar rates of satisfaction with the services.<sup>44</sup> A survey of rural physician practices in northern Maine and public health nurses statewide found that health professionals receiving and providing educational and clinical genetic services via videoconferencing generally found it to be a positive and satisfying experience.<sup>45</sup> One experimental study randomized general practice teams in the United Kingdom to the use of computerized decision support software that aided in familial risk assessment of breast, ovarian, and colorectal cancer or to a comparison group that received education and guidelines; it found that with decision support, there were significantly more genetics referrals, and these referrals were more likely to be consistent with referral guidelines.<sup>46</sup>

Regarding direct-to-consumer marketing of genetic services, an observational study that assessed nutrigenomics tests found that the genetic test results provided little influence on the assessment and recommendations provided by the test companies, and test results frequently included recommendations for the consumer to purchase costly dietary supplements.<sup>47</sup> A survey of primary care physicians and consumers in the United States found that a small percentage (14%) of consumers were aware of nutrigenomic testing and of those who had a nutrigenomics test, only 10% had discussed the results with their physicians.<sup>48</sup>

**Barriers to Clinical Integration of Genomic Medicine**

We identified 20 articles that described barriers to the clinical integration of genomic medicine. These articles were further classified as relating to health professionals' knowledge, attitudes, beliefs, and abilities; lack of oversight of genetic testing; and privacy, confidentiality, and genetic discrimination concerns (TABLE 5).

Fifteen articles described health professionals' knowledge, attitudes, beliefs, and abilities pertaining to medical genetics. This included 1 systematic review, 10 surveys, 2 observational studies, 1 descriptive study, and 1 qualitative study.

The systematic review included 18 studies that dealt with primary care physicians' perceived barriers concerning the provision of genetic services. The studies were published between 1993 and 2001 and included 7 surveys, 4 pre/post tests, 4 qualitative studies, 1 observational study, and 1 cluster RCT. These studies found that physicians reported that they lack sufficient knowledge and confidence relating to provision of genetic services and they have limited time to obtain family history.<sup>49</sup> These themes were also identified in the other 14 articles.

The 10 surveys and the qualitative study we found assessed genetics knowledge and attitudes of a variety of health professionals from the United States, Australia, and the Netherlands, and these studies found similar results to the systematic review,<sup>49</sup> with respondents feeling underprepared for assessing and managing genetic issues in their practice and lacking basic genetic knowledge.<sup>50-60</sup>

The 2 observational studies and the descriptive study we retrieved described health professionals' abilities to collect, document, and interpret family history. These studies found that a majority of patients with a strong familial risk for a common disease lacked documentation of key family history elements in their medical record, as well

**Table 5.** Evidence Table of the Challenges or Barriers to the Clinical Integration of Genomic Information

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
<b>Health Professionals' Knowledge, Attitudes, Beliefs, and Abilities</b>				
Suther and Goodson, <sup>49</sup> 2003	Systematic literature review (1991-2001)	Empirical reviews on topics of genetics and primary care in peer-reviewed journals	Review primary care physicians' perceived barriers concerning provision of genetic services	Of 18 articles, 12 identified inadequate knowledge as barrier to providing genetic information or services; limited time to obtain detailed family history was barrier in 4, lack of referral guidelines barrier in 3; 3 described decreased confidence with assessing and referring patients with genetic risks
Lapham et al, <sup>50</sup> 2000	Cross-sectional survey (United States, 1998)	3600 Members of 6 national health professional organizations; 1958 respondents	Determine genetics education needs of dietitians, occupational therapists, physical therapists, psychologists, speech-language-hearing specialists, and social workers	Less than 20% had referred patients for genetic counseling; 15% referred patients for genetic testing; 26% had confidence in eliciting genetic information; only 16% reported having high confidence in discussing genetic basis of conditions with patients
Wilkins-Haug et al, <sup>51</sup> 2000	Cross-sectional survey (United States, 1998-1999)	1248 Fellows of ACOG; 564 respondents	Assess current practice patterns and opinions on genetic screening of gynecologists	Only 24% of respondents did not routinely review family histories; when genetic testing is called for, 21% provide counseling, 54% refer to geneticist, 22% do both; 21% identified as sole provider of information and counseling to patients, but most (65%) note they are not confident of knowledge
Freedman et al, <sup>52</sup> 2003	Cross-sectional survey (United States, 1999-2000)	1763 Physicians; 1251 respondents	Assess attitudes about genetic testing for cancer susceptibility among physicians providing care for adults in certain specialties	29% reported feeling qualified to provide counseling to patients; 40% of primary care physicians felt qualified to recommend testing to patients compared with 84% of oncologists; 81% had concerns about potential insurance discrimination for patients with positive results; 53% thought it was difficult to ensure confidentiality of results
Gramling et al, <sup>53</sup> 2004	Cross-sectional survey (Massachusetts, 2002)	91 Family physicians; 300 respondents	Assess physicians' attitudes about predictive genetic testing for cancer	87% Believe screening for hereditary cancer susceptibility with family history is important; 62% confident of ability to recognize patients with hereditary cancer risk
Maradiegue et al, <sup>54</sup> 2005	Survey (United States) <sup>a</sup>	46 Graduate APN students at 2 northeastern US universities	Assess medical genetic knowledge and perceptions	34% Stated they felt comfortable speaking with family diagnosed with genetic condition; 22% felt they could draw pedigree; 95% reported no prior training during undergraduate programs regarding 21 common genetic disorders
Chen and Goodson, <sup>55</sup> 2007	Cross-sectional survey (United States) <sup>a</sup>	8058 Public health educators; 1607 respondents	Assess attitudes toward genomic competencies, awareness of efforts to promote genomics, knowledge of genomics	49% Valued their practice of genomic competencies proposed for public health educators even though most (89%) supported these competencies; 51% of answers to 6 items regarding basic and applied genomic knowledge were correct
Baars et al, <sup>56</sup> 2005	Cross-sectional survey (the Netherlands 1997-1999)	2377 Medical students nearing graduation; 291 respondents	Assess medical genetics knowledge	Mean percentage of correct answers on genetic examination, 62%; mean score for essential knowledge that all physicians should know, 71%; for desirable knowledge, 56%; for specialized knowledge, 44%
Metcalfe et al, <sup>57</sup> 2002	Qualitative study and survey (Victoria, Australia, 1999-2000)	Primary care providers: 39 focus group participants and 875 eligible survey participants; 160 respondents	Assess genetics knowledge and educational needs	Believe their knowledge is poor and they are inadequately prepared to manage patients with genetic conditions; want to know more about prenatal testing, counseling, and drawing pedigrees; report low use of genetic services, that genetics is not very relevant to current practice, and that referral and management process is often patient-driven
Doksum et al, <sup>58</sup> 2003	Survey (United States, 1998)	2250 Internists, obstetrician-gynecologists, oncologists; 803 respondents	Assess nongeneticist physicians' knowledge and experience with <i>BRCA</i> testing	Only 13% of internists, 21% of obstetrician-gynecologists, and 40% of oncologists correctly answered 4 knowledge questions about genetics of breast cancer and testing; knowledge only significantly associated with ordering <i>BRCA</i> testing among oncologists
Wideroff et al, <sup>59</sup> 2003	Cross-sectional survey (United States, 1999-2000)	1763 Physicians; 1251 respondents	Assess use of genetic testing for cancer susceptibility among certain specialties	31% Had ordered cancer susceptibility test or referred patients in previous 12 mo; testing and referral significantly associated with practice location in the Northeast, feeling qualified to recommend testing, receiving cancer susceptibility testing advertisements, and having patients who asked about test
Sandhaus et al, <sup>60</sup> 2001	Cross-sectional survey (Cleveland, Ohio, 2000)	124 Family practitioners, general internists, and gynecologists not currently ordering <i>BRCA1/2</i> testing; 82 respondents	Assess ability of physicians to interpret genetic testing laboratory report that provided <i>BRCA1/2</i> genetic test results and probabilistic information about cancer risk	32% Did not demonstrate sufficient knowledge to provide accurate genetic risk assessment; knowledge of cumulative risk strongly associated with comprehension of cancer risk information

(continued)

as documentation of genetic risk assessment or referral for genetics evaluation.<sup>61-63</sup> A survey of family physicians also found that most (87%) believed that family history screening is important; however, only 62% were confident in the ability to recognize patients with hereditary risk.<sup>53</sup>

One article described oversight of genetic testing. A survey of 190 genetic testing laboratory directors found that most would support formal registration under a genetic testing specialty regulated by the Clinical Laboratory Improvement Amendments and that proficiency testing could improve the quality of genetic testing.<sup>64</sup>

Four articles described concerns about privacy and genetic discrimination. Two articles used data from the same qualitative comparative analysis of states with and without laws prohibiting genetic discrimination by health insurers. One article found that there are no well-documented cases of

**Table 5.** Evidence Table of the Challenges or Barriers to the Clinical Integration of Genomic Information (cont)

Source	Study Type (Location, y)	Target Population	Study Goals	Selected Findings
<b>Health Professionals' Knowledge, Attitudes, Beliefs, and Abilities</b>				
Sweet et al, <sup>61</sup> 2002	Observational (Ohio, 1999-2000)	Patients at ambulatory cancer clinic; family-history data from 362 patients compared with medical records	Assess medical record documentation of family history	Of 69 patients with high familial risk, 14 had records describing increased familial risk; 7 referred for genetic consultation; of 8 histories assessed as potential cancer syndrome, 4 had sufficient family history in record to corroborate assessment; of 54 patients with no history documented, 15 were assigned high familial risk based on computer data entry
Frezzo et al, <sup>62</sup> 2003	Observational (Illinois, 2001-2002)	78 patients in internal medicine practice	Assess the documentation of family history in medical records; 2 collection methods, self-administered questionnaire and pedigree interview by genetic counselor, compared with medical record	All individuals at increased risk by review of medical records also identified as having increased risk by questionnaire or pedigree interview; questionnaires revealed 32 patients with increased risk compared with 18 identified with record review; pedigree analysis identified 30 patients with increased risk compared with 15 with record review
Murff et al, <sup>63</sup> 2004	Descriptive (Boston, Massachusetts, 2001-2002)	995 Consecutive new patients seen by primary care physicians	Determine completeness of documented cancer family history information	68% Had some form of cancer family history information in records; age at diagnosis documented in 51% of relatives with colon cancers, 38% with breast cancer, and 27% with ovarian cancer; 17% of patients who met criteria for testing referred for services
<b>Oversight and Regulation of Genetic Testing</b>				
Hudson et al, <sup>64</sup> 2006	Cross-sectional survey (United States) <sup>a</sup>	345 Molecular and biochemical genetic testing laboratory directors; 190 respondents	Assess participation in proficiency testing for genetic tests and attitudes of laboratory directors toward current regulation	84% Indicated that laboratory participated in some form of external proficiency testing; 60% found it very useful to improve quality of genetic testing; 73% agreed that CLIA should create genetic testing specialty for molecular and biochemical tests
<b>Privacy and Confidentiality Concerns</b>				
Hall and Rich, <sup>65</sup> 2000	Qualitative comparative case study (United States, 1995-1997)	Representatives from insurance industry (47), genetics professionals (29), and patient advocates (5) from 7 states with laws and 6 states without laws on use of genetic information in health insurance	Evaluate whether state laws reduce extent of genetic discrimination by health insurers	No well-documented cases of health insurers either asking for or using presymptomatic genetic test results in underwriting decisions, either before or after laws or in states with or without laws
Hall and Rich, <sup>66</sup> 2000	Qualitative-comparative case study (United States, 1995-1997)	Representatives from insurance industry (47), genetics professionals (29), and patient advocates (5) from 7 states with laws and 6 states without laws on use of genetic information in health insurance	Assess attitudes regarding genetic discrimination	Patients' and clinicians' fear of genetic discrimination in health insurance exceeds reality, may deter genetic testing, particularly for costlier tests and adult-onset diseases; most professionals are aware of federal and state laws prohibiting discrimination, but many underestimate protections
Hall et al, <sup>67</sup> 2005	Cross-sectional survey (United States and Canada, 2001-2003)	86 859 Primary care patients; 78 942 respondents with complete data	Assess concern about insurance problems related to genetic testing for hemochromatosis	African American and Asian individuals significantly much less likely and Hispanic more likely than white individuals to express concern about insurance discrimination; participants younger than 65 y, US residents (compared with Canadians), those without high school diploma, and those with lower mental health scores were substantially more likely to express concern
Hall et al, <sup>68</sup> 2007	Survey (United States and Canada)	1154 Primary care patients screened for iron overload phenotypes and HFE genotypes; 832 respondents	Assess extent of insurance and employment problems associated with population screening for hereditary hemochromatosis and iron overload after 1 y	Three respondents (0.4%) had verified insurance or employment problems that they believed were related to hereditary hemochromatosis and iron overload; 2 had problems with life insurance and 1 with long-term care insurance; no problems verified for health insurance or employment

Abbreviations: ACOG, American College of Obstetricians and Gynecologists; APN, advanced practice nursing; CLIA, Clinical Laboratory Improvement Amendments.  
<sup>a</sup>Year not stated.

health insurers either asking for or using presymptomatic genetic test results for underwriting purposes.<sup>65</sup> The other study found that patients' and clinicians' fears of genetic discrimination in health insurance exceeds reality, and this fear may deter genetic testing, especially for high-cost tests and adult-onset diseases.<sup>66</sup>

A cross-sectional survey of 86 859 patients in primary care settings participating in a hemochromatosis screening study in North America found that African American and Asian individuals were less likely to have concerns about genetic discrimination, and younger participants, US residents, and those with less than a high school education were more likely to have these concerns.<sup>67</sup> A follow-up survey of 832 participants from this cohort who were screened for iron phenotypes and *HFE* genotypes associated with hemochromatosis found that after 1 year, none reported problems with health insurance or employment and only 3 (0.4%) reported problems with life insurance or long-term care insurance.<sup>68</sup>

## COMMENT

Genomic advances hold the promise to improve care and prevention of common chronic diseases. Although that promise has yet to be fully realized, new genetic discoveries make the reality of that promise seem closer than ever before. However, if past experience with other health care advances is any guide, patients will not realize the full benefit of genomic advances without a thorough understanding of the organization, clinician, and patient needs that are required to translate these advances into improved clinical outcomes. Our systematic review reveals a large gap between what knowledge is available and what health systems still need to know about the outcomes, consumer needs, organization of health services, and barriers, to ensure appropriate and effective clinical integration of genomic information and technologies for common chronic disease.

The most important and consistent finding from our literature review is that the primary care workforce, which will be required to be on the front lines of

the integration of genomics into the regular practice of medicine, feels woefully underprepared to do so. Remediation of this deficiency should be a top priority, and more studies are needed to test models for how this can be feasibly accomplished.

A second theme we identified is that consumers have unclear and dissonant notions about the value of genetic testing for common chronic disease. In general, consumers knew little about genetics/genomics but were interested in the prospect of this technology helping to better identify diseases for which they and their family members were at increased risk. Consumers were also worried about the possible adverse consequences of genetic testing, particularly the privacy issues and discrimination in health insurance and employment. Therefore, another research need is the development and testing of interventions to promote greater understanding of genomic medicine among consumers. Such interventions may need to be tailored for the needs of specific populations.

A third theme we identified is that there is a great need to better understand the outcomes of genomic medicine interventions for common chronic disease. To date most studies have assessed these outcomes using weak pre/post study designs, and in general these studies have assessed changes in psychological, affective, and cognitive outcomes of patients receiving genetic counseling and testing for single-gene disorders. More research describing clinical outcomes is needed: do patients who receive counseling and testing have better clinical outcomes in terms of mortality, decreases in incidence of disease, and better clinical responses to pharmaceuticals? And at what cost?

We identified other barriers to the clinical integration of genomic medicine for common chronic disease, in addition to the perceived inadequacy of the primary care workforce to participate in this. The most prominent of these include health professionals' lack of basic knowledge about genetics and their lack of confidence in interpreting familial patterns of disease, which limits their

ability to appropriately counsel their patients, order and accurately interpret genetic tests, and refer their patients for genetics consultation. In addition, there may not be sufficient numbers of genetics professionals available to meet the demand for genetic services.

Our review has several limitations. First was the difficulty in identifying health services studies of genomic medicine for common chronic disease. We know of no empirical assessments identifying an optimal search strategy for such studies as, for example, there exist optimal search strategies to identify RCTs and studies of risk and prognosis. We searched MEDLINE using reasonable search terms, but we acknowledge it is likely that we have failed to identify some studies of relevance. However, given the consistency of the studies we did identify, we believe it is unlikely that missing literature would substantially change our main conclusions.

Second, we did not address the literature dealing with prenatal genetics, pediatric genetics, genetic conditions with pediatric onset experienced by adults, or rare single-gene disorders presenting in adulthood. Our focus was on the opportunities and challenges of genomics interventions for common chronic diseases of adulthood. Even then we found that the evidence regarding these conditions is largely limited to single-gene disorders that manifest as common diseases in adulthood, particularly cancer.

Third, because this literature was a heterogeneous combination of study questions, designs, populations, and outcomes, synthesizing the study findings involved making a certain number of judgments on our part. We tried to be explicit and describe these judgments as fully as possible so readers can understand what we did.

## CONCLUSIONS

In summary, this review of health services research studies revealed many gaps in the organization, clinician, and patient needs that must be filled to realize the full benefits of genomics. These studies reported that consumers need more and better information to under-

stand the value of genomic medicine for common chronic diseases; that the primary care workforce is not prepared to meet the challenge of integrating common disease genetics/genomics into the regular practice of medicine; that the genetics workforce appears to have inadequate numbers to respond to genetic service needs for adult-onset conditions; that few models of integration into primary care have been successfully implemented on a wide scale; and that a host of barriers exist, such as lack of oversight for genetic testing technologies and concerns about privacy and discrimination. All of these issues need attention. It will be a lost opportunity if the health services research components of genomic medicine fail to keep pace with the rapid basic science advances and clinical discoveries.

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**Study concept and design:** Scheuner, Sieverding, Shekelle.

**Acquisition of data:** Scheuner.

**Analysis and interpretation of data:** Scheuner, Shekelle.

**Drafting of the manuscript:** Scheuner, Sieverding, Shekelle.

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