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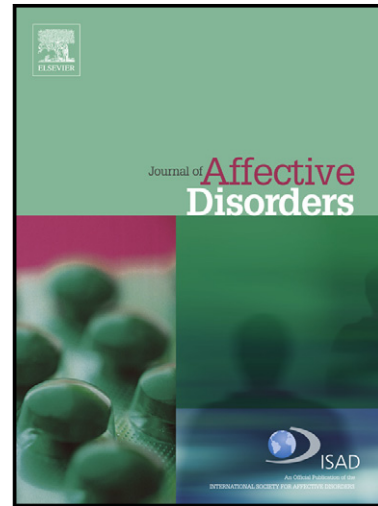
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# Author's Accepted Manuscript

Suicidal ideation and physical illness: does the link lie with depression?

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**Suicidal ideation and physical illness: does the link lie with depression?**

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**ABSTRACT**

**Objective:** Medical illness is a risk factor for suicidality; however, disorder-specific risks are not well-known and these relationships are often explained by major depressive disorder (MDD). We aimed to investigate the relationship between suicidal ideation, MDD and medical illnesses in an age-stratified, population-based sample of men participating in the Geelong Osteoporosis Study.

**Methods:** Suicidal ideation and medical conditions were self-reported. Medical conditions were confirmed by medical records, medication use or clinical data where possible. MDD

was determined using the Structured Clinical Interview for DSM-IV-TR Research Version, Non-patient edition.

**Results:** Of the 907 men, 8.5% reported suicidal ideation. Thyroid disorders (OR 3.85, 95%CI 1.2-12.1), syncope and seizures (OR 1.96, 95%CI 1.1-3.5), liver disorders (OR 3.53, 95%CI 1.1-11.8; younger men only) and alcoholism (OR 2.15, 95%CI 1.1-4.4) were associated with increased odds of suicidal ideation, independent of age and MDD. Major vascular events doubled the odds of suicidal ideation but this was explained by MDD. No association was evident with high medical burden, musculoskeletal disease, metabolic factors, gastrointestinal disorders, headaches, cardiovascular disease, COPD, cancer and psoriasis.

**Conclusion:** Health care professionals should focus on identification, assessment and management of suicidal ideation in the medically ill in patients both with and without MDD.

**Keywords:** comorbidity; depression; medical illness; suicidal ideation

## INTRODUCTION

Although the rate of suicide in Australia has been seen to be dropping over time, over 2,000 Australians complete suicide each year (Large and Nielssen, 2010, Australian Bureau of Statistics, 2012). It has been estimated that the lifetime prevalence of suicidal ideation, suicide plan and suicide attempt is 13.3%, 4.0% and 3.2%, respectively (Johnston et al., 2009), with men more likely to have a successful attempt (13.9 per 100 000 males, versus 3.96 in females) (Large and Nielssen, 2010).

It is well-known that physical and mental illness are strongly linked (Liew, 2012, Roy-Byrne et al., 2008). Over the past 15 years, researchers have systematically investigated the association between suicidality and medical conditions, yet study cohorts are usually restricted to elderly populations (Waern et al., 2002, Juurlink et al., 2004, Quan et al., 2002) or psychiatric/inpatient settings (Furlanetto and Stefanello, 2011, Webb et al., 2012, Botega et al., 2010) with few population-based studies (Druss and Pincus, 2000, Scott et al., 2010). There is also controversy surrounding whether suicide is more likely to be associated with general medical burden rather than a specific condition (Webb et al., 2012, Scott et al., 2010, Waern et al., 2002). Understanding the role of medical conditions in suicidal ideation is complex due to frequent comorbidity with major depressive disorder (MDD). Webb and colleagues demonstrated a higher suicide risk among people affected by coronary heart disease (CHD), stroke, chronic obstructive pulmonary disease (COPD) and osteoporosis, but these associations were explained by adjustment for MDD (Webb et al., 2012). On the other hand, Scott and colleagues recently found physical conditions to be a risk factor for suicidal behaviour independent of mental disorders in a large, population based cross-national sample of 37,915 men and women (Scott et al., 2010).

Considering suicidality as a continuum between passive death-related thoughts and self-inflicted death, we aimed to investigate the association between suicidality, MDD, medical conditions and overall medical burden in a population based sample of men spanning the full adult age range.

## METHOD

### Participants

This study examined data collected from the 5-year follow-up of men participating in the Geelong Osteoporosis Study (GOS) (Pasco et al., 2012), an epidemiological population-based study involving individuals randomly selected from the Commonwealth of Australia Electoral Rolls for the Barwon Statistical Division. A total of 1540 male participants aged 20-97 years were randomly recruited between 2001 and 2006 (67% response), with 978 returning for the 5-year follow up (81% of eligible men). Reasons for non-participation included death (n=141), change of region (n=41), incapacity to provide written informed consent (n=16), inability to be contacted (n=139) and 225 declined participation.

Of the 978 participants, 22 did not provide medical information and 49 participants did not complete the suicidal ideation question and were thus excluded from the current analysis, resulting in a sample of 907 eligible men aged 25-98 years. The study was approved by the Barwon Health Human Research Ethics Committee and written informed consent was obtained from all participants.

**Assessments****Outcomevariable**

Suicidal ideation was determined from a self-reported question eliciting a binary yes/no response: Have you had for a two-week period, recurrent thoughts of death or thoughts of suicide, or a plan for committing suicide?

**Exposure variables**

The presence of medical conditions (lifetime) was self-reported and confirmed by medical records, medication use or clinical data where possible. Low bone mineral density (BMD) self-reported osteoarthritis, ankylosing spondylitis, psoriatic arthritis, rheumatoid arthritis, muscle disease or weakness, adult low trauma fracture and self-reported or medicated gout (agents used in gout or hyperuricaemia) were termed Musculoskeletal disease. Low BMD at the lumbar spine (L2-L4) and/or femoral neck was measured by Dual Energy X-ray Absorptiometry (DXA) using GE Lunar Prodigy (Prodigy GE Lunar Madison, WI, USA) and identified as T-score less than -1 (Henry et al., 2010). Thyroid disorders included self-reported or medicated (thyroid hormones and anti-thyroid agents) hyperthyroidism, hypothyroidism, Graves' disease, Hashimoto's disease, thyroiditis and other unspecified thyroid conditions. A diagnosis of diabetes, defined by self-report or current medication use (oral hypoglycaemic agents and insulin preparations), obesity defined by a body mass index (BMI) greater than or equal to  $30\text{kg/m}^2$ , self-reported or medicated hypercholesterolemia

(cholesterol-lowering agents) and hypertension (self-report and current use of antihypertensive medication/Beta-adrenergic blocking agents/diuretics, or systolic blood pressure of >140mmHg or diastolic blood pressure of >90mmHg) were collectively termed Metabolic risk factors. BMI ( $\text{kg/m}^2$ ) was calculated from measurements of height and weight to the nearest 0.1cm and 0.1kg, respectively. Gastrointestinal disorders encompassed peptic ulcer, chronic gastritis and causes of malabsorption such as pancreatitis, gastric surgery, chronic diarrhoea, irritable bowel syndrome, inflammatory bowel syndrome and coeliac disease. Hypertension (as detailed above) or a combination of self-reported or medicated (beta-adrenergic blocking agents, diuretics, anti-arrhythmic, anti-angina, cardiac inotropic agents, adrenergic stimulants, other cardiovascular agents) stroke, ischaemic cardiomyopathy, arrhythmia and valve and vascular diseases were collectively termed Cardiovascular diseases. Major vascular events included stroke and ischaemic cardiomyopathy. Epilepsy, blackouts, fainting and dizzy spells were grouped together as syncope and seizures. Recurrent headaches included migraine and other recurrent headaches. Diagnoses of asthma, emphysema and chronic bronchitis were grouped as pulmonary disease. Psoriasis was defined by self-report. Liver disease included fatty liver, hepatitis, cirrhosis and liver failure. Malignant tumours including non-melanoma skin cancer were grouped as Cancer. A diagnosis of three or more conditions listed above awarded the term high medical burden.

Past and current alcoholism, including alcohol abuse and dependence and MDD were assessed using the Structured Clinical Interview for DSM-IV-TR Research Version, Non-patient edition (SCID-I/NP) (First et al., 2002). Clinical interviewers were trained in administering the SCID-I/NP and held qualifications in psychology.

Information on lifestyle and other health factors was obtained via questionnaire. Participants were asked to bring in a list of medications or containers to assist with accurate recording of details. Cigarette smoking was documented and grouped as current, past or never. Men participating in light to vigorous activity on a regular basis were classed as active. Socio-economic status (SES) was defined based on quintiles of the Index of Relative Socioeconomic Advantage/Disadvantage (IRSAD), derived from the Socio-Economic Index for Areas (SEIFA) (Australian Bureau of Statistics, 2006).

### **Statistical Analysis**

The prevalence of medical conditions in participants with and without suicidal ideation was analysed using chi square analysis and Kruskal-Wallis, where applicable. Age- and age and MDD- adjusted binary logistic regression were performed to evaluate the relationship between lifetime suicidal ideation and lifetime medical conditions. Interaction terms were tested for effect modification. Post hoc analyses incorporating alcoholism into the models were performed. Statistical analysis was performed using Minitab (version 16; Minitab, State College, PA).

## RESULTS

Seventy-seven men (8.5%) were identified as having a history of suicidal ideation. Characteristics of men with and without suicidal ideation are listed in Table 1. There were no differences in age, BMI, physical activity, smoking status, SES or alcohol consumption between the groups. Males with MDD were more likely to have suicidal ideation than those without.

Table 2 presents both age- and age/MDD -adjusted odds ratios for medical conditions in men with a lifetime history of suicidal ideation. Thyroid disorders were associated with a 4-fold increased odds of suicidal ideation (age adjusted OR 4.0, 95% CI 1.4-11.6,  $p=0.009$ ), which persisted following adjustment for MDD (OR 3.9, 95% CI 1.2-12.1,  $p=0.02$ ). Self-reported syncope and seizures were associated with a two-fold increased risk of suicidal ideation before (age adjusted OR 2.4, 95% CI 1.4-4.1,  $p=0.002$ ) and after adjustment for MDD (OR 2.0, 95% CI 1.1-3.5,  $p=0.02$ ). Major vascular events were associated with a two-fold increased risk of suicidal ideation (age-adjusted OR 2.1, 95% CI 1.1-4.2,  $p=0.03$ ); however, this was attenuated following adjustments for MDD (OR 1.6, 95% CI 0.8-3.4,  $p=0.19$ ). Age was an effect modifier in the association between liver disorders and suicidal ideation. Liver disorders were associated with a 3-fold increase in risk of suicidal ideation among younger men both before (OR 4.0, 95% CI 1.3-11.9,  $p=0.01$ ) and after (OR 3.5, 95% CI 1.1-11.8,  $p=0.04$ ) adjustment for MDD, but not among those aged over 60 years ( $p>0.05$ ). Alcoholism was associated with an increased risk of suicidal ideation both before (OR 3.2, 95% CI 1.7-6.2),  $p<0.001$ ) and after (OR 2.2, 95% CI 1.1-4.4,  $p=0.04$ ) adjusting for MDD.

Further adjustments for BMI, physical activity, smoking status, SES, alcohol consumption and alcoholism did not impact on the odds ratios.

There was no association between suicidal ideation and musculoskeletal disease, metabolic risk factors, gastrointestinal disorders, recurrent headaches, cardiovascular diseases, pulmonary disease, cancer, psoriasis and high medical burden (all  $p > 0.05$ ).

## DISCUSSION

Our data demonstrate that suicidality is associated with several medical conditions; thyroid disorders, syncope and seizures, alcoholism and liver disorders among younger men only, independent of age, MDD, sociodemographic factors and other lifestyle factors. There were no associations detected between suicidality and musculoskeletal disease, metabolic risk factors, gastrointestinal disorders, recurrent headaches, cardiovascular diseases, pulmonary disease, cancer, psoriasis and high medical burden and the significant relationship between suicidality and major vascular events was lost following adjustment for MDD.

The high odds of suicidality in men with thyroid dysfunction and young men with liver disorders, corroborate recent data (Duval et al., 2010, Kristiansen et al., 2011). Similarly, our results confirm previous observations of a positive association between suicidality and neurological disorders such as blackouts, dizzy spells and epilepsy (Christensen et al., 2007), and alcohol abuse and dependence (Clark, 2003), regardless of a diagnosis of depression. It is notable that Clark suggested that alcoholism can lead to suicidal behaviour in an indirect

way by affecting mood, but also in a direct way by enhancing impulsivity (Clark, 2003). However, our results show that the association between medical conditions and suicidality is independent of alcohol abuse/dependence. The relationship between major vascular events and suicidal ideation was influenced by MDD. This result supports that by Scott and colleagues who reported a 2.7 fold increased risk of planned suicide attempts amongst those with past history of stroke/heart attack was not significant after adjusting for mental disorders in their analysis of World Mental Health surveys (Scott et al., 2010).

There was no evidence of an increased odds of suicidal ideation associated with high medical burden; being in accordance with Webb and colleagues who reported that heightened risk of suicide was associated with multiple physical diseases for women only (Webb et al., 2012). However, in another study, a high overall medical burden has been associated with an almost threefold increase in rate of self-inflicted death in elderly men (Waern et al., 2002). It is noteworthy that cut-off points differed between the studies; high medical burden was categorised as 3 or more and 10 or more medical disorders, respectively.

Our results confirm previous data showing no association between suicidality and metabolic risk factor such as diabetes, hypertension and obesity (Harris and Barraclough, 1994) and gastrointestinal disorders such as peptic ulcer (Quan et al., 2002) and raise questions regarding other known associations with cardiovascular disease (Larsen et al., 2010,

Lossnitzer et al., 2009), COPD (Goodwin, 2011), psoriasis (Gupta and Gupta, 1998), cancer (Scott et al., 2010) and recurrent headaches (Scott et al., 2010).

Diseases were grouped based on organs/systems affected in order to give sufficient power for analyses, therefore examining larger groups rather than individual illness. This may help to explain the differences between our observations and those of others. For example, it has been previously reported that osteoarthritis is protective against suicidal ideation whereas osteoporosis is a risk factor (Webb et al., 2012); however, in our analysis these diseases were pooled reporting no significant association.

Reasons for the relationship between suicide and medical illness are still unknown and explanatory pathways are likely to be different for different conditions. Depression is a possible explanation, however, life-threatening characteristics of the condition, lack of social support/coping capacities (Marusic and Goodwin, 2006), functional status (Kaplan et al., 2007), subjective perception of the illness (Olfson et al., 1996) or chronic pain (Purcell et al., 1999) are also potential mechanisms.

It is necessary to note the methodological characteristics of the study. Strengths include the use of a randomly-selected population-based sample of men spanning the full adult age range, thus allowing generalization of our findings to the adult population and assessment of possible age-related associations. Suicidality has been previously shown to differ between elderly and young physically-ill patients (Viilo et al., 2005). Furthermore, self-reported data

were confirmed by medical records, medication use or clinical data where possible and a gold standard tool was used to assess mood and alcohol use disorders. Limitations of our study include potential recall bias, healthy participant bias and the absence of illness severity and functional disability. It is possible that the relationship between suicidal ideation and medical illness is driven by severity of illness rather than the physical disease per se. Although the total sample size was moderate, the small size of some of the subgroups of medical conditions, albeit likely to be representative of the prevalence of the medical condition in the general population, may have limited the power to detect a difference between the groups. Furthermore, medication effects that may induce self-harm ideation have not been taken into consideration. We evaluated self-reported passive and active death-related thoughts through a question with a binary (yes/no) response, rather than using a detailed rating scale. Furthermore, we investigated suicidal thoughts rather than suicidal behaviour as data on suicide attempt and completed suicides were not available. It is estimated that only a small proportion of individuals who exhibit suicidal ideation go on to attempt suicide. However, desire of death, suicidal ideation and suicide planning are main predictors of suicide behaviour (Baca-Garcia et al., 2011). Finally, the cross-sectional nature of our study does not enable conclusions about causal directionality, but we can speculate that there might be a reciprocal relationship between health status and self-harm ideation.

Past research has shown that many patients who commit suicide have seen their primary care physician within one month (Luoma et al., 2002) and often within the week of their death (Conwell, 1997) with many physicians unaware of their patients' intentions (Murphy,

1975). Suicidality, including in its cognitive expression, is a condition often independent of a depressive syndrome, and thus it is a responsibility of any clinician monitoring a patient's health, both physical and mental. In light of this, primary care physicians should be trained in screening patients for suicidal ideation, both active and passive. In addition, information and awareness programs should be implemented at the level of the general population to educate and reduce stigma surrounding suicidality. Considering desire for death, suicidal ideation and suicidal planning as elements on a continuum, we suggest that a correct assessment and management of these factors could improve patients' quality of life, and have the capacity to prevent the progression to the last step represented by completed suicide. In conclusion, our data suggest that suicidality is associated with several medical conditions outside of hospital or psychiatric settings. Thus, awareness of this relationship and identification and management of suicidal ideation should be a priority.

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**Table 1. Characteristics between men with or without lifetime history of suicidal ideation. Values are given as median (interquartile range) or n (%).**

Medical Condition (ever)	Total n=907	Suicidal ideation (ever)		p value	
		Yes n=77	No n=830		
Age at interview(yr), median (IQR)	59.6 (45.7, 73.2)	56.1 (44.4,68.3)	60.0 (45.7, 73.5)	0.15	
Major Depressive Disorder	133 (14.8%)	39 (52.0%)	94 (11.4%)	<0.001	
BMI (kg/m <sup>2</sup> ), median (IQR)	27.1 (24.7, 29.7)	26.8 (24.3, 30.2)	27.1 (24.7, 29.6)	0.86	
Physical Activity (active)	650 (71.7%)	54 (70.1%)	596 (71.9%)	0.74	
Smoking (current)	98 (10.8%)	10 (13.0%)	88 (10.6%)	0.53	
Socioeconomic Status (IRSAD)	Quintile 1 (low)	144 (15.9%)	14 (18.2%)	130 (15.7%)	0.23
	Quintile 2	186 (20.5%)	18 (23.4%)	168 (20.2%)	
	Quintile 3	179 (19.7%)	10 (13.0%)	169 (20.4%)	
	Quintile 4	195 (21.5%)	22 (28.6%)	173 (20.8%)	
	Quintile 5	203 (22.4%)	13 (16.9%)	190 (22.9%)	
Alcohol consumption	0	93 (10.5%)	8 (10.5%)	85 (10.5%)	0.41
	1-2 glasses/day	341 (51.0%)	24 (31.6%)	317 (39.1%)	
	≥3 glasses/day	452 (38.5%)	44 (57.9%)	408 (50.4%)	
Musculoskeletal disease	679 (76.1%)	60 (79.0%)	619 (75.9%)	0.55	
Thyroid disorders	21 (2.3%)	5 (6.5%)	16 (1.9%)	0.01	
Metabolic risk factors	636 (90.1%)	54 (88.5%)	582 (90.2%)	0.67	
Gastrointestinal disorders	158 (17.4%)	14 (18.2%)	144 (17.4%)	0.85	
Recurrent headaches	48 (5.3%)	7 (9.1%)	41 (4.9%)	0.12	
Syncope and seizures	150 (16.5%)	22 (28.6%)	128 (15.4%)	0.003	
Cardiovascular disease	575 (81.8%)	49 (75.4%)	526 (82.5%)	0.16	
Major vascular events	130 (14.3%)	15 (19.5%)	115 (13.9%)	0.19	
Pulmonary disease	175 (19.3%)	15 (19.5%)	160 (19.3%)	0.97	
Liver disorders	55 (6.1%)	8 (10.4%)	47 (5.7%)	0.10	

<b>Age &lt;60yo</b>	18/459 (3.9%)	5/44 (11.4%)	13/415 (3.1%)	0.007
<b>Age ≥60yo</b>	37/448 (8.3%)	3/33 (9.1%)	34/415 (8.2%)	0.86
<b>Cancer</b>	157 (17.3%)	16 (20.8%)	141 (17.0%)	0.40
<b>Alcoholism</b>	65 (7.2%)	14 (18.2%)	51 (6.1%)	<0.001
<b>Psoriasis</b>	39 (4.3%)	3 (3.9%)	36 (4.3%)	0.86
<b>High medical burden</b>	358 (48.6%)	35 (52.2%)	323 (48.2%)	0.53

Missing data: MDD n=10, BMI n=27, Physical Activity n=1, Smoking n=3, Musculoskeletal disease n=15, Metabolic risk factors n=201, Cardiovascular diseases n=204, High medical burden n=170

**Table 2. Age- and MDD/age-adjusted odds ratios for physical illness in men with a lifetime history of suicidal ideation.**

	Suicidal ideation			
	Model	Odds ratio	95% CI	p value
<b>Musculoskeletal disease</b>	I	1.29	0.72 – 2.31	0.40
	II	1.23	0.65 – 2.31	0.53
<b>Thyroid disorders</b>	I	4.04	1.42 – 11.55	0.01
	II	3.85	1.22 – 12.13	0.02
<b>Metabolic risk factors</b>	I	0.95	0.41 – 2.20	0.90
	II	0.91	0.35 – 2.35	0.84
<b>Gastrointestinal disorders</b>	I	1.15	0.62 – 2.13	0.66
	II	1.04	0.54 – 1.99	0.91
<b>Recurrent headaches</b>	I	1.99	0.86 – 4.62	0.11
	II	1.52	0.61 – 3.76	0.37
<b>Syncope and seizures</b>	I	2.38	1.39 – 4.07	0.002
	II	1.96	1.10 – 3.50	0.02
<b>Cardiovascular disease</b>	I	0.79	0.42 – 1.49	0.47
	II	0.76	0.37 – 1.55	0.45
<b>Major vascular events</b>	I	2.11	1.07 – 4.19	0.03
	II	1.63	0.78 – 3.40	0.19
<b>Pulmonary disease</b>	I	1.01	0.56 – 1.82	0.98
	II	0.79	0.41 – 1.51	0.48
<b>Liver disorders &lt;60yo*</b>	I	3.97	1.32 – 11.93	0.01
	II	3.53	1.06 – 11.81	0.04
<b>Liver disorders ≥60yo*</b>	I	1.06	0.30 – 3.71	0.93
	II	0.56	0.14 – 2.27	0.42
<b>Cancer</b>	I	1.54	0.83 – 2.85	0.17
	II	1.80	0.93 – 3.49	0.08
<b>Alcoholism</b>	I	3.23	1.68 – 6.20	<0.001

	II	2.15	1.05 – 4.40	0.04
<b>Psoriasis</b>	I	0.95	0.29 – 3.18	0.94
	II	0.80	0.22 – 2.88	0.74
<b>High medical burden</b>	I	1.53	0.85- 2.77	0.16
	II	1.09	0.57 – 2.06	0.80

Model I: Age-adjusted    Model II: Age / MDD-adjusted

\* Alcohol consumption-adjusted

### Conflict of interest

Livia Sanna, Amanda L Stuart and Mark A Kotowicz have no conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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#### **Author contribution**

LS and AS were involved in the conception and design of the study, analysis of data and interpretation of data. JP, MK and LW were involved in the conception and design of the study and interpretation of data. MB and PG were involved in the interpretation of data. All authors were involved in the drafting, revision process and gave final approval of the published version of the manuscript

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