Genomics and Insurance in the United Kingdom: Increasing Complexity and Emerging Challenges

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ABSTRACT

This article identifies issues relating to the use of genetics and genomics in insurance that may challenge existing regulatory models in the UK and elsewhere. We discuss three core issues: (1) As genomic testing advances, and results are increasingly relevant to guide healthcare across an individual's lifetime, the distinction between diagnostic and predictive testing that the current UK insurance code relies on becomes more blurred and this has consequences what constitutes a genetic "result" (2) The emerging category of pharmacogenomic tests which are predictive only the in the context of a specific prescribing moment (3) The increasing availability and affordability of polygenic scores that are neither clearly diagnostic nor highly predictive, but which nonetheless might have incremental value for insurance underwriting beyond conventional factors. We also outline the broad scope of possible regulatory responses to these developments. At present in the UK, consumers are not obliged to declare results of predictive genetic tests except in very specific scenarios, meaning that pricing is not actuarially fair (premiums paid in such cases are likely to be lower than the expected value of the compensation received). We suggest a deliberative approach is required to establish where these deviations from actuarially fair pricing should be upheld, and whether there might be situations in which they should be withdrawn.

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1. Introduction

This article identifies emerging issues relating to the use of genomics and genetics[1] in insurance. These issues relate to clinical, research, technological, and economic developments that may disrupt prevailing regulatory models intended to support the efficient and equitable provision of insurance. Our focus is on the specific regulatory context of the United Kingdom, but the general issues we raise will apply to varying extents in other jurisdictions.

The challenges that genetic testing and genetic data may pose to insurance have long been anticipated. In 1935, R.A. Fisher gave a lecture at the International Congress on Life Assurance Medicine in London on 'Linkage studies and the prognosis of hereditary ailments', which argued for the "great importance" of characterizing linkage groups so that inheritance could be estimated and "to predict the occurrence of other factors of greater individual importance, such as those producing insanity, various forms of mental deficiency, and other … diseases" (1, 2). Diagnostic tests for genetic conditions began to be used by the UK insurance industry to inform offers of cover in the 1990s, in light of which a "Genetic Testing Code of Practice" was introduced by the Association of British Insurers (ABI) in December 1997 (3). A version of this agreement has existed in various forms ever since and has been subject to amendments over time (4) .

The current version of the Code (5, 6), a voluntary agreement between the UK government and the ABI, refers to two types of genetic test. Diagnostic genetic tests are defined as those that confirm or rule out a diagnosis. Predictive genetic tests assess future disease risk in individuals without symptoms of a "genetic disorder".

[1] We use "genetics" and "genomics" interchangeably throughout

The Code embodies two core principles. The first prohibits insurers from requiring or pressuring applicants for insurance policies to take either type of genetic test. The second relates to predictive tests, the results of which may be considered only if the test is specifically named in the Code and if the financial sum to be assured exceeds limits defined in the Code. Only one such test currently meets these criteria, which is a predictive genetic test for Huntington's disease in relation to applications for life insurance cover over £500,000.

However, the code does not define how predictive a test has to be, and these will range from strongly predictive (e.g. for Huntington's disease) to weakly predictive for diseases where only a small proportion of those tested ultimately develop the disease (e.g. some of the genetic tests predicting cardiac arrhythmias). The Code does not prevent the use of family history for a disease or trait. Strongly heritable conditions will sometimes have a family history and insurers can and do use this information as an indirect genetic test of disease risk.

A long-standing concern (7-16) that motivated the original version of the code and its subsequent iterations has been the possibility of genetic discrimination, which could involve the denial of insurance, restrictions to coverage, or substantially higher premiums to those with particular genetic profiles (11, 17, 18). This could lead to individuals refusing to take genetic tests that were otherwise indicated for fear that their results (or the mere fact of taking the test) could result in exclusion or in unfavourable terms when seeking insurance. On the other side of the market, prohibitions or limitations on the ability of insurers to use genetic information in risk-based pricing could threaten their solvency or lead to the withdrawal of particular insurance products (19, 20).

These types of concern were, in some cases, motivated by an expectation that genetic tests would be substantially more predictive and discriminating than they have proved to be (21). To date, evidence from annual reports of the operation of the Code (6) and elsewhere suggests the overall impact of these phenomena has been limited, including for highly penetrant monogenic disorders (21) where their impact might be expected to be greatest.

However, even in the absence of radical increases in the diagnostic or predictive capacities of genetic testing, recent developments in identifying genetic contributions to disease susceptibility, longevity, and drug responses, may merit new forms of oversight to support the interests of both insurers and their policyholders (12, 19, 22-26). We describe three developments that may increase the salience of genetic data for – in particular -life insurance and health insurance.

The first development relates to the fact that, as genetic testing routinely encompasses ever greater portions of the genetic code, the distinction between diagnostic and predictive genetic testing becomes blurred. A “typical” person has around 100,000 rare variants in their genome (27) - some of these may help diagnose a condition already known about, others may predict disease (with varying degrees of accuracy) and yet others be entirely uncertain as to what their effects may be. This blurs the distinction alluded to in the Code and has consequences for what elements of a genomic analysis might constitute a “result”.

The second area relates to pharmacogenetics, which is the study of how genetic variation can affect an individual's response to medicines, particularly with respect to drug efficacy and safety. However, predictions of response at an individual level are imperfect, the medicine in question may never be required, and identification of the risk of serious adverse events could increase the cost of future healthcare and therefore potentially the costs of

insurance (if no effective alternative treatments are available) or reduce these costs (if treatment is more effective when informed by pharmacogenetics).

The third area relates to the increasing availability and affordability of “polygenic scores” that measure a component of risk for common disease, and so are neither clearly diagnostic nor highly predictive. The contribution of a polygenic score to absolute risk may be very small. Nonetheless, there is evidence that polygenic scores might add some value to underwriting beyond conventional factors. We discuss these three issues below after first briefly reviewing the principles of insurance, risk rating and actuarial fairness.

2. Insurance, risk rating and actuarial fairness

Insurance protects against loss of income associated with unpredictable events. While an event may be expected (such as some form of prolonged ill health) or certain (death), its timing and consequences are likely to be unpredictable. Faced with uncertainty about the timing, scope and extent of medical and other spending, individuals derive value from pooling risks with others in the population. Within a risk pool, the majority of individuals who do not make claims contribute to meet the cost of the minority who do make claims.

The premium and terms of insurance contracts are typically based on the assessed risk that a prospective customer may experience such an event that necessitates a claim, as well as the costs borne by the insurer in providing cover. Higher assessed risk generally results in higher premiums to be paid by customers, and/or more restrictive contract terms. The converse will generally be true for lower assessed risk. The need to gauge risk accurately motivates the disclosure obligations central to almost all insurance contracts. The price of insurance reflects, in large part, the average expected cost within risk pools of individuals (or organizations) with similar risk profiles.

From an actuarial perspective, a fair insurance contract is one that accurately prices risk. Systematic mispricing of insurance by a single provider, in the sense of overcharging or undercharging certain groups given the risks and therefore the costs associated with each group, will result in a competitive disadvantage and will not be sustainable. However, actuarial fairness - while a critical consideration – is rarely the sole criterion that determines the availability, structure and cost of insurance products made available.

In part, this is due to complications of agency, which arise because, unlike in most other markets, the likelihood of incurring significant cost in the process of providing the service of insurance depends in a fundamental way on the (potentially unobservable) characteristics of the buyer and the (potentially unobservable) actions this buyer might take (28). We consider an important example of agency problems – adverse selection – below in our discussion of how polygenic scores could contribute to insurance underwriting.

Reliance on actuarial fairness "expresses the moral judgment that fair underwriting practices must reflect the division of people according to actuarially accurate determination of their risks"(13). Wider considerations beyond actuarial concerns may involve access to insurance by different groups, the cost and quality of insurance, privacy issues, market functioning, and ultimately how best to achieve the fundamental goal of protecting against future events that compromise health given these types of constraint.

In this context, some individuals may (29, 30) regard genetic risk factors differently from more conventional rating factors used in insurance (such as age, sex, occupation, smoking status and many others) (29). For example, privacy issues in relation to genetic data are at least as important as for other health data (30). Genetic data also has an inherently familial dimension (31-34) which may influence people's willingness to share these data with

insurers compared to other types of health data. Below, we consider how increasing volumes of genetic data allied to the growing complexity of defining which of the many genomic variants found during a test should be considered a “result” merit renewed attention.

3. The meaning of a genetic “result”

The cost of genetic testing continues to fall, and the volume of data that such testing produces continues to increase (35). Identifying relevant, meaningful variants that have or are likely to have health implications for the individual concerned is increasingly challenging. To place the scale of variation in context, there are on average 4-5 million differences between the reference human genome and any typical human genome (27) – and many of these differences will be challenging to interpret in terms of their medical impact.

Indeed, large numbers of variants that have historically been considered to be pathogenic (associated with specific health outcomes) have in fact turned out to be common in individuals who do not show the associated phenotype (36), suggesting that either their original classification was wrong, or that their impact on health is more subtle or context-dependent than previously appreciated. Beaumont et al (37) illustrated the challenge of interpreting people’s genomic data, showing that while large gene panels may maximize diagnostic yield, they are also likely to identify several variants that look hypothetically concerning though are probably benign: most people have at least one rare variant in the coding regions of the genome in panels containing over five hundred disease genes. Even for ‘well-understood’ pathogenic genetic variants, context matters: Jackson et al (38) found that people with cancer-predisposing genetic variants were at significantly less elevated risk of

cancer in the absence of a family history. These issues are likely to be amplified by initiatives to undertake whole genome sequencing of all newborn children within a population.

The predictive value of a specific variant identified via genetic testing in the absence of phenotype and positive family history may therefore be low (35, 39, 40). Prior to very recent expansions in the scale and speed of genetic testing, genetic tests examining a limited number of carefully chosen genes were typically only offered to people with a personal or family history that strongly suggested a genetic condition. In this scenario, if a potentially concerning variant was identified there was a much higher probability of it being medically relevant, permitting greater confidence in diagnosis.

As genetic tests become broader, a distinction has emerged between using genetic results for diagnoses (in tandem with other clinical information) and the use of genetic data for other purposes (such as prediction of disease risk) outside of a clear familial or phenotypic context. For example, in the former case, a high degree of confidence might be expected in reaching an overall diagnostic assessment for a particular individual. In the latter, inferences about disease risk are likely to be less meaningful at the level of the individual. Where this distinction was more stark, positive diagnostic genetic test results in an individual would in many cases motivate the use of predictive tests in family members.

This changing distinction between diagnostic and predictive results may also be influenced in some contexts by prognostic information. For example, in some cases an underlying genetic cause for a clinical diagnosis may change the prognosis associated with a particular condition. For example, knowledge that an individual has congenital long QT syndrome (which is associated with irregular or abnormal heart beats) may change the prognosis associated with the risk of future cardiac arrests (41).

There is also increasing interest in polygenic scores (42). Polygenic scores are aggregated summaries analyzing many points of variation in the genome to estimate liability to disease incidence, disease progression or related outcomes. Does knowledge that an individual has high polygenic risk for a particular condition constitute a genetic "result"?

Without additional information, knowledge that an individual is in the top decile or even the top percentile of a polygenic distribution for incident disease may indicate only a marginal increase in lifetime risk, and furthermore could miss most cases that occur in people other centiles. For example, women in the top 5% of polygenic risk for ovarian cancer have a lifetime risk of 2.1% for developing this condition, compared a population average risk of 1.6% (43). The overall distribution of the polygenic risk at the population level may be informative for disease etiology, even if knowledge of an individual's polygenic risk in itself does not contribute much, if anything, to knowledge of "which particular individuals will succumb" (44) to the condition of interest. Below in Section 5 we explore other potential consequences of polygenic scores for insurance in the context of increasing knowledge of the association between genotype and healthcare costs.

Insurance company perspectives

Even if genetic variants found by genomic tests can- in certain contexts- help predict disease, one may argue that no changes to current practices are required. This would be the case if, in fairly assessing risks, insurers recognize that many apparently pathogenic genetic variants may in fact turn out to be clinically insignificant, and as such avoid gross distortions to the pricing of risk. However, the situation may be more complicated than this given the responses that insurers and individuals may make to genetic information. Lacaze et al (45) note, that this is "contingent on the insurer actually understanding the concepts of

incomplete penetrance (and variable expression (degrees of disease severity)) in the population, and excluding these variants from risk calculations for that individual."

Ashcroft (46) refers to irrational discrimination by insurers arising from "false beliefs" about genetic information. In this case, the identification of a variant, or a combination of variants, may at best lead to mispricing of the associated risk, or at worst an actuarially unjustified refusal to insure an individual. In either case, there would be too little insurance offered at too high a price.

For example, pathogenic variants in *MYBPC3* gene increase the risk of developing hypertrophic cardiomyopathy (47), a disease caused by dysfunction in the cardiac muscles which can lead to arrhythmia and sudden death (48). Many people, even within the same family, with the same pathogenic *MYBPC3* variant may have no or few symptoms, will never develop hypertrophic cardiomyopathy and are unaware that they have this genotype (49). These individuals are at increased risk of developing hypertrophic cardiomyopathy but the genetic test result itself does not mean they have the condition. Nevertheless, some individuals with these variants (and not necessarily expressing the associated phenotype) are reported to have encountered actuarially unjustified obstacles when applying for insurance (50).

These possibilities and concerns are also informed by historical precedents for these practices in relation to new and complex health challenges such as the emergence of HIV. For example, following guidelines issued in 1987 by the Association of British Insurers, applicants for life insurance were asked if they had taken an HIV antibody test (51). This led to concerns that merely taking the test would lead to insurance being withheld or becoming

more expensive, and moreover could lead to serious health consequences by deterring people from HIV testing, leading to increased rates of HIV transmission (51).

Response of individuals

A further consideration relates to the responses of individuals, and potential excessive insurance against negligible risks associated with variants that could theoretically increase the risk of developing a given phenotype but which ultimately are likely to be clinically insignificant. As McLean and Gannon (30) put it , "…the aura of scientific certainty which pervades much of the discourse on genetics may lead the unwary or the ignorant into weighing genetic evidence more heavily in the decision-making scales than is actually merited".

Viewed from one perspective, this may not require policy intervention if individuals are considered to be the most competent judges of their own self-interest. However, concerns about the consequences of exaggerated expectations regarding the informativeness of genetic tests for future disease risk, such as increased, but unwarranted, demand on primary care, may provide a rationale for intervention. On the other hand, there is evidence that some at-risk individuals refuse or are inclined to refuse genetic testing from fear of discrimination by insurers (52-56).

System level impacts

The resources needed to confirm the consequences for an individual of a particular "finding" may be considerable, including cases where the finding is not of consequence for an individual's health. These resources, all with competing alternative uses, will include patient time, clinical input, and potentially also financial consequences for the individual as well as

the health system confirmed. For example, McGurk et al (57) considered recommendations for reporting of secondary findings in clinical sequencing and the list of genes in which secondary findings should be sought made by the American College of Medical Genetics and Genomics. For people with truncating variants in one such gene (TTN) associated with dilated cardiomyopathy and a one-off reassuring cardiac MRI aged 64 years, it would require approximately 8,000 person years of surveillance (amounting to 1,600 cardiovascular magnetic resonance scans under a 5- yearly imaging schedule) to prevent one death over the subsequent four years.

4. Pharmacogenetics

The complex practical implications involved in defining which results merit interventions, and when, also arise in the context of pharmacogenetics. Response to medicines vary between individuals, in part, because of genetic variation. If a pharmacogenetic test determines that an individual is less likely to respond to a certain medication, then an alternative treatment (if one is available) may be less effective, which – alongside the health consequences for the individual concerns– will have implications for future treatment costs. Pharmacogenetic testing is not easily classified as either predictive or diagnostic, as has historically been the case for other types of genomic tests.

For example, *CYP2C19* is an important drug metabolizing enzyme (58). Genetic variation in *CYP2C19* is associated with diminished tolerance, treatment failure, and adverse reactions for many drugs (59). For instance, *CYP2C19* catalyzes the activation of clopidogrel, a widely prescribed anti-platelet drug. Individuals with two *CYP2C19* loss-of-function alleles (“poor metabolizers”) will experience diminished platelet inhibition when prescribed clopidogrel, compared to the rest of the population (60).

A genetic result showing that an individual carries a loss of function variant in *CYP2C19* means that their CYP2C19 enzyme will have reduced activity. This result represents a measurable physiological state in that individual which is present at the time of genotyping. As such, *CYP2C19* genotyping could be considered diagnostic in nature. However, the negative clinical impact of being a CYP2C19 poor metabolizer is only experienced in certain contexts, such as when the individual is prescribed clopidogrel or another antiplatelet medicine. In that regard, one could consider the test to be more akin to a predictive test. This blurring between the diagnostic and predictive creates challenges when attempting to consider the insurance implications of a given pharmacogenetic test result.

5. Predicting costs and related phenotypes from genotype

Arrow (61) noted that health status is costly to verify, and therefore health insurance proceeds not on in-kind basis or an indemnity basis that specifies payouts in each possible state of health (i.e. health is non-contractible) but instead as payments conditional on medical expenditure (62). Health insurance (but not life insurance) pay-outs to the individual will therefore typically be an increasing function of expenditure. Variables that influence health care costs will therefore be of interest to insurers. Two types of evidence suggest that knowledge of genetic risk for costs and mortality will become increasingly feasible and potentially of interest (24) to individuals making decisions concerning their insurance coverage. The first is new evidence on the heritability of health care costs, and the second is new evidence on the association between genotype and healthcare costs.

Heritability refers the proportion of variance in a phenotype that is attributable to genetic variance in a given population. Lakhani et al (63) used an American health insurance dataset to examine the heritability of monthly healthcare cost amongst 56,396 twin pairs. They

estimated that the heritability of average monthly cost was 0.29, meaning that 29% of the variance in average monthly healthcare cost between individuals in that study population was attributable to genetic factors. de Zeeuw et al (64) studied 16,726 participants in the Netherlands Twin Register and estimated similar heritabilities between 0.29 and 0.38. Although debates continue about the extent to which twin studies might over-estimate heritability (65), it is noteworthy that these estimates for healthcare cost heritability are comparable to estimates of the twin-heritability (33%) for incident cancer (66).

Second, Mendelian randomization analyses – the use of common genetic variation indicating liability to particular phenotypes in instrumental variable analyses – has demonstrated that genotypes associated with a variety of diseases (67), traits (68-70) and behaviours (71) are associated with healthcare costs as well as with closely related outcomes such as rates of hospital admission (69). Data on genetic susceptibility to incur healthcare costs could give rise to adverse selection.

Adverse selection arises in circumstances where individuals who expect to incur high future health costs differentially prefer more generous or comprehensive insurance plans, and individuals who expect relatively low costs select less comprehensive and less expensive plans (72). This may result in an adverse selection "death spiral" – the insurance product or the insurance company itself becomes commercially unviable because insuring individuals with adverse risk profiles increases premiums, which deters low-risk customers, which further increases premiums.

One means to overcome adverse selection is to reduce the informational asymmetry between customer and insurer so that the latter can more readily identify risks, and offer contracts priced according to individual risk profiles. This, of course, may conflict with the

wider concerns and priorities concerning insurance in the presence of more extensive and richer genetic data than the insurance industry has heretofore encountered. The overall magnitude of adverse selection informed by knowledge of polygenic risk in relation to longevity or future healthcare costs remains to be assessed, and may be small in general (73) or large for some groups (20, 74).

Nevertheless, there is already some evidence that individuals already appear to alter their purchasing of insurance products when they receive information about genetic liability to disease, at least for penetrant monogenic variants. For example, Oster et al (75) find that individuals who know they carry genetic predisposition for Huntington's disease are up to five times more likely to have this type of insurance than are matched controls. More recently, polygenic scores have been assessed as a tool for insurance underwriting. For example, Linner and Koellinger (76) found that a polygenic score could detect a substantially shorter median lifespan in the top decile of total genetic liability independent of other factors used in conventional insurance underwriting. Maxwell et al (18) suggests that the use of polygenic scores provides additional information for insurance underwriting beyond these conventional risk factors. The actuarial models of MacDonald and McIvor (77) and Adams et al (78) suggest adverse selection in the presence of polygenic risk for breast cancer (i.e. people with a higher polygenic risk for breast cancer will tend to choose more comprehensive policies).

6. Toward deliberative processes

A central task that for any new regulatory response that involves wider considerations than only the actuarial pricing of genetic risk will be to identify individuals and groups on whom these costs fall and on whom they ought to fall. For example, normative considerations

might suggest people at risk of some types of condition ought not to lose access ought not to lose access to insurance or to face high premiums because of their genetic risk. A *per se* rejection of risk-based pricing for these individuals shifts their costs onto those with lower (genetic) risk, with the effect that a cross-subsidy is created from low to high-risk individuals. The overall impact of this cross-subsidy is unlikely to "net off" to zero costs; for example, depending on the nature of the risks and proportions of people in each risk category, it is possible (if not likely) that the reduction in costs for high risks is not as great as the increase in costs for the low risks. In this scenario, the aggregate costs of insurance become higher for society as a whole.

The risks faced by individuals are not abolished simply because some groups do not face actuarially fair risk-based pricing for their insurance products; instead, there will necessarily be impacts on the price and availability of insurance. There may be second order effects on the dynamics of competition amongst insurance. For example, adverse selection is still possible even if those with the highest genetic risk do not face premiums based on their actuarial risk. Higher prices amongst the lower risk groups may reduce their use of insurance, resulting in future avoidable health impairments and economic detriment. On the other hand, appropriate regulatory protections could prevent individuals being penalized from undertaking genetic testing where indicated (79).

The analytic challenges therefore involve characterizing and modelling the trade-offs involved (10, 80). These trade-offs include the quantitative impact of genetic information on the terms and price of insurance, increasing knowledge of genetic contributions to disease and mortality, the predictive capacity of polygenic and other genetic risk scores, the demand for insurance, and the behavioural responses of consumers. If genetic data cannot

be used in risk based-pricing, then variables correlated with these data could potentially be used (if available) and this may frustrate to some degree the prohibition on the use of genetic data (81, 82). The feasibility of finding robust proxies for genetic data may be more limited than for more traditional risk factors such as gender (83) but this is likely to vary by context.

The normative issues require, we suggest, a deliberative approach to identify what deviations from actuarially fair pricing are appropriate. The final product of a deliberative process is “guidance shaped by judgements” (84). What judgements matter or ought to matter in this context? A fundamental consideration is to establish which conditions and which genetic risks (and their consequences) society assesses should be borne by the individual and which should be shared more widely. A starting point in this space is perhaps to recognize the value of insurance, and the need to ensure its sustainable provision. An overarching approach could be to minimize the overall cost of insurance, subject to specific exemptions the costs of which are either managed through cross-subsidy imposed on lower risk groups of individuals or met through some other mechanism. An alternative starting point could be to ensure that those facing the greatest possible handicap (however defined) from genetic conditions retain access on reasonable terms.

A multitude of other models could be proposed, each of which will embody their own trade-offs and give rise to different cost profiles and health outcomes. This will also give rise to a host of ethical issues. Should the treatment of genetic information be different from other personal characteristics that influence insurance premiums but over which the individual concerned has no control, such as sex and age? Is discrimination by insurance companies on the basis of genotype normatively the same as discrimination according to sex, the use of

which as a rating factor the European Union prohibited in December 2012? Can and should there be separate ethical frameworks for different types of insurance?

Possible impacts across jurisdictions

These and other questions will need to be addressed in the context of different existing regulatory models. The issues we describe above are arguably more important for non-health insurance in the UK given comprehensive and free at the point of use health care provided by the National Health Service. The initial impact of these developments may also be felt initially in non-health insurance markets in the United States, where the Genetic Information Nondiscrimination Act (GINA) was signed into law in 2008 by the federal government (85). It prohibits the use of genetic information in determining the offer of health insurance, but not other forms of insurance, including life insurance. There is also variation at the state level in how genetic data may be used for insurance underwriting.

There is some scope for insurers to use genetic data to inform the offer of insurance in Australia (22). The Financial Services Council, the self-regulated industry representative body, introduced a moratorium in 2019 for some types of insurance cover. The Canadian federal legislature enacted in 2017 the Genetic Non-Discrimination Act (85, 86) which contains prohibitions on requesting disclosure of the results of genetic tests or being forced to take such tests in order to obtain access to goods and services including insurance. This stance was challenged in the Supreme Court of Canada, which confirmed in 2020 that parliament had the authority to prohibit genetic testing and the mandatory disclosure of genetic test results (87).

7. Conclusion

The potential for genetic data to be used in insurance underwriting has long been recognised. This has recently been accompanied by increasing concern that the use of these data could result in unintended adverse impacts on both insurers as well as current and potential policy holders. We contend that expansions in the volume and quality of genetic data, the blurring of diagnostic and predictive genetic testing, and new evidence on the association between genotype and healthcare costs and mortality mean that conversations about their consequences and new regulatory developments are now much needed. Future regulatory developments in this area will involve identifying and quantifying these costs, as well developing mechanisms for their distribution amongst individuals.

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References

1. Edwards AWF. Haldane and Fisher – scientific interactions. Journal of Genetics. 2017;96(5):747-52.
2. Harper PS. 194The Human Gene Map. 2008 [cited 8/18/2022]. In: A Short History of Medical Genetics [Internet]. Oxford University Press, [cited 8/18/2022]; [0]. Available from: https://doi.org/10.1093/med/9780195187502.003.0008_update_001.
3. Committee HoCSaT. Science and Technology - Fifth Report. London; 2001.

4. Department of HEalth and Social Care. Code on Genetic Testing and Insurance: 3-year review 2022. London; 2022.
5. ABI HA. Code on Genetic Testing and Insurance. 2018.
6. ABI ABI Annual Report: Code on Genetic Testing and Insurance. London; 2022.
7. Prince AER. Political economy, stakeholder voices, and saliency: lessons from international policies regulating insurer use of genetic information. Journal of Law and the Biosciences. 2018;5(3):461-94.
8. Prince AER. Insurance risk classification in an era of genomics: is a rational discrimination policy rational? Nebraska law review. 2017;96(3):624.
9. Prince AER, Uhlmann WR, Suter SM, Scherer AM. Genetic testing and insurance implications: Surveying the US general population about discrimination concerns and knowledge of the Genetic Information Nondiscrimination Act (GINA). Risk Management and Insurance Review. 2021;24(4):341-65.
10. Ossa DF, Towse A. Genetic screening, health care and the insurance industry. Should genetic information be made available to insurers? The European journal of health economics : HEPAC : health economics in prevention and care. 2004;5(2):116-21.
11. Holmes EM. Solving the insurance/genetic fair/unfair discrimination dilemma in light of the Human Genome Project. Ky LJ. 1996;85:503.
12. Rothstein MA. Time to End the Use of Genetic Test Results in Life Insurance Underwriting. The Journal of Law, Medicine & Ethics. 2018;46(3):794-801.
13. Daniels N. The Functions of Insurance and the Fairness of Genetic Underwriting. In: Rothstein MA, editor. Genetics and Life Insurance: Medical Underwriting and Social Policy. Cambridge MA: MIT Press; 2004. p. 119-45.
14. Joly Y, Dalpé G, Dupras C, Bévière-Boyer B, De Paor A, Dove ES, et al. Establishing the International genetic discrimination Observatory. Nat Genet. 2020;52(5):466-8.
15. Joly Y, Dupras C, Pinkesz M, Tovino SA, Rothstein MA. Looking Beyond GINA: Policy Approaches to Address Genetic Discrimination. Annu Rev Genomics Hum Genet. 2020;21:491-507.
16. Tiller JM, Bakshi A, Brotchie AR, Green RC, Winship IM, Lacaze P. Public willingness to participate in population DNA screening in Australia. J Med Genet. 2022:jmg-2022-108921.
17. Harper PS. Genetic testing and insurance. J R Coll Physicians Lond. 1992;26(2):184-7.
18. Maxwell JM, Russell RA, Wu HM, Sharapova N, Banthorpe P, O'Reilly PF, et al. Multifactorial disorders and polygenic risk scores: predicting common diseases and the possibility of adverse selection in life and protection insurance. Annals of Actuarial Science. 2021;15(3):488-503.
19. Born P. Genetic Testing in Underwriting: Implications for Life Insurance Markets. Journal of Insurance Regulation. 2019;38(5):1-18.
20. Howard RCW. Genetic testing model: if underwriters had no access to known results. Canadian Institute of Actuaries http://www cia-ica ca/docs/default-source/2014/214082e pdf. 2014.
21. Macdonald A, Yu F. The Impact of Genetic Information on the Insurance Industry: Conclusions from the 'Bottom-Up' Modelling Programme. ASTIN Bulletin. 2011;41(2):343-76.
22. Tiller J, Morris S, Rice T, Barter K, Riaz M, Keogh L, et al. Genetic discrimination by Australian insurance companies: a survey of consumer experiences. Eur J Hum Genet. 2020;28(1):108-13.
23. Roberts JS, Dolinoy DC, Tarini BA. Emerging Issues in Public Health Genomics. Annual Review of Genomics and Human Genetics. 2014;15(1):461-80.
24. Conley D. From Fraternities to DNA: The Challenge Genetic Prediction Poses to Insurance Markets. The Milbank quarterly. 2019;97(1):40-3.
25. Peter R, Richter A, Thistle P. Endogenous information, adverse selection, and prevention: Implications for genetic testing policy. J Health Econ. 2017;55:95-107.
26. Rodriguez-Rincon D, Parkinson S, Hocking L, Evans H, Hudson E, Morley KI. Assessing the impact of developments in genetic testing on insurers' risk exposure. Santa Monica, CA: RAND Corporation; 2022.

27. Auton A, Abecasis GR, Altshuler DM, Durbin RM, Abecasis GR, Bentley DR, et al. A global reference for human genetic variation. Nature. 2015;526(7571):68-74.
28. Cutler DM, Zeckhauser RJ. The anatomy of health insurance. Handbook of health economics. 1: Elsevier; 2000. p. 563-643.
29. Ashcroft R. Should genetic information be disclosed to insurers? No. BMJ (Clinical research ed). 2007;334(7605):1197-.
30. McLean SAM, Gannon P. Genetics and insurance. In: Sorrell T., editor. Health care, ethics and insurance: Routledge; 1998. p. 103-16.
31. Parker M, Lucassen A. Concern for families and individuals in clinical genetics. J Med Ethics. 2003;29(2):70.
32. Lucassen A, Clarke A. In the family: access to, and communication of, familial information in clinical practice. Hum Genet. 2022;141(5):1053-8.
33. Reid NJ, Brockman DG, Elisabeth Leonard C, Pelletier R, Khera AV. Concordance of a High Polygenic Score Among Relatives: Implications for Genetic Counseling and Cascade Screening. Circ Genom Precis Med. 2021;14(2):e003262.
34. Carmi S. Cascade screening following a polygenic risk score test: what is the risk of a relative conditional on a high score of a proband? bioRxiv. 2021:2021.04.11.439329.
35. Horton RH, Lucassen AM. Recent developments in genetic/genomic medicine. Clin Sci (Lond). 2019;133(5):697-708.
36. Cassa CA, Tong MY, Jordan DM. Large Numbers of Genetic Variants Considered to be Pathogenic are Common in Asymptomatic Individuals. Hum Mutat. 2013;34(9):1216-20.
37. Beaumont RN, Wright CF. Estimating diagnostic noise in panel-based genomic analysis. Genet Med. 2022.
38. Jackson L, Weedon MN, Harrison JW, Wood AR, Ruth KS, Tyrrell J, et al. Influence of family history on penetrance of hereditary cancers in a population setting. medRxiv. 2022:2022.07.08.22277415.
39. Horton R, Crawford G, Freeman L, Fenwick A, Wright CF, Lucassen A. Direct-to-consumer genetic testing. BMJ. 2019;367:l5688.
40. Horton R, Lucassen A. Ethical Considerations in Research with Genomic Data. The New Bioethics. 2022:1-15.
41. Arthur AMW, Ahmad SA, Pieter GP. Diagnosis, management and therapeutic strategies for congenital long QT syndrome. Heart. 2022;108(5):332.
42. Sud A, Horton RH, Hingorani AD, Tzoulaki I, Turnbull C, Houlston RS, et al. Realistic expectations are key to realising the benefits of polygenic scores. BMJ. 2023;380:e073149.
43. Sud A, Turnbull C, Houlston R. Will polygenic risk scores for cancer ever be clinically useful? npj Precision Oncology. 2021;5(1):40.
44. Smith GD. Epidemiology, epigenetics and the 'Gloomy Prospect': embracing randomness in population health research and practice. Int J Epidemiol. 2011;40(3):537-62.
45. Lacaze P, Ryan J, Woods R, Winship I, McNeil J. Pathogenic variants in the healthy elderly: unique ethical and practical challenges. J Med Ethics. 2017;43(10):714-22.
46. Ashcroft R. Should genetic information be disclosed to insurers? No. BMJ. 2007;334(7605):1197-.
47. Marian AJ, Roberts R. The Molecular Genetic Basis for Hypertrophic Cardiomyopathy. J Mol Cell Cardiol. 2001;33(4):655-70.
48. Marston S, Copeland ON, Gehmlich K, Schlossarek S, Carrrier L. How do MYBPC3 mutations cause hypertrophic cardiomyopathy? J Muscle Res Cell Motil. 2012;33(1):75-80.
49. Marian AJ, Braunwald E. Hypertrophic cardiomyopathy: genetics, pathogenesis, clinical manifestations, diagnosis, and therapy. Circ Res. 2017;121(7):749-70.
50. Christiaans I, Kok TM, van Langen IM, Birnie E, Bonsel GJ, Wilde AAM, et al. Obtaining insurance after DNA diagnostics: a survey among hypertrophic cardiomyopathy mutation carriers. Eur J Hum Genet. 2010;18(2):251-3.

51. Barton S, Roth P. Life insurance and HIV antibody testing. BMJ: British Medical Journal. 1992;305(6859):902.
52. Hall MA, Rich SS. Genetic privacy laws and patients' fear of discrimination by health insurers: The view from genetic counselors. J Law Med Ethics. 2000;28(3):245-57.
53. Allain DC, Friedman S, Senter L. Consumer awareness and attitudes about insurance discrimination post enactment of the Genetic Information Nondiscrimination Act. Fam Cancer. 2012;11(4):637-44.
54. Haga SB, Barry WT, Mills R, Ginsburg GS, Svetkey L, Sullivan J, et al. Public Knowledge of and Attitudes Toward Genetics and Genetic Testing. Genetic Testing and Molecular Biomarkers. 2013;17(4):327-35.
55. Wauters A, Van Hoyweghen I. Global trends on fears and concerns of genetic discrimination: a systematic literature review. J Hum Genet. 2016;61(4):275-82.
56. Robinson JO, Carroll TM, Feuerman LZ, Perry DL, Hoffman-Andrews L, Walsh RC, et al. Participants and Study Decliners' Perspectives About the Risks of Participating in a Clinical Trial of Whole Genome Sequencing. J Empir Res Hum Res Ethics. 2016;11(1):21-30.
57. McGurk KA, Zheng SL, Henry A, Josephs K, Edwards M, de Marvao A, et al. Correspondence on “ACMG SF v3.0 list for reporting of secondary findings in clinical exome and genome sequencing: a policy statement of the American College of Medical Genetics and Genomics (ACMG)” by Miller et al. Genet Med. 2022;24(3):744-6.
58. Gaedigk A, Sangkuhl K, Whirl-Carrillo M, Klein T, Leeder JS. Prediction of CYP2D6 phenotype from genotype across world populations. Genet Med. 2017;19(1):69-76.
59. Botton MR, Whirl-Carrillo M, Del Tredici AL, Sangkuhl K, Cavallari LH, Agúndez JAG, et al. PharmVar GeneFocus: CYP2C19. Clin Pharmacol Ther. 2021;109(2):352-66.
60. Scott SA, Sangkuhl K, Stein CM, Hulot JS, Mega JL, Roden DM, et al. Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C19 Genotype and Clopidogrel Therapy: 2013 Update. Clin Pharmacol Ther. 2013;94(3):317-23.
61. Arrow KJ. Uncertainty and the Welfare Economics of Medical Care. The American Economic Review. 1963;53(5):941-73.
62. Geoffard P-Y. Incentive and selection effects in health insurance. The Elgar Companion to Health Economics, Second Edition: Edward Elgar Publishing; 2012.
63. Lakhani CM, Tierney BT, Manrai AK, Yang J, Visscher PM, Patel CJ. Repurposing large health insurance claims data to estimate genetic and environmental contributions in 560 phenotypes. Nat Genet. 2019;51(2):327-34.
64. de Zeeuw EL, Voort L, Schoonhoven R, Nivard MG, Emery T, Hottenga JJ, et al. Safe Linkage of Cohort and Population-Based Register Data in a Genomewide Association Study on Health Care Expenditure. Twin Res Hum Genet. 2021;24(2):103-9.
65. Young AI. Solving the missing heritability problem. PLOS Genetics. 2019;15(6):e1008222.
66. Mucci LA, Hjelmborg JB, Harris JR, Czene K, Havelick DJ, Scheike T, et al. Familial Risk and Heritability of Cancer Among Twins in Nordic Countries. JAMA. 2016;315(1):68-76.
67. Dixon P, Harrison S, Hollingworth W, Davies NM, Smith GD. Estimating the causal effect of liability to disease on healthcare costs using Mendelian Randomization. Econ Hum Biol. 2022:101154.
68. Dixon P, Hollingworth W, Harrison S, Davies NM, Davey Smith G. Mendelian Randomization analysis of the causal effect of adiposity on hospital costs. J Health Econ. 2020;70:102300.
69. Hazewinkel A-D, Richmond RC, Wade KH, Dixon P. Mendelian randomization analysis of the causal impact of body mass index and waist-hip ratio on rates of hospital admission. Econ Hum Biol. 2022;44:101088.
70. Lee J, Jukarainen S, Dixon P, Davies NM, Smith GD, Natarajan P, et al. Quantifying the causal impact of biological risk factors on healthcare costs. medRxiv. 2022:2022.11.19.22282356.
71. Dixon P, Sallis H, Munafo M, Smith GD, Howe L. The causal effect of cigarette smoking on healthcare costs. medRxiv. 2022:2022.07.05.22277228.

72. Cutler DM, Zeckhauser RJ, editors. Adverse selection in health insurance1998 1998: De Gruyter.
73. MacMinn RD, Brockett PL, Raeburn JA. Health Insurance, Genetic Testing and Adverse Selection. Annals of Actuarial Science. 2007;2(2):327-47.
74. Hoy M, Witt J. Welfare effects of banning genetic information in the life insurance market: the case of BRCA1/2 genes. J Risk Insur. 2007;74(3):523-46.
75. Oster E, Shoulson I, Quaid K, Dorsey ER. Genetic adverse selection: Evidence from long-term care insurance and Huntington disease. Journal of Public Economics. 2010;94(11):1041-50.
76. Karlsson Linnér R, Koellinger PD. Genetic risk scores in life insurance underwriting. J Health Econ. 2022;81:102556.
77. Macdonald AS, McIvor KR. Modelling Adverse Selection in The Presence of a Common Genetic Disorder: the Breast Cancer Polygene. ASTIN Bulletin. 2009;39(2):373-402.
78. Adams C, Donnelly C, Macdonald A. The impact of known breast cancer polygenes on critical illness insurance. Scandinavian Actuarial Journal. 2015;2015(2):141-71.
79. Filipova-Neumann L, Hoy M. Managing genetic tests, surveillance, and preventive medicine under a public health insurance system. J Health Econ. 2014;34:31-41.
80. Wilson D. Acquisition and disclosure of genetic information under alternative policy regimes: an economic analysis. Health Economics, Policy and Law. 2006;1(3):263-76.
81. Aseervatham V, Lex C, Spindler M. How Do Unisex Rating Regulations Affect Gender Differences in Insurance Premiums? The Geneva Papers on Risk and Insurance - Issues and Practice. 2016;41(1):128-60.
82. Pope DG, Sydnor JR. Implementing Anti-discrimination Policies in Statistical Profiling Models. American Economic Journal: Economic Policy. 2011;3(3):206-31.
83. Oxera. The use of gender in insurance pricing: Analysing the impact of a potential ban on the use of gender as a rating factor. 2010.
84. Culyer AJ. NICE's use of cost effectiveness as an exemplar of a deliberative process. Health economics, policy, and law. 2006;1(Pt 3):299-318.
85. Bélisle-Pipon J-C, Vayena E, Green RC, Cohen IG. Genetic testing, insurance discrimination and medical research: what the United States can learn from peer countries. Nat Med. 2019;25(8):1198-204.
86. Bombard Y, Heim-Myers B. The Genetic Non-Discrimination Act: critical for promoting health and science in Canada. Can Med Assoc J. 2018;190(19):E579.

87. Supreme Court of Canada. Reference re Genetic Non-Discrimination Act 2020 [Available from: https://www.scc-csc.ca/case-dossier/cb/2020/38478-eng.aspx.