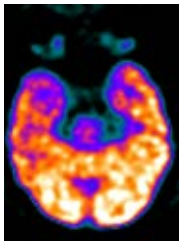
research

Specialist palliative care most effective when targeted at those with complex needs p 59



Dementia prevalence in England and Wales to rise to 4.4% by 2040 p 60

No or little association found between benzodiazepine initiation and mortality p 62

ORIGINAL RESEARCH Systematic review and meta-analysis

Effect of specialist palliative care services on quality of life in adults with advanced incurable illness in hospital, hospice, or community settings

Gaertner J, Siemens W, Meerpohl JJ, et al

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Find this at: http://dx.doi.org/10.1136/bmj.j2925

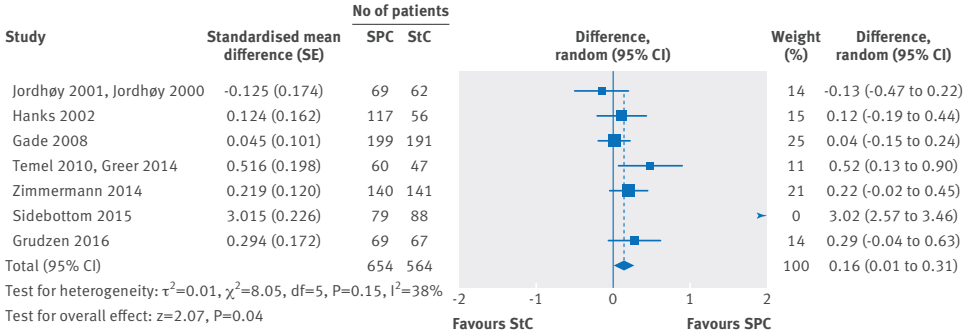
Study question Does multiprofessional specialist palliative care, in addition to standard care, improve quality of life of patients with advanced illness?

Methods Systematic review and meta-analysis of randomised controlled trials. Medline, Embase, CENTRAL, PsycINFO, and trial registers were searched until July 2016. Studies in adult inpatients or outpatients treated in hospital, hospice, or community settings with any advanced illness were included. Standard care plus specialist palliative care (provided by a multiprofessional team) was compared with standard care alone. The primary outcome was quality of life. Two reviewers independently screened and extracted data, assessed the risk of bias, and evaluated the quality of evidence. Results are reported as standardised mean difference (SMD) and are also re-expressed on the global health/QoL scale (item 29 and 30, respectively) of the QLQ-C30 (0-100, high values=good quality of life, minimal clinically important difference 8.1).

Study answer and limitations Of 3967 publications, 12 were included (10 randomised controlled trials with 2454 patients randomised, of whom 72% (1766) had cancer). In no trial was integration of specialist palliative care triggered according to patients' needs as identified by screening. Overall, there was a small effect in favour of specialist palliative care (SMD 0.16, 95% confidence interval 0.01 to 0.31; QLQ-C30 global health/QoL 4.1, 0.3 to 8.2; n=1218, six trials). Sensitivity analysis showed an SMD of 0.57 (−0.02 to 1.15; global health/QoL 14.6, −0.5 to 29.4; n=1385, seven trials). The effect was marginally larger for patients with cancer (0.20, 0.01 to 0.38; global health/QoL 5.1, 0.3 to 9.7; n=828, five trials) and especially for those who received specialist palliative care early (0.33, 0.05 to 0.61, global health/QoL 8.5, 1.3 to 15.6; n=388, two trials). The results for pain and other secondary outcomes were inconclusive. Some methodological problems (such as lack of blinding) reduced the strength of the evidence.

What this study adds Recommendations from different institutions urge physicians to cooperate closely with providers of specialist palliative care. These recommendations were based on expert opinion or systematic reviews (without meta-analysis). This study used highest standards of evidence based medicine (such as assessment of risk of bias and quality of evidence) to quantify the effect of specialist palliative care in meta-analyses with different subgroup and sensitivity analyses. It shows that specialist palliative care might be most effective when it is provided in addition to general palliative care for patients with complex needs rather than to all patients in the palliative stages of their diseases.

Funding, competing interests, data sharing, systematic review registration See bmj.com.



Effect on total quality of life (primary outcome) in review of studies on specialist palliative care (SPC) versus standard care (StC) (study by Sidebottom et al was not included in meta-analysis)

Dementia trends in England and Wales

ORIGINAL RESEARCH Modelling study

Temporal trend in dementia incidence since 2002 and projections for prevalence in England and Wales to 2040

Ahmadi-Abhari S, Guzman-Castillo M, Bandosz P, et al

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Find this at: http://dx.doi.org/10.1136/bmj.j2856

Study question What is the future burden of dementia in England and Wales if population based estimates of increasing life expectancy and declining incidence of dementia and cardiovascular disease are taken into account?

Methods In this modelling study the authors analysed data from six waves of the representative English Longitudinal Study of Ageing (2002-13). Dementia was as certained based on repeated assessments of cognition and function using constant objective criteria. A robust joint modelling technique was used to estimate the trend in dementia incidence over the past 15 years, correcting for bias as a result of selective dropout of study participants. A health state transition (Markov) model (IMPACT-Better Ageing Model, IMPACT-BAM) was developed to integrate trends in cardiovascular disease, cognitive and functional impairment, dementia, and mortality to predict dementia prevalence and number of cases to 2040.

Study answer and limitations Age and sex adjusted incidence of dementia declined by 2.7% (95% confidence interval 2.4% to 2.9%) relatively each year between 2002 and 2013. According to Markov model estimates, 767 000 (95% uncertainty interval 735 000 to 797 000) people were living with dementia in England and Wales in 2016, representing a prevalence of 3.6% in the population aged 50 years or older. Dementia cases (prevalence) are projected to increase to 872 000 (3.8%), 1 092 000 (4.3%), and 1 205 000 (4.4%) in 2020, 2030, and 2040, respectively. In contrast, the projection based on no further decline in dementia incidence indicates that 1 909 000 people would be living with dementia in 2040. Uncertainties in model parameters were addressed by sensitivity analyses.

COMMENTARY Robust models forecast a dramatic increase in the number of people with dementia

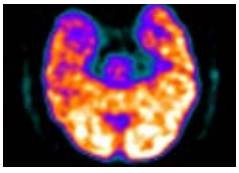
Because the most prominent risk factor for dementia is aging, the urgent need to address the public health challenges of dementia is heightened by the "greying" of societies worldwide. In 2015, nearly 47 million people around the world had dementia. If age and sex specific prevalence of dementia stays constant over time, there will be 130 million cases by 2050.[1]

Uncertainties

And yet changes over time in both dementia incidence (the rate at which new cases arise in a population over a specified period, among people at risk) and duration (time from the overt clinical onset to death) are plausible, so dementia prevalence, which is the product of incidence and average duration, could remain stable, decrease, or increase accordingly. In a linked paper, Ahmadi-Abhari and colleagues develop a Markov model to estimate the direction and magnitude of these and other trends to 2040 in England and Wales.[2]

Trends in prevalence[3] and incidence of dementia[4] have been previously reported in the Medical Research Council's Cognitive Function and Ageing Study (CFAS), which was purposely designed and powered to detect any such changes. The study found a reduction in incidence, although in men only, and a reduction in prevalence in those aged 80 or more years. However, the net effect of the incidence reduction is uncertain, and whether sex and age standardised prevalence of dementia is declining in Western countries is still unclear.

Differential participation and attrition of participants cannot be ruled out because dementia risk at baseline is likely associated with non-participation and shorter survival. Dementia shares risk factors with other non-communicable diseases of old age,[5] which might also increase all cause mortality. Finally, uncertainty remains over whether and by how much changes in the prevalence of and mortality from vascular and other risk factors will modify the magnitude of the expected dementia epidemic.



High quality epidemiological studies are still needed to monitor actual changes in dementia prevalence, incidence, and associated mortality over time

Ahmadi-Abhari and colleagues found a statistically significant 2.7% annual reduction in dementia incidence between 2002 and 2013, after accounting for differential attrition.[2] To estimate projections of dementia prevalence in England and Wales up to 2040, the authors applied advanced statistical methodologies that accounted for varying competing risks and mortality rates, and their potential opposite effect on changes in dementia prevalence over time.

The novel and advanced statistical models and the extensive set of sensitivity analyses conducted to test their robustness are major strengths of this study. Although a decline in the overall age standardised prevalence of dementia was estimated between 2016 and 2040, there will be up to a 57% increase in the absolute number of those affected by 2040 because of the expected demographic changes. These results are in line with those of previous studies.[6]

Limitations

Some design characteristics and methodological limitations suggest that the results of this rich set of secondary analyses from the ELSA study should be interpreted cautiously. Dementia diagnosis requires demonstration of cognitive decline (from a previous level of functioning), demonstration that the decline socially and functionally impairs patients, and the exclusion of "other causes" (including depression and delirium). Although the criteria to establish dementia caseness were kept constant over time in the ELSA study, they were not formally validated, were not equal for all participants at each wave, and do not seem to conform to

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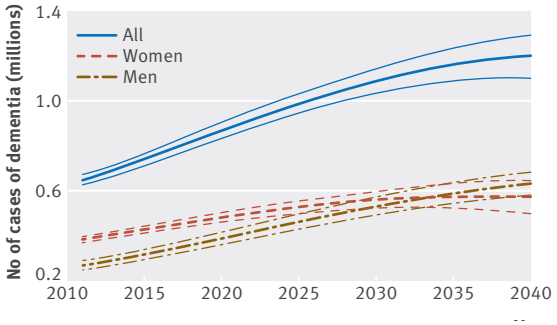

Projected number of people with dementia in England and Wales 2016-40 obtained from IMPACT-BAM health state transition model

What this study adds Representative data collected between 2002 and 2013 indicates that age specific incidence of dementia is declining. Even if the decline in incidence continues, aging of the population means future growth in numbers of people with dementia will continue to pose a major challenge to society.

Data sharing, funding, competing interests This study is funded by grants from the British Heart Foundation (RG/13/2/30098, RG/16/11/32334). The authors have no competing interests.

DSM-IV (diagnostic and statistical manual of mental disorders, fourth edition) or other criteria.

Evidence of a major decline in cognitive function compared with the previous level of functioning was not sought in all participants; and dementia diagnosis based on self reported doctor diagnosis and the use of an informant questionnaire, which was used in the subsample of those with no cognitive assessment, were likely prone to bias.

Both cognitive and functional impairment may be due to depression, delirium, or other mental disorders, but these were not assessed. The possibility that observed declines in both incidence and prevalence of dementia might be in part (or entirely) due to a reduction in the occurrence of depression cannot be ruled out.

Finally, although temporal trends in mortality due to dementia are difficult to study, and were not reported, it is possible that future longer survival of patients with dementia (which is desirable) may counterbalance the effects of a reduced incidence on prevalence.

Given these limitations, it is too early to abandon current assumptions that age specific prevalence of dementia will remain constant over time,[6] and too early to amend current dementia forecasts.[1]

However, the results from the ELSA study do confirm that the absolute number of people with dementia will increase substantially in the coming years in England and Wales, as a result of an aging population, and it is these numbers that matter most to policy makers planning future care and services. The study also confirms that high quality epidemiological studies are still needed to monitor actual changes in dementia prevalence, incidence, and associated mortality over time. The WHO global plan on dementia, which was unanimously adopted on 29 May 2017 at the 70th session of the World Health Assembly in Geneva,[7] provides the opportunity to revitalise epidemiological research in Europe, which has worryingly stalled in the past 15 years.[1]

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Elizabeth Loder explains why decision letters from *The BMJ* often arrive quickly and at odd hours

The journal that never sleeps

The research editors of *The BMJ* have been working hard to speed up our processes and improve our service to authors. The most common "service" we provide, though, is a rejection letter.

We receive thousands of research papers each year and are able to publish only a few hundred. In many cases we know almost immediately that a paper is not right for the journal. For example, *The BMJ* does not publish animal studies, early phase clinical trials, or studies without any health related outcomes. These papers are rejected without additional editorial or peer review. We aim to do this rapidly so that authors will not be delayed in submitting elsewhere.

But is it possible to be too fast? We worry authors might be affronted if they receive a rejection letter within an hour or so of submission. However, my email tells me that most authors prefer a rapid decision, even if it is not the one they wanted. Decision letters are sent to the corresponding author, but all coauthors are copied in. Someone usually forgets who sent the original email and hits "reply all," thus including the handling editor in the ensuing chain of comments. Many authors express anger or sadness about the decision, but nearly all seem grateful that we haven't wasted their time.

There are limits though. Decision letters that arrive on weekends, holidays, or in the middle of the night are especially likely to provoke indignation. My theory is that authors imagine a sleepy editor who isn't giving their paper proper attention. The reality is that *The BMJ* is an international journal with research editors in China, Croatia, Portugal, the US, Austria, and the UK. Thus, a decision letter arriving in the middle of the night was probably sent by an editor in another part of the world.

Such was the case a few weeks ago, when I awoke on a Saturday morning to a "reply all" discussion among the European authors of a paper I had rejected on Friday. "I suspect the editors haven't read our manuscript, or a robot did it between 6 pm and 4 am," opined one of the authors. Nope. It was me, working in the US. You might be snoozing, but somewhere, even on weekends and holidays, a research editor of *The BMJ* is hard at work.

Elizabeth Loder is head of research, *The BMJ*

Benzodiazepines and risk of all cause mortality in adults

Patorno E, Glynn RJ, Levin R, Lee MP, Huybrechts KF

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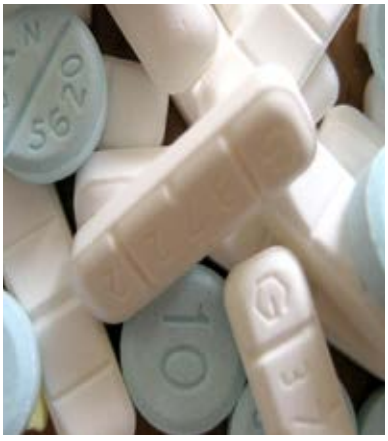
Find this at: http://dx.doi.org/10.1136/bmj.j2941

Study question What is the risk of all cause mortality associated with benzodiazepine initiation in adults?



Methods The researchers carried out a retrospective cohort study using a large US commercial healthcare database. They matched patients initiating benzodiazepines between 2004 and 2013 to non-initiators with a medical visit around the same time (n=1 252 988). To address treatment barriers and confounding, patients were required to have evidence of medication use before the index date and were matched using a high dimensional propensity score that included more than 300 covariates. The risk of all cause mortality was assessed using Cox proportional hazards regression.

Study answer and limitations

Over a six month follow-up, 5061 and 4691 deaths occurred among benzodiazepine initiators versus non-initiators (9.3 *v* 9.4 events per 1000 person years; hazard ratio 1.00, 95% confidence interval 0.96 to 1.04). A 4% to 9% increase in risk was observed for follow-ups of 12 and 48 months and in subgroups of younger patients and patients using short acting agents. Certain relevant clinical information might not have been completely captured in the source data, and this may have led to residual confounding which may have driven the small positive associations observed in selected analyses.

What this study adds This study found either no increase or at most a minor increase in risk of all cause mortality associated with benzodiazepine initiation. If a detrimental effect exists, it is likely to be much smaller than previously reported and to have uncertain clinical relevance.

Funding, competing interests, data sharing This study was funded by the Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA. KFH was supported by a career development grant (K01MH099141) from the National Institute of Mental Health. The authors have no competing interests. No additional data are available.

Risk of mortality associated with benzodiazepine initiation versus non-initiation in unadjusted and high dimensional propensity score matched analyses within six months' follow-up, and in sensitivity and subgroup analyses

	Benzodiazepine initiators				Benzodiazepine non-initiators				
Analysis	No of patients	No of events	Person years	Incidence/1000 person years	No of patients	No of events	Person years	Incidence/1000 person years	Hazard ratio (95% CI)
Main analyses									
Unadjusted	1 686 410	8945	733 918	12.2	1 930 159	5347	772 958	6.9	1.78 (1.73 to 1.85)
1:1 matched	1 252 988	5061	546 435	9.3	1 252 988	4691	500 932	9.4	1.00 (0.96 to 1.04)
Subgroup and sensitivity analyses									
Follow-up duration (months):									
12	1 252 988	7671	986 396	7.8	1 252 988	6552	855 316	7.7	1.04 (1.01 to 1.08)
48	1 252 988	13 532	2 241 015	6	1 252 988	10 299	1 696 159	6.1	1.05 (1.02 to 1.07)
Patient age (years):									
<65	1 156 209	2160	504 932	4.3	1 156 209	1843	462 811	4	1.09 (1.02 to 1.15)
≥65	92 273	2599	39 716	65.4	92 273	2708	36 438	74.3	0.89 (0.85 to 0.94)
Drug duration of action:									
Short acting	1 011 732	4973	440 142	11.3	1 011 732	4370	403 954	10.8	1.06 (1.02 to 1.10)
Long acting	412 976	869	181 483	4.8	412 976	1341	165 450	8.1	0.60 (0.55 to 0.65)