

Title: NSAID use, gastrointestinal complications, and burden of disease in osteoarthritis: Nordic registry study with emphasis on patients below 60 years

Authors list: Tore K Kvien^{1,2}, Johan L Hansen^{3,4}, Robert Böttger⁵, Rita Freitas⁵, Jan Jastorff⁵, Elena Mascia⁵, Manfred Gross⁶

1. Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway
2. Institute of Clinical Medicine, University of Oslo, Oslo, Norway
3. Quantify Research, Stockholm, Sweden
4. Institute of Health and Society, University of Oslo, Oslo, Norway
5. Grünenthal GmbH, Aachen, Germany
6. Center for Endoscopy-Gastroenterology, Starnberg, Germany

Correspondence details:

Corresponding author: Jan Jastorff

Email address: jan.jastorff@grunenthal.com

Appendix tables

Supplementary Table 1. Overview of data sources

Type of register	Norway	Sweden	Finland	Variables
Patient registers	Norwegian Patient Register, NDH (2008)	Swedish National Patient Register, NBHW (1987/2001)	Care register for health care, THL (1969/1994)	Diagnosis codes (ICD-9/10), dates and types of visit
Prescription registers	Norwegian Prescription Database, NIPH (2004)	Swedish Prescribed Drug Registry, NBHW (2005)	The Reimbursement Register, Kela (1995)	Dispatch dates, type of medication, strengths and dosage info
Information on work absence	FD-Trygd, Statistics Norway (1993/1998)	MIDAS (2005), The Swedish Social Insurance Agency	The sickness insurance Register, KELA (2004) and Finnish Center for Pensions (ETK)	Dates, extent of sick-leave, diagnosis rational, early retirement
Population registers	The Norwegian population register, Statistics Norway (1975)	The National Population Register, Statistics Sweden (1968)	The Population Register, Statistics Finland (1970)	Age, Sex (for id of matched comparison cohort)

Supplementary Table 2. Diagnoses used to identify patients with osteoarthritis

Diagnoses	ICD-10 codes
Polyosteoarthritis	M15
Osteoarthritis of hip	M16
Osteoarthritis of knee	M17
Osteoarthritis of first carpometacarpal joint	M18
Other and unspecified osteoarthritis	M19

Supplementary Table 3. ICD-10 codes for the Elixhauser comorbidity index

AIDS/HIV	B20, B21, B22, B24	1
Alcohol abuse	E52, F10, T51, G621, I426, K292, K700, K703, K709, Z502, Z714, Z721	1
Blood loss anaemia	D500	1
Cardiac arrhythmias	I47, I48, I49, I441, I442, I443, I456, I459, R000, R001, R008, T821, Z450, Z950	1
Chronic pulmonary disease	J40–47, J60–67, I278, I279, J684, J701, J703	1
Coagulopathy	D65, D66, D67, D68, D691, D693, D694, D695, D696	1
Congestive heart failure	I43, I50, I099, I110, I130, I132, I255, I420, I425, I426, I427, I428, I429, P290	1
Deficiency anaemia	D51, D52, D53, D508, D509	1
Depression	F32, F33, F204, F313, F314, F315, F341, F412, F432	1
Diabetes, complicated	E102, E103, E104, E105, E106, E107, E108, E112, E113, E114, E115, E116, E117, E118, E122, E123, E124, E125, E126, E127, E128, E132, E133, E134, E135, E136, E137, E138, E142, E143, E144, E145, E146, E147, E148	1
Diabetes, uncomplicated	E100, E101, E109, E110, E111, E119, E120, E121, E129, E130, E131, E139, E140, E141, E149	1
Drug abuse	F11, F12, F13, F14, F15, F16, F18, F19, Z715, Z722	1
Fluid and electrolyte disorders	E86, E87, E222	1
Hypertension, complicated	I11, I12, I13, I15	1

Hypertension, uncomplicated	I10	1
Hypothyroidism	E00, E01, E02, E03, E890	1
Liver disease	B18, I85, K70, K72, K73, K74, I864, I982, K711, K713, K714, K715, K717, K760, K762, K763, K764, K765, K766, K767, K768, K769, Z944	1
Lymphoma	C81, C82, C83, C84, C85, C88, C96, C900, C902	1
Metastatic cancer	C77, C78, C79, C80	1
Obesity	E66	1
Other neurological disorders	G10, G11, G12, G13, G20, G21, G22, G32, G35, G36, G37, G40, G41, R56, G254, G255, G312, G318, G319, G931, G934, R470	1
Paralysis	G81, G82, G041, G114, G801, G802, G830, G831, G832, G833, G834, G839	1
Peptic ulcer disease excluding bleeding	K257, K259, K267, K269, K277, K279, K287, K289	1
Peripheral vascular disorders	I70, I71, I731, I738, I739, I771, I790, I792, K551, K558, K559, Z958, Z959	1
Psychoses	F20, F22, F23, F24, F25, F28, F29, F302, F312, F315	1
Pulmonary circulation disorders	I26, I27, I280, I288, I289	1
Renal failure	N18, N19, I120, I131, N250, Z490, Z491, Z492, Z940, Z992	1

Rheumatoid arthritis/collagen vascular diseases	M05, M06, M08, M30, M32, M33, M34, M35, M45, L940, L941, L943, M120, M123, M310, M311, M312, M313, M461, M468, M469	1
Solid tumour without metastasis	C00–26, C30–34, C37–41, C43, C45–58, C60–76, C97	1
Valvular disease	I05, I06, I07, I08, I34, I35, I36, I37, I38, I39, A520, I091, I098, Q230, Q231, Q232, Q233, Z952, Z953, Z954	1
Weight loss	E40–46, R64, R634	1

Supplementary Table 4. Diagnosis codes used to define GI complications

Code	Description
I85.0	Oesophageal varices with bleeding
K22.6	Gastro-oesophageal laceration-haemorrhage syndrome (Mallory–Weiss syndrome)
K22.8	Other specified diseases of oesophagus: Haemorrhage of oesophagus NOS
K25.0	Gastric ulcer – acute with haemorrhage
K25.2	Gastric ulcer – acute with both haemorrhage and perforation
K25.4	Gastric ulcer – chronic or unspecified with haemorrhage
K25.6	Gastric ulcer – chronic or unspecified with both haemorrhage and perforation
K26.0	Duodenal ulcer – acute with haemorrhage
K26.2	Duodenal ulcer – acute with both haemorrhage and perforation
K26.4	Duodenal ulcer – chronic or unspecified with haemorrhage
K26.6	Duodenal ulcer – chronic or unspecified with both haemorrhage and perforation
K27.0	Peptic ulcer, unspecified – acute with haemorrhage
K27.2	Peptic ulcer, unspecified – acute with both haemorrhage and perforation
K27.4	Peptic ulcer, unspecified – chronic or unspecified with haemorrhage
K27.6	Peptic ulcer, unspecified – chronic or unspecified with both haemorrhage and perforation
K28.0	Gastrojejunal ulcer – acute with haemorrhage
K28.2	Gastrojejunal ulcer – acute with both haemorrhage and perforation

K28.4	Gastrojejunal ulcer – chronic or unspecified with haemorrhage
K28.6	Gastrojejunal ulcer – chronic or unspecified with both haemorrhage and perforation
K29.0	Acute haemorrhagic gastritis
K51	Ulcerative colitis
K57	Diverticular disease of intestine
K62.5	Gastrointestinal haemorrhage, unspecified
K92.0	Haematemesis
K92.1	Melaena
K92.2	Gastrointestinal haemorrhage, unspecified, unless present with a secondary or subsidiary diagnosis of lower gastrointestinal disease (C17.1–C21, K50–K52, K55–K57 or K60–K63)

Supplementary Table 5: Patient characteristics (Elixhauser comorbidity), by country and cohort

	Norway		Sweden		Finland	
	OA cohort	Matched comparison cohort	OA cohort	Matched comparison cohort	OA cohort	Matched comparison cohort
	N (%)		N (%)		N (%)	
Number of individuals	189,553	189,553	341,548	341,548	218,253	218,253
Elixhauser: AIDS/HIV	105 (<0.1%)	121 (<0.1%)	92 (<0.1%)	93 (<0.1%)	40 (<0.1%)	52 (<0.1%)
Elixhauser: Alcohol abuse	1,385 (0.7%)	1,391 (0.7%)	4,224 (1.2%)	3,945 (1.2%)	3,143 (1.4%)	2,913 (1.3%)
Elixhauser: Blood loss anaemia	535 (0.3%)	519 (0.3%)	335 (<0.1%)	257 (<0.1%)	442 (0.2%)	305 (0.1%)
Elixhauser: Cardiac arrhythmias	14,017 (7.4%)	11,826 (6.2%)	23,487 (6.9%)	19,211 (5.6%)	16,912 (7.7%)	13,139 (6.0%)
Elixhauser: Chronic pulmonary disease	10,112 (5.3%)	8,524 (4.5%)	14,096 (4.1%)	10,485 (3.1%)	9,746 (4.5%)	6,432 (2.9%)
Elixhauser: Coagulopathy	878 (0.5%)	695 (0.4%)	1,656 (0.5%)	1,153 (0.3%)	582 (0.3%)	329 (0.2%)

	Norway		Sweden		Finland	
Elixhauser: Congestive heart failure	3,366 (1.8%)	3,630 (1.9%)	8,548 (2.5%)	8,283 (2.4%)	5,288 (2.4%)	4,731 (2.2%)
Elixhauser: Depression	6,531 (3.4%)	5,259 (2.8%)	9,511 (2.8%)	7,486 (2.2%)	6,558 (3.0%)	4,200 (1.9%)
Elixhauser: Diabetes, complicated	3,923 (2.1%)	3,761 (2.0%)	7,366 (2.2%)	7,494 (2.2%)	3,683 (1.7%)	2,982 (1.4%)
Elixhauser: Diabetes, uncomplicated	11,276 (5.9%)	9,877 (5.2%)	16,955 (5.0%)	14,088 (4.1%)	8,476 (3.9%)	6,025 (2.8%)
Elixhauser: Drug abuse	703 (0.4%)	555 (0.3%)	1,684 (0.5%)	1,100 (0.3%)	490 (0.2%)	300 (0.1%)
Elixhauser: Fluid and electrolyte disorders	3,497 (1.8%)	4,040 (2.1%)	3,286 (1.0%)	3,396 (1.0%)	1,683 (0.8%)	1,470 (0.7%)
Elixhauser: Hypertension, complicated	2,137 (1.1%)	1,603 (0.8%)	1,936 (0.6%)	1,617 (0.5%)	1,793 (0.8%)	1,221 (0.6%)
Elixhauser: Hypertension, uncomplicated	20,743 (10.9%)	16,049 (8.5%)	56,734 (16.6%)	40,339 (11.8%)	26,145 (12.0%)	16,904 (7.7%)
Elixhauser: Hypothyroidism	2,942 (1.6%)	2,051 (1.1%)	7,748 (2.3%)	5,101 (1.5%)	3,408 (1.6%)	2,038 (0.9%)

	Norway		Sweden		Finland	
Elixhauser: Liver disease	1,352 (0.7%)	1,106 (0.6%)	2,794 (0.8%)	2,247 (0.7%)	1,522 (0.7%)	1,129 (0.5%)
Elixhauser: Lymphoma	773 (0.4%)	828 (0.4%)	1,352 (0.4%)	324 (<0.1%)	913 (0.4%)	171 (<0.1%)
Elixhauser: Metastatic cancer	1,050 (0.6%)	1,731 (0.9%)	1,979 (0.6%)	608 (0.2%)	311 (0.1%)	117 (<0.1%)
Elixhauser: Obesity	3,720 (2.0%)	1,380 (0.7%)	7,113 (2.1%)	2,642 (0.8%)	5,002 (2.3%)	1,446 (0.7%)
Elixhauser: Other neurological disorders	3,241 (1.7%)	3,703 (2.0%)	5,542 (1.6%)	6,640 (1.9%)	4,013 (1.8%)	4,356 (2.0%)
Elixhauser: Paralysis	388 (0.2%)	310 (0.2%)	1,253 (0.4%)	1,617 (0.5%)	368 (0.2%)	259 (0.1%)
Elixhauser: Peptic ulcer disease excluding bleeding	664 (0.4%)	537 (0.3%)	1,316 (0.4%)	911 (0.3%)	556 (0.3%)	327 (0.1%)
Elixhauser: Peripheral vascular disorders	5,138 (2.7%)	4,674 (2.5%)	4,666 (1.4%)	4,953 (1.5%)	3,373 (1.5%)	3,202 (1.5%)
Elixhauser: Psychoses	529 (0.3%)	1,014 (0.5%)	1,225 (0.4%)	2,447 (0.7%)	1,447 (0.7%)	2,194 (1.0%)

	Norway		Sweden		Finland	
Elixhauser: Pulmonary circulation disorders	984 (0.5%)	985 (0.5%)	2,092 (0.6%)	1,664 (0.5%)	1,230 (0.6%)	785 (0.4%)
Elixhauser: Renal failure	3,080 (1.6%)	2,853 (1.5%)	4,024 (1.2%)	3,572 (1.0%)	1,808 (0.8%)	1,378 (0.6%)
Elixhauser: Rheumatoid arthritis/collagen vascular diseases	8,822 (4.7%)	4,595 (2.4%)	12,880 (3.8%)	6,739 (2.0%)	8,542 (3.9%)	3,748 (1.7%)
Elixhauser: Solid tumour without metastasis	9,855 (5.2%)	10,162 (5.4%)	16,618 (4.9%)	4,722 (1.4%)	10,962 (5.0%)	2,464 (1.1%)
Elixhauser: Valvular disease	6,653 (3.5%)	5,621 (3.0%)	5,903 (1.7%)	5,243 (1.5%)	4,502 (2.1%)	3,722 (1.7%)
Elixhauser: Weight loss	941 (0.5%)	1,405 (0.7%)	479 (0.1%)	523 (0.2%)	264 (0.1%)	244 (0.1%)

N, number; OA, patients with osteoarthritis