Twenty questions in genetic medicine—an assessment of World Wide Web databases for genetics information at the point of care

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Purpose: The aim of this article was to determine the accuracy and efficiency of World Wide Web (“Web”) resources to help nongeneticists answer four clinical questions about each of five common genetic conditions. **Methods:** Correct answers were established by literature review. Two open-access genetics resources and seven general subscription resources were reviewed. Scoring criteria were established to define complete, partial, vague, inconsistent, not found, and wrong answers. The main outcome measures were number of answers found, accuracy, and completeness of answers. Efficiency (time per answer found) was a secondary measure. **Results:** Overall, the databases contained complete answers 33.3% of the time but contained no information as frequently (33.9%). The best database had complete answers 70% of the time, whereas the worst contained no complete answers. Five of the seven subscription databases had a total of eight wrong answers. The other two subscription databases and the two open-access genetics databases had no wrong answers. Search time ranged from 3.2 to 18.3 minutes per complete answer. **Conclusions:** Nongeneticist providers do not have a Web resource that is accessible, accurate, and efficient to answer genetic questions that might arise in practice. *Genet Med* 2008;10(9):659–667.

Key Words: World Wide Web information resources, point of care, primary care, accuracy, efficiency

All providers treat patients with genetic conditions. In a recent survey, genetic medicine consumers rated the genetic knowledge of their nongenetics providers as “poor” 31% of the time.¹ They perceived problems in coordination of care and in awareness of the medical and psychosocial impacts of genetic disorders. Despite this, a majority identified a nongeneticist as the most important provider in overall management of the patient’s condition.

Expectations to integrate genetics into daily patient care are growing, and often exceed providers’ training, knowledge, and confidence.^{2–7} Primary care providers need to be able to recog-

nize when a genetic issue or diagnosis may exist, answer some initial questions for the patient, and make appropriate specialty referral(s). Frequently, an existing genetic condition must be considered when making recommendations about other medical problems. To manage these responsibilities, clinicians need information that is accurate, accessible, and applicable to a specific clinical problem.^{7–12}

Time is scarce in healthcare.^{12,13} Primary care physicians spend less than 2 minutes searching for the answer to a medical question.^{14,15} To be useful in the busy clinical setting, a point-of-care resource must answer questions quickly.

In a 1999 study of primary care physicians, 2% sought answers to clinical questions in electronic resources.¹⁴ By 2005, this proportion had grown to 16%.¹²

Web resources with genetics content include open access and subscription databases. The open access databases are written by and for geneticists. However, nongeneticists, with limited genetics knowledge, may find these resources difficult to understand and use. The subscription databases are more general and are intended for point-of-care use by a broad range of clinicians.

We examined the accuracy and completeness of selected World Wide Web resources in answering 20 clinical questions about genetic conditions. We also evaluated the time required per answer found.

MATERIALS AND METHODS

For five common genetic conditions, we wrote one question each about signs and symptoms, diagnosis, management, and

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inheritance. The intent was to highlight issues that should be considered or may become relevant in a nongenetics clinical setting. These questions were pilot-tested for clarity in five online databases. After the pilot, we refined the questions and the scoring categories to their final form.

We searched the primary literature to determine the correct answers to all 20 questions. All information found in at least three independent references (with no contradictory references) was deemed required for a “complete” answer. Information found in fewer than three references, or where references disagreed, was deemed acceptable, meaning it was neither required for a complete answer nor considered “wrong.” Conditions, questions, required answers, and acceptable answers are shown in Table 1.

We developed a scoring system to evaluate each resource’s answer to each question. To be complete, an answer had to contain all of the required information. There was no penalty for containing or lacking any of the information deemed acceptable. We assigned a score of “partial” when some of the required information was missing, and “not found” when none of the required information was present. Answers that required the user to have any basic genetics knowledge were scored as “vague,” even if they were otherwise complete. Other criteria for vague and criteria for scores of “inconsistent” and wrong are described in Table 2.

Two genetics databases and seven general databases were selected for review (Table 3). Five-Minute Clinical Consult is available within InfoRetriever, but was excluded from the specific analysis of InfoRetriever. During the last 2 weeks of January 2007 each author independently reviewed six of the nine databases. Two authors examined each database; each pair of authors shared three databases.

We compared the two assigned scores for each question. If both reviewers scored the answer as complete or not found, that was the final score. If matching scores of partial were assigned, we merged the detailed notes taken by each investigator. If the combination included all required content, a final score of complete was assigned. If not, the final score remained partial. The third investigator reviewed all scores of vague, inconsistent, or wrong, and all disagreements between the two primary reviewers. The third investigator reviewed the detailed notes of the primary reviewers and the database itself, assigning the most appropriate final score.

Each reviewer recorded total time to answer all 20 questions for each database. We calculated the efficiency of each resource in two different ways. First, the time required by the fastest searcher was divided by the total number of answers found, regardless of accuracy or completeness of the answers. We then performed a more rigorous calculation of efficiency for finding correct answers. This was determined as the time required by the fastest searcher divided by the total number of complete answers for each database.

Statistical analysis was conducted using Stata 9.2 (Stata-Corp) and StatXact 7.0.0 (Cytel Software Corporation) software. Inter-reviewer agreement was measured using the kappa statistic (κ). McNemar’s test was used to test scores of com-

plete versus all other scores in comparisons between two databases, question types, or disorders. Cochran’s Q test was used to test scores of complete versus all other results when comparing more than two databases, question types, or disorders.

RESULTS

Internal consistency

For two databases (DynaMed and Online Mendelian Inheritance In Man [OMIM]), there was poor agreement between the initial reviewers (45% and 50%, respectively). The other seven databases had 65–80% agreement between the initial scores. Overall agreement between reviewers was good ($\kappa = 0.57$). The most common disagreements were complete versus vague (26% of disagreements) and vague versus not found (19% of disagreements). In the 28 disagreements over whether or not the information found was complete, 18 (64%) were assigned a final score of complete. Overall, the arbitrator chose a higher score 23 times and a lower score 34 times.

Accuracy of information

Of the 180 answers (20 questions in each of nine databases), 60 (33.3%) were considered complete and 61 (33.9%) were not found. Partial and vague final scores were common (22 and 27 times, respectively). Final scores of inconsistent were assigned twice and wrong eight times (Fig. 1).

GeneReviews was the most accurate resource containing 70% complete answers and 90% either complete or partial. It had significantly more complete answers than the four worst performing databases (Table 4). There was no significant difference compared with the two next-best performers. Fifty-five percent of the content in UpToDate was scored as complete, but no other resource contained more than 50% complete responses. Importantly, GeneReviews, OMIM, UpToDate, and Physician’s Information and Education Resource (PIER) contained no wrong answers (Fig. 2).

There were no significant differences in the number of complete answers among the five conditions (Cochran’s Q test; $P = 0.62$). Across the databases, cystic fibrosis had the most complete answers (15 of 36; 41.7%) (Fig. 3). Hemochromatosis, neurofibromatosis 1, and fragile X syndrome were similar, with 30.6–36.1% answers scored as complete. Hereditary breast and ovarian cancer questions had the fewest complete answers (25.0%). Of the eight wrong answers found, half were for questions about hereditary breast and ovarian cancer. Only fragile X syndrome had no wrong answers. The differences in number of wrong answers among the five conditions were not statistically significant (Cochran’s Q test; $P = 0.23$).

Finally, we examined the data by question type (signs and symptoms, diagnosis, management, inheritance) (Fig. 4). Significant differences were seen for number of complete answers (Cochran’s Q test; $P = 0.003$) and for wrong answers (Cochran’s Q test; $P = 0.05$). Fifty percent of the wrong answers were in the diagnosis category and 25% each were in the management and inheritance categories. There were no wrong answers

Table 1
Conditions, questions, and answers for the study

Question	Required for complete answer	Acceptable answers	References
Hemochromatosis			
List the major clinical manifestations of untreated hemochromatosis.	Fatigue, lethargy and/or weakness Arthropathy and/or arthritis Hepatomegaly, hepatic fibrosis or hepatic cirrhosis Hepatocellular carcinoma Hypogonadism (including impotence, reduced libido, amenorrhea) Diabetes mellitus Hypothyroidism Cardiomyopathy Arrhythmia	Liver enzyme elevation Skin hyperpigmentation Osteopenia or osteoporosis	18–23
Which of the following is the best test to establish a clinical diagnosis of hemochromatosis? (Choose from <i>HFE1</i> gene mutation analysis; serum ferritin; transferrin saturation.)	Transferrin saturation	None	18–23
Which clinical manifestations of hereditary hemochromatosis are unlikely to improve with phlebotomy?	Diabetes Hypogonadism Arthropathy Risk of hepatocellular carcinoma (if cirrhosis is present)	Cirrhosis Hypothyroidism	18–22,24,25
Members of what racial or ancestral group are most likely to carry a mutation in the <i>HFE1</i> gene for hemochromatosis?	Any one or more of: Northern European Caucasian Celtic	None	18–23,26
Neurofibromatosis-1			
What percentage of people with neurofibromatosis-1 has a learning disability?	30–65%	None	27–30
List the diagnostic criteria for neurofibromatosis-1.	Six or more café-au-lait macules >5 mm in diameter (before puberty) or >15 mm in diameter (after puberty) Two or more neurofibromas of any type or one plexiform neurofibroma Freckling in the axillary or inguinal regions (skin folds) Optic pathway glioma Two or more lisch nodules (iris hamartomas) Dysplasia of the sphenoid bone, or dysplasia or thinning of the cortex of the long bones (e.g., tibia) First-degree relative with NF1	None	28,29,31,32
Other than essential hypertension, what etiology must be considered in a child or adolescent with neurofibromatosis-1 who develops high blood pressure?	Renal artery stenosis/renovascular hypertension	Coarctation of aorta	28,29,31–33
In what percentage of neurofibromatosis-1 patients would you expect to find an affected parent?	50%	None	28,31,34,35
Cystic fibrosis			
What percentage of cystic fibrosis cases present with meconium ileus?	10–20%	None	36–38

(Continued)

Table 1
Continued

Question	Required for complete answer	Acceptable answers	References
What tests are acceptable to establish a clinical diagnosis of cystic fibrosis?	Genetic test showing two CFTR mutations Elevated sweat chloride on two separate occasions Abnormal transepithelial nasal potential difference on two separate occasions	None	36,38–40
Other than a gastroenterologist and a pulmonologist, what other healthcare providers should be involved in a cystic fibrosis management team?	Nurse Nutritionist/dietician Social worker and/or psychologist Respiratory therapist Physical and/or occupational therapist	Geneticist and/or genetic counselor	41–46
If a woman of Northern European ancestry has a negative standard 25-mutation cystic fibrosis carrier screening test, what is the remaining chance that she may still be a carrier? (Choose from zero: reduced, but not zero; the general population carrier frequency.)	Reduced, but not zero	None	39,40,47
Hereditary breast and ovarian cancer (HBOC)			
What cancers, other than breast and ovarian, are associated with mutation of the <i>BRCA1</i> or <i>BRCA2</i> genes?	Peritoneal Pancreatic Prostate	Colon Fallopian tube Stomach Malignant melanoma Buccal cavity or pharynx Liver Gall bladder and bile ducts	48–60
What proportion of hereditary breast cancer is attributable to mutation in the <i>BRCA1</i> or <i>BRCA2</i> genes?	Approximately 80%	None	61–64
Oophorectomy may be offered to women with a <i>BRCA1</i> mutation to reduce the risk of breast and ovarian cancer. What effect is oophorectomy likely to have on the risk of peritoneal carcinoma?	No change	None	48–51
A woman had an aunt and grandmother on her father's side with breast cancer. A second woman had the same pattern on her mother's side. Which woman is at greater genetic risk for breast cancer?	Equal	None	59,65,66
Fragile X			
List 2 clinical problems that may occur in men and/or women with milder mutations of the <i>FMRI</i> gene that don't cause the full fragile X syndrome.	Fragile X associated tremor ataxia syndrome (FXTAS) Premature ovarian failure	None	67–77
What is the minimum number of tri-nucleotide repeats to unequivocally establish a diagnosis of fragile X syndrome?	200	None	67,68,70,72,73,75,77,78
What specialty consultations or tests are recommended when a child is newly diagnosed with fragile X syndrome?	Speech and/or language therapy Occupational therapy Behavior specialist Genetic counselor	Physical therapy Special education Psychology	67,71,72,77,78
A boy is diagnosed with Fragile X syndrome. His mother and father both have pregnant sisters. Which of these pregnant women is at risk for having a child with fragile X syndrome?	Mother's sister	None	67,68,70,71,73,77,78

Table 2
Criteria for scoring databases

Score	Criteria
Complete	Contains all items required for a completely correct answer A numerical answer must be within the defined correct range
Partial	Missing one or more items required for a completely correct answer
Vague	Information that likely would not be explicitly clear to an average user, especially if it requires any genetic knowledge or more than a single mathematical calculation "X-linked recessive with 60% penetrance" is vague "The inherited rate is 1/100 and the new mutation rate is 1/500 in this autosomal dominant with 70% penetrance" is vague To determine the frequency of symptomatic individuals, "80% are clinically normal" (meaning 20% have symptoms) is acceptable
Inconsistent	Contains conflicting information, none of which is wrong
Wrong	Any information relevant to the question is wrong
Not found	No clearly identifiable information was found

Table 3
Databases in this study

Open access genetic databases	Subscription databases
GeneReviews	UpToDate
OMIM	First Consult
	PIER
	DynaMed
	5-Minute Clinical Consult
	Epocrates
	InfoRetriever

OMIM, Online Mendelian Inheritance in Man; PIER, Physician's Information and Education Resource.

in the signs and symptoms category. The only significant pair-wise difference for complete answers was between signs and symptoms (17 of 45; 37.8%) and management (11 of 45, 24.4%) (McNemar's test; $P = 0.03$). No pair-wise comparisons for wrong answers were significant at the 0.05 level.

Efficiency

When we looked at time per any answer found (regardless of the accuracy of the information), GeneReviews and UpToDate were the most efficient at <3 minutes per answer (Table 5).

Using the more rigorous standard of "time per complete answer found," the efficiency of GeneReviews' was 3.2 minutes. The next most efficient resource was UpToDate at 4.5

Fig. 1. Final categorization of database answers.

Table 4
Comparison of GeneReviews to other databases for number of complete answers

Comparison database	No. of complete answers (%)	McNemar's test, P (two sided)
GeneReviews	14 (70)	—
UpToDate	11 (55)	0.45
First Consult	9 (45)	0.23
OMIM	7 (35)	0.07
PIER	7 (35)	0.07
DynaMed	5 (25)	0.004
5-Minute Clinical Consult	4 (20)	0.006
Epocrates	3 (15)	0.003
InfoRetriever	0 (0)	<0.001

OMIM, Online Mendelian Inheritance in Man; PIER, Physician's Information and Education Resource.

minutes. No other database was below 7 minutes per complete answer found. All of the databases exceeded the critical 2 minute per question standard by at least 50%.

DISCUSSION

In an ideal world, the information needed to care for a patient would be accessible, clinically relevant, accurate, and found quickly. When new or complex issues arise, clinicians need an information resource to assist with appropriate evaluation, management, and referral. They often look for point-of-care answers in secondary sources that have demonstrated

Fig. 2. Answers by database.

Fig. 3. Answers by condition.

authority.^{11,12} It has been proposed that they are using the authority of the source as a proxy for accuracy, trusting that the author or editor has validated the information.¹¹

This study examined nine online resources in January 2007. Overall, there was a lack of genetic information across the databases. Answers were scored not found as frequently as they were scored complete. No database was efficient enough to meet the time demands of the typical busy primary care clinician.

The best resource was GeneReviews. It provided 14 complete answers and four partial answers to the 20 questions, with no wrong answers. As an open access database, it is freely available to anyone. GeneReviews was also the most efficient database judged by either the “any answer” or the “complete answer” criterion. However, it still took 3.2 min-

utes per complete answer, which is too long for a primary care setting.^{14,15}

OMIM did especially poorly on questions about management and inheritance (data not shown). However, this database describes itself as a catalog of human genes and genetic disorders. It is not intended as a clinical management resource. In addition, because OMIM is written for use primarily by genetics professionals, it assumes that the user has some basic genetics knowledge. This caused OMIM to be rated as vague for three of the four inheritance questions.

Each of the nongenetics databases describes itself as intended to assist with clinical decision support at the point-of-care. The best of them, UpToDate and First Consult, each answered about half of our questions completely. However, they were less accurate and less efficient than GeneReviews (Fig. 2

Fig. 4. Answers by question type.

Table 5
Database efficiency

Database	Fastest time (minutes)	Total answers found ^a	Min per any answer found ^a	Complete answers found	Min per complete answer found
GeneReviews	45	19	2.4	14	3.2
UpToDate	50	18	2.8	11	4.5
First Consult	81	19	4.3	9	9.0
OMIM	65	14	4.6	7	9.3
PIER	50	8	6.3	7	7.1
DynaMed	50	16	3.1	5	10.0
5-min Clinical Consult	33	11	3.0	4	8.3
Epocrates	55	11	5.0	3	18.3
InfoRetriever	30	3	10.0	0	N/A ^b

^aIncludes "Complete," "Partial," "Vague," "Inconsistent," and "Wrong" answers.

^bNo complete answers found for infoRetriever.

OMIM, Online Mendelian Inheritance in Man; PIER, Physician's Information and Education Resource.

and Table 5). All of the nongenetics resources are accessible only by subscription or membership.

Limitations

The primary goal of this study was to evaluate point-of-care databases for completeness. We continued searching even after finding a partial answer, searching for the most complete answer possible. As a result, efficiency is probably underestimated for each database. Balancing that, however, using the fastest individual searcher's time biases the data toward more efficiency. The primary reviewers routinely use all the databases except InfoRetriever and DynaMed, minimizing any bias toward faster searches in individual databases.

We have not formally established the relevance of our 20 questions. However, they were written by active clinicians with experience and training in primary care and genetics. We believe they represent realistic issues that may arise in a clinical encounter with a nongeneticist.

Our scoring criteria assumed that a user has no more than minimal genetic knowledge. Less rigorous criteria probably would have resulted in fewer partial or vague answers and more complete answers. This is especially true for the two genetics resources, GeneReviews and OMIM.

We studied only 20 questions per database. This may have limited our ability to detect differences between resources.

These findings are applicable only for the selected databases as they existed on the World Wide Web in January 2007. These resources have undoubtedly changed since this evaluation.

Comparison with other studies

Ely et al.¹² directly observed primary care physicians and recorded their attempts to answer clinical questions. Answers were found easily 41% of the time, with difficulty 31% of the time, and not at all 28% of the time. In 2001, Alper et al.¹⁶ concluded that "point-of-care searching is not yet fast enough to address most clinical questions identified in routine prac-

tice.” They studied 14 databases and found that 20–70% of 20 general primary care questions were answered adequately, requiring 2.4–6.5 minutes per answer. They defined “adequate” as good enough to guide clinical decision-making, but the accuracy of the answers was not examined. In 1999, Graber et al.¹⁷ searched 16 Web resources for predefined accurate answers to 10 common questions posed by primary care clinicians. The success rate was 0–60%. Our results are similar, finding any answer (without regard to accuracy) 15–95% of the time and complete answers 0–70% of the time.

Implications

It is worrisome that more than half of the databases in this study provided wrong answers. One might assume that a subscription database has greater authority and accuracy than a free resource. However, all of the wrong answers in this study were found in sources that require a paid subscription for access.

The most frequently asked questions in primary care are about diagnosis and management.^{14,15} Our study found that diagnosis questions had the most wrong answers and management questions had the fewest complete answers. This significantly decreases the utility of the databases for nongenetics providers caring for patients with genetic conditions.

Many World Wide Web databases do not answer clinical questions about genetic conditions accurately. None of the resources we tested are efficient enough for point-of-care use. As genetics becomes more prominent in daily patient care, providers will need an efficient, accurate, and accessible source of information.

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