

# Pain and subsequent mortality and cancer among women in the Royal College of General Practitioners Oral Contraception Study

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## SUMMARY

Recent research suggested associations between pain and subsequent all-cause and cancer-specific mortality. This study examined death and cancer development within six years of reporting pain, among women in the Royal College of General Practitioners Oral Contraception Study. We found no associations between 'any' or 'chronic' pain and subsequent all-cause mortality or cancer. We found a higher risk of death from respiratory disease among women reporting pain (adjusted odds ratio [AOR] = 2.5), a higher mortality among women reporting chronic chest pain (AOR = 1.75), and a higher risk of subsequent cancer among women reporting head or abdomen pain. Given the high prevalence of pain symptoms, these findings may be important, and warrant further research.

**Keywords:** pain; chronic pain; cancer; mortality; cohort study.

## Introduction

PAIN is a common problem in the community and, when chronic, has a high impact on physical, psychological and social health.<sup>1-3</sup> A recent study by Macfarlane *et al* found that people who reported widespread pain had an increased risk of death, mainly from cancer, over the subsequent five years.<sup>4</sup> The authors highlighted the importance of corroborating this novel finding, because of its implications for long-term follow-up of patients presenting with pain. We explored the relationship between pain and subsequent mortality and cancer using another large prospective dataset.

## Method

The Royal College of General Practitioners Oral Contraception Study<sup>5</sup> began in 1968, when 1400 general practitioners (GPs) throughout the United Kingdom recruited 47 000 women, to examine the effects of oral contraception. The GPs subsequently supplied, for women still in their care, information about new episodes of illness, including cancer. In the mid-1970s, about 75% of the cohort was flagged at the NHS Central Registries at Southport and Edinburgh for cancer and death notifications (the remainder having already left the study). Deaths and illnesses were coded using the International Classification of Diseases, 8th Revision (ICD-8).

Between November 1994 and July 1995, 11 797 of the 12 303 women still in the study were sent a health survey questionnaire,<sup>5</sup> which included two pain questions:<sup>6</sup>

- During the past month have you had an ache or pain that lasted for one day or longer? (Used to identify individuals with 'any pain'.)
- Did the pain start more than three months ago? (Used to identify individuals with 'chronic pain'.)

Responders also indicated the pain site(s): head, neck, shoulder(s), arm(s), chest, back, abdomen/stomach, hip(s), leg(s). By combining health survey information with death and cancer notifications between August 1995 and September 2001, we calculated adjusted odds ratios (AORs) for the chances of dying or developing cancer among those with 'any' and 'chronic' pain. The odds ratios were adjusted for age, social class, and number of cigarettes smoked at recruitment using, as appropriate, individuals without 'any' or 'chronic' pain as reference groups. Women reported by the GP or registry as having cancer before the survey were excluded from the cancer analysis.

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Submitted: 21 January 2002; Editor's response: 3 July 2002; final acceptance: 4 September 2002.

©British Journal of General Practice, 2003, 53, 45-46.

**HOW THIS FITS IN***What do we know?*

Pain, including chronic pain, is a common and important symptom in the community. It has been found that people who report widespread pain are at greater risk of death, particularly from cancer, in the subsequent five years.

*What does this paper add?*

These findings do not confirm the associations between pain, mortality and cancer. They suggest an association between some kinds of pain and subsequent mortality, particularly from respiratory disease, and between some kinds of pain and subsequent cancer. They highlight the need for further research in this area.

**Results**

There were 10 073 responders to the survey (response rate = 85.4%), with a mean age of 56.1 years (range = 42 to 81). Some 52.7% (95% CI = 51.7% to 53.7%) reported 'any pain' and 38.4% (95% CI = 37.4% to 39.4%) reported 'chronic pain'. Overall, women reporting pain had similar chances of dying to those without (Table 1). Women with chronic chest pain ( $n = 585$ ) had elevated odds ratios for all mortality (AOR = 1.75, 95% CI = 1.18 to 2.59). No other pain site was significantly associated with overall mortality and there was no relationship with the number of sites of pain. Women with 'any' or 'chronic' pain were more likely to die from respiratory disease, a risk that was particularly associated with chronic back pain (AOR = 2.74, 95% CI = 1.29 to 5.81).

Some 258 women had a first ever cancer registered since August 1995. There was no significant association overall between 'any' or 'chronic' pain and subsequent cancer. However, there was a slightly higher risk of subsequent cancer following a report of 'any' pain in the head (AOR = 1.50, 95% CI = 1.03 to 2.18) or the abdomen (AOR = 1.57, 95% CI = 1.01 to 2.43).

**Discussion**

In this cohort, which had similar prevalences of pain to other studies,<sup>1,3,4</sup> we found no evidence of increased all-cause or

cancer-specific mortality among those reporting pain. This is in contrast with Macfarlane's findings<sup>4</sup> and confirms the need for further research, whose findings will inform the importance to primary care of pain as a presenting symptom. The findings of increased risk of respiratory death, particularly in association with back pain, and the associations between head or abdominal pain and subsequent cancer were unexpected, and may be the result of random error. Although there are several possible mechanisms for associations between pain, mortality, and cancer,<sup>7</sup> this study has not provided confirmation. Given the high prevalence of pain and cancer, calls for further explanatory research<sup>4,7</sup> are appropriate. Ideally, this will include purpose-designed prospective studies.

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**Acknowledgements**

We thank the GPs who have contributed data to the RCGP Oral Contraception Study and the thousands of women who completed our questionnaires. The study has received funding from the Royal College of General Practitioners, Medical Research Council, Imperial Cancer Research Fund, British Heart Foundation, Schering AG, Schering Health Care Ltd, Wyeth Ayerst International, Ortho Cilag and Searle. Dr Blair Smith is supported by an NHS R&D Career Scientist Award, funded by the Scottish Executive, Department of Health.

Table 1. Association between pain in 1994/1995 and cause of subsequent death. Odds ratios (95% CI), adjusted for age (continuous variable), social class ('manual' or 'non-manual', based on husband's occupation), and smoking (number of cigarettes per day at recruitment).

Cause of death	ICD-8 codes	Number of deaths	Any pain <sup>a</sup>		Chronic pain <sup>b</sup>	
			AOR (95% CI)	P-value	AOR (95% CI)	P-value
All causes		400	1.10 (0.89-1.36)	0.40	1.01 (0.81-1.26)	0.95
All cancers	140-209 230-239	187	1.00 (0.74-1.38)	0.98	0.85 (0.62-1.18)	0.34
Cardiovascular disease	390-458	106	1.10 (0.73-1.65)	0.65	0.95 (0.63-1.44)	0.81
Respiratory disease	460-519	44	2.50 (1.21-5.16)	0.014	2.22 (1.12-4.39)	0.022
Other diseases	All other codes	36	1.10 (0.53-2.30)	0.79	1.08 (0.52-2.27)	0.84
All external causes	E800-E999 N800-N999 Y00-Y89	5	0.59 (0.10-3.57)	0.57	0.99 (0.16-5.93)	0.99

<sup>a</sup>Reference group = 'no pain'; <sup>b</sup>reference group = 'no chronic pain'.