

# BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [editorial.bmjopen@bmj.com](mailto:editorial.bmjopen@bmj.com)

# BMJ Open

## The provision of medical assistance in dying: protocol for a scoping review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-017888
Article Type:	Protocol
Date Submitted by the Author:	23-May-2017
Complete List of Authors:	Oczkowski, Simon; McMaster University, Medicine (Critical Care); Hamilton Health Sciences, Critical Care Ball, Ian; London Health Sciences Centre, Medicine Saleh, Carol; McMaster University, Medicine Kalles, Gaelen; Hamilton Health Sciences, Critical Care Chkaroubo, Anatoli; Hamilton Health Sciences, Pharmacy Kekewich, Mike; Ottawa Hospital, Clinical and Organizational Ethics Miller, Paul; Hamilton Health Sciences, Emergency Medicine; McMaster University, Medicine (Emergency Medicine) Dees, Marianne; Radboudumc, Radboud Institute for Health Sciences Frolic, Andrea; Hamilton Health Sciences, Clinical and Organizational Ethics
<b>Primary Subject Heading</b>:	Palliative care
Secondary Subject Heading:	Anaesthesia, Ethics, Intensive care
Keywords:	Adult palliative care < PALLIATIVE CARE, MEDICAL ETHICS, ANAESTHETICS

SCHOLARONE™  
Manuscripts

only

**Title:** The provision of medical assistance in dying: protocol for a scoping review

**Author Names and Affiliations:**

Simon JW Oczkowski MD MHSc (1,2)

Ian Ball MD MSc (3)

Carol Saleh MD (4)

Gaelen Kalles RN (2)

Anatoli Chkaroubo (2)

Mike Kekewich MA (5)

Paul Miller MD (2,6)

Marianne Dees MD PhD (7)

Andrea Frolic PhD (2)

1. Division of Critical Care, Department of Medicine, McMaster University, Hamilton Canada
2. Hamilton Health Sciences, Hamilton Canada
3. Division of Critical Care Medicine, Department of Epidemiology and Biostatistics, Western University
4. Department of Medicine, McMaster University, Hamilton Canada
5. Department of Clinical and Organizational Ethics, The Ottawa Hospital, Ottawa Canada
6. Division of Emergency Medicine, Department of Medicine, McMaster University Hamilton Canada
7. IQ Healthcare, Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands

**Corresponding Author:**

Simon Oczkowski MD MHSc

[oczkowski@mcmaster.ca](mailto:oczkowski@mcmaster.ca)

Juravinski Hospital, Room A3-20

711 Concession St.

Hamilton ON

L8V 1C3

**Word Count:** 1623

## ABSTRACT

### Introduction

Medical assistance in dying (MAID), a term encompassing both euthanasia and assisted suicide, was decriminalized in Canada in 2015. Although Bill C-14 legislated eligibility criteria under which patients could receive MAID, it did not provide guidance regarding the technical aspects of providing an assisted death. Therefore, we propose a scoping review to map the characteristics of the existing medical literature describing the medications, settings, participants, and outcomes of MAID, in order to identify knowledge gaps and areas for future research.

### Methods and analysis

We will search electronic databases (MEDLINE, EMBASE, CINAHL, CENTRAL, PsycINFO), clinical trial databases, conference abstracts, and professional guidelines and recommendations from jurisdictions where MAID is legal. Eligible report types will include technical summaries, institutional policies, practice surveys, practice guidelines, and clinical studies. We will include all descriptions of MAID provision (either euthanasia or assisted suicide) in adults who have provided informed consent for MAID, for any reason, including reports where patients have provided consent to MAID in advance of the development of incapacity (*eg.* dementia). We will exclude reports in which patients receive involuntary euthanasia (*eg.* capital punishment). Two independent investigators will screen and select retrieved reports using pilot-tested screening and eligibility forms, and collect data using standardized data collection forms. We will summarize extracted data in tabular format with accompanying descriptive statistics and use narrative format to describe their relevance to the provision of MAID in Canada, identify knowledge gaps, and suggest topics for future research.

### Ethics and dissemination

This scoping review will map the range and scope of the existing literature on the provision of MAID in jurisdictions where the practice has been decriminalized. The review will be disseminated through conference presentations and publication in a peer-reviewed journal. These results will be useful to clinicians, policy makers, and researchers involved with MAID.

## INTRODCUTION

### Background

In its 2015 ruling *Carter v Canada*, the Supreme Court of Canada (SCC) struck down the criminal prohibition on assisting individuals in suicide, if physicians deemed such individuals to be competent adults with a “grievous and irremediable medical condition” causing “enduring suffering intolerable to the individual.”[1] The SCC suspended the ruling for one year to provide the Canadian federal government with time to develop a legislative framework for medical assistance in dying (MAID).[2] In June 2016, the federal government passed Bill C-14, which decriminalized assisted dying for capable patients with intolerable suffering for whom death was “reasonably foreseeable.”[3]

### Study rationale

Although Bill C-14 legislated eligibility criteria under which patients could receive MAID, the law did not provide clinicians or organizations with guidance regarding the technical aspects of providing MAID, including fundamental issues as whether it should be in the form of assisted suicide (in which a person self-administers a lethal medication prescribed and provided by a health care professional) or euthanasia (in which a person receives a lethal dose of medication at the hands of a health care professional). As a result, Canadian clinicians and organizations have struggled with many practical questions about providing MAID, including:

1. Should MAID be provided in the form of assisted suicide, euthanasia, or a combination of the two?
2. Which pharmaceuticals, doses and routes of administration should be used for MAID?
3. Should MAID provision take place in the community, institutional settings, or in dedicated, expert centres?
4. What is the appropriate role, scope of practice, and training of MAID providers?
5. How should patients’ families be involved in the provision of MAID?
6. How can organ donation be incorporated into the provision of MAID?

Given concerns about variation in consistency and quality of MAID, including the possibility of technical problems with medication administration, and the potentially high impact of the practice upon patients, families and health care providers, there is an urgent need to develop an evidence base to guide the provision of MAID.[5,6] While several other jurisdictions permit MAID in the form of assisted suicide (Switzerland, and the American states of Oregon, Montana, Washington, California, Colorado, Vermont, Washington DC), euthanasia (Columbia and

1  
2  
3 Belgium), or both (The Netherlands and Luxembourg), there is little readily-available evidence to  
4 assist Canadian clinicians and organizations in addressing these fundamental questions about  
5 providing MAID.[4,5]  
6  
7

8 Therefore, we propose a scoping review on the provision of MAID from all jurisdictions  
9 where assisted dying is legal, in order to determine the range, scope, and content of the existing  
10 medical literature on the provision of MAID in consenting adults, and to identify evidence gaps  
11 to guide future research in MAID care.  
12  
13

### 14 15 16 **Study Objectives**

- 17 1) To describe the existing medical literature on the provision of MAID
- 18 2) To summarize the existing medical literature and provide an overview of the technical  
19 aspects of MAID provision (including pharmaceuticals and procedures; location of provision;  
20 the role, scope of practice, and training of health care professionals; role of patients'  
21 families; rates of adverse events; and integration of MAID organ donation)  
22  
23 3) To identify evidence gaps to guide future research in MAID  
24  
25  
26  
27  
28

### 29 30 **METHODS AND ANALYSIS**

31 The methods of in this scoping review protocol are based upon those described in the  
32 Joanna Briggs Institute Reviewer's Manual.[7]  
33  
34  
35

### 36 37 **Inclusion and exclusion criteria**

38 As opposed to a systematic review, the selection of studies and reports in a scoping  
39 review is an iterative process, and inclusion and exclusion criteria may undergo revision as the  
40 review progresses, taking into account findings which emerge during the course of the  
41 review.[7-9] In this protocol, we outline our initial inclusion and exclusion criteria (Table 1), while  
42 any changes made during the course of the review will be described in the final review  
43 manuscript.  
44  
45  
46  
47

### 48 49 **Types of participants**

50 We will include reports which include adult (age>18) patients who have provided  
51 informed consent for MAID in the form of either assisted suicide or euthanasia, for any reason,  
52 or are intended for use with such patients. We will include studies where patients have provided  
53 informed consent to MAID in advance of the development of incapacity (eg. advanced directives  
54  
55  
56  
57  
58  
59  
60

for MAID), but exclude reports in which patients receive euthanasia without having provided informed consent (eg. execution).

#### Types of interventions

We will include reports which describe the provision of MAID by either assisted suicide or euthanasia, using any method, in any location. We will exclude reports where patients receive assisted suicide or euthanasia without the involvement of a health care professional such as a physician, nurse, or pharmacist; reports which solely describe the assessment of patient eligibility for MAID; and descriptions of public or healthcare provider opinions about about acceptability or ethics MAID. We will also exclude reports describing other end-of-life practices, including withholding or withdrawing of life-sustaining treatment; palliative sedation, or unintentional hastening of death via medications for symptom management (eg. the doctrine of double effect), unless such reports also include separate descriptions of MAID.

#### Types of sources

We will include technical reports, institutional policies, practice surveys, clinical practice guidelines, and clinical studies (case report, observational studies or clinical trials). Opinion pieces/letters will be excluded. We will impose no restrictions based upon methodological quality, study location, language, or publication date.

*Table 1: Inclusion & Exclusion Criteria*

	Inclusion Criteria	Exclusion Criteria
<b>Types of sources</b>	Technical report	Opinion piece/letter
	Institutional policy	
	Practice survey	
	Clinical practice guideline/recommendation	
	Case report	
	Observational study	
	Clinical trial	
	Other (describe)	

<b>Types of patients</b>	Adults (age >18 years)	Patients receiving involuntary euthanasia (capital punishment)
	Provided informed consent for MAID (assisted suicide or euthanasia), for any reason	
<b>Types of interventions</b>	Provision of assisted suicide or euthanasia with involvement of a health care professional (physician, nurse, pharmacist, etc.)	Assisted suicide or euthanasia without involvement of a health professional
		Description of assessment/ eligibility for MAID alone
		Description of ethics or acceptability of MAID
		Non-MAID end-of-life practices, including withdrawing/withholding treatments; palliative sedation; or palliative care

### Search strategy

We will conduct systematic searches of multiple databases, including MEDLINE, EMBASE, CINAHL, CENTRAL, and PsycINFO from database inception to the current date for the the concept of MAID (“[medical] aid [assistance] in dying,” “euthanasia,” “assisted suicide,” “[physician] assisted dying,” “[physician] assisted death,” “termination of life,” “death with dignity,” “compassionate dying,” “end of life choice”) and the concept of medication administration (“practice patterns,” “drug administration,” “medication management,” “drug utilization,” “drug therapy”). The electronic search will be supplemented by extensive grey literature searches, including clinical trial databases, conference abstracts from palliative care conferences (Canadian Hospice Palliative Care Conference, International Congress on Palliative Care), technical reports of MAID protocols, and institutional policies for MAID. In jurisdictions where MAID is legal, we will contact professional groups (eg. medical associations), as well as government agencies which monitor and regulate health care (eg. ministries of health) in order to obtain protocols and reports describing the provision of MAID.

### Selection Process

Report eligibility will be determined in two stages: first by screening of titles and abstracts, and secondly by full-text screening. At each stage, two investigators (CS, SO) will pilot-test the screening and eligibility forms on the first 10 reports in order to ensure consistent



1  
2  
3 application of inclusion and exclusion criteria. Following pilot-testing and completion of any  
4 necessary modifications to the screening and eligibility forms, two investigators will  
5 independently review each report for inclusion eligibility in the review. In the event of  
6 disagreement over report eligibility which cannot be resolved by discussion between the two  
7 investigators, a third investigator will make the final determination of eligibility. To provide a  
8 measure of the consistency of application of the inclusion and exclusion criteria at each stage, a  
9 weighted kappa statistic will be calculated as a measure of inter-rater reliability.[10]  
10  
11  
12  
13

14  
15 If during the course of the review, the investigators believe that a change to the inclusion  
16 or exclusion criteria is warranted, this will be discussed with the entire investigative team for  
17 review and approval, to ensure that the proposed changes are consistent with the study  
18 objectives. Any such changes will be clearly delineated in the final review manuscript in order to  
19 ensure methodological transparency.  
20  
21  
22  
23

#### 24 **Extraction of results**

25  
26 Data will be collected by two investigators (CS, SO) using structured data extraction  
27 forms. An initial set of data items is listed below (Table 2), however the final set of data items to  
28 be collected may change as review progresses, based upon the data contained in the included  
29 reports. The two investigators will independently chart data from the first five included reports to  
30 pilot-test the data extraction form and to ensure consistent data collection. As the review  
31 progresses, the investigators will discuss and collate results, and consider updating the data  
32 charting forms to ensure that the collected data is consistent with the review's objectives. The  
33 initial data collection forms will collect data related to three major concepts: report  
34 characteristics; methods of MAID provision (medications, locations, participants); and MAID  
35 outcomes.  
36  
37  
38  
39  
40  
41  
42  
43

44 *Table 2: Data collection items*

46 <b>Report Characteristics</b>	47 <b>Description</b>
48 Author(s)	49 Profession and or specialization
50 Year of publication	
51 Origin of report	52 jurisdiction of report (eg. Country, state)
53 Report type	54 technical report, practice survey, clinical practice guideline, 55 observational study, clinical trial, other (describe)
56 Report purpose	57 stated or inferred

Report audience	stated or inferred
Report citation	primary documents upon which the report is based (if relevant)
<b>MAID Provision: medications</b>	<b>Description</b>
Pharmaceutical used	Each pharmaceutical name, dose, route, frequency, speed of administration, stated or inferred purpose of each medication (eg. anxiolytic, sedation, pain control, anti-emetic, paralytic) and frequency of use (optional vs. obligatory); alternative medications in case of allergy
Other equipment used	If relevant
Safety checks and documentation	eg. use of a checklist; confirmation of consent; backup medications available etc.
Organ donation	Methods by which organ donation is incorporated in to MAID provision
<b>MAID Provision: location</b>	<b>Description</b>
Location of provision	home, hospital, hospice, other, nursing home's psychiatric institutions provider's profession or specialization, self administration or euthanasia?
<b>MAID Provision: participants</b>	<b>Description</b>
Role of health care provider(s)	Profession, training/expertise, role in assisted dying
Role of families	Training/preparation; follow-up care; bereavement care
Safety checks and documentation	eg. use of a checklist; confirmation of consent; backup medications available etc.
Aftercare	Health care providers/families/ others
<b>Outcomes</b>	<b>Description</b>
Complications- technical	eg. IV malfunction, need to use a second kit; vomiting; allergic reaction
Complications- patient/family distress	eg. patient pain; family agitation/anger during provision
Complications- provider distress	eg. anxiety during provision
Scores or measurements to assess quality of care or quality of dying	eg. Quality of Dying and Death score, reporting checklist

### Presentation of results

We will organize the collected data according to the three major concepts listed above (report characteristics; MAID provision; and MAID outcomes). We will summarize the report

1  
2  
3 characteristics, including date of publication, publication type, and geographic origin of  
4 publication in a table with accompanying univariate descriptive statistics (eg. frequency,  
5 proportion) in order to provide an overview of the characteristics of the existing medical  
6 literature on the provision of MAID.  
7  
8

9  
10 We will summarize data about the provision of MAID and about MAID outcomes in  
11 tables categorized as follows: pharmaceuticals and equipment; location of provision; personnel;  
12 documentation; and aftercare, with accompanying descriptive statistics of frequency or  
13 proportion for categorical data, and mean and standard deviation or median and interquartile  
14 range for continuous data. The tables will summarize the collected data, for assisted suicide and  
15 euthanasia separately, where appropriate (eg. pharmaceuticals, personnel). We will summarize  
16 the tabulated data and provide a description of their relevance to the provision of MAID in  
17 Canada, identify knowledge gaps, and formulate topics for future research.  
18  
19  
20  
21  
22

## 23 24 **ETHICS AND DISSEMINATION**

25 This scoping review will provide a comprehensive description of the range and scope of  
26 the existing literature on the provision of MAID, and a summary of the technical aspects of  
27 providing MAID. We will describe the relevance of the existing literature to the provision of MAID  
28 in Canada, and identify knowledge gaps and topics for future research. The results of the  
29 review will be submitted for presentation as a conference abstract, and publication in a peer-  
30 reviewed journal.  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**REFERENCES**

1. Carter v. Canada (Attorney General) [2015] SCC 5.
2. Attaran A. Unanimity on Death with Dignity — Legalizing Physician-Assisted Dying in Canada. *N Engl J Med* 2015;372:2080–2.
3. Bill C-14: An Act to amend the Criminal Code and to make related amendments to other Acts (medical assistance in dying). First Session of the Parliament of Canada (2016).
4. Veldink JH, Wokke JHJ, van der Wal G, et al. Euthanasia and Physician-Assisted Suicide among Patients with Amyotrophic Lateral Sclerosis in the Netherlands. *N Engl J Med* 2002;346:1638–44.
5. Hendin H. Physician-Assisted Suicide and Euthanasia in the Netherlands. *J Am Med Assoc* 1997;277:1720.
6. Groenewoud JH, van der Heide A, Onwuteaka-Philipsen BD, et al. Clinical Problems with the Performance of Euthanasia and Physician-Assisted Suicide in the Netherlands. *N Engl J Med* 2000;342:551–6.
7. Peters M, Godfrey C, Mclnerney P, et al. "The Joanna Briggs Institute Reviewers' Manual 2015: Methodology for JBI Scoping Reviews." 2015.
8. Arksey H, O'Malley L. "Scoping studies: towards a methodological framework." *Int J Soc Res Methodol* 2005;8(1):19-32.
9. Levac D, Colquhoun H, and O'Brien KK. "Scoping studies: advancing the methodology." *Implement Sci* 2010;5(1):69.
10. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. *Fam Med*. 2005;37(5):360-3.

**AUTHOR'S CONTRIBUTIONS**

SO conceived the idea for the project and developed the initial draft of the manuscript. All authors developed the review methodology and edited and revised the manuscript for essential content and formatting details, and approved the final version of the manuscript for submission. SO and CS will conduct the data collection, data extraction for the review. All authors will contribute to the analysis of the review data.

**ACKNOWLEDGEMENTS**

Dr. Simon Oczkowski is supported by an Internal Career Award from the Department of Medicine at McMaster University.

**COMPETING INTERESTS**

The authors have no competing interests to declare.

**FUNDING STATEMENT**

This review was supported by a grant from the Hamilton Academic Health Sciences Organization Innovation Fund.

# BMJ Open

## The provision of medical assistance in dying: protocol for a scoping review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2017-017888.R1
Article Type:	Protocol
Date Submitted by the Author:	19-Jun-2017
Complete List of Authors:	Oczkowski, Simon; McMaster University, Medicine (Critical Care); Hamilton Health Sciences, Critical Care Ball, Ian; London Health Sciences Centre, Medicine Saleh, Carol; McMaster University, Medicine Kalles, Gaelen; Hamilton Health Sciences, Critical Care Chkaroubo, Anatoli; Hamilton Health Sciences, Pharmacy Kekewich, Mike; Ottawa Hospital, Clinical and Organizational Ethics Miller, Paul; Hamilton Health Sciences, Emergency Medicine; McMaster University, Medicine (Emergency Medicine) Dees, Marianne; Radboudumc, Radboud Institute for Health Sciences Frolic, Andrea; Hamilton Health Sciences, Clinical and Organizational Ethics
<b>Primary Subject Heading</b>:	Palliative care
Secondary Subject Heading:	Anaesthesia, Ethics, Intensive care
Keywords:	Adult palliative care < PALLIATIVE CARE, MEDICAL ETHICS, ANAESTHETICS

SCHOLARONE™  
Manuscripts

only

**Title:** The provision of medical assistance in dying: protocol for a scoping review

**Author Names and Affiliations:**

Simon JW Oczkowski MD MHSc (1,2)

Ian Ball MD MSc (3)

Carol Saleh MD (4)

Gaelen Kalles RN (2)

Anatoli Chkaroubo (2)

Mike Kekewich MA (5)

Paul Miller MD (2,6)

Marianne Dees MD PhD (7)

Andrea Frolic PhD (2)

1. Division of Critical Care, Department of Medicine, McMaster University, Hamilton Canada
2. Hamilton Health Sciences, Hamilton Canada
3. Division of Critical Care Medicine, Department of Epidemiology and Biostatistics, Western University
4. Department of Medicine, McMaster University, Hamilton Canada
5. Department of Clinical and Organizational Ethics, The Ottawa Hospital, Ottawa Canada
6. Division of Emergency Medicine, Department of Medicine, McMaster University Hamilton Canada
7. IQ Healthcare, Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands

**Corresponding Author:**

Simon Oczkowski MD MHSc

[oczkowski@mcmaster.ca](mailto:oczkowski@mcmaster.ca)

Juravinski Hospital, Room A3-20

711 Concession St.

Hamilton ON

L8V 1C3

**Word Count:** 1841

## ABSTRACT

### Introduction

Medical assistance in dying (MAID), a term encompassing both euthanasia and assisted suicide, was decriminalized in Canada in 2015. Although Bill C-14 legislated eligibility criteria under which patients could receive MAID, it did not provide guidance regarding the technical aspects of providing an assisted death. Therefore, we propose a scoping review to map the characteristics of the existing medical literature describing the medications, settings, participants, and outcomes of MAID, in order to identify knowledge gaps and areas for future research.

### Methods and analysis

We will search electronic databases (MEDLINE, EMBASE, CINAHL, CENTRAL, PsycINFO), clinical trial registries, conference abstracts, and professional guidelines and recommendations from jurisdictions where MAID is legal, up to June 2017. Eligible report types will include technical summaries, institutional policies, practice surveys, practice guidelines, and clinical studies. We will include all descriptions of MAID provision (either euthanasia or assisted suicide) in adults who have provided informed consent for MAID, for any reason, including reports where patients have provided consent to MAID in advance of the development of incapacity (eg. dementia). We will exclude reports in which patients receive involuntary euthanasia (eg. capital punishment). Two independent investigators will screen and select retrieved reports using pilot-tested screening and eligibility forms, and collect data using standardized data collection forms. We will summarize extracted data in tabular format with accompanying descriptive statistics and use narrative format to describe their clinical relevance, identify knowledge gaps, and suggest topics for future research.

### Ethics and dissemination

This scoping review will map the range and scope of the existing literature on the provision of MAID in jurisdictions where the practice has been decriminalized. The review will be disseminated through conference presentations and publication in a peer-reviewed journal. These results will be useful to clinicians, policy makers, and researchers involved with MAID.



### Strengths and limitations of this study

- This will be the first scoping literature review on the provision of medical assistance in dying
- The search strategy includes a comprehensive and systematic search of five electronic databases, conference proceedings, clinical trial registries, and grey literature from jurisdictions where medical assistance in dying has been decriminalized
- Although the study will provide a descriptive overview of how medical assistance in dying may be provided, no formal assessment of the quality of evidence for any given approach will be conducted
- Though this review will not provide recommendations for how to provide medical assistance in dying, an overview of current practices and knowledge gaps may still inform clinicians, policy makers, and researchers working in this area

## INTRODUCTION

### Background

In its 2015 ruling *Carter v Canada*, the Supreme Court of Canada (SCC) struck down the criminal prohibition on assisting individuals in suicide, if physicians deemed such individuals to be competent adults with a “grievous and irremediable medical condition” causing “enduring suffering intolerable to the individual.”[1] The SCC suspended the ruling for one year to provide the Canadian federal government with time to develop a legislative framework for medical assistance in dying (MAID).[2] In June 2016, the federal government passed Bill C-14, which decriminalized assisted dying for capable patients with intolerable suffering for whom death was “reasonably foreseeable.”[3]

### Study rationale

Although Bill C-14 legislated eligibility criteria under which patients could receive MAID, the law did not provide clinicians or organizations with guidance regarding the technical aspects of providing MAID, including fundamental issues as whether it should be in the form of assisted suicide (in which a person self-administers a lethal medication prescribed and provided by a health care professional) or euthanasia (in which a person receives a lethal dose of medication at the hands of a health care professional). As a result, Canadian clinicians and organizations have struggled with many practical questions about providing MAID, including:

1. Should MAID be provided in the form of assisted suicide, euthanasia, or a combination of the two?
2. Which pharmaceuticals, doses, and routes of administration should be used for MAID?
3. Should MAID provision take place in the community, institutional settings, or in dedicated, expert centres?
4. What is the appropriate role, scope of practice, and training of MAID providers?
5. How should patients’ families be involved & supported in the provision of MAID?

Given concerns about variation in consistency and quality of MAID, including the possibility of technical problems with medication administration, and the potentially high impact of the practice upon patients, families and health care providers, there is an urgent need to develop an evidence base to guide the provision of MAID.[5,6] While several other jurisdictions permit MAID in the form of assisted suicide (Switzerland, and the American states of Oregon, Montana, Washington, California, Colorado, Vermont, Washington DC), euthanasia (Columbia), or both (Belgium, The Netherlands, and Luxembourg), there is little readily-available evidence to assist

1  
2  
3 Canadian clinicians and organizations in addressing these fundamental questions about  
4 providing MAID.[4,5]

5  
6 Therefore, we propose a scoping review on the provision of MAID from all jurisdictions  
7 where medically assisted dying is not illegal, in order to determine the range, scope, and  
8 content of the existing medical literature on the provision of MAID in consenting adults.  
9  
10

### 11 12 **Study Objectives**

- 13 1) To describe the existing medical literature on the provision of MAID
- 14 2) To summarize the existing medical literature and provide an overview of the technical  
15 aspects of MAID provision (including pharmaceuticals and procedures; location of provision;  
16 the role, scope of practice, and training of health care professionals; role of patients'  
17 families; rates of adverse events)
- 18 3) To identify evidence gaps to guide future research in MAID  
19  
20  
21  
22  
23  
24  
25

### 26 **METHODS AND ANALYSIS**

27 The methods of this scoping review protocol are based upon those described in the  
28 Joanna Briggs Institute Reviewer's Manual.[7]  
29  
30  
31

#### 32 **Inclusion and exclusion criteria**

33 As opposed to a systematic review, the selection of studies and reports in a scoping  
34 review is an iterative process, and inclusion and exclusion criteria may undergo revision as the  
35 review progresses, taking into account findings which emerge during the course of the  
36 review.[7-9] In this protocol, we outline our initial inclusion and exclusion criteria (Table 1), while  
37 any changes made during the course of the review will be described in the final review  
38 manuscript.  
39  
40  
41  
42  
43  
44

#### 45 **Types of participants**

46 We will include reports which include adult (age>18) patients who have provided  
47 informed consent for MAID in the form of either assisted suicide or euthanasia, for any reason,  
48 or are intended for use with such patients. We will include studies where patients have provided  
49 informed consent to MAID in advance of the development of incapacity (e.g. advanced  
50 directives for MAID), but exclude reports in which patients receive euthanasia without having  
51 provided informed consent (e.g. execution).  
52  
53  
54  
55  
56  
57  
58  
59  
60

### Types of interventions

We will include reports which describe the provision of MAID by either assisted suicide or euthanasia, using any method, in any location. We will exclude reports where patients receive assisted suicide or euthanasia without the involvement of a health care professional such as a physician, nurse, or pharmacist; reports which solely describe the assessment of patient eligibility for MAID; and descriptions of public or healthcare provider opinions about acceptability or ethics of MAID. We will also exclude reports describing other end-of-life practices, including withholding or withdrawing of life-sustaining treatment; palliative sedation, or unintentional hastening of death via medications for symptom management (e.g. the doctrine of double effect), unless such reports also include separate descriptions of MAID.

### Types of sources

We will include technical reports, institutional policies, practice surveys, clinical practice guidelines, and clinical studies (case reports, observational studies or clinical trials). Opinion pieces/letters will be excluded. We will impose no restrictions based upon methodological quality, study location, language, or publication date.

*Table 1: Inclusion & Exclusion Criteria*

	Inclusion Criteria	Exclusion Criteria
<b>Types of sources</b>	Technical report	Opinion piece/letter
	Institutional policy	
	Practice survey	
	Clinical practice guideline/recommendation	
	Case report	
	Observational study	
	Clinical trial	
	Other (describe)	
<b>Types of patients</b>	Adults (age >18 years)	Patients receiving involuntary euthanasia (capital punishment)
	Provided informed consent for MAID (assisted suicide or euthanasia), for any reason	

<b>Types of interventions</b>	Provision of assisted suicide or euthanasia with involvement of a health care professional (physician, nurse, pharmacist, etc.)	Assisted suicide or euthanasia without involvement of a health professional
		Description of assessment/ eligibility for MAID alone
		Description of ethics or acceptability of MAID
		Non-MAID end-of-life practices, including withdrawing/withholding treatments; palliative sedation; or palliative care

### Search strategy

We will conduct systematic searches of multiple databases, including MEDLINE, EMBASE, CINAHL, CENTRAL, and PsycINFO from database inception to June 2017 for the concept of MAID (“[medical] aid [assistance] in dying,” “euthanasia,” “assisted suicide,” “[physician] assisted dying,” “[physician] assisted death,” “end of life choice”) and the concept of medication administration (“practice patterns,” “drug administration,” “medication management,” “drug utilization,” “drug therapy”) (available as a supplementary file). The electronic search will be supplemented by extensive grey literature searches, including clinical trial databases, conference abstracts from palliative care conferences (Canadian Hospice Palliative Care Conference, International Congress on Palliative Care), technical reports of MAID protocols, and institutional policies for MAID. In jurisdictions where MAID is legal, we will contact professional groups (e.g. medical associations), as well as government agencies which monitor and regulate health care (e.g. ministries of health) in order to obtain protocols and reports describing the provision of MAID. The search will be complete by June 30, 2017.

### Selection process

Report eligibility will be determined in two stages: first by screening of titles and abstracts, and secondly by full-text screening. Two investigators (CS, SO) will pilot-test the screening and eligibility forms on the first 100 abstracts and the first 10 full-text reports in order to ensure consistent application of inclusion and exclusion criteria at each stage. Following pilot-testing and completion of any necessary modifications to the screening and eligibility forms, the same two investigators will independently review each report’s eligibility for inclusion in the review. In the event of disagreement over report eligibility which cannot be resolved by

discussion between the two investigators, a third investigator will make the final determination of eligibility. To provide a measure of the consistency of application of the inclusion and exclusion criteria at each stage, a weighted kappa statistic will be calculated as a measure of inter-rater reliability.[10]

If during the course of the review, the investigators believe that a change to the inclusion or exclusion criteria is warranted, this will be discussed with the entire investigative team for review and approval, to ensure that the proposed changes are consistent with the study objectives. Any such changes will be clearly delineated in the final review manuscript in order to ensure methodological transparency.

### Extraction of results

Data will be collected by two investigators (CS, SO) using structured data extraction forms. An initial set of data items is listed below (Table 2), however the final set of data items to be collected may change as review progresses, based upon the data contained in the included reports. The two investigators will independently chart data from the first five included reports to pilot-test the data extraction form, thereby ensuring consistent and comprehensive data collection. Following pilot testing and, if necessary, modification of the data extraction forms, the two investigators will continue with duplicate data extraction. As the review progresses, the investigators will compare and discuss the extracted data, and consider updating the data extraction forms to ensure that the collected data is consistent with the review's objectives. The initial data collection forms will collect data related to three major concepts: report characteristics; methods of MAID provision (medications, locations, participants); and MAID outcomes.

Table 2: Data collection items

Report Characteristics	Description
Author(s)	Profession and or specialization
Year of publication	
Origin of report	jurisdiction of report (e.g. Country, state)
Report type	technical report, practice survey, clinical practice guideline, observational study, clinical trial, other (describe)
Report purpose	stated or inferred
Report audience	stated or inferred

Report citation	primary documents upon which the report is based (if relevant)
<b>MAID Provision: medications</b>	<b>Description</b>
Pharmaceutical used	Each pharmaceutical name, dose, route, frequency, speed of administration, stated or inferred purpose of each medication (e.g. anxiolytic, sedation, pain control, anti-emetic, paralytic) and frequency of use (optional vs. obligatory); alternative medications in case of allergy
Other equipment used	If relevant
Safety checks and documentation	e.g. use of a checklist; confirmation of consent; backup medications available etc.
<b>MAID Provision: location</b>	<b>Description</b>
Location of provision	home, hospital, hospice, other, nursing home's psychiatric institutions provider's profession or specialization, self administration or euthanasia?
<b>MAID Provision: participants</b>	<b>Description</b>
Role of health care provider(s)	Profession, training/expertise, role in assisted dying
Role of families	Training/preparation; follow-up care; bereavement care
Safety checks and documentation	e.g. use of a checklist; confirmation of consent; backup medications available etc.
Aftercare	Health care providers/families/ others
<b>Outcomes</b>	<b>Description</b>
Complications- technical	e.g. IV malfunction, need to use a second kit; vomiting; allergic reaction
Complications- patient/family distress	e.g. patient pain; family agitation/anger during provision
Complications- provider distress	e.g. anxiety during provision
Scores or measurements to assess quality of care or quality of dying	e.g. Quality of Dying and Death score, reporting checklist

## Presentation of results

We will organize the collected data according to the three major concepts listed above (report characteristics; MAID provision; and MAID outcomes). We will summarize the report characteristics, including date of publication, publication type, and geographic origin of publication in a table with accompanying univariate descriptive statistics (e.g. frequency,

1  
2  
3 proportion) in order to provide an overview of the characteristics of the existing medical  
4 literature on the provision of MAID.  
5

6 We will summarize data about the provision of MAID and about MAID outcomes in  
7 tables categorized as follows: pharmaceuticals and equipment; location of provision; personnel;  
8 documentation; and aftercare, with accompanying descriptive statistics of frequency or  
9 proportion for categorical data, and mean and standard deviation or median and interquartile  
10 range for continuous data. The tables will summarize the collected data, for assisted suicide and  
11 euthanasia separately, where appropriate (e.g. pharmaceuticals, personnel). We will synthesize  
12 this information in narrative format, describing the type and range of the available evidence and  
13 its relevance to the five questions described in the study rationale, above. Though a formal  
14 appraisal of the quality (certainty) of the evidence is not routinely conducted in a scoping  
15 review,[7] we will comment upon the reliability and trustworthiness of the available evidence,  
16 based upon the methods of each report and the consistency, or lack of consistency, of results  
17 between reports. We will summarize the data's potential relevance to the provision of MAID in  
18 Canada, as compared to other clinical and legal contexts. In doing so, we will identify  
19 knowledge gaps and formulate topics for future research.  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29

### 30 **ETHICS AND DISSEMINATION**

31 This scoping review will provide a comprehensive description of the range and scope of  
32 the existing literature on the provision of MAID, and a summary of the technical aspects of  
33 providing MAID. We will describe the relevance of the existing literature to the provision of MAID  
34 in Canada, and identify knowledge gaps and topics for future research. The results of the  
35 review will be submitted for presentation as a conference abstract, and publication in a peer-  
36 reviewed journal.  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



**REFERENCES**

1. Carter v. Canada (Attorney General) [2015] SCC 5.
2. Attaran A. Unanimity on Death with Dignity — Legalizing Physician-Assisted Dying in Canada. *N Engl J Med* 2015;372:2080–2.
3. Bill C-14: An Act to amend the Criminal Code and to make related amendments to other Acts (medical assistance in dying). First Session of the Parliament of Canada (2016).
4. Veldink JH, Wokke JHJ, van der Wal G, et al. Euthanasia and Physician-Assisted Suicide among Patients with Amyotrophic Lateral Sclerosis in the Netherlands. *N Engl J Med* 2002;346:1638–44.
5. Hendin H. Physician-Assisted Suicide and Euthanasia in the Netherlands. *J Am Med Assoc* 1997;277:1720.
6. Groenewoud JH, van der Heide A, Onwuteaka-Philipsen BD, et al. Clinical Problems with the Performance of Euthanasia and Physician-Assisted Suicide in the Netherlands. *N Engl J Med* 2000;342:551–6.
7. Peters M, Godfrey C, Mclnerney P, et al. "The Joanna Briggs Institute Reviewers' Manual 2015: Methodology for JBI Scoping Reviews." 2015.
8. Arksey H, O'Malley L. "Scoping studies: towards a methodological framework." *Int J Soc Res Methodol* 2005;8(1):19-32.
9. Levac D, Colquhoun H, and O'Brien KK. "Scoping studies: advancing the methodology." *Implement Sci* 2010;5(1):69.
10. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. *Fam Med*. 2005;37(5):360-3.

## **AUTHOR'S CONTRIBUTIONS**

SO conceived the idea for the project and developed the initial draft of the manuscript. All authors developed the review methodology and edited and revised the manuscript for essential content and formatting details, and approved the final version of the manuscript for submission. SO and CS will conduct the searches, screening, data extraction, and data summaries for the review. All authors will contribute to the analysis of the review data.

## **ACKNOWLEDGEMENTS**

Dr. Simon Oczkowski is supported by an Internal Career Award from the Department of Medicine at McMaster University.

## **COMPETING INTERESTS**

The authors have no competing interests to declare.

## **FUNDING STATEMENT**

This review was supported by a grant from the Hamilton Academic Health Sciences Organization Innovation Fund.

### Supplementary File 1: MAID Scoping Review Search Strategies

*OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, OVID MEDLINE(R) Daily and OVID MEDLINE(R) 1946 to Present - June 16, 2017*

1. right to die.ti,ab,kf. or Right to Die/	5226
2. ((medical* aid* or medical* assist*) adj2 (dying or die or death*).ti,ab,kf.	50
3. ((physician* assist* or physician aid* or doctor* assist* or doctor aid*) adj2 (death* or dying or die)).ti,ab,kf.	442
4. end of life choice*.ti,ab,kf.	64
5. Euthanasia, Active, Voluntary/ or Euthanasia, Active/	3366
6. euthanasia.ti,ab,kf.	21294
7. Suicide, Assisted/	5337
8. assisted suicide*.ti,ab,kf.	2884
9. assisted death*.ti,ab,kf.	405
10. practice patterns, physicians/ or patient care guideline/ or guideline/ or (guideline* or guidance or consensus).ti,ab,kf.	516025
11. pharmacist/ or physician/ or nurse/	124347
12. patient care management/	2992
13. medication therapy management/	1299
14. (medication utilization or medication therap* or "medication use" or medication*).ti,ab,kf.	262031
15. drug delivery systems/	49065
16. drug administration routes/	5309
17. administration, oral/	131323
18. administration, intravenous/	5358
19. injections/	40348
20. (drug delivery or drug administration or bolus or inject*).ti,ab,kw.	788480
21. Analgesics, Opioid/	35560
22. opi*.ti,ab,kf.	186417
23. Neuromuscular Blocking Agents/	3299
24. (paraly* or neuromuscular block*).ti,ab,kf.	66603
25. "Hypnotics and Sedatives"/	27048

26. (hypno* or sedat* or an?sthe*).ti,ab,kf.	506435
27. Drug Prescriptions/	25165
28. (prescribe* or prescription*).ti,ab,kf.	156126
29. drug utilization/ or "drug utilization review"/	22289
30. (drug utili?ation or drug therap* or "drug use").ti,ab,kf.	89717
31. drug therapy/	29902
32. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	26210
33. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31	2433657
34. 32 and 33	6324
35. 34 not animals/	5325

#### EMBASE - 1974 to 2017 June 14

1. euthanasia/ or active euthanasia/ or voluntary euthanasia/	14939
2. assisted suicide/	4550
3. ((medical* aid* or medical* assist*) adj2 (dying or die or death*)).ti,ab,kf.	57
4. ((physician* assist* or physician aid* or doctor* assist* or doctor aid*) adj2 (death* or dying or die)).ti,ab,kf.	435
5. right to die/ or right to die.ti,ab,kw.	4339
6. end of life choice*.ti,ab,kw.	73
7. euthanasia.ti,ab,kw.	11853
8. (assisted suicide* or assisted death*).ti,ab,kw.	3348
9. clinical practice/ or medical practice/ or professional practice/ or practice guideline/	616940
10. (clinical practice or medical practice or professional practice or practice guideline or guideline* or guidance or consensus).ti,ab,kw.	835272
11. patient care/ or management/	292402
12. (patient care or patient management).ti,ab,kw.	91135
13. prescription/ or pharmacist/ or medication therapy management/ or drug therapy/	646407
14. (prescri* or pharmac* or medic* therap* or drug therapy).ti,ab,kw.	1238500

15. drug delivery system/ or drug administration/ or oral drug administration/ or intravenous drug administration/ or bolus injection/ or injection/	946330
16. (drug delivery or drug administration or bolus or inject*).ti,ab,kw.	998587
17. neuromuscular blocking agent/	7115
18. (paraly* or neuromuscular block*).ti,ab,kf.	71322
19. opiate/	65315
20. opioi*.ti,ab,kf.	92154
21. hypnotic agent/	10032
22. (hypno* or sedat* or an?ssthe*).ti,ab,kf.	384836
23. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	24284
24. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	4722340
25. 23 and 24	5844
26. 25 not animals/	5550

*PsychINFO - 1806 to June Week 2 2017*

1. *assisted suicide/ or euthanasia/	1975
2. (assisted suicide or assisted death).mp.	1468
3. *euthanasia/	1265
4. euthanasia.mp.	2176
5. ((medical* aid* or medical* assist*) adj2 (dying or die or death*)).ti,ab,kf.	16
6. ((physician* assist* or physician aid* or doctor* assist* or doctor aid*) adj2 (death* or dying or die)).ti,ab,kf.	176
7. end of life choice*.mp.	32
8. right to die.mp.	240
9. exp Clinical Practice/ or exp Health Care Services/ or exp Caring Behaviours/ or exp Treatment Guideline/	120988
10. (clinical practice* or health care or medical care or treatment* or clinical practice* or medical practice* guideline* or guidance or consensus).mp.	812357

11. drugs/ or drug dosages/ or "prescribing (drugs)"/ or self-medication/ or injections/ or drug administration methods/ or intravenous injections/ or drug self administration/ or Drug Therapy/	163484
12. (drug delivery or drug administration or bolus or injection or medication utilisation or medical utilization or medication therapy or medication or prescribe or prescription or drug utilisation or drug utilization or drug therapy).mp.	203881
13. exp Clinicians/ or exp Nurse/ or exp Physicians/ or exp Pharmacists/	49394
14. exp HYPNOTIC DRUGS/	5599
15. (hypno* or sedat*).mp.	30936
16. exp ANALGESIC DRUGS/	17811
17. opi*.mp.	77671
18. exp ANESTHETIC DRUGS/	19333
19. an?sthe*.mp.	13116
20. exp Muscle Relaxing Drugs/ or exp Cholinergic Receptors/ or exp Synapses/ or exp Neurotransmission/ or exp Paralysis/	36296
21. (paraly* or neuromuscular block*).mp.	6790
22. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	3043
23. 9 or 10 or 11 or 12 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21	1038761
24. 22 and 23	1603
25. 24 not animals/	1600

### Central- May 2017

1. right to die.mp. or Right to Die/	4
2. ((medical* aid* or medical* assist*) adj2 (dying or die or death*)).mp.	0
3. ((physician* assist* or physician aid* or doctor* assist* or doctor aid*) adj2 (death* or dying or die)).mp.	1
4. end of life choice*.mp.	1
5. Euthanasia, Active, Voluntary/ or Euthanasia, Active/	3
6. euthanasia.ti,ab,kf.	44
7. Suicide, Assisted/	0
8. assisted suicide*.ti,ab,kf.	3

9. assisted death*.ti,ab,kf.	0
10. practice patterns, physicians/ or patient care guideline/ or guideline/ or (guideline* or guidance or consensus).ti,ab,kf.	23569
11. pharmacist/ or physician/ or nurse/	3
12. patient care management/	104
13. medication therapy management/	58
14. (medication utilization or medication therap* or "medication use" or medication*).ti,ab,kf.	46253
15. drug delivery systems/	834
16. drug administration routes/	312
17. administration, oral/	20558
18. administration, intravenous/	490
19. injections/	2311
20. (drug delivery or drug administration or bolus or inject*).ti,ab,kw.	140195
21. Analgesics, Opioid/	5705
22. opi*.ti,ab,kf.	18444
23. Neuromuscular Blocking Agents/	250
24. (paraly* or neuromuscular block*).ti,ab,kf.	4273
25. "Hypnotics and Sedatives"/	3052
26. (hypno* or sedat* or an?sthe*).ti,ab,kf.	54931
27. Drug Prescriptions/	419
28. (prescribe* or prescription*).ti,ab,kf.	15186
29. drug utilization/ or "drug utilization review"/	443
30. (drug utilization or drug therap* or "drug use").ti,ab,kf.	283688
31. drug therapy/	300
32. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	49
33. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31	389871
34. 32 and 33	23
35. 34 not animals/	20

## CINAHL - 1981 to June 16, 2017

S1. (MH "Right to Die") OR "right to die"	1405
S2. (("medical* aid*" or "medical* assist*") N2 ("dying" or "die" or "death*"))	52
S3. "end of life choice*"	49
S4. (MH "Euthanasia+") OR "euthanasia"	5844
S5. (MH "Suicide, Assisted") OR "assisted suicide"	2785
S6. "assisted death*" or "assisted dying"	543
S7. (("physician* assist*" or "physician aid*" or "doctor* assist*" or "doctor aid*") N2 ("death*" or "dying" or "die"))	243
S8.(MH "Practice Patterns") OR (MH "Prescribing Patterns") OR (MH "Medical Practice")	12815
S9. (MH "Patient Care Plans") OR "patient care management"	3773
S10. (MH "Medication Management") OR "medication therapy"	350
S11. (MH "Drugs, Prescription") OR (MH "Prescriptions, Drug") OR "drug prescription"	16355
S12. (MH "Drug Utilization") OR "drug utilization"	4434
S13."prescribe*" or "prescription*"	46349
S14. (MH "Drug Therapy+") OR "drug therapy" OR (MH "Drug Therapy, Combination+")	312444
S15. (MH "Drug Administration Routes") OR "drug administration routes" OR (MH "Administration, Intravenous") OR (MH "Self Administration") OR (MH "Administration, Oral")	14588
S16. (MH "Analgesics, Opioid+") OR (MH "Narcotics+") OR "opi*"	51110
S17. (MH "Neuromuscular Nondepolarizing Agents+") OR (MH "Neuromuscular Blocking Agents+") OR (MH "Neuromuscular Depolarizing Agents+") OR (MH "Neuromuscular Agents+") OR (MH "Neuromuscular Blockade") OR "neuromuscular blockers"	4704
S18. (MH "Hypnotics and Sedatives+") OR "hypnotic*" OR "sedat*" OR (MH "Sedatives, Barbiturate+") OR (MH "Sedatives, Nonbarbiturate+") OR (MH "Sedation") OR (MH "Midazolam")	15810
S19. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7	8368
S20. S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18	404373
S21. S19 AND S20	1234



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60