Picturing ELSI+: a visual representation of ethical, legal, and social issues, and patient experiences in Health Technology Assessment in Canada

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Objectives. Consideration of ethical, legal, and social issues plus patient values (ELSI+) in health technology assessment (HTA) is challenging because of a lack of conceptual clarity and the multi-disciplinary nature of ELSI+. We used concept mapping to identify key concepts and inter-relationships in the ELSI+ domain and provide a conceptual framework for consideration of ELSI+ in HTA.

Methods. We conducted a scoping review (Medline and EMBASE, 2000–2016) to identify ELSI+ issues in the HTA literature. Items from the scoping review and an expert brainstorming session were consolidated into eighty ELSI+-related statements, which were entered into Concept Systems® Global MAX™ software. Participants ($N = 38$; 36 percent worked as researchers, 21 percent as academics; 42 percent self-identified as HTA experts) sorted the statements into thematic groups, and rated them on importance in making decisions about adopting technologies in Canada, from 1 (not at all important) to 5 (extremely important). We used Concept Systems® Global MAX™ software to create and analyze concept maps with four to sixteen clusters.

Results. Our final ELSI+ map consisted of five clusters, with each cluster representing a different concept and the statements within each cluster representing the same concept. Based on the concepts, we named these clusters: patient preferences/experiences, patient quality of life/function, patient burden/harm, fairness, and organizational. The highest mean importance ratings were for the statements in the patient burden/harm (3.82) and organizational (3.92) clusters.

Conclusions. This study suggests an alternative approach to ELSI+, based on conceptual coherence rather than academic disciplines. This will provide a foundation for incorporating ELSI+ into HTA.

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Health technology assessment (HTA) is a form of policy research which synthesizes and appraises information, mainly from systematic reviews and cost-effectiveness analyses, to inform a policy question (1). Over recent decades, it has become apparent that decisions about health technologies (adoption, optimal use, disinvestment) are not only scientific questions, but are heavily value-laden. HTA agencies, governments, and researchers have been exploring methods to better integrate the consideration of ethical, legal, and social issues (ELSI) into HTA (2–10). They have also recognized the importance of patient and public perspectives (11–13), and embraced methods to integrate them into decision processes (14).

However, this is challenging work. While unequivocally important, ELSI is arguably the broadest and most heterogeneous of HTA domains. Ethical issues abound, not only with respect to the use of technologies, but also with the methods and processes by which technology is appraised. Social values include equity, solidarity, population health, resource sufficiency, and more. Legal considerations are complex, and growing as a field of study.

In addition, patients' values and preferences, quality of life, experiences, and satisfaction are essential considerations in the appraisal of health technologies. These heterogeneous constructs underlie the "plus" in our "ELSI+". Their complexity is compounded by the variety of professionals who study them (bioethicists, lawyers, psychologists, social scientists, health economists, and clinicians) and the various methods they use (bioethical analyses, surveys, quality of life and utility studies, and qualitative research). Finally, different professions adopt different terminologies to refer to very similar constructs (9). An economist is interested in preferences for health states. A qualitative researcher studies patient experience. A psychologist studies quality of life, function, or satisfaction. While these ideas are not identical, there is surely some congruence and overlap.

We believe there is a fundamental lack of clarity regarding key ELSI+ concepts (15), which lies at the heart of the challenge of integrating ELSI+ into HTA. For example, is there an underlying construct, or set of constructs, for "ELSI+"? What are the relationships between ethics, patient preferences, patient perspectives, quality of life, and social values? The literature characterizing the relationships between these ideas is limited. There have been a few systematic attempts to understand ethical considerations (8;16), and patient preferences (17;18), but little transdisciplinary work that spans the entire ELSI+ domain.

The objective of this study was to identify the key concepts in the ELSI+ domain and their inter-relationships, using concept mapping. A visual and conceptual representation of ELSI+ may provide a foundation for literature search strategies and a conceptual roadmap for HTA researchers and decision makers.

Methods

This study was approved by the Research Ethics Board of the University Health Network, Toronto, Canada.

Concept mapping is an analytic method used to guide evaluation and planning in health and medicine (19–21). It combines qualitative approaches with quantitative analytical tools to visually represent ideas and their relationships in a picture or map (19), and thus is useful for exploring and understanding complex phenomena (21). The steps in a typical concept mapping process include (22;23):

(1) Preparation—outlining the research goals and developing the focus of the study; identifying participants;
(2) Generation of statements—gathering knowledge and opinions to create a set of ideas;
(3) Structuring of statements—engaging participants to sort the statements into categories, and rate them on one or more attributes; combining the individual sorting and rating results into matrices based on how many participants grouped statements together and how they rated the statements;
(4) Concept mapping analysis—analyzing the statement relationships using computer software for concept mapping;
(5) Interpretation of maps—conducting group sessions to discuss and interpret the conceptual structure of the maps.

We followed these steps in our study, as described below.

(1) Preparation

Our goal was to understand the range and inter-relationships of ELSI+ concepts. We aimed to recruit participants working or studying in social science, bioethics, law, patient advocacy, health economics, and HTA.

(2) Generation of statements

Scoping Review

We followed the Joanna Briggs methodology (24) for scoping reviews to examine the extent and nature of issues, ideas, and concepts related to ethical, legal, social, and patient values in the HTA literature (25). The search strategy (Supplementary Table 1), developed by an experienced librarian and peer-reviewed (26), included terms related to social/societal or legal or ethics or quality of life (utility) or patient preferences/satisfaction or social values/norms. These were combined with terms related to technology or HTA.

We searched the following databases: (1) Ovid MEDLINE®: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, (2) Ovid MEDLINE® Daily, (3) Ovid MEDLINE® 1946-Present, (4) Ovid Embase® 1974-Present. We limited the searches to English language studies published from 1 January 2000 (approximately when ELSI was introduced into HTA) to 2 March 2017.

Results from all searches were combined in a bibliographic database and duplicates deleted. The titles and abstracts of the remaining articles were reviewed independently by members of the study team. Duplicate papers that had not been identified previously were excluded. We retrieved full-text articles if the abstract reported on HTA, or at least one treatment, device, technology, or program; and ethical, legal, or social issues, or compliance, adherence, patient satisfaction, values, or preferences. Four reviewers (KEB, JB, JW, TT; see Acknowledgements) independently reviewed the selected full-text articles, and assessed their content for relevance to ELSI+ in HTA. The following data were extracted from the included articles and entered into an Excel database: first author, year of publication, journal title, topic of paper, and items describing the ELSI+ concepts and ideas. The extracted items were categorized into "ethical," "legal," "social," "patient values and preferences," "patient adherence/compliance/satisfaction," "quality of life and utilities," and "patient priorities." This classification was used to organize items in the data. Because this was not a meta-analysis, we did not record the frequency with which ideas were mentioned.

Brainstorming Session

We approached ten individuals who, based on the literature and our personal knowledge, had expertise in health economics, health policy, social science, and health outcomes, including from the patient perspective, for participation in a brainstorming session. The purpose of this in-person session, with a video-teleconference option, was to discuss the relevance of the ELSI+ items found in the scoping review and to elicit others. Six academic researchers/professionals and a patient advocate were available to participate. Five representative scenarios from the literature were presented: (1) screening for fetal abnormalities, (2) a drug for terminal cancer, (3) a universal vaccine, (4) telehomecare for chronic illness, and (5) genomics and genetic tests. Participants were asked to think of and discuss ELSI+-related issues for each, and some ideas and issues mentioned in the literature were then shown and discussed. Notes were taken, and the session was audio-recorded with the verbal consent of participants. The recording was later reviewed and the notes were augmented.

Review and Consolidation of Items

We reviewed all items derived from the scoping review and the brainstorming session. We sorted items with similar ideas into groups, selected the most representative terminology, and eliminated duplicate ideas. A maximum of 100 statements is considered manageable for the tasks required for concept mapping (22;23). We aimed for no more than eighty statements in our consolidation, to limit the burden on participants.

(3) Structuring of statements

We used The Concept Systems® Global MAX™ software (27) to conduct and analyze the study. The list of statements was entered into the brainstorming page, and a randomization function shuffled the list and assigned statement numbers. These statements were used for the rest of the study.

The tasks required from online participants were "sorting" and "rating" the statements. The sorting task asked participants to place the statements into groups based on common themes that made sense to them, and then name the groups. Rating involved assigning each statement a number on a five-point Likert scale. Our question for rating was: "How important do you think that each of the issues below are to decisions about whether or not a technology should be adopted for use in Canada? Please select the number that best describes how important you think each of the concepts below should be in Health Technology Assessment." The scale anchors were 1 = not at all important and 5 = extremely important, with 2, 3, and 4 (unlabeled) in-between. Demographic-related questions (gender, age group, type of work, area of expertise) were included to characterize the participants. Participants signed in anonymously or with their name, and they could save their responses at any time and return later to reduce task burden.

Participants

We searched the websites of thirteen Canadian universities for names and e-mail addresses of academics and researchers working in bioethics, health policy, or social sciences or law related to HTA. We also searched the websites of Canadian HTA agencies to identify individuals involved in HTA research, health economics, or patient advocacy, and scanned the author lists of the articles included in the scoping review to identify additional Canadians involved in ELSI+ endeavors.

We sent e-mails describing the study to 133 potential participants. We inquired about their interest in the study and asked them to forward the e-mail to others in their institution who might be interested. We received one "undeliverable" reply, and could not contact that person. We received automatic "out-of-office" replies from eight people on leave. Two people forwarded the information about the study to their group. All respondents who expressed interest in the study were e-mailed the consent form (to be signed and returned via e-mail) and the link to the online sorting and rating tasks, described above. We sent reminder e-mails to people who did not return the consent form within 10 days.

All forty-eight respondents who returned consent forms began the sorting task, and thirty-nine of them began the rating task. At least sixty of the eighty statements had to be sorted or rated to be considered a complete response for the purpose of analysis. Thirty-eight people completed the sorting task; one person sorted seventy-nine statements, and the others sorted eighty statements. A total of thirty-eight people completed the rating task, although one rated only seventy-three statements and three individuals rated seventy-nine statements. One person who assigned the same rating to all statements was excluded. Therefore, we analyzed sorting data from thirty-eight participants and rating data from thirty-seven participants.

(4) Concept mapping analysis

We used the Concept Systems® Global MAX™ software (27) to create point and cluster maps from the sorting and rating data. A point map locates each statement as a separate point on a two-dimensional (x, y) map, based on the frequency that statements were put in the same pile by the participants (22;23). Hierarchical clustering of the multidimensional scaling (x, y) co-ordinates was used to create clusters from the points, based on their proximity on the point map (23). The Concept Systems® Global MAX™ software (27) allows researchers to create several cluster maps, each with a different number of clusters. The cluster maps require interpretation for the selection of a final concept map.

(5) Interpretation of maps

We created cluster maps with as many as sixteen and as few as four clusters. Two clusters were merged as each map with fewer clusters was created. For example, in going from fifteen clusters to fourteen clusters, two clusters (and their statements) were merged to form one cluster. By examining how statements were merged to form progressively fewer clusters, we decided on the number of clusters that best fit the purpose of the study. The goal was to find the number of clusters that retained meaningful differences between the clusters but also kept statements together that seemed to belong together (23). The Concept Systems® Global MAX™ software (27) assigned labels to each cluster based on the names the participants gave to their groups of statements in the sorting task. These labels could be revised by the research team.

We used other analytical tools offered by The Concept Systems® Global MAX™ software (27) to analyze the point map and the cluster maps. For example, "bridging" analysis provided a value for each statement that described how well it reflected other statements in its vicinity on the map (23). A statement with a low bridging value is an "anchor"—it was sorted with nearby statements by many people. A "bridging" statement has a high bridging value—it was sorted with statements somewhat distant from it on the map. The bridging analysis therefore provided information about the relationship of that statement to statements nearby and far away.

The results of the rating task were used to create point-rating and cluster-rating maps, in which the average ratings for each statement and for each cluster were super-imposed on a point and cluster map, respectively (23;27).

Results

Scoping Review

A total of 26,890 articles were retrieved from Medline (11,155) and Embase (15,735), and 6,882 duplicates were removed to yield 20,008 articles, which were entered into bibliographic software. Another 1,248 duplicates were removed when reviewing article titles, resulting in 18,760 unique articles. After reviewing the titles and abstracts,

546 articles were retrieved for a full review. Information was extracted from 251 full articles (Supplementary Figure 1).

Brainstorming Session

The brainstorming session confirmed that the scoping study was comprehensive. However, the discussion generated some new ideas, such as parents making decisions for their unborn child in the case of screening for fetal abnormalities, the preferences of the family in the case of a drug for terminal cancer, and the consequences of knowing one's risk for disease in the case of genomics or genetic tests.

Review and Consolidation of Items; Generation of Statements

Approximately 300 ideas were compiled from the scoping review and the brainstorming session. These were consolidated into 100 statements that were further reduced to eighty statements (Table 1). Statements were concise and to the point to facilitate understanding and limit ambiguity. Supplementary Table 2 describes examples of how statements were consolidated.

Participants

The characteristics of the participants are shown in Supplementary Table 3. Participants were working as researchers (36 percent), and academics (21 percent), and 42 percent self-identified as experts in HTA. Study recruitment and data collection were completed within 2 months.

The Point Map

The point map (Supplemental Figure 2) shows the two-dimensional non-metric multidimensional scaling of the sorting data (23). The numbers correspond to the statement numbers (Table 1). The proximity of the points is determined by how likely they were to have been sorted in the same group by the participants. For example, six statements (26, 42, 44, 50, 58, and 74) are very close together. These statements are about sleep, disruption to daily life, mood and emotions, daily activities, and anxiety and stress (Table 1). Five statements (2, 27, 31, 34, and 69) are close to each other but not as close as the other six. These five statements concern universal access, rare diseases, equity, and distribution of health care and benefits (Table 1). Examination over the entire map indicated that the positions of the statements made sense (23). The point map was the basis for all other maps, and its structure did not change.

Cluster Maps

We created maps with varying numbers of clusters. Given eighty statements, a map with twenty clusters would have an average of four statements per cluster, while a map with ten clusters would have an average of eight statements per cluster. We aimed to select a map in which the clusters represented different concepts and the statements within each cluster represented the same concept. We began with an overall ELSI+ domain comprised of ethical, legal, and social issues, and patients' values and preferences, so we anticipated that fewer than four clusters would not be practical, nor would more than sixteen.

Two members of the study team (MK, KB) and two of the study participants (VR, TT, see Acknowledgments) reviewed the cluster maps in order to select the optimal number of clusters for the ELSI+ map. We started with sixteen clusters and observed which statements were merged with the formation of fifteen clusters. At this point, we independently asked ourselves if the statements that were merged into one cluster belonged together. We each recorded whether the merge made sense (yes, no, undecided), and why it did or did not make sense (23). We then looked at the fourteen-cluster map and examined the two clusters that were merged with its formation. Again, we recorded if we thought that the merged cluster included statements that belonged together. We continued this process until the map had four clusters. Figures 1A and 1B show the maps with sixteen and four clusters, respectively. It is possible to see which clusters were merged in going from sixteen to four clusters.

The four reviewers unanimously agreed with most of the merges from sixteen to five clusters, with two exceptions that were resolved through discussion. However, when the four-cluster map was created by merging a cluster with statements about patients' financial costs, location of care, and continuum of care with a cluster about incorrect test results, incidental findings, and ease of use, none of the reviewers thought the merge was appropriate. The statements in the first cluster were about operational matters and those in the second cluster were about risks and usability. Therefore, in assessing the merges made in going from sixteen to four clusters, it was decided that the map with five clusters was the most appropriate one. Each of the five clusters described a different concept, while the statements within each cluster described a singular concept. Table 2 describes the structure of the map with five clusters with the cluster labels given by The Concept Systems® Global MAX™ software (27).

We reviewed the statements in each cluster and the cluster labels (27) (Table 2). After some discussion, we renamed "Preferences" to "Patient preferences and experiences" and renamed "Patient quality of life" to "Patient quality of life and function." "Fairness" was judged to be appropriate for the third cluster. "Characteristics of the technology" was renamed "Patient burden/harm" and the "Access" cluster was renamed "Organizational." Figure 2 shows the final ELSI+ concept map with five clusters.

We analyzed the bridging values and importance ratings for the final ELSI+ concept map. The bridging value for each statement and the mean bridging value for each cluster are shown in Table 2. Statements and clusters with lower bridging values reflect the content in their vicinity well, whereas statements with high bridging values relate to other statements that are more distant from it on the map (23). "Patient quality of life and function," "Fairness," and "Patient burden/harm" have statements with lower bridging values than the other two clusters (Table 2). "Patient quality of life and function" has the lowest mean bridging value (.09), while "Organizational" has the highest (.73).

We also obtained the mean rating on importance in HTA for each statement and for each cluster (Table 2, Figure 2). The mean importance ratings for all clusters were above 3.5. The concept of "Fairness" was considered more important (mean rating 3.69) than "Patient preferences and experiences" (mean importance rating 3.61), or "Patient quality of life and function" (mean rating 3.65). However, "Patient burden/harm" was rated more important than any of these (3.82), as was the "Organizational" cluster (3.92). On average, the statements rated least important were religious beliefs, desire to fit in with other people, how much life-style or behavior choices cause disease or illness, and the statement

Table 1. Final List of Eighty Statements for the Sorting and Rating Tasks

1.	Quality of life
2.	Universal access
3.	Additional financial costs to patients or family
4.	Solidarity; society is willing to share good and bad health
5.	We should help the people who need help the most
6.	How much do life-style or behavior choices cause disease or illness
7.	Potential for addiction or abuse of a drug
8.	Parents' responsibility to children
9.	Equity in health outcomes
10.	Intrusion into personal life
11.	Patient preferences for outcomes
12.	Patient preferences for treatment
13.	Desire to "fit in" with other people
14.	False positive results = over-diagnosis, over-treatment
15.	Society's acceptance of disability and illness
16.	Interaction/relationship with healthcare provider
17.	Risk of harm
18.	Social stigma, embarrassment
19.	Difficult decisions arise after test results
20.	Ease of use; usability
21.	People value life more at the end of life
22.	Complexity of technology or treatment
23.	Continuum of patient care
24.	Communication with healthcare provider
25.	Consequences for family members
26.	Sleep; interference with sleep
27.	Rare diseases: if a few people need a very expensive treatment, we should help them regardless of cost
28.	Home-based vs. facility-based care
29.	Patient expectations
30.	Discrimination because of genetic test results
31.	Equity in access to treatment and health care
32.	Energy
33.	Physician–patient relationship
34.	If the costs are equal, we should help many people with a common disease instead of a few people with a rare disease
35.	False negative results = false reassurance; patients disregard symptoms
36.	Children's rights to make their own choices
37.	Realistic expectations
38.	Basic human rights
39.	Individual choice vs. societal choice
40.	Privacy of information
41.	Ability to obtain informed consent (ill, disabled)
42.	Amount of disruption to daily life

(Continued)

Table 1. (*Continued.*)

43.	Burden of treatment or technology
44.	Effects on mood, emotions
45.	Patient satisfaction
46.	Balance between individual's benefit and societal good
47.	Adaptive preferences: patients adapt to disability
48.	Patient empowerment
49.	Applicability to clinical practice
50.	Relief from symptoms; time to relief from symptoms
51.	Follow-up resources (e.g. treatment, genetic counseling)
52.	To be treated with dignity, respect, courtesy
53.	Freedom of choice
54.	Confidentiality
55.	Patient self-efficacy
56.	Receiving accurate and adequate information
57.	Handicapped and disabled people have their own society and culture
58.	Effects on daily activities
59.	Beneficence; do no harm
60.	Legal liability and responsibility for malfunctioning equipment, technical problems
61.	Anxiety about test results
62.	Desire to be treated as a whole person
63.	Side effects and adverse events
64.	Effects on physical activities
65.	Risks of incidental findings from a test
66.	Effects on social function
67.	Discrimination because of illness
68.	Preferences of general public (taxpayers, "veil of ignorance") vs. patients
69.	Maximum benefits for the most people
70.	Individuals have a responsibility to society
71.	Respect for patients
72.	Cultural beliefs and norms
73.	Religious beliefs
74.	Anxiety and stress
75.	Autonomy; personal choice
76.	Discrimination because of treatment
77.	Feasibility of implementation and use
78.	Patient involvement in decisions
79.	Risks of incorrect test results
80.	Preferences and values of family

about rare diseases (if a few people need a very expensive treatment, we should help them regardless of cost). The statement "quality of life" had the highest mean rating on importance in HTA (4.68), but other highly rated statements were basic human rights (4.56), equity in access to treatment and health
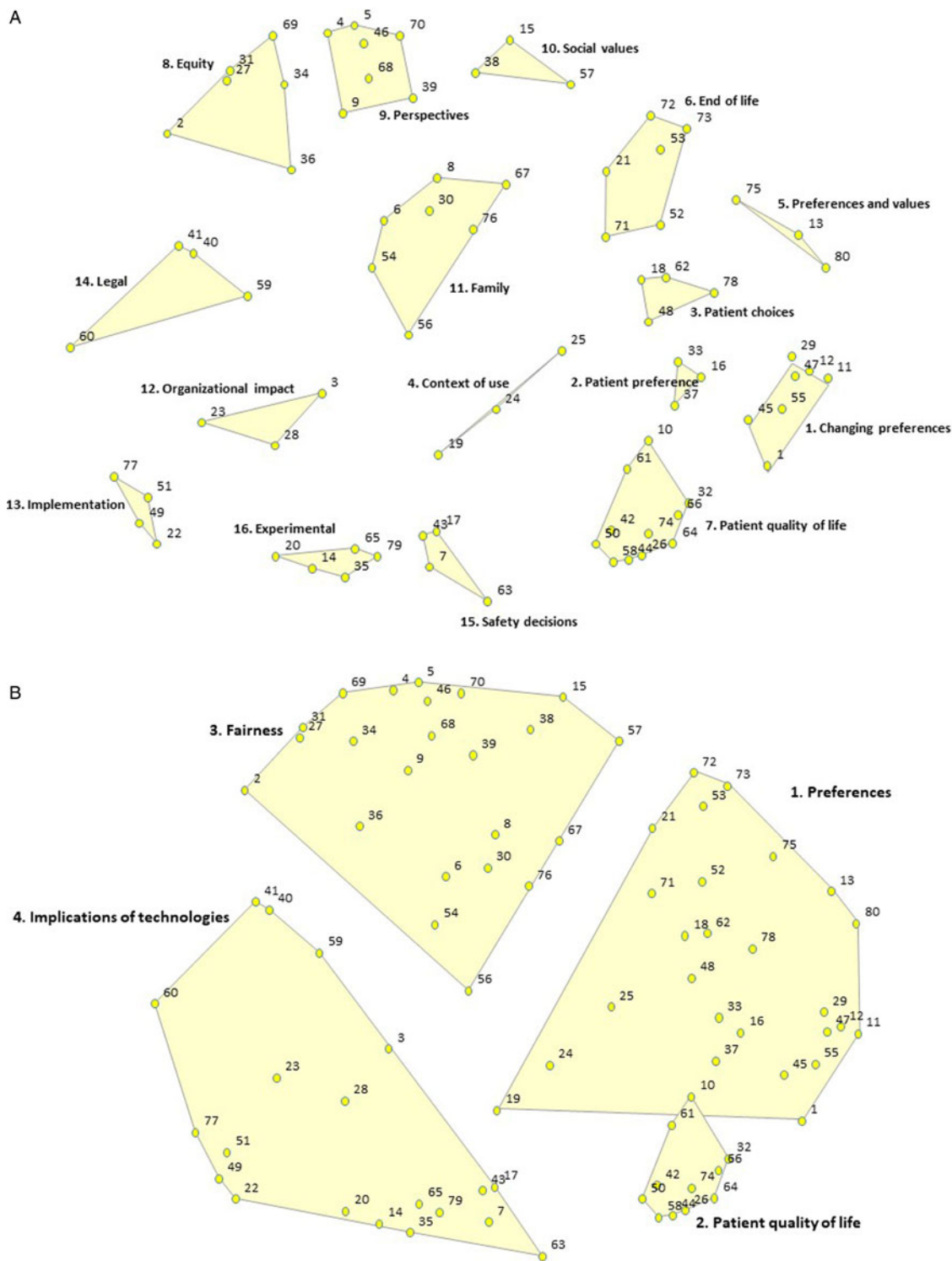
Fig. 1. Cluster map creation. (A) The map with sixteen clusters. (B) The map with four clusters.

care (4.54), receiving accurate and adequate information (4.5), and risk of harm (4.5).

Discussion

This study used qualitative and quantitative research methods to characterize ideas related to ELSI+ in HTA. We extracted eighty statements related to ELSI+ from the literature and a focus group. Although this extraction involved some subjective judgment, all members of the research team agreed on its inclusiveness and appropriateness. Moreover, after reading over 200 articles, saturation was reached. We used concept mapping to visually represent ELSI+ ideas and their relationships (19). We selected a concept map with five clusters, each of which

Table 2. The Clusters Comprising the ELSI+ Concept Map with Five Clusters With Statements, Mean Importance Ratings, and Bridging Values

Cluster name from software—*revised cluster name*		Importance rating	Bridging value
1. Preferences—*Patient preferences and experiences*		***3.65***	***.36***
37	Realistic expectations	3.89	.22
33	Physician–patient relationship	3.51	.22
16	Interaction/relationship with healthcare provider	3.38	.23
45	Patient satisfaction	3.76	.24
48	Patient empowerment	3.64	.25
29	Patient expectations	3.38	.25
62	Desire to be treated as a whole person	3.86	.25
71	Respect for patients	4.24	.29
78	Patient involvement in decisions	3.97	.3
47	Adaptive preferences: patients adapt to disability	3.54	.32
12	Patient preferences for treatment	3.89	.33
11	Patient preferences for outcomes	**4.28**	.34
55	Patient self-efficacy	3.73	.34
18	Social stigma, embarrassment	3.24	.34
24	Communication with healthcare provider	3.70	.36
1	Quality of life	**4.68**	.36
52	To be treated with dignity, respect, courtesy	**4.33**	.37
25	Consequences for family members	3.70	.38
72	Cultural beliefs and norms	3.24	.41
75	Autonomy; personal choice	4.00	.44
19	Difficult decisions arise after test results	3.22	.44
73	Religious beliefs	2.78	.44
53	Freedom of choice	4.00	.49
21	People value life more at the end of life	3.14	.51
80	Preferences and values of family	3.38	.53
13	Desire to "fit in" with other people	2.43	.58
2. Patient quality of life—*Patient quality of life and function*		***3.61***	***.09***
26	Sleep; interference with sleep	3.54	0
44	Effects on mood, emotions	3.62	.01
58	Effects on daily activities	**4.08**	.02
64	Effects on physical activities	**4.03**	.03
74	Anxiety and stress	3.54	.05
42	Amount of disruption to daily life	3.68	.08
32	Energy	3.00	.1
50	Relief from symptoms; time to relief from symptoms	**4.22**	.13
66	Effects on social function	3.75	.17
61	Anxiety about test results	3.05	.21
10	Intrusion into personal life	3.19	.22
3. Fairness—*Fairness*		***3.00***	***.33***
5	We should help the people who need help the most	3.89	.07
46	Balance between individual's benefit and societal good	4.08	.11

(Continued)

Table 2. (*Continued.*)

Cluster name from software—*revised cluster name*		Importance rating	Bridging value
	Statement Number		
4	Solidarity; society is willing to share good and bad health	3.49	.13
70	Individuals have a responsibility to society	3.43	.16
69	Maximum benefits for the most people	4.03	.19
34	If the costs are equal, we should help many people with a common disease instead of a few people with a rare disease	3.49	.22
68	Preferences of general public (taxpayers, "veil of ignorance") vs. patients	3.47	.23
39	Individual choice vs. societal choice	3.57	.24
31	Equity in access to treatment and health care	**4.54**	.3
67	Discrimination because of illness	3.73	.31
27	Rare diseases: if a few people need a very expensive treatment, we should help them regardless of cost	2.84	.31
9	Equity in health outcomes	4.14	.33
15	Society's acceptance of disability and illness	3.24	.33
76	Discrimination because of treatment	3.65	.34
30	Discrimination because of genetic test results	3.41	.36
57	Handicapped and disabled people have their own society and culture	3.11	.38
38	Basic human rights	**4.56**	.41
8	Parents' responsibility to children	3.70	.42
54	Confidentiality	3.86	.45
56	Receiving accurate and adequate information	**4.50**	.5
36	Children's rights to make their own choices	3.05	.58
6	How much do life-style or behavior choices cause disease or illness	2.92	.59
2	Universal access	4.27	.61
4. Access—*Organizational*		***3.82***	***.73***
22	Complexity of technology or treatment	3.27	.45
49	Applicability to clinical practice	**4.11**	.5
51	Follow-up resources (e.g. treatment, genetic counseling)	3.97	.58
77	Feasibility of implementation and use	**4.32**	.58
3	Additional financial costs to patients or family	3.92	.75
59	Beneficence; do no harm	**4.24**	.79
28	Home-based vs. facility-based care	3.36	.82
41	Ability to obtain informed consent (ill, disabled)	3.68	.83
40	Privacy of information	3.89	.86
23	Continuum of patient care	3.73	.87
60	Legal liability and responsibility for malfunctioning equipment, technical problems	2.50	1
5. Characteristics of technology—*Patient burden/harm*		***3.92***	***.31***
79	Risks of incorrect test results	4.03	.21
63	Side effects and adverse events	**4.43**	.22
65	Risks of incidental findings from a test	3.43	.25
17	Risk of harm	**4.51**	.26
35	False negative results = false reassurance; patients disregard symptoms	3.81	.27
7	Potential for addiction or abuse of a drug	3.32	.29
14	False positive results = over-diagnosis, over-treatment	4.00	.34

(*Continued*)

Table 2. (*Continued.*)

Cluster name from software—*revised cluster name*		Importance rating	Bridging value
Statement Number			
43	Burden of treatment or technology	**4.05**	.38
20	Ease of use; usability	3.73	.54

Mean importance and bridging values for each cluster are bolded italics. Statements within each cluster are ordered by bridging value. The three highest importance ratings within each cluster are bolded.
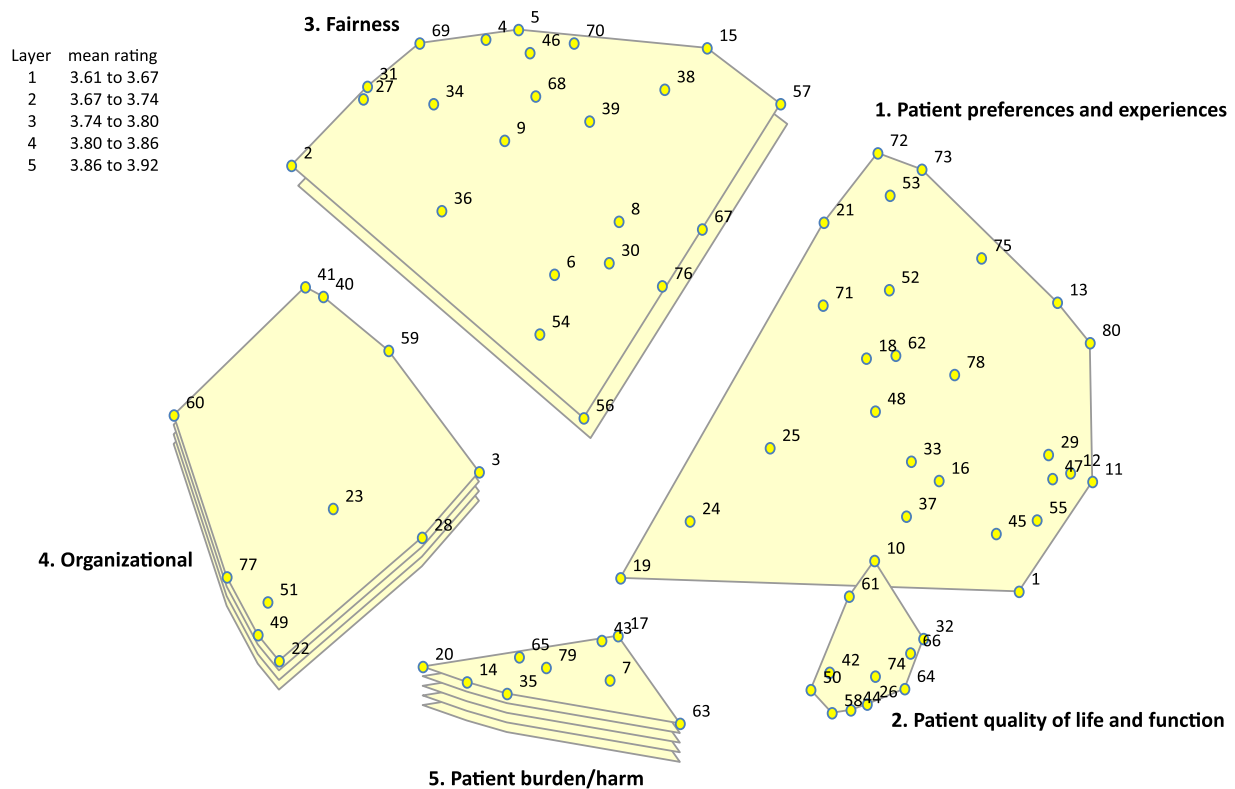

Fig. 2. Final cluster map with five clusters for ELSI+ with mean importance ratings.

represented a different concept and, at the same time, the statements within each cluster represented the same concept. The five clusters were (i) Patient preferences and experiences, (ii) Patient quality of life and function, (iii) Fairness, (iv) Patient burden/harm, (v) Organizational.

Our final clusters were not completely congruent with the original "ELSI+" conceptualization. The four moral principles commonly used in biomedical ethics (28) were found in all five clusters. Statements related to *beneficence* were in the "Patient preferences and experiences" cluster (patient satisfaction, patient preferences for treatment and outcomes), as well as the "Fairness" (maximum benefits for the most people, we should help the people who need help the most), and "Organizational" (beneficence; do no harm) clusters. *Non-maleficence* was addressed in almost all of the statements in "Patient burden/harm," and in "Patient quality of life and function" (anxiety and stress, effects on daily activities, amount of disruption to daily life), and "Organizational" (additional financial costs to patients or family). The principle of *autonomy* was evident in the "Patient preferences and experiences" cluster (freedom of choice, autonomy/personal choice, patient self-efficacy, patient empowerment, patient involvement in decisions), but also in the

"Fairness" (children's rights to make their own choices, receiving accurate and adequate information), and "Organization" clusters (ability to obtain informed consent (ill, disabled)). Most of the statements related to *justice* were included in "Fairness" (basic human rights, equity in access to treatment and health care, equity in health outcomes, universal access, balance between individual's benefit and societal good, individual choice vs. societal choice), but were also expressed in "Patient preferences and experiences" (respect for patients, desire to be treated as a whole person).

Statements about legal concerns were grouped in the "Organizational" (legal liability and responsibility for malfunctioning equipment, technical problems) and the "Fairness" (discrimination because of illness, treatment, or genetic test results) clusters.

Eleven social values relevant to HTA were identified by Giacomini: (1) Quality; (2) Evidence-informed policy; (3) Effectiveness; (4) Resource stewardship; (5) Resource sufficiency; (6) Equity; (7) Solidarity; (8) Population health; (9) Patient-centered care; (10) Collaboration; and (11) Shared responsibility for health (1). Many of these social values were distributed across our clusters. For example, equity, solidarity, and population

health were included in the "Fairness" cluster, while patient-centered care was expressed in "Patient preferences and experiences." The "Organizational" cluster included ideas related to resource stewardship and resource sufficiency.

With respect to the "+" in our ELSI+, three clusters addressed the patient perspective: preferences and experiences, quality of life and function, and burden/harm. The "Organizational" cluster also included statements that were relevant to patients, such as financial costs, and privacy of information. Although the "Fairness" cluster was more about patients as a group, its statements included discrimination, disability, and receiving information. Our conceptualization of ELSI+, therefore, appears to be very patient-centric.

Limitations

Representation from the public and patient communities would have allowed us to include their voices and assess similarities and differences between them and our participants.

Conclusions

This study offers an innovative approach to guide the integration of ELSI+ into HTA, applicable to any setting in which HTA is conducted. Articles in our scoping review were from Europe, the United Kingdom, the United States, Canada, and Asia.

Rather than a fundamentally profession-centric approach, we conceptualized ELSI+ based on the congruence of the underlying ideas, and in terms of patient preferences and experiences, patient quality of life and function, burden and harm, fairness (individual and societal), and organizational issues. This implies that the professions and academic disciplines that work within the ELSI+ domain (e.g. bioethics, social science, law, economics) cover a heterogeneous, but overlapping, set of concepts, which would benefit from multi-disciplinary and cross-disciplinary study.

Future work should (i) use a larger and more comprehensive sample of respondents, including patients, (ii) identify research methods associated with each concept, and (iii) create a validated search string for identification of the relevant literature.

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