

BRIEF COMMUNICATION

Marketing of Personalized Cancer Care on the Web: an Analysis of Internet Websites

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Abstract

Internet marketing may accelerate the use of care based on genomic or tumor-derived data. However, online marketing may be detrimental if it endorses products of unproven benefit. We conducted an analysis of Internet websites to identify personalized cancer medicine (PCM) products and claims. A Delphi Panel categorized PCM as standard or nonstandard based on evidence of clinical utility. Fifty-five websites, sponsored by commercial entities, academic institutions, physicians, research institutes, and organizations, that marketed PCM included somatic (58%) and germline (20%) analysis, interpretive services (15%), and physicians/institutions offering personalized care (44%). Of 32 sites offering somatic analysis, 56% included specific test information (range 1–152 tests). All statistical tests were two-sided, and comparisons of website content were conducted using McNemar's test. More websites contained information about the benefits than limitations of PCM (85% vs 27%, $P < .001$). Websites specifying somatic analysis were statistically significantly more likely to market one or more nonstandard tests as compared with standard tests (88% vs 44%, $P = .04$).

The genomics revolution has created unprecedented opportunities and challenges for cancer care delivery. While somatic and germline testing stands to dramatically improve patient outcomes, the paucity of genetic testing regulation (1) may undermine high-quality cancer care if unproven products are promoted. Increasingly, for-profit companies, hospitals, and academic centers are marketing care that is based on genomic or tumor-derived data (personalized cancer medicine [PCM]) over the Internet. In light of the potential benefits and harms of internet marketing, there is an urgent need to understand the types of "personalized" genomic products and claims that patients may encounter online. In order to address this need, we systematically analyzed internet websites marketing PCM. In light of prior

work (2–5), we hypothesized that there would be more information on websites about the benefits of PCM as compared with the limitations of PCM and that commercial websites would promote more nonstandard tests than standard tests, as compared with professional or government websites.

We systematically screened the top 30 websites on Google, Yahoo, and Bing, using 54 search terms (Supplementary Table 1, available online) related to personalized or genomic cancer care (4860 websites), as well as websites identified through a literature review and an abstraction of exhibitor information from a national oncology conference (50 websites). In order to capture websites that market cancer-related germline testing, genomic interpretative services, and providers who advertise

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Table 1. Examples of benefit and limitation marketing claims from those websites providing benefit or limitation information*

Marketing claim subtype	No. (%)	Examples of marketing claims
Benefit subtype	47 (100)	
Tailor/personalize your therapy	44 (94)	<p>“Personalized oncology means to match the right drug to the right patient at the right time.”</p> <p>“By identifying the alterations in each tumor’s information pathways, molecular profiling enables the individualization of a patient’s treatment by matching those tumor alterations with one or more drugs.”</p>
Identify more effective treatment	31 (66)	<p>“Every option we present to you has passed rigorous scrutiny and has been proven to have a direct and positive impact on the treatment of your particular form of cancer.”</p> <p>“Our laboratory analyzes your tumor’s response to 8–16 drugs and combinations to identify which treatments will work best to kill your cancer. Why use your body to investigate a drug’s effectiveness, when we can garner the results safely and in a timely manner?”</p> <p>“Similarly, no good doctor should attempt to choose drugs based solely on genomic analyses.... By testing your tumor in its native state, ‘functional profiling’ performed at (our company) takes not just your genomic make-up into consideration, but your cells’ entire biology.”</p>
Outcome benefit	22 (47)	<p>“Through these enhanced treatment options our patients experienced a greater life expectancy, often with significantly less side effects than standard treatment.”</p> <p>“This late stage pancreatic cancer patient’s life was extended five years by (our product)-guided treatment.”</p>
Identify clinical trials	16 (34)	<p>“A clinical trial matching service...which helps connect each patient with relevant clinical trials based on each patient’s tumor type and unique tumor molecular profile, clinical history, and personal considerations.”</p>
Decrease side effects	14 (30)	<p>“We want you to have the peace of mind that comes from knowing you are doing everything you can to maximize the success of your treatment and limit treatment side effects as much as possible.”</p>
Improve prevention/risk prediction	10 (21)	<p>“Individualized, personalized, comprehensive cancer care may yield the best results. Early detection of cancer and preventative measures are offered to every patient.”</p>
Cost savings	10 (21)	<p>“Reduce trial and error at the prescription pad, genetic testing is a tool for better patient care, greater accuracy, lower costs, enhanced care, that is our promise.”</p>
Benefit to physicians	6 (13)	<p>“With the documentation and education (our company) provides, your doctor will have the information they need to understand the value of these additional/optional tests and treatments.”</p>
Access to cutting-edge technology/ new models of care	2 (4)	<p>“(Our company) has also developed technology that uses patient-specific tumor alterations to create a simple blood test for tumor detection and monitoring.”</p> <p>“Our team has helped patients become aware of, and gain rapid access to, innovative treatments that were not initially prescribed by their oncologists.”</p>
Psychological benefits	6 (13)	<p>“If you want the peace of mind that comes from knowing that you are doing everything possible to beat your cancer with the least amount of side effects and the shortest recovery time possible, let (our company) prepare a (personalized plan) for you.”</p>
Limitation subtype	15 (100)	
Test failure	6 (40)	<p>“Although unlikely, in 8–10% of cases, testing cannot be completed.”</p>
Negative result	3 (20)	<p>“It is possible that your tumor does not have any of the mutations tested.”</p>
Challenges of data interpretation	3 (20)	<p>“The sheer volume of data produced by next generation sequencing far exceeds the ability of individual physicians, drug developers and healthcare providers to stay up to date on its potential clinical relevance.... As sequencing costs continue to fall, increased emphasis will be placed on the interpretation of sequencing data.”</p>
Potential for discrimination	3 (20)	<p>“Although confirmed cases of genetic discrimination are thankfully rare, the fear of discrimination by insurance companies is one of the main reasons people hesitate to pursue access to their genetic information...”</p>
Lack of benefit of personalized therapy	2 (13)	<p>“As yet, there are no solid data available confirming the advantages of a patient-individualized or marker-guided therapy. For that reason, deviation from the standard therapies does not make sense at present.”</p>
False positive/false negative	2 (13)	<p>“Next generation sequencing approaches may provide incorrect sequence or mutational data because of insufficient coverage in specific regions of the genome, inability to distinguish highly related human sequences, and sequencing errors.”</p>

Table 1. Continued

Marketing claim subtype	No. (%)	Examples of marketing claims
Uncertain clinical utility	1 (7)	“(Some) reports are based on peer-reviewed, published research where the findings still need to be confirmed by the scientific community. They also include topics where there may be contradictory evidence.”
Ethical/social	1 (7)	“Because genetic information is hereditary, knowing something about your genetics also tells you something about those closely related to you. Your family may or may not want to know this information as well, and relationships with others can be affected by learning about your DNA.”
Tests may not be FDA approved	1 (7)	“(The test) has not been cleared or approved by the US Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.”
Results not intended to be medical advice	2 (13)	“This (web) Site Does Not Provide Medical Advice. All of the material provided on the Site, such as text, treatments, dosages, outcomes, charts, patient profiles, graphics, photographs, images, advice, messages, forum postings, and any other material provided on the Site are for informational purposes only and are not a substitute for professional medical advice or treatment.”

* No. = number of websites. % represents the proportion of websites providing the particular benefit/limitation subtype of those websites that provide benefit (n = 47) or limitation (n = 15) information. FDA = US Food and Drug Administration.

personalized care, we broadly defined PCM as products or services that could be used to tailor, personalize, or individualize care based on genomic or tumor-derived data. Websites were selected for analysis if they marketed PCM. Duplicate, non-English, and linked external websites were excluded. Sites were defined as commercially sponsored if they appeared to sell a product or service for profit, excluding sites sponsored by academic, private, or research institutions or physician practices.

Two coders (SG and KJ) independently coded all websites in REDCap (6) between December 14, 2012 and January 5, 2013. In order to classify PCM tests as “standard” or “nonstandard,” we conducted a systematic literature review followed by a modified Delphi panel (Supplementary Methods and Supplementary Table 2, available online). We classified PCM tests as standard or nonstandard based on evidence of clinical utility, drawing upon the definitions set forth by the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) working group (Supplementary Table 3, available online) (7). Because we wanted to identify PCM tests that had well-established clinical utility, we considered tests to be standard if 90% or more of the 14 expert panelists classified a test as standard.

Intercoder reliability was calculated for all items. Subsequent analyses were conducted after discordant data were resolved by consensus. McNemar’s test was used to evaluate whether websites provided more information about the benefits of PCM, as compared with its limitations, and to determine whether websites were more likely to market one or more standard tests as compared with nonstandard tests. Fisher’s exact test was used to evaluate the association between website sponsor (commercial vs noncommercial) and whether the website included benefit information. In sensitivity analyses, we varied the threshold for the Delphi consensus required for tests to be considered standard at 100%, 75%, and 50%. Statistical analyses were conducted in STATA 11.2 (8) and R (9). All statistical tests were two-sided.

Fifty-five websites marketed PCM products over the Internet (Supplementary Table 4, available online). Across all variables, intercoder agreement was 86%.

Website and search characteristics are displayed in Supplementary Table 5 (available online). While the majority of websites were sponsored by a commercial entity (56%), other

sponsors included academic institutions (20%), private institutions (15%), and individual physicians (2%). Of commercial sites, 29% provided guidance to patients about discussing PCM products with their physician and 10% included a directory of physicians who could provide the test or service. About half of the commercial websites included the cost of testing; test prices ranged from \$99 to \$13 000.

Thirty-one percent of websites offered multiple PCM services (Supplementary Figure 1, available online): 58% percent of all websites (n = 32) marketed somatic analysis and 20% of websites offered germline analysis (n = 11). Websites marketed a wide range of testing (Figure 1). Websites also marketed healthcare institutions or clinical practices offering personalized cancer care (44%) and interpretive services (15%). Eighteen websites marketing somatic testing specified the tests that they offered (Supplementary Table 6, available online). The number of specific tests offered ranged from one to 152 with a median of four. Of websites specifying somatic analysis, several websites marketed guideline-endorsed tests such as EGFR and BRAF (28% of sites), whereas 88% percent marketed one or more nonstandard tests (Supplementary Figure 2, available online). Websites were more likely to market nonstandard tests than standard tests (88% vs 44%, $P = .04$). Across all sensitivity models, nonstandard tests were marketed on more than 80% of websites that specified tumor testing.

Commercial websites were more likely than noncommercial sites to specify the type of somatic testing offered (55% vs 4%, $P < .001$), include a gene/protein list (42% vs 0%, $P = .04$), and market chemotherapy sensitivity testing (19% vs 0%, $P = .03$). We were not able to test our hypothesis that commercial websites would promote more nonstandard PCM as compared with noncommercial sites because only one noncommercial website specified somatic testing, which was whole-exome/whole-genome sequencing. PCM was offered for a variety of tumor types, most commonly for breast, colorectal, and lung cancer (Supplementary Figure 3, available online).

Eighty-five percent of all websites (47/55) included benefit information, whereas 27% (15/55) included limitation information (Table 1 and Supplementary Table 7, available online). Websites included more information on the benefits of PCM than the limitations of PCM ($P < .001$). Compared with noncommercial

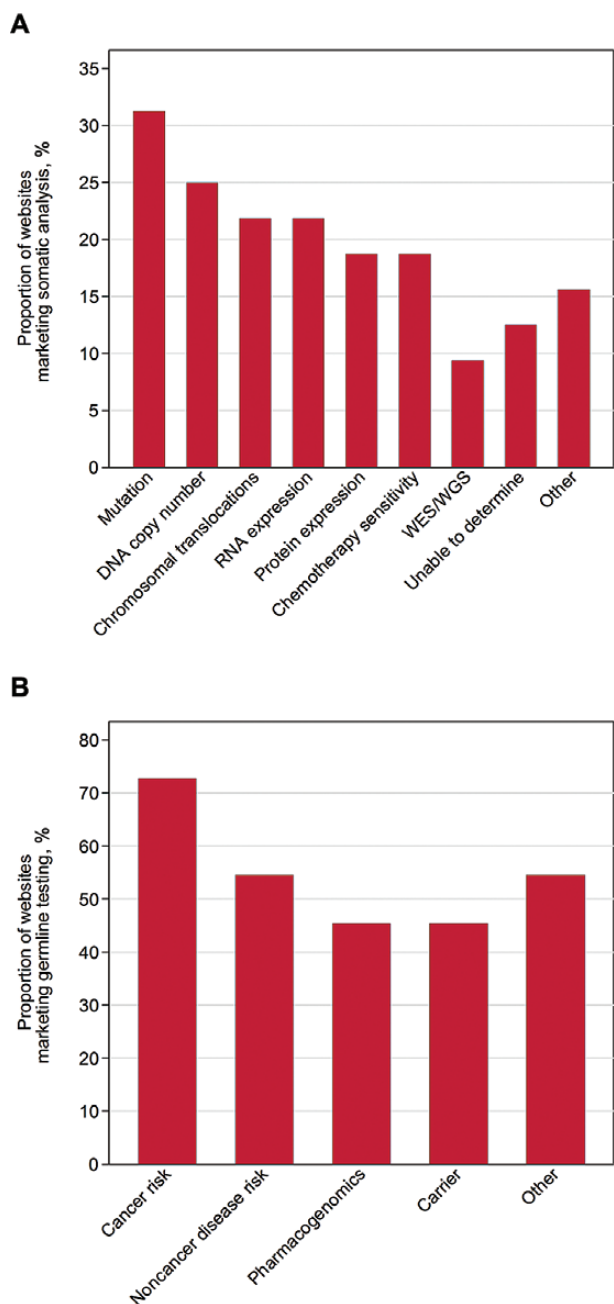


Figure 1. Types of somatic and germline testing offered on the internet. **A)** Types of somatic testing offered among 32 websites marketing somatic analysis. Categories are not mutually exclusive. **B)** Types of germline testing offered among 11 websites marketing germline analysis. Categories are not mutually exclusive. WES = whole exome sequencing; WGS = whole genome sequencing.

websites, commercial websites were more likely to provide information on the benefits of PCM (100% vs 67%, $P < .001$).

Because online marketing of PCM is a recent phenomenon, few data evaluate the effect of such marketing on patient care. Prior work has shown that mass media and print-based marketing can increase referrals for genetic testing and influence patients' attitudes, knowledge, and decision-making (10–12). While few data describe the uptake of online PCM products, several examples provide evidence that demand may be substantial. For example, from 2007 to 2013 over 500 000 people purchased direct-to-consumer (DTC) genetic tests (13), and one

prominent company reported selling over 22 000 somatic tests in 2014, corresponding to revenues of \$9.7 million (14).

In addition, we found that the vast majority of companies that market somatic tests online promote tests that do not have evidence of clinical utility. For example, six websites offered chemotherapy sensitivity testing despite the fact that technology assessments from the American Society of Clinical Oncology (ASCO) have found insufficient evidence to recommend such tests (15,16). While it is likely that patients could use a subset of marketed nonstandard tests to help select clinical trials, it is not clear that Internet marketing of PCM is an effective way to identify alterations indicating trial eligibility.

Our findings support the hypothesis that PCM websites emphasize the benefits and downplay the potential limitations of testing. These results are consistent with prior work showing that marketing materials for genetic tests, medications, and imaging studies often include more benefit than risk information (2,17–19). While we did not assess the validity of claims made on PCM sites, others have found that online genetic testing claims are infrequently supported by scientific evidence (18–22). In the setting of cancer care, information on the limitations of PCM may be particularly important because of the uncertainties inherent in genomic analysis and interpretation.

The debate over genomic marketing is bound to intensify in the wake of the US Food and Drug Administration's (FDA's) demand that the genomics company 23andMe “immediately discontinue marketing” its Personal Genome Service out of concerns for the “public health consequences of inaccurate results” (13,23–25). Since 2008, the Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) has recommended that the FDA regulate all laboratory tests, including genomic tests (1,26), and the FDA has reported that it intends to do so (1,27). Perhaps companies that market genomic tests over the internet should be required to provide consumers with balanced benefit and limitation information, similar to what is required in pharmaceutical marketing (28). When considering legislation, policy makers will need to consider whether new regulations can adequately protect public health while at the same time continue to foster an environment that promotes medical innovation.

Online marketing of PCM also raises several questions about health care utilization and cost. Marketed tests ranged in price from \$99 to \$13 000, and 10% of websites provided patients with a directory of physicians through whom they could order PCM products. While online marketing of PCM may improve access to testing, more work is needed to determine whether such testing will be covered by insurance, to examine the downstream implications of testing and to understand the financial and medical impact of care that may bypass traditional physician-patient relationships.

Until genomic tests are more highly regulated, and perhaps even after regulatory changes are in place, oncology providers will need to guide patients as they navigate decisions about PCM. Providers might want to view such encounters as “teachable moments” and help to educate patients about issues related to clinical validity, clinical utility, and the generalizability of research findings (29,30). Such opportunities for patient education may be missed, however, if oncology providers are not well versed in genomics. Prior work has shown that there is considerable variation in providers' genomic confidence and that inadequate provider education may limit the appropriate integration of genomic tests into clinical care (29,31–33).

Our study adds to the literature by evaluating sites selling “personalized” services beyond genetic tests and employing

rigorous methods to determine whether marketed tests have evidence of clinical utility. Our study also has a number of limitations. While we used systematic methods to determine PCM standards, a different Delphi panel may have classified tests in a different way. Second, it is possible that our findings might have varied if different coders had evaluated the sites or if the coding had been done at a different time. In fact, a recent search of the evaluated websites revealed that nine URLs were nonfunctional; however, we identified alternative URLs for seven of the websites. Changes such as these highlight some of the challenges of studying the dynamic Internet environment. Finally, while we screened over 4900 websites for inclusion, it is possible that we missed websites marketing PCM.

In summary we identified 55 websites that market a broad range of tests and services that promise the ability to personalize cancer treatment. While such marketing may help to disseminate information about evidence-based tests, most companies also market tests that have little or no evidence substantiating the ability to improve patient outcomes. Given the lack of uniform regulation over internet marketing, disproportionate claims of benefit, and promotion of nonstandard technologies, it is essential that clinicians and patients critically evaluate online products.

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