

# Chronic widespread pain and increased mortality: biopsychosocial interconnections

Jose A P Da Silva,<sup>1</sup> Rinie Geenen,<sup>2</sup> Johannes W G Jacobs<sup>3</sup>

Chronic widespread pain (CWP) is associated with excess mortality. Robust evidence is provided in *ARD* by a study that included over half a million participants and a meta-analysis.<sup>1</sup> This adds to the (already overwhelming) recognised burden of CWP and imposes an additional urgency in improving our understanding and management of the condition. Reducing excess mortality in patients with chronic pain requires an accurate knowledge of relevant mechanisms and mediators. Previous research and this new study indicate that this excess mortality is, to a large extent, explained by lifestyle factors such as decreased physical activity, increased body mass index, unhealthy diets and smoking. In this editorial, we will offer arguments and evidence emphasising the need to also take account of psychological factors to explain the link between CWP and early death.

## BIOPSYCHOSOCIAL MODEL OF CHRONIC PAIN

Decades of research led to the current concept that chronic pain encompasses multiple and mutually interacting biological, psychological and social factors. These include—but are not limited to—nature of pain, peripheral and central pain processing mechanisms, physical disability, sleep disturbance, obesity, smoking, alcoholism and other health risks, psychological resilience and vulnerabilities (emotions, cognitions, behaviour) and social factors (work, support, facilities, financial resources). Relations between all factors of this biopsychosocial model are recognised to be dynamic and reciprocal, with mutually influencing pathways similar to a hanging mobile toy, in which

movement of one component may induce change in all others and back. The weight of the distinct factors differs between individuals.

Psychological factors are important players in this context. To start with, they are core determinants of unhealthy lifestyles that turned out to be important in the recent study.<sup>1</sup> For instance, reduced physical activity has been shown to be influenced by fear of movement-related pain (kinesiophobia)<sup>2</sup> and by catastrophising cognitions (ie, rumination, magnification and helplessness).<sup>3</sup> Lifestyle factors including unhealthy diet, excess weight and smoking are also (reciprocally) associated with psychological determinants. Thus, addressing the lifestyle factors contributing to increased mortality would certainly require consideration of the psychological dimensions affecting their adoption and correction. However, the potential roles of psychological dimensions in the link between CWP and mortality are more complex.

## PSYCHOLOGICAL VULNERABILITIES PREDICT EXCESS MORTALITY

Depression has been associated with increased all-cause mortality in a large variety of settings, from the general population (relative risk (RR) 1.52<sup>4</sup>) to different disease conditions. Especially in cardiovascular disease, meta-analyses have demonstrated an association between depressive symptoms and the incidence of coronary events (RR 1.81<sup>5</sup>), myocardial infarction (RR 1.32<sup>6</sup>) and stroke (RR 1.45<sup>7</sup>). Psychological stress and depression have also been associated with a higher incidence,<sup>8</sup> faster progression<sup>9</sup> and increased mortality<sup>10</sup> of cancer.

In a hallmark study,<sup>11</sup> it was shown that depression predicted risk of death in older persons. Early death was more likely in major than minor depression, but risk of death was still significantly higher in minor depression, even after correction for age, education level, chronic disease, smoking, obesity and sedentary lifestyle. In a study from the UK, over 68 000 members of the general population aged

35 years and over, at baseline free of cardiovascular disease and cancer, were included and followed up for an average of 8.2 years, accumulating more than 8000 deaths. A dose–response relation between intensity of psychological distress at baseline and mortality was shown, which remained significant after controlling for age, gender, comorbidity and behavioural and socioeconomic factors.<sup>12</sup> Of note, this association was observed across the full range of distress, including people enduring common, subclinical levels of distress, who would not usually require mental health assistance.

Neuroticism has been directly and indirectly associated with a negative impact on a variety of health dimensions,<sup>13</sup> including all-cause mortality.<sup>14 15 16</sup> In the UK Health and Life-Style Survey publication of 2007,<sup>17</sup> 1 SD increase in neuroticism was associated with a 9% HR 1.09 (95% CI 1.03 to 1.16) increased risk of mortality from all causes.

## PSYCHOLOGICAL RESILIENCE PROMOTES LONGEVITY

Conversely, a variety of resilience factors has been identified that protect against early death. We will discuss optimism as an example of a cognition, positive affect and social support.

In a pivotal study, optimism was measured in a sample of 7007 college students.<sup>18</sup> Forty years later, 91.1% of the most pessimistic students were still alive as compared with 94.1% of the most optimistic group. Similar results were observed in a recent publication of the Nurses Health Study<sup>19</sup> involving more than 70 000 participants: a higher degree of optimism was associated with a lower mortality risk, which remained significant after adjustment for sociodemographic confounders, health behaviours, health conditions and depression (HR 0.91, 95% CI 0.85 to 0.97). The associations were verified for various causes of death, including cancer, heart disease, stroke, respiratory disease and infection. Data from a cohort of 602 Dutch elders, followed for 9 years, corroborated the view that optimism is associated with increased longevity.<sup>20</sup>

Also positive affect has been associated with increased longevity.<sup>21 22</sup> A truly prospective study analysed handwritten biographies of 180 catholic nuns composed when the sisters joined the congregation at a mean age of 22.<sup>23</sup> Emotion words in the biographies were counted and related to survival between ages 75 and 90. The results showed a

<sup>1</sup>Department of Rheumatology, Faculty of Medicine and University Hospital, Coimbra, Portugal

<sup>2</sup>Department of Psychology, Utrecht University, Utrecht, Netherlands

<sup>3</sup>Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands

**Correspondence to** Professor Jose A P Da Silva, Department of Rheumatology, Faculty of Medicine and University Hospital, 3000-075 Coimbra, Portugal; jdasilva@ci.uc.pt

strong positive correlation between the number and variety of positive emotional expressions in the early life biographies and longevity in later life, resulting in a 2.5-fold difference between the lowest and highest quartiles (figure 1). An important aspect of this study is that the nuns shared a very similar lifestyle, thus reducing its potential confounding role in the observations.

Findings of a pioneering study showed that social support predicted 30-month longevity in an elderly community population, even after controlling for age, sex, race, economic status, physical health status, self-care capacity, depressive symptoms, cognitive functioning, stressful life events and smoking.<sup>24</sup> This finding has been consistently replicated in all kinds of groups. An interesting prospective study on mortality showed that providing social support may be even more beneficial than receiving it.<sup>25</sup>

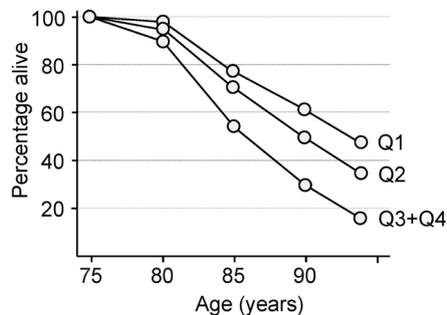
Thus, overall, studies show that psychological vulnerability factors predict mortality but also that psychological resilience predicts longevity. All of these psychological factors are, to a certain extent, amenable to change, but how do they link CWP and mortality?

### PSYCHOLOGICAL DIMENSIONS OF CWP

Most accumulated evidence indicates that CWP is associated with a high prevalence of the vulnerability factors and a significant scarcity of the resilience factors described above. CWP has been consistently associated with an increased prevalence of a number of distressful psychological conditions, with emphasis on depression, anxiety and 'overall' negative affect.<sup>26 27 28</sup> The annual prevalence of major depressive disorder among patients with fibromyalgia has been estimated at 22%, which is three times higher than in individuals without fibromyalgia.<sup>29 30</sup> Other studies report even higher prevalence estimates.

Although CWP seems not strictly linked to a *specific* type of personality,<sup>31</sup> some studies indicate that fibromyalgia is associated with higher rates of neuroticism.<sup>32 33 34</sup> We have shown that healthcare professionals are able to distinguish patients with fibromyalgia from healthy controls, based solely on a limited set of items extracted from a personality profile, most being related to neuroticism.<sup>35</sup>

Depression, anxiety and neuroticism have well-established positive correlations with the prevalence and severity of pain, comorbid symptomatology and disability, in patients with CWP and in the general population.<sup>36 37 38</sup> Psychosocial



**Figure 1** Positive emotion expression at average age 22 and survival after age 75 years. Q1: highest quartile of number of positive emotion sentences; Q2: second highest quartile; Q3+Q4: quartiles 3 and 4 together (because of overlap), reflecting lowest number of sentences with positive emotions. Adapted from Danner *et al.*<sup>23</sup>

distress and stress have been identified as a predictor of new-onset CWP,<sup>39 40</sup> and neuroticism has been shown to predict joint pain even over 23 years.<sup>41</sup>

Conversely, patients with CWP seem to present lower levels of resilience factors such as positive affect<sup>42 43</sup> and social support.<sup>44 45 46</sup> All of these risk and resilience factors have demonstrated correlations with daily intensity of fibromyalgia symptoms and have been the object of promising intervention studies in this context.

### CLINICAL IMPLICATIONS

The results presented by Macfarlane *et al* reinforce the evidence that CWP is associated with increased mortality of all causes, underlining the importance of developing our understanding of this condition to improve the care we provide to these patients. The complexity of the potential causative interactions underlying these observations cannot be overexpressed. Our editorial emphasises the importance of also attending to the psychosocial domains of CWP and their multifaceted potential consequences, including the mediation between CWP and increased mortality. This claim neither refutes the importance of lifestyle factors nor does it exclude the participation of yet additional risk factors, such as the adverse effects of non-steroidal anti-inflammatory drugs and other medications commonly used in this clinical context. The socioeconomic context also continues to deserve attention as it has been associated with both the prevalence of CWP<sup>47 48</sup> and with higher overall cardiovascular and cancer mortality.<sup>49</sup> Similar observations apply to sleep deprivation.<sup>50</sup>

We stress the potential importance of psychological domains, as they appear to have key influences in all 'phases' of these complex interactions, from the origin or maintenance of CWP, to the emotional and behavioural response to pain, the adoption of unhealthy lifestyles and the overall risk of death.

This is especially important in view of the efficacy of psychological therapies on CWP and its psychological correlates sleep problems, depression, functional status and catastrophising.<sup>51</sup> A recent population-based intervention study<sup>52</sup> demonstrated that a depression management programme significantly improved the long-term survival among older adults with high levels of medical comorbidity, which supports the view that targeting depression and other psychological correlates of CWP might decrease early mortality.

### CONCLUSION

CWP should be seen as a biopsychosocial condition requiring a biopsychosocial understanding and therapeutic approach.

**Contributors** All authors contributed equally to the text through provision of ideas, writing, discussing and editing.

**Competing interests** None declared.

**Provenance and peer review** Commissioned; externally peer reviewed.

© Article author(s) (or their employer(s) unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.



**To cite** Da Silva JAP, Geenen R, Jacobs JWG. *Ann Rheum Dis* 2018;**77**:790–792.



► <http://dx.doi.org/10.1136/annrheumdis-2017-211476>

*Ann Rheum Dis* 2018;**77**:790–792.  
doi:10.1136/annrheumdis-2017-211893

### REFERENCES

- Macfarlane GJ, Barnish MS, Jones GT. Persons with chronic widespread pain experience excess mortality: longitudinal results from UK Biobank and meta-analysis. *Ann Rheum Dis* 2017;**76**:1815–22.
- Vlaeyen JW, Crombez G, Linton SJ. The fear-avoidance model of pain. *Pain* 2016;**157**:1588–9.
- Sullivan MJ, Rodgers WM, Wilson PM, *et al.* An experimental investigation of the relation between catastrophizing and activity intolerance. *Pain* 2002;**100**:47–53.
- Cuijpers P, Vogelzangs N, Twisk J, *et al.* Comprehensive meta-analysis of excess mortality in depression in the general community versus patients with specific illnesses. *Am J Psychiatry* 2014;**171**:453–62.

- 5 Nicholson A, Kuper H, Hemingway H. Depression as an aetiological and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies. *Eur Heart J* 2006;27:2763–74.
- 6 Meijer A, Conradi HJ, Bos EH, et al. Adjusted prognostic association of depression following myocardial infarction with mortality and cardiovascular events: individual patient data meta-analysis. *Br J Psychiatry* 2013;203:90–102.
- 7 Pan A, Sun Q, Okereke OI, et al. Depression and risk of stroke morbidity and mortality. *JAMA* 2011;306:1241–9.
- 8 Chida Y, Hamer M, Wardle J, et al. Do stress-related psychosocial factors contribute to cancer incidence and survival? *Nat Clin Pract Oncol* 2008;5:466–75.
- 9 Spiegel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry* 2003;54:269–82.
- 10 Pinquart M, Duberstein PR. Depression and cancer mortality: a meta-analysis. *Psychol Med* 2010;40:1797–810.
- 11 Penninx BW, Geerlings SW, Deeg DJ, et al. Minor and major depression and the risk of death in older persons. *Arch Gen Psychiatry* 1999;56:889–95.
- 12 Russ TC, Stamatakis E, Hamer M, et al. Association between psychological distress and mortality: individual participant pooled analysis of 10 prospective cohort studies. *BMJ* 2012;345:e4933.
- 13 Lahey BB. Public health significance of neuroticism. *Am Psychol* 2009;64:241–56.
- 14 Jokela M, Pulkki-Råback L, Elovainio M, et al. Personality traits as risk factors for stroke and coronary heart disease mortality: pooled analysis of three cohort studies. *J Behav Med* 2014;37:881–9.
- 15 Mroczek DK, Spiro A, Turiano N. Do health behaviors explain the effect of neuroticism on mortality? longitudinal findings from the VA normative aging study. *J Res Pers* 2009;43:653–9.
- 16 Wilson RS, Krueger KR, Gu L, et al. Neuroticism, extraversion, and mortality in a defined population of older persons. *Psychosom Med* 2005;67:841–5.
- 17 Shipley BA, Weiss A, Der G, et al. Neuroticism, extraversion, and mortality in the UK Health and Lifestyle Survey: a 21-year prospective cohort study. *Psychosom Med* 2007;69:923–31.
- 18 Brummett BH, Helms MJ, Dahlstrom WG, et al. Prediction of all-cause mortality by the Minnesota Multiphasic Personality Inventory Optimism–Pessimism Scale scores: study of a college sample during a 40-year follow-up period. *Mayo Clin Proc* 2006;81:1541–4.
- 19 Kim ES, Hagan KA, Grodstein F, et al. Optimism and cause-specific mortality: a prospective cohort study. *Am J Epidemiol* 2017;185:21–9.
- 20 Giltay EJ, Geleijnse JM, Zitman FG, et al. Dispositional optimism and all-cause and cardiovascular mortality in a prospective cohort of elderly dutch men and women. *Arch Gen Psychiatry* 2004;61:1126–35.
- 21 Okely JA, Weiss A, Gale CR. The interaction between stress and positive affect in predicting mortality. *J Psychosom Res* 2017;100:53–60.
- 22 Zhang Y, Han B. Positive affect and mortality risk in older adults: A meta-analysis. *Psych J* 2016;5:125–38.
- 23 Danner DD, Snowdon DA, Friesen WV. Positive emotions in early life and longevity: findings from the nun study. *J Pers Soc Psychol* 2001;80:804–13.
- 24 Blazer DG. Social support and mortality in an elderly community population. *Am J Epidemiol* 1982;115:684–94.
- 25 Brown SL, Nesse RM, Vinokur AD, et al. Providing social support may be more beneficial than receiving it: results from a prospective study of mortality. *Psychol Sci* 2003;14:320–7.
- 26 Burri A, Hilpert P, McNair P, et al. Exploring symptoms of somatization in chronic widespread pain: latent class analysis and the role of personality. *J Pain Res* 2017;10:1733–40.
- 27 Burri A, Ogata S, Vehof J, et al. Chronic widespread pain: clinical comorbidities and psychological correlates. *Pain* 2015;156:1458–64.
- 28 Clauw DJ, Crofford LJ. Chronic widespread pain and fibromyalgia: what we know, and what we need to know. *Best Pract Res Clin Rheumatol* 2003;17:685–701.
- 29 Kassam A, Patten SB. Major depression, fibromyalgia and labour force participation: a population-based cross-sectional study. *BMC Musculoskelet Disord* 2006;7:4.
- 30 Pae CU, Luyten P, Marks DM, et al. The relationship between fibromyalgia and major depressive disorder: a comprehensive review. *Curr Med Res Opin* 2008;24:2359–71.
- 31 Malin K, Littlejohn GO. Personality and fibromyalgia syndrome. *Open Rheumatol J* 2012;6:273–85.
- 32 Malin K, Littlejohn GO. Neuroticism in young women with fibromyalgia links to key clinical features. *Pain Res Treat* 2012;2012:1–7.
- 33 Bucourt E, Martailé V, Mulleman D, et al. Comparison of the big five personality traits in fibromyalgia and other rheumatic diseases. *Joint Bone Spine* 2017;84:203–7.
- 34 Frølund Pedersen H, Frøholm L, Søndergaard Jensen J, et al. Neuroticism and maladaptive coping in patients with functional somatic syndromes. *Br J Health Psychol* 2016;21:917–36.
- 35 Da Silva JAP, Jacobs JW, Branco JC, et al. Can health care providers recognise a fibromyalgia personality? *Clin Exp Rheumatol* 2017;35:43–9.
- 36 Stubbs B, Vancampfort D, Veronese N, et al. Depression and pain: primary data and meta-analysis among 237 952 people across 47 low- and middle-income countries. *Psychol Med* 2017;22:1–12.
- 37 Croft P. The Epidemiology of Chronic Widespread Pain. *J Musculoskelet Pain* 2002;10:191–9.
- 38 Bair MJ, Robinson RL, Katon W, et al. Depression and pain comorbidity: a literature review. *Arch Intern Med* 2003;163:2433–45.
- 39 Gupta A, Silman AJ, Ray D, et al. The role of psychosocial factors in predicting the onset of chronic widespread pain: results from a prospective population-based study. *Rheumatology* 2007;46:666–71.
- 40 Generaal E, Vogelzangs N, Macfarlane GJ, et al. Biological stress systems, adverse life events and the onset of chronic multisite musculoskeletal pain: a 6-year cohort study. *Ann Rheum Dis* 2016;75:847–54.
- 41 Charles ST, Gatz M, Pedersen NL, et al. Genetic and behavioral risk factors for self-reported joint pain among a population-based sample of Swedish twins. *Health Psychol* 1999;18:644–54.
- 42 van Middendorp H, Lumley MA, Jacobs JW, et al. Emotions and emotional approach and avoidance strategies in fibromyalgia. *J Psychosom Res* 2008;64:159–67.
- 43 Hassett AL, Simonelli LE, Radvanski DC, et al. The relationship between affect balance style and clinical outcomes in fibromyalgia. *Arthritis Rheum* 2008;59:833–40.
- 44 Kool MB, Geenen R. Loneliness in patients with rheumatic diseases: the significance of invalidation and lack of social support. *J Psychol* 2012;146:229–41.
- 45 Lynch-Jordan AM, Sil S, Bromberg M, et al. Cross-sectional study of young adults diagnosed with Juvenile Fibromyalgia: social support and its impact on functioning and mood. *J Adolesc Health* 2015;57:482–7.
- 46 Crofford LJ. Psychological aspects of chronic musculoskeletal pain. *Best Pract Res Clin Rheumatol* 2015;29:147–55.
- 47 Macfarlane GJ, Pye SR, Finn JD, et al. Investigating the determinants of international differences in the prevalence of chronic widespread pain: evidence from the European Male Ageing Study. *Ann Rheum Dis* 2009;68:690–5.
- 48 Davies KA, Silman AJ, Macfarlane GJ, et al. The association between neighbourhood socio-economic status and the onset of chronic widespread pain: results from the EPiFUND study. *Eur J Pain* 2009;13:635–40.
- 49 Stringhini S, Carmeli C, Jokela M, et al. Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women. *Lancet* 2017;389:1229–37.
- 50 Itani O, Jike M, Watanabe N, et al. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. *Sleep Med* 2017;32:246–56.
- 51 Glombiewski JA, Sawyer AT, Gutermann J, et al. Psychological treatments for fibromyalgia: a meta-analysis. *Pain* 2010;151:280–95.
- 52 Gallo JJ, Hwang S, Joo JH, et al. Multimorbidity, depression, and mortality in primary care: randomized clinical trial of an evidence-based depression care management program on mortality risk. *J Gen Intern Med* 2016;31:380–6.