

## Summary and conclusions

SBU has evaluated the efficacy and risks of adverse events of commonly used pharmaceuticals for osteoarthritis, painful diabetic neuropathy and pain from vertebral compression fractures in older persons<sup>1</sup>. We also have evaluated the risk in older persons for acute renal failure and gastrointestinal bleeding and ulcers with NSAIDs and opioids and the risk of fall. In addition, we have evaluated experiences of care for older persons with pain. Finally, we have identified health-economic and ethical aspects and conducted a practice survey regarding drug prescription patterns in this area.

### Conclusions

- ▶ **Pharmaceuticals for common and long-term pain conditions in older persons<sup>1</sup> have a very small efficacy on group level compared with placebo. NSAID and opioids can also cause rare but serious adverse events. However, some individuals may benefit from the treatment, which is currently offered to many older persons.**
- ▶ **In studies with qualitative methods, older persons<sup>1</sup> with pain have experienced that they are overlooked in the consultation with health care professionals because of their age. They have felt that they are being belittled and not taken seriously. It may therefore be justified to investigate, problematise and, if necessary, improve the attitudes of health care personnel towards pain in the older persons.**
- ▶ **In studies with qualitative methodology, both personnel in health care and older persons<sup>1</sup> with pain have experienced that health care professionals have insufficient knowledge**

**about pain and pain management. Older persons have also experienced communication deficiencies in the consultation with health care staff.** This justifies examining the state of knowledge of health care professionals about pain and pain treatment of older persons and considering whether this knowledge needs to be improved.

- ▶ **There is a need of studies of high quality on pain-relieving drugs for older persons with multiple co-morbidities.** To date, this group has most often been excluded from such studies.

### Background and aim

Several common pain drugs may not be suitable for the treatment of older persons (65 years and older) due to an increased risk of adverse events, which in some cases may be serious. In the light of this problem, long-term pain conditions are the focus of this evaluation. In addition, several problems and shortcomings have been identified in the care of pain in older persons.

The purpose of this report has been to evaluate the efficacy and risk of common adverse events of drugs in common and long-term pain conditions in older persons, the risk of rare but potentially serious adverse events of these drugs, and experiences in the care of pain in older persons, both in patients and health care professionals. The aim has also been to highlight the health-economic and ethical aspects of the area and to include a practice survey of the prescription patterns in the field.

### Important definitions

In the case of common pain conditions, this assessment includes the efficacy and risk of adverse events in older persons with osteoarthritis, diabetic neuropathy and vertebral compression fractures. Regarding the risk of rare but potentially serious adverse events,

<sup>1</sup> For a description of the age composition of the patient populations in included studies and the handling of assessing the certainty of the scientific basis, see "Main findings".

the evaluation is confined to NSAIDs and the risk of acute renal and gastrointestinal perforations, bleeding or ulcer (PUB) in older persons, and to opioids and the risk of falls in older persons. These pain conditions and adverse events were chosen based on the pain mechanism that causes the condition and the prevalence of the conditions and the adverse events.

## Method

Systematic literature reviews were carried out in accordance with SBU's hand book (as of January 2020), for quantitative and qualitative questions.

Ethical, social and societal aspects were highlighted through discussions in the project group, partly based on several questions taken from SBU's guidelines for assessment of ethical issues in health care.

In order to highlight health-economic aspects, data from The Dental and Pharmaceutical Benefits Agency, TLV's price and decision database, Swedish Association of Local Authorities and Regions' KPP database, the Swedish National Board of Health and Welfare's weight lists for NordDRG and two surveys from the National Board of Health and Welfare on the morbidity related to pharmaceuticals in older persons were used. In addition, a literature search was conducted for studies evaluating the impact of drug therapy on resource use in the pertinent patient populations.

The Stockholm County Health Database VAL was used for the practice survey. The study used de-iden-

tified data on diagnoses and prescribed drugs that had been dispensed from pharmacies.

## Main findings

### Efficacy and risk of adverse events in drug treatment of common pain conditions of older persons

The results for osteoarthritis pain are based on five systematic reviews, which in turn are based on 165 randomized, double-blind and controlled (primarily placebo-controlled) studies. The results for painful diabetic neuropathy are based on 35 randomized, double-blind and controlled (primarily placebo-controlled) studies. The average age in the included studies was around 60 years. The populations in the included studies were only partly equivalent to the populations solicited in our questions, which generated a deduction for transferability when assessing the certainty of the scientific evidence. The follow-up period was in most cases between 4 and 12 weeks. There were no studies evaluating commonly used pain-relieving drugs for vertebral compression fractures.

Drug treatment of the evaluated pain conditions has a very small efficacy on group-level compared with placebo. The risk increase for common adverse events with these drugs is in most cases moderate or high. Paracetamol has a frequency of adverse event that is comparable with placebo (elevated levels of liver enzymes in blood plasma excluded). The risk increase for treatment discontinuations due to adverse reactions with oral NSAID appears to be small. However, most

**Table 1** Efficacy and risk of common adverse events in drug treatment of common pain conditions in older persons.

	Efficacy	Risk of adverse events
<b>Osteoarthritis pain (scale 0-100)</b>		
Paracetamol	⊕⊕⊕○ Moderate certainty for a <i>very small</i> efficacy on pain, 3 counts better than placebo	⊕⊕⊕○ Moderate certainty for paracetamol having a frequency of adverse reactions <i>comparable</i> to placebo, risk ratio 1.01 (95% CI, 0.92 to 1.11)
Oral NSAID	⊕⊕○○ Low certainty for a <i>very small</i> efficacy on pain, 7 counts better than placebo	⊕⊕○○ Low certainty for a <i>small</i> risk increase for treatment discontinuation due to adverse events, risk ratio 1.16 (95% CI, 1.02 to 1.32)
Opioids (excluding Tramadol)	⊕⊕⊕○ Moderate certainty for a <i>very small</i> efficacy on pain, 6 counts better than placebo	⊕⊕⊕○ Moderate certainty for a <i>high</i> risk increase for treatment discontinuation due to adverse events, risk ratio 3.76 (95% CI, 2.93 to 4.82)

The table continues on the next page

**Table 1** continues

	<b>Efficacy</b>	<b>Risk of adverse events</b>
Tramadol	⊕⊕○○ Low certainty for a <i>very small</i> efficacy on pain, 4 counts better than placebo	⊕⊕○○ Low certainty for a <i>high</i> risk increase for treatment discontinuation due to adverse events, risk ratio 2.64 (95% CI, 2.17 to 3.20)
<b>Painful diabetic neuropathy (scale 0-100)</b>		
Pregabalin, duloxetine and oxycodone respectively	⊕⊕⊕○ Moderate certainty for a <i>very small</i> efficacy on pain, 5–9 counts better than placebo	A <i>moderate</i> risk increase for treatment discontinuation due to adverse events, absolute risk increase with approximately 12 weeks of treatment: ⊕⊕⊕○ Moderate certainty: Pregabalin: 7% (95% CI, 4% to 12%) Duloxetine 7% (95% CI, 3% to 10%) ⊕⊕○○ Low certainty: Oxycodone 8% (95% CI, 0 to 15%) compared to placebo.
<b>Pain from vertebrae compression</b>		
Paracetamol, NSAID and opioids	Studies are missing	Studies are missing

CI = confidence interval; NSAID = Non-steroidal Anti-Inflammatory Drugs

included studies did not present this outcome measure, which contributed to the low certainty of the magnitude of this risk increase, see Table 1. In the case of topical NSAID, topical diclofenac was shown to have a very small efficacy on knee osteoarthritis compared to vehicle (moderate certainty). The scientific basis for the efficacy of topical ketoprofen in osteoarthritis of the knee has very low certainty.

The results for NSAID and risk of acute renal failure are based on four non-randomised studies with a total of 140 000 participants. The average age of participants in the studies was between 74 and 78. The results for NSAID and the risk of gastrointestinal PUB are based on analysis of individual patient data for participants over 60 years of age from a systematic review that included 754 randomised and controlled studies. In the case of opioids and the risk of cases, the results are based on a meta-analysis (from a systematic survey) of eight non-randomised studies with 267 000 participants. The average age of participants in the studies was between 74 and 88. The populations in the included studies were considered to correspond to the populations that were specified in our research questions.

In all cases except one, there was a moderate risk increase in older persons for rare but potentially serious

adverse events of NSAID preparations and opioids with regard to the risk of acute renal influence, gastrointestinal PUB and falls, respectively. See Table 2.

### Experiences in the care of pain in older persons

The results of this part of the assessment are based on 20 studies with qualitative methodology that explored experiences among both older persons with pain and health care professionals. The older persons in the included studies had an average age of between 65 and 88 years and suffered from various types of long-term pain, mainly osteoarthritis and other musculoskeletal pain. The populations of the included studies were considered to correspond to the populations that were specified in our research questions.

The studies were descriptive and many used qualitative content analysis. Most of the studies investigated the experiences of older persons living at home, but there were also studies from residential care facilities and home-based care. The studies also included several different categories of staff, such as home care staff, nurses, occupational therapists and doctors from primary care. Four of the studies were conducted in Sweden. The results of the studies were similar regardless of the country in which the studies were conducted.

**Table 2** Risk of rare but potentially serious adverse reactions to NSAID preparations and opioids in older persons.

Risk of adverse events in older persons	Comparison	Results and certainty in scientific data
Hospitalization due to acute kidney failure	NSAID use compared to no NSAID use	⊕⊕○○ Low certainty for a moderate risk increase, odds ratio 1.59
Gastrointestinal PUB	tNSAID compared to placebo	⊕⊕⊕○ Moderate certainty for a moderate risk increase, annual absolute risk increase 0.87% (NNH=115)
Gastrointestinal PUB	Coxibs compared to placebo	⊕⊕⊕⊕ High certainty for low risk increase (annual absolute risk increase 0.37% (NNH=270)
Case	Opioid use compared to no opioid use	⊕⊕○○ Low certainty for a moderate risk increase, odds ratio 1.60

**Coxiber** = selective cox-2 inhibitors, e.g. celecoxib; **NNH** = numbers needed to harm; **PUB** = Perforations, ulcer or bleeding; **tNSAID** = traditional NSAID, e.g. ibuprofen and diclofenac

Experiences of older persons with pain and their encounters with the health care professionals are presented in Table 3.

**Table 3** Summary of assessment of the certainty of level 3 descriptive themes for metasynthesis about experiences of encounters with care.

Theme level 3	Number of Studies (subject-based participants)	Grade-CERQual certainty	Reasons for deductions
Older persons with pain felt overlooked in their meeting with health care professionals	12 (419)	High ⊕⊕⊕⊕	–
Health care professionals' lack of knowledge about pain and pain treatment led to frustration in older persons, which affected the care meeting	8 (318)	High ⊕⊕⊕⊕	–
Lack of communication in the care meeting led to dissatisfaction among older persons with pain	9 (292)	High ⊕⊕⊕⊕	–

The experience of older persons with pain relieving medication is presented in Table 4.

**Table 4** Summary of the assessment of the certainty of level 3 descriptive themes for metasynthesis on experiences of pain relieving drug treatment.

Theme level 3	Number of Studies (participants who support the theme)	Grade-CERQual scientific evidence	Reasons for deductions
Older persons with pain made decisions about taking drugs based on information about the drug and their own experience of the drug	9 (330)	Moderate ⊕⊕⊕○	Insufficient data: –1

The experiences of the health care staff in the meeting with older persons with pain are presented in Table 5.

**Table 5** Summary of the assessment of the certainty of level 3 descriptive themes for the experiences of nursing staff in caring for older persons with pain.

Theme level 3	Number of Studies (participants who support the theme)	Grade-CERQual scientific evidence	Reasons for deductions
The experience of the health care staff was that older persons with long-term pain were a difficult group to manage	6 (193)	High ⊕⊕⊕⊕	–
The experience of the health care staff was that there were obstacles to optimal treatment both in health care and among older persons with pain	4 (131)	High ⊕⊕⊕⊕	–
The experience of the health care staff was that the choice of treatment for pain in the older persons was a balance between risk and benefit	4 (88)	Moderate ⊕⊕⊕○	Insufficient data: –1

### Health economy

Health-economic aspects in the context of this evaluation include:

- The majority of pertinent pain relieving drugs have a very low price, which means that they can be considered to be highly cost-effective despite a very small efficacy with regards to pain, function and quality of life.
- It is unclear (studies are missing) whether treatment with pain-relieving drugs result in a reduced consumption of care or a reduced need for home care.
- Rare but serious adverse events of NSAID and opioids in older persons can result in significant care costs, in addition to suffering from the adverse event itself.

### Ethical, social and societal aspects

A main result of this assessment is that drugs for relieving long-term pain have a very small efficacy compared to placebo on group-level and that they increase the risk of adverse events, which in some cases may be serious. It is unethical to treat patients with methods where the risks exceed the benefits. Treatment of pain in older persons therefore requires a thorough information to the patient and a careful follow-up of efficacy versus adverse events or risk of adverse events in each patient.

The results of studies with qualitative methodology included in this assessment show that older persons with pain feel that they are overlooked because they

are old, that they are belittled and not taken seriously. Treating patients with a lack of respect because they are old is clearly contrary to the principle of human dignity in the Swedish parliamentary ethical platform and the Swedish Health Care Act.

In addition, studies with qualitative methodology show that older persons with pain describe that the health care personnel had insufficient knowledge about pain and pain treatment, that communication in the health care consultation was inadequate and that there was a lack of time that had a negative impact on the health care consultation. These aspects pose an ethical problem.

### Practice survey

The practice survey showed that a large proportion of older persons with the evaluated pain conditions are offered treatment with commonly used pain relief drugs. The study does not answer the question for how long, in which dose, etcetera older persons use these drugs. However, the fact that a large proportion of older persons with common pain conditions are prescribed these drugs underlines the importance of continuous monitoring and review of the treatment administered to each individual. In other respects, the prescription patterns seem to be largely in line with current treatment recommendations.

### Summary discussion and impact assessment

One limitation of this assessment is the relatively few associated pain conditions (osteoarthritis pain, painful diabetic neuropathy and pain from vertebral compression fractures) and severe adverse events (NSAID and risk of acute renal failure and gastroin-

testinal PUB, opioids and risk of falling). However, there are several systematic reviews in the literature that evaluate drug treatment in other common pain conditions and risks of other serious adverse events in older persons. The results of these reviews are very similar to the results of our evaluation.

The results in this evaluation are presented at group level. However, drug treatment for long-term pain can be valuable on an individual level. But the small efficacy at group level and the risks of adverse events highlight the importance of careful, continuous and individually designed follow-up when pain relieving drugs are prescribed for long term pain. The follow-up aims to review the benefits and risks of treatment to the individual and to assess whether the treatment needs to be changed, adjusted or terminated. Persistent drug treatment without sufficient benefit or associated with unacceptable adverse events is not only a problem in itself, but also contributes to unnecessary polypharmacy for older persons that in turn can increase the risk of drug interactions and the individual's difficulty in managing and getting an overview of their entire drug treatment.

Other methods of treatment against long-term pain conditions, such as physiotherapy and psychological treatments, may be worth considering. Several systematic reviews in the literature evaluate such methods.

A methodological limitation in the included studies in this evaluation concerns the difficulty of quantitatively estimating the efficacy on the subjective experience of pain. In conclusion, this means challenges in assessing the exact efficacy of analgesic drugs. We have therefore taken some caution in this assessment and are only talking about the order of magnitude of the efficacy of these drugs.

Our results regarding older persons experiences of uninterested health care professionals are consistent with the results of previous SBU reports, which concerned other groups with chronic conditions, such as older persons with arm fracture or women with endometriosis.

It seems justified to investigate and problematise the attitudes of health care personnel to pain in older persons. It is important that health care professionals understand how older persons with pain are affected by their pain and their expectations for recovery. It is also important that care for older persons with pain is person-centred and is designed in consultation with the patient based on their needs and resources.

The results also show that both older persons with pain and the health care staff have insufficient knowledge. Both groups also believe that the time and the resources are too scarce to adequately treat older persons with pain. This justifies examining the state of knowledge of health care professionals about pain and pain treatment of the older persons and considering whether this knowledge needs to be improved.

### **Knowledge gaps and research needs**

There is a lack of studies investigating the risk and benefit of common pain relief drugs for pain in vertebral compression fractures. There is also a lack of randomised studies evaluating the efficacy and adverse events of analgesic drugs in the oldest and in patients with multiple comorbidities. There is also a lack of studies with a long follow-up period and larger studies evaluating combination therapy of various pain-relieving drugs.

No studies with qualitative methodology were found that primarily aimed at examining how older persons with pain experience the consultation with health care professionals. Included studies with qualitative methodology in this evaluation had broader purposes than simply investigating experiences of this consultation. There is also a lack of studies focusing on how health care consultations should be designed to enable older persons to perceive it as a good consultation. There is also a lack of qualitative studies that include only the oldest individuals, for example 80 years old and older.

### **Appendices ([www.sbu.se/315e](http://www.sbu.se/315e))**

- Search strategies
- Table of excluded studies
- Table of included studies

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