



16th South Thames Acute Pain Group Conference
11-12th November 2010

Prevalence and risk factors for chronic pain after surgery

Julie Bruce PhD, Principal Research Fellow
Clinical Trials Unit, University of Warwick, UK

Presentation

- definitions / terminology
- approaches to measurement
- evidence on risk factors → acute setting?
- model for research / future work
- epidemiological perspective

Definition – IASP

Chronic pain

“intermittent or continuous pain which persists beyond normal tissue healing time”

“**3** months most convenient division between acute & chronic but for research purposes, **6** months will often be preferred”

(IASP, Classification of Chronic Pain, 1984)

Definition

Criteria for chronic pain after surgery

(Macrae & Davies, 1999):

- i. Pain must develop after a surgical procedure;
- ii. Pain is of at least **2** months duration;
- iii. Other causes for the pain have been excluded;
- iv. The possibility that the pain is from a pre-existing problem should be explored and exclusion attempted.

Terminology

“Chronic post-surgical pain”

post-surgical neuralgia

post-operative traumatic nerve injury

neuroma pain

persistent scar pain

Procedure-specific syndromes

Breast

Post-mastectomy pain syndrome (PMPS)

Post-axillary dissection pain

Intercostobrachial nerve entrapment syndrome

Hernia

Mesh inguinodynia

Mesh ilioinguinal neuropathy

chronic genitofemoral neuralgia

Thoracic/cardiac: Post-thoracotomy pain syndrome

Internal mammary artery syndrome (IMAS)*etc.*

Mechanism

- **Nociceptive pain:** activation of peripheral sensory neurons by noxious stimuli
 - ~ local increase in sensitivity
 - ~ prolonged high intensity stimulus, fades on removal
- **Inflammatory pain:** response to tissue injury & inflammation
 - ~ drives acute postop pain until wound healed, usually reversible
- **Neuropathic pain:** can arise after nerve injury
 - ~ intraoperative nerve trauma from cautery, dissection etc.

Characteristics

Chronic post-surgical pain

Sensation: loss or alteration of sensation (touch, temp, pressure)

Allodynia: pain evoked by non-noxious stimuli

Hyperalgesia: amplified response

- Predominantly neuropathic (Kehlet 2006, Steegers 2008)
- **Pain descriptors**
 - stabbing, shooting, burning, numbness, pins & needles, tingling.....

Burden of disease

How common?

Historically,

- rare syndrome, literature from 1970s: 0.1% to 4%
- 'mild side effect' (Brit J Cancer, 1992)

Survey of UK outpatient pain clinics (Crombie et al. 1998)

The contributors to the development of pain in 5130 patients	
Putative cause	% of patients ^a
Degenerative	34.2
Surgery	22.5
No definite cause	20.2
Trauma	18.7
Infective	7.2
Inflammatory	6.7
Tumour	3.5
Others	6.2

Chronic pain after breast surgery

Prevalence studies

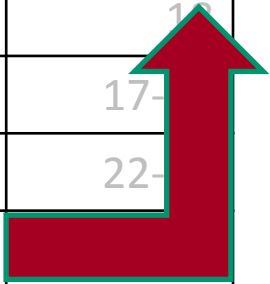
Author	Country	Year	S/Size	Follow-up	Pain (%)
Vecht	Netherlands	1990	38	0.5yr	18
Kroner	Denmark	1992	69	6 yr	17-31
Polinsky	USA	1994	223	8 yr	22-32
Stevens	USA	1995	95	NR	20
Tasmuth	Finland	1995	93	1 yr	24
Tasmuth	Finland	1995	469	2 yr	49
Wallace	USA	1996	282	1 yr	31-49
Smith	Scotland	1999	408	3 yr	43
Johansen	Denmark	2000	266	6 yr	15
Fassoulaki	Greece	2005	55	6 mo.	57
Macdonald	Scotland	2005	175	9 yrs	50

Chronic pain after breast surgery

Danish nationwide cross-sectional survey (87% responded)

Author	Country	Year	S/Size	Follow-up	Pain (%)
Gartner <i>et al.</i>	Denmark	2009	3253	2 yrs	47
Vecht	Netherlands	1990	38	0.5yr	18
Kroner	Denmark	1992	69	6 yr	17-
Polir				yr	22-
Stev				R	
Tasmuth	Finland	1995	95	1 yr	24
Tasmuth	Finland	1995	469	2 yr	49
Wallace	USA	1996	282	1 yr	31-49
Smith	Scotland	1999	408	3 yr	43
Johansen	Denmark	2000	266	6 yr	15
Fassoulaki	Greece	2005	55	6 mo.	57
Macdonald	Scotland	2005	175	9 yrs	50

Of women with pain, n=796 (52%) reported moderate to severe pain (JAMA, 2009)



Inguinal hernia repair

Systematic review

Authors	Published	No. of studies	S/Size	Definition of CPSP	% chronic pain
Poobalan <i>et al.</i>	1987- 2000	N=40	Any	>3 months	10-30% (5% severe)

A Review of Chronic Pain After Inguinal Herniorrhaphy

*Amudha S. Poobalan, M.B.B.S., M.Sc., *Julie Bruce, M.Sc., *W. Cairns
S. Smith, M.D., M.F.P.H.M., F.R.C.P, †Peter M. King, F.R.C.S., †Zygmunt H. Krukowski, F.R.C.S., and
W. Alastair Chambers, M.D., F.F.A.R.C.S.

Clin J Pain, 2003

Pain prevalence after hernia surgery

Systematic reviews

Authors	Published	No. of studies	S/Size	Definition of CPSP	% chronic pain
Poobalan <i>et al.</i>	1987-2000	N=40	Any	>3 months	10-30% (5% severe)
Aasvang & Kehlet	2000-3	N=35	>100	> 6 months	12% Testicular pain 6%

Chronic postoperative pain: the case of inguinal herniorrhaphy

E. Aasvang and H. Kehlet*

Brit J Anaes 2005

Increased recognition

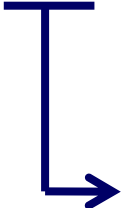
Surgical adverse event

- growing body of literature → hernia, breast, cardiac, orthopaedic, amputation, gynae surgery....
- UK NICE – primary outcome after herniorrhaphy
- studies published in key medical (& surgical) journals

Prognosis?

Grampian study pain after breast surgery

175/ 408 (43%) chronic pain 3 years post-mastectomy (Pain, 1999)

- 
- alive & eligible
 - mean 9 years postoperatively, 82% responded
 - re-assessed post-mastectomy pain: MPQ, VAS, body maps etc.
 - **still had pain, (n=59; 52%)**
 - **pain resolved (n=54; 48%)**

Long-term follow-up of breast cancer survivors with post-mastectomy pain syndrome

Brit J Cancer, 2005

L Macdonald¹, J Bruce^{*,2}, NW Scott², WCS Smith² and WA Chambers¹

¹Department of Anaesthesia, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZN, UK; ²Department of Public Health, University of Aberdeen, Polwarth Building, Medical School, Foresterhill, Aberdeen AB25 2ZD, UK

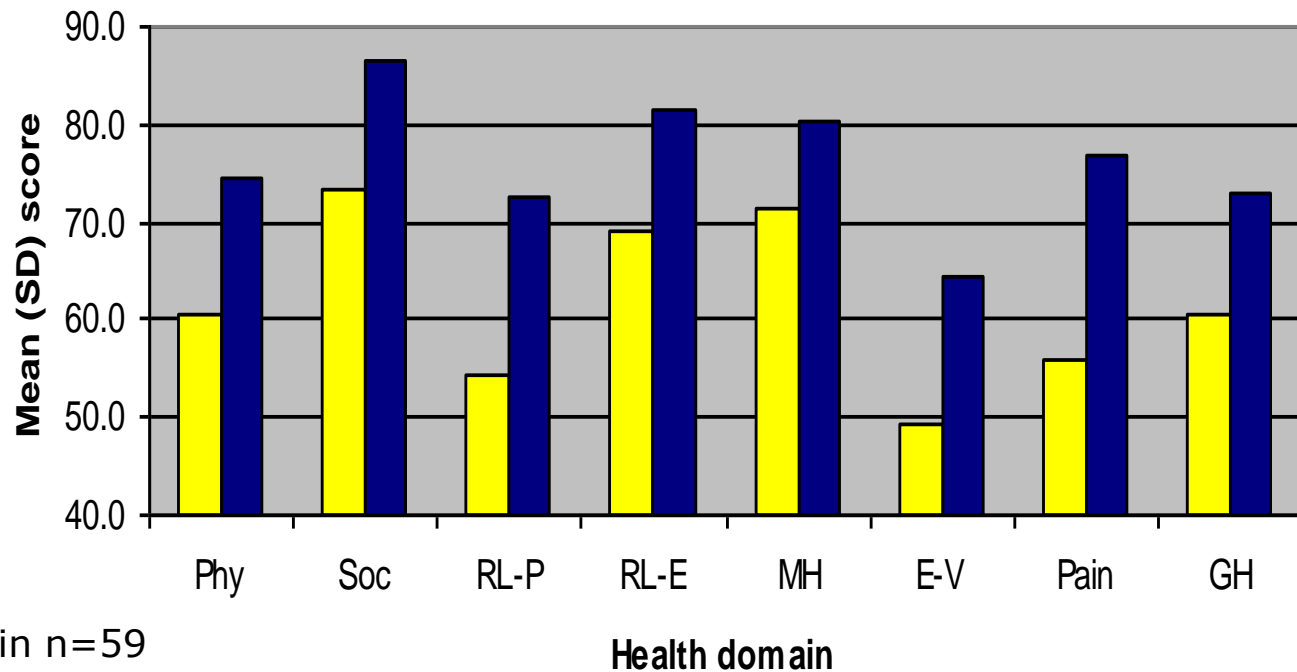
Impact on quality of life

9 years post-mastectomy, n=113 patients

- (52%) pain resolved: QoL improved over time

- (48%) **persistent pain**: QoL scores lower

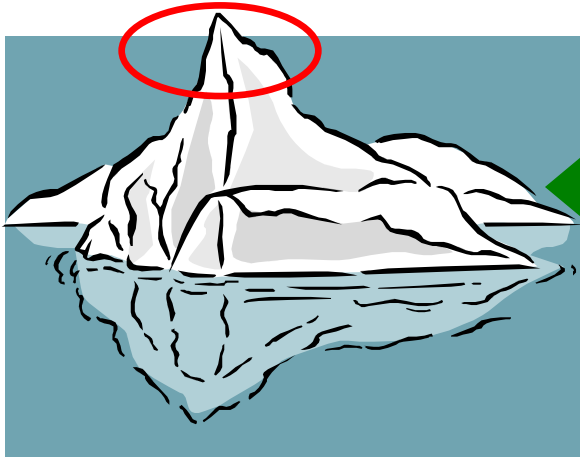
($P < 0.01$; all domains)



■ Chronic pain n=59
■ Pain resolved n=54

Measurement

Clinical vs epidemiological approach



Clinical e.g. pain clinic
detailed assessment of
individuals
individual approach to
investigation & treatment

Epidemiological
Population level
Cross sectional surveys
Prospective surgical cohorts



Epidemiological studies

Case ascertainment



Defining 'chronic'

Have you had pain in the last day?

Have you had this pain for more than 2 / 3 / 6 months?

Location of pain

Attributable to surgery?

Is this pain the same as the pain before surgery? [*recall bias*]

Is the pain due to surgery?



Surgical cohort studies



Model for investigation



Pain characteristics

Intensity

e.g. VAS, VRS, BPI

Character:

MPQ, s-LANSS, DN4 etc.

Timeline:

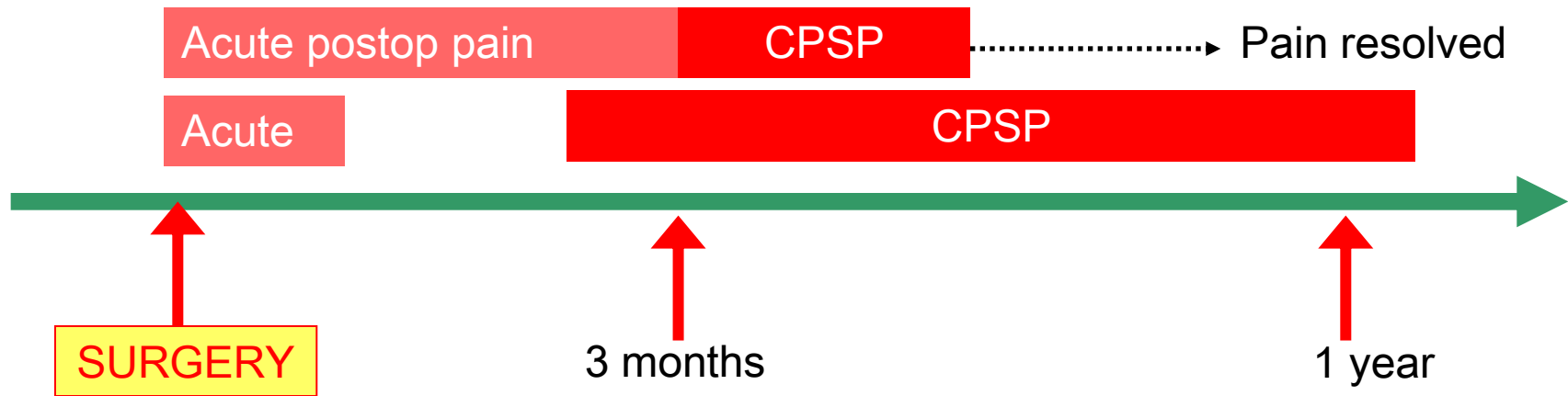
onset & pattern

Impact on QoL:

BPI, SF36 etc

Surgical cohort studies

Pain onset & trajectory



Pain after mastectomy
(Smith *et al.*, Pain, 1999)

1/4 had late onset pain

Time of onset of pain	Number	Percentage
Immediate	52	30
Less than one month	44	25
1-3 Months	26	15
More than 3 months	42	24
Not reported	11	6

Chronic post-surgical pain

Risk factors?

Demographic

Younger age

- breast, hernia, cardiac, thoracic (e.g, Maguire, 2006)

- severe pain common in younger patients (Aasvang & Kehlet, 2005)

Age	Aberdeen studies*		
	% CPSP		
	Breast N=408	Hernia N=351	Cardiac N=1080
<50	↓ 65%	↓ 58%	↓ 55%
50-70	40%	40%	38%
>70	↓ 26%	↓ 14%	↓ 34%

*Smith 1999; Poobalan 2001; Bruce 2003

Sex

- chronic pain more common in women
- evidence less consistent after surgery

Genetic susceptibility

- pain perception & susceptibility variable (Diatchenko, 2005)
- chronic neuropathic pain after breast cancer surgery (Nissenbaum 2010)

Surgical factors

e,g, type of implant, surgeon experience, volume & outcome (Tasmuth 1995)

- duration of surgery increases risk (Peters 2007)
- extent of injury & severity of pain?
 - high rates after major invasive procedures
 - higher rates after open vs. laparoscopic surgery
 - Not a consistent or linear r/ship (Kehlet 2006)
 - many studies suggest short-term benefits
 - video-assisted approaches (thoracic) – reduced acute pain but not difference in rates of chronic pain (eg. Stammberger 2000)

Nerve injury

Intraoperative trauma:

e.g. nerve stretching, contusion, entrapment, compression, diathermy, sutures, staples...etc.

Evidence from trials of elective nerve division?

- ICBN dissection: no difference in chronic pain or sensory deficit (Salmon 1998)
- ICBN dissection: no difference in chronic pain but more sensory deficit (Freeman, 2003)
- n=973 hernia repairs, identification, dissection or preserved (Alfieri, 2006)
 - ~ identification of nerve structures associated with lower chronic pain
 - ~ risk of pain increased with number of nerves not detected.

Preoperative pain

Pain at site of surgery

-limb amputation, spinal surgery, knee replacement, hernia repair

(see Nickolajsen 2007; den Boer 2006; Thorvaldsen & Sorensen 1990; Brander 2003; Liem 2003)

Other painful conditions

Chronic pain 5 years post-hernia more common in those with existing painful condition

e.g. backache, headache, IBS (Wright 2002)

Danish breast cancer survey (Gartner 2009)

- more common in women with backache/headache ($p < 0.001$)

Chronic preop pain

Chronic pain before surgery

- knee replacement, n=855 (Puolakka, 2010)
- duration of preoperative pain? longer duration = higher risk
- adjusted OR 2.8 (95%CI 1.4, 8.7)

Mechanism?

- sustained nociceptive input
- sensitization, exaggerated pain response
- does surgery trigger / accelerate pain response?

Psychological factors

Surgical studies – r/ship with acute postop pain

- ❑ depression (Katz 2005, Poleshuck 2006)
- ❑ anxiety (Katz 2005, Poleshuck 2006)
- ❑ pain catastrophising (Granot 2005; Sullivan 2009)
- ❑ pain / recovery expectations (Iversen 1998)
- ❑ optimism (Peters 2007)

Acute postop pain

Severe acute postoperative pain predicts chronic pain

- breast cancer surgery
- knee replacement
- thoractomy
- other surgeries

see Tasmuth 1995, Poleshuck 2005; Rosseland 2008; Katz, 1996; Gottshalk 2008; Peters 2007 etc...

Severity of acute pain

Data from n=855 TKRs (Puolakka, 2010)

- independent of age, sex, type of joint revision etc

Table 3 Results of multivariate logistic regression analysis

Variable	OR	95% CI
Bilateral versus primary arthroplasty	0.8864	0.4802 – 1.5875
Revision versus primary arthroplasty	1.0904	0.3650 – 2.8885
Duration of presurgical pain >12 months	2.8431	1.1448 – 8.6517
Age, centred at 70 years	1.0141	0.9855 – 1.0434
Age, squared and centred at 70 years	1.0027	1.0007 – 1.0048
Sex, female	1.9084	1.1434 – 3.2787
Moderate postsurgical pain versus mild	3.1135	1.5857 – 6.6186
Severe postsurgical pain versus mild	8.1686	4.0428 – 17.8303
Unbearable postsurgical pain versus mild	10.6857	3.6304 – 32.6282

CI, confidence interval; OR, odds ratio.

Summary of risk factors

from current literature

- younger age, existing pain, chronic painful condition, females (~?), more invasive procedures of longer duration
- anxious/depression, low expectation of pain relief & long-term recovery of function
- **severe acute postoperative pain**
- **BUT** many studies are small & methodologically flawed

Research agenda

Future directions

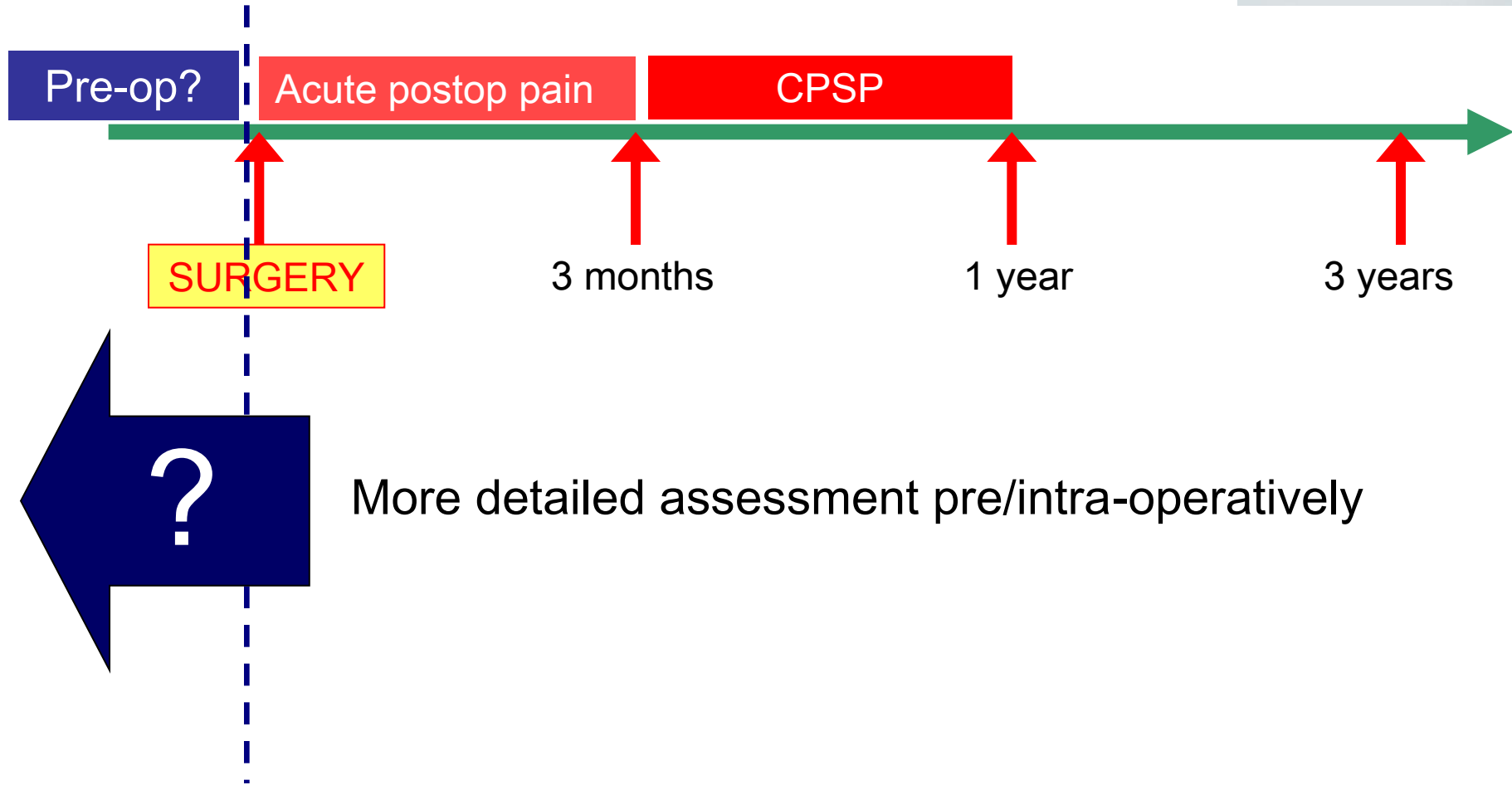
- shift from prevalence → better quality studies with larger sample sizes
- identify patients “at risk” preoperatively



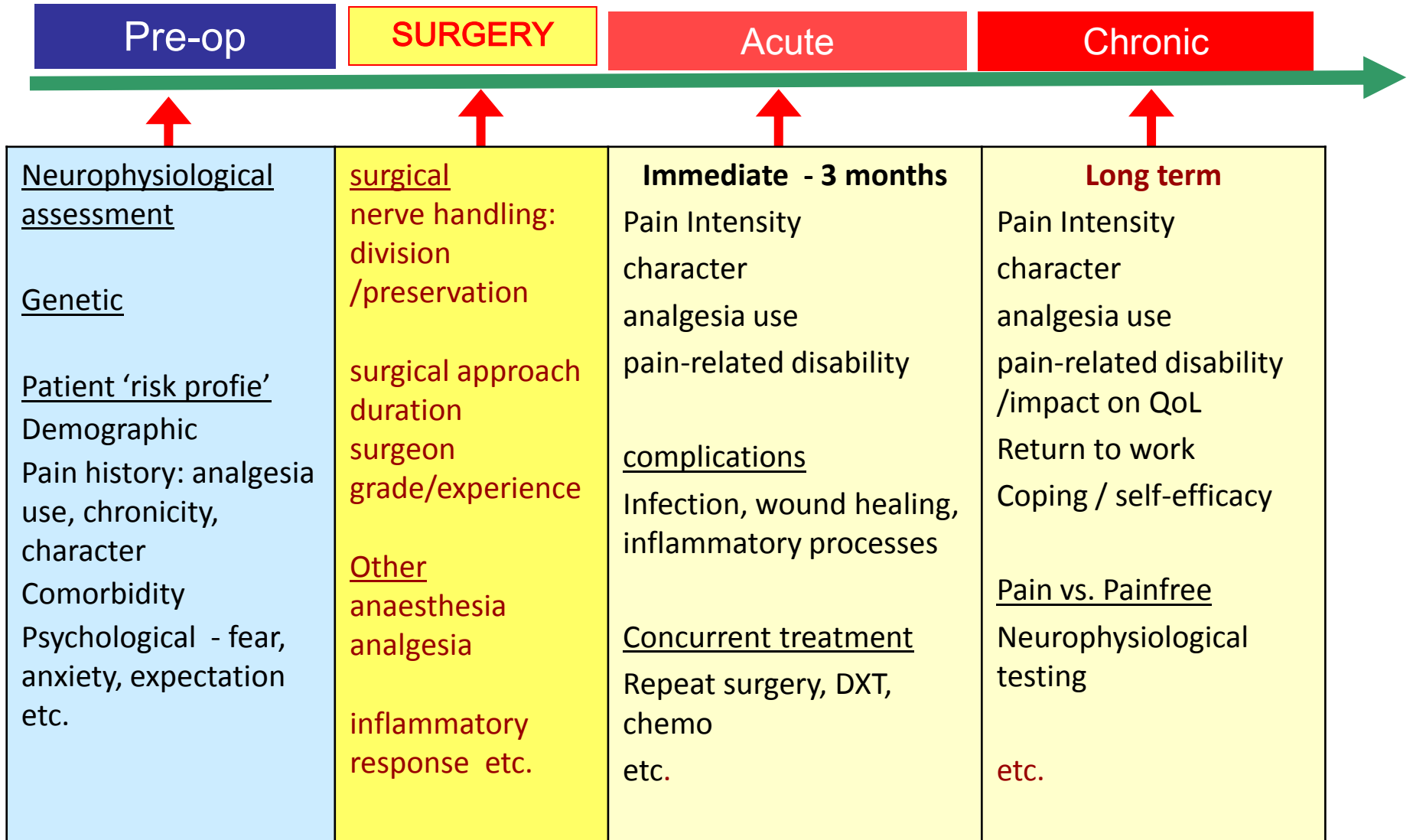
Surgical cohort studies



Model for investigation



Assessment of multiple factors



Collaborative initiatives

Current work



The Netherlands

- hysterectomy
- **pre**, acute pain, 6 & 12 months



Canada

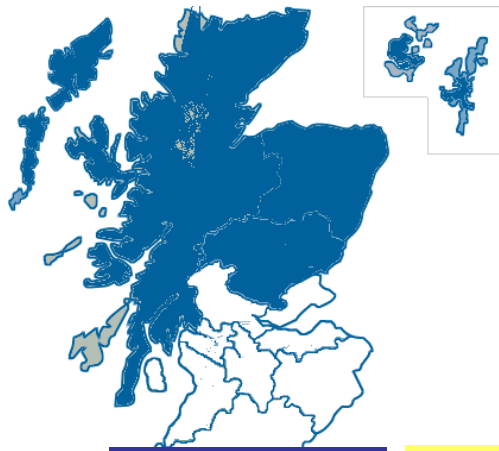
- hysterectomy
- **pre**, acute pain, 6 & 12 months



Scotland

- breast cancer surgery
- **pre**, acute pain, 4 & 9 months





North of Scotland study of pain after breast cancer surgery

n=405 mastectomy +/- axillary surgery



Demographic

Age, education, m
etc.

ICBN injury
etc.

Pain status

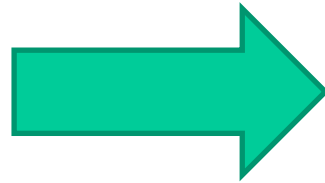
Comorbidity /chronicity
BPI, MPQ, DN4

Physical functioning

QoL

Psychological

PCS, HADS, STAI,
optimism/fear etc.



Pain status

NRS 0-10
BPI, MPQ,
NeuP (DN4 /SLANSS)

Physical functioning

QoL

currently > 90% follow-up @ 9 months

Conclusion

- common postoperative complication, increased awareness
- nerve injury contributes not sufficient in itself, pain occurs in susceptible subgroups
- transition from acute to chronic is complex
- Need for more detailed pre/intraoperative assessment to improve knowledge on risk prediction

Acknowledgements

Collaborators

Prof W Alastair Chambers
Prof W Cairns Smith
Dr Amudha Poobalan
Prof Zyg Krukowski
Mr Peter King
Prof Steven D Heys
Ms Susan Marfizo
Prof Alastair Thompson
Ms Alison Thornton
Dr Rachael Powell
Dr Louise Macdonald
Prof Marie Johnston
Dr Neil Scott
Dr William Macrae

International collaborators

Prof Madelon Peters
Dr Liz van den Kerkoff



Thank you!