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Prevalence of depression in granted and refused requests for euthanasia and assisted suicide: a systematic review

Ilana Levene, Michael Parker

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The Ethox Centre, Department of Public Health, University of Oxford, Oxford, UK

Correspondence to
Ilana Levene, The Ethox Centre, University of Oxford, Badenoch Building, Old Road Campus, Oxford OX3 7LF, UK;
ilana.levene@doctors.org.uk

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ABSTRACT

Background There is an established link between depression and interest in hastened death in patients who are seriously ill. Concern exists over the extent of depression in patients who actively request euthanasia/physician-assisted suicide (PAS) and those who have their requests granted.

Objectives To estimate the prevalence of depression in refused and granted requests for euthanasia/PAS and discuss these findings.

Methods A systematic review was performed in MEDLINE and PsycINFO in July 2010, identifying studies reporting rates of depression in requests for and cases of euthanasia/PAS. One author critically appraised the strength of the data using published criteria.

Results 21 studies were included covering four countries. There was considerable heterogeneity in methods of assessing depression and selecting patients. In the highest quality studies, in the Netherlands and Oregon, 8–47% of patients requesting euthanasia/PAS had depressive symptoms and 2–17% of completed euthanasia/PAS cases had depressive symptoms. In the Netherlands, depression was significantly higher in refused than granted requests, and there was no significant difference in the rate of depression between euthanasia cases and similar patients who had not made a request for euthanasia.

Conclusion It is unclear whether depression increases the probability of making a request for euthanasia/PAS, but in the Netherlands most requests in depressed patients are rejected, leaving a depression rate in cases that is similar to the surrounding population. Less evidence is available elsewhere, but some level of depression has been identified in patients undergoing euthanasia/PAS in all the countries studied. Whether the presence of depression is ever compatible with an ethical decision on euthanasia/PAS is discussed.

BACKGROUND

Rationale

Clinical depression has an established link with suicidal ideation, suicide attempts and completed suicide.[1 2] Several studies have also shown that depression is correlated with an interest in euthanasia (a doctor ending a patient's life at explicit request) and physician-assisted suicide (PAS; a doctor prescribing medication for a patient to end their own life) in patients with serious and terminal illnesses.[3–5] However, only a small percentage of those who state an interest in euthanasia/PAS will actually discuss this with a doctor and make a clear request—for example, in Oregon where 17% of respondents were potentially interested in aid in dying, only 1–2% formally requested it.[6] In addition, depressed patients may have increased apathy and lack of motivation, which could reduce the likelihood of interest in euthanasia/PAS leading to an active request. The rate of depression in requests and cases must therefore be assessed directly.

Depression is a concern in requests for euthanasia/PAS because it is potentially reversible and may affect the patients' competency, particularly in the relative weighting they give to positive and negative aspects of their situation and possible future outcomes. Depressed patients can be viewed as a vulnerable population in this context as their request for death may be part of their illness, with the correct response being treatment rather than assistance in dying.

The application of techniques from evidence-based medicine to ethics is in its infancy. Partly this is because only a small number of ethical arguments are related to testable hypotheses, and these hypotheses do not lend themselves easily to the randomised controlled trial, generally considered to be the most robust of study designs. However, tools are being developed to assess the quality of other study designs, including analysis of prevalence data.[7 8] The principles of systematic review, critical appraisal of the quality of the available evidence and its interpretation in relation to the question under consideration are therefore possible and valuable in reducing bias when making conclusions in the field of ethics.[9] If the evidence is not reviewed systematically, there is a risk of making biased conclusions.

Objectives

This study was undertaken to assess the prevalence of depression in adult patients requesting euthanasia and PAS and in those requests that were granted, and to discuss these findings. The systematic review was conducted using PRISMA guidelines[10] for high quality reporting (see PRISMA checklist in appendix 1 in the online supplement).

METHODS

Search methods

MEDLINE (1950 to present) was searched using terms [(euthanasia OR "assisted suicide") AND (depression OR depressive OR characteristic OR characteristics OR descript* OR describ* OR psychiatri*) NOT veterinar* NOT neonat* NOT nazi NOT infant NOT nonhuman] with limits set to humans only. The same positive search terms (without negative search terms or limits) were used

to search titles in PsycINFO (1950 to present). The last searches were run in July 2010. Additional studies were sought from recent reviews,[11–13] reference lists of included articles and through examining records that had cited included articles. The systematic review was not registered and the search protocol has not been previously published.

Eligibility criteria

Studies were included if they sampled patients who had made an active request for euthanasia/PAS or died from these practices, and collected information relating to depressive symptoms of patients. Studies with and without a control group were considered but had to include more than 10 participants. No language, publication status or time period restriction was applied to the search. Review articles and studies where general interest in hastened dying was reported, without an active request for euthanasia/PAS, were excluded. Studies specific to children were also excluded. The search terms specifically excluded only neonates and infants whereas the eligibility criteria excluded all children. This was because the use of MEDLINE age limits in the search was found to be non-specific and removed studies that fitted the eligibility criteria. Eligibility criteria were defined broadly with the knowledge that this research field is at an early stage, with few studies using high-quality evidence-based methods.

One author (IL) assessed the search results for inclusion in an unblinded fashion.

Data were extracted using a priori categories of setting (geographical and time period), method (how patients were sampled, number of patients, response rate, method of identifying depression and categorising severity) and results (prevalence of depression in each subcategory of patients and/or severity). The summary measure was expected to be the percentage of patients in each category with depression.

Each study was assessed against 10 quality criteria. These criteria were constructed using a published checklist for assessing the quality of studies reporting prevalence data[8] and are described in box 1. The overall performance against the 10 quality criteria was used to divide the studies into high, medium and low quality. This division was performed by comparing the number of criteria that each study fulfilled, although no strict score was used as quality scores have been shown to correlate poorly with outcomes.[14]

Data management

Where statistical significance was not reported in the original paper, χ^2 tests were performed as appropriate.

Box 1 Criteria for assessing the quality of included studies*

1. Were subjects recruited prospectively—that is, at the time that the request for euthanasia/PAS was made rather than after a decision was made or after death? (Prospective: yes/no)
2. Were all consecutive patients making an euthanasia/PAS request included? Or, alternatively, was the population sampled randomly? (Consecutive: marked yes/no—yes if positive to either question)
3. Were all patients assessed for depression in the same way using the same criteria? (All assessed: marked yes/no)
4. Was the sample generalisable—that is, was it representative of the majority of euthanasia/PAS requests? (Generalisable: marked likely/unlikely)
5. Was there a control group? In this setting, two useful control groups were possible—first, contrasting refused with granted requests and, second, contrasting patients who have made a euthanasia/PAS request with similar patients who have not made a request. (Control: marked yes/no for both control types)
6. Was the method of assessing for depression transparent and standardised—that is, were DSM-IV or ICD-10 criteria used or were established tools for diagnosing depression used? (Standardised: marked yes/no)
7. Were categories that have beenused to divide results clearly defined—for example, in terms of the severity of the depression or whether the depression was felt to be a motivating factor in the euthanasia/PAS request? (Categories: marked yes/no or not applicable if no diagnostic categories were used)
8. Was the sample size large? The size of the group of patients making a euthanasia request was divided into four categories: <50 (marked 0), ≥ 50 but <200 (marked 1), ≥ 200 but <500 (marked 2) and ≥ 500 (marked 3). Larger samples were considered to be higher quality (Sample size: marked 0–3)
9. Was the response rate high enough (Response $\geq 70\%$: marked yes/no or not applicable)
10. Were CIs and/or statistical probability testing reported? (Statistics: marked yes/no)

If sufficient information was not included in the published report to be able to make a decision on a particular criterion, the study was marked as not achieving the criterion.

*These were constructed from a published checklist for assessing the quality of prevalence data.[8] Appendix 2 in the online supplement marks each study against these criteria using the titles given in brackets above.

RESULTS

Figure 1 shows a flowchart of search results following the PRISMA template. The search generated 1579 independent results. Twenty-one research studies met the inclusion criteria which were reported in 24 publications. Appendix 2 in the online supplement reports the full characteristics, results and quality assessment of the studies. Data covered the Netherlands, Switzerland and Oregon State (where euthanasia and/or PAS are legal; see appendix 3 in the online supplement for details of their regulatory systems), as well as Canada and states in the USA other than Oregon where both practices are illegal. Twenty-nine studies were excluded, as detailed in appendix 4 in the online supplement.

Eight studies were categorised as high quality,[15–22] six were categorised as medium quality[23–28] and seven as low quality.[29–35] Tables 1–3 show the prevalence of depression in different categories of patients in high-, medium- and low-quality studies, respectively. Because of the variation in study designs, sample populations and measures of depression, meta-analysis of data is not possible.

High-quality results

In the Netherlands, 8–47% of people requesting euthanasia/PAS were reported as having 'severe depression'[16 21] (not formally classified) or depression using the Hospital Anxiety and Depression Scale (HADS) or Composite International Diagnostic Interview (CIDI).[15] In contrast, 0–17% of similar

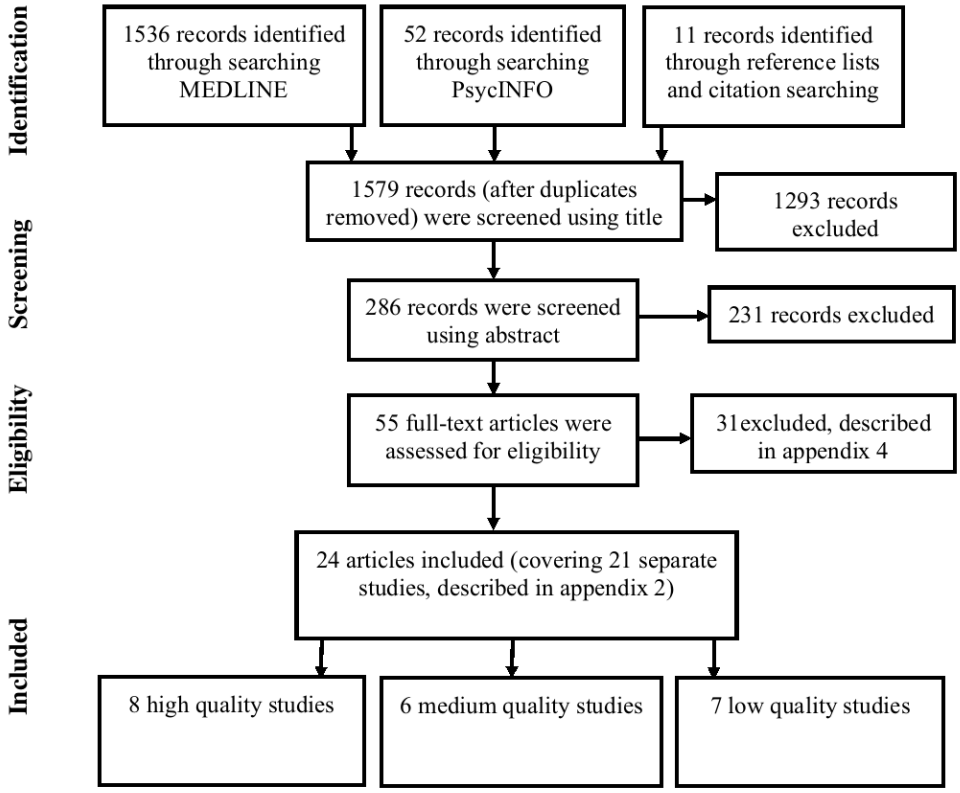

Figure 1 Flowchart of search results.

patients who did not request euthanasia/PAS were reported as having 'severe depression'[16 17 21] or positive HADS/CIDI screening,[15] as shown in table 1. When those who have requested euthanasia/PAS were compared directly with those who have not in the same study design, two studies (one of which was specific to patients with terminal cancer) found no significant difference in the prevalence of depression.[17 21] In contrast, another study in patients with terminal cancer found significantly more depression in those requesting euthanasia/PAS when using the HADS score but no significant difference when using the CIDI (on a smaller number of patients).[15]

Overall, in the Netherlands, 12–39% of people whose request for euthanasia/PAS was refused were classified as having 'severe depression',[16] 'depression',[18] 'depression as a reason for the request',[18] 'depression that was predominant in the request'[19] (none of which were formally defined criteria) or a psychiatric diagnosis of mood disorder (the latter were cases where a psychiatrist had been involved in assessing whether the request met legal guidelines).[20] In contrast, 2–10% of people whose request for euthanasia/PAS was granted were classified as depressed using the same categories.[16–20] When refused and granted requests were compared directly in the same study

Table 1 High-quality evidence on the prevalence of depression in different categories of patients

	Prevalence of depression in all euthanasia/PAS requests	Prevalence of depression in refused euthanasia/PAS requests	Prevalence of depression in granted euthanasia/PAS requests	Prevalence of depression in control group not requesting euthanasia/PAS
The Netherlands	17% of terminal cancer patients had major depression on CIDI (2/12). 47% had depression on HADS (14/30)[15]			0% of terminal cancer patients had major depression on CIDI (0/17). 17% had depression on HADS (18/107)[15]
	8% of all patients had severe depressive symptoms in last 24 h of life[16]	12% of all patients had severe depressive symptoms in last 24 h of life[16]	2% of all patients had severe depressive symptoms in last 24 h of life[16]	3% of all patients had severe depressive symptoms in last 24 h of life[16]
			10% of terminal cancer patients had severe depressive feelings (11/106)[17]	8% of terminal cancer patients had severe depressive feelings (5/64)[17]
		32% of all patients had depression, 18% had depression as a reason for the request[18]	9% of all patients had depression, 4% had depression as a reason for the request[18]	
		39% of all patients had depression as predominant complaint[19]	3% of all patients had depression as predominant complaint[19]	
		20% of patients where a psychiatrist was consulted had a psychiatric diagnosis of mood disorder (25/124)[20]	7% of patients where a psychiatrist was consulted had a psychiatric diagnosis of mood disorder (5/67)[20]	
	13% of terminal cancer patients had severe depressive feelings (2/16)[21]			6–8% of terminal cancer patients had severe depressive feelings (4/69)[21]
Oregon state, USA	26% of all patients had depression in a structured interview/HADS (15/58)[22]	30% of all patients had depression in a structured interview/HADS (12/40)[22]	17% of all patients had depression in a structured interview/HADS (3/18)[22]	

Absolute numbers are given in brackets where available.
CIDI, Composite International Diagnostic Interview; HADS, Hospital Anxiety and Depression Scale; PAS, physician-assisted suicide.

Table 2 Medium-quality evidence on the prevalence of depression in different categories of patientsc

	Prevalence of depression in euthanasia/PAS requests	Prevalence of depression in granted euthanasia/PAS requests	Prevalence of depression in population not requesting euthanasia/PAS
The Netherlands		25% of all patients had depression to great/very great extent, 29% to a lesser extent[23]	
		5% of all patients had depression as a motivating factor (4/87)[24]	
		12% of ALS patients used antidepressants in end-stage, 11% had symptoms of depression in end-stage, 23% had anhedonia, 21% depressed mood, 13% feelings of guilt[25]	11% of ALS patients used antidepressants in end-stage, 16% had symptoms of depression in end-stage, 24% had anhedonia, 18% depressed mood, 9% feelings of guilt[25]
Non-legal: Washington state, USA	55% of all patients had severe depression or depressed mood (114/207)[26]		
Non-legal: Toronto, Canada	50% of HIV patients had a diagnosis of depression (10/20)[27]		17% of HIV patients had a diagnosis of depression (2/12)[27]

Absolute numbers are given in brackets where available.
ALS, amyotrophic lateral sclerosis; PAS, physician-assisted suicide.

design, all four studies found a significantly higher rate of depression in patients whose requests were refused compared with those whose requests were granted.[16 18–20] One study compared patients with terminal cancer whose euthanasia/PAS request was granted with a similar population who had not made a request. It found no significant difference in the rate of 'severe depressive feelings' between the two groups (10% vs 8%).[17]

In the single Oregon study, 26% of people requesting PAS were found to be depressed in a structured interview or using HADS. There was no significant difference in the rate of depression between those whose request was refused and those whose request was granted,[22] but the study only contained 18 patients whose request was granted and therefore the number who were depressed was extremely small (3 patients). The study also reported that the majority of patients requesting PAS did not rank depression as a motivating factor in their request (the median score for the extent to which depression motivated their request was 1 (IQR 1–1), where 1 was defined as not at all important).[36]

Medium-quality results

In the Netherlands 5–25% of people whose requests for euthanasia/PASwere granted had depression 'to a great or very great extent'[23] (not formally defined) or as a 'motivating factor' in their request.[24] 11–23% of amyotrophic lateral sclerosis (ALS) patients were usinganti-depressants or showed specific depressive symptoms (anhedonia,depressed mood and feelings of guilt) in the end-stage of disease.[25] In contrast, 11–24% of ALS patients who had not made a euthanasia/PASrequest were using anti-depressants or had specific depressive symptoms in the end-stage, which was not a significantdifference.

Two studies were conducted in non-legal settings in America and Canada. Here, 50–55% of people requesting euthanasia/PAS were defined as having 'severe depression or depressed mood'[26] or had a coexisting diagnosis of depression[27] (none of which were formally defined). The latter definition was used in patients with HIV in Toronto.[27] In contrast, 17% of people with HIV who were not interested in euthanasia/PAS had a coexisting diagnosis of depression. This was not a significant difference but the sample size was very small.[27]

The final medium-quality study showed that 49% of hospice patients in Oregon whose request for PAS had been granted had the same level of depression (not formally defined) as other hospice patients who had not made a request. Twenty-eight percent of those who had requested PAS were reported as having less depression than the control group and 23% as having more.[28]

Low-quality results

One low-quality study in Oregon reported that 20% of people making a request for PAS had 'symptoms of depression'[29] (not formally defined). Two other studies using scales to assess whether depression was a motivating factor in PAS requests found that the majority of patients were not classified as having depression as a motivating factor for the request.[34 35]

In Switzerland, 27% of people whose request for PAS was granted (within a prominent right-to-die organisation) were defined as depressed[30] (not formally defined) and at least 2% of people using the same right-to-die organisation to commit PAS in a different time period were found to have a psychiatric diagnosis of depression in the records of public psychiatric institutions, with another 4% having a psychiatric diagnosis of dysthymia.[31]

In Michigan, USA where euthanasia/PAS are not legal, 13% of people who were assisted in euthanasia by Dr Jack Kevorkian

Table 3 Low-quality evidence on the prevalence of depression in different categories of patients

	Prevalence of depression in euthanasia/PAS requests	Prevalence of depression in granted euthanasia/PAS requests
Oregon state, USA	20% of all patients had symptoms of depression (28/143)[29]	
Switzerland		27% of all patients were depressed (24/90)[30]
		At least 2% of all patients had a psychiatric diagnosis of depression (1/46), at least 4% had a psychiatric diagnosis of dysthymia (2/46)[31]
Non-legal: states other than Oregon, USA	0% of all patients had probable major depression assessed by a psychiatrist (0/35), 9% had possible major depression (3/35), an additional 14% had depressive symptoms (5/35)[32]	
Non-legal: Michigan, USA		13% of all patients had depressive symptoms (9/69)[33]

Absolute numbers are given in brackets where available.
PAS, physician-assisted suicide.

had depressive symptoms[33] (not formally defined). A separate study interviewed patients and family of patients from across the USA who were requesting euthanasia/PAS. When interviews were assessed by a psychiatrist, no patients were classified as having probable major depression according to DSM-IV criteria, 9% were classified as having possible major depression, and a further 14% were classified as having depressive symptoms not fitting full DSM-IV criteria.[32]

DISCUSSION

It is clear that both undefined depressive symptoms and clinical depression are found at high levels in patients making requests for euthanasia/PAS, with most studies across the quality spectrum estimating that a quarter to a half of requests came from depressed patients.[15 22 26 27] Two out of three high-quality studies comparing those who made a request for euthanasia/PAS with similar patients who did not request euthanasia/PAS found no significant difference in depression rate between the two groups,[9 21] which could imply that the high depression rate is not necessarily correlated with the euthanasia/PAS request but with the terminal and serious conditions that these patients generally have. However, the study which did show a higher depression rate in those requesting euthanasia/PAS was the only one to independently assess patients during their lifetime with standardised depression assessment tools.[15] In addition, one of the studies showing no difference included only a small sample of 16 people making a request for euthanasia/PAS.[21] The current evidence on whether depressed patients are a vulnerable population for making euthanasia/PAS requests is therefore conflicting. Large and robust studies that directly assess patients' depression in a standardised fashion are necessary for more confident conclusions.

There are also significant levels of depression in completed euthanasia/PAS cases, but this may vary according to the system regulating the way in which euthanasia and PAS occur. In the Netherlands, where euthanasia and PAS are legal, high-quality studies showed a depression rate of 2–10% in euthanasia/PAS cases.[16–20 23 24] There is convincing evidence to show that depression is a significant factor in refusing euthanasia/PAS requests,[16 18–20] with supporting high- and medium-quality evidence showing that the rate of depression in completed euthanasia/PAS cases is no different from the surrounding population of seriously ill patients.[16 17 25] This implies that the Dutch system may be successful at screening out many requests motivated by depression. Whether it is acceptable for depression to occur in euthanasia/PAS cases at any level, regardless of the depression rate in the surrounding population, is discussed further below.

Data on the rate of depression in completed cases in other countries are of lower quality and are more sparse, and therefore conclusions are tentative. In Oregon, where PAS is legal, one high-quality study showed that clinical depression had definitely been missed in patients who had been approved for PAS prescription,[22] but there is no comparison with rates in patients not making a request. Only one of the three patients identified with clinical depression stated that depression was a factor in her request, and this patient underwent PAS even after her depression was treated and in remission. The other two patients stated that depression was not a factor in their requests and refused the treatment offered by the study team. The issue of whether treating depression will affect the PAS decision is discussed further below.

Evidence from Switzerland, where PAS is legal, was of low quality but showed a high level of apparent depression in granted PAS requests, as assessed by lay volunteers (27%).[30] This may be a particular cause for concern over the informality of the way that Switzerland regulates PAS, where there is no official reporting and most cases have extensive involvement of lay people in the assessment process. Certainly there are also qualitative data raising concern over the way PAS is used in Switzerland, with known cases of patients being admitted to psychiatric hospital for suicidal ideation and completing PAS while on home leave.[37]

The single study representing completed euthanasia cases in non-legal settings (analysing a subset of Dr Kevorkian's patients) was also of low quality and was unlikely to be representative of typical cases. However, the rate of depression noted (13%[33]) was comparable to that seen in Oregon and the Netherlands. Given the single low-quality data point, there is not enough evidence available to comment on whether legalisation of euthanasia/PAS has an impact on depression in completed cases.

In summary, the strongest data are from the Netherlands and do not convincingly show that depression is more common in patients making a request for euthanasia/PAS than in the surrounding population of terminally or seriously ill patients, although this may be due to methodological shortcomings in the studies. When a request is made, significantly more patients who are refused assistance are depressed than those who are granted. The same relationship may not be true in Oregon, but less evidence is available. However, in all countries, some patients who have undergone euthanasia/PAS have been depressed.

The final conclusion raises two important questions—first, whether depression should exclude a patient from having their request for euthanasia/PAS granted and, second, whether there are effective structures available to identify and treat such patients' depression. These issues will be discussed further with reference to research outside the systematic review—this should be considered narrative review.

Depression may affect a patient's competence due to cognitive difficulties and weighting of positive and negative information. However, most people with major depression retain competence to make medical decisions.[38] The legalisation of euthanasia/PAS acknowledges that active hastening of death can be a valid choice in terminal or severe illness so, if competency can be retained in depression, it is possible for euthanasia/PAS to be a valid choice despite the presence of depression. Therefore, there must be some assessment of whether the depression is a factor in the desire for hastened death, not simply whether it is present.

To understand this relationship, data on the potential for treatment of depression to change the patient's request for euthanasia/PAS would be useful. For this to occur, improvement in depression in terminally ill patients must be possible, despite problems such as short life expectancy and unacceptable side effects at the end of life. Some studies have shown that treatment with medication and psychotherapy can improve depressive symptoms in terminal illness even with a short timescale, but the potential for full remission in clinical depression is less certain.[39 40]

Few studies have looked specifically at the effect of treatment for depression on requests for hastened death. An Australian study showed that successful treatment of depression reduces the number of patients who would accept euthanasia if offered to them in their current state and in a hypothetical life-threatening illness with good outcome, but did not change the number who would accept euthanasia in a hypothetical life-threatening illness with uncertain outcome.[41] An American investigation

showed that treatment of severe depression changed current and theoretical preferences of elderly patients for withholding or withdrawing life-sustaining treatment, but there was no difference in the preferences of patients with mild or moderate depression.[42] A very small Japanese study included three depressed patients who ceased requesting euthanasia or palliative sedation after a week of treatment with tricyclic antidepressants.[40]

This evidence shows that there is potential for treatment of depression to affect a request for euthanasia/PAS, but much more investigation is needed to clarify whether this is limited to severely depressed patients or those with less serious underlying illnesses. If so, it may be that only a very small number of patients requesting euthanasia/PAS would change their minds if treated for depression, although treatment would be recommended regardless to reduce psychological suffering.

The second question covers the identification of depression in patients requesting euthanasia/PAS. Neither of the two major models of legalisation—the Netherlands and the state of Oregon—mandate psychiatric assessment, although it has been extensively debated. Arguments against it include the burden placed on terminally and seriously ill patients and the creation of a gatekeeper role for psychiatrists that may interfere with the relationship of the patient and the psychiatrist. Many patients who request euthanasia/PAS in the Netherlands die before a decision is made, and any extra regulation will raise this number or may encourage patients to seek euthanasia/PAS earlier than they would ideally want it to make sure they can fulfil all the requirements.

It is unknown whether mandatory psychiatric assessment would be worth these negative effects by increasing the identification of depression, or whether patients identified in this way would accept treatment. The Rights of the Terminally Ill Act in Australia, which briefly legalised euthanasia in the Northern Territory in 1996, included mandatory psychological assessment. Although only a small number of cases occurred before the law was repealed, there have been questions over whether this was effective in picking up psychiatric disorders in these patients and whether patients were fully honest in the psychiatric assessments.[43]

Psychiatrists are not confident that they could easily identify all cases of depression in these patients—only 6% of Oregonian psychiatrists felt they could assess whether psychiatric factors were affecting a patient's judgement in a PAS request during a single consultation.[44] In contrast, 35% of non-psychiatrists in Connecticut were very confident they could assess whether a psychiatric disorder was impairing the judgement of a patient requesting PAS if they knew them well, in contrast to only 5% if the patient was new to them.[45] This implies that having an existing relationship with the patient is important for competency assessment, which is difficult if the patient does not have such a relationship with any doctor or if their longstanding doctor does not wish to assist in euthanasia/PAS. It is therefore far from clear how all cases where depression is motivating a request for euthanasia/PAS can be identified and offered treatment. It may be more effective to strengthen screening of all terminally and seriously ill patients for depression to pick up these issues before a request for euthanasia/PAS is made and give more time for treatment to take effect. However, this laudable goal is unlikely to solve the problem entirely.

The conclusions from the results reported are limited by various factors. There are several methodological challenges that are difficult to overcome in assessing both end-of-life decisions and depression in the chronically and terminally ill. In countries where euthanasia/PAS are illegal, under-reporting, lack of clarity in the explicit nature of the request and difficulty in recruitment are likely. Measuring depression during physical illness is complicated by the fact that physical symptoms such as fatigue and sleep disturbance that are used in defining depression may be caused by an underlying illness.[46] All studies in the review that stated their approach were inclusive,[22 32] attributing any depression-related symptoms to depression rather than physical illness, but most did not declare their approach. Although both inclusive and exclusive approaches can be justified, any use of an exclusive approach would affect comparisons because eliminating physical symptoms can halve the estimated prevalence of depression in patients with cancer.[47]

The studies reviewed also show limitations which could be overcome by changes in study design. The highest quality design would include direct prospective assessment of patients for depression with validated psychological tools or against DSM-IV criteria, and also have a large sample size. For the highest relevance there would be a comparison between groups requesting euthanasia/PAS, those that were refused, those that were granted and a control population who had made no request for euthanasia/PAS. Unfortunately, no studies achieved high levels of quality in all of these areas. Research was dominated by the Netherlands and Oregon, with very little or no data from Switzerland, Belgium and non-legal settings. Given the importance of assessing the impact of different forms of regulation on vulnerable patients, research is encouraged elsewhere, including states with recent legislation such as Washington State and Luxembourg. In addition, the systematic review suffers from broad limitations such as publication bias and selective reporting within studies. Researchers are likely to have an opinion on the ethics behind euthanasia/PAS which may affect the way in which they structure studies and report results.

CONCLUSION

Up to half of patients requesting euthanasia/PAS may show symptoms of depression but, in the Dutch regulatory system, most patients with depression have their requests refused and the rate of depression in cases is not significantly different from that of the surrounding population. There is little evidence as to whether other systems act in a similar manner, including informal systems acting where these practices are illegal. In all countries studied, depression occurs in some patients who undergo euthanasia/PAS.

Whether it is acceptable to have any level of depression in deaths from euthanasia/PAS is debated because depression does not necessarily make patients incompetent and there is little evidence on whether treatment will be acceptable to patients at the end of life, or will change end-of-life decisions. Although assessment for depression in patients requesting euthanasia/PAS is extremely important, it is likely to be more successful to improve screening and treatment for depression in all terminally and seriously ill patients. More high-quality investigation and discussion is necessary in this area to increase the protection for vulnerable patients while not compromising patient autonomy.

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REFERENCES

1. **Goldney RD,** Wilson D, Dal Grande E, *et al*. Suicidal ideation in a random community sample: attributable risk due to depression and psychosocial and traumatic events. *Aust NZ J Psychiatry* 2000;**34**:98—106.
2. **Beautrais AL,** Joyce PR, Mulder RT, *et al*. Prevalence and comorbidity of mental disorders in persons making serious suicide attempts: a case-control study. *Am J Psychiatry* 1996;**153**:1009—14.
3. **Wilson KG,** Chochinov HM, McPherson CJ, *et al*. Desire for euthanasia or physician-assisted suicide in palliative cancer care. *Health Psychol* 2007;**26**:314—23.
4. **Chochinov HM,** Wilson KG, Enns M, *et al*. Desire for death in the terminally ill. *Am J Psychiatry* 1995;**152**:1185—91.
5. **Blank K,** Robison J, Doherty E, *et al*. Life-sustaining treatment and assisted death choices in depressed older patients. *J Am Geriatr Soc* 2001;**49**:153—61.
6. **Tolle SW,** Tilden VR, Drach LL, *et al*. Characteristics and proportion of dying Oregonians who personally consider physician-assisted suicide. *J Clin Ethics* 2004;**15**:111—18.
7. **Tooth L,** Ware R, Bain C, *et al*. Quality of reporting of observational longitudinal research. *Am J Epidemiol* 2005;**161**:280—8.
8. **Donner-Banzhoff N,** Kunz R, Rosser W. Studies of symptoms in primary care. *Fam Pract* 2001;**18**:33—8.
9. **Strech D.** Evidence-based ethics—what it should be and what it shouldn't. *BMC Med Ethics* 2008;**9**:16.
10. **Moher D,** Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;**6**:e1000097.
11. **Werth JL Jr.** The relationships among clinial depression, suicide, and other actions that may hasten death. *Behav Sci Law* 2004;**22**:627—49.
12. **Rosenfeld B.** Assisted suicide, depression, and the right to die. *Psychol Public Policy Law* 2000;**6**:467—88.
13. **Emanuel EJ.** Depression, euthanasia, and improving end-of-life care. *J Clin Oncol* 2005;**23**:6456—8.
14. **Juni P,** Witschi A, Bloch R, *et al*. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999;**282**:1054—60.
15. **van der Lee ML,** van der Bom JG, Swarte NB, *et al*. Euthanasia and depression: a prospective cohort study among terminally ill cancer patients. *J Clin Oncol* 2005;**23**:6607—12.
16. **Onwuteaka-Philipsen BD,** Rurup ML, Pasman HR, *et al*. The last phase of life. Who requests and who receives euthanasia or physician-assisted suicide? *Med Care* 2010;**48**:596—603.
17. **Georges JJ,** Onwuteaka-Philipsen BD, Van Der Wal G, *et al*. Differences between terminally ill cancer patients who died after euthanasia had been performed and terminally ill cancer patients who did not request euthanasia. *Palliat Med* 2005;**19**:578—86.
18. **Jansen-van der Weide MC,** Onwuteaka-Philipsen BD, Van Der Wal G. Granted, undecided, withdrawn, and refused requests for euthanasia and physician-assisted suicide. *Arch Intern Med* 2005;**165**:1698—704.
19. **Haverkate I,** Onwuteaka-Philipsen BD, van Der HA, *et al*. Refused and granted requests for euthanasia and assisted suicide in the Netherlands: interview study with structured questionnaire. *BMJ* 2000;**321**:865—6.
20. **Groenewoud JH,** Van Der Heide A, Tholen AJ, *et al*. Psychiatric consultation with regard to requests for euthanasia or physician-assisted suicide. *Gen Hosp Psychiatry* 2004;**26**:323—30.
21. **Georges JJ,** Onwuteaka-Philipsen BD, Van Der Heide A, *et al*. Requests to forgo potentially life-prolonging treatment and to hasten death in terminally ill cancer patients: a prospective study. *J Pain Symptom Manage* 2006;**31**:100—10.
22. **Ganzini L,** Goy ER, Dobscha SK. Prevalence of depression and anxiety in patients requesting physicians' aid in dying: cross sectional survey. *BMJ* 2008;**337**:a1682.
23. **Van Der Wal G,** van Eijk JT, Leenen HJ, *et al*. [Euthanasia and assisted suicide by physicians in the home situation. 2. Suffering of the patients] (In Dutch). *Ned Tijdschr Geneeskd* 1991;**135**:1599—603.
24. **Georges JJ,** Onwuteaka-Philipsen BD, Muller MT, *et al*. Relatives' perspective on the terminally ill patients who died after euthanasia or physician-assisted suicide: a retrospective cross-sectional interview study in the Netherlands. *Death Stud* 2007;**31**:1—15.
25. **Maessen M,** Veldink JH, Onwuteaka-Philipsen BD, *et al*. Trends and determinants of end-of-life practices in ALS in the Netherlands. *Neurology* 2009;**73**:954—61.
26. **Back AL,** Wallace JI, Starks HE, *et al*. Physician-assisted suicide and euthanasia in Washington State. Patient requests and physician responses. *JAMA* 1996;**275**:919—25.
27. **Lavery JV,** Boyle J, Dickens BM, *et al*. Origins of the desire for euthanasia and assisted suicide in people with HIV-1 or AIDS: a qualitative study. *Lancet* 2001;**358**:362—7.
28. **Ganzini L,** Harvath TA, Jackson A, *et al*. Experiences of oregon nurses and social workers with hospice patients who requested assistance with suicide. *N Engl J Med* 2002;**347**:582—8.
29. **Ganzini L,** Nelson HD, Schmidt TA, *et al*. Physicians' experiences with the Oregon Death with Dignity Act. *N Engl J Med* 2000;**342**:557—63.
30. **Bosshard G,** Ulrich E, Ziegler SJ, *et al*. Assessment of requests for assisted suicide by a Swiss right-to-die society. *Death Stud* 2008;**32**:646—57.
31. **Frei A,** Schenker TA, Finzen A, *et al*. Assisted suicide as conducted by a "Right-to-Die" society in Switzerland: a descriptive analysis of 43 consecutive cases. *Swiss Med Wkly* 2001;**131**:375—80.
32. **Bharucha AJ,** Pearlman RA, Back AL, *et al*. The pursuit of physician-assisted suicide: role of psychiatric factors. *J Palliat Med* 2003;**6**:873—83.
33. **Roscoe LA,** Malphurs JE, Dragovic LJ, *et al*. A comparison of characteristics of Kevorkian euthanasia cases and physician-assisted suicides in Oregon. *Gerontologist* 2001;**41**:439—46.
34. **Carlson B,** Simopolous N, Goy ER, *et al*. Oregon hospice chaplains' experiences with patients requesting physician-assisted suicide. *J Palliat Med* 2005;**8**:1160—6.
35. **Ganzini L,** Goy ER, Dobscha SK. Why Oregon patients request assisted death: family members' views. *J Gen Intern Med* 2008;**23**:154—7.
36. **Ganzini L,** Goy ER, Dobscha SK. Oregonians' reasons for requesting physician aid in dying. *Arch Intern Med* 2009;**169**:489—92.
37. **Strnad J,** Grosjean S, Schupbach B, *et al*. [Suicide of psychiatric inpatients assisted by euthanasia advocacy groups. Cases of assisted suicide?] (In German). *Nervenarzt* 1999;**70**:645—9.
38. **Grisso T,** Appelbaum PS. Comparison of standards for assessing patients' capacities to make treatment decisions. *Am J Psychiatry* 1995;**152**:1033—7.
39. **Akechi T,** Okuyama T, Onishi J, *et al*. Psychotherapy for depression among incurable cancer patients. *Cochrane Database Syst Rev* 2008;(2):CD005537.
40. **Kugaya A,** Akechi T, Nakano T, *et al*. Successful antidepressant treatment for five terminally ill cancer patients with major depression, suicidal ideation and a desire for death. *Support Care Cancer* 1999;**7**:432—6.
41. **Hooper SC,** Vaughan KJ, Tennant CC, *et al*. Preferences for voluntary euthanasia during major depression and following improvement in an elderly population. *Aust J Ageing* 1997;**16**:3—7.
42. **Ganzini L,** Lee MA, Heintz RT, *et al*. The effect of depression treatment on elderly patients' preferences for life-sustaining medical therapy. *Am J Psychiatry* 1994;**151**:1631—6.
43. **Kissane DW,** Street A, Nitschke P. Seven deaths in Darwin: case studies under the rights of the Terminally Ill Act, Northern Territory, Australia. *Lancet* 1998;**352**:1097—102.
44. **Ganzini L,** Fenn DS, Lee MA, *et al*. Attitudes of Oregon psychiatrists toward physician-assisted suicide. *Am J Psychiatry* 1996;**153**:1469—75.
45. **Curry L,** Gruman C, Blank K, *et al*. Physician-assisted suicide in Connecticut: physicians' attitudes and experiences. *Conn Med* 2000;**64**:403—12.
46. **Akechi T,** Nakano T, Akizuki N, *et al*. Somatic symptoms for diagnosing major depression in cancer patients. *Psychosomatics* 2003;**44**:244—8.
47. **Bukberg J,** Penman D, Holland JC. Depression in hospitalized cancer patients. *Psychosom Med* 1984;**46**:199—212.

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Ilana Levene and Michael Parker

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