study investigated whether an analgesic plasma concentration could be determined for oxycodone and which factors affect it.

Methods: 1000 women undergoing breast cancer surgery were recruited to the study. Demographic data were collected and their cold and heat pain sensitivity and anxiety scores were measured preoperatively. After surgery, rest and motion pain intensities were measured. Intravenous oxycodone was administered until the patients reported satisfactory pain relief (NRS <4/10). At this point, plasma concentrations of oxycodone and its metabolites were determined. A second plasma sample for oxycodone determination was taken when the patient requested a new dose of oxycodone. Genomic DNA was extracted from whole blood samples and the patients were genotyped for CYP2D6, CYP3A4 and CYP3A5

**Results:** The two oxycodone concentrations showed a strong correlation (r = 0.84). The pain intensity measured during motion before oxycodone dosing correlated significantly with the plasma oxycodone concentration (geometric mean 35.3 ng/ml and CV% 66.4) required to achieve satisfactory analgesia (r = 0.38,  $p = 1.5 \times 10^{-33}$ ). The most important factors associating with postoperative pain intensity were type of surgery (breast conserving or mastectomy with or without axillary clearance) and the age of the patient. Older patients reported lower pain scores and required smaller oxycodone concentrations for satisfactory analgesia. CYP2D6, CYP3A5 or CYP3A4 genotypes did not significantly affect the oxycodone concentrations, but CYP2D6 genotype significantly affected the formation of the metabolites oxymorphone and noroxymorphone. CYP3A4 and CYP3A5 genotypes did not affect the metabolite formation.

**Conclusions:** Our results indicate that the more pain the patient experiences postoperatively the greater her minimum plasma oxycodone concentration must be to achieve satisfactory analgesia. Type of surgery and age significantly affect postoperative pain intensity.

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## Sport participation and physical activity level in relation to musculoskeletal pain in a population-based sample of adolescents: The Young-HUNT Study



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Aims: Studies have shown conflicting results regarding associations between physical activity (PA) and musculoskeletal pain among adolescents, and few have evaluated the impact of sport participation. Therefore, the aims of this study were to examine the associations between sport participation and persistent weekly pain by body region in a population-based sample of adolescents.

Methods: In this cross-sectional study, data from the adolescent part of the Nord-Trøndelag Health Study (Young-HUNT3) were used. Participants were asked how often during the last 3 months they had experienced pain in the neck-and-shoulders (NSP), low back (LBP) or lower extremities (LEP). The impact of sport participation and PA level on pain was evaluated using logistic regression analyses, stratified by gender, and adjusted for age, socioeconomic status and psychological distress.

Results: In total, 3765 boys and 3831 girls were included, mean age 15.8 years (SD 1.7). NSP was most prevalent (17%). Adolescents who participated in endurance sports had lower odds of NSP and LBP compared to non-participants. Participation in technical sports was associated with increased odds of LBP, and participation in team sports with increased odds of LEP, vs. no participation in the respective sports. Participation in strength sports and risk sports, vs. no participation, was related to higher levels of pain in all regions. Compared to a low PA level, a moderate PA level reduced the odds of NSP and LBP, whereas a high PA level increased the odds of LEP.

**Conclusion:** This study identified sports potentially protective, as well as sports associated with higher odds of NSP, LBP and LEP in a large population-based sample, and has increased the understanding of participation in sports as potential determinants of musculoskeletal pain among adolescents. Our findings highlight that types of sport adolescents participate in should be considered by healthcare professionals when evaluating their musculoskeletal pain.

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## "Tears are also included" - women's experience of treatment for painful endometriosis at a pain clinic



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Aims: To explore how women perceive and are affected by treatment for painful endometriosis.

Method: Qualitative methodology with emergent design was used. Sixteen semi-structured interviews (including 3 follow-ups) with 13 women (age 20-47) treated at a pain clinic, were analysed with Grounded Theory.

Results: A preliminary model describes how women experience treatment for painful endometriosis and its consequences in one core category and three categories. The core category; Surviving painful endometriosis, described the women's promoting strategies like Knowledge, Adaption and Planning, and inhibiting reactions as Anxiety and Resignation. The three interacting categories; Woman with painful endometriosis, included experiences of "The self" and "The body". "The environment/significant others" described the environments' support. Missed opportunities were described as a lack of participation in important life areas; "Social life", "Career" and "Descendants". "New possibilities" were experienced when pain disappeared or could be controlled. Dependent on health care included the experiences of "Treatments" from helpful to harmful and "Encounters with health care" from empowering to humiliating.

**Conclusions:** The suffering of women when exposed to painful endometriosis can lead to missed opportunities in several important areas of life. Hormonal and symptomatic treatments, as well as positive encounters of health care are important for the women's possibility to develop working surviving strategies.

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## Predictors of long-term opioid use among chronic nonmalignant pain patients: A register-based national open cohort study



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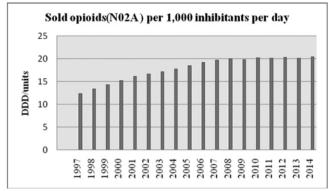
**Aims:** (1) To determine the distribution and determinants of opioid use among chronic nonmalignant pain (CNP) patients. (2) To identify the patient, treatment and socioeconomic characteristics as determinants for potential risk groups.

We hypothesized that CNP patient who use opioids for more than 1 year would differ in demographics and comorbidity from other patients who use opioids for less than 6 months.

**Methods:** National registers were used to include patients beginning opioid therapy in the period 01/01/2000–31/12/2014 (incl.). The cohort consists of adults aged 16 years or older who redeemed at least one prescription for an opioid product and residing in Denmark, analysing only patients who survived for at least two years. Follow-up minimum one year after the last redeemed opioid prescription or to 31/12/2015. Participants are included at first redeemed prescription for an opioid product using the ATC codes N02AA01–N02AX06. Patients were then classified as either opioid use for more than 1 year (group A), as opioid use for more than 6 months but less than 1 year (group B) and opioid use equal to or less than 6 months (group C).

**Results:** The quantity of sold opioids has been increasing during 1997–2008, with a fairly stable but high level since. It is expected that we will be able to determine patterns and the distribution of opioid use among CNP patients in Denmark. Consequently, describing potential risk groups of opioid use based on patient, treatment, comorbidity, socioeconomic and demographic characteristics. Data analysis is ongoing.

**Conclusions:** It is expected that this study will serve as a significant supplement of existing knowledge in the area of opioid consumption among CNP patients in Denmark. In a future perspective of prevention and health promotion initiatives of the growing public health problem CNP, it might be beneficial to include perspectives of risk assessment of long-term opioid use.



http://medstat.dk/ statistics for annual sales of medicines in Denmark 1996-2014.

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# Coupled cell networks of astrocytes and chondrocytes are target cells of inflammation



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**Aims:** Systemic low-grade inflammation can be initiated *in vivo* after traumatic injury or in chronic diseases as neurodegenerative, metabolic and autoimmune diseases. Coupled cell networks are target cells leading to the spread of inflammation and changes in biochemical cellular parameters. Do astrocytes and chondrocytes behave in a similar way in an inflammatory reactive state with respect to Ca<sup>2+</sup> signaling, actin filaments rearrangement, receptor properties, pro-inflammatory cytokine release etc?

**Methods:** Primary cultures of astrocytes and chondrocytes, respectively, were incubated with lipopolysaccharide (LPS) (10 ng/ml, 24 h) or interleukin-1 $\beta$  (IL-1 $\beta$ ) (5 ng/ml, 24 h) to induce inflammatory reactivity. Ca<sup>2+</sup> signaling, Na<sup>+</sup>/K<sup>+</sup>-ATPase-, connexin 43 (Cx43)-, and Toll-like receptor 4 (TLR4)- expressions, actin filament organization, and IL-1 $\beta$  release were analyzed.

**Results:** Stimulation with IL-1 $\beta$  or LPS altered the Ca<sup>2+</sup> signaling from single peaks to oscillating waves and increased the expression of Cx43 and TLR4, and decreased expression of Na<sup>+</sup>/K<sup>+</sup>-ATPase. A disruption of the actin filaments with more pronounced ringformed structures was found in inflammatory induced astrocytes and chondrocytes which in turn affects Ca<sup>2+</sup> oscillations. Additionally a release of active matrix metallopeptidase-13 was found in media from IL-1 $\beta$  stimulated chondrocytes.

**Conclusions:** Our data show that cellular mechanisms of healthy chondrocytes as well as inflamed, resemble the coupled cell networks of astrocytes. Chronic, low-grade inflammation can influence coupled cell networks in one or several organs, leading to co-morbidity. It is crucial that inflammatory affected cells in various