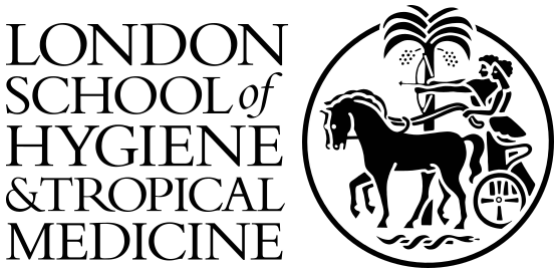

Title

Comparing end-of-life practices in different policy contexts: a scoping review

Authors and affiliations

- Antoine Boivin, MD, PhD. Charles-Lemoyne Hospital Research Center, Department of family and emergency medicine. Université de Sherbrooke, Canada (antoine.boivin@usherbrooke.ca) .
- Isabelle Marcoux, PhD. Faculty of health science. University of Ottawa, Canada (imarcoux@uottawa.ca).
- Geneviève Garnon, MSc. Université de Sherbrooke, Canada (Genevieve.Garnon@USherbrooke.ca).
- Pascale Lehoux, PhD. Institut de recherche en santé publique de l'Université de Montréal, Canada (Pascale.lehoux@umontreal.ca).
- Nicholas Mays, FFPH. Health Services Research and Policy department. London School of Hygiene and Tropical Medicine, United Kingdom (nicholas.mays@lshtm.ac.uk).
- Marie-Claude Prémont, PhD. École nationale d'administration publique, Canada (marie-claude.premont@enap.ca).
- Yi-Sheng Chao, MD, PhD. Université de Sherbrooke, Canada (Yi-Sheng.Chao@USherbrooke.ca)
- Evert van Leeuwen, PhD. Scientific Institute for Quality of Healthcare, Radboud University Nijmegen, Netherlands (E.vanLeeuwen@iq.umcn.nl).
- Raynald Pineault, MD, PhD. Institut National de Santé Publique du Québec; Département de santé publique de Montréal, Canada (raynald.pineault@umontreal.ca).

Corresponding author:

Antoine Boivin, MD, PhD
Adjunct professor
Department of family and emergency medicine
Charles-Lemoyne Research Center
Université de Sherbrooke, Longueuil Campus
150 Place Charles-Lemoyne, Bureau 200 (9e étage)
Longueuil (QC) J4K 0A8, Canada
antoine.boivin@usherbrooke.ca

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Abstract

Context
End-of-life policy reforms are being debated in many countries. International evidence is used to support different hypothesis about the effects of policy change on end-of-life practices. It is unclear whether reliable international comparisons can be made between policy contexts of prohibition and legalization.

Objectives
To assess the potential for comparisons between end-of-life practices across different policy contexts.

Methods
We conducted a scoping review of studies on medical end-of-life practices. We ~~built~~ developed a descriptive classification of end-of-life practices that distinguishes practices according to their legal status. We focused our review on the intentional use of lethal drugs by physicians, because of variations in the legal status of this practice across jurisdictions. MEDLINE, EMBASE, CINAHL, and Google Scholar searches were supplemented by expert consultation and hand-searching of reference lists. The sensitivity of the search strategy was tested using a set of 77 articles meeting our inclusion criteria. Two research assistants extracted data on end-of-life practice definitions and labeling, study methods, and comparisons across policy contexts. Canadian decision-makers were involved at different stages of the review to increase its policy relevance.

Results
333 empirical studies on the intentional use of lethal drugs by physicians were identified, including data from 19 countries. The bibliographic search captured 76 of the 77 studies initially identified ~~studies~~ as meeting the inclusion criteria (sensitivity=98.7%). Studies on the frequency of lethal drug use were conducted in jurisdictions with permissive (61.7%) and restrictive policies (43.3%). The most common study objectives related to the frequency of end-of-life practices, determinants of practices, and conformity with regulatory standards. Large variations in definitions and research methods were noted across studies. The use of a descriptive classification of end-of-life practices was useful to deal with international variations in definitions and labeling. A few international studies compared end-of-life practice in countries with different policies, using consistent research methods. We identified no systematic review comparing international end-of-life practices in different policy contexts.

Conclusions
A growing number of empirical studies have assessed medical end-of-life practices in the context of prohibition and legalization. The use of a descriptive classification is helpful to distinguish practices with different legal status and to deal with international variations in definitions and labeling. A systematic review of international evidence is needed to assess the impact of end-of-life policies on medical practice.

Introduction

End-of-life policy reforms are being debated in many countries. In Canada, the Criminal Code prohibition on the intentional use of lethal drugs by physicians is currently being challenged in court[1], and in parliament[2]. In the United States, several referendums and policy proposals were recently held on "right to die" legislation[3]. Similar legislative reforms have been debated in France[4], and the United Kingdom[5]. These developments create strong pressure on governments and challenge existing end-of-life policies.

Different assumptions are made about the potential effects of policy change on end-of-life practices. The "slippery slope hypothesis" hold that legalization of certain medical end-of-life practices could lead over time to a broadening application of proposed legal norms, leading to undesirable consequences on vulnerable patients[6-9]. Conversely, the "transparency hypothesis" hold that legalization could lead to more open and regulated medical practices, thus resulting in better respect of proposed safeguards [10-13].

International evidence is being used in support of these different hypotheses by proponents and opponents of policy reforms. For example, Canadian court documents and policy proposals included an extensive discussion of international evidence to support their position [1,10,14,15]. Similarly, the House of Lords in the United Kingdom included a lengthy review of international experiences [5], as did the recent Sicard report in France [4].

It is unclear whether reliable international comparisons can be made from evidence collected in different legal contexts. For example, the feasibility of documenting medical practices that are prohibited could be problematic and limit the ability to test the impact of policy change. Also, interpreting international evidence is far from straightforward, because of potential variations in definitions and classifications of end-of-life practices, study methods, health system characteristics and regulation.

As a first step toward the completion of a full systematic review, we sought to map available international evidence on medical end-of-life practices, and to assess the potential for reliable international comparisons across different policy contexts. Mapping available evidence is important to clarify what can realistically be expected from existing studies, and to identify current gaps in research. Our review focused on two core research questions: 1) what empirical evidence is available on medical end-of-life practices in contexts of prohibition and legalization; 2) what is the potential and what are the limitations of the empirical evidence to compare the frequency of medical end-of-life practices in different legal contexts?

Methods:

Design

We conducted a scoping review of studies on medical end-of-life practices, with a focus on practices whose legal status differ across jurisdictions (described below). Scoping reviews aim at mapping the main sources and types of evidence available in a field of

interest[16]. Scoping studies are ~~especially~~ best suited for complex areas of research, and can be useful to determine gaps in the existing literature and assess the value of conducting a full systematic review.

Classification of medical end-of-life practices and scoping review focus

Legal definitions and classifications of medical end-of-life practices vary, and no consensus exists at the international level[17]. For example, definitions of terms like "euthanasia" have evolved over time and across countries[18-20]. In preparation for the scoping review, we developed a descriptive classification of end-of-life practices that: 1) distinguishes medical practices according to their legal status; 2) is related to observable practices that can be studied empirically; and 3) allows for the potential translation of different end-of-life practice definitions into comparable categories across countries.

Our descriptive classification distinguishes between:

1. Withdrawing or withholding of treatments that have the potential to prolong life (e.g. cessation of an artificial ~~respirator~~ventilator, not initiating chemotherapy ~~to~~ for a patient with cancer, stopping antibiotics for a patient with pneumonia);
2. Use of a drug justifiable by its specific effect on symptom management or treatment of a health condition, even if an unintended side-effect may be to shorten life (e.g. thrombolysis for myocardial infarction, chemotherapy for cancer, use of opiates ~~adjusted~~ titrated to pain control, use of specific sedative medication ~~adjusted~~ titrated to refractory symptom control by reduction in patient consciousness[21]);
3. Intentional use (prescription, advice, supply, or administration) of a lethal drug that is not justified by a specific effect on symptom control or treatment of a medical condition (e.g. injection of a neuromuscular blocker without respiratory support, injection of potassium chloride to a patient with a normal potassium level, injection of a massive dose of opiates above what is necessary for pain control, continuous use of sedatives without artificial hydration above what is needed for symptom control).

We emphasize that this classification seeks to distinguish practices according to their legal status in different jurisdictions, rather than their ethical or deontological justification. For example, some ethicists contest the distinction between withdrawing life-sustaining treatment, using drugs whose unintended side-effect may be to shorten life, and the intentional use of lethal drugs[22,23]. However, these practices currently have different legal status in many jurisdictions[17].

We should also highlight that, while category #3 refers to the intentional use of lethal drugs that is "not justified" by a specific effect on symptom control or treatment of a medical condition, this does not mean that no other legal justification can exist for this practice. While many jurisdictions prohibit the intentional use of lethal drugs by physicians (e.g. Canada, United-Kingdom, France, New Zealand), other jurisdictions recognize specific circumstances in which such practice can be legally justified. Legal conditions for the intentional use of lethal drugs vary across jurisdictions, and can include one or many of the following criteria (this is not an exhaustive list):

- Voluntary request by a competent patient (e.g. Oregon, Vermont, Montana, Washington, Belgium, Luxemburg, Netherlands, Switzerland) [17,24,25];

Commented [AB1]: I added more details, based on definitions of palliative sedation therapy proposed by an international expert group in Graeff et al. 2007

- Presence of an advanced directive by a previously competent patient (e.g. Netherlands, Belgium, Luxemburg) [19,26,27];
- Presence of a substituted request in the case of an incompetent patient (e.g. Netherlands) [8,28,29]
- Presence of unbearable suffering (e.g. Netherlands, Belgium, Luxemburg)[17];
- Presence of a terminal illness with limited life expectancy (e.g. Oregon, Vermont, Washington);
- The self-administration of lethal drugs by the patient himself (e.g. Oregon, Vermont, Montana, Washington, Switzerland);
- The absence of self-interest by the person providing lethal drugs (e.g. Switzerland)[30].

To reflect these differences in end-of-life policies across jurisdictions, our descriptive classification further distinguishes if the intentional use of a lethal drug is carried out: a) with a voluntary and informed request made by the patient prior to death; b) if a voluntary advanced directive was made by a previously competent patient, c) if a substitute request was made by the proxy decision-maker of an incompetent patient, or d) if the medical practice is carried without a patient or substitute request. We also distinguish when a lethal drug is administered by the patient himself or by someone else.

As illustrated in Table 1, the descriptive classification distinguishes end-of-life practices that have different legal statuses across jurisdictions. To yield a manageable number of studies, we focused the scoping review on the intentional use of lethal drugs not justified by a specific effect on symptom control or treatment of a health condition (category #3 of the descriptive classification). This choice was justified by variation in the legal status of this practice across different jurisdictions.

Data sources and search strategy

We conducted two bibliographic searches sequentially. First, we ran an open search strategy in Google Scholar using the search terms "end-of-life decisions", "euthanasia", "assisted suicide", "assisted dying", "assisted death", "assisted dying", "medical aid in dying", "termination of life", "medical behaviors that shorten life". This was supplemented with hand searching of reference lists and expert consultation. This initial search identified a set of studies meeting our inclusion criteria, which were used to develop and test a more focused search strategy in electronic databases. Our final search strategy was run in March 2012 in three electronic databases (MEDLINE, EMBASE, and CINAHL) using the search terms listed in Appendix 1.

Inclusion and exclusion criteria

The scoping review proceeded in two stages, with a progressive restriction of the inclusion criteria between each stage. In Stage 1 (mapping of the topic area), we included all empirical qualitative or quantitative studies on the use of lethal drugs by physicians with data on actual medical practices. We excluded studies on physicians' attitudes and opinions, studies on the use of lethal drugs without physician involvement (e.g. injection by a nurse without a physician's prescription), or studies on lethal drug use outside the medical context (e.g. prisoner execution). We also excluded studies without an abstract, animal studies and those published in a language other than English or French. In Stage 2 (comparability of international frequency studies), we further restricted our analysis to quantitative studies on the *frequency* of physicians' lethal use of drugs. Two research assistants screened each reference against the inclusion and exclusion

criteria. Disagreements were resolved through team discussion with the principal investigator (AB).

Data extraction

We extracted data on *study methods* (design, objectives, country, year of data collection, sampling strategy, source of data collection, data collection method, number of participants and response rate, respondents), on how *medical practices* were defined and measured (definitions, question wording, type of drugs used, and assessment of its lethal potential), and on the presence of *comparisons* within and across jurisdictions with different policies. Data extraction was conducted by two research assistants using a structured extraction sheet. Extracted data were imported in a FilemakerPro database developed with the help of an information technology specialist.

Data analysis

In stage 1, we used content analysis to map the main study objectives of all empirical studies on the use of lethal drugs by physicians. Key themes were charted and analyzed using the theory of planned behavior as an original template[31]. In Stage 2, we used descriptive statistics to report on the main characteristics of frequency studies, seeking to identify the main sources of heterogeneity and the potential for conducting international comparisons. We classified the policy context as "permissive" when the intentional use of lethal drugs was allowed by public policies at the time of the study (e.g. Belgium after 2002[19], Oregon after 1997[25]) and "restrictive" when the intentional use of lethal drugs was prohibited by public policies.

Integrated knowledge translation strategy

We followed an integrated knowledge translation strategy to increase the policy relevance of the review[32]. We set up an advisory committee composed of key medical, legal, governmental, and public organizations involved in end-of-life policymaking in Canada, including organizations with different views on end-of-life policies. Two one day meetings were organized over a one year period: the first meeting focused on agreeing roles and responsibilities, discussing scoping review objectives, and discussing the descriptive classification of end-of-life practices; and the second meeting aimed at reviewing preliminary findings and identify priorities for further research. While the advisory committee's recommendations informed research decisions, the researchers remained ultimately responsible for the scientific integrity of the review.

Results:

Identified studies

Figure 1 describes the flow of included studies. 1308 unique abstracts were screened, yielding a total of 333 empirical studies on the use of lethal drugs by physicians published between 1998 and 2012 (Table 2). Our final bibliographic search captured 76 of the 77 initially identified studies meeting the inclusion criteria (sensitivity=98.7%), meaning that our search strategy was highly sensitive to capturing empirical studies on the use of lethal drugs by physicians. Most studies (N=248, 74.4%) used quantitative research designs.

Table 3 includes the main study objectives covered by the 333 empirical studies on the use of lethal drugs by physicians. The most frequent study objectives related to determinants of requests

and practices (N=64, 19.2%), frequency of lethal drug use (N=60, 18.0%), and conformity of practices with regulatory standards (N=48, 14.4%). We identified few empirical studies on medical complications of lethal drug use (N=6, 1.8%) and their impact on relatives (N=8, 2.4%).

Sixty quantitative articles aimed at assessing the frequency of lethal drug use, and these articles were analyzed in more detail to assess their potential for international comparisons (Table 4). There was a large clustering of articles from a few countries, with multiple articles reporting results of the same study. For example, 6 large cross-sectional surveys conducted in the Netherlands, Belgium, Denmark, Italy, Sweden, and Switzerland accounted for 45% (N=27) of all articles on the frequency of lethal drug use by physicians. While all articles reported data on the intentional use of lethal drugs by physicians (as per the inclusion criteria), other end-of-life practices were also reported in these studies, including the use of drugs justified by symptom control (N=24, 40.0% of articles) and the withholding/withdrawal of life-sustaining treatment (N=29, 48.3%). Only 58% (N=35) of studies included data on the use of lethal drugs without patient request.

Labelling, definitions, and classification of medical end-of-life practices

Among the 60 quantitative articles on the frequency of end-of-life practices, there were large variations in terms of labeling, definitions, and classifications of medical end-of-life practices. In 33% of articles (N=20), no definitions of different end-of-life practices were included. When definitions were provided, similar labels were found to have different meanings across studies, countries, and over time. For example, some studies used "euthanasia" to refer to the administration of lethal drugs by physicians, without distinguishing if this was carried with or without voluntary patient request[33]. Other studies had more restrictive definitions, and used "euthanasia" to refer to the intentional administration of a lethal drug with a patient request[34-36]. Other labels used to refer to the intentional use of lethal drugs by physicians included "physician assisted dying"[37], "physician assisted suicide"[38], "help to die"[39], "ending of life"[40], "life-terminating act"[41], and "using drugs to end life"[42].

Wording of study questionnaires varied across studies, and 25% of articles (N=15) did not provide information about how questions were framed. Some questions made it difficult to distinguish between the intentional use of lethal drugs and treatment withholding/withdrawal (e.g. "Have you ever taken deliberate action that would directly cause a patient's death?"[43]). Other ~~differences in~~ questions related to the framing of physicians' intentions, which was sometimes described as ending the patient's life [38,44-46], bringing about the patient's death [47], hastening the patient's death [28,48,49], or shortening the patient's life[13].

Distinguishing between practices with different legal statuses was sometimes difficult because of inconsistencies between empirical practice studies and public policies. For example, the Belgian Euthanasia Act of 2002 defines euthanasia as the "intentional life-terminating action by someone other than the person concerned, at the request of the latter"[19]. However, empirical studies from Belgium and other European countries exclude from the euthanasia category all use of lethal drugs with a "partial" intention to hasten death[35,49], a distinction that is not reflected in public policies. This means that some practices that meet the legal definition of euthanasia would not be classified as such in those empirical studies. Other examples of inconsistencies include grouping together the frequency of lethal drug use in children and adults[13,35,49], despite the fact that policies in the studied countries have different legal provisions for lethal drug use in these age

categories. The grouping of practices with mixed legal statuses was most problematic with categories labeled as "intensification of symptom alleviation", "terminal sedation" and "continuous deep sedation" [50-52]. Proper analysis of these categories is complex because of incomplete outcome reporting[53] and discrepancies between the reporting of the same studies in different languages[40,54].

A related but distinct problem is the absence of information on the actual lethal potential of drugs used by physicians. Only 33% of studies (N=20) reported data on the type of drugs used, and 8% (N=5) appraised their actual lethal potential by external experts. This means that observed differences between countries could simply reflect physicians' subjective reporting of their intentions rather than changes in actual practices (e.g. what drugs are used, at what dose initiation/escalation, and with what lethal potential). This limitation is important given the fact that intentions have been found imperfect to predict end-of-life practices[54] and because up to 76% of drugs used by physicians with the intention to cause death have low lethal potential[55]. While the problem of end-of-life categories with mixed legal status would tend to underestimate the frequency of intentional lethal drug use by physicians, absence of data on drug lethality would tend to over-estimate the frequency of physicians' practices that actually cause patients' deaths.

Potential for international comparisons of end-of-life practice frequencies

Studies on the frequency of lethal drug use by physicians were conducted in countries with permissive (N=37, 61.7%) and restrictive policies (N=26, 43.3%)[1], thus offering some potential for international comparisons. All frequency studies used cross-sectional study designs, some with repeated measurement over time and across countries . Twenty-seven percent of articles (N=16) included comparison of end-of-life practice frequencies before and after a change in public policies (e.g. before and after the adoption of the 2002 Euthanasia Act in Belgium)[34,56], and 28.3% (N=17) included comparisons across countries with different policies (e.g. comparison between different European countries)[35,57,58].

A number of differences in sampling strategy, data collection methods, and outcome measures were noted, all of which could influence comparisons of end-of-life practice frequencies. Data on end-of-life practices were mostly collected from physicians' self-administered questionnaires (N=44, 72.3%), individual interviews (N=13, 21.7%) , or physicians' self-reporting to external authorities (N=5, 8.3%) . Data were most often collected retrospectively, with professionals being asked to recall a death they had attended. ~~In~~ Only in rare cases were end-of-life practice data collected prospectively[59].

Response rates varied significantly across studies, ranging from 34% to 91%. Some countries with restrictive policies on lethal drug use had higher response rates than permissive countries, suggesting that variables other than the legal status of end-of-life practices influenced respondents [35,57]. Response rates varied according to country, the data collection method, and the strategy used to ensure respondents' anonymity.

Three main patterns of sampling methods and outcome measures were identified:

[1] These two categories are not mutually exclusive.

1. Half of the identified articles were based on stratified samples of death certificates. These studies reported the frequencies of medical practices in relation to the percentage of all annual deaths[13,35,40,49,56].
2. A second group of studies used similar outcome measures (% of all annual deaths), but a different sampling method based on professional registries[36,59-62].
3. A third group of studies used sampling methods and outcome measures based on the total number of physicians (eg. proportion of physicians who reported ever having intentionally used a lethal drug in their career)[33,58].

Some studies focused on the frequency of lethal drug use in specific populations (e.g. children)[28,57] and among specific professional groups (e.g. general practitioners)[61]. A few studies ~~aimed~~ sought to provide~~at providing~~ national frequency estimates, but specifically excluded end-of-life practices in children [13,35,49,50,52,56,63]. These exclusions could limit the comparability of frequency estimates across studies addressing different sub-populations.

We identified a number of empirical studies that used consistent methodologies to compare end-of-life practice frequencies in different countries, and to assess changes of practices over time. One example is the EURELD research consortium funded by the European Commission, which conducted two international studies of medical end-of-life practices in 2001 and 2002. The 2001 EURELD study used nationally representative sample of death certificates to compare the annual frequency of medical end-of-life practices in 6 European countries with different legislative frameworks (Netherlands, Belgium, Switzerland, Sweden, Italy, and Denmark)[35,50,52]. The 2002 EURELD study used a random sample of physicians to compare the lifetime prevalence of end-of-life practices in 7 countries in Europe and Australia[58]. National surveys conducted in the Netherlands (1990, 1995, 2001, 2005, 2010)[34,40,59,64,65], Belgium (1998, 2001, 2007)[13,49,56] and France (2009)[63] used similar sampling strategies and questionnaires than the 2001 EURELD study[2].

We found no systematic review of international evidence about the effects of public policies on end-of-life practices. A few published reviews have assessed changes in medical practices in selected countries (e.g. the Netherlands, Belgium, and the USA[6,34,66,67]) or on specific populations[68].

Discussion

To the best of our knowledge, this is the first rigorous scoping review to assess the potential for reliable ~~end-of-life practice~~ comparisons between end-of-life practices across different policy contexts. Our findings indicate that it is feasible to conduct studies on end-of-life practices in the context of legalization and prohibition, as demonstrated by the number of studies on the intentional use of lethal drugs by physicians in countries where this practice is authorized, and in those where it remains prohibited.

This review documents an important growth in international empirical evidence on end-of-life practices in the past 25 years. We identified a substantial number of studies that used consistent

[2] The 2001 Dutch and Belgium national surveys were conducted as part of the 2001 EURELD consortium study.

methods to compare end-of-life practice frequencies in different policy contexts, thus supporting the need and potential for a full systematic review on this topic. Another important contribution of this review is the development of a descriptive classification of end-of-life practices, which helps address differences in labels and definitions across studies, and facilitates the distinction of practices with different legal status. Such descriptive classification could be implemented in a full systematic review of international evidence.

This scoping review also brings greater clarity regarding the main methodological challenges for making reliable international comparisons. Heterogeneity in sampling strategy, data collection methods, and outcome measures limits the potential for valid comparisons between many studies. Dealing with low response rates is another challenge, particularly when non-response differentially affects a specific policy context. Most studies estimate the frequency of end-of-life practices based only on physicians' reported intentions, without details of which behaviors were actually performed and what their lethal potential is. Finally, the fact that available studies are observational in nature, with a limited number of measures before and after policy reform, is likely to limit, but not entirely prevent, the ability to attribute changes in end-of-life practices to public policies or to other contextual factors (e.g. health system characteristics, cultural attitudes, and professional norms). Thus, rigorous quality assessment of included studies is essential in any future systematic review of international evidence.

Policy implications

The main implication from this scoping review is that policymakers should be careful in drawing straightforward conclusions about the effects of different end-of-life policies. While empirical studies are frequently quoted in public and policy debates, acknowledgement of the heterogeneity of study methods, risks of biased frequency estimates, and relevance to the particular context is rarely discussed. Failure to recognize these limitations could lead to inappropriate conclusions by policymakers and the public. Policymakers should prioritize robust systematic reviews of empirical evidence rather than selected analysis of single studies to assess what is known and unknown of policy effects. To reduce as much as possible the above problems of misinterpretation of findings and to contextualize appropriately the available international evidence, greater collaboration between research teams, decision-makers and policy experts would be highly recommended..

Study strengths and limitations and directions for future research

A strength of this scoping review is that it reveals the range of empirical evidence available from different policy contexts. Testing of our search strategy on a large set of studies initially identified as meeting the study inclusion criteria showed that it was highly sensitive to identifying empirical studies on the intentional use of lethal drugs by physicians. The comprehensiveness of our review may however have been hampered by its focus on medical databases and the screening of frequency studies based on published abstracts alone. Also, scoping reviews focus on breath of coverage, rather than depth of analysis[16], and so we neither conducted a systematic quality assessment of included studies, nor did we synthesize study results. This review nonetheless represents a valuable preliminary step toward the completion of a full systematic review of international comparative evidence, by: 1) documenting the feasibility of comparing similar end-of-life practices in different legal contexts; 2) identifying a set of international studies comparing end-of-life practices using consistent research methods; 3) developing a descriptive classification of end-of-life practices to address international variations

in definitions and labels; 4) highlighting the main methodological challenges that should be taken into account in quality assessment of comparative studies.

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Conclusion

A growing number of empirical studies have assessed medical end-of-life practices in different policy contexts (prohibition and legalization), using consistent methods, thus offering some potential for reliable international comparisons. The use of a descriptive classification of end-of-life practices is helpful to distinguish practices with different legal status, and to deal with international variations in definitions and labeling. A better understanding of the strengths and limitations in end-of-life practice studies is key for providing policy guidance that is both context-sensitive and informed by an international set of evidence. A systematic review of international evidence is needed to assess the impact of end-of-life policies on medical practice, and thereby contribute meaningfully to policymaking.

Authors' contribution

AB assumed primary responsibility for the study design, supervised data collection and analysis, and drafted the manuscript. IM, PL, RP, NM, EvL, MCP, and GG contributed to study design. AB, IM, and PL led the integrated knowledge translation process with advisory committee members. GG led data collection and analysis. All authors contributed to the interpretation of findings, revised the manuscript critically for important intellectual content, and approved the submitted version of the article. AB is the guarantor.

Competing interests

All authors declare no support or relationships with any organizations that might have an interest in the submitted work, and no other relationships or activities that could appear to have influenced the submitted work.

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Sylvie Bellot, Virginie Ferrera, and Jenissa Gagné contributed to study screening and data extraction. Stéphane Ratté developed the bibliographic search strategy. Blaise Fotso contributed to the analysis of international end-of-life policies. Suzanne Philips-Nootens provided advice on end-of-life policies and legislation. Julie Caron-Malenfant (Institut du Nouveau Monde) provided advice on our integrated knowledge translation strategy. Amel Zertal helped coordinate the project.

Participants in the Advisory Committee meetings included Jeff Blackmer (Canadian Medical Association); Marie-Dominique Beaulieu and Bill Sullivan (College of Family Physicians of Canada); Pierre Deschamps, Bernard Grenier, Ann Soden, and Robert Delorme (Canadian Bar Association); Jean Rodrigue, Jeanine Auger, and Louis Dufresne (Ministère de la santé et des services sociaux du Québec); Yves Robert and Michelle Marchand (Collège des médecins du Québec); Jean-Pierre Ménard and Marc Sauvé (Barreau du Québec); Justine Farley and Danielle Drouin (Réseau des soins palliatifs du Québec); Ghislaine de Langavant (Commissaire à la santé et au bien-être du Québec). The authors remain sole responsible for research conclusions, which do not necessarily reflect the position of the individuals and organizations represented on the Advisory Committee.

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Figure 1: Flow chart of included studies

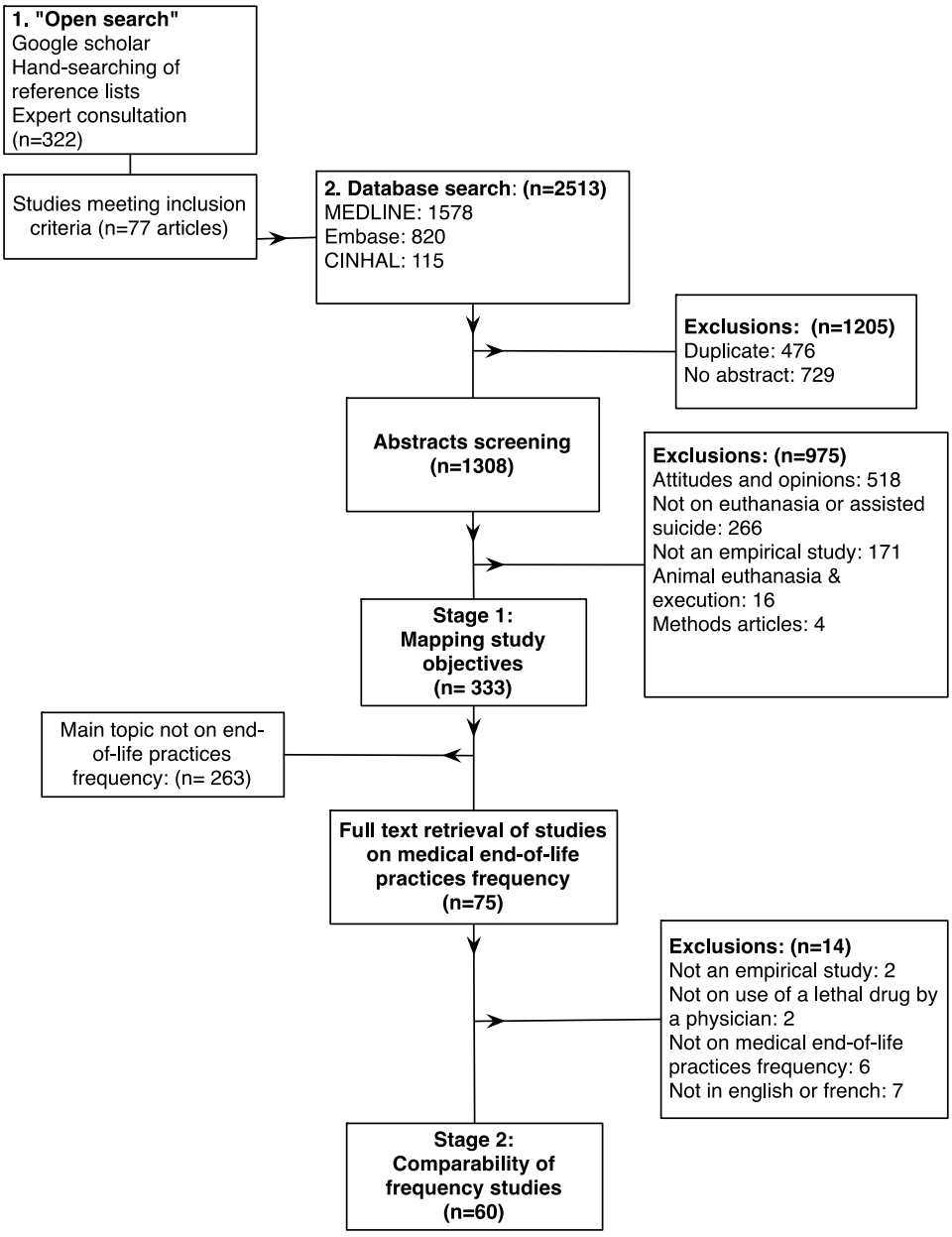

Table 1: Relationship between descriptive classification and legal status of end-of-life practices

Descriptive classification of end-of-life practices		Legal status of practices in selected jurisdictions			
		Canada, United Kingdom, France, New Zealand	Oregon, Washington, Vermont, Montana, Switzerland	Belgium, Luxemburg	Netherlands
1. Witholding/withdrawal of life-sustaining treatment					
2. Use of drugs justified by symptoms management or treatment of a medical condition					
3. Intentional use of lethal drugs not justified by symptom management or treatment of a medical condition	Self-administered by the patient, upon voluntary request				
	Administered by professional with voluntary patient request or prior advanced directive of a previously competent patient				
	Administered by professional to an incompetent patient with substituted request of a proxy decision-maker				

Table 1 legend: Yellow = authorized practices under restricted conditions; Red = prohibited practices.

Table 2: Characteristics of all included studies on lethal drug use by physicians (n=333 articles)

Year of publication	N	%
<1990	1	0%
1990-1994	19	0,06%
1995-1999	62	0,18%
2000-2004	82	0,24%
2005-2009	107	0,32%
2010-2012	66	0,20%
Country		
Netherlands	158	(47,4%)
Belgium	65	(19,5%)
United States (other than Oregon)	40	(12,0%)
Oregon	25	(7,5%)
Scandinavia (Norway, Danemark, Sweden)	22	(6,6%)
UK	17	(5,1%)
Switzerland	16	(4,8%)
Australia	15	(4,5%)
France	5	(1,5%)
Italy	5	(1,5%)
Argentina	3	(0,9%)
Germany	2	(0,6%)
Japan	2	(0,6%)
Spain	1	(0,3%)
New Zealand	1	(0,3%)
Austria	1	(0,3%)
Bosnia	1	(0,3%)
Luxembourg	1	(0,3%)
Study design		
Quantitative	248	(74,5%)
Qualitative	77	(23,1%)
Systematic reviews	8	(2,4%)

Table 3: Main objectives of all included studies on lethal drug use by physicians (n=333 articles)

Themes	N=number of articles	(%)=percentage of articles	Article focus/Main objective
Determinants of the requests and practices of the use of a lethal drug	64	(19,2%)	The determinants of the requests and practices of euthanasia/assisted suicide.
Medical end-of-life practices frequency*	60	(18,0%)	Data on the frequency of medical end-of-life practices.
Medical end-of-life practices regulation and control mechanisms	48	(14,4%)	The consistency of medical end-of-life practices with the existent standards and control mechanisms.
Specific populations	29	(8,7%)	The medical end-of-life practices among specific populations (elderly, new born, diagnostic, etc.)
Nurse's role	25	(7,5%)	The nurse's attitudes, practices and role in the use of lethal drugs and their involvement in the decision process and the care for patients that request and/or receive euthanasia.
Assessment of use of lethal drug requests	15	(4,5%)	Present data on health professional's assessment of the use of a lethal drug requests.
Impacts on health professionals	13	(3,9%)	The impacts (legal, emotional) of the requests and practices the use of a lethal drug on health professionals.

Communication and consultations in the decision process of euthanasia	12	(3,6%)	The communications between the people involved in the end-of-life decision process (patient, relatives, health professionals) including the consultation of outside expertise (consultants, experts).
Impacts on patients and publics	9	(2,7%)	Data on the impact of asking or being administered a lethal drug on the experience of death (*death experience quality*). Some articles in that thematic focus on the possible drifts and abuses or positive impacts on the public of legalizing euthanasia and assisted suicide.
Impacts on relatives	8	(2,4%)	Data on the impact of the use of lethal drugs on relative's mental health and mourning process.
Naming and labeling	7	(2,1%)	How medical end-of-life practices are named and labeled within various populations and settings.
Medical complications	6	(1,8%)	Medical complications reported by health professionals with preparation and administration of a lethal drug.

Psychiatric consultations and euthanasia	4	(1,2%)	The value of a psychiatric consultation and of the involvement of a psychiatric expertise in the assessment of requests of the use of lethal drugs.
Pharmacist's practices	2	(0,6%)	Data on the attitudes and practices of pharmacists regarding end-of-life medical practices.

Note: *see Table 4 for detailed statistics on studies of medical end-of-life practice frequencies.

Table 4: Comparability of studies on the frequency of lethal drugs use by physicians (n=60 articles)

Sampling method	N (%)
Sampling of all deaths	30 (50.0%)
Sampling of professionals	30 (50.0%)
Data collection method	
Postal self-administered questionnaires	44 (73.3%)
Interviews	13 (21.7%)
Examination of medical records of reported cases	5(8.3%)
Medical practice under study	
Intentional use of lethal drugs by physicians	60 (100%)
At the patient's request administered by the patient	47 (78.3%)
At the patient's request administered by a health professional	49 (81.7%)
Without the patient's request	35 (58.3%)
Use drugs justified by symptom control	24 (40.0%)
Withholding or withdrawal of medical treatment that has the potential to prolong life	29 (48.3%)
Information on medical end-of-life practices	
Definition within article	41 (68.3%)
Questions within article	46 (76.7%)
Data on drug used	20 (33.3%)
Data on dosage	6 (10.0%)
Lethal potential as perceived by the clinician	19 (31.7%)
Lethal potential as perceived by experts	5 (8.3%)
Legislative context	
Permissive policies	37 (61.7%)
Restrictive policies	26 (43.3%)
Comparaisons of end-of-life practices frequencies	
Before and after a change in public policy	16 (26.7%)
Between jurisdictions with different public policies	17 (28.3%)

Appendix 1: Search strategy

	Concepts	MEDLINE	Embase	CINAHL
#1	Intentional use of lethal drugs by physicians	Euthanasia[MAJR:NOEXP] OR Euthanasia, active[MAJR:NOEXP] OR Euthanasia, Active, Voluntary[MAJR] OR Suicide, assisted[MAJR] OR Euthanasia*[TI] OR Assisted suicide[TI] OR Assisted suicides[TI] OR Assisted death[TI] OR Assisted deaths[TI] OR Assisted dying[TI] OR "Aid in dying" [TI] OR "End of life decision"[TI] OR "End of life decisions"[TI] OR "Termination of life"[TI] OR ((Medical behaviors[TI] or Medical behavior[TI] or Medical behaviour[TI] or Medical behaviours[TI]) AND (Shorten life[TI] or Shortens life[TI]))	*Euthanasia/ or *Active euthanasia/ or *Voluntary euthanasia/ OR *Assisted suicide/ OR (Euthanasia* OR Assisted suicide OR Assisted suicides OR Assisted death OR Assisted deaths OR Assisted dying OR "End of life decision" OR "Aid in dying" OR "End of life decisions" OR "Termination of life" OR ((Medical behaviors or Medical behavior or Medical behaviour or Medical behaviours) AND (Shorten$ life or Shortens life))).ti	MM "Euthanasia" OR TI (Euthanasia* OR Assisted suicide OR Assisted suicides OR Assisted death OR Assisted deaths OR Assisted dying OR "End of life decision" OR "End of life decisions" OR "Termination of life" OR ((Medical behaviors or Medical behavior or Medical behaviour or Medical behaviours) AND (Shorten? life or Shortens life)))

#2	Empirical studies	"Data Collection"[MH:NOEXP] OR "Cross-sectional studies"[MH] OR "Cohort studies"[MH] OR Questionnaires[MH] OR "Empirical Research"[MH] OR "Qualitative research"[MH] OR "Interviews as topic"[MH] OR Clinical Trial[PT] OR Comparative study[PT] OR Practice Guideline[PT] OR "Statistics and numerical data"[SH] OR (Data[TIAB] AND (Collected[TIAB] OR Colllection[TIAB] OR Collecting[TIAB])) OR Cross-sectional study[TIAB] OR Cohort[TIAB] OR Empirical Research[TIAB] OR Empirical Study[TIAB] OR Quantitative Research[TIAB] OR Quantitative Study[TIAB] OR Qualitative research[TIAB] OR Qualitative study[TIAB] OR Interview*[TIAB] OR Questionnaire*[TIAB] OR Survey[TIAB] OR Survey*[TIAB] OR Systematic review[TIAB] OR Clinical Trial[TIAB] OR Comparative study[TIAB] OR Practice guideline[TIAB]	Data collection method/ OR Cross-sectional study/ OR Cohort analysis/ OR Prospective study/ OR Retrospective study/ OR Exp Questionnaire/ OR Empirical Research/ OR Qualitative research/ OR Exp Interview/ OR Systematic review/ OR Exp Clinical Trial/ OR Comparative study/ OR Practice Guideline/ OR ((Data AND (Collected OR Colllection OR Collecting)) OR Cross-sectional study OR Cohort OR Empirical Research OR Empirical Study OR Quantitative Research OR Quantitative Study OR Qualitative research OR Qualitative study OR Interview* OR Questionnaire* OR Survey* OR Systematic review OR Clinical Trial OR Comparative study OR Practice guideline).ti,ab	MH "Data Collection" OR MH "Data Collection Methods+" OR MH "Cross Sectional Studies" OR MH "Prospective studies+" OR MH "Retrospective design" OR MH "Questionnaires+" OR MH "Empirical Research" OR MH "Qualitative Studies+" OR MH "Experimental studies+" OR MH "Systematic review" OR MH "Comparative studies" OR MH "Practice guidelines" OR TI ((Data AND (Collected OR Colllection OR Collecting)) OR Cross-sectional study OR Cohort OR Empirical Research OR Empirical Study OR Quantitative Research OR Quantitative Study OR Qualitative research OR Qualitative study OR Interview* OR Questionnaire* OR Survey* OR Systematic review OR Clinical Trial OR Comparative study OR Practice guideline) OR AB ((Data AND (Collected OR Colllection OR Collecting)) OR Cross-sectional study OR Cohort OR Empirical Research OR Empirical Study OR Quantitative Research OR Quantitative Study OR Qualitative research OR Qualitative study OR Interview* OR Questionnaire* OR Survey* OR Systematic review OR Clinical Trial OR Comparative study OR Practice guideline)
#3	Has abstract	Hasabstract	Limité à Embase et Abstract	Exclude Medline et Abstract

#4	Humans	Animals[MH] NOT Humans[MH]	(Animals/ OR Nonhuman/) NOT Human/	MH "Animals+" NOT MH "Humans"
#	Combine	(#1 AND #2 AND #3) NOT #4	(#1 AND #2 AND #3) NOT #4	(#1 AND #2 AND #3) NOT #4