BMJ Open

Presentation and recognition of Suicidal behavior in Dutch general practice 1983-2013 – a dynamic cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2015-010868
Article Type:	Research
Date Submitted by the Author:	15-Dec-2015
Complete List of Authors:	de Beurs, Derek; Nederlands Instituut voor Onderzoek van de Gezondheidszorg, Hooiveld, Mariëtte; NIVEL (Netherlands institute for health services research), Kerkhof, Ad; Vrije Universiteit Amsterdam Faculteit der Psychologie en Pedagogiek, clincial psychology Korevaar, J; Netherlands Institute for Health Services Research (NIVEL), Donker, G; NIVEL, Sentinel practice network
Primary Subject Heading:	Mental health
Secondary Subject Heading:	Epidemiology
Keywords:	Suicide & self-harm < PSYCHIATRY, PRIMARY CARE, EPIDEMIOLOGY

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Presentation and recognition of suicidal behavior in Dutch general practice 1983-2013 – a dynamic cohort study

Derek P. de Beurs, Mariette Hooiveld, Ad J.F.M. Kerkhof, Joke C. Korevaar, Gé A. Donker

Corresponding author:
Derek de Beurs, Netherlands Institute for Health Services Research (NIVEL)
derekdebeurs@gmail.com
Otterstraat 118-124,
3513CR Utrecht

Mariette Hooiveld, Netherlands Institute for Health Services Research (NIVEL),
m.hooiveld@nivel.nl
Ad Kerkhof, department of clinical psychology, VU Amsterdam, ajfm.kerkhof@vu.nl
Joke Korevaar, Netherlands Institute for Health Services Research (NIVEL),
j.korevaar@nivel.nl
Ge Donker, Netherlands Institute for Health Services Research (NIVEL), g.donker@nivel.nl

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Strengths and Limitations

- First study on changes of presentation and recognition of suicidal behavior in primary care in the years 1983-2013
- First study on suicide rates in primary care using joint point regression modeling
- Focus on presentation and recognition of male suicidal behaviour in primary care
- General Practitioners answered questions on suicidal behaviour retrospectively, possibly resulting in re-call bias
- Underreporting of suicidal behaviour may have occurred

Abstract

Objectives:

To analyze changes of presentation and recognition of suicidal behavior in primary care in the years 1983-2013, especially after the recent economic recession.

Settings:

40 general practices in the Netherlands during the period 1983-2013

Primary and secondary outcomes:

Age-adjusted and gender-specific trends in reported suicides (342) and suicide attempts (1614), were analysed using joint-point regression models. Frequency of suicides and suicide attempts were related to reported patient characteristics such as age and history of depression. To analyse change in presentation or recognition due to the financial crisis, we described frequencies for the periods 1983-2003, 2004-2007 and 2008-2013.

Results

Joint-point analyses revealed a significant rise in male suicides from 2008, specifically in the age group of 40-49. Female suicidal behavior showed a steady decrease from 1989-2013. In 63% of the suicides, a history of depression was reported. Almost half of the suicidal patients were in contact with a GP within 30 days before the event. In hindsight, GPs stated during this consultation, suicidal behaviour was a reason for concern in 24% of the cases. A history of depression was less often reported by GPs among patients who died by suicide after 2007.

Discussion

Since 2008, there was a rise in male suicidal behaviour while female suicide behaviour kept on declining. GP's less often reported a history of depression within both males and females that died by suicide after 2007 than before.

Introduction

In the Netherlands, suicides and attempted suicides are registered by general sentinel practices participating in NIVEL Primary Care Database, formerly known as the Dutch Sentinel General Practice Network [1]. After reporting a suicide or a suicide attempt, general practitioners (GPs) fill in additional questionnaires on the demographics, history of depression and characteristics of care provision such as last consultation of the GP of the suicidal patient. Previous analysis found that between 1983 and 2003 the annual number of suicide and suicide attempts decreased by 50% [2]. Also, 53% of those who died because of suicide and 54% of those who attempted suicide had been in contact with their GP in the 30-days period before the event. A history of depression was reported in 60% of these patients. GPs noted that suicide ideation was an important symptom of the depression in 7% of suicidal patients [2, 3]. One of the recommendations from previous studies on NIVEL Primary Care data was that GPs should ask more frequently and persistently for suicidal ideation in depressed patients [2, 4, 5]. This was also one of the recommendations from the Dutch Multidisciplinary Practice Guideline on the Assessment and Treatment of Suicidal Behaviour which was released in 2012 [6]. Another initiative in the last decade to improve recognition of suicidal ideation within depressed patients was the European Alliance Against Depression [7]. Based on the success of a four-level intervention program to improve care for depressed and suicidal patients in Germany, the Netherlands joined the European Alliance against Depression (EAAD) [7] in 2004. An important focus was to improve the attitude and skills of GPs towards recognition and treatment of depressed and suicidal patients via workshops and other educational interventions [7]. In Germany, the program resulted in a sustainable decline in suicidal behavior of 32.4% in the three years after the start of the intervention [8].

In the current study we analyzed trends in incidence of suicides and suicide attempts as registered in the sentinel general practices of NIVEL Primary Care Database during1983-2013. Using joint model analysis, we determined whether the incidence started rising, remained stable or declined. Given the earlier recommendations, and the start of the EAAD in the Netherlands in 2004, we expected to see a decrease in reported suicides and suicide attempts from 2004 until 20007. Comparable to other studies, we expected a rise in incidence of male suicidal behavior in response to the recession [9-11]. As several studies found no relation between a financial crisis and female suicidal behavior[11-14], we expected no significant change for females. Several studies attribute the rise in suicide rate to the increase of more impulsive male suicidal behavior[15, 16]. Therefore we expected that GP's less often reported a history of depression among males that died by suicide after the crisis, when compared to males that died before the crisis.

Methods

In the Dutch health care system, >99% non-institutionalized citizens are enlisted as patients in a practice and the GP acts as a gatekeeper to secondary care. Cases of suicide or attempted suicide were registered by sentinel general practices participating in the NIVEL Primary Care Database [1]. Since 1970, the Dutch Sentinel Practices consists of about 40 general practices with a practice population covering about 0.8% of the Dutch population. The practices are nationally representative by age, gender, geographic distribution and population density.

The participating GPs weekly report about certain illnesses, events and procedures in general practice that cannot be collected from routinely registered data. Since 1979, concerning suicides and attempted suicide cases aged 15 years or older, the GP fills out an additional questionnaire addressing patient characteristics such as age and gender, previous contact with the GP, a history of depression and whether the GP thought suicidal behaviour was a concern in patients who visited the GP 30 days before the suicidal event. The registration included suicides and attempted suicides among all enlisted patients, also when the patient was seen by another GP on duty, was treated at an emergency ward, or

when hospitalised, although underreporting may have occurred in these cases. As we were not able to retrieve the data from 1979-1982, we used the data from the period 1983-2013.

Statistical analysis

To estimate national incidence rates, we applied direct age standardisation, taking the age distribution of the Dutch population in 2011 as the standard [17]. An adjustment factor was applied when estimating incidence rates for incomplete years. We calculated the 3 year moving average to smooth out short term fluctuations and to be able to highlight longer term trends.

To analyse changes in trends of reported suicides and suicide attempts we applied joint point regression models [18], using the Surveillance Epidemiology and End Results statistical software[19]. The software takes trend data (in our case the age adjusted 3 year moving average of suicides or suicide attempts) and fits them to the simplest joint-model that the data allow. The program tests the null-hypotheses of no joint point with the alternative of one or more joint points. Because of the well-established differences in suicidal behaviour between men and women [20], we stratify trend analyses by gender.

Using descriptive statistics, we described the number of suicides and suicide attempts in relation to several patient characteristics such as age and gender. We restrict the analyses to reported suicide(attempts) that where the first report for the individual in order to exclude influences of the results by a limited number of persons with (many) repeated suicide attempts.

To examine change in presentation and recognition of suicidal behaviour by gender before and after the recession, we compared the frequency of patient characteristics by gender of the period 1983-2003 with the period of 2004-2007 and 2008-2013.

As the actual number of events of suicidal behaviour in the last two periods will be relatively low, we will not test for significance, but only describe the data.

Results

Suicide and attempted suicide from 1983 until 2013.

From 1983-2013, data were collected from 1956 patients with (attempted) suicide. 342 patients died because of suicide (229 males, 112 females), and there were 1614 reported suicide attempts (561 males, 1041 females). In figure 1, the 3 years moving average for the number of suicide attempts and suicides, by gender are presented.
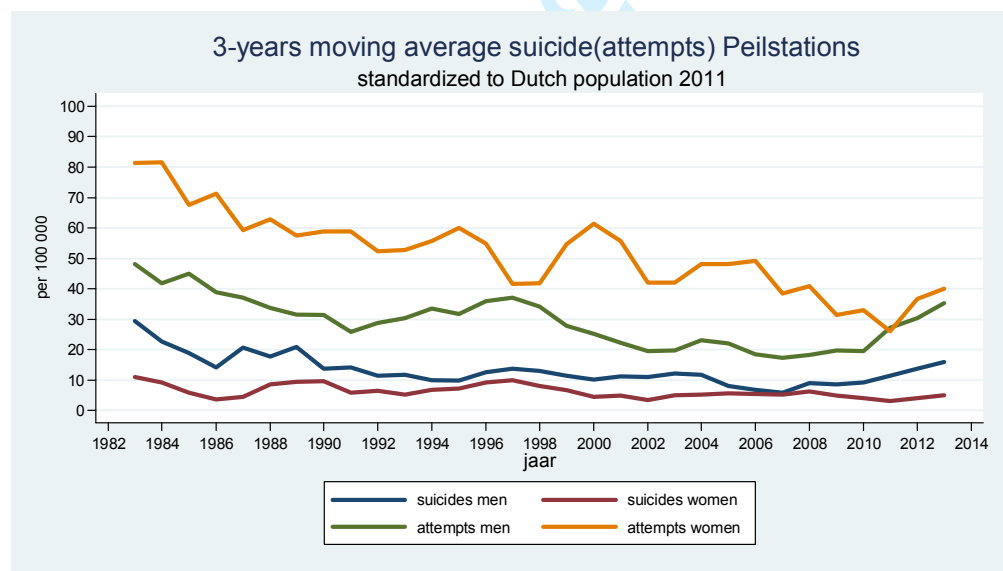

Fig 1: age adjusted 3 years moving average for the number of suicide attempts and suicides, stratified by gender

Trend analysis

Suicide and gender

Male suicides

When analysing incidence of male suicides, two significant trend changes joint points are observed, one in 1994 and one in 2007 (fig 2). After a significant decrease from 1983-1994 (b = -0.06, SE = 0.03, p < 0.001), the trend stabilized from 1994-2003 (b = 0.00, SE = 0.02, p = 0.8). Next, there was a decline, although not significantly, in the period 2003-2007 (b -0.16, SE = 0.1, p = 0.1). From 2007-2013 there was a sudden significant increase (b = 0.32, SE = 0.1, p = 0.008).

3 Joinpoints

Legend:
- Observed
- 1983-1994 APC = -6.41^
- 1994-2003 APC = 0.60
- 2003-2007 APC = -15.60
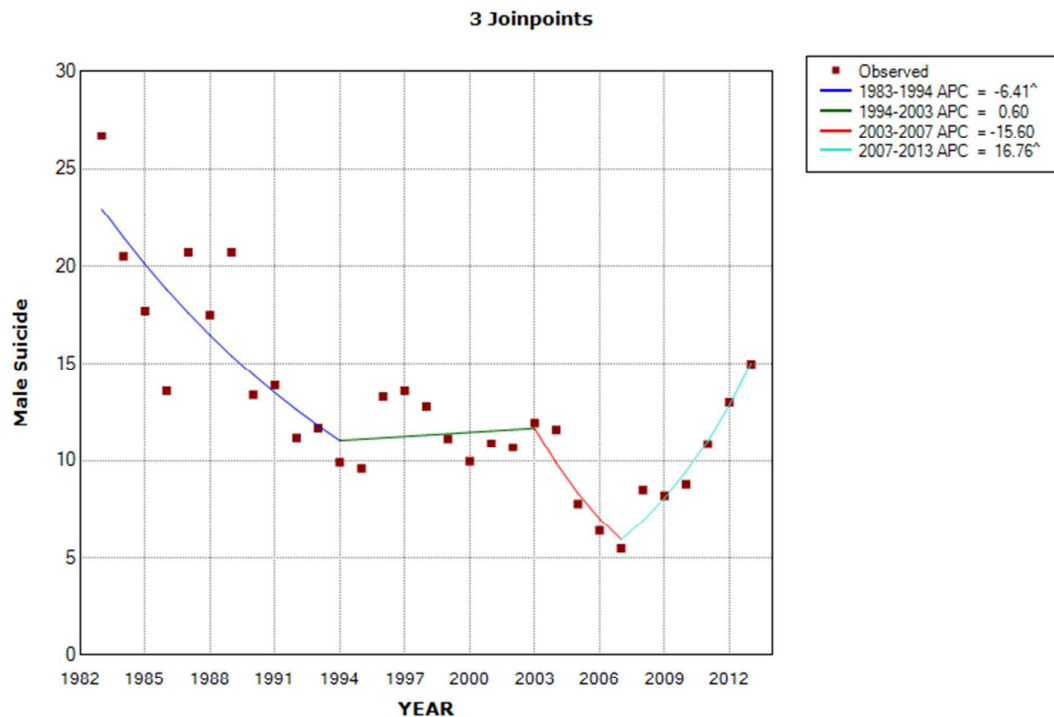- 2007-2013 APC = 16.76^

Fig 2: joint point regression analysis of suicide incidence among men 1983-2013

Male attempts

Compared to male suicides, we find a similar decline in male attempts from 1983-1991 (b = -0.05, SE = 0.01, p < 0.001). From 1991 until 1997 we find a significant rise in incidence (b = 0.1, SE = 0,02, p < 0.001). From 1997 until 2009 there was a decline in incidence, in which the period from 1997-2001 was significant (b = -0.2, SE = 0.06, p = 0.004). Starting from 2009, there is a significant increase (b = 0.19, SE = 0.04, P < 0.001).

Female suicides

Since 1989, there has been a significant decrease of the incidence of female suicides. (b = -0.03, SE = 0.007, p < 0.0001) (fig 3.). Fig 3 does show a non-significant rise in female suicides in 2012-2013.
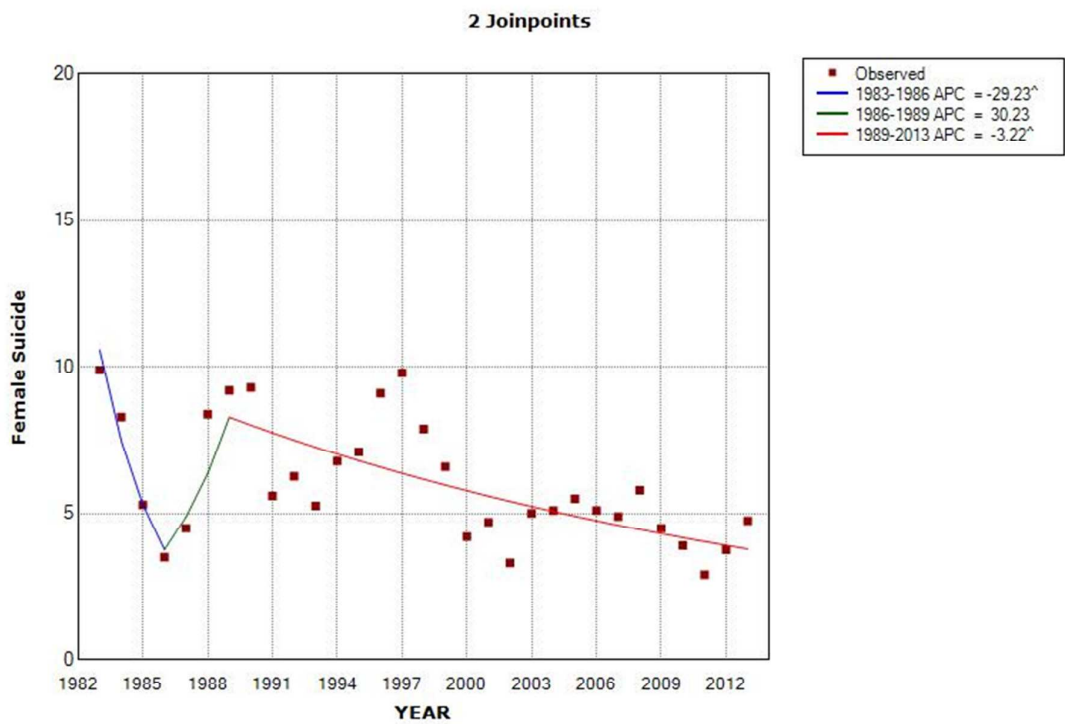

Fig 3: joint point regression analysis of suicide incidence among women 1983-2013

Female attempts

Regarding female attempts, the data showed a constant significant decline over the period 1989-2013 (b = -0.02, SE = 0.002, p < 0.001)

Age distribution

About 50% of the suicides and 65% of the suicide attempts took place in the age group of 20-50. The peak of male suicides and attempts was around the age of 30-39. Female suicides peaked at 40-49 while female attempts peaked between 20-29 (fig 4).
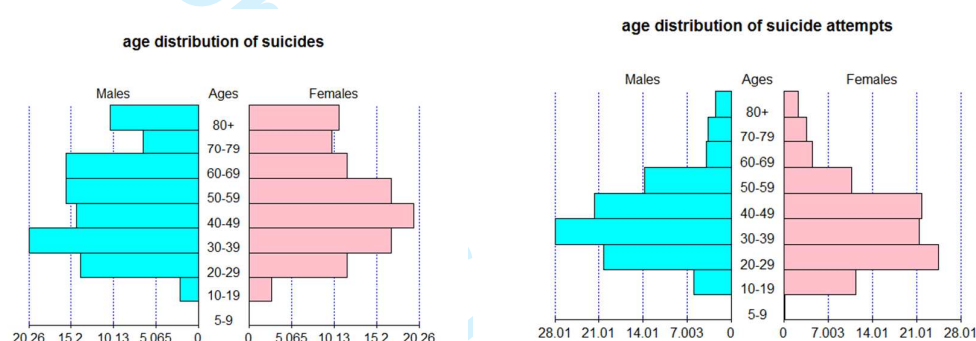

Fig 4: age distribution for suicides and suicide attempts in percentage, split for gender

History of depression, and contact 30 days before event: 1983-2013

In 63% of the patients that died by suicide GPs recalled a history of depression (57% for males, 74% for females), compared to 58% of the suicide attempts (49% for males, 63% for females). Suicide ideation was recalled to be an important feature of the depression of 13% of the suicidal patients. Of the patients with a history of depression, 40% had previously received antidepressants, of which 41% were SSRIs. GPs indicated that 57% of patients (53% men, 60% female) who later would engage in fatal or non-fatal suicidal behaviour had been under treatment by a specialized mental health professional. Almost half of the suicidal patients (48% of the patients who attempted and 49% of the patients who died by suicide) were in contact with a GP within 30 days before the event. In hindsight,

GPs stated that suicidal behaviour was a reason for concern during the consultation in 31% of the cases that died by suicide and in 22% of patients showed non-fatal behaviour within the next 30 days. More than half of the patients that died by suicide lived alone (56% for men, 52% for women). Suicide attempters tended to live with two or more persons (55% for men, 73 % for women).

Suicidal behavior from 1983-2003, 2004-2007 and 2008-2013

Change in Age distribution

Compared to the period before 2007, the peak of male suicidal behaviour shifted from the age group of 30-39 years to the age group of 40-49. The peak of female suicidal behaviour shifted from 20-29 to 40-59 after the crisis. From 2004-2007, GPs more often recalled a history of depression within male patients who died by suicide when compared to 1983-2003 (71% and 59% respectively, table 1). This rate dropped to 46% in the period from 2008-2013. Within females, depression was recognized in 77% of the patients that died by suicide before 2007, compared to 60% within patients that died after the crisis. Additionally, in 2008-2013, there was a decrease in male suicidal patients who had been treated by a mental health professional compared to the years before (44% and 54% respectively). Treatment for female suicidal patients seems to be have increased over the years (from 60% to 67%). Referral rates after a suicide attempt of both men and women increased from 64% in 1983-2003 to 90% in 2008-2013.

	1983-2003	2004-2007	2008-2013

	(suicides = 173, attempts = 432)	(suicides = 20, attempts = 48)	(suicides = 36, attempts = 81)
SUICIDE			
GP recalled history of depression of patient who died by suicide	59%	71%	46%
Patient had been under treatment of mental health professional before suicide	50%	64%	52%
30 days contact before suicide	46%	35%	42%
Suicidal behaviour of concern during last visit before suicide? (% YES)	34%	17%	28%
ATTEMPTED SUICDE			
GP recalled history of depression of patient who attempted suicide	49%	48%	49%
Patient had been under treatment of mental health professional before suicide attempt	54%	59%	41%
30 days contact before suicide attempt? (% YES)	43%	29%	44%
Suicidal behaviour of concern during last visit before attempt? (% YES)	20%	17%	19%
Referred to specialized care after attempt? (% YES)	59%	86%	88%

NB: Number of suicides and suicide attempts over which percentages were calculated may differ from total number due to missing values.

Table 1: Characteristics of male suicidal behaviour over three time periods.

Discussion

We found no significant change in female suicidal behaviour, but a rise in suicidal behaviour since 2008 in males. The study is consistent with national trends in suicidal behaviour [21]. Analogue to the national data, the rise was mainly explained by an increase in male fatal suicidal behaviour around the age of 40-49. As is often argued[22], the rise in middle and older aged male suicidal behaviour might be explained by the economic recession, during which this group was more at risk to lose their job or remain unemployed. Losing one's job, long term unemployment, or being incapable to work due to long-term illness or handicap influences well-known risk factors for suicidal behaviour, such as hopelessness, feelings of defeat, entrapment and lack of future perspective [10, 23-26]. Several authors [27, 28] question the relationship between unemployment and suicide because of other pre-existing potential confounders such as a history of mental illness. However, a meta-analysis [29] demonstrated that unemployment is indeed associated with greater risk of suicide after adjusting for prior mental disorder. Importantly, a recent article showed that a higher suicide rate preceded a rise in unemployment [12]. The authors hypothesise that males more often die because of suicide in response to the anticipated stress of possible unemployment. This might also explain why in our study, a history of depression was less often reported among males that died by suicide after the recession. The suicide act might have been more impulsive, as a result of intense feeling of entrapment, without any earlier overt signs of depression.

We found no significant change in female suicidal behaviour. This is in line with many other studies, that indicate no relation between unemployment or occupational instability and female suicidal behaviour[11, 13, 14, 30]. We did however found that, after the recession, the peak of female suicidal behaviour shifted from the age group of 20-29 years to the age group of 40-59 years. Also, depression was less often recognized for females that committed suicide after 2007. This indicates that although there is no overall rise in suicidal behaviour among females after the recession, suicidal behaviour among the middle aged women indeed seems to have increased. Comparable to male suicidal patients,

after the crisis the GP less often recognized a history of depression, perhaps indicating more impulsive suicidal behaviour among middle aged females as well.

Finally, we did observe a non-significant increase in female suicides from 2010, but follow up research is necessary to analyse whether this is a natural fluctuation or a significant change.

Many suicidal patients in our database had previously been in contact with mental health professionals, which is in line with an earlier study on reports of the Dutch Health Inspectorate [31]. They must have been referred to mental health care by GPs previously for good reasons, for some patients including suicidal ideation. Specialised mental health care therefore has been available and accessible for many patients who later on engaged in fatal and non-fatal suicidal behaviours. We did find that the rate of males that had been under treatment of a mental health professional before the suicidal event decreased after the economic crisis. This might mean that in times of economic recession depression becomes less important as a risk factor to suicide compared to financial hardship.

Limitations

The data was collected in a subsample of 40 general practices participating in the Dutch NIVEL Primary Care Database. Although the sample is nationally representative by age, gender, regional distribution and population density, the sample is relatively small in relation to the low incidence of suicide (attempts).Underreporting of suicidal behaviour may have occurred in our study as cases were only counted after correct ICPC coding of suicidal behaviour (P77). In routine daily practice some incorrect coding may occur. In addition, GPs were asked to record the questionnaire after a notification of suicidal behaviour. This might have influenced their answers, possibly inducing memory bias[32]. GPs might be more susceptible to report noticing risk factors predicting the suicidal behaviour than was actually the case. As we only have data on registered actual suicidal behaviour, we have no idea how the actions of the GP (treatment, medication, referral) effectively prevented suicidal behaviour in other cases. The decline in suicide rates and suicidal behaviour from 2003-2007 among men, and the continuous decline of suicidal behaviour among women over the last 30 years could be the result of better assessment, treatment and referral by GPs. In 63% of the patients who died by

suicide, GPs reported a history of depression. This remains an underestimation of the true prevalence of about 87% diagnosable depression in suicidal patients [33]. Previous studies have shown that training GPs in the recognition of depression can influence the suicide rates [8, 34].

Despite several initiatives [2-4, 7] to increase the assessment of suicide risk in depressed patients, the percentage of cases in which the GP report suicidal ideation as one of the four most important symptoms of depression remained stable over the years (11%). This may be related to the unwillingness of suicidal patients to reveal their suicidal thoughts and plans, or that perhaps at that moment the patient did not have suicidal ideation at all, but developed suicidal plans days and weeks after the last visit. Perhaps this points to GPs finding other symptoms more important, or that they underestimate the predictive power of suicidal communication [35]. In one out of every 4 cases of patients who engaged in suicidal behaviour within 30 days (and questioned about this with hindsight knowledge of the actual suicidal behaviour), GPs identified suicidal ideation as an important concern during the last visit. In many other cases the suicidal behaviour has come as a surprise.

This points towards the difficulty GPs face in responding to depressed patients when suicidal ideation is not overtly presented. The Dutch College of General Health Practitioners(NHG) reports the identification of suicidal ideation within depression as an important part of estimating the severity of the depression [36]. Also, the NHG endorsed the Multidisciplinary Practice Guideline for the Assessment and Treatment of suicidal behaviour. At the same time, GPs generally do not have any formal training in suicide risk identification [37]. Nor in undergraduate, nor in postgraduate education is suicide prevention part of their systematic training. Notwithstanding some local initiatives for postgraduate training, the majority of Dutch GPs did not follow systematic education in this respect [37].

In sum, we saw a rise in male suicidal behaviour while the female suicide behaviours gradually kept on declining. The rise in suicidal behaviour among middle and older aged men is alarming, and asks for new insights in male suicidal behaviour during an economic recession. A study combining cause of death statistics from the national statistics centre with the NIVEL primary care database could inform us on the different health care paths among individuals in the years before the actual suicidal behaviour[38]. This new information on specific risk factors for male suicidal behaviour could help GPs

to earlier and more accurately identify latent suicidal behaviour. For now, we advise GPs to be especially aware of middle aged male patients who are (long term) unemployed, incapacitated or at risk of losing their job or income. We found that more than half of the participants who died by suicide lived alone. In the near future, many more (older) people will be living alone[39, 40]. Especially for men, this is a well-documented risk factor for suicidal behaviour[41-43]. Therefore, GPs should not forget to assess (change in) household composition, when assessing risk for suicidal behaviour. Communities and municipalities may also concentrate on offering special social and sports programmes for these target groups.

In the Netherlands, since 2014, the GP has been given a much more central role in the assessment, treatment and referral of psychiatric patients [44]. The ministry of Health advocates the transition from specialized mental health care to primary care. More psychiatric patients should be treated by the GP and nurses with psychiatric training, so that care can be provided closer to home and at lower cost. Also, chronic psychiatric patients will be treated for a shorter period in specialized mental Health Care, and are encouraged to return to society as soon as possible. These developments, in combination with the ongoing economic recession, are bound to influence the numbers of GP-reported suicides and suicide attempts, and forces the GPs and supporting teams to be more aware of suicidal behaviour. Recently, a multidisciplinary training program focusing on the structural assessment of suicidal behaviour in specialized mental health care led to improved confidence regarding the assessment of suicidal behaviour among professionals, and a quicker recovery of suicidal thoughts among depressed suicidal patients [45, 46]. We argue that a similar structured implementation program in primary care might improve the recognition rate of suicide ideation within depressed patients.

Contributorship statement

DP did the analysis and drafted the manuscript. MH prepared the data for data analysis and checked the analysis. GD has been responsible for the data collection for the last decade. All authors worked on earlier versions of the manuscript and contributed substantially to the text. All approve of the last version to be submitted.

Competing interests

All authors declare to have no competing interests

Data sharing statement

Data can be found via the Dutch Data Achieving and Networked services (DANS)

http://www.nwo.nl/en/about-nwo/organisation/nwo-divisions/dans

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract PAGE 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found PAGE 3-4
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported PAGE 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses PAGE 5
Methods		
Study design	4	Present key elements of study design early in the paper PAGE 5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection PAGE 5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up PAGE5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable PAGE 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group PAGE 5
Bias	9	Describe any efforts to address potential sources of bias PAGE 5
Study size	10	Explain how the study size was arrived at PAGE 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why PAGE 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding PAGE 6
		(*b*) Describe any methods used to examine subgroups and interactions PAGE 6
		(*c*) Explain how missing data were addressed PAGE 6
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses PAGE 6
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed PAGE 7
		(b) Give reasons for non-participation at each stage PAGE 7
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Page11-13
		(b) Indicate number of participants with missing data for each variable of interest Page11-13
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included Page11-13
		(*b*) Report category boundaries when continuous variables were categorized NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Page11-13
Discussion		
Key results	18	Summarise key results with reference to study objectives PAGE14-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias PAGE 15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence PAGE15-16
Generalisability	21	Discuss the generalisability (external validity) of the study resultsPAGE15-16
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Trends in suicidal behaviour in Dutch general practice 1983–2013 – a retrospective observational study

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Trends in suicidal behaviour in Dutch general practice 1983-2013 – a retrospective observational study

Derek P. de Beurs, Mariette Hooiveld, Ad J.F.M. Kerkhof, Joke C. Korevaar, Gé A. Donker

Corresponding author:
Derek de Beurs, Netherlands Institute for Health Services Research (NIVEL)
derekdebeurs@gmail.com
Otterstraat 118-124,
3513CR Utrecht

Mariette Hooiveld, Netherlands Institute for Health Services Research (NIVEL),
m.hooiveld@nivel.nl
Ad Kerkhof, department of clinical psychology, VU Amsterdam, ajfm.kerkhof@vu.nl
Joke Korevaar, Netherlands Institute for Health Services Research (NIVEL),
j.korevaar@nivel.nl
Ge Donker, Netherlands Institute for Health Services Research (NIVEL), g.donker@nivel.nl

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Abstract

Objectives:

To analyze trends in suicidal behaviour as reported by Dutch sentinel general practices from 1983-2013. Second, to examine the relationship between suicidal behaviour and several patient characteristics. Finally, to compare the relationship between suicidal behaviour and patient characteristics before (1983-2007) and after (2008-2013) the start of the crisis.

Setting

40 general practices in the Netherlands during the period 1983-2013

Participants

Patients with an ICPC code of P77 (suicide attempt)

Primary and secondary outcomes

Primary outcomes were age-adjusted and gender-specific trends in reported suicides (342) and suicide attempts (1614). Secondary outcomes were the relationship between suicidal behaviour and age, household composition, history of depression, recognition of suicide ideation, treatment before the suicidal behaviour and contact within the last month before suicidal behaviour for the period 1983-2013. Additionally, separate frequencies for the periods 1983-2007 and 2008-2013 were presented.

Results

Join-point analyses revealed a significant rise in male suicides from 2008 (b = 0.32, SE = 0.1, p = 0.008), and an increase in male suicide attempts since 2009 (b = 0.19, SE = 0.04, P < 0.001). Female suicidal behaviour showed a steady decrease from 1989-2013(b = -0.03, SE = 0.007, p < 0.0001 for female suicide, b = -0.02, SE = 0.002, p < 0.001 for female attempts). Before 2007, a history of depression was reported in 65% (168/257) of the suicides. After the start of the recession, a depression was recognized in 44% (22/50) of the patients that died by suicide.

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Conclusions

Since 2008, there was a rise in the male suicide rate while female suicide behaviour has continued to decline. GPs less often reported a history of depression within patients that died due to suicide after 2007 than before. Training in the early recognition of suicide ideation in depressive patients might improve suicide prevention in primary care.

Strengths and Limitations

- First study on trends of suicidal behaviour in Dutch primary care in the years 1983-2013
- First study on suicide rates in primary care using join point regression modeling
- GPs collected additional information on patient characteristics of suicidal patients.
- GPs answered questions on suicidal behaviour retrospectively, possibly resulting in a re-call bias
- Underreporting of suicidal behaviour may have occurred

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Introduction

The general practitioner (GP) plays an important role in suicide prevention. In many countries, the GP is the first accessible contact for patients with mental health problems, making them important gatekeepers to identify suicidal ideation at an early stage[1]. The integrated motivational volitional model (IVM) argues that patients gradually move from suicidal thoughts (the motivational phase) to actual suicidal behaviour (the volitional phase)[2]. Early identification of suicidal thoughts within general practice can prevent the patient from going further in the suicidal process, and prevent the patient from reaching the volitional phase. In Germany, a multifaceted program that improved the attitude and skills of GPs towards recognition and treatment of depressed and suicidal patients via workshops and other educational interventions resulted in a sustained decline in suicidal behaviour of 32.4% in the three years after the start of the intervention [3 4].

A review found that on average 45% of the suicidal patients had been in contact with their GP in the 30-days period before the suicidal event[5]. However, NIVEL data also showed that risk for suicide was only identified in 31% of the cases, indicating that the early timely recognition of suicidal behaviour is difficult within primary practice[6].

In the Dutch health care system, most of the non-institutionalized citizens are enlisted as patients in a practice and the GP acts as a gatekeeper to secondary care[7]. For mild psychological problems, the GP, supported by a mental health nurse, can offer antidepressants and different forms of psychological counseling. Patients with more severe psychiatric symptoms or an actual psychiatric disorder are referred to specialized mental health care[7]. The availability and accessibility of GPs give them an important preventive function for suicidal behaviour. This is different for example in Belgium, where patients are free to consult any care provider, and GPs were found to be moving back from the first line of care for suicidal patients[8]. Also, compared to patients in the Netherlands, Belgium patients feel there is more stigma associated with consulting their GP for psychological problems[9].

From 2007-2013, Dutch suicide rates have risen by 5% each year, from 1353 suicides in 2007 to 1854 in 2013[10]. The average suicide rate increased from 10 to 11 per 100.000. Although this is often

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attributed to the rise in unemployment, the unemployment rates in the Netherlands only started going up in 2009[10]. The start of an economic recession typically results in more people feeling entrapped, via (the anticipation of) lay-offs, financial problems and increased hopelessness about the future. The IVM model of suicidal behaviour and the recent Dutch multidisciplinary guideline on the assessment and treatment of suicidal behaviour give entrapment a central role in the transition from suicidal thoughts to actual suicidal behaviour[2 11]. Also, during a recession, more people may feel defeated, that they have failed in life, and that they have become a burden upon others. Defeat, failure and perceived burdensomeness are additional crucial elements for suicidal behaviour in both the IVM and the interpersonal psychological theory of suicidal behaviour[2 12].

In the Netherlands, suicides and attempted suicides are registered by general sentinel practices participating in NIVEL Primary Care Database[13]. After reporting a suicide or a suicide attempt, GPs fill in additional questionnaires on the demographics, history of depression and characteristics of care provision such as the last consultation with the GP of the suicidal patient. The last analysis of suicidal behaviour within NIVEL Primary Care Database was done for the period of 1983-2003[7]. In the current study we analyzed trends in incidence of suicides and suicide attempts logged in the NIVEL Primary Care Database during 1983-2013. Using join model analysis, we determined whether the incidence started rising, remained stable or declined over a period of 30 years. Comparable to other studies and in line with the IVM and the IPT, we expected a rise in incidence of suicidal behaviour in response to the global recession which started in 2007[14-16]. As several studies found no relation between a financial crisis and female suicidal behaviour[16-19], we expected no significant change for females. The relationship between patient characteristics such as history of depression and suicidal behaviour will be analyzed for the period 1983-2013. To offer insights into changes of patient characteristics of suicidal patients after the recession we will also present descriptives of patient characteristics and suicidal behaviour separate for the period before and after the recession.

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Methods

Cases of suicide or attempted suicide were registered by sentinel general practices participating in the

NIVEL Primary Care Database [13]. Since 1970, the Dutch Sentinel Practices has consisted of about 40

general practices with a practice population covering about 0.8% of the Dutch population. The

practices are nationally representative by age, gender, geographic distribution and population density.

The participating GPs weekly report about certain illnesses, events and procedures in general practice

that cannot be collected from routinely registered data. Since 1979, concerning suicides and attempted

suicide cases in patients aged 15 years or older, the GP fills out an additional questionnaire addressing

patient characteristics the following patient characteristics: age, gender, household composition,

history of depression, recognition of suicide ideation, treatment before the suicidal behaviour and

contact within the last month before suicidal behaviour. Registration included suicides and attempted

suicides among all registered patients, including when the patient was seen by another GP on duty,

was treated at an emergency ward, or when hospitalised, although underreporting may have occurred

in these cases. We used the data from the period 1983-2013.

Statistical analysis

Primary outcomes

To estimate national incidence rates, we applied direct age standardisation, taking the age distribution

of the Dutch population in 2011 as the standard [20]. An adjustment factor was applied when estimating

incidence rates for incomplete years. We calculated the 3 year moving average to smooth out short

term fluctuations and to be able to highlight longer term trends.

To analyse changes in trends of reported suicides and suicide attempts we applied join point regression

models [21], using the Surveillance Epidemiology and End Results statistical software[22]. The software

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takes trend data (in our case the age adjusted 3 year moving average of suicides or suicide attempts) and fits them to the simplest join-model that the data allow. The program tests the null-hypotheses of no join point with the alternative of one or more join points. Because of the well-established differences in suicidal behaviour between men and women [23], we stratify trend analyses by gender.

Secondary outcomes:

Using descriptive statistics, we described the number of suicides and suicide attempts in relation to the following patient characteristics: age, gender, household composition, history of depression, recognition of suicide ideation, treatment before the suicidal behaviour and contact within the last month before suicidal behaviour. We restricted the analyses to reported suicide (attempts) tp the first report for the individual in order to exclude influences of the results by a limited number of persons with (many) repeated suicide attempts. The relation between patient characteristics and suicidal behaviour is presented as a percentage. For example, when we are interested in the percentage of male suicides, we will divide the number of male suicides with the total number of suicides. To indicate the number of participants with missing data, we will present the number of actual cases (n) with the total available sample data (N) for each variable of interest.

To examine changes in characteristics of suicidal behaviour before and after the recession, we compared the frequency of patient characteristics from 1983-2017 and 2008-2013. As the actual number of events of suicidal behaviour in the period after the recession will be relatively low, we will not test for significance, but only describe the data.

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Results

Suicide and attempted suicide from 1983 until 2013.

From 1983-2013, data were collected on 1956 patients with fatal or non-fatal suicidal behaviour. 342 patients died due to suicide (229 males, 112 females), and there were 1614 reported suicide attempts (561 males, 1041 females). In figure 1, the 3 years moving averages for the number of suicide attempts and suicides, are presented by gender.

Figure one About Here

Fig 1: age adjusted 3 years moving average for the number of suicide attempts and suicides, stratified by gender

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Trend analysis

Suicide and gender

Male suicides

When analysing incidence of male suicides, two significant trend changes join points are observed, one in 1994 and one in 2007 (fig 2). After a significant decrease from 1983-1994 (b = -0.06, SE = 0.03, p < 0.001), the trend stabilized from 1994-2003 (b = 0.00, SE = 0.02, p = 0.8). Next, there was a decline, although not significantly, in the period 2003-2007 (b = -0.16, SE = 0.1, p = 0.1). From 2007-2013 there was a sudden significant increase (b = 0.32, SE = 0.1, p = 0.008).

FIGURE 2 ABOUT HERE

Fig 2: join point regression analysis of suicide incidence among men 1983-2013

Male attempts

Compared to male suicides, we find a similar decline in male attempts from 1983-1991 (b = -0.05, SE = 0.01, p < 0.001). From 1991 until 1997 we find a significant rise in incidence (b = 0.1, SE = 0,02, p < 0.001). From 1997 until 2009 there was a decline in incidence, in which the period from 1997-2001 was significant (b = -0.2, SE = 0.06, p = 0.004). Starting from 2009, there is a significant increase (b = 0.19, SE = 0.04, P < 0.001).

Female suicides

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Since 1989, there has been a significant decrease of the incidence of female suicides. (b = -0.03, SE = 0.007, p < 0.0001) (fig 3.). Fig 3 does show a non-significant rise in female suicides in 2012-2013.

FIGURE 3 ABOUT HERE

Fig 3: join point regression analysis of suicide incidence among women 1983-2013

Female attempts

Regarding female attempts, the data showed a constant significant decline over the period 1989-2013 (b = -0.02, SE = 0.002, p < 0.001)

Patient characteristics and suicidal behaviour: 1983-2013

48% (166/340) of the suicides and 68% (1098/1603) of the suicide attempts took place in the age group of 20-50. The peak of male suicides and attempts was around the age of 30-39 (table 1). Female suicides peaked at 40-49 while female attempts peaked between 20-29.

Of the patients that died due to suicide GPs recalled a history of depression in 63% (194/308) of the cases (57% for males, 74% for females), compared to 58% (871/1503) of the suicide attempts (49% for males, 63% for females). Suicide ideation was recalled to be an important feature of the depression of 13% of the suicidal patients (116/923). GPs indicated that 57% of patients (1039/1825) (53% men, 60% female) who later would engage in fatal or non-fatal suicidal behaviour had been receiving treatment by a specialized mental health professional. Almost half of the suicidal patients (48% (902/1878)) were in contact with a GP within 30 days before the event. In hindsight, GPs stated that suicidal behaviour was a reason for concern during the consultation in 31% (54/175) of the cases that died due to suicide and in 29% (185/834) of patients showed non-fatal behaviour within the next 30 days. 43% (147/340) of the patients that died due to suicide lived alone (42% (95/228) for men, 46%

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(51/111) for women. Suicide attempters lived alone in 30.3% (486/1604) of the cases (36% (203/558) for men, 27% (275/1034) for women).

Suicidal behaviour after 2007

Compared to the period before 2007, the peak of male suicides shifted from the age group of 30-39 years to the age group of 60-69 in the period 2008-2013 (table 1). The median age peak of female suicides shifted from 30-39 to 50-59 after the start of the crisis. The median age of suicide attempt for males rose from 30-39 to 40-49. For female suicide attempts, the median age changed from 20-29 to 50-59. Recognition of a history of depression of male patients who died by suicide decreased from 60% (102/171) of the male patients to 46% (16/35) . For females it decreased from 47% (45/96) to 40% (9/15). The number of male suicidal patients who had been treated before the suicide remained stable (52%, 99/182) after 2007 but decreased for females (table 1).

	MALES			FEMALES		
	1983-2013	1983-2007	2008-2013	**1983-2013**	1983-2007	2008-2013
SUICIDES (N)	**229**	193	36	**112**	97	15
Median age group	**30-39 (46/227)**	30-39 (42/191)	60-69 (11/36)	**40-49 (22/112)**	30-39 (19/97)	50-59 (10/15)
Living alone (% Yes)	**42% (95/228)**	41% (79/192)	44% (16/36)	**46% (51/111)**	47% (45/96)	40% (9/15)
GP recalled history of depression of patient who died by suicide	**57% (118/206)**	60% (102/171)	46% (16/35)	**74% (75/101)**	77% (66/86)	60% (6/15)
Patient had been under treatment of mental health	**52% (108/209)**	52% (99/182)	52% (14/27)	**64% (67/104)**	66% (61/93)	55% (7/11)

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professional before suicide						
30 days contact before suicide	**45% (98/219)**	45% (83/184)	43% (15/35)	**59% (63/107)**	57% (52/92)	73% (11/15)
Suicidal behaviour of concern during last visit before suicide? (% YES)	**31% (34/109)**	33% (31/93)	23% (3/13)	**30% (20/66)**	30% (16/54)	50% (4/8)
ATTEMPTED SUICDE (N)	**561**	480	81	**1041**	929	112
Median age group	**30-39 (156/557)**	30-39(142/475)	40-49 (30/81)	**20-29 (253-1035)**	20-29 (231/923)	50-59 (25/112)
Living alone (% yes)	**36% (203/558)**	34% (166/292)	46% (37/80)	**27%(275/1034)**	25% (234/923)	37% (41/111)
GP recalled history of depression of patient who attempted suicide	**49% (256/524)**	49% (217/445)	49% (39/79)	63% (609/967)	64% (547/861)	58% (62/106)
Patient had been under treatment of mental health professional before suicide attempt	**53% (277/574)**	54% (251/461)	42% (26/63)	**60% (581/975)**	59% (527/896)	68% (54/79)
30 days contact before suicide attempt? (% YES)	**42% (226/540)**	42% (192/462)	44% (34/78)	**52% (512/999)**	52% (462/893)	47% (50/106)
Suicidal behaviour of concern during last visit before attempt? (% YES)	**21% (56/265)**	20% (44/222)	28% (12/43)	**23% (127/563)**	22% (111/509)	30% (16/54)

Table 1: Gender specific characteristics of suicidal behaviour from the period 1983-2013, and split for

1983-2007 and 2008-2013.

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Discussion

Since 2008, there has been a rise in the male suicide rate while female suicide behaviour kept on declining. The rate in male suicide attempt started rising since 2009. The trend found in our study is consistent with national trends in suicidal behaviour [10]. Similarly to the national data, the rise was mainly explained by an increase in male fatal suicidal behaviour around the age of 60-69. As is often argued, the rise in middle and older aged male suicidal behaviour might be explained by the economic recession, during which this group was more at risk of losing their job or remaining unemployed[24]. Losing one's job, long term unemployment, or being incapable to work due to long-term illness or handicap influences well-known risk factors for suicidal behaviour, such as hopelessness, feelings of defeat, entrapment and lack of future perspective [15 25-28]. Several authors [29 30] question the relationship between unemployment and suicide because of other pre-existing potential confounders such as a history of mental illness. However, a meta-analysis [24] demonstrated that unemployment is indeed associated with greater risk of suicide after adjusting for prior mental disorder. Importantly, a recent article showed that a higher suicide rate preceded a rise in unemployment [17]. The authors hypothesise that males more often die because of suicide in response to the anticipated stress of possible unemployment. This might also explain why in our study, a history of depression was less often reported among males who died by suicide after the recession. The suicide act might have been more impulsive, as a result of intense feeling of entrapment, without any earlier overt signs of depression.

We found no significant change in female suicidal behaviour. This is in line with many other studies, that indicate no relation between unemployment or occupational instability and female suicidal behaviour[16 18 19 31]. However, we did find that, after the recession, the peak of female suicidal behaviour shifted from the age group of 20-29 years to the age group of 40-59 years. Also, depression

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was less often recognized for females that died of suicide after 2007. This indicates that although there is no overall rise in suicidal behaviour among females after the recession, suicidal behaviour among the middle-aged women seems to have increased. Comparable to male suicidal patients, after the crisis the GP less often recognized a history of depression, perhaps indicating more impulsive suicidal behaviour among middle aged females as well.

Finally, we did observe a non-significant increase in female suicides from 2010, but follow-up research is necessary to analyse whether this is a natural fluctuation or a significant trend.

Many suicidal patients in our database had previously been in contact with mental health professionals, which is in line with an earlier study on reports of the Dutch Health Inspectorate [32]. They must have been referred to mental health care by GPs previously for good reasons, for some patients possibly including suicidal ideation. Specialised mental health care therefore has been available and accessible for many patients who later on engaged in fatal and non-fatal suicidal behaviours. We observed that the rate of males under treatment of a mental health professional before the suicidal event decreased after the economic crisis. This might mean that in times of economic recession depression becomes less important as a risk factor to suicide compared to financial hardship.

Limitations

The data was collected in a subsample of 40 general practices participating in the Dutch NIVEL Primary Care Database. Although the sample is nationally representative by age, gender, regional distribution and population density, the sample is relatively small consistent with the low incidence of suicide (attempts).Underreporting of suicidal behaviour may have occurred in our study as cases were only counted after correct ICPC coding of suicidal behaviour (P77). In routine daily practice some incorrect coding may occur. In addition, GPs were asked to record the questionnaire after a notification of suicidal behaviour. This might have influenced their answers, possibly inducing memory bias[33]. GPs might be more susceptible to report noticing risk factors predicting the suicidal behaviour than was actually the case.

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The retrospective analysis of GP records following suicide deaths and attempts is a useful means of establishing the ways in which mortality and morbidity from suicide could be prevented or addressed. However the main limitation of this approach is the absence of a comparator group of patients who did not go on to attempt or complete suicide. Therefore, we cannot for example examine whether the percentage of suicidal patients that live alone is relatively high or low compared to other patients. Also, we only have data on registered actual suicidal behaviour, we have no idea how the actions of the GP (treatment, medication, referral) effectively prevented suicidal behaviour in other cases. The decline in suicide rates and suicidal behaviour from 2003-2007 among men, and the continuous decline of suicidal behaviour among women over the last 30 years could be the result of better assessment, treatment and referral by GPs. In 63% of the patients who died by suicide, GPs reported a history of depression. This remains an underestimation of the true prevalence of about 87% diagnosable depression in suicidal patients [34]. Previous studies have shown that training GPs in the recognition of depression can influence the suicide rates [4][35].

Despite several initiatives [3][6][36][37] to increase the assessment of suicide risk in depressed patients, the percentage of cases in which the GP report suicidal ideation as one of the four most important symptoms of depression has remained stable over the years. This does not mean that the GP did not discuss suicide ideation, but that GPs found other symptoms more important. As we know that suicide ideation is an important predictor for future suicidal behaviour, GPs might be trained to learn about the predictive power of suicidal communication [38]. Future studies should ask GP to the routinely record suicidal ideation to give a more complete picture of how often suicidal ideation was discussed with depressed or suicidal patients.

In one out of every 4 cases of patients who engaged in suicidal behaviour within 30 days (and who were questioned about this with hindsight knowledge of the actual suicidal behaviour), GPs identified suicidal ideation as an important concern during the last visit. In many other cases the suicidal behaviour has come as a surprise. This may be related to the hesitation of suicidal patients to reveal their suicidal thoughts and plans, or that perhaps at that moment the patient did not have suicidal ideation at all, but developed suicidal plans days and weeks after the last visit.

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This points towards the difficulty GPs face in responding to depressed patients when suicidal ideation is not overtly presented. The Dutch College of General Health Practitioners (NHG) reports the identification of suicidal ideation within depression as an important part of estimating the severity of the depression [39]. Also, the NHG endorsed the Multidisciplinary Practice Guideline for the Assessment and Treatment of suicidal behaviour. At the same time, GPs generally do not have any formal training in suicide risk identification [40]. Suicide prevention is not part of their systematic training in undergraduate, nor in postgraduate education. Notwithstanding some local initiatives for postgraduate training, the majority of Dutch GPs did not follow systematic training in this respect [40].

The Dutch rise in suicide rate was among the highest in Europe since the crisis. Only Greece showed a higher increase in suicide rate. However, it is good to realize that even in 2013, the Dutch suicide rate is low compared to surrounding countries such as Belgium and Germany. Also, to halt the rise, the ministry of Health has launched a national prevention strategy. Many gatekeepers such as teachers and bailiffs and professionals have been trained in the recognition of suicide ideation. GPs and mental health nurses have had access to e-learning and training since 2014. Future studies will give insight into the effects of these interventions.

To sum up, we saw a rise in male suicidal behaviour while the female suicide behaviours gradually continued to decline. The rise in suicidal behaviour among middle and older aged men is alarming, and asks for new insights in male suicidal behaviour during an economic recession. A study combining cause of death statistics from the national statistics centre with the NIVEL primary care database could inform us on the different health care paths among individuals in the years before the actual suicidal behaviour[41]. This new information on specific risk factors for male suicidal behaviour could help GPs to earlier and more accurately identify latent suicidal behaviour. For now, we advise GPs to be especially aware of middle aged male patients who are (long term) unemployed, incapacitated or at risk of losing their job or income. Also, all reports of suicidal thoughts need to be taken seriously, even if those thoughts are not a dominant feature of the depression. In the near future, many more (older) people will be living alone[42 43]. Especially for men, this is a well-documented risk

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factor for suicidal behaviour[44-46]. Therefore, GPs should not forget to assess (change in) household composition, when assessing risk for suicidal behaviour. Communities and municipalities may also concentrate on offering special social and sports programmes for these target groups.

In the Netherlands, since 2014, the GP has been given a much more central role in the assessment, treatment and referral of psychiatric patients [7]. The Ministry of Health advocates the transition from specialized mental health care to primary care. More psychiatric patients should be treated by the GP and nurses with psychiatric training, so that care can be provided closer to home and at lower cost. Also, chronic psychiatric patients will be treated for a shorter period in specialized mental health are, and are encouraged to return to society as soon as possible. These developments, in combination with the ongoing economic recession, are bound to influence the numbers of GP-reported suicides and suicide attempts, and forces the GPs and supporting teams to be more aware of suicidal behaviour. Recently, a multidisciplinary training program focusing on the structural assessment of suicidal behaviour in specialized mental health care led to improved confidence regarding the assessment of suicidal behaviour among professionals, and a quicker recovery of suicidal thoughts among depressed suicidal patients [47 48]. We argue that a similar structured implementation program in primary care might improve the recognition rate of suicide ideation within depressed patients.

Contributorship statement

DP did the analysis and drafted the manuscript. MH prepared the data for data analysis and checked the analysis. GD has been responsible for the data collection for the last decade. All authors worked on earlier versions of the manuscript and contributed substantially to the text. All approve of the last version to be submitted.

Competing interests

All authors declare to have no competing interests

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Data sharing statement

No additional data available.

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3-years moving average suicide(attempts) Peilstations
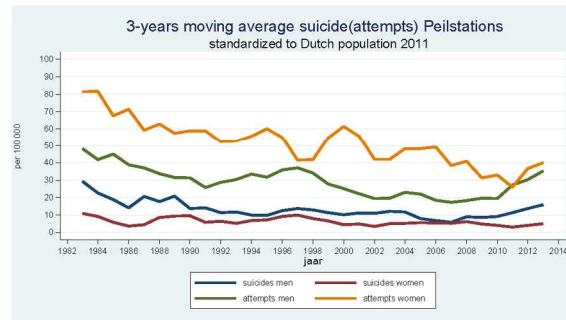standardized to Dutch population 2011

Fig 1: age adjusted 3 years moving average for the number of suicide attempts and suicides, stratified by gender
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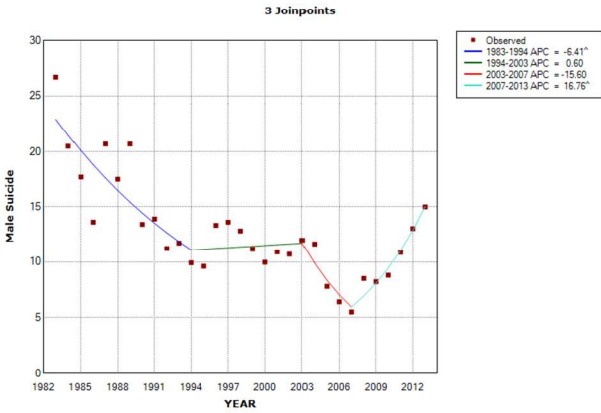51
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Fig 2: join point regression analysis of suicide incidence among men 1983-2013
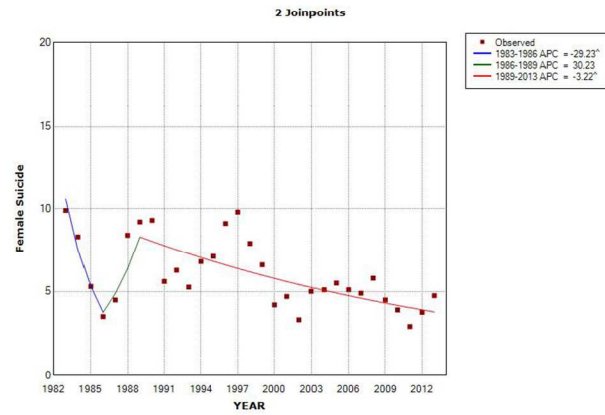210x297mm (127 x 127 DPI)

Fig 3: join point regression analysis of suicide incidence among women 1983-2013
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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract PAGE 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found PAGE 2-3
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported PAGE 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses PAGE 5
Methods		
Study design	4	Present key elements of study design early in the paper PAGE 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection PAGE 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up PAGE 6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable PAGE 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group PAGE 6
Bias	9	Describe any efforts to address potential sources of bias PAGE 6 and discussion: PAGE 15
Study size	10	Explain how the study size was arrived at PAGE 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why PAGE 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding PAGE 6-7
		(*b*) Describe any methods used to examine subgroups and interactions PAGE 6-7
		(*c*) Explain how missing data were addressed PAGE 7
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses Not Applicable
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed PAGE 12-13(Table 1)
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Page12-13(table 1)
		(b) Indicate number of participants with missing data for each variable of interest Page12-13(table 1)
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and

		their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included PAGE 9-11
		(*b*) Report category boundaries when continuous variables were categorized NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Page11-13

Discussion

Key results	18	Summarise key results with reference to study objectives PAGE14-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias PAGE 15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence PAGE 15-17
Generalisability	21	Discuss the generalisability (external validity) of the study results PAGE 15-16

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based PAGE 18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.