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Guidance for considering ethical, legal, and social issues in health technology assessment: Application to genetic screening

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Objectives and Methods: Many authors have argued that ethical, legal, and social issues ("ELSIs") should be explicitly integrated into health technology assessment (HTA), yet doing so poses challenges. This discussion may be particularly salient for technologies viewed as ethically complex, such as genetic screening. Here we provide a brief overview of contemporary discussions of the issues from the HTA literature. We then describe key existing policy evaluation frameworks in the fields of disease screening and public health genomics. Finally, we map the insights from the HTA literature to the policy evaluation frameworks, with discussion of the implications for HTA in genetic screening.
Results and Conclusions: A critical discussion in the HTA literature considers the definition of ELSIs in HTA, highlighting the importance of thinking beyond ELSIs as impacts of technology. Existing HTA guidance on integrating ELSIs relates to three broad approaches: literature synthesis, involvement of experts, and consideration of stakeholder values. The thirteen key policy evaluation frameworks relating to disease screening and public health genomics identified a range of ELSIs relevant to genetic screening. Beyond straightforward impacts of screening, these ELSIs require consideration of factors such as the social and political context surrounding policy decisions. The three broad approaches to addressing ELSIs described above are apparent in the screening/genomics literatures. In integrating these findings we suggest that the method chosen for addressing ELSIs in HTA for genetic screening may determine which ELSIs are prioritized; and that an important challenge is the lack of guidance for evaluating such methods.

Keywords: Genetic screening, Ethical, legal, and social issues, Health technology assessment

HEALTH TECHNOLOGY ASSESSMENT: THE RATIONALE FOR CONSIDERING ETHICAL, LEGAL, AND SOCIAL ISSUES

Health technology assessment (HTA) is typically described as including values considerations within its scope, having been defined as " . . . a multidisciplinary field of policy analysis [that] studies the medical, social, ethical, and economic implications of development, diffusion, and use of health technology" (30). In practice, though, HTAs have focused mainly on questions of technical and clinical effectiveness (16;37;38). While ethical, legal, and social issues ("ELSIs") are embedded within HTA *implicitly* by virtue of the inherent normative nature of generating and summarizing evidence (43), many suggest that they should be more *explicitly* integrated, based on three main arguments. First, HTA reports that discuss ELSIs may be more useful to policy makers, because ELSIs are important to policy decisions (3;28;32;51). Second, the distinction between clinical or technical issues and ELSIs may be artificial (22;36;37;39;49;50). Indeed, appropriately considering clinical evidence and using resources wisely are essential to ethical policy decision making. More profoundly, it has been argued that society and technologies exist in a dynamic relationship (22;36;39;49;51); as part of a "sociotechnical network" of people (technology designers, users, society) and technologies, a health technology thus both reflects and influences values, such that its normative nature cannot be ignored (36, p. 50); directly identifying and incorporating the issues in the process of HTA is an acknowledgement of this normativity. Third, it has been suggested that ELSIs need to be formally integrated in HTA (and in HTA reports) to ensure that they are considered in policy decisions (3;32;39).

GENETIC SCREENING: ETHICAL, LEGAL, AND SOCIAL ISSUES IN POLICY DECISION MAKING

Considering whether and how to address ELSIs in HTA may be particularly relevant for technologies considered controversial or ethically complex, such as genetic screening programs. The distinguishing features of genetic screening as a technology are its ability to identify risk of heritable or genetic conditions, and the notion that it is a program (including the screening test itself, as well as relevant ancillary services such as education, counseling, and follow-up diagnostic care) that is offered to all members of a population or population sub-group, rather than a test provided to individuals who have specifically sought clinical care or advice (48;56). These features have led to discussions of the particular ELSIs that may be most important to genetic screening policy decisions: the definition of a health problem (e.g., the ethical implications of defining a serious condition in prenatal genetic screening); the purpose of a technology (e.g., for information versus clinical benefits); psychosocial benefits and harms to individuals and families (e.g., from carrier detection, labeling, false positives,); choice and consent (e.g., parents making decisions for children, models of consent and choice in mass screening); privacy and confidentiality (e.g., data protection, family disclosure of information); equity (e.g., targeted versus universal screening, access to screening and follow-up care); and

discrimination or stigmatization (e.g., discrimination against carriers of genetic mutations, the disability rights critique of prenatal genetic screening) (e.g., 18;42;48).

PURPOSE

The HTA community has recently given considerable attention to the challenge of addressing ELSIs, particularly ethical issues, in HTA reports (e.g., 31;39;53). Here we aim to explore the application of these insights to the example of genetic screening. Specifically, we: (i) Provide a brief overview of contemporary discussions about integrating ELSIs in HTA, drawn from the HTA literature; (ii) Describe key frameworks for evaluating screening programs and/or genetic tests, based on the disease screening and public health genomics literatures, with an emphasis on how ELSIs are addressed in these frameworks; and (iii) Map the screening and genetics policy frameworks to the insights summarized from the HTA literature, with discussion of the implications for approaches to HTA in the field of genetic screening.

To inform our overview of guidance from the HTA literature, we relied on recent reviews and seminal discussion papers, identified in a nonsystematic search using MEDLINE, reference lists of reviews, and focused searching in the International Journal of Technology Assessment in Health Care. To identify evaluation frameworks for disease screening and/or genetic testing technologies, we used nonsystematic MEDLINE searches, reference lists, and searches in the grey literature (e.g., searching the Web sites of the CDC's National Office of Public Health Genomics, the PHG Foundation, and the Genome-based Research and Population Health International Network). Our aim was not to systematically review all existing evaluation frameworks but to describe an illustrative sample of key frameworks published in recent years (since approximately 2000) so as to understand current thinking about the role of ELSIs within approaches to the evaluation of genetic screening programs.

INSIGHTS FROM THE HTA LITERATURE

Analysis within the HTA literature of the conceptual and methodological challenges presented in addressing ELSIs within HTA reports has included both a critical discussion of the scope of ethical issues and social values and how they relate to HTA (i.e., defining the issues); and guidance on methods for addressing them. With respect to the critical discussion, it has been argued that HTA should go beyond an examination of social and ethical issues as *impacts* of a technology, to a more far-reaching exploration of the dynamic relationships among technology, individuals, and society (a "social shaping" perspective) (5;20;36;37;39;57). For example, HTA might question why particular technologies are developed, whose interests they serve, how they relate to knowledge, and how they both reflect and influence relationships and power dynamics (36;37;57). Some authors further suggest a "reflexive" approach that explores normative aspects of the HTA process itself (5;20;28). Finally, a related development both in HTA and in wider discussions of policy-oriented research, is an emphasis on "contextualizing" findings to increase their relevance for policy (4;27;38;40). "Contextual evidence" has been described in terms of issues such as current practice patterns, health system factors, or organizational characteristics (38); or more broadly as encompassing a broad range of factors beyond scientific evidence that influence policy, including ethical issues (4, p.1465; 40, p.15). This relates to the social shaping perspective, because, for example, those who develop and use a technology may be considered part of the relevant social and political context.

In terms of specific guidance on approaches to integrating ELSIs into HTA, three broad categories of methods are apparent in the HTA literature (we note that these are not mutually exclusive and that a distinction is typically not made between the HTA process and the HTA report as a product, such that this description of methods assumes that the process will be reflected in the product): (i) the identification and consideration of ELSI-relevant literature in a knowledge synthesis component of HTA (31;39); (ii) the involvement of experts in fields such as bioethics, health law, and sociology (3;5;22;28;31;39); and (iii) the consideration of "stakeholder" values (e.g., views of patients and families, health professionals, and citizens) (3;5;22;31;37;39;50;57;60). The latter two categories encompass several related approaches. For example, with respect to (ii), although the literature offers few recommendations for the specific contributions of ELSI experts (as direct participants or external consultants), there is ongoing controversy about the appropriate ethical theory and method of analysis (a review of the competing approaches is beyond the scope of this study) (5;22;28;53). In terms of category (iii), stakeholder involvement in HTA, and particularly consumer involvement, encompasses several passive and active approaches and has recently been emphasized in its own right (in addition to the discussion of its potential for addressing ELSIs), in parallel with broader trends highlighting public engagement in health policy decision making (1;14;25;39;40;50–52).

EVALUATION FRAMEWORKS FOR SCREENING PROGRAMS AND GENETIC TESTS

We identified three types of evaluation frameworks from the disease screening and public health genomics literatures, based on the following: (i) established criteria for evaluating disease screening programs; (ii) systematic review methods for evaluating screening and/or diagnostic tests; and (iii) methods for policy-oriented evaluations of genetic tests (Tables 1 to 3).

Table 1. Frameworks Based on Disease Screening Criteria

Framework	Brief description	Consideration of ELSIs
Criteria for appraising the viability, effectiveness and appropriateness of a screening programme (47)	• Criteria for evaluating screening programs • Based in part on Wilson and Jungner, but with more focus on evidence-based approaches and potential harms (45) • Current version includes criteria specific to genetic screening	• Recent versions emphasize promoting informed choice as the goal of screening (46), which requires adequate information • Highlights importance of acceptability (to population screened, health professionals, public) • Acceptability to family members and carriers specifically addressed in relation to genetic screening • Psychosocial harms & benefits considered, including impacts on carriers
Appraising organized screening programmes for testing for genetic susceptibility to cancer (19)	• Criteria for evaluating screening programs for genetic susceptibility to cancer • Developed as an extension of the Wilson and Jungner criteria	Criteria developed with a particular emphasis on ELSIs, for example by: • Expanding "acceptability" to encompass psychosocial, ethical, legal, and social impacts on various stakeholder groups • Expanding "cost" to include psychological and social costs • Considering potential adverse effects for both the screened and non-screened populations • Overarching recommendation to observe basic human rights principles
Application of population screening principles to genetic screening for adult-onset conditions (7)	• Framework for public health policy in genetic screening • Describes 3 stages in evaluation (criteria embedded in stages): 1) Assessment: evaluation of benefits and harms 2) Policy development: using a consensus process, collectively considering the evidence 3) Program evaluation (information only available when screening underway; or information changes over time)	ELSIs considered in all stages: • Asssessment: psychological and social consequences, potential risks of stigmatization or discrimination • Policy development: stakeholder participation and consideration of context, including community values • Program evaluation: acceptability to target population, adverse events Importance throughout of attention to consent and confidentiality
Decision support guide for population-based genetic screening programs (2; Andermann et al., unpublished report, 2007)	• Analytic approach specifically designed to support policy decisions regarding population-based genetic screening • Includes four components: 1) Fundamental principles underlying the decision-making process and the screening program 2) "Decision nodes" to make explicit different perspectives & levels of analysis: (i) utility of screening strategy for individuals & families, (ii) relevance of implementing screening program for particular target population & context, (iii) judicious resource allocation at societal level 3) Criteria grouped according to each of 3 decision nodes 4) Suggested supporting evidence to assess whether each criterion upheld and to make criteria more explicit	ELSIs incorporated in various ways: • Underlying principles: transparency; equity; context (e.g., regulatory framework, stakeholder positions, ethical & legal context); stakeholder acceptability; values (both healthcare system & societal) • Decision nodes: focus on stakeholder groups for each decision node, including individuals and families; the target population to be screened; and society more broadly • Criteria and supporting evidence: benefits and harms; broad social/ethical concerns (e.g., discrimination); principles of respect for autonomy, accountability; informed consent, privacy, cultural context

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Table 2. Frameworks Based on Methods for Systematic Reviews of Screening Tests

Framework	Brief description	Consideration of ELSIs
Current methods of the U.S. Preventive Services Task Force (23;26;55)	• Methods used for systematic review and recommendation development re: clinical preventive services, including screening • Supported by analytic framework that considers overall screening program as well as specific "links" within program (e.g., effectiveness of screening in identifying disease; and effectiveness of early disease treatment) • Focused on transparent, evidence-based methods and an independent process	• Clinical and ELSI questions guided by the analytic framework; ELSIs are addressed as part of the general assessment of benefits and harms • Acknowledges value judgments necessary in weighing benefits and harms • Some ELSI considerations (e.g., related to medicolegal context or insurance coverage) explicitly left for consideration by decision makers
Medical Services Advisory Committee guidelines for the assessment of diagnostic technologies (44)	• Guidelines for health technology assessment related to diagnostic tests (also applicable to screening) • Based on USPSTF guidelines and other methodological literature • Focused on systematic review methods • Describes potential use of "linked evidence," as in USPSTF	• ELSIs addressed as part of systematic evaluation of benefits and harms • Ethics and acceptability listed as potential considerations other than safety, effectiveness, cost-effectiveness in preparation of review protocol • ELSIs may be addressed at "integration of evidence" stage, which includes overall assessment of evidence and consideration of other factors

Frameworks Based on Disease Screening Criteria

A common approach to evaluating population-based screening programs uses a set of published criteria, often based on the World Health Organization's principles of disease screening (61). These principles have been updated and adapted, both with a focus on screening programs generally (e.g., 47), and specific to genetic screening (e.g., 19) (Table 1). Given that the purpose of criteria-oriented frameworks is to specify the conditions under which a screening test is considered acceptable (or fundable), and not necessarily how this should be demonstrated, these frameworks have tended to emphasize the particular ELSIs that should be considered, rather than the methods for addressing them.

The original Wilson and Jungner principles incorporate some ELSI-related concepts, including a criterion of public acceptability and two criteria that suggest social value judgments related to priority-setting (one criterion states that the screened condition should be an important health problem; another stipulates that the costs of case-finding should be "economically balanced" in relation to other healthcare costs) (61). Recent adaptations of these criteria have addressed ELSIs more directly by specifying additional issues such as psychosocial benefits and harms, impacts on stakeholder groups, informed choice, equity, discrimination, and human dignity (19;47) (Table 1).

Within the area of genetic screening, some groups have incorporated disease screening criteria within comprehensive frameworks for policy decision making (Table 1). For example, by including a "policy development" stage in the assessment framework (7) or in presenting a set of underpinning principles as well as key "decision nodes" to guide policy decisions (2), these frameworks highlight ELSIs that may be particularly important at the decision-making stage (e.g., related to context) (Table 1).

Frameworks Based on Methods for Systematic Reviews of Screening Tests

Frameworks for evaluating screening (or diagnostic) technologies that are based on systematic review methods include methods used by the U.S. Preventive Services Task Force (USPSTF) (23;26;55) and a related Australian framework from the Medical Services Advisory Committee (MSAC) (44) (Table 2). Both consider research evidence relating to a screening program overall but recognize that often reviewers must rely instead on evidence relating to separate components of a program (e.g., evidence relating to the effectiveness of screening for early disease detection; and evidence on the health impact of early treatment). Both frameworks also mention ELSIs, mainly in relation to psychosocial benefits and harms. Given the nature of the guidelines, literature reviewing is implied as a method for considering ELSIs (Table 2).

Frameworks for Policy-Oriented Assessments of Genetic Tests

Frameworks for policy-oriented evaluations of genetic tests (not necessarily specific to screening) (Table 3) often make reference to the performance criteria suggested by the U.S. Task Force on Genetic Testing: analytic validity (the extent to which a test accurately measures a particular analyte);

Table 3. Frameworks for Policy-Oriented Assessments of Genetic Tests

Framework	Brief description	Consideration of ELSIs
ACCE: a model process for evaluating data on emerging genetic tests (24)	• Guidelines for systematic evaluation of emerging genetic tests; primarily based on evidence synthesis • Model provides an analytic framework of 44+ questions organized within four components: 1) **a**nalytic validity 2) **c**linical validity 3) **c**linical utility 4) **e**thical, legal, and social issues	• ELSIs shown in diagram as "penetrating pie slice", permeating model • Integrated into clinical utility component (addressing impact on socially vulnerable populations, information needs, consent, informed choice) • Also summarized separately through specific ELSI questions: 1) Stigmatization, discrimination, disparities, privacy/confidentiality, personal/family/societal issues 2) Legal issues (consent, ownership, property rights, disclosure) 3) Safeguards (Methods for gathering this information: pilot trials, generic insights; expert legal review; information from elsewhere in review on safeguards) • Acknowledges need for multidisciplinary involvement in preparing and reviewing reports, including fields of law and social sciences
Gene Dossier (34;59).	• Based in part on ACCE • Focused mainly on evaluating tests for single gene disorders • Lists nine criteria/characteristics to be evaluated by panel: seriousness of condition; prevalence of condition; purpose of test; complexity of test; context of test use; characteristics of test (e.g., sensitivity, specificity, positive predictive value); clinical utility of test; ethical, legal, and social considerations; cost	Ethical, legal, and social issues are represented as one of nine considerations used by the evaluation panel
Framework for the assessment of genetic testing in the Andalusian Public Health System (41)	• Three phases of research for assessing genetic test: test performance (analytical & clinical validity); test results (clinical utility: effectiveness & safety); impact on health services & society (organizational, economic, ethical, societal implications) • Discusses linked evidence approach (USPSTF) & its limitations • Assessment framework with four components: 1) Test performance (analytical and clinical validity) 2) Test results (clinical utility and safety) 3) Social impact and ethical implications 4) Impact on health services (economic and organizational)	ELSIs considered in two areas: 1) Clinical utility assessment (psychosocial benefits & harms) 2) Assessment of social and ethical implications (examples of ELSIs relevant to genetic tests: psychosocial impact, discrimination, eugenics, inequities in access, need for counseling and information, family disclosure, genetic testing in children) States that views of healthcare system managers, health professionals, and citizens should be taken into account

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Table 3. Continued.

Evaluation of Genomic Applications in Practice and Prevention (EGAPP) (58)	• Initiated in 2004; building on the ACCE model • Also incorporates methodologies (e.g., formal assessment of the quality of studies and overall strength of evidence) from initiatives such as USPSTF and international HTA processes • Five evidence reports completed and first recommendation statement published in December 2007	• Independent EGAPP working group focused mainly on clinical outcomes but has also identified family/societal outcomes, reflecting psychosocial and ethical implications • Due to scarcity of empirical research on non-clinical outcomes, developed set of "contextual issues" to be raised within recommendations
Moving beyond ACCE: An expanded framework for genetic test evaluation (9)	Builds on ACCE and draws from multidisciplinary theories/frameworks; 3 broad dimensions of genetic test evaluation: • Evaluation of assay: analytic validity, reliability/reproducibility • Clinical validity: gene-disease association, test performance • Clinical utility: ○ purpose of a test (legitimacy, efficacy, effectiveness, appropriateness) ○ feasibility of test delivery (acceptability, efficiency, optimality, equity)	ELSIs incorporated within several aspects of assessing clinical utility, e.g.: • Legitimacy (social preferences related to ethical principles, values, laws, regulations, with consideration of test purpose) • Appropriateness (balance of benefits & harms, including social impacts) • Acceptability (views of patients and families) • Equity (distribution of benefits among individuals and groups)
Confronting the "gray zones" of technology assessment: evaluating genetic testing services for public insurance coverage in Canada (17)	• Developed for technology assessment/coverage decision making regarding emerging predictive genetic tests • Domains include: evaluation criteria; cutoffs or standards for deciding coverage within each criterion; coverage conditions when standards met conditionally • If uncertain whether technology meets standard for a criterion, technology placed in "gray zone" for that criterion • Evaluation criteria: ○ intended purpose of technology (i.e., whether worthwhile) ○ effectiveness/clinical utility ○ "additional effects" (other than intended purpose) ○ aggregate costs ○ demand ○ cost-effectiveness	• ELSIs considered in describing purpose (e.g., whether goals of a test are considered worthwhile), documenting benefits & harms (e.g., psychosocial benefits and harms, impacts on society, equity in distribution of benefits and harms) • Framework emphasizes policy options (aside from coverage or non-coverage) for addressing uncertainty and potential harms, e.g.: ○ applying technology in a research context ○ stipulating provision of services to mitigate potential adverse effects ○ establishing clinical or ethical guidelines ○ using formal regulatory mechanisms ○ periodic re-evaluation
Providing genetic testing through the private sector. A view from Canada (12)	• Framework for considering whether a test should be offered, and, if offered, whether should be covered by public funding • Thresholds or criteria to consider: 1) overall moral acceptability of test 2) analytic validity (including laboratory quality assurance) 3) usefulness 4) potential harms 5) whether test should be publicly funded 6) whether test should be available for purchase, if meets thresholds 1 through 4 but not publicly funded	ELSIs integrated throughout: • Threshold 1, moral acceptability: suggests need for public engagement • Thresholds 3 and 4 involve weighing benefits & harms, including psychosocial & social impacts on individuals & society • Potential means of alleviating potential harms through regulatory mechanisms considered in threshold 4 • Threshold 5 includes considerations of equity in access and stakeholder values in making coverage decision • Threshold 6 considers potential regulation for services not publicly funded

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clinical validity (the extent to which a test predicts clinical phenotype); and clinical utility (the assessment of benefits and harms) (29). As pointed out by Grosse and Khoury (21), the concept of "clinical utility" was initially defined as encompassing all benefits and harms, including social impacts (29), yet recently it has sometimes been defined more narrowly in terms of clinical outcomes, with ELSIs considered separately (e.g., 6;24;35).

A key framework that relies on these criteria is the U.S. "ACCE" model (**a**nalytic validity; **c**linical validity; **c**linical utility; and **e**thical, legal, and social issues) for evaluating emerging genetic tests (24). Several additional frameworks are based in part on ACCE, including the United Kingdom Genetic Testing Network (UKGTN)'s "Gene Dossier" approach to genetic test evaluation (34;54;59), and a framework for assessing genetic tests developed by the Andalusian Agency for Health Technology Assessment (AETSA) (41). In both ACCE and the AETSA framework, ELSIs are included as part of clinical utility and are also summarized as a separate component (Table 3). These criteria-oriented frameworks do include some details regarding methods, which focus on reviewing scientific evidence but also mention expert legal review (24) and the need to consider local context (41) when addressing ELSIs. Finally, recent developments in this area include the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) project, initiated as a follow-up to ACCE (58) (Table 3); and recent work that places a strong emphasis on the purpose of a genetic test (i.e., for morbidity or mortality reduction, health information, or reproductive decision making) (9;10) and broadens the scope of clinical utility to include a range of ELSIs and other factors (9) (Table 3).

A related framework is the "three-domain model" developed in Ontario, Canada, for technology assessment and coverage decision making regarding emerging predictive genetic tests (17) (Table 3), which uses a unique approach to address uncertainty in whether a test meets the standard for any given criterion. ELSIs are considered mainly in defining a technology's purpose (which is presented as a fundamental step in framing an evaluation) and in documenting costs and benefits. Finally, Caulfield and colleagues (12) proposed an analytic framework for evaluating genetic tests based on a Canadian generic healthcare coverage decision-making model (15). This framework presents a series of thresholds to determine whether a genetic test should be offered and whether it should be covered (12) (Table 3). The framework integrates ELSIs throughout and emphasizes overall moral acceptability as the first threshold.

INTEGRATION AND IMPLICATIONS FOR HTA IN GENETIC SCREENING

From the HTA literature, we summarized above recent discussions about the definition and scope of ELSIs in relation to HTA; as well as discussions about what "addressing" or "integrating" ELSIs might entail in practice. Specifically, authors have recommended including within HTA not only those ELSIs that may be viewed as impacts of technologies, but also those that describe the complexity of the relationship between technologies and society, including the social and political context in which technologies are developed and used. We described three broad approaches recommended in the HTA community for integrating ELSIs in HTA: literature synthesis, involvement of ELSI experts, and consideration of stakeholder values.

From the disease screening and public health genomics literatures, we identified three types of evaluation frameworks (based on disease-screening criteria, systematic review methods, and policy-oriented evaluations of genetic tests). ELSIs relevant to genetic screening that were mentioned in the frameworks included human rights, eugenics, accountability, transparency, equity, autonomy, stigmatization and discrimination, psychosocial harms and benefits, acceptability to stakeholders, choice and consent, privacy and confidentiality, and intellectual property (Tables 1 to 3). In accordance with current discussions in the HTA literature, several of these issues (e.g., human rights, eugenics, and stigmatization) suggest some consideration in an evaluation of how the development of technologies both reflects and contributes to societal and cultural values. Issues such as equity, acceptability, privacy, and intellectual property relate to the social and political context surrounding genetic screening policy decisions.

Although not all of the disease screening and genetic test evaluation frameworks described specific methodological approaches, where methods were stated or suggested, we found examples of the same three approaches to addressing ELSIs that were identified in the HTA literature (Tables 1 to 3). For example, the systematic review-based frameworks (26;44) and some genetic test evaluation frameworks (e.g., 24) emphasized knowledge synthesis methods. Involvement of ELSI experts was rarely explicitly mentioned (although see 24); however, we did not review the composition of the groups who developed the frameworks or that of policy evaluation bodies, so this does not suggest that ELSI expertise is not incorporated in practice. The need to consider stakeholder values was frequently mentioned and three frameworks directly recommended stakeholder participation (7;9;12). Finally, three frameworks placed particular emphasis on the need to address context (2;7;9).

Putting this together, it seems useful to consider how the issues defined as ELSIs in the field of genetic screening may be integrated with the methods identified for their consideration. For example, an assessment of psychosocial harms and benefits might best be carried out using systematic review methods; assessing public acceptability suggests a need to consider stakeholder values; and issues such as human rights, privacy, and intellectual property likely require input from experts in health law or bioethics. This mapping

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of methods against issues also reveals the implications of the choice of method on ELSI considerations. For example, systematic review methods may prioritize ELSIs that are amenable to empirical assessment (e.g., individual benefits and harms) rather than broader societal issues.

In turn, this relates to a discussion of whether ELSIs are best considered separately from other elements of an evaluation, or integrated throughout the HTA process (28). In genetic screening, their treatment as a separate entity has been argued to have hindered the role of ELSIs research in contributing to population health (8), and some authors have integrated ELSIs to avoid their marginalization (19). Based on the above, though, if ELSIs are embedded into an assessment of clinical utility, there is a risk that evaluations may focus more narrowly on "benefits and harms", excluding considerations that are important but cannot easily be reduced to an "effectiveness" dimension (unless clinical utility itself is viewed more broadly [e.g., 9]). For example, a critical examination of the perspectives and roles of patients, healthcare providers, and commercial interests (i.e., the sociotechnical network surrounding a screening test [36]) may improve our understanding of why and how a test is developed and used, and yield insights into how it might be regulated (11–13).

Finally, accepting the argument that it is important to incorporate ELSIs into HTA for genetic screening and recognizing (as we have described) that there are methods for doing so, a key remaining question is how to judge impact. What criteria should we use to decide whether a chosen method is appropriate and whether it has been applied well? To address this question we might turn to the stated reasons for incorporating ELSIs in HTA. For example, if the intent of addressing ELSIs is to increase the relevance of HTA to policy makers and other target audiences, then some measure of usefulness (based on the views of these groups) will be necessary. However, if part of the rationale for addressing ELSIs is an argument that ELSIs *should* be considered in HTA (regardless of whether policy makers would find HTAs that address ELSIs more useful), evaluation of the process will be more complex. The rapid evolution of the technologies involved in genetic screening presents a further challenge in assessing the impact of HTA methodology.

Others have also recognized the challenges in evaluating approaches to considering ethics in HTA (28;51) and in evaluating ethical guidelines for health policy generally (33). Kenny and Giacomini compared the current development of ethical guidelines to earlier stages in the field of clinical guidelines development, whereby guidelines were taken at face value and used to evaluate practice; now the guidelines themselves are subject to evaluation (33). Similarly, ethics guidelines for health policy will eventually themselves require assessment, including, where possible, the accumulation of empirical evidence. In the meantime, Hofmann notes that while we cannot ensure a high-quality ethical analysis in HTA, "... we may still discuss the goodness of an inquiry. An assessment that spells out the relevant moral aspects related to a technology and makes it easy for the reader to get hold of the moral complexity will be better than one that does not" (28, p. 317).

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REFERENCES

1. Abelson J, Giacomini M, Lehoux P, Gauvin FP. Bringing 'the public' into health technology assessment and coverage policy decisions: From principles to practice. *Health Policy*. 2006;82:37-50.
2. Andermann A, Blancquaert I, Beauchamp S, Dery V. Revisiting Wilson and Jungner in the genomic age: A review of screening criteria over the past 40 years. *Bull World Health Organ*. 2008;86:317-319.
3. Autti-Ramo I, Makela M. Ethical evaluation in health technology assessment reports: An eclectic approach. *Int J Technol Assess Health Care*. 2007;23:1-8.
4. Battista RN, Hodge MJ. The evolving paradigm of health technology assessment: Reflections for the millennium. *CMAJ*. 1999;160:1464-1467.
5. Braunack-Mayer AJ. Ethics and health technology assessment: Handmaiden and/or critic? *Int J Technol Assess Health Care*. 2006;22:307-312.
6. Burke W, Atkins D, Gwinn M, et al. Genetic test evaluation: Information needs of clinicians, policy makers, and the public. *Am J Epidemiol*. 2002;156:311-318.
7. Burke W, Coughlin SS, Lee NC, Weed DL, Khoury MJ. Application of population screening principles to genetic screening for adult-onset conditions. *Genet Test*. 2001;5:201-211.
8. Burke W, Khoury MJ, Stewart A, Zimmern RL. The path from genome-based research to population health: Development of an international public health genomics network. *Genet Med*. 2006;8:451-458.
9. Burke W, Zimmern R. *Moving beyond ACCE: An expanded framework for genetic test evaluation*. A Paper for the United Kingdom Genetic Testing Network. www.phgfoundation.org. 2007.
10. Burke W, Zimmern R, Kroese M. Defining purpose: A key step in genetic test evaluation. *Genet Med*. 2007;9:675-681.
11. Burke W, Zimmern RL. Ensuring the appropriate use of genetic tests. *Nat Rev Genet*. 2004;5:955-959.
12. Caulfield T, Burgess MM, Williams-Jones B. Providing genetic testing through the private sector. A view from Canada. *ISUMA: Can J Policy Res*. 2001;2:72-81.
13. Caulfield TA. The informed gatekeeper?: A commentary on genetic tests, marketing pressure and the role of primary care physicians. *Health Law Rev*. 2001;9:14-18.
14. Culyer AJ. Involving stakeholders in healthcare decisions – the experience of the National Institute for Clinical Excellence (NICE) in England and Wales. *Healthc Q*. 2005;8:54-58.
15. Deber RB, Narine L, Baranek P, et al. The public-private mix in health care. In: National Forum on Health, ed. *Striking a balance: Health care systems in Canada and elsewhere*. Sainte-Foy, Québec: Éditions MultiMondes; 1998.
16. Draborg E, Gyrd-Hansen D, Poulsen PB, Horder M. International comparison of the definition and the practical application of health technology assessment. *Int J Technol Assess Health Care*. 2005;21:89-95.
17. Giacomini M, Miller F, Browman G. Confronting the "gray zones" of technology assessment: Evaluating genetic testing services for public insurance coverage in Canada. *Int J Technol Assess Health Care*. 2003;19:301-316.
18. Godard B, ten Kate L, Evers-Kiebooms G, Ayme S. Population genetic screening programmes: Principles, techniques, practices, and policies. *Eur J Hum Genet*. 2003;11(Suppl 2):S49-S87.
19. Goel V. Appraising organised screening programmes for testing for genetic susceptibility to cancer. *BMJ*. 2001;322:1174-1178.
20. Grin J. Health technology assessment between our health care system and our health. Exploring the potential of reflexive HTA. *Poiesis Prax*. 2004;2:174.
21. Grosse SD, Khoury MJ. What is the clinical utility of genetic testing? *Genet Med*. 2006;8:448-450.
22. Grunwald A. The normative basis of (health) technology assessment and the role of ethical expertise. *Poiesis Prax*. 2004;2:175-193.
23. Guirguis-Blake J, Calonge N, Miller T, et al. Current processes of the U.S. Preventive Services Task Force: Refining evidence-based recommendation development. *Ann Intern Med*. 2007;147:117-122.
24. Haddow JE, Palomaki GE. ACCE: A model process for evaluating data on emerging genetic tests. In: Khoury MJ, Little J, Burke W, eds. *Human genome epidemiology*. Cambridge: Oxford University Press; 2004:217-233.
25. Hailey D, Nordwall M. Survey on the involvement of consumers in health technology assessment programs. *Int J Technol Assess Health Care*. 2006;22:497-499.
26. Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: A review of the process. *Am J Prev Med*. 2001;20:21-35.
27. Health Technology Assessment Task Group. *Health technology strategy 1.0. Final report*. Federal/Provincial/Territorial Advisory Committee on Information and Emerging Technologies. http://www.hc-sc.gc.ca/hcs-sss/pubs/ehealth-esante/2004-tech-strateg/index_e.html. 2004.
28. Hofmann B. Toward a procedure for integrating moral issues in health technology assessment. *Int J Technol Assess Health Care*. 2005;21:312-318.
29. Holtzman NA, Watson MS. *Promoting safe and effective genetic testing in the United States. Final report of the Task Force on Genetic Testing*. National Institutes of Health. www.genome.gov/10001733. 1997.
30. INAHTA. *INAHTA website. Definitions*. http://www.inahta.org/HTA/. 2007.
31. INAHTA Ethics Working Group. *Final report*. INAHTA. www.inahta.org/HTA/Ethics. 2005.
32. Johri M, Lehoux P. The great escape? Prospects for regulating access to technology through health technology assessment. *Int J Technol Assess Health Care*. 2003;19:179-193.
33. Kenny N, Giacomini M. Wanted: A new ethics field for health policy analysis. *Health Care Anal*. 2005;13:247-260.
34. Kroese M, Zimmern RL, Farndon P, Stewart F, Whittaker J. How can genetic tests be evaluated for clinical use? Experience

of the UK Genetic Testing Network. *Eur J Hum Genet*. 2007;15:917-921.
35. Kroese M, Zimmern RL, Sanderson S. Genetic tests and their evaluation: Can we answer the key questions? *Genet Med*. 2004;6:475-480.
36. Lehoux P. *The problem of health technology. Policy implications for modern health care systems*. New York: Routledge; 2006.
37. Lehoux P, Blume S. Technology assessment and the sociopolitics of health technologies. *J Health Polit Policy Law*. 2000;25:1083-1120.
38. Lehoux P, Tailliez S, Denis JL, Hivon M. Redefining health technology assessment in Canada: Diversification of products and contextualization of findings. *Int J Technol Assess Health Care*. 2004;20:325-336.
39. Lehoux P, Williams-Jones B. Mapping the integration of social and ethical issues in health technology assessment. *Int J Technol Assess Health Care*. 2007;23:9-16.
40. Lomas J, Culyer T, McCutcheon C, McAuley L, Law S. *Conceptualizing and combining evidence for health system guidance*. Canadian Health Services Research Foundation. http://www.chsrf.ca/other_documents/evidence_e.php. 2005.
41. Marquez Calderon S, Briones Perez de la Blanca E. *Framework for the assessment of genetic testing in the Andalusian Public Health System*. Seville: Andalusian Agency for Health Technology Assessment. http://www.juntadeandalucia.es/salud/contenidos/aetsa/pdf/Marco_pruebas_geneticas_eng_def.pdf. 2006.
42. McNally E, Cambon-Thomsen A, Brazell C, et al. *25 Recommendations on the ethical, legal and social implications of genetic testing*. European Commission. http://ec.europa.eu/research/conferences/2004/genetic/pdf/recommendations_en.pdf. 2004.
43. Molewijk AC, Stiggelbout AM, Otten W, Dupuis HM, Kievit J. Implicit normativity in evidence-based medicine: A plea for integrated empirical ethics research. *Health Care Anal*. 2003;11:69-92.
44. Medical Services Advisory Committee (MSAC). *Guidelines for the assessment of diagnostic technologies*. MSAC. http://www.health.gov.au/internet/msac/publishing.nsf/Content/C1F4569D79E542FACA257161001F1389/$File/guidelines2.pdf. 2005.
45. National Screening Committee (NSC). *First report of the National Screening Committee*. NSC. www.library.nhs.uk/screening. 1998.
46. National Screening Committee (NSC). *Second report of the UK National Screening Committee*. NSC. www.library.nhs.uk/screening. 2000.
47. National Screening Committee (NSC). *Criteria for appraising the viability, effectiveness and appropriateness of a screening programme*. NSC. www.library.nhs.uk/screening. 2003.
48. Nuffield Council on Bioethics. *Genetic screening: A supplement to the 1993 report by the Nuffield Council on Bioethics*. Council. www.nuffieldbioethics.org. 2006.
49. Oortwijn W, Reuzel R, Decker M. Introduction. *Poiesis Prax*. 2004;2:97-101.
50. Reuzel R. Interactive technology assessment of paediatric cochlear implantation. *Poiesis Prax*. 2004;2:119-137.
51. Reuzel R, Oortwijn W, Decker M, et al. Ethics and HTA: Some lessons and challenges for the future. *Poiesis Prax*. 2004;2:247-256.
52. Royle J, Oliver S. Consumer involvement in the health technology assessment program. *Int J Technol Assess Health Care*. 2004;20:493-497.
53. Sacchini D, Virdis A, Refolo P, Pennacchini M, Carrasco de Paula I. Health Technology Assessment (HTA): Ethical aspects. *Med Health Care Philos*. 2008;
54. Sanderson S, Zimmern R, Kroese M, et al. How can the evaluation of genetic tests be enhanced? Lessons learned from the ACCE framework and evaluating genetic tests in the United Kingdom. *Genet Med.* 2005;7:495-500.
55. Sawaya GF, Guirguis-Blake J, LeFevre M, Harris R, Petitti D. Update on the methods of the U.S. Preventive Services Task Force: Estimating certainty and magnitude of net benefit. *Ann Intern Med.* 2007;147:871-875.
56. Secretary's Advisory Committee on Genetics, Health, and Society. *U.S. system of oversight of genetic testing: A response to the charge of the secretary of Health and Human Services*. http://www4.od.nih.gov/oba/sacghs/reports/SACGHS_oversight_report.pdf. 2008.
57. ten Have H. Ethical perspectives on health technology assessment. *Int J Technol Assess Health Care*. 2004;20:71-76.
58. Teutsch SM, Bradley LA, Palomaki GE, et al., on behalf of the EGAPP Working Group. The evaluation of genomic applications in practice and prevention (EGAPP) initiative: Methods of the EGAPP working group. *Genet Med.* 2008. In press.
59. UK Genetic Testing Network (UKGTN) steering group. *Procedures and criteria for the evaluation of genetic tests for NHS Service (Gene Dossier)*. UKGTN. www.genetictestingnetwork.org.uk/gtn/. 2003.
60. Van Der Wilt GJ, Reuzel R, Banta HD. The ethics of assessing health technologies. *Theor Med Bioeth*. 2000;21:103-115.
61. Wilson JMG, Jungner G. *Principles and practice of screening for disease*. Geneva: World Health Organization; 1968.