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Eachempati, P

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Title: Developing an integrated multi-level model of uncertainty in health care – A qualitative systematic review and thematic synthesis

Authors:

Lead and corresponding author:

Dr Prashanti Eachempati

Professor and Head of Prosthodontics,

Faculty of Dentistry,

Manipal University College Malaysia,

Melaka 75150

Malaysia

Email: prashanti.eachempati@manipal.edu.my

ORCID iD: <https://orcid.org/0000-0003-1263-7423>

Co-authors:

Mr Roland Brian Büchter

Institute for Research in Operative Medicine (IFOM), Faculty of Health - School of Medicine,

Witten/Herdecke University, Cologne, Germany

Email: roland.buechter@uni-wh.de

ORCID iD: <https://orcid.org/0000-0002-2437-4790>

Dr Kiran Kumar KS

Professor in department of Prosthodontics

Faculty of Dentistry

Manipal University College Malaysia,

Melaka 75150

Malaysia

Email: kiran.kumar@manipal.edu.my

ORCID iD: <https://orcid.org/0000-0001-6638-0120>

Dr Sally Hanks

Associate Head School: Teaching and Learning, Peninsula Dental School
Professor of Primary Care Dentistry.

University of Plymouth

Email: sally.hanks@plymouth.ac.uk

Orcid: <https://orcid.org/0000-0002-4072-4594>

Dr John Martin

Sustainable Earth Institute,

University of Plymouth

Email: J.Martin-2@plymouth.ac.uk

<https://orcid.org/0000-0003-3363-8855>

Dr Mona Nasser

Associate Professor of Evidence Based Dentistry

Peninsula Dental School (Faculty of Health)

University of Plymouth

Email: mona.nasser@plymouth.ac.uk

<https://orcid.org/0000-0003-2220-6491>

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ABSTRACT:

Introduction: Uncertainty is an inevitable part of health care and a source of confusion and challenge in decision making. Several taxonomies of uncertainty have been developed, but mainly focus on decisions in clinical settings. Our goal was to develop a holistic model of uncertainty that can be applied to both clinical as well as public and global health scenarios.

Methods: We searched Medline, Embase, CINAHL, Scopus and Google scholar in March 2021 for literature reviews, qualitative studies and case studies related to classifications or models of uncertainty in health care. Empirical articles were assessed for study limitations using the CASP checklist. We synthesised the literature using a thematic approach and developed a dynamic multi-level model of uncertainty. We sought patient input to assess reliability of the model and applied it to two case examples.

Results: From the 4125 studies obtained in the search, we included 15 empirical studies, 13 literature reviews and 5 case studies. We identified 77 codes and organized these into 26 descriptive and 11 analytical themes of uncertainty. These related to global issues, public health, health care systems, clinical care, ethics, interpersonal relationships, personal issues, knowledge exchange, epistemology, unpredictability, and model parameters. The themes were included in a model which captures the macro, meso and micro levels and the interrelatedness of uncertainty. We successfully piloted the model on one public health example and an environmental topic. The main limitations are that the research input into our model predominantly came from North America and Europe, and that we have not yet tested the model in a real-life setting.

Conclusion: We developed a model that can comprehensively capture uncertainty in public and global health scenarios. It builds on models that focus solely on clinical settings by

including social and political contexts and emphasising the dynamic interplay between different areas of uncertainty.

KEY FINDINGS

What is already known?

- Uncertainty is inherent to clinical care and can be a source of confusion and a challenge to decision making.
- Uncertainty can become even more pronounced for public or global health scenarios as the Covid-19 pandemic has made painfully obvious.
- Current models of uncertainty in health care mainly focus on clinical decision making within a restricted health care system context.

What are the new findings?

- The synthesis highlights specific challenges that increase uncertainty in public and global health contexts such as political dimensions, social circumstances and equity issues.
- Uncertainty can occur at a micro, meso and macro level, is interconnected and can interact dynamically.

What do the new findings imply?

- In tackling public and global health challenges, a variety of uncertainties and their interplay should be considered.
- Possible applications of our model of uncertainty include exercises to identify and map specific uncertainties to aid the development of public and global health recommendations, priority setting for health research and situational analyses.

- More case studies are required on the application of models of uncertainty to public and global health challenges.

BACKGROUND

“Uncertainty is the only certainty there is and knowing how to live with insecurity is the only security.”- John Allen Paulos¹

Uncertainty is an inevitable part of clinical practice.² It can occur at every step of the clinical pathway: in delineating a disease, narrowing down a diagnosis, choosing a procedure, ascertaining which outcome is important to a particular patient and assessing the outcome or interpreting the findings of a measurement, for example. As the condition of patients becomes more complex e.g. due to multimorbidity, layers of uncertainty add up. In such cases, health professionals and patients not only strive to make sense of, and consider numerous, conflicting health problems, but also to ensure the optimum coordination of care.³ Trying to choose the ‘best’ option from different alternatives may pose a challenge; at the same time, any decision, even when well-informed and supported by high quality evidence, can lead to less desirable outcomes for the patients. It is often difficult to appreciate how intricately complex these tasks are and how easily wrong conclusions can be deduced.

Numerous definitions of uncertainty have been proposed in healthcare. Mishel 1990 defined uncertainty as ‘the inability to determine the meaning of illness-related events and occurs in situations where the decision maker is unable to assign definite values to objects and events and/ or is unable to accurately predict outcomes because sufficient cues are lacking’. After examining the various definitions, the common features related to uncertainty can be summarised to obtain a working definition which suggests that uncertainty is a subjective perception and a cognitive state of mind where there is conscious awareness of being unsure and represents a multi-dimensional phenomenon. Although it has been identified as a multi-dimensional phenomenon, a taxonomy which captures the dynamic nature of uncertainty is lacking.^{2 4-12}

Fox⁷ in 1957 and Light⁸ in 1979 each developed a conceptual framework of medical residents' experiences of uncertainty. Mishel⁹ has written extensively about patients' experiences of 'uncertainty in illness' in the nursing literature. Later, Beresford¹⁰ proposed a new classification of uncertainty based on interviews with clinicians from a variety of healthcare settings. In order to harmonize the literature, Han et al. proposed a three-dimensional taxonomy based on the sources, issues and loci that characterise uncertainty in health care.² Recently, three scoping reviews further classifying uncertainty in health care have been reported. Pomare et al.⁵ added categories to Han's framework² to develop a taxonomy of uncertainty in complex healthcare settings. Lee et al.¹¹ developed a framework of clinical uncertainty for medical education while Hong et al.¹² evaluated uncertainty in communicating cancer related genetic risk information.

Previous models of uncertainty focus on decision making scenarios in clinical settings. These have typically classified uncertainty in a discrete and segmented manner and have not accounted for the dynamic interplay between different types of uncertainty at multiple levels, such as the clinical, public and global levels. When a patient makes a clinical decision on an individual level, the decisions on public or global level directly and indirectly affects them. The global pandemic is a good example of this interaction: the political issues that affect population-level decisions on mask or vaccine, either directly affect individual decisions through changes in national guidelines or indirectly through the media attention towards the political controversy and uncertainties. In this paper, we focused on a broader range of decisions that not only focussed on uncertainty arising in clinical decision making which looks primarily at individual interactions between patients and clinicians but also involved population-level decisions. In this paper, we use the term public health level and global health level as separate definitions. Public health decisions focus on issues that affect the health of the population of a particular community or country. Ref lancet. Global health decisions involve

‘health issues that transcend national boundaries and governments and call for actions on the global forces’. References Lancet We recognize that there is a lot of overlap between these concepts but we wanted to have categories that differentiate population-level decisions that might be on community level, local or national level, from population-level decisions that happen on global scale. Our rationale was that decisions in communities that are closer to us (what we refer here is public health level) might affect us more than global level decisions (that happen on a global political level that transcend national boundaries and governments).

The objective of this paper is to see whether there is a unified or generalisable taxonomy of uncertainty for health care; and if not, to develop a holistic model that covers different levels of decision making in health care based on findings from a systematic review. Further, we show how the model can be used in one health (water fluoridation) and one non-health scenario (landscaping). The examples are intended to show how the model can be applied to health care (from where the data has been derived) and also more broadly to other areas (where further data is needed to support the model).

METHODS

All methods used in this review were pre-specified in a study protocol, which was registered in the open science framework (Publication DOI: <https://doi.org/10.17605/OSF.IO/QEP9H>). The review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹³ An initial scoping search was performed as a preliminary step to develop and refine the methods and identify existing conceptual models of uncertainty from articles, reviews, books, and book chapters.

Search strategy: Identification of papers and relevant databases

Search technique:

The SPIDER¹⁴ question format which is adapted from the PICO tool was used to search for studies as shown in Table 1.

Table 1: SPIDER question format

S ample	Studies describing types/classifications/taxonomies/conceptual models of uncertainties related to people/patients/health care providers/policymakers/health care systems
P henomenon of I nterest	Uncertainties in health care
D esign	Any, e.g., Qualitative, quantitative, and mixed-method studies
E valuation/outcome	A conceptual framework or taxonomy of uncertainties or elements identified from the research that can be contributed to the framework
R esearch tool	Any tool for collecting data (e.g., interviews, surveys, analysis of secondary data)

We searched five databases to identify articles related to taxonomies of uncertainty in healthcare (Medline via Ovid, Embase via Ovid, CINAHL via EBSCO Host, Scopus via Ovid and Google scholar). We combined subject headings and free text terms using truncation and appropriate Boolean operators, as available. Search terms included synonyms for uncertainty, health care and taxonomy as follows: ("uncertain*" OR "ambiguity" OR "doubt "OR "confusion "OR "unsure" OR "equivocal") AND (taxonom* OR classification OR variet* OR conceptual model* OR typology) AND ("healthcare" OR "health related information" OR "medical" OR "dental" OR "nursing"). Reference lists of the potentially included articles were searched and screened for eligibility. Searched were conducted on March 21st, 2021.

Study selection criteria:

Studies that had the primary objective of developing a taxonomy or conceptual model of uncertainty in health care, or to identify and classify different types of uncertainty derived from the literature or empirical research were included. Studies that presented an expansion, subtype, or modification of an existing framework, model, or taxonomy of uncertainty in health care and case studies which used cases to classify uncertainty were also included. Excluded studies did not develop a new taxonomy and used an existing taxonomy to map uncertainties in their specific context. The inclusion criteria allowed for studies reported in all languages.

Assessment strategy: Process of appraisal of papers to include in the review

The results obtained were screened in Rayyan software by two authors (Prashanti Eachempati (PE) and Kiran Kumar (KK)) applying the study selection criteria. We piloted the screening process with 100 articles to build a common understanding on how to apply the eligibility criteria before screening the rest of the articles. Disagreements were resolved by discussion and by consulting the arbiter if needed (Mona Nasser (MN)). Full texts for the potentially included articles were obtained and screened for inclusion by two authors (PE and KK). Disagreements were to be resolved by consulting an arbiter (Roland Büchter (RB)), however, this was not required. Reasons for exclusion were noted in the characteristics of excluded studies table. (*Supplementary file 1*)

Synthesis strategy: Data extraction and quality assessment

We developed a data extraction form and piloted it with 10 studies before applying it to the rest of the studies. We extracted data from the included studies on publication date, geographical location, type of study and model of uncertainty reported (original / extension of existing). Data extraction was performed by PE and KK independently and in duplicate.

We conducted a quality assessment using the CASP qualitative analysis tool¹⁵ to develop classifications from empirical research studies. We did not exclude studies based on the quality appraisal. No weighting or overall rank was given to the items, and we presented the judgement in each area so readers can assess areas of stronger and weaker methods and reporting. Thresholds for judgements were discussed during piloting of the data extraction form. All judgements were made independently by two authors (PE and KK) and disagreements were resolved through discussion.

Synthesis strategy: Data analysis

The data obtained from literature review articles was subject to descriptive analysis. For the studies using empirical research and the case studies, thematic synthesis was conducted as described by Thomas and Harden.¹⁶ Thematic synthesis was performed in three stages. First, the findings were coded line by line; second, 'free codes' were organised into related areas and 'descriptive' themes constructed; and finally, we organised the descriptive themes into overarching 'analytical' themes.

Stages one and two: coding text and developing descriptive themes

N-VIVO 12 pro software was used to store and manage the data from decisions that the researchers made during the thematic analysis. We coded the studies for themes relevant to the questions of interest. Coding was applied to the text labelled as 'results' or 'findings' and 'discussion' for studies pertaining to empirical research and to the entire text for case studies. Coding was done by PE. In addition, a sample of 6 studies each were coded by two additional authors with different backgrounds (RB, MN) to gain a broader understanding of the issue and to increase reflexivity. Descriptive themes basically remain 'close' to the primary studies, (what is identified from the articles) and the analytical themes 'represents a stage of interpretation where reviewers 'go beyond' the primary studies and generate new interpretive constructs.'¹⁶

Stage three: generating analytical themes

Analytical themes were identified by giving our own meaning to the data obtained. It was dependent on the judgement and insights of the reviewers. Hence a consensus meeting was conducted among three reviewers (PE, MN and RB) to segregate the descriptive themes into analytical themes representing areas of uncertainty in health care and defining them.

In keeping with quality standards for rigour in qualitative research, we considered our own views and opinions of uncertainty in healthcare and possible influences on the decisions made during the coding process and on how the emerging results of the study influenced those views and opinions. Reflexivity was recorded during the coding process. The audit trail was generated to provide some transparency and give readers an insight into the lens through which we have viewed our data. (*Supplementary file 2*).

Deviations from the protocol are recorded in the differences between protocol and review section. (*Supplementary file 3*).

Using the findings of the thematic synthesis, we proposed an interdependent multi-level conceptual model of uncertainty in health care. (Figure 1)

RESULTS

Search results

A total of 4125 titles were found through the five databases searched. After deduplication, 4107 remained. Through title and abstract screening, 4025 studies were excluded. A total of 82 studies were considered for full text screening. From the 82 articles, we checked the cross references and identified 59 more articles for which full text screening was done. Among the 141 screened for eligibility, 100 studies were excluded as they were not related to taxonomies of uncertainty. Eight studies which were pertaining to uncertainty but could not be considered

for inclusion, were excluded with reasons (e.g., authors summarised uncertainty given by others but have not given their own classification or uncertainty classification did not relate to health care setting). These are presented in characteristics of excluded studies table (Supplementary file 1). Thirty-three studies were included in the final analysis. (Figure 2)

Study Characteristics of included studies

The 33 included articles were published from 1957 to 2021. The majority of the included articles were reported from North America, 18 from the USA,^{2,4 7-9 15 17-27} three from Canada,^{10 28 29} and two from Mexico.^{30 31} Of the remaining, six studies were reported from Europe,³²⁻³⁷ two from Asia,^{12 38} one from Australia⁵ and one from New Zealand.¹¹

Fifteen studies used empirical research to develop classifications, of which twelve used a qualitative methodology,^{4 10 21 23 25 26 28 29 32 34 37 38} two used quantitative methodology,^{9 18} and one used a mixed-methods approach.³¹ From the mixed-method study only the qualitative component which pertained to classification development was considered. Five of the included studies were case studies.^{24 33 35 36 39} The remaining thirteen reports were literature reviews of which three were book chapters^{7 17 22} and three were scoping reviews.^{5 11 12}

Interviews were the predominantly used method of data collection in the qualitative studies,^{4 10 21 23 28 29 37 38} and mixed-method study.³¹ Focus group discussions were used in one study,²⁶ secondary data from NICE documents³² in another; and another²⁵ used open ended questionnaires to collect data. The two quantitative studies used surveys to collect data.^{9 18}

Study participants included medical doctors,^{7 10 26-28 30} medical residents,^{8 21 31} medical students,¹¹ emergency crisis management teams,³⁵ patients^{9 12 18 23 33 34 36 37} and parents of patients.^{25 38} Details of data extracted from included studies are provided in *supplementary file 4*.

Quality assessment

The quality assessment of all twelve qualitative studies^{4 10 21 23 25 26 28 29 32 34 37 38} and the qualitative component of the mixed-method study³¹ are presented using the CASP tool in *supplementary file 5*. All the studies reported a clear statement of the aims and were justified in using qualitative methodology to address the aims of the research. (For further details refer *supplementary file 5*).

Results of data analysis from different types of papers:

This section will be discussed in two ways:

- a. Narrative of different types of uncertainty classifications derived from the literature
- b. Thematic synthesis of empirical research and case studies

a. Uncertainty classifications derived from literature:

The description of the 13 literature review studies developing taxonomies are presented in Supplementary file 6 and Table 2. We listed the classifications proposed by the individual authors in supplementary file 6. All authors except of JM are current or previous health professionals with experience in clinical research. JM is an environmental scientist. The themes and codes were initially coded by [PE, MN, RB] and then double checked by [KK, SH and JM]. JM provided a non-health care viewpoint to reduce the impact of the authors health care background on categorising and grouping of studies.

We recognise that the uncertainties discussed in these papers are heterogenous as some discuss what causes of uncertainty (Knowledge deficits^{2,7,11, 12,15,17, 22, 27, 30} or probability^{2,7,12,15,17, 22, 30}) while some discuss the issues causing it (health care system^{2,5,11,20} or clinical practice^{2,8,11,12,15,19,22,27}). Some papers discuss the uncertainty caused due to interpersonal

relationships^{2,8,11,19} or patient experiences^{15,19,22} and some discussed two or more categories.

We tried to segregate papers with some common patterns and presented in Table 2.

Table 2: Common patterns across papers

Common concepts identified in the included studies	Studies discussing the concept	Description of the concepts
Uncertainty pertaining to knowledge deficit and qualities of knowledge or epistemic uncertainty	Fox 1957 ⁷ Mishel 1988 ¹⁵ Smithson 1989 ¹⁷ Babrow 1998 ³⁰ Djulbergovic 2011 ²² Han 2011 ² Wray 2015 ²⁷ Hong 2020 ¹² Lee 2020 ¹¹	This source of uncertainty can be limited knowledge or limitations in the quality of knowledge. Moreover, if the knowledge is provided in a way that is not understandable or ambiguous for the receiver or the audience it can lead to uncertainty. Complexity in the information or the context that the information is provided or used can also lead to uncertainty.
Uncertainty due to unpredictability or aleatoric uncertainty	Fox 1957 ⁷ Mishel 1988 ¹⁵ Smithson 1989 ¹⁷ Babrow 1998 ³⁰ Djulbergovic 2011 ²² Han 2011 ² Hong 2020 ¹²	Random error is a well-known aspect in scientific research. Although up-to-date evidence informs us on treatment or interventions with a higher probability to show certain effects on the patients, there is a variability in these effects due to random error. The latter can introduce uncertainty in the health care context.
System related uncertainty	Begun 2004 ²⁰ Lee 2020 ¹¹ Pomare 2019 ⁵ Han 2011 ²	Health care decisions are made in a wider health care system that introduces several levels of complexities and consequently uncertainty on the delivery and impact of the health care decisions.

Uncertainty in clinical practice	Light 1979 ⁸ Mishel 1988 ¹⁵ Penrod 2001 ¹⁹ Djulbergovic 2011 ²² Han 2011 ² Wray 2015 ²⁷ Hong 2020 ¹² Lee 2020 ¹¹	Although this category of uncertainty has an overlap with the healthcare system uncertainty, this pertains primarily to scientific uncertainty encountered in clinical practice - concerning to diagnosis, analysis, and treatment. Most of the included studies in this category discussed the complex interplay of variability in patients, disease presentations and clinical practices leading to uncertainty.
Uncertainty in patient experiences	Penrod 2001 ¹⁹ Mishel 1988 ¹⁵ Djulbergovic 2011 ²²	Patients' previous experiences and cultural contexts that they live in, shape what outcomes they prefer or what they find acceptable. That can become an additional level of uncertainty in the health care decision making process especially if there are conflicting values or interests between the information provider or health care professional and the patient.
Uncertainty due to relationships	Penrod 2001 ¹⁹ Light 1979 ⁸ Han 2011 ² Lee 2020 ¹¹	The different type of relationships that are shaped between doctor-patient or their families, can affect the nature of uncertainty that the individuals need to consider when they make a decision.

b. Thematic synthesis of empirical research and case studies

Free codes were identified using the line-by-line coding method and this allowed us to translate concepts of one study to another. As we coded each new study we added to our 'bank' of codes and developed new codes when a new concept was identified. Some of the sentences were categorised using several codes, e.g., in one study a parent whose child's diagnosis was uncertain commented: *"I am also anxious about knowing exactly what her diagnosis is so I can be aware when I have more children"*. This sentence was coded under both patients' personal fears as well as diagnostic uncertainties. In another example a physician commented on dilemmas due to lack of resources: *"For us it hasn't been a choice between patient A or patient B. We've never had a situation that clear....problem of balancing patients with quite different conditions who need access to the same bed, personnel, or equipment"*. This was coded under both ethical dilemmas and lack of resources. The initial coding process allowed us to identify 107 codes which were revised to eliminate overlaps. The final 77 codes were organized into 26

descriptive and 11 analytical themes based on the judgement and discussions among the authors. (*Supplementary file: 7*)

We defined the 11 analytical themes and described them by citing examples from the primary studies included in synthesis. These themes are not necessarily mutually exclusive. There are overlapping areas. For example, whether COVID, cancer, or heart disease, all raise uncertainty that is simultaneously experienced by individuals, health care institutions communities and societies, and that ultimately cross boundaries and require cooperation of different countries for effective management. And conversely, individual issues managed in the single exam room also raise uncertainties at the aggregate level. However, we discuss the themes independently to demonstrate the special challenges or limitations that they introduce.

Theme: Global uncertainty

Global uncertainty deals with health issues which evade, undermine, or go beyond the territorial and political boundaries, and thus require the cooperation of different countries to manage them effectively.

For example: Epidemics/pandemics and the impact of climate change on health create uncertainty that transcend national boundaries. One characteristic of this uncertainty is the involvement of more than two countries, with at least one outside the traditional regional groupings. Global politics, media and internationalisation can influence the extent or impact of the uncertainty.

An example from the primary studies is the global uncertainty created by the Zika virus pandemic.³⁵

*'Uncertainty, in sum, was crucial in categorizing the Zika crisis as an international emergency. This was a particular form of unknowing, however, understood by key global health institutions, most notably the WHO, as the confusion created by the absence of a scientific consensus on the nature of the association between ZIKV infection and microcephaly.'*³⁵

Theme: Public Health Uncertainty

Uncertainty that focuses on issues that affect the health of the population of a particular country or community or society, which are within the realms of national boundaries.

This uncertainty relates to issues pertaining to improving and protecting community health and well-being, and disease prevention strategies among the public. Uncertainty in public level data such as lack of epidemiological data on risk distribution or lack of uniformity in national health campaigns to prevent infectious diseases in the community leading to health inequalities, are examples in this category.

An example from the primary studies includes how the Zika virus pandemic impacted public health at the national level due to lack of epidemiological data.³⁵

*'...public health uncertainty was initially exacerbated by the intensification of surveillance efforts. The need to standardize clinical reporting protocols brought greater scrutiny to practices of prenatal and perinatal care, revealing shortcomings across the country, including limitations in the national system for registering congenital and birth abnormalities.'*³⁵

This uncertainty is different from global health uncertainty. Although public health uncertainty is also affected by political and social issues, global health issues cross national boundaries and add in another layer of complexity not only from political but also social and cultural aspect. Hence, we felt this requires a category of its own to demonstrate the uncertainty introduced in the decision-making process.

Theme: Health care system uncertainty

Uncertainty emerging from the manner in which services and systems are structured and organised, while involving the navigation of the patient in the complexities of the health care delivery.

This includes uncertainty that arises from challenging pathways for complex health problems that cause confusion and anxiety for those involved, leading to different approaches depending on how individuals perceive them.

An example from the primary studies includes resident uncertainty during transition of care²¹ and surgeon's uncertainty due to resource constraints.²⁸

'...the major categories observed included uncertainty in decision making at times of transition of care, specifically the determination of whether patients required escalation of care (eg, transfer to the intensive care unit) or were prepared for discharge'²¹

'...scheduling-related issues of being on call, staffing, time pressures, and equipment-related issues such as the availability and function of tools [led to uncertainty].'²⁸

Global (inherent globalisation), public health (geo-political localisation and interdependence) and health care system uncertainty (individualisation) have an unavoidable overlap and create triplication uncertainty.

Theme: Clinical uncertainty

Uncertainty experienced during patient-physician encounters in a clinical setting when confronted with the dilemmas relating to diagnosis, treatment, and prognosis due to variability in disease presentation, in feasible investigations, or multiple co-morbidities.

The following example from the primary studies showed that uncertainty clearly affected the clinical practice of the physicians in the area of diagnostic testing.

*'The reasons for this seem to be linked to physicians' desires to provide assurance to patients [...] or more generally to their pursuit of diagnostic certainty.'*¹⁰

Theme: Ethical uncertainty

Uncertainty which arises due to the inability to determine the right course of moral action in a given situation.

In health care, ethical uncertainty can arise due to conflicts between the autonomy of a patient and the beneficence to the patient in situations when

- a. patient might prefer an option that is inferior from a purely clinical standpoint or
- b. a choice has to be made between two equally unsatisfactory options or
- c. proxy decisions need to be made on behalf of the patient

The ethical dilemma faced by the clinicians when they had to decide whether the D-feed (a medical device that is used to feed an individual who is unable to take food by mouth safely) had to be removed or continued provides an example from one of our primary studies:¹⁰

*"The next of kin were out of the country and could not be reached. We had no indications of the patient's advance wishes at all. We had some very, very vague indication that the person we were dealing with would not have wanted to prolong life"*¹⁰

Theme: Relational uncertainty

Uncertainty arising from interpersonal relations and interactions among the various stakeholders in the context of healthcare.

The interaction could be between the physician and the patient or another physician, or patients' family members as shown in the following quote:

*'Working with other professionals and family members to achieve a management plan created troubling uncertainty.'*¹⁰

Uncertainty can also arise when the clinician networks with other clinicians or while working as a member of the health care team as shown in the following example where second opinions led to even more uncertainty:

*'When the diagnosis was uncertain, AiTs tried to use referral networks, pathways and advice from colleagues, while not always obtaining a usable opinion....my second opinion (from a trainer) I got no diagnosis, all I got was an option that the patient had already used that did not work' (AiT12- M).'*¹⁰

Theme: Personal uncertainty

Uncertainty experienced individually by all stakeholders in the health care system due to their personal beliefs, values, fears, previous experiences, risk perceptions and tolerance level.

For example, individuals who are less risk averse might not consider a specific amount of uncertainty a barrier to decision making, while for others it would be the cause of anxiety and indecisiveness.

An example from the primary studies is the uncertainty faced by a mother whose child had 'orphan illness': *"So it's not cancer, right?" Despite the conversation she had just had with an oncologist about the benign vascular anomaly, she was concerned that the birthmark had other health risks'*²⁵

Theme: Knowledge exchange related uncertainty

Uncertainty which arises due to the approaches taken when knowledge is communicated and exchanged.

For example, uncertainty can arise due to the inability to access updated information by patients or clinicians. People often research information online or talk to others about their experiences:

*'parents' information-seeking behaviours in response to their negative appraisal of uncertainty recurrently led to more uncertainty'*²⁵

Lack of patient-centred or individually tailored communication strategies exaggerate this type of uncertainty.

An example includes a mother of an 11-week-old daughter who expressed concern about the physicians' uncertainty about surgery. She stated, "...they were discussing the treatment option in front of me as 'experimental' and I wasn't sure they really felt it would work."²⁵

Theme: Epistemic uncertainty

Uncertainty related to quantity and quality of knowledge.

This could be attributed to lack of information leading to inadequate knowledge; or to the quality of information which lacks clarity or is ambiguous.²

Too much information with unexplained inconsistency, and lack of evidence can also lead to uncertainty exemplified in the following quotes:

*'There is paucity of data to predict the effects of certain factors in the progress of a disease or the outcomes of certain interventions'*¹⁰

*'Paradoxical and ambivalent uncertainty dilemma between treatment-related danger and recovery-related hope that influences decision-making. This dilemma confirms that more information can increase uncertainty and compromises parents' decision-making abilities'*¹⁰

Theme: Aleatoric uncertainty

Uncertainty which is inherent in healthcare due to unpredictability of events

This uncertainty arises due to a chance factor and makes it difficult to predict the variations in disease incidence or outcome of treatment.

*'The trouble is that you can't tell.... when you take on a seventy-five-year-old man or woman with coronary-artery disease, ... Some of them do very well and some of them just exist and after a few months ...major catastrophe and die or be left even more crippled.'*¹⁰

Theme: Parameter uncertainty

Uncertainty arising due to limitation in knowledge related to the values of each of the parameters included in the model or the absence of evidence about parameter values.

For example, a variable that is considered prognostically important for a particular patient and that is not included in the prediction model recommended in the local guideline can impede quantification or question the validity of data.

An example from the included studies is model inadequacy:

*'[uncertainty arising due to] limitations in either the theoretical or empirical models (e.g., genes, animal systems) used to represent gene-disease mechanisms.'*⁴

Model development

Based on themes identified from the thematic synthesis, we developed an overarching model of uncertainty (Figure 1). The representation of the model in concentric circles demonstrates the interdependency and interrelatedness of the different types of uncertainty in healthcare although they happen at different levels. We illustrated the model at three distinct yet interdependent levels: the macro, meso and micro level. We define macro level uncertainty as those affecting communities and societies as a whole and hence categorised the global, public health and health care system uncertainties in this level. The meso level pertains to the groups and relationships between the entities such as physician patient interaction or interaction of the

clinician with the members of the healthcare team. We mapped the clinical, relational and knowledge exchange uncertainties in this level. The micro level relates to individual level uncertainty affected by personal values, beliefs, and trust issues and hence we mapped the personal level uncertainty in this level. The epistemic, aleatoric, ethical and parametric uncertainties happen at all the three levels and form a link between the levels.

DISCUSSION

This systematic review was able to de-construct the separate layers of uncertainty affecting health decisions and demonstrate their dynamic interplay which was not adequately illustrated in previous papers. This is consistent with the complex cognitive processes required to deal with uncertainty in decision making⁴⁰ and raises the question whether we should conceptualise and study uncertainty as a ‘system problem’ rather than studying single aspects of uncertainty in isolation from each other. This approach allows us to acknowledge that uncertainty can change and evolve during interaction between different people.

As we mentioned, our updated model for the taxonomy of uncertainty emphasizes the dynamic nature and interrelation of different elements in the decision-making process. It can be used to better guide future communication and engagement strategies to support patients and clinicians and help in managing uncertainty in decision making. For example, our model discusses specific issues like uncertainty around the data, along with broader issues like global uncertainty which considers the changing global political environment.

Although we did not conduct any extensive interviews with stakeholders, we involved patients in this systematic review and sought their views on our newly developed model. Patients from different backgrounds, age groups and gender who had experienced health related uncertainty were contacted. Seven agreed to participate. We shared a video explaining the uncertainty model we developed and asked them to remark whether they could relate to the different types

of uncertainty we had classified and share their experiences of uncertainty in writing. Participants shared the same with us via email or phone. We explored how these patient experiences related to our proposed model. All the participants predominantly had uncertainty in the micro level (personal uncertainty) and meso-level (clinical, relational and knowledge exchange uncertainty). Epistemic uncertainty was identified by majority of the participants, and health care system uncertainty and aleatoric uncertainty were also identified.

Although there were no new categories of uncertainty added to the model, the PPI involvement allowed us to appreciate better the dynamic interaction of one uncertainty with another in a given situation, as experienced by the participants. It demonstrated that even smaller clinical decisions that only affect one person can have multiple layers of uncertainty affecting those decisions. The patient involvement unveiled that the complexity of a decision is not necessarily correlated with how many people it influences; a clinical decision involving one individual can in certain contexts have multiple layers of uncertainty. It became apparent that even very personal decisions have many levels of complexities involving a range of uncertainties. For example, a participant related how she had fertility issues and faced not only clinical uncertainty related to treatment outcomes, but also personal and relational uncertainties due to lack of much mental support from family and doctors. Another example is of a mother of a new-born baby who spoke about her personal uncertainty due to lack of support especially after childbirth and epistemic uncertainty she faced due to lack of knowledge on how to handle the baby in the initial few days. She narrated how it was assumed that breastfeeding would come naturally and was treated unkindly by the nurses and lactation consultants, leading to relational and healthcare system uncertainties. Our review also raises the question whether conceptualising these elements as separate and isolated issues is useful or if we should see them as dynamic items that can change over time and in different contexts even for the same decisions. We intend to evaluate this in future research.

We have used the micro, meso and macro levels to facilitate the understanding, the broadness of issues and the number of people that are affected by healthcare decisions (Figure 2). Similar to the other elements, they are not mutually exclusive, and decisions can be mapped across more than one level. For example, the meso level can refer to decisions made by regional health directors and affecting individuals in their region or it can refer to the individual decisions of the people in a region, which are affected by policies that were set on regional level. However, there is not necessarily a direct relation between broadness of the issues (number of people affected) and complexity of decision (or at least not from this review).

We demonstrated the applicability of the model in health care using the example of water fluoridation^{41 42} (Table 3) and showcased how different uncertainties co-exist in a particular situation that contains many layers of complexity.

Table 3: Application of the integrated multi-level conceptual model using water fluoridation as an example

Type of uncertainty	Definition	Example: Fluoride debate- Israel water fluoridation case ^{45 46}
Micro level		
Personal	Uncertainty experienced individually by all stakeholders in the health care system due to their personal beliefs, values, fears, previous experiences, risk perceptions and tolerance level.	People against water fluoridation are reluctant to voice out their views against the decision made by the government due to personal fears. Personal uncertainty is also caused by the fear of chronic fluoride toxicity causing cancer especially to those with history of losing near ones due to cancer.
Meso Level		

Type of uncertainty	Definition	Example: Fluoride debate- Israel water fluoridation case^{45 46}
Clinical	Uncertainty experienced during patient-physician encounters in a clinical setting when confronted with the dilemmas relating to diagnosis, treatment, and prognosis.	Parents from water fluoridated areas often consult dentists regarding the white spots on the developing dentition of their children and the possible influence of fluoridated water. It is difficult for the clinicians to confirm the aetiology of the hypoplastic lesions and ascertain the role of fluoridated water.
Relational	Uncertainty arising from interpersonal relations and interactions among the various stakeholders in the healthcare team.	In the Israel fluoridation case two groups were created for and against. Controversies and debates between all the involved stakeholders created another level of uncertainty due to interpersonal relationships.
Knowledge exchange	Uncertainty around how knowledge is communicated and exchanged.	To create a sense of certainty (despite uncertainty), policymakers and health professionals withhold information and provide ‘ready-made meal’ for providing convenient information to the public. (Israel water fluoridation case). Misleading information exchange leads to uncertainty.
Macro level		
Healthcare system	Uncertainty emerging from the manner in which services and systems are structured and organised, while involving the navigation of the patient in the complexities of the health care delivery.	Water fluoridation is not usually part of the health system and hence in many contexts, it doesn’t add a direct uncertainty to these decisions. However, there are other systems e.g. water system in countries that introduce uncertainty in these decisions. For example, certain cities might have mutual water systems where one city may agree for water fluoridation while the other does not. It introduces uncertainty whether we can implement water fluoridation considering where the water comes from, who is responsible for it and how many communities share the same water system and what other water sources are contaminated through this system.
Public health	Uncertainty that focus on issues that affect the health of the population of a particular country or community or society which are within the realms of national boundaries.	A typical example is the Israeli case of water fluoridation where in order to establish mandatory regulation, health ministry officials expressed information in an unbalanced format, promoting the topic of fluoridation by framing it in exclusively positive terms creating public level uncertainty.

Type of uncertainty	Definition	Example: Fluoride debate- Israel water fluoridation case^{45 46}
Global	Uncertainty related to health issues which evade, undermine, or go beyond the territorial and political boundaries, and are thus beyond the capacity of individual countries to resolve.	Despite the contradicting evidence, Centres for Disease Control and Prevention and American Dental Association support mandatory water fluoridation and call oppositions against it as ‘myths’ while referring to arguments in favour of fluoridation as ‘facts’.
Uncertainty across all three levels		
Epistemic	Uncertainty related to quantity and quality of knowledge.	Cochrane’s systematic review of water fluoridation concluded that there is very little updated and high-quality evidence indicating that fluoridation reduces dental caries. In spite of lack of evidence, water fluoridation is done globally highlighting its benefits creating uncertainty.
Aleatoric	Uncertainty which are inherent in healthcare due to unpredictability of events.	Effect of fluoride on individuals may vary and it is difficult to predict the adverse outcomes with certainty.
Parametric	Uncertainty due to lack of estimate of uncertainties or uncertainties in the model underlying the cause-effect relation or it might be lack of inclusion of these quantitative information in official updated clinical guidelines used by the clinician.	The current example did not use a modelling of data to inform their decision making due to the nature of studies around fluoride e.g. clinical studies along with biomedical studies. If in other contexts, decisions makers use a model of clinical and pre-clinical studies to make these decisions. Then uncertainty can arise from the existence or lack of estimate of uncertainty in these models.
Ethical	Uncertainty which arise due to inability to determine the right course of moral action in a given situation.	The main ethical arguments against water fluoridation are infringement of personal freedom of consuming water without fluoride, infringement of personal freedom of consuming ‘natural’ water without additives and coercing people to consume the water as supplied.

However, some health decisions have overlapping social or environmental components. For example, in some countries the decisions to remove amalgam as a restorative material was

based primarily on its environment impact and not clinical adverse events.^{43 44 45} Keeping this in mind we have piloted our framework on an example with an environmental focus (landscape uncertainty)^{46 47} and were able to map all the decisions across it. (Refer <https://doi.org/10.17605/OSF.IO/QEP9H> for details). Although the model wasn't validated for environmental decisions, landscaping has gone through a similar evolution as health decisions, having evolved from a more didactic decision-making process by managers and policy makers to a more participatory decision-making process. This might explain why the framework was easily mapped across those decisions. However, this needs to be evaluated further.

Some authors⁴⁸ have argued that the diversity and intricacy of uncertainty works against developing a comprehensive and specific conceptual model of uncertainty in healthcare. We agree with this position but believe that models should be advanced conceptually to better reflect the evolving complexities and contexts of decision making in health care. Health care has also moved away from the more didactic approach to decision making to a more participatory approach. It has transitioned from a paternalistic model of decision making (where the key driver was related solely to the doctor's experience and expertise) to a shared decision-making model where patient factors including patient experience and preferences, family members, information that they are exposed to on internet, add additional layers of complexity to the process. Despite its limitations (which we acknowledge), the existence of this updated framework of uncertainty will enable us to design better studies to capture what is required in health care decisions happening at different levels involving different stakeholders that we could not do otherwise.

The main limitation of this review is the limited scope and the narrow context of the included studies. We need more studies from more diverse populations exploring how the uncertainty can be different in different ethnic groups, countries, health systems etc and how we need to

consider them in engaging or communicating health information or support health decisions. In future research, we will use this model to study in a multi-ethnic group how individuals deal with different layers of uncertainty. Another limitation is that we did not apply and test the model in a real-life setting. Possible applications include, for example: identifying uncertainties that evolved during the Covid pandemic; identifying uncertainties on public health matters in order to develop guideline recommendations; identifying model parameters and their uncertainties for predictive models (“forecasting”) or assessing their limitations; mapping uncertainties regarding public or global health issues and identifying research priorities.

Finally, although three reviewers (PE, MN, RB) with different positions and experiences working in different health care contexts took part in the analysis, we acknowledge that it is impossible to completely prevent our personal experiences taint the analysis. That said, we have made an effort to make the data used to derive the themes and model as transparent as possible.

CONCLUSION

This systematic review has contributed to the development of a new expanded taxonomy and model of uncertainty in health care decisions that reflects our current transitions from a more didactic to more participatory decision-making processes across different levels of the health care systems. It acknowledges the dynamic nature of uncertainty and how it can change and evolve; and incorporates the global/public health perspectives that previous models did not include.

The model is built from the macro, meso and micro levels and includes 11 themes which are global, public health, healthcare system, clinical, relational, ethical, parametric, epistemic, knowledge exchange related, personal and aleatoric uncertainties. We suggest a fresh perspective that explicitly states the levels at which uncertainty occurs and meaningfully

interweaves them with the nature of uncertainty while keeping in mind the actors involved and their relationships.

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LEGENDS FOR FIGURES

Figure 1: Interdependent multi-level model of uncertainties in health care

Figure 2: Prisma Chart