Legal Liability and the Uncertain Nature of Risk Prediction: The Case of Breast Cancer Risk Prediction Models

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Abstract
Background: The rapidity of technological change in genetics is not always matched by the uptake of this new knowledge into practice. Increasing genetic knowledge has already led to legal liability for those who have not used it properly, such as not informing patients or their families of potential genetic risk. A similar outcome is also of concern in the case of risk prediction models used for hereditary breast cancer. Results: No legal case has directly addressed the use of risk prediction models. However, as genetic medicine and risk prediction models become more widely used, the prospect of a lawsuit will also increase. Current case law is instructive on the circumstances under which medical liability actions could be pursued and circumstances under which liability is unlikely, such as the provision of faulty family history information by a patient. Conclusions: There is existing case law on family history and genetics that parallels in many respects the use of risk prediction models. However, the idea of a bad ‘prediction’ is a difficult legal concept. Outside of a plain misuse or failure to use a risk prediction model when circumstances clearly required it, there is little legal guidance presently available to determine the risk for medical liability.

Introduction
A woman goes to her physician and discloses a family history of breast cancer, but does not know of any genetic mutation in the family linked to the cancers. Taking this information into account, the physician uses a risk prediction model to estimate the patient’s risk for carrying a genetic mutation and developing breast cancer. Following a determination that the risk is high enough to warrant further action, the physician refers the patient to a genetic counsellor (or medical geneticist or other qualified genetic health professional) for a further discussion of her options.

This is how we expect our health care system to work: the patient has a potential problem, and the physician identifies it and refers the patient to the appropriate health specialist. However, this system is made up of individuals who do not always perform as expected and may have incomplete information and understanding, especially in a
field where technology is far from static and can change how health care providers respond to particular challenges.

There are thus many opportunities for something to go awry and for the patient to receive too little or too much care. Do we know that the information provided by the patient is accurate? Do we know that the physician used the correct risk prediction model? Even if the correct model was used, do we know that the information was correctly analyzed and the patient appropriately referred? These are all questions that arise as a result of changes in technology and new scientific discoveries, which are not always integrated into medical practice in a timely fashion.

One consequence of technical ability outpacing understanding and uptake is the intervention of the legal system. If, for example, the physician in the scenario above misapplied the risk prediction model, what happens? If the patient is provided with treatment (or not) based upon an erroneous interpretation, are there consequences for the physician or genetic counsellor? What is the patient’s responsibility in this process? Legal liability, while always a concern for health professionals, can have potentially greater impact when dealing with a new technology or practice when there are many unknowns and the technology itself is constantly shifting [1].

**Legal Liability and Genetic Medicine**

Increasing genetic knowledge has already led to legal liability for those who have not used it properly. In the US, for example, a court held a physician liable for not informing the daughter of a patient about the hereditary aspects of the cancer that caused the patient’s death [2]. This decision effectively questioned traditional notions of confidentiality as well as the view of genetic information as individual and ‘exceptional’. It also held the physician to a standard of disclosure that was not fully recognized by the medical profession at that time.

Similarly in Canada, a Quebec trial court found a physician liable for failing to inform the mother of a child of a suspected genetic disorder even though he had informed the father [3]. The judgment, stemming from events nearly 40 years earlier, had the potential to drastically alter the confidentiality and privacy practices in Quebec and disregarded statements by experts that under the circumstances and at the time, the physician fulfilled any duty he may have had by informing the father. However, this decision was overturned on appeal and the appellate court adopted a more tempered approach, recognizing that the physician’s actions were consistent with his responsibility to inform the parents of the child and that it was the father’s failure to convey the information to his wife and, in turn, her family that broke ‘the chain of causation’ [4].

These cases, much like previous cases on confidentiality [5], rapidly altered the practice of physicians – changing both what is ethical and what is legal. In this way, the ebb and flow of legal decisions, legislation and regulation are difficult to predict, much like advancements in medical science.

Today, the discussion by researchers, clinicians and policymakers over how genetic information is used and disclosed in medical treatment is ongoing, with little solid ethical guidance and even less legal guidance. As new ways of identifying, diagnosing and treating diseases with genetic causes continue to be developed, physicians are faced with ever more information, much of which becomes obsolete as new discoveries are made. Implementing this information in clinical practice – and anticipating and addressing new developments – poses substantial challenges to traditional medical practice and gives rise to difficulties parsing out what we know and do not yet know when trying to treat patients. These challenges are exceedingly visible in the case of hereditary breast cancer risk prediction.

**Breast Cancer Risk Prediction Models: The Known-Knowns, Known-Unknowns, and Unknown-Unknowns**

Former US Secretary of Defense Donald Rumsfeld unwittingly provided a perfectly descriptive, if imperfectly received, framework of genetic knowledge. At a briefing in response to a question regarding Iraq, Secretary Rumsfeld replied ‘… as we know, there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns – the ones we don’t know we don’t know’. [6]. Of course, questions about Iraq in the lead-up to war are a far cry from genetics, but the statement still rings true even in the very different context of medical science. These distinctions in knowledge – known-knowns, known-unknowns, and unknown-unknowns – represent the current state of genetic knowledge, albeit in a simplified manner.
Since the linkage between specific BRCA genetic mutations and breast and ovarian cancer in the 1990s, great strides have been made in predicting who might develop cancer as well as ways to prevent its development. The association between family history and cancer was long known [7], but the breakthrough discovery of a genetic basis permitted additional avenues of prediction. These are, quite simply, the known-knowns of genetic medicine: mutations found through substantial and validated research to have a measurable impact on individuals’ risk for developing disease. Unfortunately, the costs and implications of genetic testing mean that not everyone is tested for the presence of mutations known to increase the potential for cancer.

More recently, risk prediction models were developed as additional tools to help clinicians recommend particular courses of preventive treatment or genetic testing for breast cancer in the absence of previous genetic testing of the patient. These models incorporate family history, statistical models, experiential data, and other information to determine the probability of the patient being a mutation carrier or of developing cancer. A number of models have been formulated, including BOADICEA, BRCAPro, Gail, the Manchester Scoring System, and the Myriad tables [8, 9]. Each model takes in different information and provides different results. Some have been validated in specific populations and not others, and some models were developed as variations of existing models to address a particular population [9].

These models are not substitutes for genetic testing; they do not definitively inform patients whether they have or have not a particular genetic mutation or cancer or risk for developing cancer – the known-unknowns, where we know that good answers may not be found. Rather, these tools have been used to determine who might be eligible for additional care, including genetic testing or preventive treatment [10]. Furthermore, as some jurisdictions have minimum risk thresholds that an individual must meet before testing is recommended [11], these models can be used to ensure that those who need additional care are offered it.

However, even as new models are being developed, investigators have examined the value of those already in use. For example, the Penn II model was recently compared to a number of similar models and found to perform slightly better [12]. In a different study, BOADICEA was found to be more accurate than other models (though to be fair, the Penn II study did not examine BOADICEA and the BOADICEA study did not examine Penn II) [9]. Do these studies indicate that other models should be abandoned? Are there particular benefits to older models and weaknesses of newer models? These questions further demonstrate the known-unknown aspects of risk prediction models by highlighting their shortcomings and the issues that have yet to be fully addressed – and which we know to be problematic.

Finally, the progression of genetic knowledge is continual, and over time new linkages will be found between particular mutations and various diseases. This new knowledge may impact the utility of risk prediction models as well as our understanding of the underlying causes and contributors to disease. New risk prediction models might also be developed or old ones modified to take into account this new information. In this instance, we admit to not knowing what we do not know, the unknown-unknowns, which will contract and expand as new evidence is gathered.

How does this tripod structure of genetic knowledge fit within current medical liability theories, especially in the US and Canada? Will lawyers and judges fairly judge the state of the science, and its inherent uncertainty, when deciding questions of injury and who knew what and when? The application of medical liability law to risk prediction models is a mystery at present, but previous cases involving genetic medicine are instructive.

Can Liability in Genetics Be Extended to Risk Prediction Models?

In the typical medical malpractice case, there will generally be a standard of care and a breach of that standard, causing an injury to a patient [13]. For physicians, although the specific rules might vary based on jurisdiction, the general duty is to act as a reasonable physician in a similar circumstance [14, 15]. New technologies and practices combined with sparse legal precedent make it difficult to discern how a reasonable physician would act and, therefore, how the legal system would respond to an alleged breach of the standard of care. In the instance of breast cancer risk prediction models, what is a reasonable physician to do?

For any use of new or continually developing technology, including risk prediction models, the knowledge of the health professional is central to liability. The problem with risk prediction models, though, is 2-fold. First, there are many available, so knowing which one to use for a particular patient and how to interpret the results may not be simple. Second, although many physicians are capable of taking family histories, the information provided
may be incomplete and, therefore, lead to misleading results [16, 17].

It can be easily demonstrated that a duty of care was not met if the physician in question just did not understand the technical aspects of what he or she was doing, therefore, not acting as a reasonable physician. Either the physician should not have been performing the risk assessment or should have been more knowledgeable about the requirements of the particular model. Ill-conceived decisions reflecting a lack of knowledge are essentially easy pickings in the world of medical liability.

It can also be shown that a physician acted negligently by failing to do something. If, for instance, a physician fails to perform a promised genetic test and the patient takes actions that she would not have taken had the test been done and the positive results conveyed it is the physician’s inaction that creates liability [18]. In a case examining this eventuality, Molloy v. Meier stated ‘[The physicians] should have foreseen that negligently rendering care … or erroneously reporting genetic test results … could result in the [harm]’. [18] Both negligently rendering care and erroneously reporting risk assessment results are possibilities when using risk prediction models, so judicial decisions such as Molloy should be considered when examining legal liability following the use of the models.

However, in contrast to a physician’s breach of duty, the use of a risk prediction model might also start with a caveat to the patient: ‘based on the information you have provided to me …’. This is both important to the issue of liability in the use of risk prediction models and an indication of the models’ limits. Often in medical liability, it is a clear act (or failure to act) by a physician that causes a patient’s harm. In this instance, the cause of harm could stem from the physician, the patient or both.

The only legal cases identified that closely parallel the family history component of risk prediction models demonstrate the potential confounding effect of the patient-provided information relied upon for the accurate functioning of the models. In Downey v. Dunnington, a physician recommended that his patient undergo a prophylactic mastectomy based on her family history of breast and ovarian cancer without first performing genetic testing for the patient or her mother as an alternative to invasive surgery. (It should be noted that the primary reason the physician did not refer the patient for genetic testing was the patient’s lack of financial resources and the high cost of the test, which was not covered under the state’s Medicaid program [medical insurance for those making less than a specified income]) [19]. The patient and her mother, however, provided an erroneous family history: the mother had previously been diagnosed with unilateral breast cancer and cervical cancer, not bilateral breast and ovarian cancer as they told the physician. The physician in this case prevailed, despite a number of missteps such as failing to verify the family history provided by the patient and not sending the patient to a genetic counsellor [19]. The jury essentially viewed the patient’s (and her family’s) inaccuracies as the root of the erroneous medical decisions in the case, despite the physician’s deficiencies.

An earlier case, Munro v. Regents of the University of California, likewise stemmed from a failure to order genetic testing following the collection of family information. The physician obtained from parents-to-be a genealogy to rule out risk for Tay-Sachs disease, which is more prevalent in the Ashkenazi Jewish population than the general population [20]. However, unlike in Downey where the physician’s failure to pursue the family medical history contributed to the decision to recommend potentially unnecessary surgery, the physician here had no other source of information from which to confirm the parents’ family heritage. It was only following the genetic counselling session that the physician was informed that their heritage included a French-Canadian population with a higher prevalence of the disease. When it comes to family history, information that is outside the control of the physician can shield against liability.

The outcome of situations similar to those in the above legal decisions and following the use of risk prediction models is unknown. The legal system is apt to address scientific discoveries in much the same way as medical science does: it adapts current practice and rules to these new circumstances. However, the reliance on previous case law in common law jurisdictions can greatly impact a court’s or jury’s decision as to the legal doctrines to apply in a given case (the legal concept of stare decisis).

These cases might therefore play a role in determining medical liability involving risk prediction. First, the same issues could arise – a physician could fail to assess risk when warranted by the medical evidence or could use a model inappropriately. This could occur from simple negligence, but also from a failure to understand the models or keep up with new developments in the field. Second, the results of a misapplication can be serious for a patient. For one, the decision not to pursue genetic testing or preventive treatment when an accurate use of a model would have indicated the need could cause the patient to forego monitoring in the future. Conversely, undergoing preventive surgery, as happened in Downey v.
Dunnington, could cause a patient unnecessary pain and suffering as well as emotional trauma. Even though risk prediction models are not guarantors of genetic risk, they do have real physical and emotional consequences.

**Conclusion**

In a perfect world, the ‘reasonable’ physician would have good knowledge of all the different risk prediction models and the ability to apply this knowledge to any given patient. Unfortunately, our world is not perfect, especially when it comes to the genetic knowledge of physicians at the front lines of patient care. The genetic education of physicians, especially in those specialties not directly tied to genetic medicine, is often lacking [21, 22]. It is perhaps only through a distorted perspective that we expect physicians to have a complete understanding of all things medical. Furthermore, the constant changes in medical science make it difficult for any physician, regardless of training and background, to keep up with new information and techniques.

When the expectations of patients (and society) are not met, one result can be a medical liability lawsuit. recourse to the courts is common today in the case of injury linked to medical care (even when there is no injury or no negligence) [23], and court cases on genetic risk and the family have amply demonstrated the impact that medical liability lawsuits can have not just on a particular health professional, but on medicine more broadly by changing methods of practice or avenues of care. New theories of liability are tested regularly, and the receptiveness of a judge or jury can greatly influence the practice of medicine and a decision to use or not a new technology, device or procedure.

In the case of risk prediction models the jury is, as they say, still out. There is existing case law on family history and genetics that parallels in many respects the use of risk models. However, the idea of a bad ‘prediction’ is a difficult legal concept and a poor outcome for a patient might not have the same aura of negligence that is present in many other instances of medical liability. In terms of the categorizations of genetic knowledge set forth previously in this paper, there are too many unknown-unknowns remaining in genetic risk prediction. Outside of a plain misuse or failure to use a risk prediction model when circumstances clearly required it – a known-known situation – there is little legal guidance presently available to determine the potential for medical liability following the use of a model. This does not mean that liability will never occur. Rather, it is just the legal beast lurking behind the genetics door.

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