Understanding the epidemiology of neuropathic pain

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Conflicts of Interest

- I am Chief Investigator on a study of neuropathic pain epidemiology, funded by an unrestricted educational grant from Pfizer UK Ltd
- I am co-investigator on a study of neuropathic pain epidemiology in Canada, funded by an unrestricted educational grant from Pfizer Ltd
- No other conflicts of interest

Objectives of this presentation

This presentation will review:

1. The nature and potential of epidemiological research
2. The challenges facing epidemiological study of neuropathic pain
3. Current evidence on the prevalence of neuropathic pain, and associated socio-demographic and health factors

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IASP NeuPSIG Management Committee

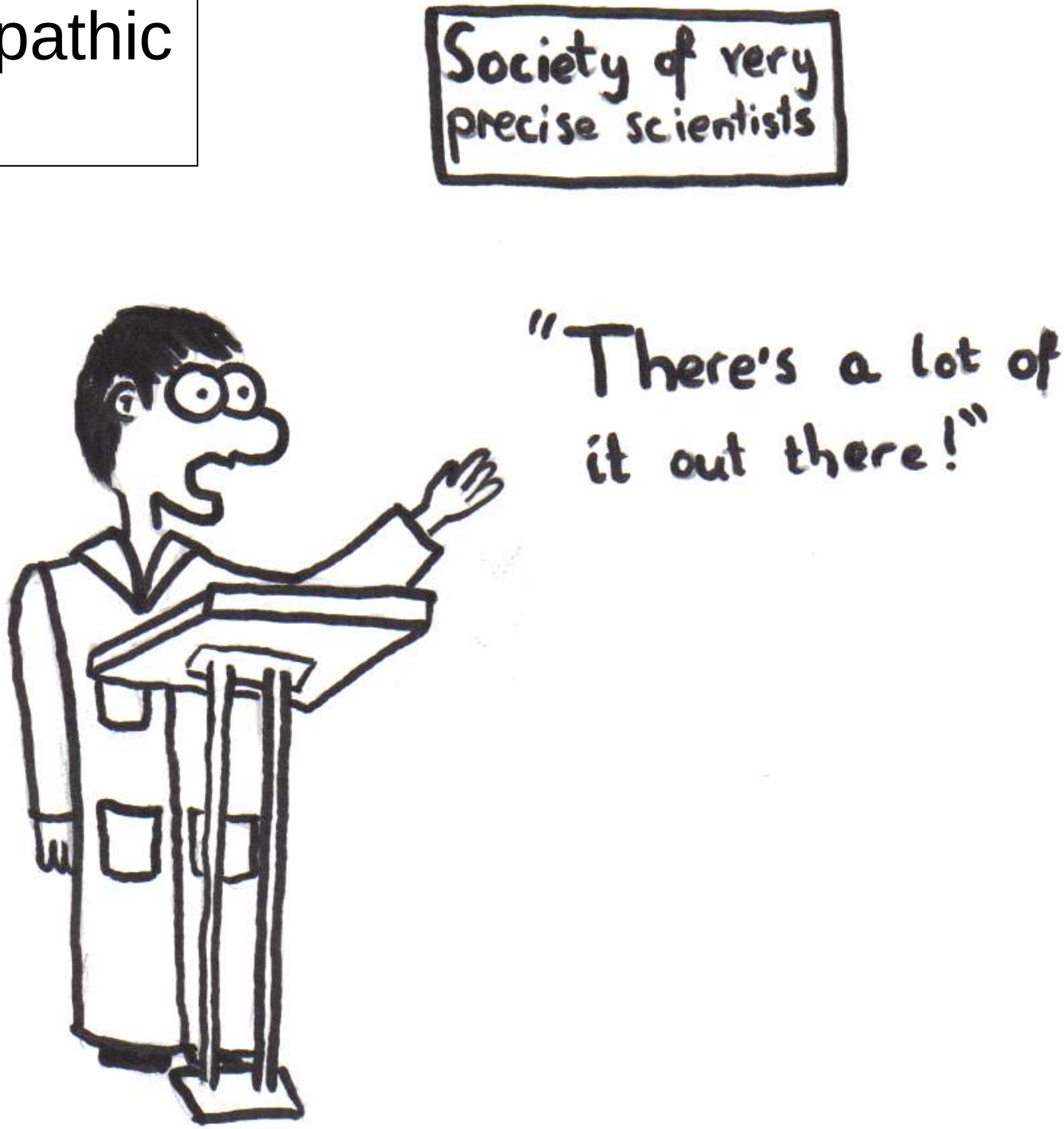

(NOTHING)


TO-DO LIST
NOTHING

We might know:

- Estimated prevalence of NeuP
- Prevalence of some conditions associated with NeuP
- Proportion of those with some of these conditions who have NeuP
- Prevalence of population responding positively to some screening instruments
- Factors associated with these (risk and impact)
- How to move from this baseline to hold more valuable information

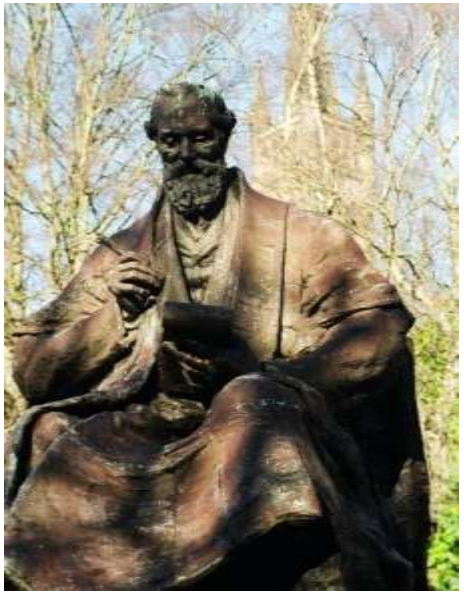
Neuropathic Pain

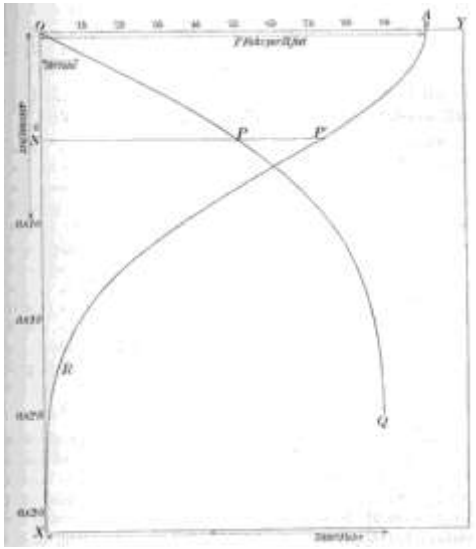


But…

“One’s knowledge of science begins when he can measure what he is speaking about and express it in numbers”.

Lord Kelvin

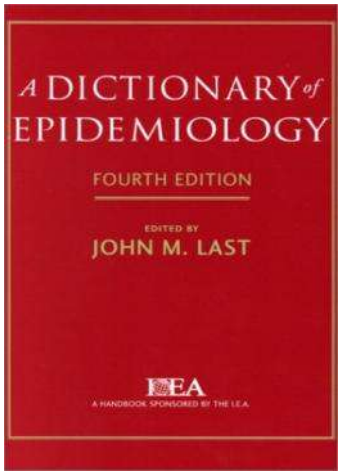




Epidemiology

"The study of the distribution and determinants of health-related states or events in specified populations *and* the application of this study to control health problems."

Last, 2001



…to control health problems

Lind J. *An inquiry into the nature, causes, and cure of the scurvy.* Edinburgh: Sands, Murray and Cochran, 1753

The famous Broad Street pump

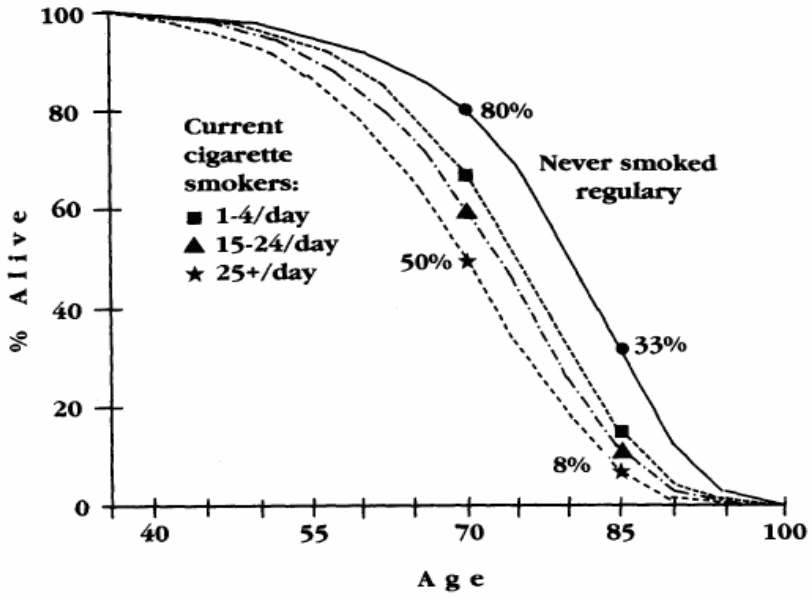
Snow J. *On the mode of communication of cholera.* London: Churchill, 1855

The doctors study

Doll R, Bradford Hill A. Mortality in relation to smoking: ten years' observation of British doctors. *Br Med J* 1964 **1** 1399-1410, 1460-67

Doll R, Peto R *et al.* Mortality in relation to smoking: 40 years' observations on male British doctors. *Br Med J 1994* **309** 901-11

Etc



Epidemiological study of (neuropathic) pain

To inform understanding, at a population level, of:

- Distribution and determinants
- Definition and classification
- Aetiology (factors which favour development and chronicity)
- Prognosis
- Prevention
- Impact on quality of life
- Design, targeting and evaluation of treatment strategies
- Allocation of health service resources
- Allocation of educational resources

Case definition

The essential starting point for epidemiological research

- "Pain initiated or caused by a primary lesion or dysfunction in the nervous system" Mersey and Bogduk, 1994
- "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" Treede *et al* 2008, Jensen *et al* 2011 [Epub ahead of print]
  - "Possible," "probable," "definite"
  - What constitutes a "(primary) lesion"
  - What constitutes a "dysfunction" or "disease"
  - Can we diagnose neuropathic pain without incontrovertible proof of these?
  - How do we address these questions in population studies?

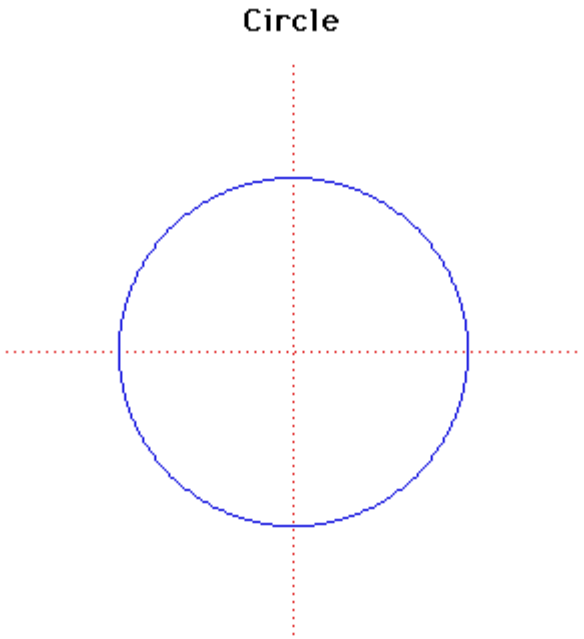
A yes / no phenomenon?

- "Pain can pain be more or less neuropathic" Rasmussen *et al*, 2004; Attal and Bouhassira, 2004; Bennett *et al* 2006
  - Gradient of neuropathic characteristics with increasing diagnostic certainty (MPQ, NPS, DN4, S-LANSS)
- So neuropathic pain can be seen as a spectrum, not a dichotomy
- Which point on the spectrum do we use for epidemiological case definition?

Epidemiological dilemma

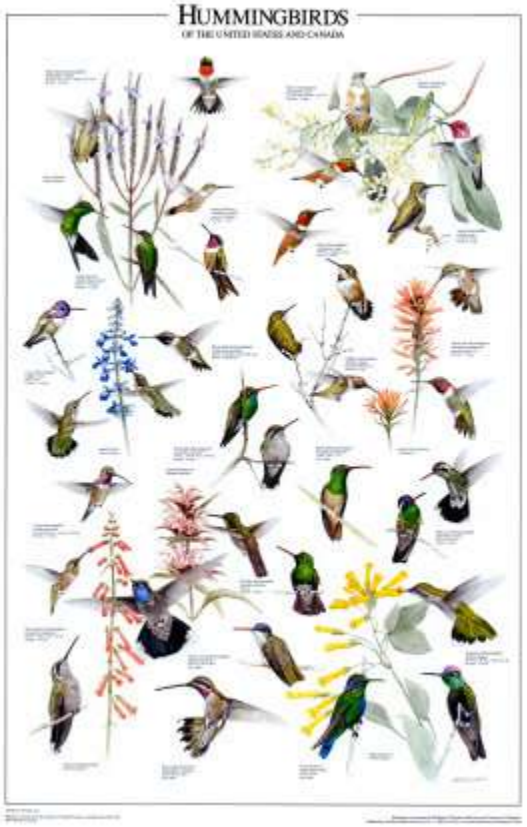
Neuropathic pain:

a single, global entity? or a diagnostic umbrella?



Compare with ornithology

More than 9,000 known species of birds



But...

"... a great number of people are unable to identify birds....[T]here are only three kinds of birds:

a) little fluttery ones,

b) big flappy ones,

c) and ducks."

Derek Parkinson, The Times, 12 January 2009

Neuropathic pain as a single entity?

- **Common features among all causes**
  - Mechanisms, symptoms, signs
  - HRQoL impact more dependent on intensity than cause – Doth *et al 2010*
- **Common response to treatments**
  - Sindrup and Jensen, 1999; Hansson and Dickenson, 2005
- **Not always possible to distinguish diagnosis**
  - Especially in primary care, also in epidemiology
- **Specific treatments available for NeuP**
  - Therefore important to identify and target unclassified and mixed cases, as well as classical syndromes
  - Daniel et al (2008) – different treatment needs from PMP for NeuP than for CLBP

But also important differences

- **Obvious aetiological differences**
  - Eg, PDN, PHN, Postsurgical pain, HIV neuropathy
- **With implications for prevention**
  - Eg treating hyperglycaemia, HZV immunisation, HIV prevention
- **Emerging evidence of clinical differences**
  - Fields *et al* 1998*:* two distinct PHN subtypes
  - Baron *et al* 2009*:* five distinct NeuP subtypes, frequencies vary in PHN and LBP
  - Grémau-Richard *et al* 2010: different response to treatment in 2 BMS subtypes
  - ?implications for treatment generally
- **Most RCTs are condition-specific**
  - Evidence limited of application to different conditions
  - Some evidence of condition-specific effects, eg HIV
    - Amitriptyline and gabapentin ineffective (Kieburtz *et al* 1998; Hahn *et al* 2004; Shay *et al* 1998)
    - Cannabis effective (Abrams *et al* 2007; Ellis *et al* 2008)

Case ascertainment

How do we determine who fulfils our case definition (for research purposes)?

- Clinical examination
  - Specialist / non-specialist? How detailed, and using what criteria? Eg Haanpää et al 2009; Haanpää et al 2010
- Interview
  - Face-to-face / telephone
- Medical records review
  - Quality and validity variable
- Questionnaire
  - How valid? What criteria?

Questionnaire screening tools

Topical review

Using screening tools to identify neuropathic pain

Michael I. Bennett , Nadine Attal, Miroslav M. Backonja, Ralf Baron, Didier Bouhassira, Rainer Freynhagen, Joachim Scholz, Thomas R. Tölle, Hans-Ulrich Wittchen, Troels Staehelin Jensen *Pain* 2007 **127** 199-203

	LANSS[a]	DN4[a]	NPQ	pain*DETECT*	ID Pain
Symptoms					
Pricking, tingling, pins and needles	•	•	•	•	•
Electric shocks or shooting	•	•	•	•	•
Hot or burning	•	•	•	•	•
Numbness		•	•	•	•
Pain evoked by light touching	•		•	•	•
Painful cold or freezing pain		•	•		
Pain evoked by mild pressure				•	
Pain evoked by heat or cold				•	
Pain evoked by changes in weather			•		
Pain limited to joints[b]					○
Itching		•			
Temporal patterns				•	
Radiation of pain				•	
Autonomic changes	•				
Clinical examination					
Brush allodynia	•	•			
Raised soft touch threshold		•			
Raised pin prick threshold	•	•			

[a] Tools that involve clinical examination.
[b] Used to identify non-neuropathic pain.

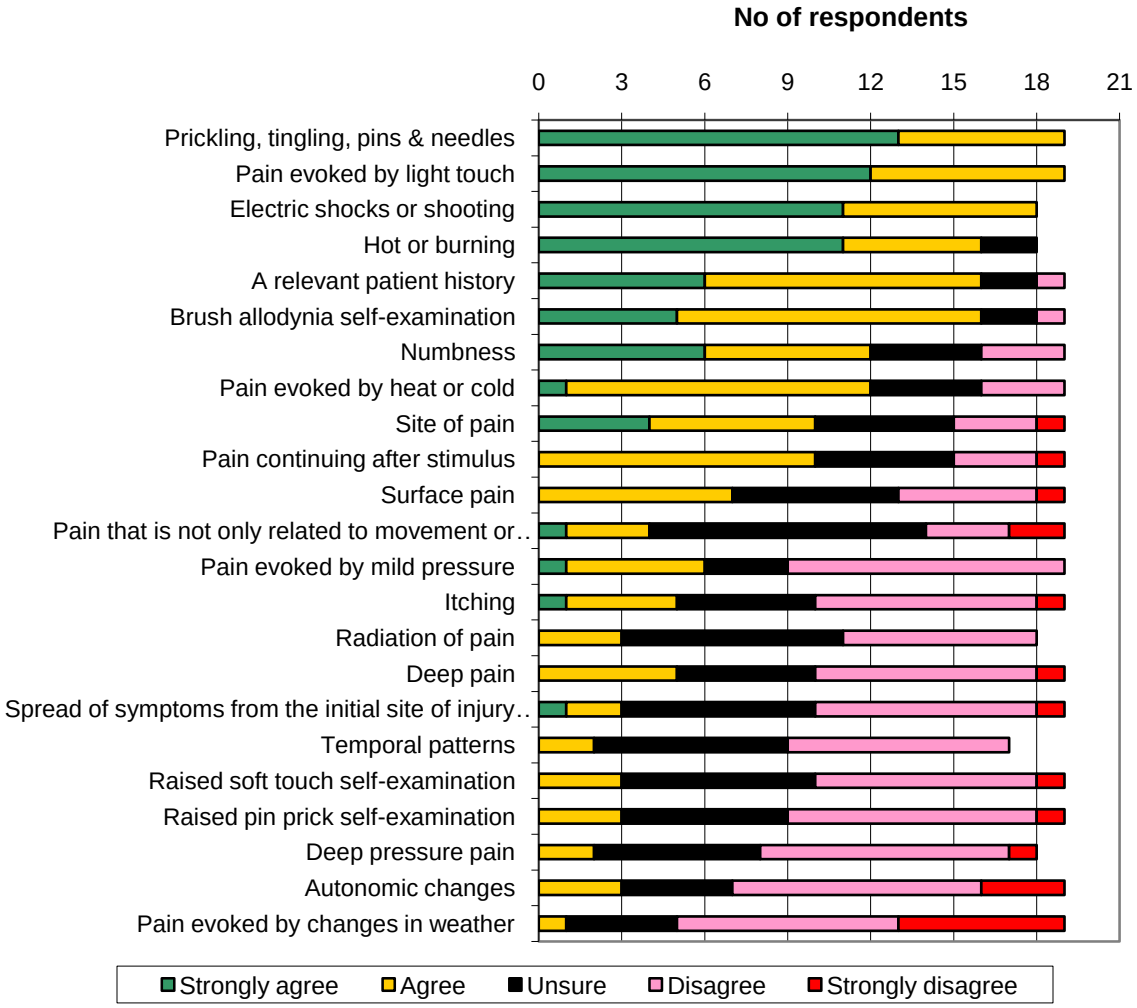

BRODYAGA.com
Photo by: Goran Zoroja
Delphi, GREECE

Delphi survey

After 3 rounds:

- 24 experts, internationally
- 6 items >75% agreement to include
- 9 items >75% agreement to exclude
- 8 items mixed agreement
- Reasonable agreement on "refractory NeuP"

Postal survey in progress across UK (n=10,000)



Smith and Torrance (*submitted*)

Information previously available

- Condition-specific estimates
- Prevalence of neuropathic pain ~1% Bowsher 1990
- Prevalence of neuropathic pain ~2% Bennett 1997

- "Thought to be more common than has been generally appreciated…" Dworkin 2002

Prevalence using screening tools

- **S-LANSS** Torrance *et al* 2006; Smith *et al* 2007; Yawn *et al* 2009
  - "Pain of predominantly neuropathic origin"
  - 8.2% (UK)
  - 8.8% (USA)

- **DN4** Bouhassira *et al* 2008;
  - "Pain with neuropathic characteristics"
  - 6.9% (France)

- Validated in pain clinic populations
- Validity and PPV unknown in general population

Therefore, this is ***not*** the prevalence of **neuropathic pain**

Prevalence of "possible neuropathic pain?" Treede *et al* 2008

Comprehensive literature review

Smith and Torrance, 2011

- Inclusion criteria
  - Epidemiological studies, 1966 to 2008
  - in general population sample
  - of condition in which NeuP is commonly recognized as a main feature, OR of NeuP as a single, global entity
- Search terms

- 1 central pain.ti,ab. (412)
- 2 myelopath$.ti,ab. (3345)
- 3 exp Neuralgia/ or exp Trigeminal Neuralgia/ or exp Facial Neuralgia/ or exp Neuralgia, Postherpetic/ (4826)
- 4 neurogenic pain.ti,ab. (132)
- 5 neuropathic pain.ti,ab. (4196)
- 6 peripheral nerve injur$.ti,ab. (1277)
- 7 peripheral neuropath$.ti,ab. (4982)
- 8 peripheral sensory neuropath$.ti,ab. (128)
- 9 polyneuropath$.ti,ab. (3951)
- 10 polyneuropathies/ or alcoholic neuropathy/ or "hereditary motor and sensory neuropathies"/ or "hereditary sensory and autonomic neuropathies"/ or polyradiculoneuropathy/ (2753)
- 11 or/1-10 (21970)
- 12 exp Pain/ (108996)
- 13 exp Incidence/ (83006)
- 14 exp Prevalence/ (86068)
- 15 exp Epidemiology/ (6644)
- 16 13 or 14 or 15 (167176)
- 17 11 and 12 and 16 (161)
- 18 limit 17 to yr="1997 - 2008" (157)
- 19 limit 18 to humans (155

Results

	NeuP as a single entity	Specific NeuP diagnoses
Original research	**4 papers** Bouhassira 2008 Dieleman 2008 Gurstorff 2008 Torrance 2006 [Toth *et al* 2009] [Yawn *et al* 2009]	**11 papers** Choo 1997 (PHN) Davies 2006 (PDN) Freynhagen 2006 (Back) Hall 2006 (multiple sites) Hall 2008 (multiple sites) Helgason 2000 (PHN) Opstelten 2002 (PHN) Sjaastad 2004 (Supra-orbital neuralgia) Wu 2007 (PDN) Yawn 2007 (PHN) Younes 2005 (Back)
Review papers	**No papers**	**2 papers** Sadosky 2008 (PDN, PHN, others) Taylor 2006 (DN, PHN, Back, CRPS)

NeuP as a single entity

	Sample size	Ascertainment method	Case definition	Main results
Bouhassira et al 2008	23,712	DN4 Postal survey	"Chronic pain with neuropathic characteristics"	Prevalence **6.9%**
Dieleman et al 2008	9,311	Medical records review	"Neuropathic pain"	Incidence **0.8%**
Gustorff et al 2008	7,707	Selected items from DN4 and LANSS Interview survey	"Neuropathic pain"	Prevalence **3.3%**
Torrance et al 2006	3,002	S-LANSS Postal survey	"Pain of predominantly neuropathic origin"	Prevalence **8.2%**
[Toth et 2009]	1,207	DN4 Telephone survey	"Chronic pain with NeP symptoms"	Prevalence **17.9%**

Specific NeuP diagnoses

- **PHN**
  - Prevalence 2.6% to 10% of those who have had HZ
  - Higher in older age-groups
- **PDN**
  - Prevalence 8% to 20% of those with Type 2 diabetes
- **Back pain neuropathy**
  - Prevalence 37% of those with CLBP (painDETECT)
  - Population prevalence 0.75% to 14.5% !

Common associated factors

- Female gender
- Older age
- Occupational factors
  - manual workers
  - being unable to work
- Indicators of deprivation
  - Social class (housing tenure)
  - Educational attainment
- Poor general health

Cross-sectional studies, so cause/effect not known.

Specific risk factors

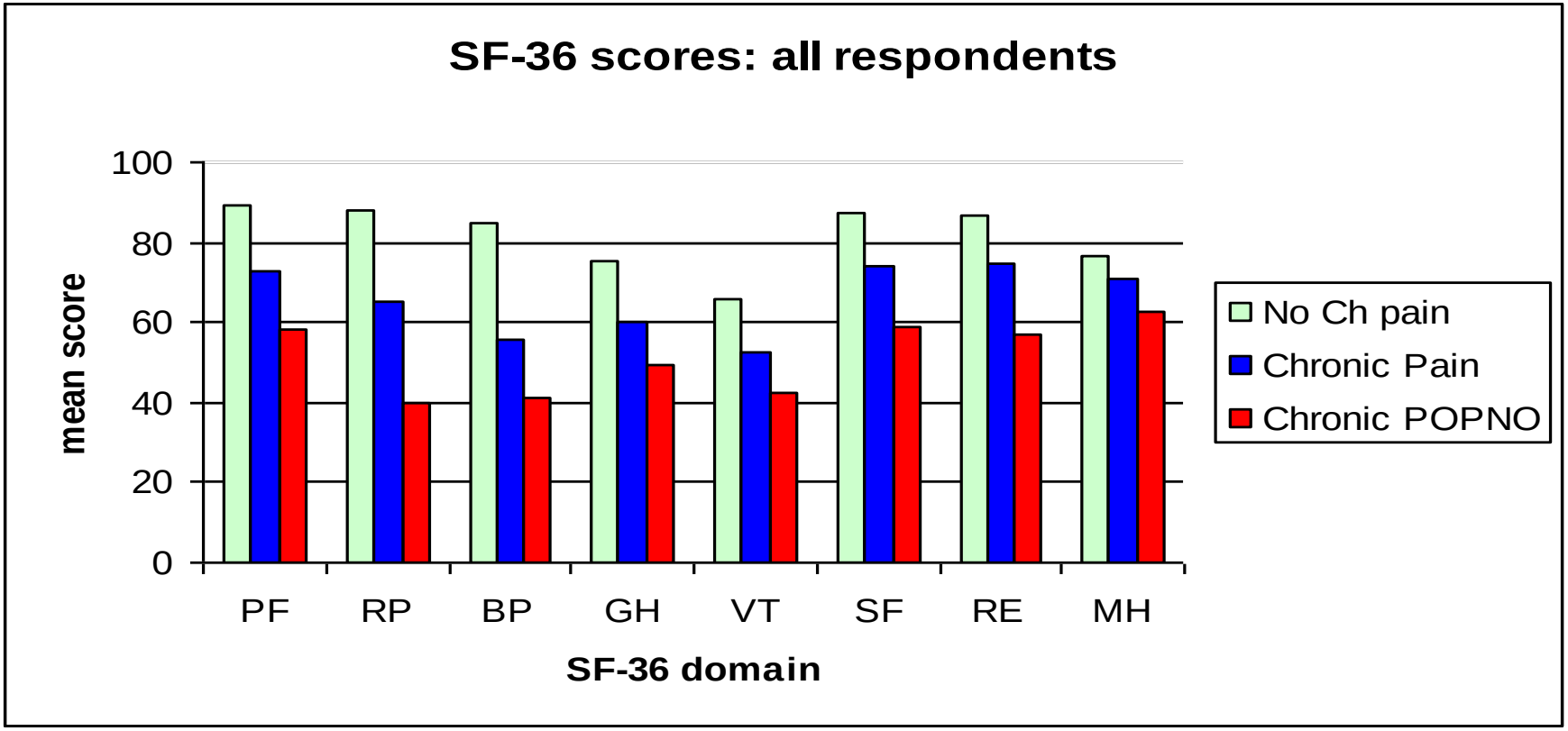
- **PDN**
  - Risk factors for DM
  - Smoking; high HbA_{1C}; duration of DM; other metabolic syndrome components; female gender Tesfaye 2005; Jensen 2006
- **PHN**
  - Older age; female gender; immunocompromise; painful prodrome; greater acute pain; more severe rash Jung 2004
- **Post-surgical pain**
  - Surgery!
  - Surgical technique/nerve damage; peri-operative pain; female gender; psychosocial factors Kehlet 2006

Consider these in planning prevention

Impact of NeuP

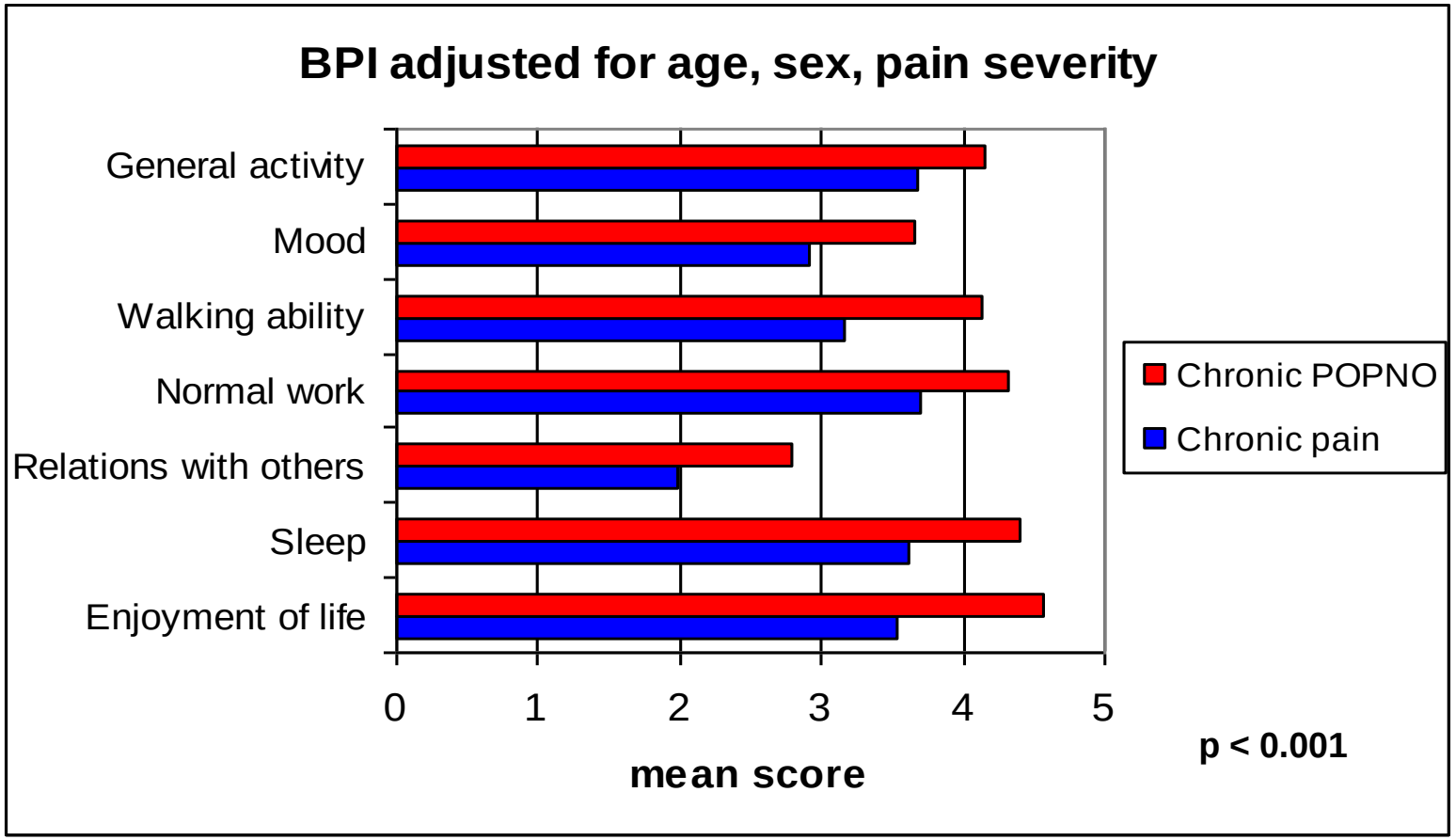
- Poor health-related quality of life Schmader *et al* 2002; Smith *et al* 2007; Jensen *et al* 2007; Doth *et al* 2010
- HRQoL most dependent on pain intensity Doth *et al* 2010
- HRQoL scores equivalent to those found in
  - Clinical depression
  - Coronary artery disease
  - Recent MI
  - Poorly controlled diabetes
- Increasing impact on society
  - Ageing population
  - Increasing prevalence of DM
  - Global burden of HIV (33.2 million have HIV; 35% have painful neuropathy)

S-LANSS and SF-36



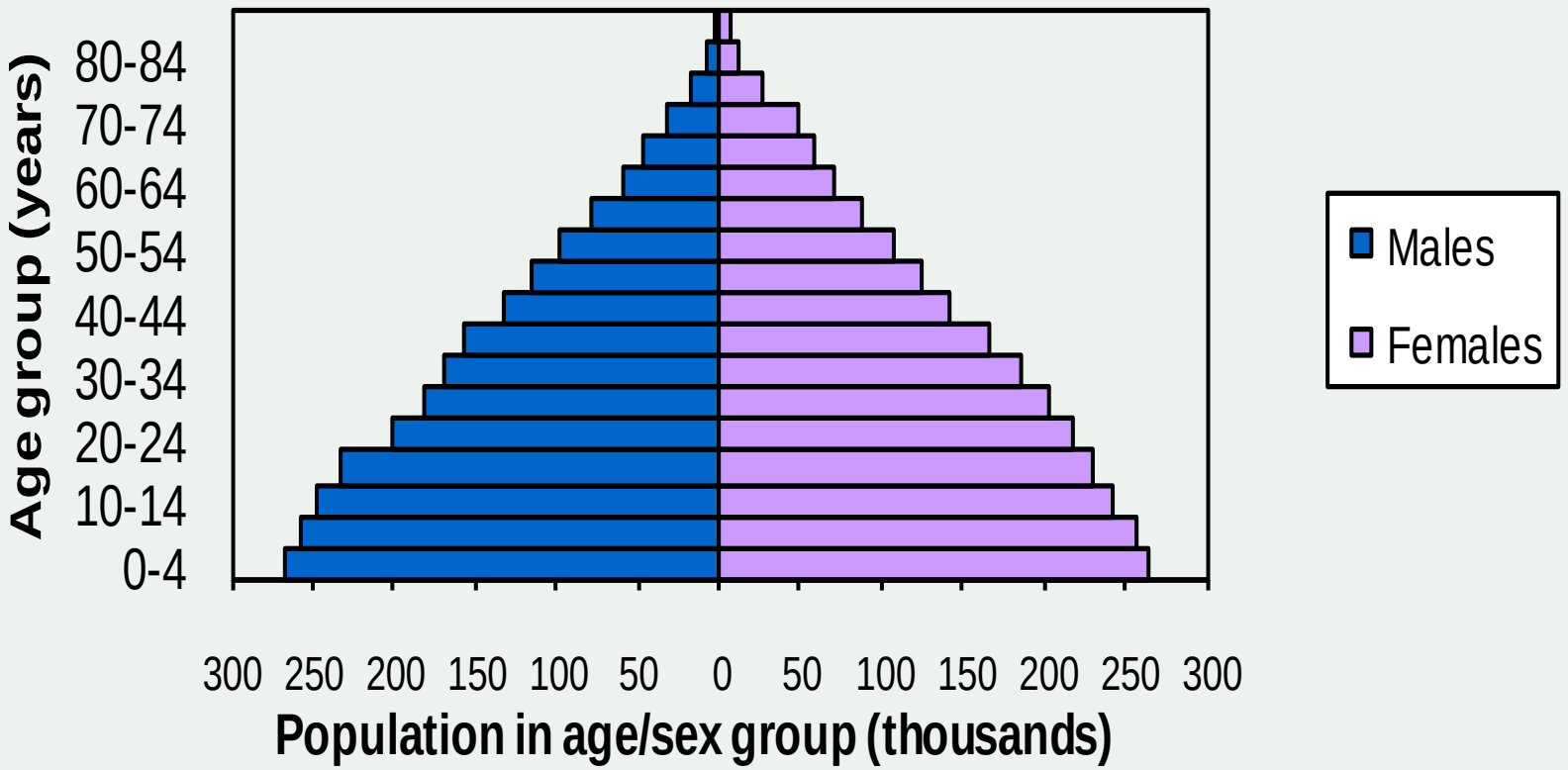
Smith *et al* 2007

Brief Pain Inventory

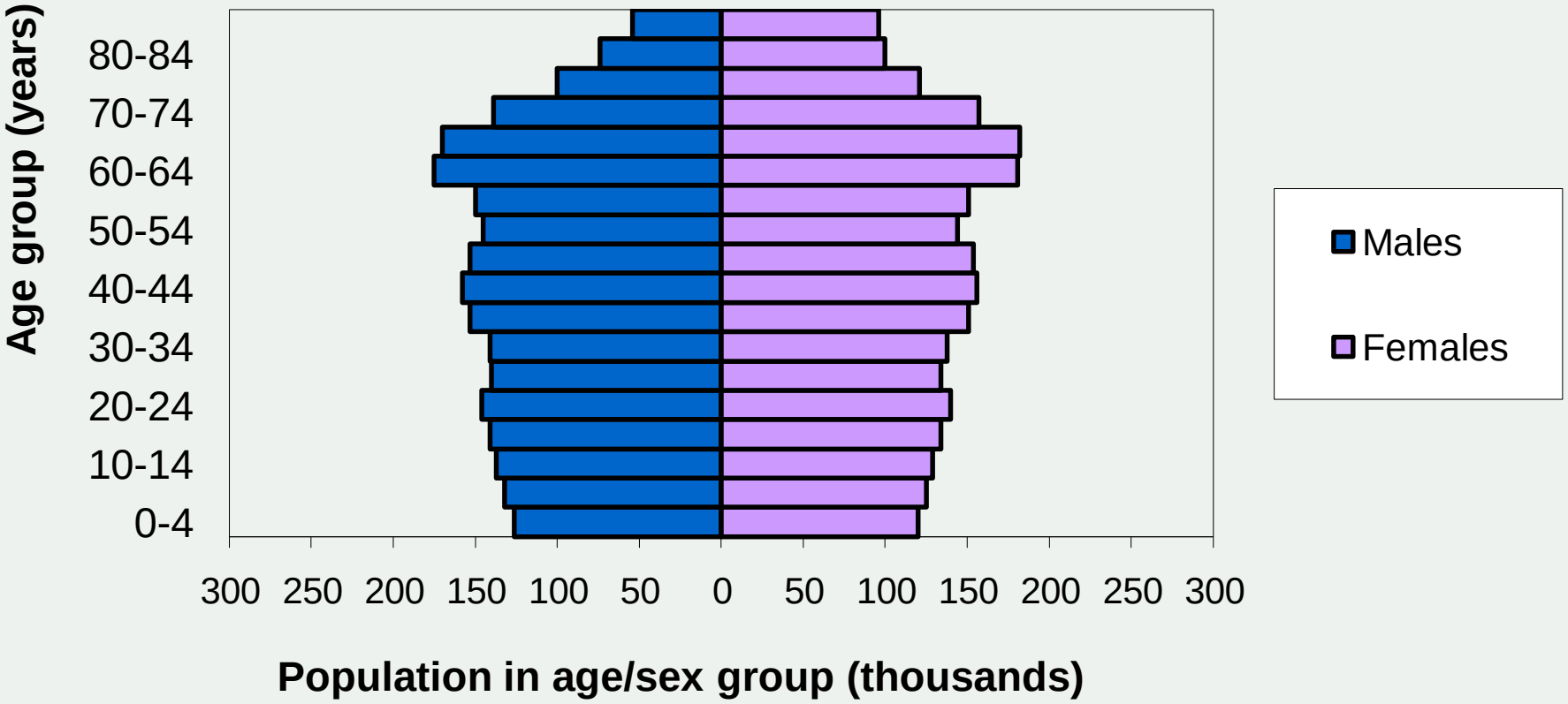


Smith *et al* 2007

Scotland 1911



Scotland 2031



Rise and rise of chronic diseases: 60% of adults

- Diabetes
- Cancer
- HIV
- Shingles
- Etc


Old age is not a disease doctor— just a challenge!
© www.growingolddisgracefully.org.uk

Summary

Available epidemiological evidence confirms that:

- Neuropathic pain is common
- Neuropathic pain is important
  - To individuals
  - To society
- There is potential to target identification and treatment strategies
- There are opportunities for prevention
- More research is needed

Research priorities

Include:

- Development of gold standard case definition
- Development of practical case ascertainment method for population-based research
- Validation of existing screening instruments for population-based research
  - Positive and negative predictive values
- Longitudinal studies, identifying risk factors
- Genetic epidemiology
- Management/prevention strategies based on these
- Differences in response to treatment, in diagnostic subgroups

Thank you for listening

"Mr. Osborne, may I be excused? My brain is full."

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