Henry J McQuay, Lesley A Smith and R Andrew Moore

1 Summary

Introduction and statement of the problem

Chronic pain is conveniently defined as any pain that persists for at least three months despite sensible treatment. It ultimately affects almost half of all adults and is most likely to occur in older people. Chronic pain is known to have significant effects on health and well-being and is a major cause of lost work days. Prevalence data alone does not capture the burden of pain, or the disability which goes with the pain. For many conditions there is no certain remedy, so that health care needs have to consider prevalence, the burden of the pain (and disability), and just how treatable the pain is. In addition, health care needs for chronic pain extend from community through to hospital care. Patients with some chronic pain conditions, such as migraine, may manage with over the counter medications; others will require prescription medication and some will need other interventions. One organisational dilemma is the overlap of pain management between community and hospital care and the overlap between pain services and other hospital services. Between primary care and the pain service there are several groups of patients who may need referral. Between the pain clinic and other hospital services the reality is that patients who fail to respond to the best endeavours of the other services find their way to the pain clinic.

Sub-categories

The sub-categories used in this chapter are based on demand in a clinic which rarely refuses referrals and which has mature relationships with other services. The main categories of pain are musculoskeletal, cancer, face/head, neuropathic, vascular, chronic postoperative and medically unexplained painful syndromes. The most problematic growth in demand is for medically unexplained painful syndromes.

Prevalence and incidence

Chronic pain is common. One in two people report chronic pain lasting for three months or more, rising to two in three over 67 years. In a Primary Care Trust population of 100 000 people there would be about 5000 to 10 000 people with severe chronic pain. Roughly half the problems will be musculoskeletal, with back pain and arthritis predominant. Pain due to nerve damage and chronic postoperative pain are two of the other big categories. Musculoskeletal conditions have the most severe impact on quality of life.

Services available

Possible interventions include drugs, the conventional analgesics from paracetamol up to morphine, the unconventional analgesics for nerve pain, antidepressants and anticonvulsants, injections including continuous infusion devices, psychological behavioural management, and operations. Patients with chronic pain who fail to respond to the best endeavours of other services find their way to the pain clinic. The pain clinic may offer injection treatments, more expert handling of neuropathic pain medication and psychological expertise unavailable in the other services.

A total of 85% of Trusts provide a chronic pain service, which can vary from the 'spoke' provision with a single-handed consultant in a district hospital to the 'hub' in the university hospital with a multi-disciplinary clinic offering a wider range of interventions. Limited cost data suggests a Primary Care Trust covering 100 000 patients should be budgeting between £100 000 and £200 000 per year for chronic pain services, allowing ten consultant sessions per 100 000 patients. Canadian data shows that users of speciality pain clinic services incur less direct health care expenditure than non users with similar conditions, about £1000 per patient per year. Without adequate provision for chronic pain management these people will bounce ineffectively and expensively around the health care system.

Effectiveness

There is a strong evidence base for pain management, for both efficacy and safety. Of the many interventions, pharmacological, non-pharmacological, invasive and non-invasive, from which to choose there is good evidence of effectiveness for many of the drug treatments, for behavioural management and for some of the invasive options. There is evidence that some of the alternative therapies do not improve pain, but may help patients cope better.

Models of care

The provision of chronic pain services should not be taken in isolation. Many treatments, drugs or procedures, are common to the different service providers; the additional expertise found in the pain service is prescribing expertise and the ability to do particular invasive procedures. The ideal promoted widely in the developed world is chronic pain services which are multidisciplinary. The medical components of such multidisciplinary services include rehabilitation, neurology, orthopaedic and psychiatric, together with clinical psychology, physiotherapy and pharmacy inputs as integral to the chronic pain service. The fact that 85% of Trusts surveyed had a chronic pain clinic is evidence that there is a perceived need for the service. There is little evidence as to what constitutes the optimal form of the service, and very little evidence on resource use and benefit gained. The current satellite and hub model of DGH and regional centre works to an extent, but there has been a dearth of organisational research into service provision. The need for good liaison with other specialities favours decentralised rather than centralised arrangements.

For the future, chronic pain, like other specialities, needs studies of complex interventions to show how to make the best of the interventions we have.

2 Introduction and statement of the problem

Chronic pain is conveniently defined as any pain that persists for at least three months despite sensible treatment, sweeping aside subtle distinctions between conditions which are always painful and conditions which are sometimes painful. Surveys that have examined the extent and significance of 'generic' chronic pain in the community have come to remarkably similar conclusions. Chronic pain ultimately affects almost half of all adults^{1–6} and is most likely to occur in older people.

Chronic pain is known to have significant effects on health and well-being⁷ and is a major cause of lost work days, from back pain⁸ to migraine,⁹ so it is important to define the extent of the problem systematically to specify health care needs. In 1999, The International Association for the Study of Pain published a book on the epidemiology of pain.¹⁰ This should be referred to for greater detail on some of the conditions mentioned throughout the chapter.

Other publications have focused on the prevalence of chronic pain due to specific disease states, such as back pain, 8,11 fibromyalgia, 12 arthritis 13 and terminal and palliative care. 14 The aim of this chapter is to consider the prevalence and treatment options and thus the need for services for the pain conditions likely to be seen in chronic pain clinics.

Organisation and perception

One common organisational dilemma is the overlap of pain management between community and hospital care, and a common source of confusion is the overlap between the pain service and other hospital services. Between primary care and the pain service there are several groups of patients who may need referral:

- patients who fail to respond to conventional analgesics and need active management of neuropathic pain, which may involve use of 'off-label' medication
- patients requiring injection procedures not available in the community
- patients who need large doses of opioids
- patients without clear diagnosis and who are difficult to manage
- patients needing services not available in the community, e.g. devices or specialist psychological input.

Between the pain clinic and other hospital services the reality is that patients who fail to respond to the best endeavours of the other services find their way to the pain clinic. The pain clinic may offer injection treatments, more expert handling of neuropathic pain medication and psychological expertise unavailable in the other services. Apparent overlaps are often minimised by local understandings. Out of back pain triage, for instance, orthopaedics may retain younger less disabled patients and refer the older and more disabled to the pain clinic. The argument that the pain clinic service could be subsumed by another service, for instance by an orthopaedic clinic, ignores the fact that the special skills of the pain clinic are of value across a variety of pain conditions which the orthopaedic clinic would not want to see. The learning, maintenance and governance of those special skills require critical mass and demand, both of which would be lost or diluted if the pain clinic was subsumed by other services.

There is a striking contrast between the standing of palliative care and that of chronic pain. Both began at roughly the same time, but palliative care, unlike chronic pain, has formal recognition and is seemingly better presented to health commissioners. A coherence has emerged about the clinical framework for palliative care which is less obvious for chronic pain. Both services are necessary, but presenting a more coherent case for chronic pain would be a great deal easier with better data. In this context it is fair to say that absence of data does not mean absence of benefit. The data needed is more management and audit rather than research.

3 Sub-categories

The pain classification in **Table 1** is the basis for the sub-categories of chronic pain used in this chapter. This was developed from the simple manoeuvre of auditing clinics for one month. This is a classification by demand in a clinic which rarely refuses referrals and which has mature relationships with other services, and joint clinics with psychiatry, neurosurgery and neurology. Cancer has been included because pain clinics commonly provide invasive options for cancer pain at the behest of the palliative care team. The classification does not use mechanism of pain, apart from the generic grouping of neuropathic pain, and is a static snapshot. The most problematic growth in demand is for medically unexplained painful syndromes.

Table 1: Pain classification.

Musculoskeletal	Back* Neck*	degenerative disc disease osteoporotic collapse stenosis facet joint post-trauma/surgery ankylosing spondylitis* no clear pathology degenerative disc disease whiplash*
	Fibromyalgia*/myofascial Arthritis	polymyalgia rheumatica* osteoarthritis, rheumatoid
Cancer	Breakthrough cancer pain*	neuropathic, movement related, poor control with oral morphine
MUPS (medically unexplained painful syndromes)		non-cardiac chest pain abdominal pelvic chest pain
Face/head pain	Migraine* Headache* Trigeminal neuralgia* Dental	atypical facial*
Neuropathic		diabetic neuropathy* postherpetic neuralgia* multiple sclerosis* post stroke* repetitive strain injury reflex sympathetic dystrophy (CRPS1) traumatic
Vascular	Peripheral Central	claudication*/Raynaud's* angina*
Chronic postoperative pain		pain after amputation (phantom* and stump) chronic postoperative breast pain* chronic postoperative thoracotomy pain* chronic postoperative cholecystectomy pain*

^{*} Asterisk means prevalence and incidence discussed below.

4 Prevalence and incidence

Chronic pain overall

Chronic pain affects almost half of all adults (**Table 2**). ¹⁻⁶ Not all of this chronic pain is severe, or the conditions disabling, but chronic pain is likely to occur in older people, and in the largest UK survey half of those with chronic pain had severe pain or were moderately disabled.

This recent data⁶ shows that the prevalence of chronic pain in the community is high. Particular population groups can differ significantly in the prevalence of chronic pain and severe chronic pain, though the importance for practice of such significant differences is not easy to perceive. ¹⁵ The causes of any variations include differences in sampling methods, diversity in disease definitions used and differences in populations studied. The main thrust of all the findings, though, is for the bulk of chronic pain to have musculoskeletal causes (**Table 2**), and to occur more frequently in older people. ⁶ Chronic pain may be particularly common in older people in nursing homes or long-term care institutions. ¹⁶ In a Primary Care Trust population of 100 000 people there would be about 5000 to 10 000 people with severe chronic pain.

Sub-categories of chronic pain

Information was sought on the prevalence and incidence of the pain conditions marked with an asterisk in **Table 1**, using the methods detailed in Appendix 1. The prevalence and incidence of the sub-categories of pain that have not been covered in depth elsewhere are presented.

Musculoskeletal pain

Musculoskeletal disorders are the commonest cause of chronic incapacity, and half are due to back pain.

Back pain

A health care needs assessment on low back pain is published in the Health Care Needs Assessment second series¹³ but it is also considered here as it is an important cause of chronic pain.

Back pain is one of the commonest causes of disability and absence from work, particularly during the productive middle years of adult life. Seven percent of UK adults consult their GP each year, and back pain costs the NHS more than £500 million a year. While 90% or more of patients with back pain recover within three months, those that do not may recover slowly and their demand for care is high.

Most recent reports estimating the burden of low back pain have focused mainly on acute back pain. There is less reliable data for chronic pain. One of the reasons for this is the lack of agreement about definitions of chronic back pain, the different time periods used and the intermittent nature of back pain.

Table 3 summarises the relevant reports. In addition, for self-reported low back pain in the community 6% of the population reported pain persisting for at least a year and 3% were still unable to work a year later. ¹¹ In a primary care trust population of 100 000 people there might be as many as several thousand with back pain that is disabling and limiting.

 Table 2: Prevalence of chronic pain.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Overall prevalence
Andersson 1994 ¹	Prospective questionnaire	Random sample of 15% of the 25–74 population of two Swedish primary care districts	Chronic pain duration longer than 3 months	1,806 questionnaires sent, 1,609 responded (89%)	25–74	High prevalence, 50,000/100,000 in men and women, with high intensity pain about 30% of this. Greater in older population. Musculoskeletal had highest prevalence.
Brattberg <i>et al.</i> 1989 ²	Postal survey	Randomly chosen individuals in a single Swedish county	Obvious pain, longer than 6 months' duration	1,009 questionnaires sent, 672 responded (67%)	18–84	38 000/100,000 in men and 42,000/100 000 in women. Peak age 45–64. Musculoskeletal had the highest prevalence.
Birse & Lander 1998 ³	Cross-sectional telephone survey	Random sample of households, and of individuals within households, in Edmonton, Canada	Chronic pain was recurrent or persistent pain of at least 6 months' duration	592 individuals, 410 responded (69%)	Over 18	35,000/100,000 in men and 66,000/100,000 in women. Peak age younger and older women and older men. Musculoskeletal had the highest prevalence. Accidents and medical or surgical procedures were most common antecedants of chronic pain.
Bowsher <i>et al.</i> 1991 ⁴	Cross-sectional telephone survey	Random selection of households in Great Britain	Chronic pain defined as lasting on or off for more than the last 3 months	2,942, 1,037 respondents (35%)	Over 15	11,500/100,000 had chronic pain. This was higher in women than men (1.5 to 1). Prevalence higher in older age groups.
Chrubasik <i>et al.</i> 1998 ⁵	Cross-sectional postal survey	Every 71st person in a county in Baden-Würtenberg, Germany	Prolonged pain in preceding 6 months	2,127 questionnaires sent, 1,420 responded (67%)	18–80	47,000/100,000 reported prolonged pain, and in 87% it had lasted over a year, and in about half the pain was severe. In about 29% of respondents pain was severe or intolerable and had lasted more than a year. Musculoskeletal pain predominated.
Elliott <i>et al.</i> 1999 ⁶	Cross-sectional postal survey	Random sample of adults in Grampian region of Scotland	Pain or discomfort that persisted continuously or intermittently for longer than 3 months	5,036 questionnaires sent, 3,605 returned (72%)	Over 25	50,000/100,000 reported chronic pain (47,000/100,000 of general population). About half had severe pain or disability. Prevalence higher in older people. Musculoskeletal pain predominated.

in **525**

 Table 3: Chronic back pain.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Overall prevalence (per 100,000)	Occurrence
Cassidy et al. 1998 ¹⁷	Retrospective survey, PSAQ	General population, random selection residents of Saskatchewan province, Canada	Point prevalence data obtained by question 'do you have LBP at the present time?' Lifetime prevalence data by question 'have you ever had LBP in your lifetime?' Mannequin diagram for location of LBP Chronic pain questionnaire for 6 month period prevalence graded in severity PI (range 0–100) disability (range 0–6)	n=2,184 recruited, 55% (n=1,133) response rate	20 to 69	*Age-adjusted point prevalence: 28,400/ 100,000 (25,600 to 31,100) *Age-adjusted lifetime prevalence: 84,100/ 100,000 (81,900 to 86,300) *Age-adjusted 6 month period prevalence: Grade 1: Low intensity/ low disability = 48,900/ 100,000 Grade 2: High intensity/ low disability = 12,300/ 100,000 Grade 3 & 4: high disability/moderately to severely limiting = 10,700/100,000	
Davies <i>et al.</i> 1995 ¹⁸	Prospective 3 year survey, questionnaire and examination by physician at clinic consultation	Patients attending 10 pain clinics with back pain, North Britain	Consultant diagnosis of back pain	n=2,007, all reported on	median age 48.5 (IQR 40–60)		Occurrence: 35,000/ 100,000 complaining of pain in low back only Duration of pain: 73% > 2 years 27% > 10 years Pain intensity: 54% moderate, 18% severe, 40% unable to work (as stated by patient) Putative cause of pain: Degenerative: 56% Trauma: 21% Failed surgery: 16% No definite cause: 15%

Table 3: Continued.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Overall prevalence (per 100,000)	Occurrence
Thomas et al. 1999 ¹⁹	Prospective 1 year survey, questionnaire + clinical exam	Patients with low back pain, registered with two GPs, Manchester, UK	Persistent disabling low back pain defined as presence of both low back pain and disability Pain rated by VASPI 0–10% scale, disability rated by Hanover back pain activity schedule 0 to 100% scale	n=442, 67% (n=246) response rate, n=180 analysed	18–75		Occurrence: at 1 week after consultation: 73% at 3 months: 48% at 12 months: 42% Period prevalence persistent disabling low back pain at each follow-up visit: 34%

Abbreviations: PSAQ – postal self-assessed questionnaire; * age-adjusted to 1995 Saskatchewan mid-year population; LBP = low back pain; PI = pain intensity; IQR = inter quartile range; VASPI = visual analogue pain intensity; DHSS = Department of Health and Social Security.

Ankylosing spondylitis

Disease prevalence

The prevalence of ankylosing spondylitis (AS) correlates with the prevalence of HLA-B27 antigen, and for the UK is estimated to be 1 to 2% of the population.²⁰ There are surveys using strict diagnostic criteria from Europe and North America (**Table 4**). The largest population-based survey was in Norway, based on 21 329 randomly selected subjects.²¹ The prevalence of AS was 1100 to 1400/100 000, and was between four and six times higher in men than in women. In a prospective study of 273 blood donors in Berlin, the prevalence of AS was 900/100 000.²² A large American population-based survey using retrospective record review of Minnesota residents between 1935 and 1989 found an age- and sex-adjusted incidence of 7.3 per 100 000 person-years (95% CI 6.1–8.4). The age-adjusted incidence was four times higher in men at 11.7 per 100 000 person-years (95% CI 9.6–13.8) than in women at 2.9 per 100 000 person-years (95% CI 2.0–3.9).²³

Pain prevalence

Of 14 539 AS patients who completed a back pain questionnaire, 2907 complained of pain.²¹ In a retrospective survey of 121 AS patients in Norway, 71 of the 100 responders reported daily pain and 60 used analgesics every day.²⁶ In the Minnesota study back pain was reported by 96% and neck pain by 27% at presentation.²³ Pain will therefore be a chronic feature for between 25% and 50% of AS patients. In a primary care trust population of 100 000 people there would be about 30 new cases of AS with pain a year.

Neck pain

Seven population-based surveys have examined the prevalence of self-reported neck pain in random samples of the general population (**Table 5**). With the exception of one Canadian and one British study, all were Scandinavian. There were no studies reporting the incidence of chronic neck pain.

The prevalence of chronic neck pain in adults was of the order of 5000 to 20 000/100 000, with most estimates about 10 000/100 000 (**Table 5**). There was some evidence that prevalence was higher in women than in men. Significantly disabling chronic neck pain affected 5000/100 000 in Canada. ²⁸ In a primary care trust population of 100 000 people there would be about 5000 cases.

Whiplash

One nine-year prospective study of patients admitted to an accident and emergency department was conducted in the UK, to determine the prevalence and incidence of neck sprain following a road traffic accident (RTA).³² Of 6149 patients admitted following injuries sustained in an RTA, 46% (2801) were diagnosed with neck sprain.

A 25 year retrospective medical record review in Holland determined the prevalence of neck sprain in all patients admitted to an accident and emergency department either due to an RTA³³ or due to injury from another cause.³⁴ Of 1374 neck sprain patients 51% (694) were sustained in a car accident and 49% (680) were not (NCA). For NCA, the five year period prevalence rates increased over time from 6.5 per 100 000 (1970 to 1974) to 28.5 per 100 000 (1990 to 1994). The age group at highest risk was 15 to 19 year olds with a prevalence of 39.2 per 100 000; accidental falls caused 25% and sports 24%. For neck sprain due to RTA, five year period prevalence rates increased over time from 34 per 100 000 (1970 to 1974) to 402 per 100 000 (1990 to 1994). The age groups at highest risk were 25 to 29 year olds with prevalence of 28.3 per 100 000, and 40 to 44 year olds with prevalence of 27.9 per 100 000.

There appears to have been a ten-fold increase over 25 years in the prevalence of neck sprain, particularly following RTA.

Table 4: Chronic pain due to ankylosing spondylitis.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Incidence	Overall prevalence	Male prevalence	Female prevalence
Braun <i>et al.</i> 1998 ²²	Survey and prospective screening with questionnaire and physical examination	Blood donors resident in Berlin, HLAB27- positive age- and sex-matched with HLAB27 negative blood donors	AS diagnosis using modified New York criteria: radiographs showing bilateral changes in SI joints > grade II	n=320 recruited, n=273 (85.3%) responded to initial questionnaire	18–65 years		AS diagnosed in 9/140 B27-positive donors calculated prevalence in population Berlin = 860/100,000		
Carbone <i>et al.</i> 1992 ²³	Retrospective review of medical records, 1935–1989	General population, residents Rochester county, Minnesota, USA	Modified New York criteria for AS: Radiographic evidence of sacroilitis with 1/3 clinical criteria (inflammatory back pain 3 month duration, limitation of movement of lumbar spine in sagittal and frontal planes, reduced chest expansion)	Population for Rochester 1930 = 18,931; 1990 = 69,995	All ages	Incidence rates calculated assuming the entire population is at risk: age- and sex-adjusted rate = 7.3/100,000 (6.1–8.4) Men: age-adjusted 11.7/100,000 (9.6–13.8) Women: age-adjusted 2.9/100,000 (2.0–3.9)			

Table 4: Continued.

Gran <i>et al</i> . 1985 ²¹	Prospective survey 1979–80, postal SAQ, clinical exam	General population, residents of Tromsø, Norway random selection (n=449, 56%) further selected for clinical examination	New York diagnostic criteria, definite AS defined as X-ray changes of sacroiliac joints	n=21,329 recruited, n=14,539 responded, (68.2%)	Adults aged 20–54		1,100 to 1,400/ 100,000	1,900 to 2,200/ 100,000	300 to 600/ 100,000
Julkunen and Korpi 1984 ²⁴	Health examination surveys, part of mini- Finland health survey, clinical exam and X-ray	General population, three population samples in Finland Study 1 and 2 were random samples, study 3 includes 196 patients with back pain	study 1: diagnosis by X-ray 10 × 10 of chest study 2: normal- sized chest X-ray study 3: lumbar spine X-ray	•	study 1 = 30+ yrs study 2 = 30+ yrs. Study 3 = 30 to 64 yrs		study 1: 400/ 100,000 study 2: 1,600/ 100,000 study 3: 1,000/ 100,000		
Underwood and Dawes 1995 ²⁵	Prospective study of patients presenting with back pain over 1 year	Suburban general practice in England	Short screening questionnaire, plus detailed diagnosis by one observer	6,600 patients	All ages	30/100,000 in 1 year (2 of 313 patients presenting with back pain)			

 Table 5: Chronic neck pain.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Prevalence (per 10	0 000)	
					(years)	Overall	Male	Female
Anderson et al. 1993 ¹	Prospective survey, PSAQ with a drawing of neck	General population, random selection of patients registered with two primary health care districts, Sweden	Persistent or regular recurrent pain more than 3 months in the neck	n=1,806, 90% (n=1,624) response rate	25–74		14,500/100,000	19,100/100,000
Bovim <i>et al.</i> 1994 ²⁷	Retrospective survey, PSAQ	General population, random selection of residents Norway	Questionnaire asked about troublesome neck pain within the last year, and duration Chronic neck pain was defined as lasting more than 6 months	n=10,000 sent questionnaire, 77% (n=7,643) response rate	18–76	13,800/100,000	10,000/100,000	19,000/100,000
Brattberg <i>et al.</i> 1989 ²	Survey, PSAQ	General population, random sample, Sweden	Any pain, or obvious pain > 6 months	n=1,009, 82 % (n=827) response rate	18–84	Point prevalence any pain > 6 months: 19,300/100,000 obvious pain > 6 months: 12,700/100,000		

Table 5: Continued.

Côté <i>et al.</i> 1998 ²⁸	Prospective survey, PSAQ	General population, random selection of residents Saskatchewan province	Acute and chronic, neck pain described as pain between occiput and 3rd thoracic vertebra Chronic neck pain questionnaire used to classify severity of pain	n=2,184 recruited, 55% (n=1,420) response rate	20–69	High-intensity/low disability 10,100/100,000 (8,200 to 11,900) significantly disabling neck pain 4,600/100,000 (3,300 to 5,800) 5.4 % had pain lasting 90 to 180 days in last 6 months		
Jacobsson <i>et al.</i> 1989 ²⁹	Prospective survey, questionnaire and physical exam	General population, random selection, residents of Malmo, Sweden	Neck pain with/ without brachalgia > 6 weeks	n=552, 81% (n=445) response rate	50–70	1 year period prevalence: 6,500/ 100,000 (4,200–8,800)	3,000/100,000	10,000/100,000
Mäkelä <i>et al.</i> 1991 ³⁰	Prospective survey, questionnaire and clinical exam	General population, random selection, residents of Finland	Current or previous neck pain for > 3 months with physical signs	n=8,000, 90% (n=7,217) response rate	over 30		Point prevalence chronic neck syndrome: 9,500/100,000	Point prevalence chronic neck syndrome: 13,500/100,000
Takala <i>et al.</i> 1982 ³¹	Retrospective survey, PSAQ and clinical exam	General population, random selection residents, Finland	Neck ache, stiffness, soreness and frequency of symptoms	n=2,439, 93% (n=2,268) response rate	40–64		1 year period prevalence: < 50 years 13,000/100,000 > 50 years 20,000/100,000	1 year period prevalence: < 50 years 13,000/100,000 > 50 years 22,000/100,000

Polymyalgia rheumatica

The incidence and prevalence of polymyalgia rheumatica (PMR) has been determined in several hospital-or clinic-based prospective studies from Scandinavia, North America and Southern Europe, all using similar diagnostic criteria (**Table 6**). All of the studies concluded that PMR is a common disease of the elderly, rarely occurring under the age of 50. Prevalence and incidence figures vary rather a lot. For instance, prevalence estimates ranged from 30/100 000 for all ages to 2000/100 000 in an over-65 population. Incidence was also age-related. In a primary care trust population of 100 000 people there would be about 50 new cases a year, and about 500 at any one time.

Fibromyalgia

Fibromyalgia (chronic widespread pain) is a poorly defined complex pain syndrome characterised by chronic widespread pain and multiple tender points. It is the third commonest rheumatic complaint in Canada (23% of new patient rheumatology referrals).⁴³

Four studies using American College of Rheumatology (ACR) criteria have been conducted to determine the prevalence of fibromyalgia in the general population (**Table 7**). All of the studies used a two stage screening process, an initial self-assessed questionnaire followed by interview, and clinical examination of tender points for those reporting chronic widespread pain. Chronic widespread pain appears to affect about 10 000/100 000 adults, though fibromyalgia may be diagnosed in 5–10% of those with chronic widespread pain. Trigger points are, however, poor indicators of fibromyalgia, ⁴⁴ and trigger point numbers are unchanged by effective treatments. ⁴⁵ It is perhaps better to think of the condition as a spectrum of musculoskeletal disorders, some of which will be severe.

In a primary care trust population of 100 000 people there would be about 10 000 cases of chronic widespread pain, with perhaps 200–1000 being defined as fibromyalgia by current criteria.

Cancer pain

Of every 100 patients with cancer some 60 will have moderate or severe pain. Most, some 80%, of these 60 will obtain at least moderate relief of their pain with appropriate use of the oral drugs on the pain 'ladder' (**Figure 1**), starting with simple analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) and then using oral opioids, usually oral morphine.

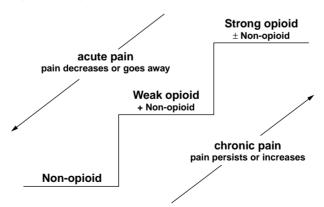


Figure 1: Pain treatment 'ladder'.

 Table 6: Chronic pain due to polymyalgic rheumatica.

Reference	Type of study	Sample source	Disease definition	Sample size	Age	Incidence (p	er 100,000 959	% CI)	
					range (years)	Overall	Men	Women	Prevalence (per 100,000 population 95% CI)
Bengtsson and Malmvall 1981 ³⁵	Retrospective review of medical records, 1973–75	Residents of a Swedish city referred to clinic or hospital	Diagnostic criteria: 1. Pain and/or stiffness affecting proximal muscle groups without evidence of inflammatory arthritis 2. ESR elevated 3. No evidence of other inflammatory or malignant disease 4. Prompt and persistent response to steroid therapy	n=126 patients identified and reported upon	51–87	PMR alone: 6.7/100,000 for all ages PMR plus GCA: 29/ 100 000 over 50s	PMR alone: 3.4/100,000 for all ages PMR plus: GCA 20/ 100,000 over 50s	PMR alone: 9.8/100,000 for all ages PMR plus GCA: 35/ 100,000 over 50s	
Boesen and Sorensen 1987 ³⁶	Prospective study, 1982–85	Residents of a Danish county, diagnosed with PMR referred to the study cohort, GP or hospital referrals	Diagnostic criteria: 1. Pain and/or stiffness affecting proximal muscle groups > 2 weeks 2. ESR > 40 mm/hour 3. Age > 50 years 4. No evidence of other inflammatory disease 5. Prompt and persistent response to steroid therapy	n=31 PMR alone n=10 PMR + temporal arteritis (TA) total population approx. 200,000	50+	19/100,000 for all ages 68/100,000 over 50s	7.4/100,000 for all ages 28/100,000 over 50s	32/100,000 for all ages 108/100,000 over 50s	30/100,000 for all ages 104/100,000 over 50s
Elling <i>et al.</i> 1996 ³⁷	Prospective, longitudinal study, 1982–94 using medical record data	Residents of 13 counties in Sweden, all incident cases of PMR recorded in 2 general hospitals reported to national patient register	States diagnosed using established criteria	n=10,818 analysed	50+	41/100,000 (30 to 67)			

Table 6: Continued.

Reference	Type of study	Sample source	Disease definition	Sample size	Age	Incidence (p	er 100,000 959	% CI)	
					range (years)	Overall	Men	Women	Prevalence (per 100,000 population 95% CI)
Gran and Myklebust 1997 ³⁸	Prospective, longitudinal survey, 1987–94, retrospective review of medical records of referrals to different hospital departments	Residents of Aust Agder county, Norway that were referred to regional hospital suspected of having PMR	PMR defined as: 1. Age > 50 years, bilateral aching and morning stiffness (> 30 min) for at least 1 month 2. Involving 2 of the following areas: neck or torso, shoulders or proximal regions of the arms and hips or proximal aspects of the thighs 3. ESR > 40 mm/hour Patients who met two of the three criteria and who had a prompt response to corticosteroid therapy also included	n=256, all patients reported on Includes 32 patients retrospectively included following initiation of drug treatment Prospective patients included in study before treatment started	50+	113/100,000	83/100,000	138/100,000	
Kyle <i>et al.</i> 1985 ³⁹	Prospective study, questionnaire, interview and clinical exam	All patients > 65 years registered with GP practice, Cambridge, UK	Diagnostic criteria: 1. Shoulder and pelvic girdle pain, primarily muscular 2. Morning stiffness 3. Duration > 2 months 4. ESR > 30 mm or C reactive protein > 6 μ /ml 5. Absence of inflammatory or muscle disease 6. Prompt and dramatic response to steroid therapy	n=5,500 patients registered, n=650 ± 65 years recruited, 89% (579) responded, n=32 studied further	± 65	About 230 per 100,000			Prevalence about 2,000 per 100,000

Table 6: Continued.

Northridge and Hill, 1995 ⁴⁰	Retrospective review of medical records	UK general practice	Patients with presumptive diagnosis treated with steroids	13,600 in one practice 72,400 in other practices	All ages	35–70/ 100,000 in one practice 55/100,000 in other practices			550/100,000 in one practice 457/100,000 in other practices
Salvarani et al. 1991 ⁴¹	Longitudinal study (1980–88), by medical record review	All residents of Reggio Emilia metropolitan area (Italy) referred to the regional hospital	PMR defined as: 1. Age > 50 years, bilateral aching and morning stiffness (> 30 min) for at least 1 month 2. Involving two of the following areas: neck or torso, shoulders or proximal regions of the arms and hips or proximal aspects of the thighs 3. Erythrocyte sedimentation rate (ESR) > 40 mm/hour Included patients met two of the three criteria or had a prompt response to corticosteroid therapy	n=76 residents identified, all included in incidence data	All ages	4.9/100,000 all ages 12.7/100,000 over 50s	3.4/100,000 all ages 9.7/100,000 over 50s	6.4/100,000 all ages 14.9/100,000 over 50s	
Salvarani et al. 1995 ⁴²	Longitudinal study (1970–91), medical record review (Mayo clinic)	Clinic-based population, all residents of Olmsted County, Minnesota, USA seeking medical care	PMR defined as: 1. Age > 50 years, bilateral aching and morning stiffness (> 30 min) for at least 1 month 2. Involving two of the following areas: neck or torso, shoulders or proximal regions of the arms and hips or proximal aspects of the thighs 3. ESR (Westergren) > 40 mm/hour Included patients met two of the three criteria or those that had a prompt response to corticosteroid therapy	n=245 residents met diagnostic criteria, all reported on and included in incidence data	50+	53/100,000 (46 to 59) in over 50s	40/100,000 (31 to 49) in over 50s	62/100,000 (52 to 71) in over 50s	Prevalence among persons > 50 years (1/1/ 92) = 627 (527 to 726)

 Table 7: Chronic pain due to fibromyalgia.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Prevalence (%)	Men	Women
Croft et al. 1993 ⁴⁶	Cross-sectional survey, SAQ	General population, two general practices in Cheshire, England	ACR definition of chronic widespread pain more than 3 months	n=2,034, 66% response rate (1,340)	18–85	Age- and sex- adjusted point prevalence: 11,200/100,000	Crude point prevalence: 9,400/100,000	Crude point prevalence: 15,600/100,000
Forseth and Gran 1992 ⁴⁷	Survey, SAQ and clinical exam	General population, random selection female residents in Arendal, Norway	ACR diagnostic criteria; widespread pain, and tenderness in at least 11/18 sites	n=2,498 women, response rate 81.5% (2038) 217 agreed to clinical exam	20–49			Point prevalence of fibromyalgia 10,500/100,000 (95% CI 6,400 to 14,600)
Prescott <i>et al.</i> 1993 ⁴⁸	National Health Interview Survey, interview and clinical exam	General population, random selection, Denmark	ACR diagnostic criteria; widespread pain, and tenderness in at least 11/18 sites	n=1,595, 1,219 interviewed, (76% response rate)	18–79	Point prevalence fibromyalgia: 660/100,000 (95% CI, 280 to 1290)		
Wolfe <i>et al.</i> 1995 ¹²	Prospective survey, PSAQ, sub-sample interviewed and examined	General population, random selection residents of Wichita, Kansas, USA	ACR diagnostic criteria; widespread pain, and tenderness in at least 11/18 sites	n=2,582 households, 74.8% response rate, n=3,006 persons n=392 categorised as having chronic, widespread pain	over 18	chronic	Point prevalence fibromyalgia: 50/100,000 (95% CI 0 to 100)	Point prevalence fibromyalgia: 340/100,000 (95% CI 230 to 460)

Abbreviations: ACR = American College of Rheumatology, SAQ = self-assessed questionnaire.

Particular problems in the 20% who do not achieve relief with this regime are found with neuropathic (nerve damage) pain, and with incident pain. Incident pain is a bad term, but encompasses movement-related and neuropathic pain. Even more confusing is the American term 'breakthrough pain', which is used both to describe incident pain and pain in patients whose oral morphine dosing is inadequate.

Breakthrough cancer pain

There are relatively few studies describing this phenomenon. On the whole these studies report the number of patients experiencing breakthrough pain, but it has either not been evaluated as a primary outcome, or it has not been defined in detail. Two studies provide the most reliable evidence for the occurrence of breakthrough pain in cancer patients (Table 8). 49,50 The first, a prospective study, reports on 63 adult patients admitted to a hospital pain service. On admission to the study, all patients had well-controlled baseline pain (moderate intensity or less). Breakthrough pain that occurred in the previous 24 hours, defined as temporary flares of severe or excruciating pain with stable opioid dose, was reported by 63% (41) patients. In a later study by the same authors, a cross-sectional survey of 178 in-patients with cancer was conducted.⁵⁰ Of the 164 who met the inclusion criteria for controlled background pain, 51% (84) experienced breakthrough pain during the previous day. In both studies the characteristics of the breakthrough pains were varied, and were experienced many times during the day (median 6; range 1-60) lasting from seconds to hours. Precipitating factors were often identified, but pains occurred without warning half of the time. Bruera et al. described observations on the occurrence and nature of incident pain in 118 cancer patients enrolled in an open uncontrolled trial.⁵¹ They identified 19% (23) with severe incident pain defined as spontaneous or provoked acute exacerbations of pain occurring against a background of good opioid pain control. Movement was the precipitating factor in all of the cases.

Face or head pain

Migraine

Numerous epidemiological studies have been published reporting prevalence rates of migraine headache. These rates vary widely from study to study depending on the disease definition used and the age and gender composition of the study population.⁵² Only population-based studies that met standard International Headache Society (IHS) diagnostic criteria for migraine headache, were conducted in European or North American adults, and that reported prevalence rates of migraine for men and women separately, were included here.

Twelve studies meeting these criteria were identified, none in the UK (**Table 9**). Ten reported prevalence and two incidence. Migraine prevalence was higher in women (14 000 to 22 000/100 000) than in men (5000 to 8000/100 000, though one small study of older adults in Italy recorded no men with migraine). In five studies investigating a range of age groups, migraine prevalence was highest in 30–45 year old women and men. These findings are consistent with those reported in a meta-analysis of 18 studies of all ages and from all countries.⁵³

The incidence of migraine headache has been estimated from two large population-based surveys in the USA. Medical records of 6478 patients with a diagnosis of headache were surveyed to determine the incidence of clinically detected migraine (IHS criteria) in 629 patients. Age-adjusted incidence was 137 per 100 000 per person-years in men, and 294 per 100 000 per person-years in women. Incidence of migraine peaked in women (20–24 years) later than in men (10–14 years). Using a cross-sectional telephone interview of 10 169 subjects and estimated migraine incidence using reported age of onset, migraine with aura peaked in men at around five years of age, and without aura between 10 and 11 years.

 Table 8: Breakthrough pain in cancer patients.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Occurrence
Bruera <i>et al.</i> 1992 ⁵¹	Open, uncontrolled trial, pain assessment	Cancer patients admitted to a palliative care unit, Canada	Incident pain defined as pain under good control with opiate analgesics while resting, and severe acute exacerbations that occurred spontaneously or on movement	118 patients admitted	63 ± 8 years	23/118 (19%) reported incident pain
Portenoy and Hagen 1990 ⁴⁹	Prospective survey, questionnaire	Cancer patients attending pain service at a cancer hospital, USA	Breakthrough defined as pain > moderate intensity following pain of moderate or less intensity for > 12 hours/day in previous 24 hours, and stable opioid dose for > 2 days Pain intensity rated on 5 point categorical scale (none, slight, moderate, severe, excruciating)	63, all patients reported on	15–81 years	Occurrence of breakthrough pain 41 (63%) in 24 hours preceding the interview Tables in paper report pain frequency, type of onset and duration Gives data on incident and spontaneous pain
Portenoy et al. 1999 ⁵⁰	Cross-sectional survey, questionnaire and interview	Hospital inpatients with cancer, randomly selected, USA	Breakthrough pain defined as one or more episodes of severe or excruciating pain in patients with controlled background pain The number of breakthrough pain episodes was recorded in addition to location, quality, and precipitating factors	178, 92% (164) included in analysis, 14 (7.8%) excluded due to uncontrolled background pain	26–77	84 (51%) reported breakthrough pain on preceding day

Table 9: Migraine.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Prevalence per 10	00 000	
			delimition			Men	Women	Overall
Breslau <i>et al.</i> 1991 ⁵⁷	Survey, face-to- face interview	HMO population, random sample, USA	IHS	1,200 84% (1007) response rate	21–30	Lifetime prevalence: 7,000/100,000 1 year period prevalence: 3,400/100,000	Lifetime prevalence: 16,300/100,000 1 year period prevalence: 12,900/100,000	Lifetime prevalence: 12,800/100,000
Franceschi et al. 1997 ⁵⁸	Longitudinal study, clinical exam	Elderly population, random sample, Italy	IHS	312	65–84	1 year period prevalence: 0/ 100,000	1 year period prevalence: 2,000/100,000	
Göbel <i>et al</i> . 1994 ⁵⁹	Survey, face-to- face interview	General population, random sample, Germany	IHS	5,000 8,1% (4,062) response rate	18 +	1 year period prevalence: 7,000 (6,000 to 9,000)	1 year period prevalence: 15,000/100,000 (13,000–17,000)	1 year period prevalence: 11,000/100,000 (10,000–13,000)
Henry <i>et al.</i> 1992 ⁶⁰	Survey, face-to- face interview	General population, stratified quota with random element, France	IHS	4,204	15 +	Lifetime prevalence: 4,000/100,000	Lifetime prevalence: 11,900/100,000	Lifetime prevalence: 8,100/100,000 (6,200–10,000)
Linet <i>et al.</i> 1989 ⁶¹	Survey, telephone interview	General population, residents of Washington County, Maryland USA	IHS	10,000	12–29	1 year period prevalence: 5,300/100,000	1 year period prevalence: 14,000/100,000	
Michel <i>et al.</i> 1996 ⁶²	Survey, PSAQ	General population, France	IHS	6,000 households 80% (n=9,411) response rate	18 +	3 month period prevalence: 8,000/100,000	3 month period prevalence: 18,000/100,000	3 month period prevalence: 15,000/100,000 (12,000–14,000)
O'Brien <i>et al.</i> 1994 ⁶³	Survey, telephone interview	General population, random sample, Canada	IHS	4,235 66% (2,922) response rate	18 +	Lifetime prevalence: 7,800/100,000 1 year prevalence: 7,400/100,000	Lifetime prevalence: 24,900/100,000 1 year prevalence: 21,900/100,000	

Table 9: Continued.

Reference	Type of study	Sample source	Disease	Sample size	Age range	Prevalence per	100 000	
			definition			Men	Women	Overall
Rasmussen et al. 1991 ⁶⁴	Prospective survey, clinical exam	General population, random sample, Denmark	IHS	1,000 75.9% (740) response rate	25–64	Lifetime prevalence: 8,000/100,000 1 year period prevalence: 6,000/100,000 (4,000–9,000)	Lifetime prevalence: 25,000/100,000 1 year period prevalence: 15,000/100,000 (12,000–19,000)	Lifetime prevalence: 16,000/100,000 1 year period prevalence: 10,000/100,000 (8,000–13,000)
Stewart <i>et al.</i> 1992 ⁶⁵	Survey, PSAQ	General population, random sample, USA	IHS	20,468 63.4% response rate	12–80	1 year period prevalence: 5,700/100,000	1 year period prevalence: 17,600/100,000	
Stewart <i>et al</i> . 1996 ⁶⁶	Survey, telephone interview	General population, USA	IHS	12,000	18–65	1 year period prevalence: 8,200/100,000	1 year period prevalence: 19,000/100,000	
						Incidence per 100 000 person-years		
						Men	Women	Overall
Rozen <i>et al.</i> 1999 ⁵⁶	Retrospective survey, medical record review, 1989–90	General population with medically recognised migrainous disorder, Olmsted County, Minnesota, USA	IHS		All ages	194/100,000	482/100,000	
Stang <i>et al</i> . 1992 ⁵⁴	Retrospective survey, medical record review, 1979–81	General population with medically recognised migrainous disorder, Olmsted County, Minnesota, USA	IHS	6,476 records reviewed	All ages	137/100,000	294/100,000	216/100,000

In women, migraine incidence with aura peaked between ages 12 and 13 and migraine without aura between 14 and 17, giving a higher migraine incidence peaking at a lower age. The difference may be due to the different data collection methods. A recent report showed an increase in the incidence of migraine in the USA in women of reproductive age.⁵⁶

A primary care trust of 100 000 people will have about 10 000 women and 2000 men who suffer from migraine. Only about one in five or six will seek medical care, the remainder using analgesics available off prescription, or no treatment at all. 67

Headache

Based on five UK population-based studies in adults, the one year period prevalence of headache ranged from 70–83% in men and 78–90% in women. These studies all used disparate, and in many cases unclear, headache definitions, and therefore do not provide reliable prevalence estimates.

When a more restricted headache definition was used, such as frequent headache as defined by IHS criteria, five population-based studies in adults from North America and Europe were found (**Table 10**). All of the studies used validated methods such as clinical examination, telephone interview or self-assessed questionnaires. In four studies, the one year prevalence of chronic tension-type headache (CTTH) was 1000 to 3000/100 000, and was reported more frequently by women than men. ^{58,73–75} One German study reported a lifetime prevalence of CTTH of 1% for women. There were no cases of CTTH reported by men in this study. ⁵⁹

The incidence of cluster headaches⁷⁶ was 10/100 000.

Trigeminal neuralgia

Incidence and prevalence of trigeminal neuralgia are difficult to estimate due to the lack of epidemiological studies with clear diagnostic criteria. Only two large population-based studies reported incidence rates for the UK⁷⁷ and USA,⁷⁸ respectively (**Table 11**).

From the medical records of the 70 000 residents of Carlisle between the years 1955–6 an incidence of 2.1/100 000 was derived.⁷⁷ The authors stated that the true incidence might have been higher because local ENT hospitals were not included. A retrospective review of the medical records of the 60 000 residents of Rochester county, Minnesota gave an annual incidence for the first episode of trigeminal neuralgia of 4.7 per 100 000 (95% CI 3.6 to 5.8).⁷⁸ Incidence rates increased with age, and were not significantly different between men and women. The authors also reported a crude prevalence rate by multiplying the annual incidence by the median survival time in years. They estimated that the prevalence of a current or recent attack of trigeminal neuralgia in a population aged 50–70 years would be < 1 in 250 or 400 per 100 000.

Only one direct estimate of trigeminal neuralgia prevalence was found.⁷⁹ In a survey of 1144 residents of a French village, 86% of the residents completed a neurological questionnaire, and three months later 261 were followed up with a neurological examination. One man was diagnosed with trigeminal neuralgia, diagnostic criteria not stated, to provide a prevalence estimate of 100/100 000.

Atypical facial pain

No studies providing reliable prevalence and incidence data for atypical facial pain were found.

Table 10: Headache.

Reference	Type of study	Sample source	Disease definition	Sample size	Age	Prevalence per 100,000			
					range (years)	Men	Women	Overall	
Franceschi et al. 1997 ⁵⁸	Longitudinal study, clinical exam	Elderly population, random sample, Italy	IHS criteria for headache classification	n=312	65–84	1 year period prevalence CTTH: 1,200/100,000	1 year period prevalence CTTH: 4,000/100,000	1 year period prevalence CTTH: 2,600/100,000	
Gobel <i>et al.</i> 1994 ⁵⁹	Survey, face-to- face interview	General population, randomly selected, Germany	IHS criteria for headache classification	n=1,200, 8,4% (n=1,007) response rate	21–30	Lifetime prevalence CTTH: 0/ 100,000	Lifetime prevalence CTTH: 1,000/100,000	Lifetime prevalence CTTH: 1,000/100,000	
Rasmussen 1995 ⁷³	Survey, recruitment by telephone followed by examination and interview by a physician	General population, randomly selected residents Copenhagen county, Denmark	IHS criteria for headache classification	n=1,000 selected, 25 unattainable, 75.9% (n=790) response rate	25–64	1 year period prevalence: Tension-type headache: 63,000/100,000 ETTH: 56,000/100,000 CTTH: 2,000/100,000	1 year period prevalence: Tension-type headache: 86,000/100,000 ETTH: 71,000/100,000 CTTH: 5,000/100,000		

						Incidence per 1	00000	
						Men	Women	Overall
Scher et al. 1998 ⁷⁵ and Schwartz et al. 1998 ⁷⁴	Survey, telephone interview	General population, randomly selected households, Baltimore County, USA	Type of headache per IHS criteria, either migraine or frequent headache Frequent headache defined as > 180 headaches/year and further subclassified: chronic tension-type headache (CTTH), frequent headache with migrainous features (FH/M) and other frequent headache (FH/O)	19,840 households selected, 6.7% could not be contacted Interview completed on 13,343 (77.4%) eligible subjects	18–65	1 year period prevalence: ETTH: 36,000/100,000 Frequent headache: 2,800/100,000 CTTH: 1,600/100,000 FH/M: 700/100,000 FH/O: 500/ 100,000	1 year period prevalence: ETTH: 42,000/100,000 Frequent headache: 5,000/100,000 CTTH: 2,600/100,000 FH/M: 1,700/100,000 FH/O: 800/100,000	1 year period prevalence: ETTH: 38,000/100,000 Frequent headache: 4,100/100,000 CTTH: 2,200/100,000 FH/M: 1,300/100,000 FH/O.: 600/100,000
Swanson et al. 1994 ⁷⁶	Case ascertainment from population	Olmsted County, Minnesota, USA	Cluster headaches, IH definition with minor variations	6,476 respondents in migraine and headache survey	Adults	15.6/100,000 (8.9–22.3)	4.0/100,000 (0.4–7.6)	9.8/100,000 (6.0–13.6)

Abbreviations: IHS = International Headache Society; CTTH = chronic tension type headache; ETTH = Episodic tension type headache.

Table 11: Trigeminal neuralgia.

						Incidence per 100 000 population				
Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Overall	Men	Women	Prevalence	Natural history
Brewis <i>et al.</i> 1966 ⁷⁷	Retrospective review of medical records	General population, residents of Carlisle, UK	Disease definition not given, but states that diagnosis by consultant physician was accepted, cases where diagnosis not clear further investigated, most excluded	n =70,000	0-85+	Annual age adjusted incidence 1955–61: 2/100,000				
Katusic <i>et al.</i> 1990 ⁷⁸	Retrospective review of medical records 1945–84 with diagnosis confirmed by a neurologist by clinical examination	General population, all residents of Rochester County, Minnesota, USA	Diagnosis of trigeminal neuralgia per Rushton and Olafson, briefly: 1. Brief paroxysms of severe pain of trigeminal nerve 2. Unpredictable remissions and exacerbations of pain 3. No evidence of sensory or motor deficit of involved nerve 4. Occurrence of trigger zones	n=222 medical records identified with diagnosis of trigeminal neuralgia, 147 excluded from study due to not meeting diagnosis criteria, not meeting residency requirements or onset outside of study time period	24-93	Annual incidence of first episode of trigeminal neuralgia 1945–84: 4.7/100,000 (3.6–5.8)	Annual incidence of first episode of trigeminal neuralgia 1945–84: 3.4/100,000 (1.9–4.9)	Annual incidence of first episode of trigeminal neuralgia 1945–84: 5.9/100,000 (4.3–7.5)	Prevalence may be derived by multiplying the annual incidence by the median survival measured in years, providing that incidence does not change with time An estimate of the prevalence of a current or recent attack of trigeminal neuralgia in a population aged 50–70 years would be < 1:250 or 400:100,000	Median number of episodes = 3 (range 1–11), 29% had 1 episode, 19% had 2, 24% had 3, 28% had 4–11 episodes Median length of an episode was 49 days, mean 116 days (range 1–1,462 days) 65% patients were estimated to have a second episode within 5 years, 77% within 10 years Among the 53 patients with 2 or more episodes, 66% experienced a third episode within 5 years of the second episode, 79% had a third episode within 10 years The 10 year survival from onset of trigeminal neuralgia to death was 46% (n=75)

Neuropathic pain

Diabetic neuropathy

Two large population-based studies have been conducted to determine the occurrence of diabetic neuropathy (**Table 12**). The first, in the UK, involved 97 034 adult patients registered with 10 general practices covering both urban and rural areas. According to strict diagnostic criteria, the occurrence of sensory neuropathy in all diabetics was 16% (95% CI 15 to 19%). There were no significant differences between prevalence rates for type I and II diabetes, or men and women. There was no specific mention of painful neuropathy. In an American survey of a random sample of 84 572 adults there were 2405 diagnosed diabetics, and 99% completed a postal self-assessed questionnaire. The occurrence of at least one symptom of sensory neuropathy in all diabetics was 38%, and pain or tingling in 23%.

These findings broadly agree with those from four clinic or hospital-based studies that determined the prevalence of sensory neuropathy in diabetic subjects having treatment (**Table 12**). The occurrence of painful neuropathy was 11% in type I diabetics with strict diagnostic criteria⁸² and 25% in all diabetics using a pain questionnaire.⁸³ Nabarro⁸⁴ found 16% painful neuropathy and O'Hare *et al.*⁸⁵ found 13%.

These studies showed that sensory neuropathy becomes more prevalent at older ages, but occurs with similar frequency in men and women. There was no significant difference between the prevalence rates for type I and type II diabetes. A primary care trust of 100 000 people will have about 2000 diabetics. About one in five will have painful neuropathy at some stage

Postherpetic neuralgia

Herpes zoster occurs in the general population at a rate of about 340/100 000 per year, ^{86,87} with 195 000 new cases a year. Following primary infection with the varicella zoster virus, the virus becomes dormant in dorsal root ganglia. Postherpetic neuralgia (PHN) is a common complication of herpes zoster, occurring in about 13–26% of cases, and including persistent pain after the onset of zoster. In the over-60s particularly, pain is common.

A summary of the occurrence of PHN is in **Table 13**, though Edmunds *et al.* also have a detailed review of the epidemiology. ^{86,87} The occurrence of painful neuropathy depended upon populations studied because of the large age-dependency. Painful neuropathy in over 40% of people aged over 50 was a common finding (**Table 13**). One incidence study ⁸⁸ indicated that a primary care group of 100 000 people could expect to see 34 new cases a year.

Multiple sclerosis

Multiple sclerosis has a crude prevalence of about 100/100 000 in England and Wales, but rates about double that in Scotland. ⁹⁵ A number of studies have examined the occurrence of chronic pain in patients with multiple sclerosis, and they are summarised in **Table 14**. Whatever definition of pain used, pain was common, occurring in about half of multiple sclerosis patients. A primary care trust of about 100 000 people in England or Wales could expect to have about 50 patients with multiple sclerosis and chronic pain. There would be about twice as many in Scotland.

Table 12: Chronic pain due to diabetic neuropathy.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Occurrence
Boulton et al. 1985 ⁸²	Prospective study, clinical exam	IDDM subjects attending diabetic clinic, Sheffield, UK	Definition of sensory polyneuropathy by strict criteria requiring presence of symptoms and signs of nerve dysfunction in the absence of peripheral vascular disease Pain sensations for at least 1 year	387 approached, 99% (n=382) agreed to participate	16–59	Painful neuropathy in 10.7%
Chan <i>et al.</i> 1990 ⁸³	Case-controlled survey, questionnaire	Patients attending a diabetic clinic, case-matched with non-diabetic control group (visitors of relatives in hospital), UK	Diabetes > 3 months duration. Chronic pain defined as pain present most of the time Patients used diagram to indicate site and radiation of pain, pain descriptors include aching, burning, and stabbing/ shooting Duration of pain also sought	Diabetics n=974 98% response rate (n=962)	adults – mean age all diabetics 58.1 ± 17.5	Chronic pain in 25.2% Burning and stabbing or shooting pain in 7.4%
Harris <i>et al.</i> 1993 ⁸¹	Cross-sectional survey, part of National Health Interview survey 1989, interview and questionnaire	General population, NIDDM adults identified from households, USA	Questions asked 'During the last 3 months have you experienced: 1. Numbness or loss of feeling in hands and feet 2. Painful sensation or tingling in hands and feet 3. Decreased ability to feel hot or cold in things you touch IDDM defined in paper'	84,572 surveyed 2,405 diagnosed diabetics, of these 99.3% (2,405) questioned further	± 18	In all diabetics over 3 months: numbness: 28.2% pain or tingling: 26.8% decreased sensation to hot or cold: 9.8% ± 1 of above symptoms: 37.9%. In type I diabetics over 3 months: numbness: 15.7% pain or tingling: 22.8% decreased sensation to hot or cold: 9.9% ± 1 of above symptoms: 30.2%.

\sim
\Box
0
\supset
$\overline{}$
•
π
a
_
\supset

Reference Type of study Sample source Disease definition Sample size Age range (years) Occurrence Nabarro Prospective Type I and type II Type I and type II diabetes as n=1,410 type I DNS In Type I: 199184 Painful neuropathy in survey, interview diabetic per WHO criteria diabetes, n=4,962 Neuropathy recorded if Type II diabetes, 16.3% with neuropathy and outpatients questionnaire attending diabetic considered to be clinically data on all patients and 2.8% of all type I clinic, 1954-88, important, DNS diagnostic In type II: London, UK criteria Painful neuropathy in 5.4% with neuropathy and 0.6% of all type II O'Hare et al. Prospective Type I and type II Type I and type II diabetes n=800, type I = 1 year period prevalence 16 - 841994⁸⁵ 336, type II = 464, survey, interview diabetics attending per standard criteria pain/paraesthesia: outpatient diabetic neuropathy criteria not data on all patients All diabetics: 13.3% and questionnaire clinic over 1 year, defined, pain intensity not Type I: 12.5% UK defined Type II: 13.8% Walters et al. Case-controlled All diabetics Diabetes defined per WHO n=97,034 patients Diabetics all ages Occurrence of 199280 survey, interview registered with 10 criteria registered in neuropathy: and clinical GP practices, case-Neuropathy defined as: 10 practices All diabetics 16.3% matched with non-1. Presence of symptoms: n=1,150 diabetics (14.6-19.0)exam diabetic controls, numbness, burning, prickling, (93.7% reviewed) Type I diabetes 12.7% UK deep aching, tenderness or (8.0-17.6)Type II diabetes 17.2% tingling present bilaterally, ± 1 year, at rest and included (15.9-18.5)in the feet 2. Loss of light touch

3. Impairment of pain

4. Absent ankle jerks in subjects < 70 years 5. Abnormal vibration perception thresholds

perception

Table 12: Continued.

 Table 13: Chronic pain due to post-herpetic neuralgia (PHN).

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Occurrence
Brown 1976 ⁸⁹	Retrospective review of medical records	Patients attending dermatology outpatients, 10 year period 1963–72, USA	PHN defined as pain > 6 weeks after initial eruption of herpes zoster	140, all reported	Not stated	All ages: pain occurred in 34% Less than 50 years: pain occurred in 6% More than 50 years: pain occurred in 43%
de Moragas and Kierland 1957 ⁹⁰	Retrospective review of medical records	Patients diagnosed with herpes zoster or PHN 1939–45, USA	PHN not defined	916 records reviewed, all reported	Less than 20 to more than 70	Pain occurred in 49% beyond 1 month Pain lasted 1–6 months in 21% Pain lasted 6–12 months in 4% Pain lasted more than 12 months in 25%
Helgason <i>et al.</i> 2000 ⁹¹	Prospective cohort study	January 1990 to June 1999 in 100,000 general practice population in Iceland	Single investigator diagnosis and questions about pain at 1, 3, 6 and 12 months	421 patients with complete ascertainment	All ages	In under-60s, 2% had pain at 3 months In over-60s, 7% had pain at 3 months and < 3% at 12 months
Lancaster et al. 1995 ⁹²	Meta-analysis of randomised trials of acute interventions to prevent long-term pain	Any randomised trial measuring pain at (at least) 1 month	Treatment of acute zoster Pain (not defined)	617 patients treated with placebo and with at least 6 months' follow-up	Adults	94/617 patients had pain at 6 months (15%)

Table 13: Continued.

Meister <i>et al.</i> 1998 ⁹³	Prospective documentation of all cases of zoster by random selection of German physicians	Patients recruited September 1994–March 1995 486 physicians contributed patients	Pain at 4–5 weeks	2,063 patients with zoster	Less than 10 to more than 70	Pain in afflicted dermatome at 4–5 weeks in 28%
Rogers and Tindall 1971 ⁹⁴	Retrospective review of medical records	Patients attending a medical centre and diagnosed with HZ or post-zoster complications, 1939–68, USA	PHN defined as pain persisting > 4 weeks after HZ infection	n=576 patients with HZ or complications n=243 age 60+ (results presented for these patients)		Pain occurred in 47% of over-60s Pain occurred in 16% of under-60s Pain lasted longer than 6 months in 58% of over-60s
						Incidence
Cockerell <i>et al.</i> 1996 ⁸⁸	Prospective 1 year study, clinical exam	Patients attending two GP surgeries, UK	Neurological disease as diagnosed by clinician	n=25,000 registered with 2 GPs	DNS	34/100,000

 Table 14: Chronic pain due to multiple sclerosis.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Occurrence of pain
Archibald <i>et al.</i> 1994 ⁹⁶	Prospective examination of consecutively referred outpatients with MS in a clinic	Clinic patients, Nova Scotia, Canada	Clinically definite MS Pain measured in a structured interview for severity, type and duration	85 of 94 approached	19–75	Pain occurred in 53%
Brochet <i>et al.</i> 1992 ⁹⁷	Prospective study, questionnaire	Multiple sclerosis patients attending outpatients, Group 1 = pain reported at least once; Group 2 = no pain, France	Pain syndromes reported: painful paraesthesias or dysaesthesias; electric shocks; lightning pain; painful leg spasms; articular and myofascial pain, also location, duration and frequency of pain	108	DNS	Pain occurred in 41%
Clifford and Trotter 1984 ⁹⁸	Retrospective medical record survey	Attendees at MS clinic between 1977 and 1983, in St Louis, Missouri, USA	Pain was defined as a major complaint that lasted at least 2 weeks	317	15–70	Pain occurred in 29%
Moulin <i>et al.</i> 1988 ⁹⁹	Retrospective review of medical records, PSAQ and telephone interview	MS patients who attended outpatient clinic between 1973 and 1985, Canada	MS by Rose criteria, 62% definite MS, 38% probable or possible MS Clinically significant pain defined as: 1. Paroxysmal stereotyped pain syndrome regarded as characteristic for MS 2. Chronic pain present intermittently or continuously over 1 month	167 patients approached, 159 responded	20 to over 60	Occurrence of any clinically significant pain in 55% Occurrence of chronic pain in 48%

Table 14: Continued.

Stenager <i>et al.</i> 1991 ¹⁰⁰	Prospective survey, questionnaire and interview	Random selection of patients with MS attending neurology clinic, Denmark	Chronic pain defined as constant or intermittent pain lasting more than 1 month Acute syndromes included transient symptoms lasting < 1 month Headaches and minor pain syndromes excluded.	117, all patients interviewed	25–55 years	Occurrence of pain at any time in 65% Occurrence of pain at interview in 45%
Vermote <i>et al.</i> 1986 ¹⁰¹	Consecutive prospective survey of MS patients	Patients with MS attending MS clinic in Belgium	MS by Schumacher criteria Pain measured by Dutch equivalent of MPQ	83	not given	Pain occurred in 54%
Warnell 1991 ¹⁰²	Prospective survey, PSAQ	MS patients attending outpatient clinic, Canada	Painful symptoms reported, including their frequency and intensity PIVAS scale	500, 73% (n=364) responders	19–74	Pain occurred in 64%

C:/Postscript/07_HCNA3_D2.3d - 10/1/7 - 8:45 [This page: 552]

552 Chronic Pain

Chronic post-stroke pain

Only one prospective study of chronic post-stroke pain has been reported. ¹⁰³ Two hundred and sixty seven adult patients were recruited to a Danish study after admission to hospital following an acute stroke. At six months, 78% had survived and the occurrence of chronic post-stroke pain, according to strict criteria, was 6.5% at six months and 8.4% at one year. The incidence of chronic post-stroke pain during the first year after stroke was 8%, of which 10/16 patients reported pain of moderate to severe intensity. In a retrospective survey of 400 cases of stroke in the UK, 2% were reported to have chronic post-stroke pain. ¹⁰⁴ The median time for onset of pain was three months from stroke, and could be as long as 24 months. In a primary care trust of 100 000 people there could be as many as 10 to 50 people with chronic post-stroke pain.

Vascular pain

There is substantial information on the incidence and prevalence of cardiovascular disease due to its high mortality and morbidity. There is limited information about the incidence and prevalence of painful symptoms.

Intermittent claudication

Accurate estimates of intermittent claudication can only be obtained from population surveys, as most subjects with claudication are not referred to hospital unless symptoms are severe enough to warrant surgery. Larger studies published since 1990 are summarised in **Table 15**. Most studies are conducted in an older adult population because this is primarily a disorder of older adults. In older adults the prevalence of intermittent claudication is of the order of 1000/100 000 to 2000/100 000, according to a review. When the age range involves mainly people in their seventh decade and older, higher prevalence rates are found. ^{106,107}

The incidence, again in older adults, is 400–1600/100 000. A typical primary care trust of 100 000 people might expect to have 400–800 people with intermittent claudication, and see 200 new cases a year.

Raynaud's phenomenon

One of the problems with prevalence estimates of Raynaud's phenomenon is that of knowing the degree of chronic pain experienced. The four population surveys identified (**Table 16**) record quite high figures for prevalence, though reducing with more exacting definitions of disorder. It is likely that even the prevalence of a clear edge between pale and normal colour overstates the prevalence of painful Raynaud's.

Angina

Many UK epidemiological studies estimating prevalence of coronary heart disease are in specific occupational groups only (Whitehall and UK heart disease prevention study), ¹¹⁶ or use methods other than the standard Rose chest pain questionnaire and ECG to estimate prevalence rates. ¹¹⁷ The Speedwell and Caerphilly survey, ¹¹⁸ Scottish Heart Health Study, ¹¹⁹ Grampian survey ⁶ and the Maidstone and Dewsbury survey ¹⁰⁶ provide reliable estimates of prevalence rates of angina in the UK (**Table 17**). Prevalence is age-dependent, because almost no angina occurs until the sixth decade of life. In all adults the prevalence is about 5000/100 000, but is about double this at 10 000/100 000 in over-50s. A US study suggests an incidence in adults between 30 and 74 years of about 1000/100 000.

A primary care trust with a population of 100 000 might expect to have about 4000 cases of angina, with about a third of them severe. There would be about 500 new cases a year.

Table 15: Claudication.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Prevalence per 100,000			Incidence per
						Overall	Men	Women	100,000
Bainton <i>et al.</i> 1994 ¹⁰⁸	Prospective, longitudinal study, part of Speedwell heart disease study, Q and clinical exam	registered	Claudication defined as: 1. pain on walking in one or both calves 2. no pain on rest 3. relieved within 10 min resting 4. never disappears when walking continued 5. pain causes subject to stop or slow down	2,550 men selected, 92% attended clinic for first visit	45–59		Prevalence 1,200/100,000 at baseline rising to 2,800/100,000 after 10 years		Annual incidence of new cases 400/100,000
Bowlin <i>et al.</i> 1994 ¹⁰⁹	Prospective study and follow-up of Israeli men	Male government employees	London School of Hygiene cardiovascular disease questionnaire	8,343 men free of coronary heart disease	40–65		baseline prevalence 2,700/100,000		Annual incidence of new cases 860/100,000
Leng et al. 1996 ¹¹⁰	Prospective, longitudinal study, SAQ and exam	Patients randomly selected from 10 GP practices, UK	Criteria for IC per Rose/WHO questionnaire, ankle brachial pressure index and reactive hyperaemia test. Grade 1 = calf pain when walking uphill or hurrying Grade 2 = pain upon walking ordinary pace on level Probable = calf pain present on exercise but not at rest	1,592 selected 65% responded	55–74	Prevalence at 5 years in those that completed WHO questionnaire: 7,100/100,000			Annual incidence 1,550/100,000

Table 15: Continued.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range (years)	Prevalence per 100,000			Incidence per
						Overall	Men	Women	100,000
Leng <i>et al.</i> 2000 ¹⁰⁶	Prospective survey of random sample of men and women	Dewsbury and Maidstone, UK	Leg pain typical of intermittent claudication if pain on walking relieved within 10 minutes	417 of 481 men and 367 of 441 women attended for ultrasound examination	56–77		6,400/100,000 (2,100–10,700) in men without femoral plaque 17,200/100,000 (12,600 to 21,800 with femoral plaque) Plaque present in 64%	6,700/100,000 (2,500–10,900) in women without femoral plaque 5,600/100,000 (2,400 to 8,800 with femoral plaque) Plaque present in 64%	
Meijer et al. 1998 ¹⁰⁵	Prospective follow-up study	Individuals aged 55 and over in Rotterdam, Holland	WHO/Rose questionnaire	10,275 invited, 7,983 responded (78%)	over 54	Prevalence 1,600/100,000	2,200/100,000	1,200/100,000	
Menotti <i>et al.</i> 2001 ¹⁰⁷	Prospective longitudinal study of men in three European countries		Rose leg pain questionnaire	2,285 men	65–84		Finland 11,000/100,000 Holland 7,600/100,000 Italy 8,400/100,000		
Smith <i>et al.</i> 1990 ¹¹¹	Prospective longitudinal study of government employees	Large prospective study	Questionnaire	18,388	40–64	Probably intermittent claudication 800/100,000 Possible intermittent claudication 1,000/100,000			

Abbreviations: IC = intermittent claudication; Q = questionnaire; SAQ = self-assessed questionnaire; PSAQ = postal self-assessed questionnaire; ECG = electrocardiogram.

 Table 16:
 Raynaud's phenomenon.

Reference	Type of study	Sample source	Disease definition	Sample size	Age	Prevalence per	100,000	
					range (years)	Overall	Men	Women
Brand <i>et al.</i> 1997 ¹¹³	Longitudinal 16 year study, questionnaire and clinical exam	General population, 2nd generation participants in Framingham Heart study (offspring and their spouses of the original participants), USA	Evidence of Raynaud's phenomenon: 1. sensitivity to cold 2. blanching of fingers when exposed to cold, with numbness followed by cyanosis, then redness and tingling or pain.	4,182 selected DNS response rate	over 20	Prevalence: 8,800/100,000	Prevalence: 8,100/100,000	Prevalence: 9,600/100,000
Maricq <i>et al.</i> 1986 ¹¹⁴	Carolina Health Survey, interviewer administered questionnaire	General population, random selection residents of South Carolina, USA	Prevalence estimates given for several different criteria: 1. reported cold sensitivity of fingers or toes 2. cold sensitivity combined with blanching and/or cyanosis 3. cold sensitivity severe enough to lead to physician consultation	1,752 subjects interviewed	over 18	Lifetime prevalence: criteria 1: 10,000/100,000 criteria 2: 4,600/100,000 criteria 3: 3,000/100,000 criteria 2 + 3: 2,000/100,000		
Palmer <i>et al.</i> 2000 ¹¹²	Random sample of adults of working age	Randomly selected adult patients from 34 selected general practices across England, Wales and Scotland, plus members of armed forces	Prevalence estimates given for several different criteria: 1. Reported cold, numb and blanched fingers 2. Brought on by cold 3. Clear edge between pale and normal colour	22,194 questionnaires, 12,907 replies (58%)	16–64	Any blanching about 15,000/ 100,000 Cold induced blanching 12,000/100,000 Clear edge 4,800/100,000	Clear edge between 1,800/ 100,000 at 16–24 up to 7,200/100,000 at 55–65	Clear edge between 3,500/ 100,000 at 16–24 up to 5,100/100,000 at 55–65

Table 16: Continued.

Reference	Type of study	Sample source	Disease definition	Sample size	Age	Prevalence per 100,000		
					range (years)	Overall	Men	Women
Silman <i>et al.</i> 1990 ¹¹⁵	Two questionnaire surveys: 1. SAQ clinic population 2. PSAQ	Two populations studied: 1. All new patients attending 5 GP practices 2. Random sample, patients registered with above 5 GPs, UK	Raynaud's phenomenon defined by presence of all 3 criteria: 1. Episodes of finger blanching 2. Precipitated by cold 3. Sensory sensations (pins and needles and numbness) Interview and clinical exam of the positive patients	1. n=1,119 (response rate not recorded) 2. n=600 69% (n=413) response rate	over 15	Prevalence: clinic attendees 19,000/100,000 postal sample 15,000/100,000	Lifetime prevalence: clinic attendees: 16,000/100,000 postal sample: 11,000/100,000	Lifetime prevalence: clinic attendees: 21,000/100,000 postal sample: 19,000/100,000

Abbreviations: IC = intermittent claudication; Q = questionnaire; SAQ = self-assessed questionnaire; PSAQ = postal self-assessed questionnaire; ECG = electrocardiogram.

Table 17: Angina.

Reference	Type of study	Sample source	Disease definition	Sample size	Age	Prevalence per 100	,000		Incidence per
					range (years)	Overall	Men	Women	100,000
Bainton et al. 1988 ¹¹⁸	Two surveys: 1. Caerphilly and, 2. Speedwell surveys Rose chest pain questionnaire and 12 lead ECG	Both surveys general population: 1. selection middle-aged men, Caerphilly, UK 2. Selection men registered with 16 GPs, Speedwell, UK	Angina defined as: grade 1 (chest pain only on walking uphill or hurrying) grade 2 (chest pain on walking at an ordinary pace on the level)	1. n=2,818 selected 89% (n=2,512) examined 2. n=2,550 selected, 92% (n=2,348) examined	45–59		Prevalence of angina 8,200/ 100,000 About 30% was more severe grade 2		
Elliott <i>et al.</i> 1999 ⁶	Random sample of the general population	Adults aged over 25 in 29 general practices in Grampian Region, Scotland	Angina defined by patient in questionnaire, with instructions and after piloting	4,611 contacted, 3,605 responses	25 and over	Prevalence of angina 4,500/100,000, almost wholly in over-55s where prevalence was 10,100/100,000	4,900/100,000	4,100/100,000	
Leng <i>et al.</i> 2000 ¹⁰⁶	Prospective survey of random sample of men and women	Dewsbury and Maidstone, UK	Rose chest pain questionnaire	417 of 481 men and 367 of 441 women attended for ultrasound examination	56–77	9,600/100,000 (6,100 to 13,100) without femoral plaque 15,400/100,000 (12,100–18,700 with femoral plaque) Plaque present in 64%			
McGovern <i>et al.</i> 2001 ¹²⁰	Retrospective survey of hospital discharges for a population	All patients discharged from metropolitan hospitals, Twin Cities, Minnesota for 1985, 1990 and 1995	From hospital notes of signs, symptoms, medical history, enzymes, complications, therapy and ECGs	For 1995, 3,615 discharge records examined	30–74				Age-adjusted incidence of angina with or without MI in 1995 was 1,357/ 100,000 for men and 495/100,000 for women

Table 17: Continued.

Reference	Type of study	Sample source	Disease definition	Sample size	Age	Prevalence per	100,000		Incidence per
					range (years)	Overall	Men	Women	100,000
Menotti et al. 2001 ¹⁰⁷	Prospective longitudinal study of men in three European countries	Men aged 65 to 84 years in 1985 from previous longitudinal study	Rose chest pain questionnaire	2,285 men	65–84		Finland 19,700/100,000 Holland 10,300/100,000 Italy 9,500/ 100,000		
Shaper <i>et al.</i> 1984 ¹¹⁷	British Regional Heart Study, administered questionnaire, 3 lead ECG	General population, random selection middle aged men, UK	Angina defined as chest pain or discomfort with exertion plus: 1. Area of pain confirmed on diagram 2. Pain causes subject to slow down or stop 3. Pain goes away if stops exertion 4. Takes < 10 minutes for pain to go away	n=7,735 selected, 78% (n=6,033) response rate	40–59		Prevalence: 8,000/100,000		
Smith <i>et al.</i> 1990 ¹¹⁹	Scottish Heart Health study, prospective survey, SAQ and physical examination with 12 lead ECG	General population, random selection from 22 GP districts, UK	Angina defined as: grade 1 (less severe) grade 2 (more severe) criteria as per Rose chest pain questionnaire	74% response rate, n=10,359 analysed	40–59		Prevalence angina 6,300/ 100,000 (3,900 to 14,800) About 30% more severe grade 2	Prevalence angina: 8,500/ 100,000 (4,300 to 17,600) About 30% more severe grade 2	

Chronic postoperative pain

The contribution of surgery to the prevalence of chronic pain has been systematically studied among outpatients attending specialist pain clinics¹²¹ and studies have been published investigating chronic pain after particular operations.¹²² In the systematic review of published studies reporting the prevalence of chronic postoperative pain after a range of common surgical operations,¹²² the methodological quality of the majority of studies was poor.

In a large survey of 10 pain clinics in the UK, information was collected about 5130 adult patients by a questionnaire filled out by the physician. ¹²¹ Chronic pain due to surgery was reported by 23% of patients. The pain had lasted longer than 24 months in 59% of these, was of moderate to severe intensity in 76%, and significantly disabling in 44%. The sites of pain most frequently reported were: abdominal (47%), anal, perineal and genital (38%) and lower limb (35%). These estimates may be higher than expected for the general population as this survey represents a selective group of patients, but it does indicate that chronic postoperative pain can be a significant part of the work of pain clinics.

In another systematic review¹²³ which included studies with information about pain 12 weeks or longer after surgery, and excluded studies smaller than 50–100 patients (apart from amputation studies with 25 patients), chronic pain after surgery was common. Many studies had information to one year or longer, and many compared different surgical approaches, or anaesthesia. Phantom limb pain was common (up to 80%), but high rates of chronic pain were reported for all surgery. Even with hernia repair, which had the lowest incidence, rates varied from 0% to 29%. Predictive factors included pre-operative pain, repeat surgery, a surgical approach with risk of nerve damage, acute and severe postoperative pain, radiation, chemotherapy and a variety of psychological and depressive symptoms.

The focus here is on the best studied areas, of phantom limb and stump pain after amputation, 124,125 of chronic postoperative pain, and breast surgery 126,127 and thoracotomy. 128,129 Detailed information on pain after hernia repair can be found in Bay-Nielsen *et al.* 130 They surveyed all repairs in Denmark over two months in 1998; 29% reported having pain in the area of the hernia within the past month, and 11% reported that the pain impaired work or leisure activities. Only 4.5% (1 in 6) had sought medical advice or received treatment for the pain.

Pain after amputation

To determine the occurrence of phantom limb pain accurately, studies must differentiate between phantom limb sensation, phantom limb pain and stump pain. This section considers the studies where phantom limb pain was described distinctly (**Table 18**). Phantom limb pain occurred in half to three quarters of amputees, persisting at seven years post-amputation.

Pain characteristics were reported in most of the studies. In the 53% of amputees reporting phantom limb pain one year following amputation, pain intensity was rated as of mild or moderate intensity by all. ¹³¹ In three other studies, mean pain intensity ranged from 5.3 to 6.9 out of a maximum of 10. ^{124,125,132} Five years after limb amputation, pain was reported by 73%, in 65% pain was experienced frequently to occasionally, and 7.5% experienced constant pain in the phantom limb. ¹³³ Most prevalence estimates are potentially biased because of small sample sizes and low response rates.

High rates of stump pain were reported in prospective surveys of military veterans, with at least half of amputees having stump pain. Rates were 49%, ¹³⁴ 57% ¹²⁵ and 62% ¹²⁴ respectively.

There are perhaps 17–20 amputees per 100 000 population in Holland, ¹³⁵, ¹³⁶ and 28/100 000 in Finland. ¹³⁷ In a typical primary care trust, about 25/100 000 may be expected, most of whom will have chronic pain problems, either phantom limb pain, or stump pain, or both.

Table 18: Phantom limb pain.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Occurrence of pain
Buchanan and Mandel 1986 ¹³⁸	Retrospective review of medical records and interview by a technician	Amputees attending prosthetic clinic 1979–80, Canada	Presence of pain asked and recorded yes/no	716 respondents, in 93 (13%) of these some data missing but not specified	< 19 to 60+	Phantom limb pain in 63%
Houghton <i>et al.</i> 1994 ¹³⁹	Retrospective survey, SAQ	Amputees at single centre	Pain intensity 0–10 scale	212 selected, 176 responded	Adults	Phantom limb pain in 78%
Kooijman <i>et al.</i> 2000 ¹³⁴	Prospective survey with questionnaire	Amputees at a single orthopaedic centre	Not clearly stated	127 subjects of whom 99 filled in a questionnaire; 27 had congenital problems, so data on 72 with acquired defects	Adults	Phantom limb pain in 51% Stump pain in 49% Phantom sensations in 76%
Jensen <i>et al.</i> 1984 ¹⁴⁰	Prospective hospital- based study April 1980 to March 1982 Interview, standard questionnaire and examination 8 days, 6 months and 2 years after limb amputation	Patients undergoing limb amputation, Denmark	Phantom pain defined as painful sensations referred to the lost body part, except stump pain	All 58 patients agreed to participate, 24 (42%) died	24–91	Patients with painful phantom limb: 8 days after amputation: 72%; 6 months: 65%; 2 years: 59%
Krebs <i>et al.</i> 1985 ¹⁴¹	Retrospective survey, interview	Patients with limb amputation 1970–77, random selection in 1983	Not stated	Of 624 amputees, 86 of 95 alive in 1983	Adults	Phantom limb pain in 52%
Pohjolainen <i>et al.</i> 1991 ¹³¹	Retrospective survey, clinical exam and interview	Amputees attending prosthetic factory	Pain intensity cat scale (mild, moderate, severe)	155 selected, 124 assessed 1 year later	Adults	1 year after amputation phantom limb pain in 53%; mostly mild or moderate intensity

Table 18: Continued.

Sherman <i>et al.</i> 1983 ¹³²	Retrospective survey, PSAQ	Military veteran amputees, randomly selected, USA	Pain intensity 0–100 scale	764 of 1,321 members		Phantom limb pain in 85%
Sherman <i>et al.</i> 1984 ¹²⁴	Retrospective survey, PSAQ	Military veteran amputees, randomly selected, USA	Stump pain and phantom pain both reported PI on 0–10 scale 0 = no pain, 10 = unbearable pain	55% responded 2,694/ 5,000		Phantom limb pain in 78% average PI = 5.3 ± 4.9 Stump pain in 62%
Steinbach <i>et al.</i> 1982 ¹³³	Retrospective survey, interview	War veterans, traumatic amputees	Frequency of phantom limb pain assessed	75 survivors, 43 assessed	Adults	5 years after amputation phantom limb pain in 73% Pain frequency: constant 7.5% occasional 45% frequent 20%
Wartan <i>et al.</i> 1997 ¹²⁵	Retrospective survey, PSAQ	Military veteran male amputees, randomly selected, UK	Pain intensity using 10 point cat scale (0 = no pain, 10 = unbearable pain) Phantom pain and stump pain evaluated Frequency, site and type of pain reported	526/590 (89%) response rate	median age 73	Phantom limb pain in 55%; Stump pain in 57% mean PI 5.6 16% complained of daily pain 16% pain always present

Chronic postoperative breast pain

Eight studies reported the occurrence of chronic post-mastectomy pain (**Table 19**). Different categories of pain were reported, including phantom breast, scar pain and pain in the ipsilateral arm. Time after operation was important, as there was a trend for some reduction in occurrence after two years or longer. While most operations were partial or total mastectomy for cancer, pain occurred after augmentation and reduction operations, and after mastectomy with reconstruction. 143

There was some variation because of time after surgery, but typically 25 to 35% of the patients reported pain more than a year after operation, and about half at one year.

Chronic postoperative thoracotomy pain

Surgical aspects of post-thoracotomy pain have been reviewed, together with reports on its occurrence. ¹⁴⁹ **Table 20** gives results from six studies in the last ten years, all of which showed that chronic pain after thoracotomy was common, and that severe pain requiring treatment is also common, occurring in 15%–25% of patients undergoing thoracotomy. Results from surveys are supported by results from randomised trials; half of the patients reported long-term pain at one and half years. ¹⁵⁰ The precise relationship between pain before, during, and after surgery, and the development of chronic pain, remains contentious.

Chronic postoperative cholecystectomy pain

Two prospective studies reported the occurrence of chronic scar pain following open cholecystectomy. At 12 months occurrence of chronic pain at the incision site was 27%, ¹⁵⁵ and at 24 months 21%. ¹⁵⁶ Two studies have attempted to compare the occurrence of chronic pain after open with the incidence after laparoscopic cholecystectomy. Stiff *et al.* reported a occurrence of 3.4% after laparoscopic compared with 9.7% after open procedure. ¹⁵⁷ Wilson and Macintyre found a similar occurrence of 7% in both groups. ¹⁵⁸

Conclusion: prevalence and burden

Health care needs for chronic pain obviously extend from community through to hospital care. Patients with some chronic pain conditions, migraine for instance, may manage with over the counter medications, others will require prescription medication and some will need other interventions. **Figure 2** summarises prevalence data for some of the conditions mentioned above.

The prevalence data contains some surprises, and shows how biased a hospital view can be, omitting as it does those conditions which trouble patients but which they manage themselves (e.g. migraine), and those conditions which are managed largely in the community (e.g. polymyalgia rheumatica). A second facet of the prevalence data is that it does not capture, and indeed it cannot capture, the burden of the pain, nor the burden of the disability which goes with the pain in many of these conditions. Much of the 'repeat business' in secondary care pain management is for conditions for which there is no certain remedy. Health care needs therefore not only have to have to consider prevalence, but also the burden of the pain (and disability), and the 'treatability' of the pain.

The disease impact of some of the conditions mentioned above, compared with other conditions, was studied in about 15 000 Dutch patients. All research groups known to examine chronic diseases in the Netherlands were contacted to see what datasets were available. ¹⁵⁹ Studies had to use a standardised quality of life instrument, have full coverage of quality of life domains, include a range of chronic diseases, be big (at least 200 patients), have medically confirmed diagnoses, be obtained since 1992 and be geographically broad. Eight datasets broadly fulfilling these categories were obtained, with information on about 15 000

Table 19: Mastectomy.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Occurrence
Ivens <i>et al</i> . 1992 ¹⁴²	Survey	Outpatient attending breast clinic	Not stated	126	28–80	Pain at 1 year 45 %, 1–2 years 37%, 2–4 years 28 %, > 4 years 20% Mostly mild, less than 20% of patients with at least moderate pain
Kroner <i>et al.</i> 1992 ¹⁴⁴	Prospective 6 year survey	Patients attending oncology and radiotherapy department	Standard questionnaire	120, 110 at 1 year, 69 at 6 years	less than 69	Phantom breast pain at 1 year = 13 % Scar pain at 1 year = 23% Phantom breast pain at 6 year = 17% Scar pain at 6 year = 31%
Polinsky 1994 ¹⁴⁵	Survey	Patients attending support group, post-mastectomy 16 months to 32 years	Pain intensity, categorical scale	314, 251 responded, 223 analysed	31–76	Pain 22–32 %
Smith <i>et al.</i> 1999 ¹⁴⁶	Retrospective consecutive cohort	All surviving women having mastectomy from 1990 to 1995 in Aberdeen, Scotland	Character, location and timing of pain	511 questionnaires sent, 457 returned and 408 fully completed	32–93	Post-mastectomy pain in 43%, and 40% had pain related to operation site Highest rate in younger women
Stevens <i>et al.</i> 1995 ¹⁴⁷	Survey	Oncology outpatients	Cancer pain questionnaire and McGill questionnaire	95	over 18	Post-mastectomy pain in 20%
Tasmuth <i>et al.</i> 1995 ¹²⁶	Retrospective study, PSAQ	Patients with breast cancer treated by surgery between 1988–91 Types of surgery: modified radical mastectomy with axillary evacuation (MRM) or breast resection with axillary evacuation (BCT), Finland	Finnish McGill pain questionnaire, Effect of chronic pain on daily lives 5 point cat scale (none, slight, mod., considerable, great), analgesic	569, response rate 92%, 467 included in analysis	29–92	49% reported pain and about a quarter reported moderate or severe pain

Table 19: Continued.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Occurrence
Tasmuth et al. 1996 ¹²⁷	Prospective, 1 year study 1993–4 Patients assessed pre-op, 1 month, 6 months and 1 year after surgery Patients assessed by a researcher by examination and questions	Patients with non- metastasised breast cancer Types of surgery: modified radical mastectomy with axillary evacuation (MRM) or breast resection with axillary evacuation (BCT), Finland	PI VAS 10-cm scale: Activities of daily living that increase pain assessed Pain in breast region or ipsilateral arm assessed	105 patients recruited, all agreed to participate, 93 (89%) included in final analysis 12 excluded due to disease complications	29 years	Chronic pain 1 year post-op in breast in 24% and in ipsilateral arm in 17%
Tasmuth <i>et al.</i> 1999 ¹⁴⁸	Prospective survey in an oncology department	Consecutive women from January to June 1996, Helsinki, Finland	VAS and McGill questionnaire Pain, chronic, and with at least a considerable effect on daily life	265 questionnaires sent, 221 responded (83%)	less than 70	Chronic pain in 56% in women operated on in high volume units, compared with 43% in those from low volume units.
Wallace <i>et al</i> . 1996 ¹⁴³	Retrospective survey	Breast cancer patients attending medical centre	Pain intensity VAS, McGill pain questionnaire	n=429 recruited, 282 responded		Pain at 1 year follow-up: post-mastectomy = 31% mastectomy/reconstruction = 49% breast augmentation = 38% breast reduction = 22%

 Table 20: Post-thoracotomy pain.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Occurrence
Dajczman et al. 1991 ¹⁵¹	Retrospective cohort study of patients who had undergone thoracic surgery between 1982–87 by one particular surgeon were reviewed, then interviewed and questionnaire completed	Post-thoracotomy patients, disease-free without metastases and at least 2 months post-op, Quebec, Canada	PIVAS 10 cm scale, shoulder pain and aggravating factors assessed	206 patients identified, 59 interview and questionnaire, 56 analysed	35–79	54% had pain at thoracotomy site, moderate or severe in about half, between 5 months and 5 years after operation
Kalso <i>et al.</i> 1992 ¹²⁸	Retrospective review of medical records, pain questionnaire sent to surviving patients	Patients who underwent a thoracotomy during 1986–88, Finland	Patients asked to describe pain as ache, burning, or tenderness and numbness, and state the duration and if analgesic required Patients asked to state if pain is associated with thoracotomy site	questioned further with pain questionnaire, 89%	less than 70	44% persistent thoracotomy pain lasting longer than 6 months. 66% received treatment for pain.
Landreneau et al. 1994 ¹⁵²	Postal questionnaire of an identified patient population	Post-thoracotomy patients > 3 months post-operation Patients had either pulmonary resection by lateral thoracotomy or video-assisted thoracic surgery (VATS) Divided into cohorts on basis of operation < 1 year or more than a year from this questionnaire contact None of patients had local recurrence of malignancy, USA	Post-thoracotomy pain defined as persistent pain along the thoracotomy scar and/or its intercostal dermatomal distribution lasting more than 2 months after operation	391, 343 (88%) responded, 165 thoracotomy, 178 VATS	mean age 59	Postoperative pain 3 months to 1 year after surgery in 44% with thoracotomy (18% treated), and 30% with VATS (11% treated) Postoperative pain more than 1 year after surgery in 29% with thoracotomy (16% treated), and 22% with VATS (6% treated)

Table 20: Continued.

Reference	Type of study	Sample source	Disease definition	Sample size	Age range	Occurrence
Matsunaga et al. 1990 ¹⁵³	Retrospective survey, surgical records	Patients of one surgeon		n=90 contacted, 77 responded		Pain in 67% 6 to 18 months post-thoracotomy, 20% required analgesics
Perttunen et al. 1999 ¹⁵⁴	Prospective cohort	Patients undergoing thoracotomy in Helsinki, Finland	Patients interviewed with standard letter at 3, 6 and 12 months	110 patients entered, with information on 62 at 1 year	19–77	Moderate or severe pain in 16% and mild pain in 45% at 1 year
Richardson et al. 1994 ¹²⁹	Retrospective analysis of medical records of patients between January 1980 and December 1991 at a general hospital	Patients had undergone a thoracotomy, UK	Post-thoracotomy neuralgia defined as chest wall pain unrelated to recurrent or persistent tumour or infection at least 2 months post-operation Unilateral chest wall pain on the side of the thoracotomy 2 months after operation taken as positive presence of neuralgia.		range 1–84 years, mean 55 years	Post-thoracotomy neuralgia in 14% at 12 months; 15% had pain sufficient for clinic referral in first year

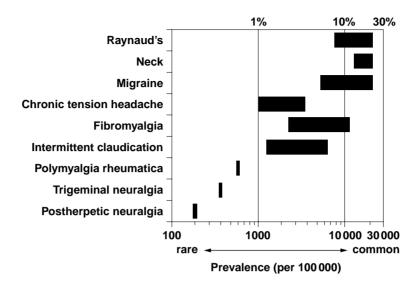


Figure 2: Prevalence of some chronic pain conditions.

people. They all used SF-36 or SF-24. These were analysed by quality of life dimension (physical functioning, physical role functioning, bodily pain, general health, vitality, social functioning and mental health) according to disease clusters (e.g. musculoskeletal conditions of osteoarthritis, joint complaints, rheumatoid arthritis and back impairments), disease categories (ranking the individual diseases within the cluster) and patient characteristics (sociodemographic variables, like age, gender, education).

The method used was the ranking of mean scores. Thus if three diseases scored (say) 5, 10 and 15 (with 5 the 'best' score), then they would be ranked 1, 2 and 3. This was done for all quality of life domains, and the ranks for individual domains added together. This summed rank produces low scores for the diseases or disease clusters causing the least distress, and high scores for those causing the most problems. The summed rank scores for chronic disease clusters are shown in **Figure 3**.

Musculoskeletal conditions, renal disease, cerebrovascular/neurological conditions and gastrointestinal conditions had the most severe impact on quality of life. In musculoskeletal conditions, osteoarthritis had more adverse impact than back impairments, which scored higher (worse) than rheumatoid arthritis. The method used for measuring quality of life, in this case SF-36, may not be perfect, but this analysis is thought-provoking for any consideration of health care needs in chronic pain, and highlights a research agenda.

The impact of the increasing age of the population, the higher prevalence of arthritis in older people and the 'worst' disease burden of musculoskeletal problems is a likely escalation of demand for pain management of arthritic problems. Co-morbidity, and treatment for that co-morbidity, can make pain management tricky in this patient group.

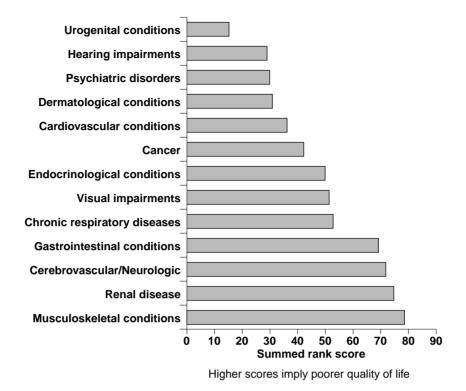


Figure 3: Summed rank scores for disease clusters. 159

5 Services available and their costs

This section outlines current interventions available to treat pain, how these interventions are provided and used (the service as a whole) and the costs of providing a chronic pain service

Interventions

There are many interventions, pharmacological, non-pharmacological, invasive and non-invasive, from which to choose to treat chronic pain. These are outlined in **Figure 4**.

Analgesics

By far the majority of acute pain is managed with analgesics alone. Most chronic pain is also managed initially with analgesics, but in contrast with acute pain, more commonly involves nerve transmission block and alternative methods. **Figure 1** (the pain treatment ladder) showed a simple plan. As acute pain wanes, weaker analgesics are used. If chronic pain increases, stronger ones are used. The same analgesics,

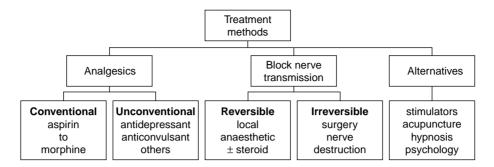


Figure 4: Treatment methods for chronic pain.

from paracetamol to NSAIDs through to opioids, are used in chronic as in acute pain. If analgesics relieve the pain to an adequate extent, and with tolerable or controllable adverse effects, then there is little reason to use other interventions. If analgesics are ineffective, other methods have to be considered. If analgesics are effective but cause intolerable or uncontrollable adverse effects then again other methods should be considered. The effectiveness and the adverse effects of the analgesics are critical.

It is known from work with cancer pain that using analgesics according to the WHO pain ladder (**Figure 1**) can relieve pain for 80% of patients. For most of the 80% the relief will be good, for a minority it will only be moderate. This presumes that the pain is managed optimally, but it is known from audit that this is often not the case. Optimal management requires that the correct drugs are available, and that they are given in the correct dose by the correct route and at the correct time. This needs staff who are well versed in the problems, and who are available to care for the patient. The second problem is the 20% of patients whose pain is not well managed by intelligent use of analgesic guidelines. The other treatment methods outlined in **Figure 4** are necessary to manage those for whom analgesics fail.

Non-opioid analgesics

Oral simple analgesics, combinations and NSAIDs

There is an old adage that if patients can swallow it is best to take drugs by mouth. Effective relief of nociceptive pain (as opposed to nerve damage pain) can be achieved with oral paracetamol, paracetamol/opioid combinations and oral NSAIDs. Paracetamol at doses of 4 gm or less per day is the safest analgesic, contrasting with NSAIDs which carry a small but finite chance of gastric bleed within the therapeutic dose range, ¹⁶⁰ and risks of renal and cardiac problems. ^{161,162}

Topical NSAIDs

Many doctors are sceptical about the efficacy of topical NSAIDs. This may not be correct, however, with topical NSAIDs, like paracetamol, having a first-line role.

Opioids

In chronic pain there are two particular problems with opioids. The first is that adequate doses are often not available or are not given, primarily because of fears of addiction. The second is that some (rarer) chronic pain states, particularly when the nervous system is damaged, may not respond fully to opioids.

Opioids used for people who are not in pain can induce physical and psychological dependence. This does not happen to patients who receive them for pain relief, for instance after an operation or for severe pain from osteoporotic vertebral collapse. Some governments restrict medical availability on the grounds that if the drugs are available medically this will worsen the street addiction problem. There is no evidence for this. The casualties are patients who are deprived of adequate pain relief.

In chronic pain opioids are usually given by mouth. The dose is worked out by titration over a period of days, and then the drug is given regularly, not waiting for the pain to come back. Initial problems with nausea or dizziness commonly settle. If constipation is likely, laxatives are given.

Patients who cannot swallow can try sublingual, transdermal or suppository dosing. Subcutaneous infusion, usually from a small (external) pump, is used for terminal patients who cannot manage these other routes. Rarely the epidural route is used for combination infusion of opioid and local anaesthetic.

If patients' pain starts to increase the dose is increased. If sensible dose increases do not produce pain relief, or if increasing the opioid dose provokes intolerable or unmanageable adverse effects, then other methods have to be considered, either as well as the opioid or instead of it. A working rule is that if the pain is in a numb area, which is a marker for a damaged nervous system, you should be less confident that opioids would necessarily produce pain relief, 164 and the threshold for using other strategies would be lower.

Unconventional analgesics

Unconventional analgesics¹⁶⁵ are drugs which have other indications in other medical settings, and are not normally thought of as analgesics. Treating chronic pain in a tertiary hospital setting these drugs are used for about one third of patients. The hall-mark is pain in a numb area, neuropathic pain.

When the patient has symptoms and signs of nervous system damage in the area of their pain it is expected that the response to conventional analgesics will be reduced. Conventional analgesics have often failed already, which is why the patient has been referred. If not, they should be tried, before empirical testing is embarked upon, to see if any of the unconventional analgesics can provide relief.

Antidepressants

Antidepressants work on the nervous system to relieve depression. They are used in much lower dosage (about half) to relieve pain. 166 Classically they were used to relieve pain that was burning rather than shooting in character, and anticonvulsants were used for shooting pains. Now antidepressants are used as first line for both types of pain, because greater success has been achieved and because it is believed that antidepressants cause fewer adverse effects.

Lower doses (median 75 mg amitriptyline nocte, maximum 150 mg) are used compared with those used to control depression. The pain-relieving effect happens, if it is going to happen, well within a week, whereas 10 days is the minimum often quoted for an antidepressant effect. The older (tricyclic) antidepressants seem to be better than the selective serotonin reuptake inhibitors as analgesics. The simplest analogy is that these older drugs are like shotguns, acting on multiple transmitter pathways, whereas the newer ones are more like rifles, designed as they are to be more selective and affect only one pathway.

Anticonvulsants

Anticonvulsants have been used for many years to treat the shooting pains of trigeminal neuralgia, painful diabetic neuropathy and postherpetic neuralgia. The catch-all explanation was that they stabilised nerve membranes, preventing them carrying spurious messages. Precisely how these channel blocking drugs work as analgesics in neuropathic pain remains unclear.

In the UK antidepressants are first choice drug therapy in neuropathic pain, supplemented or replaced by anticonvulsants if antidepressants alone provide inadequate analgesia or intolerable or unmanageable adverse effects.

Others

Clonidine and other alpha-2 adrenergic agonists have analgesic effects, both in conventional pain and in neuropathic pain. They extend the duration of local anaesthetic effect and have a synergistic effect with opioids. Their clinical utility is limited by the adverse effects of sedation and hypotension. Epidural clonidine is used in neuropathic cancer pain. Baclofen is used by intrathecal pump to treat the painful spasms of cerebral palsy. Ketamine and dextromethorphan, both drugs with NMDA antagonist action, are being used in severe neuropathic pain.

Block nerve transmission

Reversible

Local anaesthetics

Local anaesthetics block nerve conduction reversibly. When the local anaesthetic wears off the pain returns. That is the pharmacologically correct statement, but another old saying, that a series of local anaesthetic blocks can be used to 'break the cycle' of pain and effect a cure, now has some empirical support, ¹⁶⁷ even if the mechanism is not understood. Arner and colleagues showed that the duration of pain relief could far outlast the duration of local anaesthetic action, and that prolonged relief could result from a series of blocks. ¹⁶⁷ Local anaesthetic blocks can thus be diagnostic and therapeutic. Diagnosis of pain for instance from a 'trapped' lateral cutaneous nerve of thigh can be confirmed by local anaesthetic block, and a series of blocks may prevent pain recurring.

Pain clinics use such blocks commonly, for shoulder pain (suprascapular nerve block ^{168,169}), for intercostal neuralgia, for rectus sheath nerve entrapment, postoperative scar pains and other peripheral neuralgias (**Table 21**). What is not clear is the extent to which adding steroid to the local anaesthetic makes a difference, either prolonging the duration of effect of a particular procedure or increasing the chance of success of a series of blocks.

Fibromyalgia

Similar injections are done for the trigger points of fibromyalgia, but there do not appear to be any controlled comparisons of injections with other treatments. Antidepressants remain one of the few remedies of proven benefit.

Intravenous regional sympathectomy

Intravenous regional sympathetic blocks (IRSBs) are used in patients with reflex sympathetic dystrophy (complex regional pain syndrome). The blocks are useful if they facilitate mobility.

C:/Postscript/07_HCNA3_D2.3d - 10/1/7 - 8:45 [This page: 572]

572 Chronic Pain

Table 21: Common nerve blocks.

Nerve block	Common indications
Trigger point	focal pain (e.g. in muscle)
Peripheral: intercostal sacral nerves rectus sheath	pain in dermatomal distribution
Extradural (midline perineal pain)	Uni or bilateral pain (lumbosacral, cervical, thoracic etc.)
Intrathecal (midline perineal pain)	Unilateral pain (neurolytic injection for pain due to malignancy, limbs, chest etc.)
Autonomic Intravenous regional sympathectomy Stellate ganglion	reflex sympathetic dystrophy reflex sympathetic dystrophy arm pain brachial plexus nerve compression
Lumbar sympathetic	reflex sympathetic dystrophy lumbosacral plexus nerve compression vascular insufficiency lower limb perineal pain
Coeliac plexus	abdominal pain

Epidural steroids and facet joint blocks

Two other common pain clinic procedures particularly for back pain are epidural steroid injection and facet nerve blocks. However, there is considerable current controversy about the potential for epidural steroid to produce long-term neurological sequelae. Intrathecal injection of steroid can produce neurological sequelae. It is therefore important that intrathecal injection is avoided.

Classically facet joint injection with local anaesthetic and steroid is indicated when pain is worse when sitting, and pain is provoked by lateral rotation and spine extension. Recent studies suggest that whether or not the injection is actually in the facet joint makes little difference, ¹⁷⁰ and indeed cast some doubt on long-term utility. ¹⁷¹ Short-lived success (less than six weeks) with local anaesthetic and steroid is said to be improved by use of cryoanalgesia or radiofrequency blocks to the nerves to the joints.

Irreversible

The destructive procedures are aimed at cutting, burning or damaging (**Table 21**) the nerve fibres carrying the pain signals. The flaw in the logic is that the nervous system can all too often rewire, finding a way around the lesion. If that happens, and the pain returns, then it may be even more difficult to manage – severe neuropathic pain can result. In general neurolytic blocks in non-malignant pain are not recommended, because they do not last forever, and recurrent pain may be more difficult to manage, and because of the morbidity. In cancer pain these neurolytic block procedures do have a place, when there is a short (less than three month) prognosis, or where alternatives such as meticulous drug control or long-term epidural infusion are not possible. Similar distinction between cancer and non-cancer pain holds for coeliac plexus block in pancreatic pain.

The limitation is the potential for motor and sphincter damage. This risk is higher with bilateral and repeat procedures, and higher the lower the cord level of the block. Extradural neurolytics have limited efficacy. While claims have been made that the paravertebral approach is preferable, patchy results may be attributed to unpredictable injectate spread. Results of spinal infusion of a combination of local anaesthetic and opioid are superior to neurolytic blocks, providing good analgesia with minimal irreversible morbidity.

Surgery

The relevant neurosurgical interventions for orthopaedic pain include dorsal column stimulation, rhizotomy, cordotomy and dorsal root entry zone (DREZ) lesions. The indications are usually non-malignant neuropathic pain which has failed to respond to pharmacological measures.

Alternatives

TENS and acupuncture

The rationale for transcutaneous nerve stimulation (TENS) is the gate theory. ¹⁷² If the spinal cord is bombarded with impulses from the TENS machine then it is distracted from transmitting the pathological pain signal. Acupuncture is another alternative method used to address chronic pain.

Physiotherapy and variants

Pain clinics keep a very open mind about other interventions such as physiotherapy. If patients benefit from alternatives they are encouraged to continue with these methods.

Behavioural management

Back schools through to behavioural management programmes offer a range of help for patients to cope with their (usually back) pain problems. Making decisions about the benefits of psychologically-based treatments of medical problems is not easy, and especially difficult to compare with other treatments and to measure relative benefit and cost. Patients whose pain has proved intractable to all reasonable medical and other interventions are chronic consumers of health care – GP or hospital clinic time, analgesic and psychotropic drugs, repeated admissions and sometimes surgery. If rehabilitation treatment enables these patients to carry on more satisfying lives with minimum medical help, how can it be most effectively and economically offered?

Chronic pain service provision and use

Clinical Standards Advisory Group Report

A report from the Clinical Standards Advisory Group (CSAG) on services for patients with pain analysed data collected in 1997 from a national survey (238 NHS Trusts) and 12 sample sites. ¹⁷³ Of the 250 Trusts surveyed 215 (85%) provided a chronic pain service.

Activity data from the sample sites showed that only a minority (5 or 6 of 12) had activity data, and that there was wide variation in the activity levels for inpatient cases (6.4 to 35 inpatient cases annually per 100 000), day cases (72 to 155), new outpatients (67 to 158) and repeat outpatients (301 to 531).

C:/Postscript/07_HCNA3_D2.3d - 10/1/7 - 8:45 [This page: 574]

574 Chronic Pain

Consultant weekly sessions per 100 000 population served varied nationally from 0 to 2.9, considerably below the recommended provision of 10 sessions per 100 000 population. ¹⁷⁴

The national survey showed wide variation in the level of service offered (defined as particular treatments offered), and this was reflected in the data from the 12 sample sites. Only one of the sample sites offered all the 15 treatments,* but the majority did offer injection treatments, transcutaneous nerve stimulation (TENS), single shot epidurals, and supervised opioid therapy for non-cancer pain. The reasons that all sites did not offer all 15 treatments may include the fact that it was a pretty eclectic list, including interventions such as acupuncture and hypnotherapy, which clinics might not offer because of lack of efficacy evidence. For some smaller clinics single-handed consultants might not have the skill mix to offer all the treatments.

Oxford Study

The use of chronic non-malignant pain services was estimated for the Oxford Region for the Summer of 1982. The population served, 2.3 million, had a Regional Pain Relief Unit with 1115 'actively maintained records' of patients with non-malignant pain, records which had not been archived, excluding those who had died or not returned to the unit for 18 months. This gives an overall prevalence of 485 patients per million population. However, the Unit treated patients from outside the region, and adjusting for that the prevalence would be lower, at 325 patients per million.

Referrals in 1982

Referral patterns for 1982 are shown in the Table 22.

Changes since 1982

No documented evidence of change exists. Present patterns of referral and perceived changes include both patient-related and service-related factors. The patient-related factors include changes in the types of patient referred. More treatment now occurs in primary care, ¹⁷⁶ particularly in Oxfordshire. For example, antidepressants for postherpetic neuralgia will often now be initiated by GPs. More difficult patients are being referred, and in greater numbers. The service factors are that overall workloads have increased since 1982. Medical staffing has increased from one consultant and senior registrar to two consultants and a 0.5 FTE honorary consultant running what is essentially a consultant-only service, with two psychology sessions per week. Joint clinics are run with psychiatry, neurology, neurosurgery and oral surgery. There are more specialist pain centres in the UK, and in the former Oxford Region there are consultants (especially anaesthetists) specialising in pain relief.

Chronic pain services - costs

Clinical Standards Advisory Group Report

Half of the 12 sample site Health Authorities in the CSAG report provided data on tariffs charged. For first outpatient consultation these varied from £54 to £171, for repeat outpatient from £54 to £134, for elective inpatient from £553 to £1471, and for day care from £75 to £384. The more than threefold variation shows that accurate costs are not available.

^{*} Nerve blockade, TENS, X-ray assisted treatment, one-shot epidural, acupuncture, physiotherapy, supervised opioid therapy for non-cancer pain, continuous epidural, drug delivery systems: subcutaneous, psychology, drug delivery systems: intravenous, radiofrequency lesions, pain management programme, spinal cord stimulation, hypnotherapy.

Table 22: Prevalence, treatability and burden of chronic pain syndromes.

Condition	Percent	per 100,000		Treatability	Burden
Low back pain	6	6,000		variable	low to high
Ankylosing spondylitis	1.5	1,500		fair	low to high
Neck pain	15	15,000		fair	low to high
Whiplash	0.028	28		variable	low to high
Polymyalgia rheumatica	0.627	627		good	low to
					medium
Fibromyalgia	2	2,000		fair	low to
					medium
Migraine	15	15,000		good	low to
TY 1 1 (OPPRE)	_	4.000			medium
Headache (CTTH)	1	1,000		poor	low to
Trigominal nouralgia	0.4	400		fair	medium
Trigeminal neuralgia	0.4	400		fair	low to high
Diabetic neuropathy	0.4			fair	low to high
Postherpetic neuralgia		34 (incidence)	F00/	variable	low to high
Multiple sclerosis	0.05	50	50% pain prev – how many MS?	variable	low to high
Central post stroke pain	0.01-0.05	10-50	8% of strokes	poor	high
Phantom limb pain	0.025	25	75% of amputees	poor	low to high
Stump pain	0.025	25	1	poor	low to high
Claudication	1	1,000		variable	low to high
Raynaud's	2–19			variable	low to
,					medium
Angina	4	4,000		variable	low to high
Postop			say 10% of all?	variable	low to
					medium
post-mastectomy pain				variable	low to
					medium
thoracotomy				variable	low to
1 1					medium
cholecystectomy				variable	low to
					medium

Treatability; poor, fair or good. Variable if variable. Burden; low, medium or high.

Using the professional recommendation of 10 sessions per 100 000 population the requirements will be a consultant's salary, secretarial support, sessional nursing, psychology and physiotherapy, bed costs for inpatients and procedure costs for treatments. Using the CSAG activity data and tariffs yields annual costs per 100 000 population of £29 000 (lowest activity, lowest tariffs) and £210 000 (highest activity, highest tariffs). Thus a primary care trust covering 100 000 patients should be budgeting between £100 000 and £200 000 per year for chronic pain services.

As previously referred to in the section on prevalence and incidence, the burden of chronic pain seen at pain clinics has increased substantially in the last decade. Patients are usually in the sixth and seventh decade of life, so demographic imperatives will increase prevalence still further until at least about 2020. Some foresee increasing problems in recruiting and retaining staff to work in chronic pain, and this may make adequate provision more difficult.¹⁷⁷

Canadian study on costs

A detailed Canadian study of the costs incurred by users of speciality pain clinic services¹⁷⁸ showed that users of the services incur less direct health care expenditure than non-users with similar conditions. This conclusion is important and in an ideal world this study would be repeated in the UK to show the financial benefit of the service.

Of 626 patients referred to the chronic pain clinic in Hamilton, Ontario, between January 1986 and April 1988, 210 did not attend the clinic (non-attender), 180 had a consultation appointment only (consultation only), 98 had an incomplete treatment programme (incomplete treatment) and 83 had a complete treatment programme. A sample of 222 of 626 patients was used to compute the use of different types of health services and other costs. This was done by asking patients about their use of five categories of direct health services – primary care, emergency room and specialists, hospital episodes and days, and the use of seven types of other health professionals. Other direct and indirect costs for the patient and associated with their use of health care were also estimated. Money values in the paper are given in 1991 dollars, but whether these are Canadian or US dollars is not stated.

There was no demographic or condition diagnosed difference between the four groups. The results showed that the direct health care costs were lower for users of chronic pain services than for non-users. Broken down by type of cost for one year these are shown in **Table 23**.

Table 23: Annual per patient direct health care costs for patients referred to a chronic pain unit using different levels of service (1991 dollars).

Service used	Non-attender	Consult only	Incomplete treatment	Complete treatment
Number surveyed	57	80	44	41
Primary care visits	477	422	412	462
Specialists	548	642	862	817
Emergency room	206	439	266	191
Hospital stay	3,116	2,017	462	1,290
Health professional	833	396	226	237
Total	5,181	3,917	2,229	2,996

The total annual direct health costs were much lower for users of chronic pain services (even if it was only a consultation), and the savings were clearly derived mostly from reduced costs of days spent in hospital. This is shown graphically in **Figure 5**.

The 74% of the chronic pain referrals who actually used some chronic pain services had only 64% of the total costs for the referred patients. The 'saving' that came from using chronic pain services derived mainly from the intensive users of the service who had treatments, rather than those who had only a consultation.

The average direct health care cost of a patient using chronic pain services, even if that was a single consultation, was \$2947. Referred patients who did not use the service cost more, an average of \$5181. The difference between these averages was \$2234.

Using the most conservative estimate – that is, no cost inflation since 1991 and assuming that the currency was Canadian dollars with an exchange rate of about $2/\pounds$ – the average difference amounts to a saving in direct health care costs of about £1117 per patient. Using this figure with the 1982 figure of 1115 patients with non-malignant pain on the Oxford Pain Relief Unit books translates to health care savings of £1 250 000.

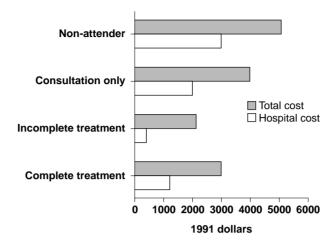


Figure 5: Total per patient direct health care costs and cost of hospital stay for patients referred to a chronic pain unit using different levels of service (1991 dollars).

This compares with the running costs (labour, consumables, estates, overheads) of the Pain Relief Unit in Oxford (with a larger workload) of £500 000 (see **Figure 6**).

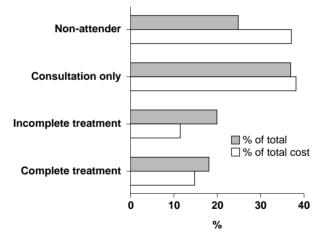


Figure 6: Percentage of total number and total direct health care costs for patients referred to a chronic pain unit using different levels of service.

6 Effectiveness of services and interventions

As mentioned previously there are many interventions, pharmacological, non-pharmacological, invasive and non-invasive, from which to choose. Whether we are making decisions for our own patients or for our service or for national or international guidelines, the same principles should apply. The relative efficacy and safety of the possible interventions, and then the cost, have to be the key determinants. This section uses systematic reviews when possible to provide the best available evidence for the various interventions, with the number-needed-to-treat (NNT) as the measure of clinical significance from quantitative systematic reviews. The arguments about best choice treatment are covered in greater detail in a Health Technology Assessment report¹⁷⁹ and in book form.¹⁸⁰

Analgesics

Figure 7 shows a league table for relative analgesic efficacy for single dose use and **Table 24** shows the NNT for some analgesic interventions. Paracetamol 1 g will produce at least 50% relief of pain for one out of four patients, ibuprofen 400 mg (and other NSAIDs analysed) for one out of two patients. The efficacy evidence thus leads to the advice to start with paracetamol, and move to combination and then to NSAID if greater efficacy is needed. This is inherently a safer strategy than leaping in with the greater efficacy NSAID, because it carries greater risk than paracetamol. (A I-1)

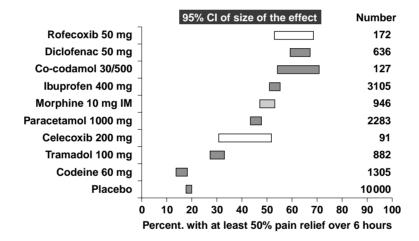


Figure 7: League table of relative efficacy for single dose analgesic use.

This philosophy is used in the American College of Rheumatologists Guidelines for arthritic pain. Two early studies suggested that there is little advantage in osteoarthritis of either NSAIDs over paracetamol ¹⁸⁹ or weak opioids in combination with paracetamol over paracetamol alone, ¹⁹⁰ but recent trials do show the expected superiority of NSAID over paracetamol.

No single-dose trial has shown any efficacy advantage of one NSAID over another. ¹⁹¹ This does not fit well with patients' reports on multiple dosing of increased efficacy from NSAIDs with greater anti-inflammatory action. The efficacy dose-response curve for NSAIDs is flat compared with the dose-response for adverse effects such as gastrointestinal symptoms, dizziness and drowsiness. ¹⁹² Increasing the dose to improve analgesia is therefore more likely to increase adverse effects than to improve analgesia.

Zhang and Li 1994¹⁸⁷

McQuay, Tramer et al. 1996¹⁸⁸

Condition	Intervention	Outcome	NNT	Reference
Postoperative pain	(good) ibuprofen 400 mg	> 50% pain relief	2	Moore, McQuay et al. 1996 ¹⁸¹
	paracetamol 1 g	> 50% pain relief	4	Moore, McQuay et al. 1996 ¹⁸¹
	(poor) codeine 60 mg oral	> 50% pain relief	> 10	Moore and McQuay 1997 ¹⁸²
Back pain	epidural steroid	> 75% relief at 60 days	> 6	Watts and Silagy 1995, McQuay and Moore 1996 ^{183,184}
Acute sprains etc.	topical NSAID (good)	> 50% pain relief	2+	Moore, Tramèr et al. 1998 ¹⁸⁵
Trigeminal neuralgia	anticonvulsants	> 50% pain relief	2.5	McQuay, Carroll et al.186
Diabetic neuropathy	anticonvulsants	> 50% pain relief	2.5	McQuay, Carroll et al.186

Table 24: Number-needed-to-treat (NNT) for some analgesic interventions.

topical capsaicin

antidepressants

NSAIDs alone produced as good analgesia as single or multiple doses of weak opioids alone or in combination with non-opioid analgesics. 192 Adverse effect incidence and patient dropout rates were the same for multiple doses of NSAIDs or weak opioids in combination with non-opioid analgesics. 192

> 50% pain relief

> 50% pain relief

4.2

2.5

In contrast to efficacy, where we see little difference between NSAIDs, the risk of NSAID-induced gastric bleeding is lowest with ibuprofen, and increases with increasing age. 193 Prophylactic misoprostol should be considered for preventing NSAID-associated gastrointestinal complications when age is greater than 75 years, cardiovascular disease, history of peptic ulcer or of gastrointestinal bleeding (NNTs to prevent one serious GI complication in one year 105, 58, 11 and 7 respectively). ^{194,195} The alternative to COX1 NSAID used with gastric protection is the COX2 specific inhibitors (COXIBs), which show similar efficacy to their forebears but with decreased risk of peptic ulceration or bleeding, ¹⁹⁶ which has economic consequences. ¹⁹⁷ Cardiac risk with NSAIDs does not appear to be improved by COXIBs.

Topical NSAIDs

Neuropathic pain

Published RCTs on chronic pain conditions (mainly knee osteoarthritis) studied over 800 subjects treated with topical NSAIDs and 322 subjects who received placebo. The analgesic response for combined placebo treatment was 30%, and for combined topical non-steroidal anti-inflammatory preparations it was 63%. For analgesic effects the odds ratio was 3.6 (2.6–4.8) and the number-needed-to-treat was 3.2 (2.6–4.1). 185 (A I-1)

Opioids

There is little strong evidence to support the intrathecal pump administration of opioid in preference to the oral route. 198 (C I-1)

- Antidepressant drugs: Antidepressants can provide good relief in neuropathic pain (NNT of 2-3, Table 24). 188 For fibromyalgia as in more classic neuropathic pain, antidepressants are one of the few remedies of proven benefit. 45 (A I-1)
- 2 Anticonvulsant drugs: Anticonvulsants can provide good relief in neuropathic pain (NNT of 2-3, Table 24). 186 Doses required for analgesic effect are close to the anticonvulsant dosing range, and carry an adverse effect burden. This systematic review suggests that there is little difference in the number of adverse effects seen with antidepressant and anticonvulsant used in neuropathic pain, but that may conceal a difference in severity (which was not reported). (A I-1)

3 Others – Alpha-2 adrenergic agonists and NMDA antagonists: Epidural clonidine is effective in neuropathic cancer pain ¹⁹⁹ (A I-2). Ketamine is used in severe neuropathic pain, with scientific rationale but little strong evidence yet of good benefit. ²⁰⁰ (C I-1)

4 Reversible block nerve transmission:

Epidural injections for back pain and sciatica: Epidural steroids in back pain have been studied in two systematic reviews. ^{183,201} Overall the combined data showed statistically significant (odds ratios) improvement for both short-term (1–60 days) and long-term (12 weeks up to one year). The clinical significance is that the NNT for short-term (1–60 days) greater than 75% pain relief from the ten trials with short-term outcomes combined, was just under 6, with 95% confidence intervals from 4 to 12. ¹⁸⁴ This means that for 6 patients treated with epidural steroid, one will obtain more than 75% pain relief short-term. (A I-1)

The NNT for long-term (12 weeks up to one year) improvement from the five trials combined, was about 11, with 95% confidence intervals from 6 to 90. This means that for 11 patients treated with epidural steroid, one will obtain more pain relief over this longer-term period. There is still the interesting question of whether local anaesthetic alone could achieve these results (breaking the cycle), or whether the steroid is an essential component. (A I-1)

Intravenous regional sympathetic blockade: A systematic review of seven RCTs of IRSBs found that none of the four guanethidine trials showed significant analgesic effect. Two reports, one using ketanserin and one bretylium, with 17 patients in total, showed some advantage of IRSBs over control.²⁰² Adding guanethidine in IRSBs does not appear to be more effective than local anaesthetic alone. (D I-1)

- 5 **Irreversible block nerve transmission:** Pain associated with pancreatic cancer responds well to coeliac plexus block,²⁰³ and it may also help those with abdominal or perineal pain from tumour in the pelvis. In chronic pancreatitis results are much less convincing. (A I-1)
- 6 **Surgery:** The difficulties of trials of uncommon surgical procedures are well known. These procedures are usually documented by glowing case series. Longer-term outcomes may not be so good.²⁰⁴ (D II-2)
- 7 **TENS:** A systematic review shows that TENS has limited efficacy in chronic pain. ²⁰⁵ (D I-1)
- 8 **Acupuncture:** Several systematic reviews discuss acupuncture in chronic non-malignant pain. ^{206–9} These show limited effect on pain outcomes. Any effect on well-being is often short-lived (three days), and is therefore expensive in time. It is difficult to know what is the real place of acupuncture, like other complementary interventions, because of the lack of trials comparing complementary with mainstream procedures. ²¹⁰ (D I-1)
- 9 **Physiotherapy:** The evidence from back pain, however, suggests that on rigorous outcome measures physiotherapy and other forms of manipulation have but limited success. Such analyses often did not include any measure of quality of life. If they make the patient feel better and they are cheap then it is a decision for the third party payer whether or not these physiotherapy manoeuvres should be offered. A number of systematic reviews are published on this subject.^{211–19} (D I-1)
- 10 **Behavioural management:** Randomised comparison of the St Thomas' four-week inpatient treatment with eight-week half-day outpatient treatment, with fitness training, planned increases in activity, activity scheduling, drug reduction, relaxation and cognitive therapy as the pain management methods taught by the same staff team, ²²⁰ showed that for every three patients treated as inpatients rather than outpatients, one patient fewer was taking analgesic or psychotropic drugs. For every four patients treated as inpatients rather than outpatients, one patient fewer sought additional medical advice in the year after treatment. For every five patients treated as inpatients rather than outpatients, one patient more had a ten-minute walking distance improved by more than 50%. For every six patients treated as inpatients rather than outpatients, one patient fewer was depressed. A number of systematic reviews exist in this area (and see McQuay et al.) for evidence of efficacy of psychological interventions). (B I-1)

Effective service provision

Once the effectiveness of an intervention is known the next step must be to check whether the interventions used in pain clinics reflect these known levels of efficacy. **Table 25** shows the attempt the Audit Commission made to make a matrix of treatment efficacy, determine the percentage of clinics in their sample which offer particular treatments, and to put the percentage offering a particular treatment on the matrix. ²³⁰ The CSAG report on pain focused more on provision and process, but has interesting data on variation in provision of services (discussed above). ¹⁷³

Table 25: Chronic pain treatments classified by evidence of effectiveness and risk of side-effects, degree of invasiveness and cost of the procedure. ²³⁰

Clinical	Effective**		Evidence of effectiveness				
risk and/ or cost:*			Thought to be effective, but with little formal evidence***		Ineffective****		
Low	Some minor oral analgesics (e.g. ibuprofen, paracetamol)		TENS provided for use at home	90%	Some minor oral analgesics (e.g. codeine alone)		
	Topical NSAIDs in rheumatological conditions (e.g. single arthritic joint pain)	90%	Relaxation therapy				
	Topical capsaicin in diabetic neuropathy, psoriasis	95%					
Medium	Antidepressant drugs (for e.g. neuropathic pain, post-herpetic neuralgia, diabetic neuropathy)	95%	Outpatient TENS courses	60%	Injection of corticosteroids in or around shoulder joints for shoulder pain	89%	
	Anticonvulsant drugs (for e.g. trigeminal neuralgia)	100%	Outpatient psychological intervention programmes	70%			
	Systematic local anaesthetic drugs for nerve injury pain	60%	Acupuncture courses by nurse or therapist	50%			
			Manipulation for back pain Epidural given once, but abandoned if ineffective Long-term, low-rate opioids Surgical intervention for back pain when surgery has not yet been tried (e.g. laminectomy for sciatica with positive neurological signs and MRI) Orthopaedic corsets, neck collars used for long periods Sclerosis injection for low back pain	21%			

C:/Postscript/07_HCNA3_D2.3d – 10/1/7 – 8:45 [This page: 582]

582 Chronic Pain

Table 25: Continued.

Clinical	Effective**		Evidence of effectiveness				
risk and/ or cost:*			Thought to be effective, but with little formal evidence***		Ineffective****		
High	Epidural for back pain and sciatica (effects for first 60 days) Inpatient psychological	25%	Acupuncture courses provided by doctors (higher salary costs) Trigeminal neuralgia	65% 30%	Epidural for back pain and sciatica (effects beyond 3 months) IRSB guanethidine	90%	
	intervention programmes		treatments using specialised/ expensive equipment (e.g. radio frequency block kit)		8		
			Lignocaine infusion as inpatient	45%			
			Epidural left in-situ for several weeks as inpatient Long-term, high doses of a cocktail of opioids and other drugs Repeated back pain surgery	84%			
			Cordotomy	11%			
			Spinal cord implanted stimulators	25%			
			Destructive nerve burning, freezing, phenol injections	95%			

^{*} Clinical risks could include side-effects, the degree of invasiveness of the procedure, and whether the effects on the body are reversible. Treatments have been placed into a category according to the professional judgement of consulted practitioners.

Source: Audit Commission; evidence of effectiveness is drawn from previous chapters; relative risk/cost from discussion with practitioners

While all of us may disagree with the particular judgements made about efficacy and safety in **Table 25**, the approach is the same approach we all use (covertly) in our professional life. What might be perceived as threatening clinical freedom, in that those paying for health care might choose to pay only for treatments in the upper left sections of **Table 25**, is in reality a matter of judging relative efficacy, safety and cost.

^{**} Treatments proved to be effective are those with a sufficient number of randomised controlled trials available to calculate a statistic called the 'number needed to treat' (NNT), and, in this context, which have values of NNT between 2 and 4.

^{***} Many treatments have not been subjected to enough randomised controlled trials to make a statistical judgement about their effectiveness.

^{****} Treatments shown to be without effect in this context are those with NNTs greater than 4.

^{% =} percentage of 20 Trusts providing each treatment is listed where known; some treatments may be provided via referral to another clinic.

Primary care prescribing

Another approach is to use the national prescribing data to see to what extent the prescribing of oral analgesics in primary care matches the efficacy league table for oral analgesics. ¹⁸⁰ Using the Government Statistical Service Prescription cost analysis for England 2001, ²³¹ which provides data on the number of prescriptions for particular categories of drug (**Table 26**), we then produced a simple scattergram of the number of prescriptions for the different drugs against the NNT for single dose analgesia ¹⁸⁰(**Figure 8**).

Table 26: UK oral analgesic prescribing and efficacy.

Analgesic studied	NNT	Prescriptions (thousands)	
Codeine	17.7	1,324	
Dihydrocodeine	9.7	2,460	
Tramadol	4.7	1,815	
Paracetamol	4.6	7,814	
Dextropropoxyphene HCl 65 mg/paracetamol 650 mg	4.4	8,775	
Ibuprofen	2.7	5,300	
Diclofenac	2.3	7,040	
Co-codamol 30 mg codeine/500 mg paracetamol	1.9	3,938	

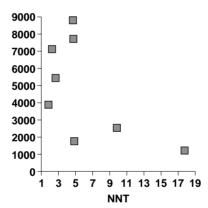


Figure 8: UK oral analgesic prescribing and efficacy (2001).

The graph shows that prescribing in primary care does a good job – there are more prescriptions for the more effective drugs. Prescribing advice will be a factor, as will cost, but most analgesics are cheap, so that efficacy should be the primary determinant. Given that there are differences between the single-dose efficacy of the different analgesics, safety issues now need to be brought into focus. A problem here is that while there may be differences in minor adverse effect incidence on single dosing, with opioids alone or in combination being the worst offenders, the real safety issues are about what happens with multiple or chronic dosing. For somebody with arthritic pain which requires months or years of analgesic use, which is the best choice, paracetamol or NSAID? At recommended doses paracetamol has minimal safety problems. Using data from four randomised trials, taking NSAIDs for more than two months carries a risk of bleeding or perforating gastroduodenal ulcer of 1 in 228 (150–479), RR 2.8 (1.2–6.2), absolute risk

C:/Postscript/07_HCNA3_D2.3d - 10/1/7 - 8:45 [This page: 584]

584 Chronic Pain

0.69%. We estimate that there is a 1 in 8.3 (12%) risk that these patients with bleed or perforation will die. Using a control event (death) rate of 0.0002% with this experimental death rate of 0.69%/8.3 = 0.083%, we calculate 160 that the average number-needed-to-kill (NNK) for a patient receiving chronic oral NSAIDs for at least two months is 1/(0.083%-0.002%) = 1/0.081% = 1235. This shows the complexity of what appears at first glance to be a simple choice between NSAID and paracetamol.

Cost-effectiveness

There is little information about the costs and benefits of chronic pain services, and what little there is barely constitutes evidence. Two possible approaches were looked at. Costs may be determined by contrasting, for instance, two or more different types of treatment for a condition and working out the costs and benefits for each. This method was precluded by lack of sufficient evidence, for instance the fact that we have no real evidence that TENS works in chronic pain. Evidence of effectiveness must come first. Rational assessment of cost—benefit needs evidence of effectiveness. Irrational assessment might just compare the cost of one ineffective therapy with another.

Another way to cost the service is to use an approach in which the disease burden is examined, changes are estimated, and judgement is made as to whether pain clinics add to costs or reduce them. Here at least there is some evidence, but not very much, and not very recent.

Do chronic pain clinics reduce other NHS expenditure? A case study

From the Canadian study described in the previous section, it can be argued that attendance at a chronic pain clinic could reduce expenditure elsewhere in the NHS, so that the cost of the clinics would more than be covered by savings. To test this idea, the Audit Commission asked a pain clinic to carry out a small study.²³⁰ A randomly-selected group of 21 patients who first attended the clinic in October 1996 were asked to take part in a telephone interview. Some of the answers were verified from clinical case notes, but mostly the results relied on the patients' memories. The interviewer (an experienced research nurse) asked the patients about their consultation and treatment histories for the six months before attending the pain clinic, and for the six months since first attending, using a structured questionnaire.

The results (**Table 27**) suggest that there may be English truth in the Canadian study, but to be sure one would need a larger sample of patients, at many more clinics, extending the period before and after the clinics, and preferably tracing patients' records rather than relying on self-report. The implication is that close liaison between the different NHS specialities could reduce excessive referral/treatment and provide a better service for patients.

These data suggest that chronic pain services not only benefit patients, but are also an efficient way of dealing with chronic pain in the community.

Table 27: Do chronic pain clinics reduce other NHS expenditure? A case study. 230

Average number per patie	In the six months			
		Before attending the pain clinic	After attending the pain clinic	Change + = increase - = reduction
Outpatient attendances:	NHS pain clinic	0.05	1.6	+97%*
	Other NHS medical specialities**	2.8	0.9	-222%*
	Total	2.8	2.5	-13%
	NHS treatments (e.g. TENS, physio, surgery)	1.0	0.9	-17%
	Days in hospital	0.2	0.5	+50%
	A/E attendances	0.1	0.05	-100%
	Different types of drug for pain	2	2.2	11%
	Visits to the GP about pain	5.0	3.0	-64%*
	Home visits by GP	0.1	0.1	_
	Other NHS home visits	0	0	_
	Private treatments	0.4	0.2	-125%*
	% of patients	Before	After	
Attending outpatient	NHS pain clinic	5%	100%	
clinics	Other NHS medical specialities**	81%	38%	
	Either	86%	100%	
Having NHS treatment	Relatively high cost treatments (e.g.	10%	5%	
_	surgery)	62%	43%	
	Medium cost (e.g. physio, nerve block)	24%	38%	
	Low cost (e.g. X-ray) Any treatment	67%	62%	
Hospital inpatient	This treatment	5%	10%	
Attending A/E		5%	5%	
Taking drugs for pain:	Opiates	14%	16%	
0 0 1	Antidepressants, tranquillisers, etc.	24%	47%	
	NSAIDs	48%	63%	
	Minor analgesics	71%	74%	
	Any type of drug	90%	90%	
Visiting the GP about	For repeat prescriptions	67%	52%	
pain:	For consultant/advice about pain	62%	24%	
•	Any reason to do with pain	86%	71%	
	Having a home visit by GP	5%	5%	
	Other NHS home visits	0	0	
Having private treatment		33%	19%	

^{*} Significant change (paired sample t-test, 1-tailed, 5% level).

** Other NHS specialities include orthopaedics, neurology, vascular surgery, gynaecology, urology, rehabilitation medicine, nephrology.

7 Models of care and recommendations

The provision of chronic pain services clearly should not be taken in isolation, and **Figure 9** shows a simple view of some major service relationships. Many treatments, drug or procedures, are common to the different service providers; the additional expertise found in the pain service is the ability to do particular invasive procedures. The ideal promoted widely in the developed world is chronic pain services which are multidisciplinary. The medical components of such multidisciplinary services are the rehabilitation, neurology, orthopaedic and psychiatric services shown in **Figure 9**, together with clinical psychology, physiotherapy and pharmacy inputs as integral to the chronic pain service.



Figure 9: Chronic pain: service relationships.

The historic pattern in the UK has been a District General Hospital (DGH) service with a more comprehensive service regionally, often in the University Hospital. The size of the DGH service varies widely, and none of those sampled by CSAG came near to the 10 consultant sessions per 100 000 population recommended by the Pain Society. There are two clear advantages to local service provision: the geographical proximity for the patient and the ability to interact easily with primary care and the other local specialities. The regional service would then provide the other speciality input or interventions not available at the DGH. The disadvantage of a small DGH service is the burden on a single-handed consultant, and lack of critical mass. It is hard to be precise about the minimum size of an effective service, but there would be few single-handed consultants if the 10 consultant sessions per 100 000 population recommendation were to be followed. Examples of a speciality intervention not usually available at a DGH would include a pain management programme.

The second level of decision in the model of care is determining which interventions a service should provide. We need to know whether the various components of the service (interventions) are effective, how much they cost, and examine whether their delivery is efficient. There are also the difficult issues of how treatable the pain syndrome is, and how big the burden is for the patient. As discussed above, in general the efficacy evidence for drug treatments (and pain management programmes) is as strong as the evidence for injection procedures is weak, but this weakness is sometimes a lack of evidence rather than evidence of lack of efficacy.

The evidence presented in the effectiveness section enables us to determine which effective treatments should be used and which ineffective interventions should be avoided:

Effective interventions

- Minor analgesics
- Combinations of different analgesics
- Anticonvulsant drugs

- Antidepressant drugs
- Systemic local anaesthetic-type drugs for nerve damage pain
- Topical NSAIDs in rheumatological conditions
- Topical capsaicin in diabetic neuropathy
- Epidural injections for back pain and sciatica.

Interventions where evidence is lacking

- Transcutaneous electrical nerve stimulation in chronic pain
- Relayation
- Spinal cord stimulator.

Ineffective interventions

- Intravenous regional sympathetic blockade
- Injections of corticosteroids in or around shoulder joints for shoulder pain.

One clear recommendation is that if paracetamol is sufficient to control the pain then the choice should be paracetamol, because of its good long-term safety at recommended doses. Taking NSAIDs for more than two months carries a risk of bleed or perforation, and in turn a risk of death. Long-term harm has important financial implications. For example, the cost of NSAID gastrointestinal adverse effects, combining hospital admission and the cost of co-prescribing gastro-protective agents, was estimated as costing the NHS a conservative £250 million in 1997/8.¹⁹⁷ And NSAID-related gastrointestinal adverse effects account for about one-third of the long-term harm. With congestive heart failure and renal failure, NSAID prescribing can result in 50 hospital admissions each year for a primary care trust of 100 000 people.²³²

Difficult commissioning decisions will emerge on a case-by-case basis, with desperate patients seeking novel treatments. Different but also difficult is the complementary and alternative medicine lobby. Acupuncture, for instance, appeared on the CSAG checklist of interventions in chronic pain. There is no credible evidence of analgesic efficacy of acupuncture in chronic pain, but acupuncture, in common with other complementary and alternative interventions, may make patients feel better even if it does not alter the pain. One way to deal with these conundrums is to fund the unproven treatments only in the context of a randomised trial.

The fact that 85% of Trusts surveyed had a chronic pain clinic is evidence that there is a perceived need for the service. There is little evidence as to what constitutes the optimal form of the service, and very little evidence on resource use and benefit gained. The current satellite and hub model of DGH and regional centre works to an extent, but there has been a dearth of organisational research into service provision.

It is foolish to be didactic about service arrangements in this area, because there is overlap between the different services which make up the provision for chronic disease and pain. A strong rehabilitation service in a district, for example, might mean that other services could be less strong. What is clear is the need, and the ageing population means that this will become more and more apparent. The pain clinic should offer a mix of drug treatment, injection treatment, devices and psychological input, and the availability of this skill mix is the important principle rather than under which service banner it appears.

One pain consultant per 100 000 of the population seems a sensible estimate for available pain expertise. Precisely how this fits into the other service provision will vary. The current hub and spoke arrangements for chronic pain may be optimal for some regions. The need for good liaison with other specialities favours decentralised rather than centralised arrangements.

8 Information and research requirements

Information requirements

In order to organise the treatment of chronic pain better, we recommend the following information is gathered, organised and made available:

- A single electronic source of high quality evidence on the *diagnosis* of various pain conditions for use in primary care.
- A single electronic source of high quality evidence on the *treatment* of various pain conditions for use in primary care. This will involve predominantly systematic reviews of randomised trials, but will also summarise where evidence does not exist (like TENS in chronic pain) and especially where treatments are known not to be effective (acupuncture).
- A single electronic source of high quality evidence about the management of chronic pain in primary and secondary care.
- Regular training courses plus distance learning to encourage lifetime learning for developing professional pain specialists in primary care.
- Referral protocols.

Research requirements

The evidence base in pain relief is one of the best in medicine. Most of the interventions commonly used in chronic pain treatment can be shown to be very effective. Some have been shown not to be effective, and their use is less common than it was. While these findings buttress much of current practice in chronic pain treatment, a common theme is that we still need to know more. In particular, information on which to base economic analysis is missing. Such information as is available indicates that pain clinics result in direct health care savings of over £1000 per patient per year, and that total savings may be twice the cost of the chronic pain service. Knowing that major demographic changes will affect the NHS over the next several decades, and that ageing populations will demand more chronic (and cancer) pain therapy, providing more information on economic as well as humanitarian benefits will be important.

Appendix 1: Methods

Studies reporting prevalence or incidence of chronic pain were sought systematically. Chronic pain is usually as defined by authors, though a minimum requirement was duration of three months or more. Several different search strategies were used to identify reports from MEDLINE (1966 to July 2001), EMBASE (1980 to January 2001), PubMed (July 2001) and the Oxford Pain Relief Database (1950 to 1994),²³³ and our own extensive literature collection in pain topics. Reference lists of retrieved reports were searched for additional studies. Abstracts and narrative review articles were not considered.

Inclusion criteria

Studies were included when they were full journal publications, studying adult community or clinic-based populations in Europe or North America, used clear and established diagnostic criteria for disease/pain conditions of interest, presented prevalence and/or incidence data for the disease/pain condition of interest and reported survey/study response rates.

Exclusion criteria

Studies were excluded if they were of occupational-based populations, used invalid or unclear diagnostic criteria, had a low response rate (below 60%) without an analysis of non-responders, or with an analysis which produced a biased result.

Data extraction

From each eligible report we extracted study design, sample source, disease/pain definition, sample size and response rate, age range, incidence and/or prevalence data. Gender and age specific rates were extracted if given, together with information on pain severity and disability.

Incidence was converted to annual incidence per 100 000 population with 95% confidence intervals (CI) where possible. Prevalence was converted to prevalence per 100 000 population with 95% CI where possible. Where pain within a condition was examined, we report the prevalence *within* the condition as occurrence, and then use prevalence information for the condition to calculate the prevalence of the *painful* condition.

References

- 1 Andersson HI, Ejlertsson G, Leden I, Rosenberg C. Chronic pain in a geographically defined general population: studies in differences in age, gender, social class, and pain localization. *Clin J Pain* 1993; **9**: 174–82.
- 2 Brattberg G, Thorslund M, Wikman A. The prevalence of pain in a general population. The results of a postal survey in a county of Sweden. *Pain* 1989; **37**: 215–22.
- 3 Birse TM, Lander J. Prevalence of chronic pain. *Canadian Journal of Public Health* 1998; **89**(2): 129–31.
- 4 Bowsher D, Rigge M, Sopp L. Prevalence of chronic pain in the British population: a telephone survey of 1037 households. *Pain Clinic* 1991; 4: 223–30.
- 5 Chrubasik S, Junck H, Zappe HA, Stutzke O. A survey on pain complaints and health care utilization in a German population sample. *Eur J Anaesthesiol* 1998; **15**: 397–408.
- 6 Wall P. Pain: the science of suffering. London: Weidenfeld and Nicolson, 1999.
- 7 Brochet B, Michel P, Barberger-Gateau P *et al.* Pain in the elderly: an epidemiological study in southwestern France. *Pain Clinic* 1991; **5**(2): 73–9.
- 8 Clinical Standards Advisory Group. Back Pain. London: HMSO, 1994.
- 9 Clarke CE, MacMillan L, Sondhi S, Wells NEJ. Economic and social impact of migraine. *QJM Monthly Journal of the Association of Physicians* 1996; **89**(1): 77–84.
- 10 Crombie IK, Croft PR, Linton SJ, LeResche L, VonKorff M (eds). Epidemiology of pain. Seattle: IASP Press, 1999.
- 11 Croft P, Papageorgious A, McNally R. Low Back Pain. In: Stevens A, Raftery J (eds). *Health care needs assessment*. Oxford and New York: Radcliffe Medical Press, 1997: 129–81.
- 12 Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995; **38**: 19–28.
- 13 Magni G, Marchetti M, Moreschi C, Merskey H, Luchini SR. Chronic musculoskeletal pain and depressive symptoms in the National Health and Nutrition Examination. I. Epidemiologic follow-up study. *Pain* 1993; **53**(2): 163–8.
- 14 Higginson I. Palliative and Terminal Care. In: Stevens A, Raftery J (eds). *Health care needs assessment*. Oxford and New York: Radcliffe Medical Press, 1997: 183–260.
- 15 Smith BH, Elliott AM, Chambers WA *et al.* The impact of chronic pain in the community. *Fam Pract* 2001; **18**(3): 292–9.
- 16 Fox PL, Raina P, Jadad AR. Prevalence and treatment of pain in older adults in nursing homes and other long-term care institutions: a systematic review. *CMA* 1999; **160**: 329–33.
- 17 Cassidy JD, Carroll LJ, Côté P. The Saskatchewan health and back pain survey. *Spine* 1998; **23**(17): 1860–6.
- 18 Davies HTO, Crombie IK, Macrae WA. Back pain in the pain clinic: nature and management. *Pain Clinic* 1995; **8**(2): 191–9.
- 19 Thomas E, Silman AJ, Croft PR, Papageorgiou AC, Jayson MI, Macfarlane GJ. Predicting who develops chronic low back pain in primary care: a prospective study. *Br Med J* 1999; **318**(7199): 1662–7.
- 20 Calin A, Fries JF. Striking prevalence of ankylosing spondylitis in 'healthy' w27 positive males and females. *N Engl J Med* 1975; **293**(17): 835–9.
- 21 Gran JT, Husby G, Hordvik M. Prevalence of ankylosing spondylitis in males and females in a young middle-aged population of Tromsø, Northern Norway. *Annals of Rheumatic Diseases* 1985; **44**: 359–67.

- 22 Braun J, Bollow M, Remlinger G *et al.* Prevalence of spondylarthropathies in HLA-B27 positive and negative blood donors. *Arthritis Rheum* 1998; **41**(1): 58–67.
- 23 Carbone LD, Cooper C, Michet CJ, Atkinson EJ, O'Fallon WM, Melton LJ III. Ankylosing spondylitis in Rochester, Minnesota, 1935–1989: Is the epidemiology changing? *Arthritis Rheum* 1992; **35**(12): 1476–82.
- 24 Julkunen H, Korpi J. Ankylosing spondylitis in three Finnish population samples. Prostatovesiculitis and salpingo-oophoritis as aetiological factors. *Scand J Rheumatol* 1984; **12**(suppl. 52): 16–8.
- 25 Underwood MR, Dawes PD. Inflammatory back pain in primary care. *Br J Rheumatol* 1995; **34**: 1074–7.
- 26 Gran JT, Skomsvoll JF. The outcome of ankylosing spondylitis: A study of 100 patients. *Br J Rheumatol* 1997; **36**(7): 766–71.
- 27 Bovim G, Schrader H, Sand T. Neck pain in general population. Spine 1994; 19: 1307-9.
- 28 Côté P, Cassidy JD, Carroll L. The Saskatchewan Health and Back Pain survey. *Spine* 1998; 23: 1689–98.
- 29 Jacobsson L, Lindgärde F, Manthorpe R. The commonest rheumatic complaints of over six weeks' duration in a twelve-month period in a defined Swedish population. *Scand J Rheumatol* 1989; **18**: 353–60.
- 30 Mäkelä M, Heliövaara M, Sievers K *et al.* Prevalence, determinants, and consequences of chronic neck pain in Finland. *Am J Epidemiol* 1991; **134**: 1356–67.
- 31 Takala J, Sievers K, Klaukka T. Rheumatic symptoms in the middle-aged population in southwestern Finland. *Scand J Rheumatol* 1982; **47**: 15–29.
- 32 Galasko CSB, Murray PM, Pitcher M et al. Neck sprains after road traffic accidents: a modern epidemic. *Injury* 1993; **24**(3): 155–7.
- 33 Versteegen GJ, Kingma J, Meijler WJ, Ten Duis HJ. Neck sprain in patients injured in car accidents: A retrospective study covering the period 1970–1994. *Eur Spine J* 1998; 7(3): 195–200.
- 34 Versteegen GJ, Kingma J, Meijler WJ, Ten Duis HJ. Neck sprain not arising from car accidents: A retrospective study covering 25 years. *Eur Spine J* 1998; **7**(3): 201–5.
- 35 Bengtsson BA, Malmvall BE. The epidemiology of giant cell arteritis including temporal arteritis and polymyalgia rheumatica. Incidences of different clinical presentations and eye complications. *Arthritis Rheum* 1981; **24**(7): 899–904.
- 36 Boesen P, Sorensen SF. Giant cell arteritis, temporal arteritis, and polymyalgia rheumatica in a Danish county. A prospective investigation, 1982–1985. *Arthritis Rheum* 1987; **30**(3): 294–9.
- 37 Elling P, Olsson AT, Elling H. Synchronous variations of the incidence of temporal arteritis and polymyalgia rheumatica in different regions of Denmark; association with epidemics of Mycoplasma pneumoniae infection. *J Rheumatol* 1996; **23**(1): 112–9.
- 38 Gran JT, Myklebust G. The incidence of polymyalgia rheumatica and temporal arteritis in the county of Aust Agder, south Norway: a prospective study 1987–94. *J Rheumatol* 1997; **24**(9): 1739–43.
- 39 Kyle V, Silverman B, Silman A *et al.* Polymyalgia rheumatica/giant cell arteritis in a Cambridge general practice. *Br Med J* 1985; **291**: 385–6s.
- 40 Northridge J, Hill SG. Polymyalgia rheumatica and giant cell arteritis in general practice. *Musculoskeletal Medicine* 1995; **2**: 13–7.
- 41 Salvarani C, Macchioni P, Zizzi F et al. Epidemiologic and immunogenetic aspects of polymyalgia rheumatica and giant cell arteritis in northern Italy. *Arthritis Rheum* 1991; 34/3(351–356).
- 42 Salvarani C, Gabriel SE, O'Fallon M, Hunder GG. Epidemiology of polymyalgia rheumatica in Olmsted County, Minnesota, 1970–1991. *Arthritis Rheum* 1995; **38**(5): 369–73.
- 43 White KP, Speechley M, Harth M, Østbye T. Fibromyalgia in rheumatology practice: a survey of Canadian Rheumatologists. *J Rheumatol* 1995; **22**: 722–6.

- 44 Croft P, Schollum J, Silman A. Population study of tender point counts and pain as evidence of fibromyalgia. *Br Med J* 1994; 309/6956(696–699).
- 45 O'Malley PG, Balden E, Tomkins G. *et al.* Treatment of fibromyalgia with antidepressants. A meta-analysis. *J Gen Intern Med* 2000; **15**: 659–66.
- 46 Croft P, Rigby AS, Boswell R *et al.* The prevalence of widespread pain in the general population. *J Rheumatol* 1993; **20**(4): 710–3.
- 47 Forseth KØ, Gran JT. The prevalence of fibromyalgia among women aged 20–49 years in Arendal, Norway. *Scand J Rheumatol* 1992; **21**: 74–8.
- 48 Prescott E, Kjøller M, Jacobsen S *et al.* Fibromyalgia in the adult Danish population: 1. A prevalence study. *Scand J Rheumatol* 1993; **22**: 233–7.
- 49 Portenoy RK, Hagen NA. Breakthrough pain: definition, prevalence and characteristics. *Pain* 1990; **41**: 273–81.
- 50 Portenoy RK, Payne D, Jacobsen P. Breakthrough pain: characteristics and impact in patients with cancer pain. *Pain* 1999; 81(1–2): 129–34.
- 51 Bruera E, Fainsinger R, MacEachern T, Hanson J. The use of methylphenidate in patients with incident cancer pain receiving regular opiates. A preliminary report. *Pain* 1992; **50**: 75–7.
- 52 Stewart WF, Simon D, Shechter A, Lipton RB. Population variation in migraine prevalence: a meta-analysis. *J Clin Epidemiol* 1995; **48**(2): 269–80.
- 53 Scher A I, Stewart W F, Lipton R B. Migraine and Headache: A meta-analytic approach. In: Crombie IK (ed). *Epidemiology of pain*. Seattle: IASP Press, 1999: 159–70.
- 54 Stang PE, Yanagihara T, Swanson JW *et al.* Incidence of migraine headache: a population-based study in Olmsted County, Minnesota. *Neurology* 1992; **42**: 1657–62.
- 55 Stewart WF, Linet MS, Celentano DD *et al.* Age- and sex-specific incidence rates of migraine with and without visual aura. *Am J Epidemiol* 1991; **134**: 1111–20.
- 56 Rozen TD, Swanson JW, Stang PE, McDonnell SK, Rocca WA. Increasing incidence of medically recognized migraine headache in a United States population. *Neurology* 1999; **53**(7): 1468–73.
- 57 Breslau N, Davis GC, Andreski P. Migraine, psychiatric disorders, and suicide attempts: an epidemiologic study of young adults. *Psychiatry Res* 1991; **37**: 11–23.
- 58 Franceschi M, Colombo B, Rossi P, Canal N. Headache in a population-based elderly cohort an ancillary study to the Italian Longitudinal Study of Aging (ILSA). *Headache* 1997; **37**(2): 79–82.
- 59 Göbel H, Petersen-Braun M, Soyka D. The epidemiology of headache in Germany: a nationwide survey of a representative sample on the basis of the headache classification of the International Headache Society. *Cephalalgia* 1994; 14: 97–106.
- 60 Henry P, Michel P, Brochet B *et al.* A nationwide survey of migraine in France: prevalence and clinical features in adults. *Cephalalgia* 1992; **12**: 229–37s.
- 61 Linet MS, Stewart WF, Celantano DD *et al.* An epidemiologic study of headache among adolescents and young adults. *JAMA* 1989; **261**(15): 2211–6.
- 62 Michel P, Pariente P, Duru G et al. MIG ACCESS: a population based, nationwide, comparative survey of access to care in migraine in France. *Cephalalgia* 1996; **16**: 50–5.
- 63 O'Brien B, Goeree R, Streiner D. Prevalence of migraine headache in Canada: a population based survey. *Int J Epidemiol* 1994; **23**(5): 1020–6.
- 64 Rasmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population-a prevalence study. *J Clin Epidemiol* 1991; **44**(11): 1147–57.
- 65 Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine headache in the United States. Relation to age, income, race, and other sociodemographic factors. *JAMA* 1992; **267**(1): 64–9.
- 66 Stewart WF, Lipton RB, Liberman J. Variation in migraine prevalence by race. *Neurology* 1996; **47**: 52–9.

- 67 Hu XH, Markson LE, Lipton RB *et al.* Burden of migraine in the United States. *Arch Intern Med* 1999; **159**: 813–8.
- 68 Waters WE. Controlled clinical trial of ergotamine tartrate. Br Med J 1970; 1(5705): 325-7.
- 69 Waters WE, O'Connor PJ. Epidemiology of headache and migraine in women. *J Neurol Neurosurg Psychiatry* 1971; **34**(2): 148–53.
- 70 Clarke GJR, Waters WE. Headache and migraine in a London general practice. In: Waters WE (ed). *The epidemiology of migraine*. Bracknell: Boehringer Ingelheim Ltd, 1974: 14–22.
- 71 Mills CH, Waters WE. Headache and migraine on the isles of Scilly. In: Waters W E (ed). *The epidemiology of migraine*. Bracknell: Boehringer Ingelheim Ltd, 1974: 49–58.
- 72 Newland CA, Illis LS, Robinson PK, Batchelor BG, Waters WE. A survey of headache in an English city. *Res Clin Stud Headache* 1978; 5: 1–20.
- 73 Rasmussen BK. Epidemiology of headache. Cephalalgia 1995; 15(1): 45–68.
- 74 Schwartz BS, Stewart WF, Simon D, Lipton RB. Epidemiology of tension-type head ache. *JAMA* 1998; **279**(5): 381–3.
- 75 Scher AI, Stewart WF, Liberman J, Lipton RB. Prevalence of frequent headache in a population sample. *Headache* 1998; **38**: 497–506.
- 76 Swanson JW, Yanagihara T, Stang PE *et al.* Incidence of cluster headaches: a population based study in Olmsted County, Minnesota. *Neurology* 1994; 44: 433–7.
- 77 Brewis M, Poskanzer DC, Rolland C, Miller H. Neurological disease in an English city. *Acta Neurol Scand* 1966; **42**(suppl 24): 1–89.
- 78 Katusic S, Beard CM, Bergstralh E, Kurland LT. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945–1984. *Ann Neurol* 1990; **27**: 89–95.
- 79 Munoz M, Dumas M, Boutros-Toni F *et al.* Neuro-epidemiological study of a small Limousin town. *Rev Neurol (Paris)* 1988; **144**(4): 266–71.
- 80 Walters DP, Gatling W, Mullee MA, Hill RD. The prevalence of diabetic distal sensory neuropathy in an English community. *Diabet Med* 1992; **9**(4): 349–53.
- 81 Harris M, Cowie C, Eastman R. Symptoms of sensory neuropathy in adults with NIDDM in the U.S. population. *Diabetes Care* 1993; **16**(11): 1446–52.
- 82 Boulton AJM, Knight G, Drury J, Ward JD. The prevalence of symptomatic, diabetic neuropathy in an insulin-treated population. *Diabetes Care* 1985; **8**(2): 125–8.
- 83 Chan AW, Macfarlane IA, Bowsher D *et al.* Chronic pain in patients with diabetes mellitus: comparison with a non-diabetic population. *Pain Clinic* 1990; **3**(3): 147–59.
- 84 Nabarro JDN. Diabetes in the United Kingdom: a personal series. Diabet Med 1991; 8: 59–68.
- 85 O'Hare JA, Abuaisha F, Geoghegan M. Prevalence and forms of neuropathic morbidity in 800 diabetics. *Ir J Med Sci* 1994; **163**(3): 132–5.
- 86 Edmunds WJ, Brisson M, Rose JD. The epidemiology of herpes zoster and potential cost-effectiveness of vaccination in England and Wales. *Vaccine* 2001; **19**: 3076–90.
- 87 Hope-Simpson R. The nature of herpes zoster: a long-term study and a new hypothesis. *J R Soc Med* 1965; **58**: 9–20.
- 88 Cockerell OC, Goodridge DMG, Brodie D *et al.* Neurological disease in a defined population: the results of a pilot study in two general practices. *Neuroepidemiology* 1996; **15**: 73–82.
- 89 Brown GR. Herpes zoster: correlation of age, sex, distribution, neuralgia, and associated disorders. *South Med J* 1976; **69**(5): 576–8.
- 90 de Moragas J, Kierland R. The outcome of patients with herpes zoster. Arch Dermatol 1957; 75: 193-5.
- 91 Helgason S, Petursson G, Gudmundsson S, Sigurdsson JA. Prevalence of postherpetic neuralgia after a single episode of herpes zoster: prospective study with long term follow up. *Br Med J* 2000; **321**: 1–4.
- 92 Lancaster T, Silagy C, Gray S. Primary care management of acute herpes zoster: systematic review of evidence from randomized controlled trials. *Br J Gen Pract* 1995; **45**(390): 39–45.

- 93 Meister W, Neiss A, Gross G *et al.* Demography, symptomatology, and course of disease in ambulatory zoster patients. *Intervirology* 1998; **41**: 272–7.
- 94 Rogers RS, Tindall JP. Geriatric herpes zoster. J Am Geriatr Soc 1971; 19(6): 495–503.
- 95 Rothwell PM, Charlton D. High incidence and prevalence of multiple sclerosis in south east Scotland: evidence of a genetic predisposition. *J Neurol Neurosurg Psychiatry* 1998; **64**: 730–5.
- 96 Archibald CJ, McGrath PJ, Ritvo PG *et al.* Pain prevalence, severity and impact in a clinic sample of multiple sclerosis patients. *Pain* 1994; **58**(1): 89–93.
- 97 Brochet B, Michel P, Henry P. Pain complaints in outpatients with multiple sclerosis: description and consequences on disability. *Pain Clinic* 1992; 5(3): 157–64.
- 98 Clifford DR, Trotter JI. Pain in multiple sclerosis. Arch Neurol 1984; 41: 1270-3.
- 99 Moulin DE, Foley KM, Ebers GC. Pain syndromes in multiple sclerosis. Neurology 1988; 38: 1830-4.
- 100 Stenager E, Knudsden L, Jensen K. Acute and chronic pain syndromes in multiple sclerosis. Acta Neurol Scand 1991; 84: 197–200.
- 101 Vermote R, Ketelaer P, Carton H. Pain in multiple sclerosis patients. *Clin Neurol Neurosurg* 1986; **88**: 87–93.
- 102 Warnell P. The pain experience of a multiple sclerosis population: a descriptive study. *Axon* 1991; **13**(1): 26–8.
- 103 Anderson IM, Tomenson BM. Treatment discontinuation with selective serotonin reuptake inhibitors compared with tricylic antidepressants: a meta-analysis. *Br Med J* 1995; **310**: 1433–8.
- 104 Bowsher D. Cerebrovascular disease. The Lancet 1993; 341: 156.
- 105 Meijer WT, Hoes AW, Rutgers D *et al.* Peripheral arterial disease in the elderly. The Rotterdam Study. *Arterioscler Thromb Vasc Biol* 1998; **18**: 185–92.
- 106 Leng GC, Papacosta O, Whincup P *et al.* Femoral atherosclerosis in an older British population: prevalence and risk factors. *Atherosclerosis* 2000; **152**: 167–74.
- 107 Menotti A, Mulder I, Nissinen A *et al.* Prevalence of morbidity and multimorbidity in the elderly male populations and their impact on 10-year all-cause mortality: The FINE study (Finland Italy, Netherlands, Elderly). *J Clin Epidemiol* 2001; **54**: 680–6.
- 108 Bainton D, Swetnam P, Baker I, Elwood P. Peripheral vascular disease: consequence for survival and association with risk factors in the Speedwell prospective heart disease study. *Br Heart J* 1994; **72**: 128–32.
- 109 Bowlin SJ, Medalie JH, Flocke SA *et al.* Epidemiology of intermittent claudication in middle-aged men. *Am J Epidemiol* 1994; **140**(5): 418–30.
- 110 Leng GC, Lee AJ, Fowkes FG *et al.* Incidence, natural history and cardiovascular events in symptomatic and asymptomatic peripheral arterial disease in the general population. *Int J Epidemiol* 1996; **25**: 1172–81.
- 111 Smith GD, Shipley MJ, Rose G. Intermittent claudication, heart disease risk factors, and mortality. The Whitehall Study. *Circulation* 1990; **82**(6): 1925–31.
- 112 Palmer KT, Griffin MJ, Syddall H *et al.* Prevalence of Raynaud's phenomenon in Great Britain and its relation to hand transmitted vibration: a national postal survey. *Occup Environ Med* 2000; **57**: 448–52.
- 113 Brand FN, Larson MG, Kannel WB, McGuirk JM. The occurrence of Raynaud's phenomenon in a general population: The Framingham Study. *Vasc Med* 1997; **2**: 296–301.
- 114 Maricq HR, Weinrich MC, Keil JE, LeRoy EC. Prevalence of Raynaud's phenomenon in the general population. *J Chronic Dis* 1986; **39**(6): 423–7s.
- 115 Silman A, Holligan S, Brennan P, Maddison P. Prevalence of symptoms of Raynaud's phenomenon in general practice. *Br Med J* 1990; **301**(6752): 590–2.
- 116 Reid DD, Brett GZ, Hamilton PJ, Jarrett RJ, Keen H, Rose G. Cardiorespiratory disease and diabetes among middle-aged male Civil Servants. A study of screening and intervention. *The Lancet* 1974; 1(7856): 469–73.

- 117 Shaper AG, Cook DG, Walker M, Macfarlane PW. Prevalence of ischaemic heart disease in middle aged men. *Br Heart I* 1984; **51**: 595–605.
- 118 Bainton D, Baker IA, Sweetnam PM *et al.* Prevalence of ischaemic heart disease: the Caerphilly and Speedwell surveys. *Br Heart J* 1988; **59**: 201–6.
- 119 Smith WCS, Kenicer MB, Tunstall-Pedoe H *et al.* Prevalence of coronary heart disease in Scotland: Scottish Heart Health Study. *Br Heart J* 1990; **64**: 295–8.
- 120 McGovern PG, Jacobs DR, Shahar E *et al.* Trends in acute coronary heart disease mortality, morbidity, and medical care from 1985 through 1997. The Minnesota Heart Survey. *Circulation* 2001; **104**: 19–24.
- 121 Crombie IK, Davies HTO, Macrae WA. Cut and thrust: Antecedent surgery and trauma among patients attending a chronic pain clinic. *Pain* 1998; **76**(1–2): 167–71.
- 122 Macrae W A, Davies H T O. Chronic Postsurgical Pain. In: Crombie IK (ed). *Epidemiology of Pain*. Seattle: IASP Press, 1999: 125–42.
- 123 Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. Anesthesiology 2000; 93: 1123-33.
- 124 Sherman R, Sherman C, Parker L. Chronic phantom and stump pain among American Veterans: results of a survey. *Pain* 1984; **18**: 83–95.
- 125 Wartan SW, Hamann W, Wedley JR, McColl I. Phantom pain and sensation among British war amputees. *Br J Anaesth* 1997; **78**: 652–9.
- 126 Tasmuth T, Von Smitten KiP *et al.* Pain and other symptoms after different treatment modalities of breast cancer. *Ann Oncol* 1995; **6**: 453–9.
- 127 Tasmuth T, von Smitten K, Kalso E. Pain and other symptoms during the first year after radical and conservative surgery for breast cancer. *Br J Cancer* 1996; 74: 2024–31.
- 128 Kalso E, Perttunen K, Kassinen S. Pain after thoracic surgery. *Acta Anaesthesiol Scand* 1992; **36**: 96–100.
- 129 Richardson J, Sabanathan S, Mearns AJ *et al.* Post-thoracotomy neuralgia. *Pain Clinic* 1994; **7**(2): 87–97.
- 130 Bay-Nielsen M, Perkins FM, Kehlet H. Pain and functional impairment 1 year after inguinal herniorraphy: a nationwide questionnaire study. *Ann Surg* 2001; **233**(1): 1–7.
- 131 Pohjolainen T. A clinical evaluation of stumps in lower limb amputees. *Prosthet Orthot Int* 1991; **15**: 178–84.
- 132 Sherman RA, Sherman CJ. Prevalence and characteristics of chronic phantom limb pain among American veterans. *Am J Phys Med* 1983; **62**(5): 227–38.
- 133 Steinbach TV, Nadvorna H, Arazi D. A five year follow-up study of phantom limb pain in post traumatic amputees. *Scand J Rehabil Med* 1982; **14**: 203–7.
- 134 Kooijman CM, Dijkstra PU, Geertzen JHB *et al.* Phantom pain and phantom sensations in upper limit amputees: an epidemiological study. *Pain* 2000; **87**: 33–41.
- 135 Pernot HF, Winnubst GM, Cluitmans JJ, De Witter. Amputees in Limburg: incidence, morbidity and mortality, prosthetic supply, care utilisation and functional level after one year. *Prosthet Orthot Int* 2000; **24**(2): 90–6.
- 136 Rommers GM, Vos LD, Groothof JW *et al.* Epidemiology of lower limb amputees in the north of The Netherlands: aetiology, discharge destination and prosthetic use. *Prosthet Orthot Int* 1997; **21**(2): 92–9
- 137 Pohjolainen T, Alaranta H. Epidemiology of lower limb amputees in Southern Finland in 1995 and trends since 1984. *Prosthet Orthot Int* 1999; **23**(2): 88–92.
- 138 Buchanan DC, Mandel AR. The prevalence of phantom limb experience in amputees. *Rehabilitation Psychology* 1986; **31**(3): 183–8.
- 139 Houghton AD, Nicholls G, Houghton AL *et al.* Phantom pain: natural history and association with rehabilitation. *Ann R Coll Surg Engl* 1994; **76**: 22–5.

- 140 Jensen TS, Krebs B, Nielsen J, Rasmussen P. Non-painful phantom limb phenomena in amputees: incidence, clinical characteristics and temporal course. *Acta Neurol Scand* 1984; **70**: 407–14.
- 141 Krebs B, Jensen TS, Kroner K, Nielsen J, Jorgensen HS. Phantom limb phenomena in amputees 7 years after limb amputation. In: Fields HL, Dubner R, Cervero F (eds). *Advances in Pain Research and Therapy*. Vol 9 edition. New York: Raven Press, 1985: 425–9.
- 142 Ivens D, Hoe Al, Podd TJ *et al.* Assessment of morbidity from complete axillary dissection. *Br J Cancer* 1992; **66**: 136–8.
- 143 Wallace MS, Wallace AM, Lee J, Dobke MK. Pain after breast surgery: a survey of 282 women. *Pain* 1996; **66**: 195–205.
- 144 Kroner K, Knudsen UB, Lundby L, Hvid H. Long-term phantom breast syndrome after mastectomy. *Clin J Pain* 1992; **8**(4): 346–50.
- 145 Polinsky ML. Functional status of long-term breast cancer. Health Soc Work 1994; 19(3): 165-73.
- 146 Smith WCS, Bourne D, Squair J et al. A retrospective cohort study of post mastectomy pain syndrome. Pain 1999; 83: 91–5.
- 147 Stevens PE, Dibble SL, Miaskowski C. Prevalence, characteristics, and impact of post-mastectomy pain syndrome: an investigation of women's experiences. *Pain* 1995; **61**: 61–8.
- 148 Tasmuth T, Blomqvist C, Kalso E. Chronic post-treatment symptoms in patients with breast cancer operated in different surgical units. *Eur J Surg Oncol* 1999; **25**: 38–43.
- 149 Rogers ML, Duffy JP. Surgical aspects of chronic post-thoractomy pain. *Eur J Cardiothorac Surg* 2000; **18**: 711–6.
- 150 Katz J, Jackson M, Kavanagh BP, Sandler A. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain* 1996; **12**(1): 50–5.
- 151 Dajczman E, Gordon A, Kreisman H, Wolkove N. Long-term postthoractomy pain. *Chest* 1991; **99**: 270–4.
- 152 Landreneau RJ, Mack MJ, Hazelrigg SR *et al.* Prevalence of chronic pain after pulmonary resection by thoractomy or video-assisted thoracic surgery. *J Thorac Cardiovasc Surg* 1994; **107**: 1079–86.
- 153 Matsunaga M, Dan K, Manabe FY. Residual pain of thoracotomy patients with malignancy and non-malignancy. *Pain* 1990; suppl 5: S148.
- 154 Perttunen K, Tasmuth T, Kalso E. Chronic pain after thoracic surgery: a follow-up study. *Acta Anaesth Scand* 1999; **43**: 563–7.
- 155 Bates T, Mercer JC, Harrison M. Symptomatic gall stone disease: before and after cholecystectomy. *Gut* 1984; **24**: 579–50.
- 156 Ros E, Zambon D. Postcholecystectomy symptoms. A prospective study of gall stone patients before and two years after surgery. *Gut* 1987; **28**(11): 1500–4.
- 157 Stiff G, Rhodes M, Kelly A, Telford K, Armstrong CP, Rees BI. Long-term pain: Less common after laparoscopic than open cholecystectomy. *Br J Surg* 1994; **81**(9): 1368–70.
- 158 Wilson RG, Macintyre IMC. Symptomatic outcome after laparoscopic cholecystectomy. *Br J Surg* 1993; **80**(4): 439–41.
- 159 Sprangers MAG, de Regt EB, Andries F *et al.* Which chronic conditions are associated with better or poorer quality of life? *J Clin Epidemiol* 2000; **53**: 895–907.
- 160 Tramer MR, Moore RA, Reynolds DJ, McQuay HJ. Quantitative estimation of rare adverse events which follow a biological progression: a new model applied to chronic NSAID use. *Pain* 2000; **85**(1–2): 169–82.
- 161 Page J, Henry D. Consumption of NSAIDs and the development of congestive heart failure in elderly patients. *Arch Intern Med* 2000; **160**: 777–84.
- 162 Merlo J, Broms K, Lindblad U *et al.* Association of outpatient utilisation of non-steroidal antiinflammatory drugs and hospitalised heart failure in the entire Swedish population. *Eur J Clin Pharmacol* 2001; 57: 71–5.

- 163 McQuay H. Opioids in chronic non-malignant pain. There's too little information on which drugs are effective and when. *Br Med J* 2001; **322**(7295): 1134–5.
- 164 Jadad AR, Carroll D, Glynn CJ, Moore RA, McQuay HJ. Morphine responsiveness of chronic pain: double-blind randomised crossover study with patient-controlled analgesia. *The Lancet* 1992; 339(8806): 1367–71.
- 165 McQuay HJ. Pharmacological treatment of neuralgic and neuropathic pain. *Cancer Surv* 1988; 7(1): 141–59.
- 166 McQuay HJ, Moore RA. Antidepressants and chronic pain. Br Med J 1997; 314(7083): 763-4.
- 167 Arner S, Lindblom U, Meyerson BA, Molander C. Prolonged relief of neuralgia after regional anesthetic blocks. A call for further experimental and systematic clinical studies. *Pain* 1990; **43**(3): 287–97.
- 168 Emery P, Bowman S, Wedderburn L, Grahame R. Suprascapular nerve block for chronic shoulder pain in rheumatoid arthritis. *Br Med J* 1989; **299**: 1079–80.
- 169 van der Heijden CJMG, van der Windt DAWM, Kleijnen J, Koes BW, Bouter LM. Steroid injections for shoulder disorders: a systematic review of randomized clinical trials. *Br J Gen Pract* 1996; **46**: 309–16.
- 170 Lilius G, Laasonen EM, Myllynen P, Harilainen A, Grönlund G. Lumbar facet joint syndrome. *J Bone Joint Surg Am* 1989; 71: 681–4.
- 171 Carette S, Marcoux S, Truchon R *et al.* A controlled trial of corticosteroid injections into facet joints for chronic low back pain. *N Engl J Med* 1991; **325**: 1002–7.
- 172 Melzack R, Wall PD. Pain mechanisms: a new theory. Science 1965; 150: 971-8.
- 173 Clinical Standards Advisory Group. Services for patients with pain. London: HMSO, 2000.
- 174 Pain Society. *Provision of pain services*. The Association of Anaesthetists of Great Britain and Ireland, 1997; 1–20.
- 175 McQuay HJ, Machin L, Moore RA. Chronic non-malignant pain: a population prevalence study. *Practitioner* 1985; **229**(1410): 1109–11.
- 176 Barsky AJ, Borus JF. Somatization and medicalization in the era of managed care. *JAMA* 1995; **274**: 1931–4.
- 177 Charlton JE. Two for the price of one is it worth it? *Anaesthesia* 2002; **57**(1): 1–3.
- 178 Weir R, Browne GB, Tunks E, Gafni A, Roberts J. A profile of users of speciality pain clinic services: predictors of use and cost estimates. *J Clin Epidemiol* 1992; **45**: 1399–11415.
- 179 McQuay HJ, Moore RA, Eccleston C, Morley S, de C Williams AC. Systematic review of outpatient services for chronic pain control. *Health Technol Assessment* 1997; 1(6).
- 180 McQuay HJ, Moore RA. *An evidence-based resource for pain relief.* Oxford: Oxford University Press, 1998.
- 181 Moore A, McQuay H, Gavaghan D. Deriving dichotomous outcome measures from continuous data in randomised controlled trials of analgesics. *Pain* 1996; **66**: 229–37.
- 182 Moore RA, McQuay HJ. Single-patient data meta-analysis of 3453 postoperative patients: Oral tramadol versus placebo, codeine and combination analgesics. *Pain* 1997; **69**(3): 287–94.
- 183 Watts RW, Silagy CA. A meta-analysis on the efficacy of epidural corticosteroids in the treatment of sciatica. *Anaesth Intensive Care* 1995; **23**: 564–9.
- 184 McQuay H, Moore RA. Epidural steroids (letter). Anaesth Intensive Care 1996; 24: 284-6.
- 185 Moore RA, Tramèr MR, Carroll D, Wiffen PJ, McQuay HJ. Quantitive systematic review of topically-applied non-steroidal anti-inflammatory drugs. *Br Med J* 1998; **316**: 333–8.
- 186 McQuay H, Carroll D, Jadad AR, Wiffen P, Moore A. Anticonvulsant drugs for management of pain: a systematic review. *Br Med J* 1995; **311**(7012): 1047–52.
- 187 Zhang WY, Li WPA. The effectiveness of topically applied capsaicin. A meta-analysis. *Eur J Clin Pharmacol* 1994; **46**(6): 517–22.

- 188 McQuay HJ, Tramer M, Nye BA, Carroll D, Wiffen PJ, Moore RA. A systematic review of antidepressants in neuropathic pain. *Pain* 1996; **68**(2–3): 217–27.
- 189 March L, Irwig L, Schwarz J, Simpson J, Chock C, Brooks P. N of 1 trials comparing a non-steroidal anti-inflammatory drug with paracetamol in osteoarthritis. *Br Med J* 1994; **309**: 1041–6.
- 190 Kjærsgaard-Andersen P, Nafei A, Skov O *et al.* Codeine plus paracetamol versus paracetamol in longer-term treatment of chronic pain due to osteoarthritis of the hip. *Pain* 1990; **43**: 309–18.
- 191 Gøtzsche PC. Patients' preference in indomethacin trials: an overview. *The Lancet* 1989; 1(8629): 88–91.
- 192 Eisenberg E, Berkey CS, Carr DB, Mosteller F, Chalmers TC. Efficacy and safety of nonsteroidal antiinflammatory drugs for cancer pain: a meta-analysis. *J Clin Oncol* 1994; **12**(12): 2756–65.
- 193 Henry D, Lim LL-Y, Rodriguez LAG *et al.* Variability in risk of gastrointestinal complications with individual non-steroidal anti-inflammatory drugs: results of a collaborative meta-analysis. *Br Med J* 1996; **312**: 1563–6.
- 194 Silverstein FE, Graham DY, Senior JR *et al.* Misoprostol reduces serious gastrointestinal complications in patients with rheumatoid arthritis receiving nonsteroidal anti-inflammatory drugs. *Ann Intern Med* 1995; **123**(4): 241–9.
- 195 Shield MJ, Morant SV. Misoprostol in patients taking non-steroidal anti-inflammatory drugs. *Br Med J* 1996; **312**: 846.
- 196 Bombardier C, Laine L, Reicin A *et al.* Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis. *N Engl J Med* 2000; **343**(21): 1520–8.
- 197 Moore RA, Phillips CJ. Cost of NSAID adverse effects to the UK National Health Service. *Journal of Medical Economics* 1999; **2**: 45–55.
- 198 Williams J, Louw G, Towlerton G. Intrathecal pumps for giving opioids in chronic pain: a systematic review. *Health Technol Assess* 2000; **4**(32).
- 199 Eisenach JC, DuPen S, Dubois M, Miguel R, Allin D. Epidural clonidine analgesia for intractable cancer pain. The Epidural Clonidine Study Group. *Pain* 1995; **61**(3): 391–9.
- 200 Bell R, Eccleston C, Kalso E. Ketamine as an adjuvant to opioids for cancer pain. *Cochrane Database Syst Rev* 2003; (1): CD003351.
- 201 Koes BW, Scholten RPM, Mens JMA, Bouter LM. Efficacy of epidural steroid injections for low-back pain and sciatica: a systematic review of randomized clinical trials. *Pain* 1995; **63**: 279–88.
- 202 Jadad AR, Carroll D, Glynn CJ, McQuay HJ. Intravenous regional sympathetic blockade for pain relief in reflex sympathetic dystrophy: a systematic review and a randomized, double-blind crossover study. *J Pain Symptom Manage* 1995; **10**(1): 13–20.
- 203 Eisenberg E, Carr DB, Chalmers TC. Neurolytic celiac plexus block for treatment of cancer pain: a meta-analysis. *Anesth Analg* 1995; **80**(2): 290–5.
- 204 Abram SE. 1992 Bonica Lecture. Advances in chronic pain management since gate control. *Reg Anesth* 1993; **18**(2): 66–81.
- 205 Reeve J, Menon D, Corabian P. Transcutaneous electrical nerve stimulation (TENS): a technology assessment. *Int J Technol Assess Health Care* 1996; **12**: 299–324.
- 206 Patel M, Gutzwiller F, Paccaud F, Marazzi A. A meta-analysis of acupuncture for chronic pain. *Int J Epidemiol* 1989; **18**(4): 900–6.
- 207 ter Riet G, Kleijnen J, Knipschild P. Acupuncture and chronic pain: a criteria-based meta-analysis. *J Clin Epidemiol* 1990; **43**(11): 1191–9.
- 208 Bhatt Sanders D. Acupuncture for rheumatoid arthritis: an analysis of the literature. *Semin Arthritis Rheum* 1985; **14**(4): 225–31.
- 209 Smith LA, Oldman AD, McQuay HJ, Moore RA. Teasing apart quality and validity in systematic reviews: an example from acupuncture trials in chronic neck and back pain. *Pain* 2000; **86**: 119–32.

- 210 Puett DW, Griffin MR. Published trials of nonmedicinal and noninvasive therapies for hip and knee osteoarthritis. *Ann Intern Med* 1994; **121**(2): 133–40.
- 211 Abenhaim L, Bergeron AM. Twenty years of randomized clinical trials of manipulative therapy for back pain: a review. *Clin Invest Med* 1992; **15**(6): 527–35.
- 212 Anderson R, Meeker WC, Wirick BE, Mootz RD, Kirk DH, Adams A. A meta-analysis of clinical trials of spinal manipulation. *J Manipulative Physiol Ther* 1992; **15**(3): 181–94.
- 213 Assendelft WJ, Koes BW, Van der Heijden GJ, Bouter LM. The efficacy of chiropractic manipulation for back pain: blinded review of relevant randomized clinical trials. *J Manipulative Physiol Ther* 1992; 15(8): 487–94.
- 214 Brunarski DJ. Clinical trials of spinal manipulation: a critical appraisal and review of the literature. *J Manipulative Physiol Ther* 1984; 7(4): 243–9.
- 215 Koes BW, Assendelft WJ, van der Heijden GJ, Bouter LM, Knipschild PG. Spinal manipulation and mobilisation for back and neck pain: a blinded review. *Br Med J* 1991; **303**(6813): 1298–303.
- 216 Koes BW, Bouter LM, Beckerman H, van der Heijden GJ, Knipschild PG. Physiotherapy exercises and back pain: a blinded review. *Br Med J* 1991; **302**(6792): 1572–6.
- 217 Ottenbacher K, DiFabio RP. Efficacy of spinal manipulation/mobilization therapy. A meta analysis. *Spine* 1985; **10**(9): 833–7.
- 218 Powell FC, Hanigan WC, Olivero WC. A risk/benefit analysis of spinal manipulation therapy for relief of lumbar or cervical pain. *Neurosurgery* 1993; **33**(1): 73–8; discussion 78–9.
- 219 Shekelle PG, Adams AH, Chassin MR, Hurwitz EL, Brook RH. Spinal manipulation for low-back pain. *Ann Intern Med* 1992; **117**(7): 590–8.
- 220 Pither CE, Nicholas MK. Psychological approaches in chronic pain management. *Br Med J* 1991; **47**: 743–61.
- 221 Williams AC. NNTs used in decision-making in chronic pain management. Bandolier 1995; 22 (Dec).
- 222 Cohen JE, Goel V, Frank JW, Bombardier C, Peloso P, Guillemin F. Group education interventions for people with low back pain. An overview of the literature. *Spine* 1994; **19**(11): 1214–22.
- 223 Cutler RB, Fishbain DA, Rosomoff HL, Abdel-Moty E, Khalil TM, Rosomoff RS. Does nonsurgical pain center treatment of chronic pain return patients to work? A review and meta-analysis of the literature. *Spine* 1994; **19**(6): 643–52.
- 224 Fernandez E, Turk DC. The utility of cognitive coping strategies for altering pain perception: a meta analysis. *Pain* 1989; **38**(2): 123–35.
- 225 Gebhardt WA. Effectiveness of training to prevent job-related back pain: a meta-analysis. *Br J Clin Psychol* 1994; **33**: 571–4.
- 226 Hyman RB, Feldman HR, Harris RB, Levin RF, Malloy GB. The effects of relaxation training on clinical symptoms: a meta analysis. *Nurs Res* 1989; **38**(4): 216–20.
- 227 Malone MD, Strube MJ, Scogin FR. Meta analysis of non medical treatments for chronic pain. *Pain* 1988; **34**(3): 231–44.
- 228 Mullen PD, Laville EA, Biddle AK, Lorig K. Efficacy of psychoeducational interventions on pain, depression, and disability in people with arthritis: a meta analysis. *J Rheumatol* 1987; **14**(suppl 15): 33–9.
- 229 Suls J, Fletcher B. The relative efficacy of avoidant and nonavoidant coping strategies: a meta analysis. *Health Psychol* 1985; **4**(3): 249–88.
- 230 Audit Commission. No feeling, no pain. London: Audit Commission, 1997.
- 231 Government Statistical Service. *Prescription cost analysis, England 2001.* London: Department of Health NHSE, 2001.
- 232 Bandolier. More on NSAID adverse effects [Web Page]. September 2000; Available at http://www.jr2.ox.ac.uk/bandolier/band79/b79-6.html. (Accessed 10 Jan 2002)
- 233 Jadad AR, Carroll D, Moore A, McQuay H. Developing a database of published reports of randomised clinical trials in pain research. *Pain* 1996; **66**: 239–46.

C:/Postscript/07_HCNA3_D2.3d - 10/1/7 - 8:45 [This page: 600]