

# **Medikationsanalyse und Update Schmerz Teil 1 : Arthrose**

**Vortrag von Dr. med. Michael Überall**

**pDL-Akademie →**



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# OSTEO-ARTHROSE

Michael A. Überall

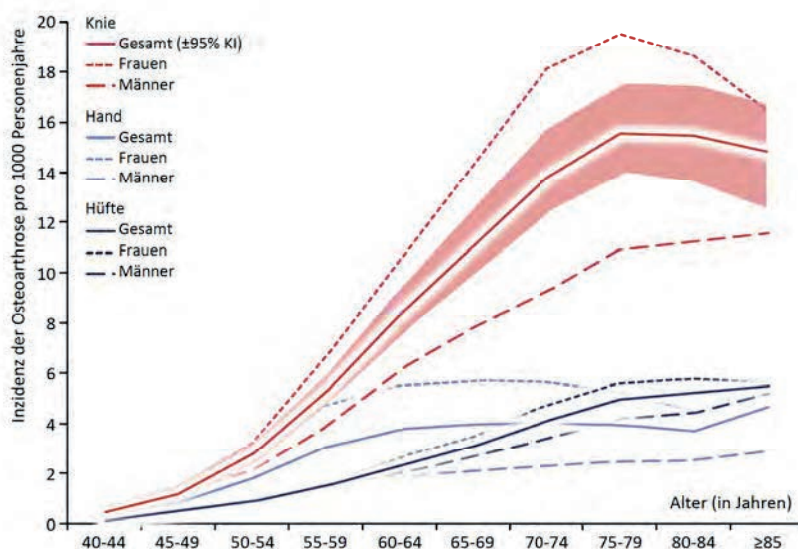
WAS SOLL / WAS KANN EINE THERAPIE MIT NSAR LEISTEN ?  
(UND WAS BESSER NICHT) ?



(UND WAS BESSER NICHT) ?

WAS SOLL / WAS KANN EINE THERAPIE MIT NSAR LEISTEN ?

## OSTEOARTHROSE - INZIDENZ



Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019; 393 (10182): 1745-1759.

Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. Eclinicalmedicine 2020; 29-30: 100587.

Steinmetz JD, Global Burden of Disease 2021 Osteoarthritis Collaborators. Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Rheumatol 2023; 5: e508-522.

## OSTEOARTHROSE - THERAPIEZIELE

### ▪ Was soll eine Schmerztherapie mit NSAR leisten?

Durch die Anwendung von NSAR sollen die Entzündungsreaktionen unterdrückt und die mit ihnen einhergehenden Beschwerden (Schmerzen, Funktionseinschränkungen, etc.) weitestgehend reduziert werden. Die Anwendung der Arzneimittel sollte einfach und nebenwirkungsfrei sein und ihr Einsatz nicht von Kontraindikationen eingeschränkt werden.

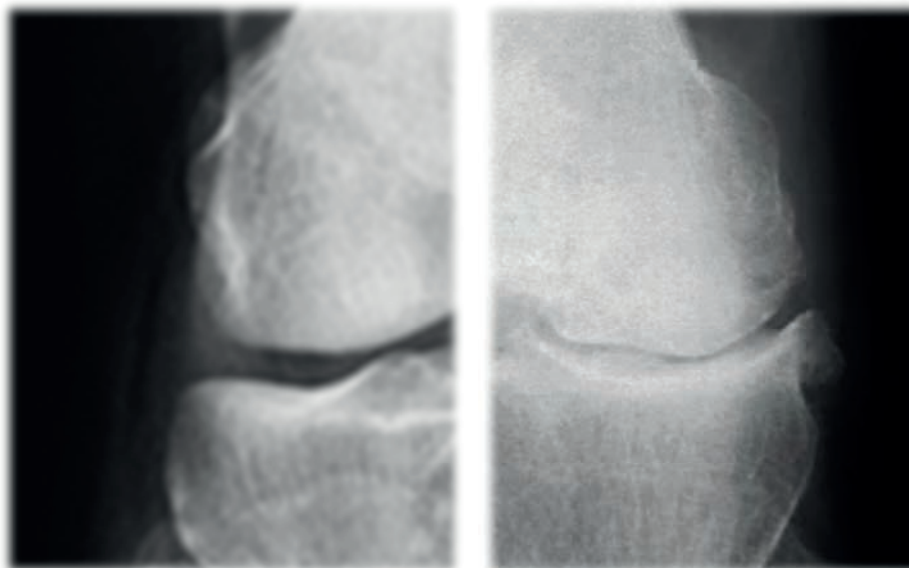
### ▪ Was kann eine Schmerztherapie mit NSAR (u.U.) leisten?

Durch die entzündungshemmende Wirkung sollen Betroffene ein weitestgehend normales Leben führen können und ggf. auch das Fortschreiten der destruktiven Umbauprozesse verzögert bzw. aufgehalten werden.

### ▪ Was sollte eine Schmerztherapie mit NSAR nicht leisten?

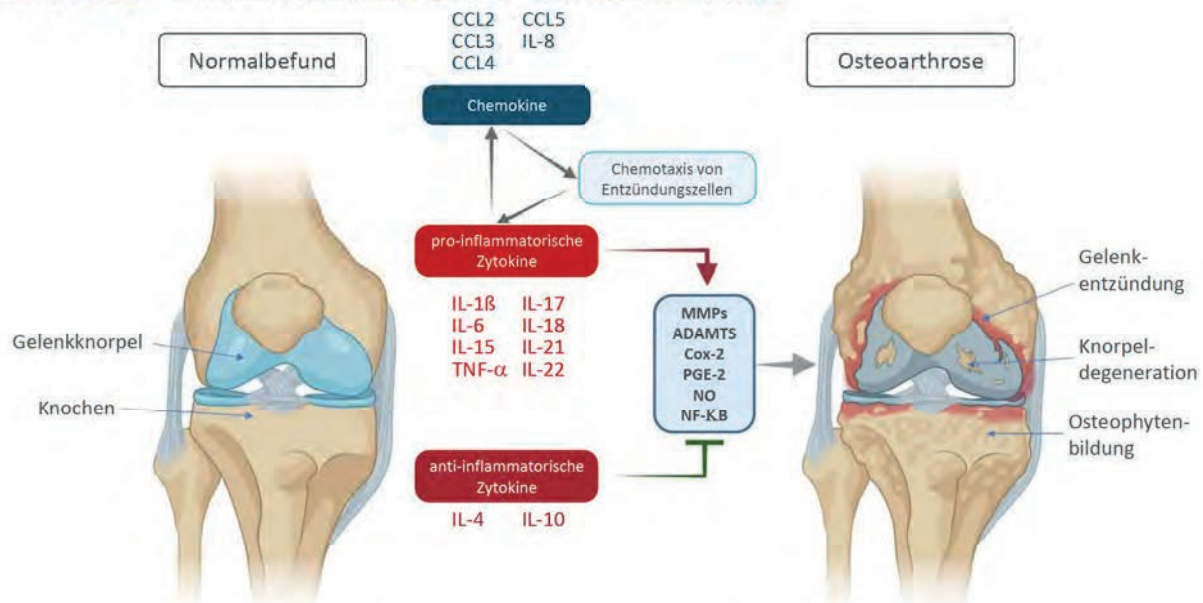
Der Einsatz der NSAR sollte keine schwerwiegenden bzw. die Wirkung der Behandlung infrage stellenden unerwünschten Arzneimittelwirkungen verursachen, nicht (bei häufig zu beobachtenden Ko-Morbiditäten und/oder Ko-Medikationen) kontraindiziert sein und nicht den Krankheitsverlauf beschleunigen.

## OSTEOARTHROSE - PATHOPHYSIOLOGIE



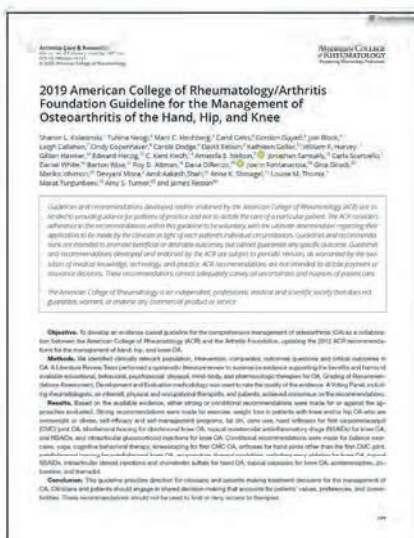


## OSTEOARTHROSE - PATHOPHYSIOLOGIE → OSTEOARTHRITIS



Molnar V, Matijevic V, Kodvanj I, Bjelica B, Jelic Z, Hudetz D, Rod E, Cukelj F, Vrdoljak T, Vidovic D, Starešinic M, Sabalic S, Dobricic B, Petrovic T, Anticevic D, Boric I, Kolir R, Zmurljak UP, Primorac D. Cytokines and chemokines involved in osteoarthritis pathogenesis. Int J Mol Sci 2021; 22, 9208. <https://doi.org/10.3390/ijms22179208>

## OSTEOARTHROSE - LEITLINIENEMPFEHLUNGEN ZUR BEHANDLUNG



Arthrose im Bereich von			Nichtmedikamentöse Maßnahmen
Hand	Knie	Hüfte	
++	++	++	Übungen
+	+	+	Balancetraining
+	++	++	Gewichtsreduktion
++	++	++	Selbstwirksamkeits- und Selbstmanagementprogramme
+	++	++	Tai Chi
+	+	+	Yoga
+	+	+	kognitive Verhaltenstherapie
+	++	++	Gehhilfen
+	+	+	tibiofemorale Knieorthese
+	+	+	patellofemorale Knieorthese
+	+	+	Kinesiotaping
++	+	+	Karpometacarpalorthese I
+	+	+	andere Handorthesen
+	+	+	orthopädisches Schuhwerk
+	+	+	keilförmige Schuheinlagen
+	+	+	Akupunktur
+	+	+	Wärmeanwendung
+	+	+	Paraffin
+	+	+	Radiofrequenzablation
+	+	+	Massage
+	+	+	Manualtherapie
+	+	+	Iontophorese
+	+	+	Schallwellentherapie
+	+	+	TENS

++ dringend empfohlen  
+ bedingt empfohlen  
keine Empfehlung  
- bedingt nicht empfohlen  
absolut nicht empfohlen



## OSTEOARTHROSE - LEITLINIENEMPFEHLUNGEN ZUR BEHANDLUNG

	Arthrose im Bereich von			Arthrose im Bereich von			Nichtmedikamentöse Maßnahmen
	Hand	Knie	Hüfte	Hand	Knie	Hüfte	
<b>Medikamentöse Maßnahmen</b>							
topische NSAR Therapie	+	++	Ø	++	++	++	Übungen
Capsaicin	o	+	Ø	Ø	+	+	Balancetraining
orale NSAR/COX-2 Therapie	++	++	++	Ø	++	++	Gewichtsreduktion
intraartikuläre Kortisoninjektion	+	++	++	++	++	++	Selbstwirksamkeits- und Selbstmanagementprogramme
ultraschallgestützte intraartikuläre Kortisoninjektion	Ø	Ø	++	Ø	++	++	Tai Chi
intraartikuläre Kortisoninjektion vs. andere Injektionen	+	+	+	Ø	+	Ø	Yoga
Paracetamol	+	+	+	+	+	+	kognitive Verhaltenstherapie
Duloxetin	+	+	+	Ø	++	++	Gehhilfen
Tramadol	+	+	+	Ø	++	Ø	tibiofemorale Knieorthese
Andere Opioidanalgetika	o	o	o	Ø	+	Ø	patellofemorale Knieorthese
Colchizin	o	o	o	+	+	Ø	Kinesiotaping
Fischöl	o	o	o	++	Ø	Ø	Karpometacarpalarthrose I
Vitamin D	o	o	o	+	Ø	Ø	andere Handorthesen
Bisphosphonate	o	o	o	Ø	o	Ø	orthopädisches Schuhwerk
Glukosamin	o	o	o	Ø	o	o	keilförmige Schuheinlagen
Chondroitinsulfat	+	o	o	+	+	+	Akupunktur
Hydroxychloroquin	o	o	o	+	+	+	Wärmeanwendung
Methotrexat	o	o	o	+	Ø	Ø	Paraffin
intraartikuläre Hyaluronsäureinjektion	o	o	o	Ø	+	Ø	Radiofrequenzablation
intraartikuläre Botulinumtoxininjektion	Ø	o	o	Ø	o	o	Massage
Proliferationstherapie	Ø	o	o	Ø	o	o	Manualtherapie
thrombozytenreiches Plasma	Ø	o	o	Ø	Ø	Ø	Iontophorese
Stammzellinjektionen	Ø	o	o	Ø	o	Ø	Schallwellentherapie
Biologica (TNF-Antagonisten, IL-1 Rezeptorantagonisten)	Ø	o	o	Ø	o	o	TENS

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Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, Callahan L, Copenhaver C, Dodge C, Felson D, Gellar K, Harvey WF, Hawker G, Herzog E, Kwoh CK, Nelson AE, Samukles J, Scanzello C, White D, Wise B, Altman RD, DiRenzo D, Fontanarosa J, Giradi G, Ishimori M, Misra D, Shah AA, Shmagel AK, Thoma LM, Turgunbaev M, Turner AS, Reston J. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis Care & Research 2020; 72: 149-162.

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intraartikuläre Kortisoninjektion	+	++	++	++	++	++	Selbstwirksamkeits- und Selbstmanagementprogramme
ultraschallgestützte intraartikuläre Kortisoninjektion	Ø	Ø	++	Ø	++	++	Tai Chi
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Chondroitinsulfat	+	o	o	+	+	+	Akupunktur
Hydroxychloroquin	o	o	o	+	+	+	Wärmeanwendung
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intraartikuläre Hyaluronsäureinjektion	o	o	o	Ø	+	Ø	Radiofrequenzablation
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Proliferationstherapie	Ø	o	o	Ø	o	o	Manualtherapie
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Biologica (TNF-Antagonisten, IL-1 Rezeptorantagonisten)	Ø	o	o	Ø	o	o	TENS

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## OSTEOARTHROSE

### THERAPIEN IM VERGLEICH

192 dbRC Studien

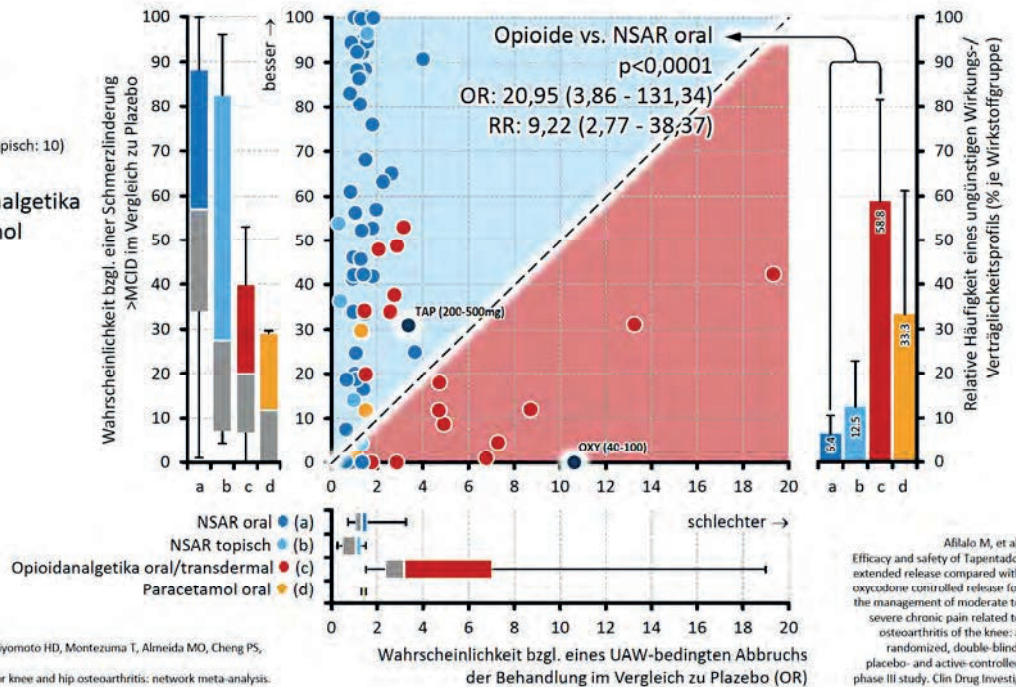
102.829 Patienten

90 verschiedene Wirkstoffe: 68 NSAR  
19 Opioidanalgetika  
3 Paracetamol

(oral: 58; topisch: 10)

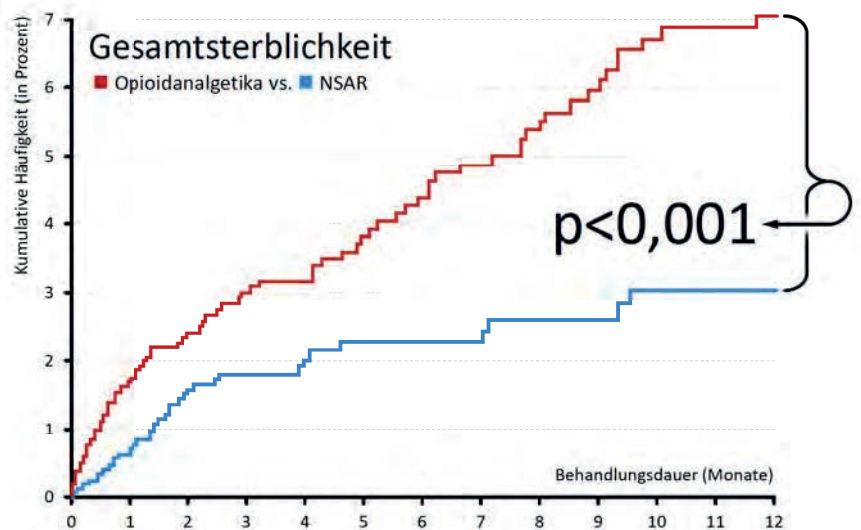


da Costa BR, Pereira TV, Saadat P, Rudnicki M, Iskander SM, Bodmer NS, Bobos P, Gao L, Kiyomoto HD, Montezuma T, Almeida MO, Cheng PS, Hincapié CA, Hari R, Sutton AJ, Tugwell P, Hawker GA, Jüni P. Effectiveness and safety of non-steroidal anti-inflammatory drugs and opioid treatment for knee and hip osteoarthritis: network meta-analysis. *BMI* 2021;375:n2321; <http://dx.doi.org/10.1136/bmj.n2321>

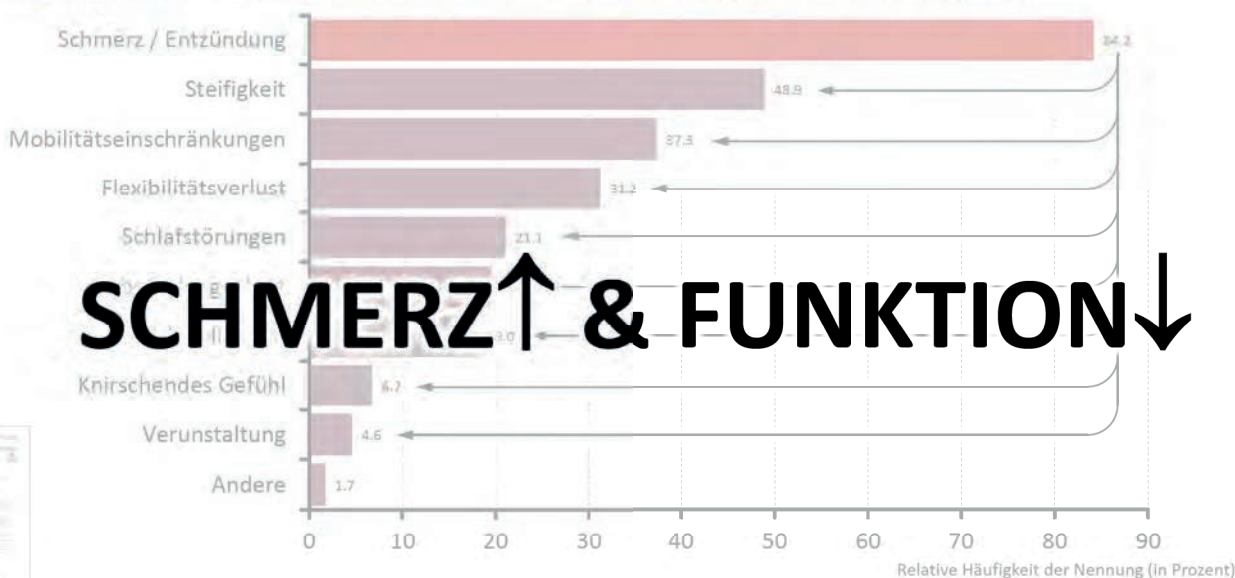


Afilalo M, et al. Efficacy and safety of Tapentadol extended release compared with oxycodone controlled release for the management of moderate to severe chronic pain related to osteoarthritis of the knee: a randomized, double-blind, placebo- and active-controlled phase III study. *Clin Drug Invest* 2010; 30(8): 489-505.

## OSTEOARTHROSE - SICHERHEIT VON OPIOIDEN VS. NSAR BEI ÄLTEREN

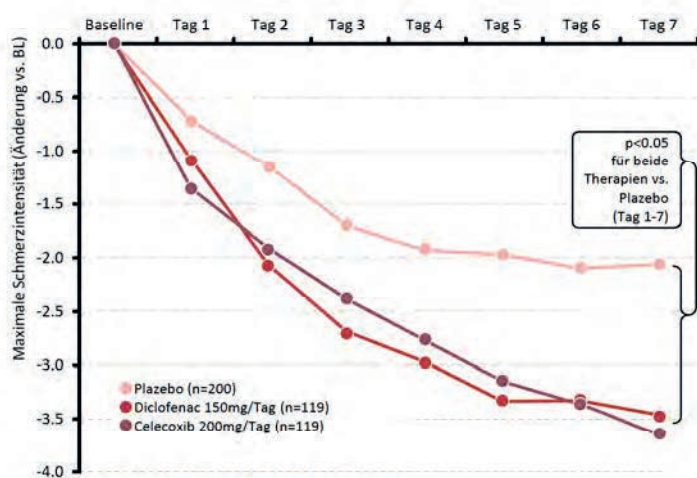


## OSTEOARTHROSE - AM STÄRKSTEN BEEINTRÄCHTIGENDE BESCHWERDEN

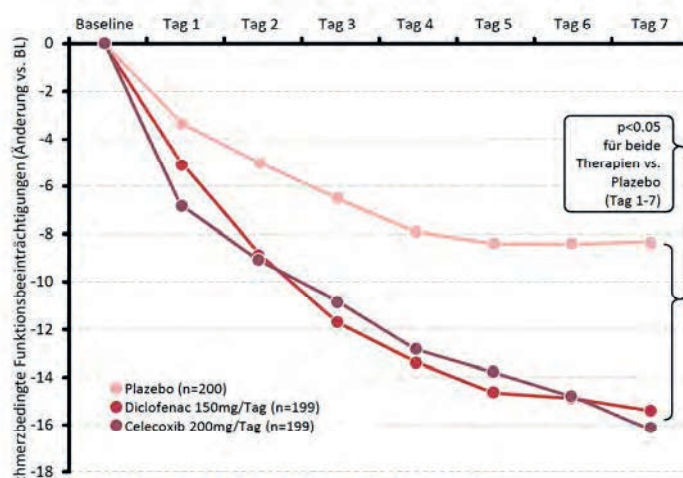


Vitaloni M, Bortolotto van Benden A, Scortino R, Carné X, Quintero M, Santos-Moreno P, Espinosa R, Billo O, Monfort I, de Abajo F, Oswald E, Matucci M, du Souich P, Möllerl, Romera Baures M, Vinci A, Scottton D, Bibas M, Eakin G, Vergnes J. A patients' view of OA: the Global Osteoarthritis Patient Perception Survey (GOAPPS), a pilot study. BMC Musculoskeletal Disorders 2020; 21: 727.

## OSTEOARTHROSE - ZIELERREICHUNG DURCH NSAR (IN KLINISCHEN STUDIEN)



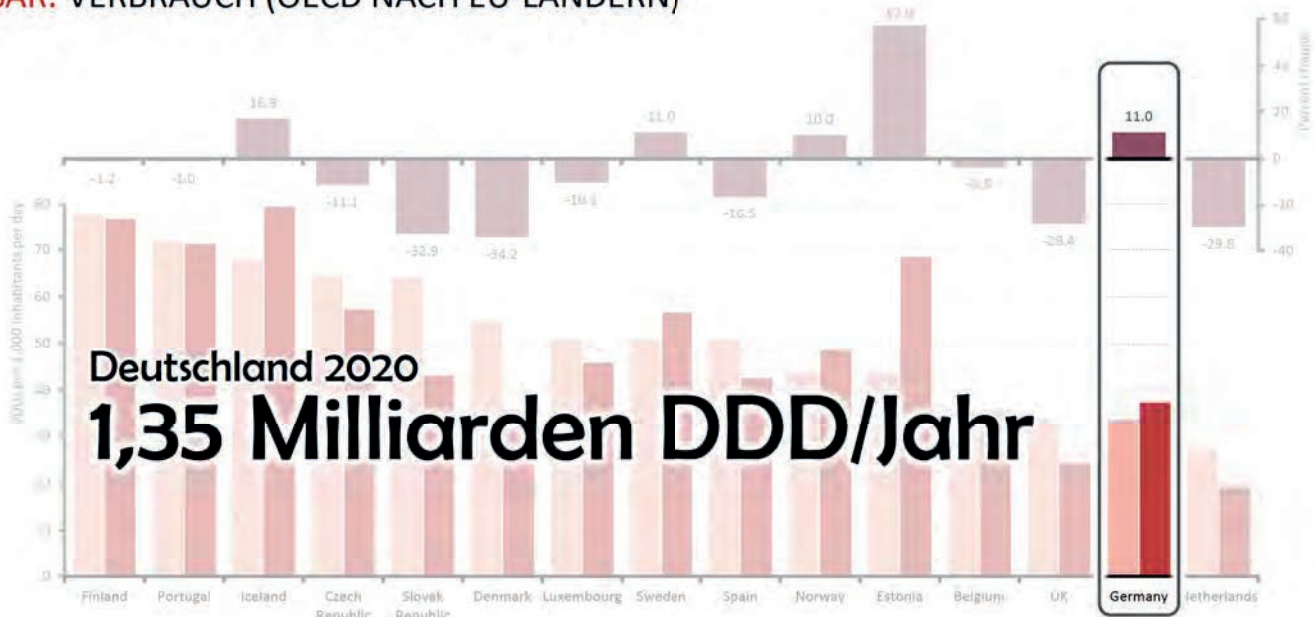
### SCHMERZLINDERUNG



### FUNKTIONSVERBESSERUNG

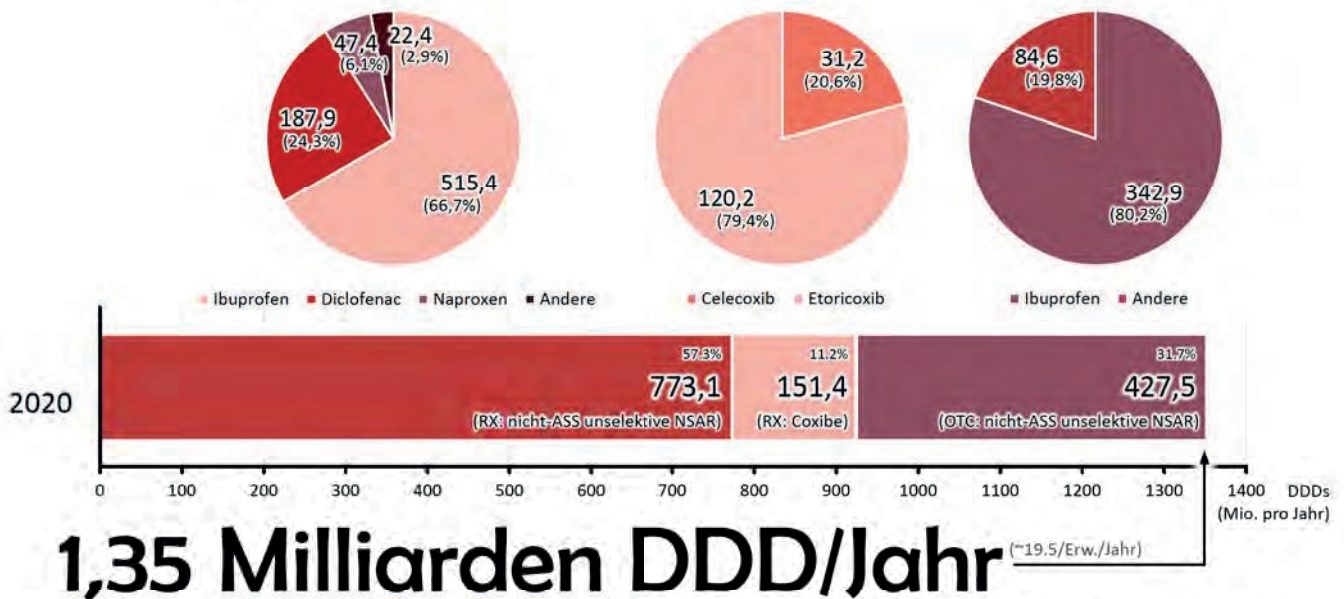


## NSAR: VERBRAUCH (OECD NACH EU-LÄNDERN)



Ludwig W-D, Mühlbauer B, Seifert R. Arzneiverordnungsreport 2021. Springer, Berlin, Germany.  
Schjerning A-M, McGettigan P, Gislason G. Cardiovascular effects and safety of (non-aspirin) NSAIDs. Nat Rev Cardiol 2020; 17(9): 574-584.

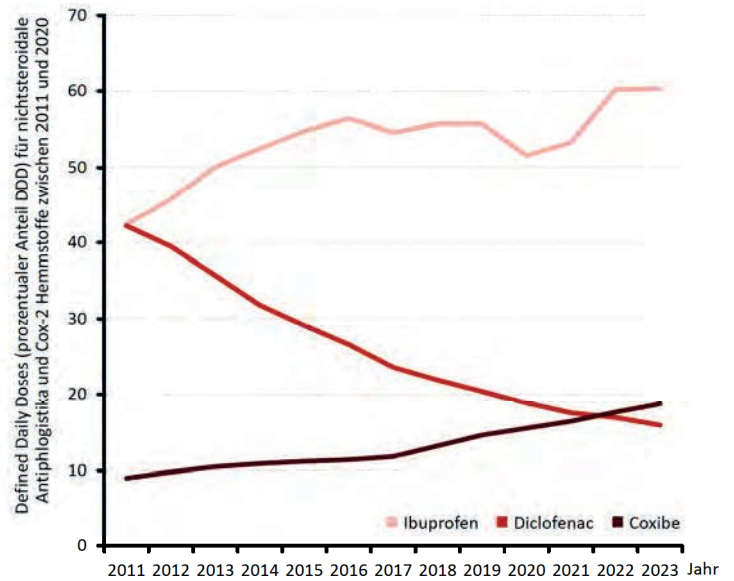
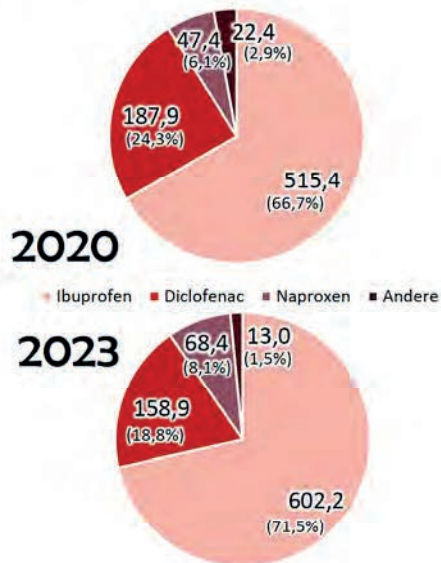
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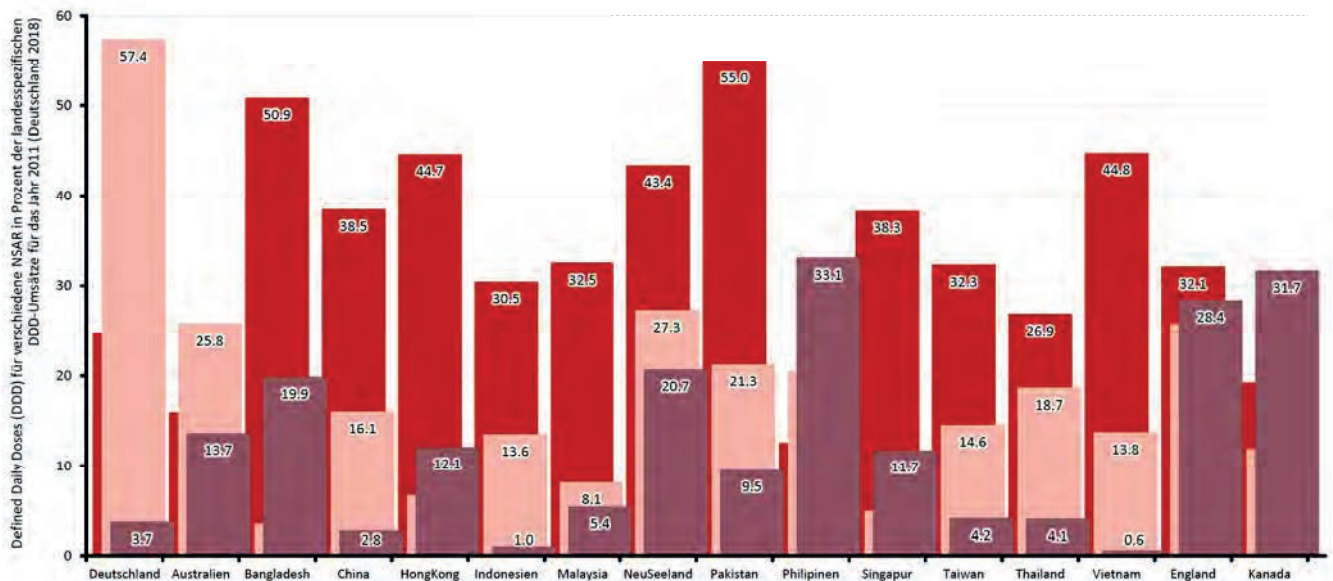
Market share of selected prescription-free analgesics in Germany 2021.  
<https://www.statista.com/statistics/820794/market-share-no-prescription-pain-relief-germany/>

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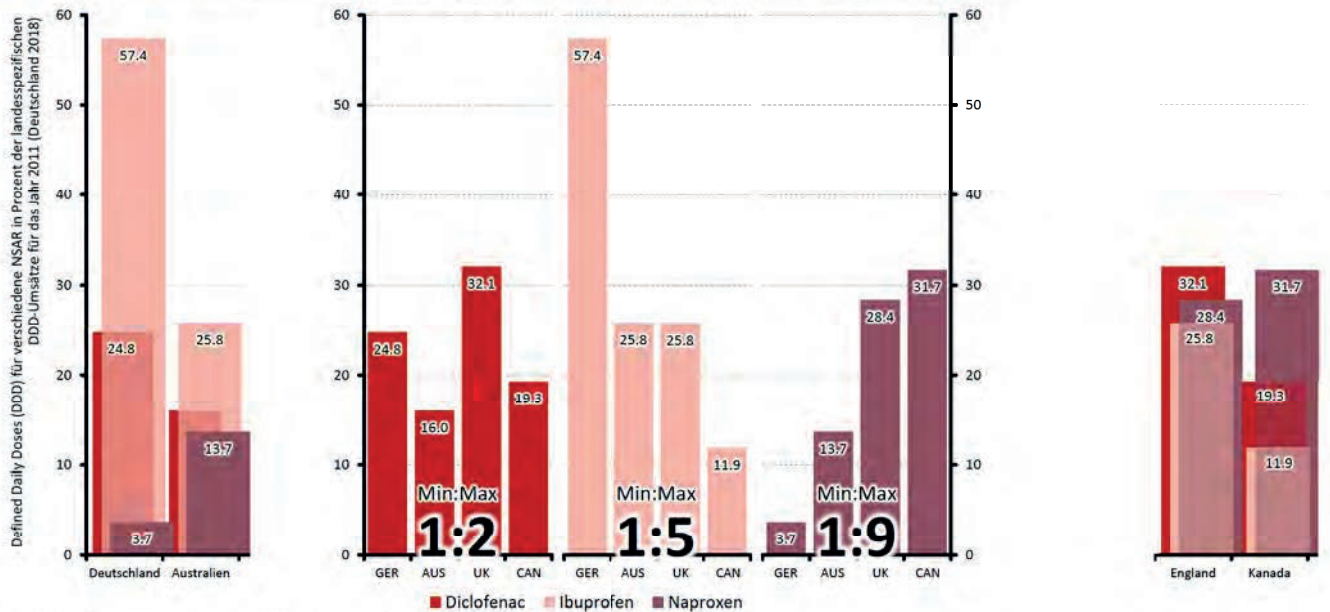
## NSAR: DIFFERENZIALTHERAPIE? → WELCHES NSAR BEI OSTEOARTHRITIS?



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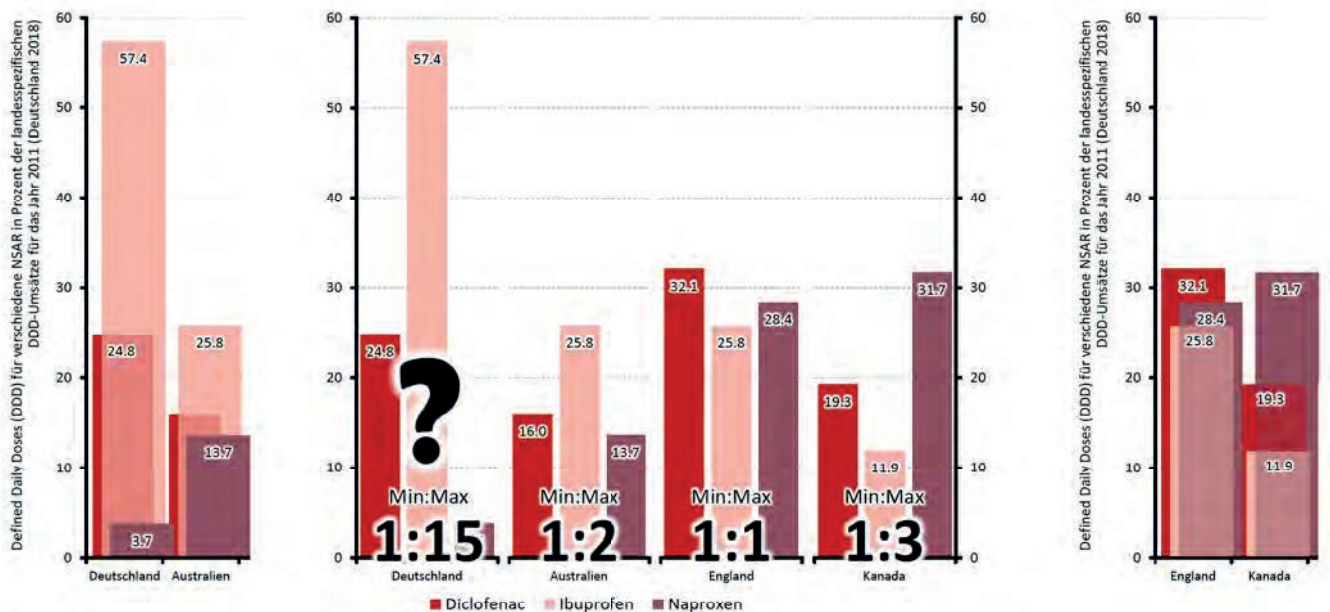
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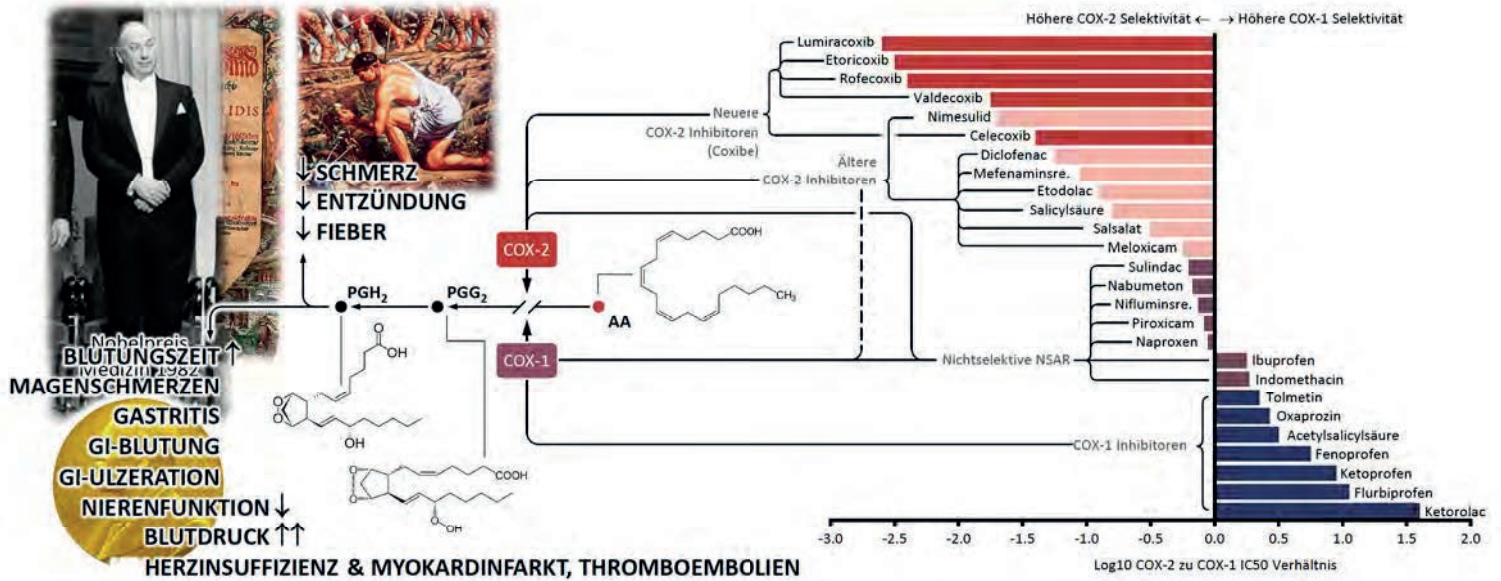


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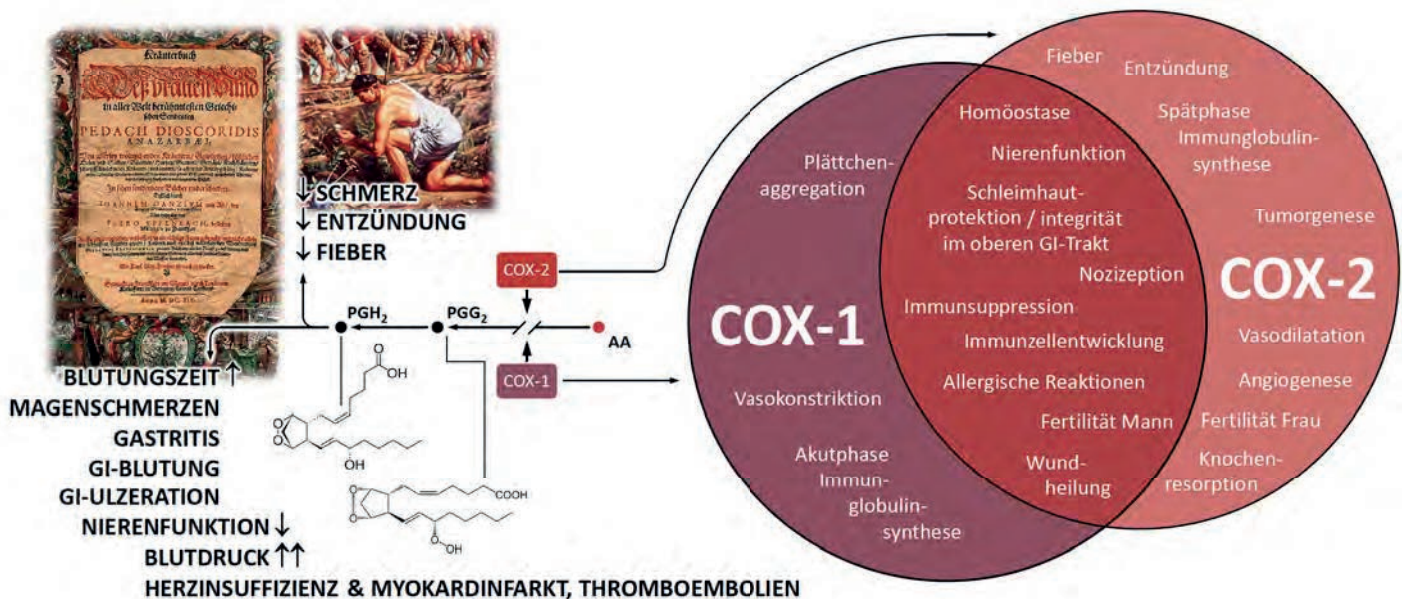


Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. Nature New Biology 1971; 231: 232-235.

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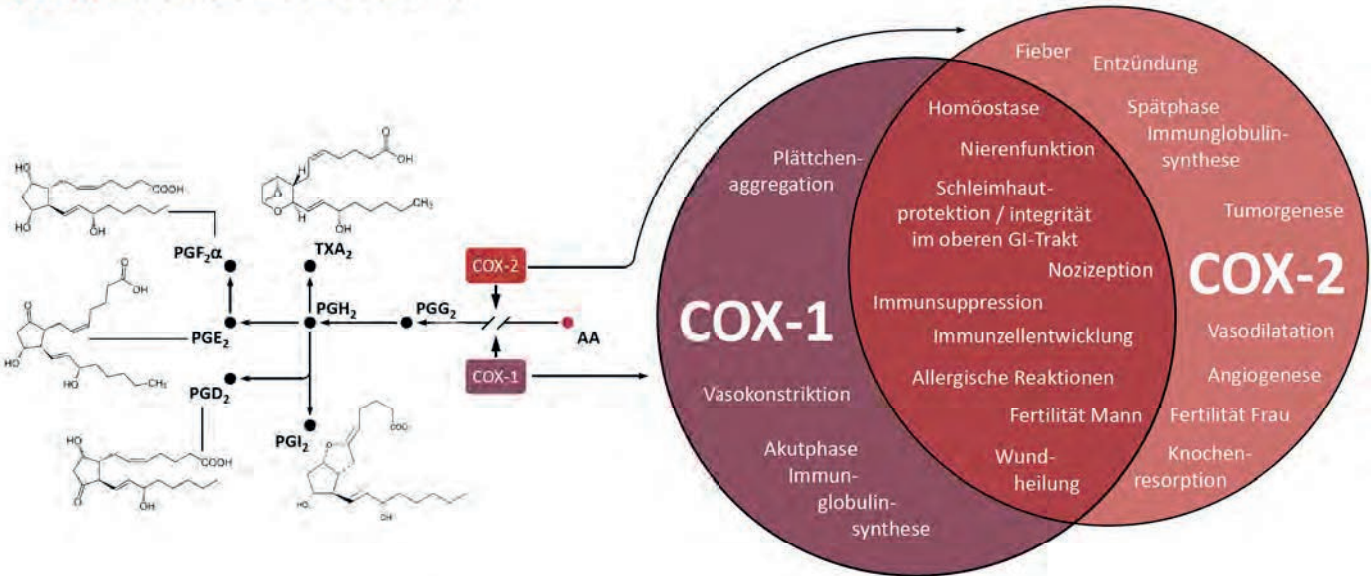
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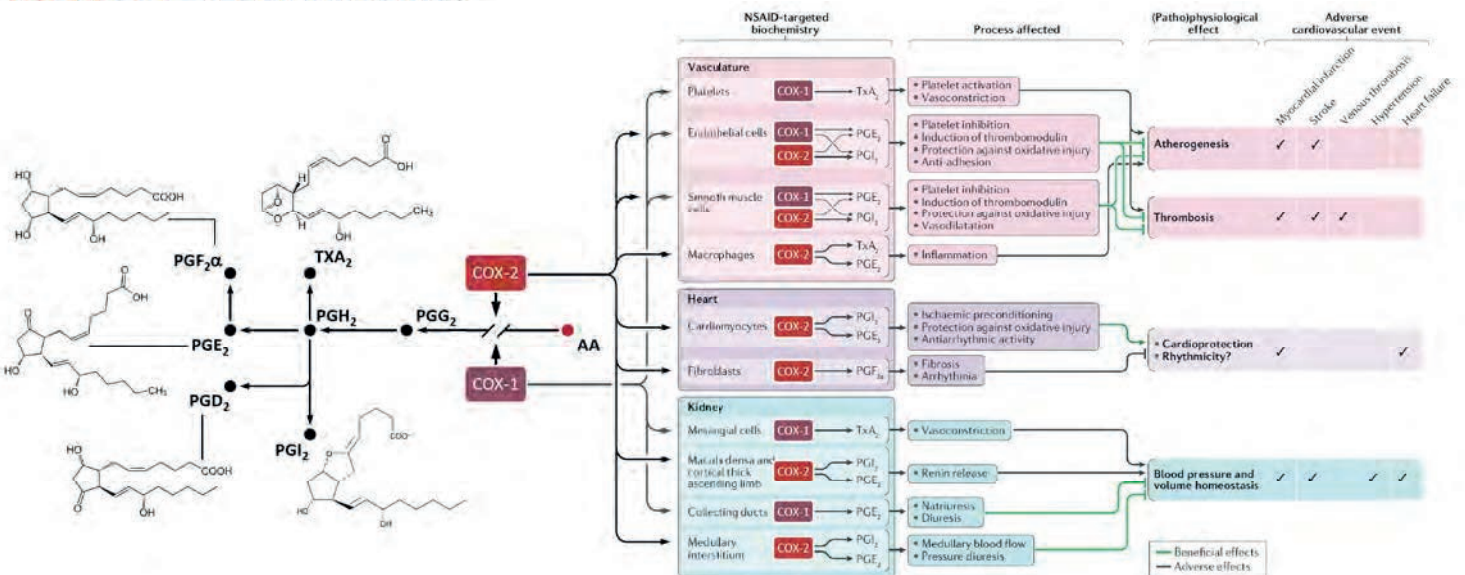


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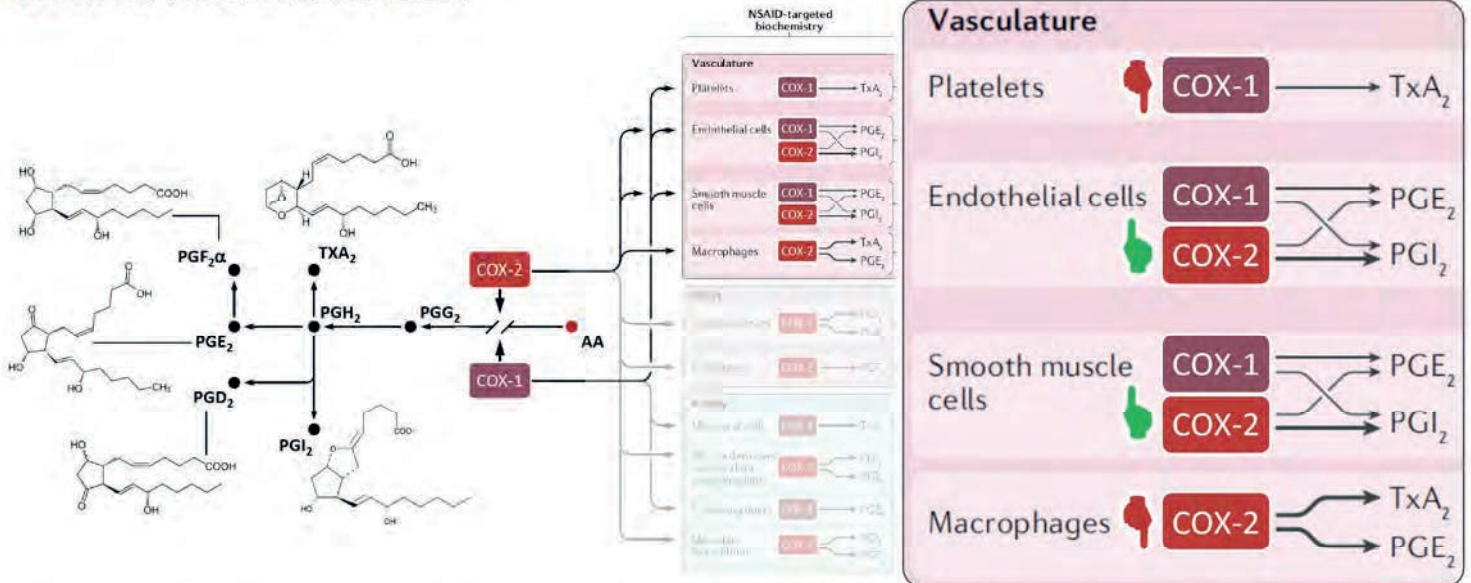
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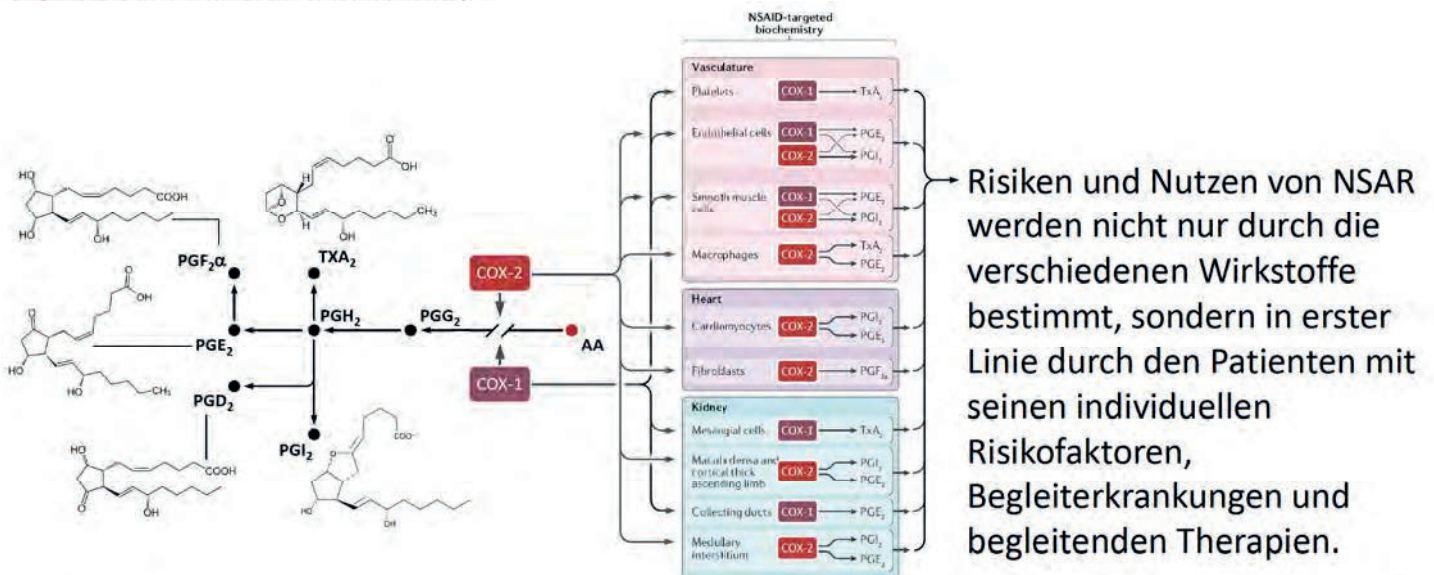
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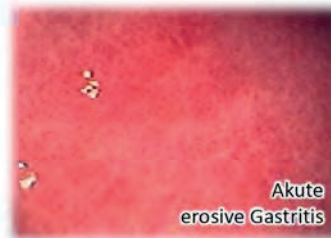
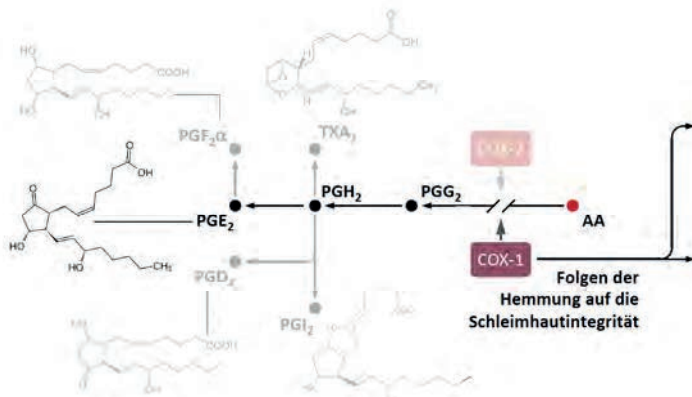
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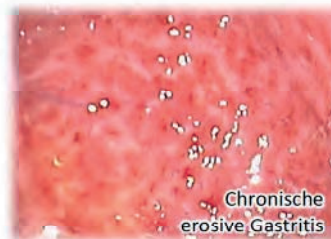
*Pharmacology & Therapeutics* 2011; 129: 195-205.



## NSAR: GI-SCHLEIMHAUTSCHÄDIGUNG



Folge von  
ASS 1000mg (Einzeldosis)



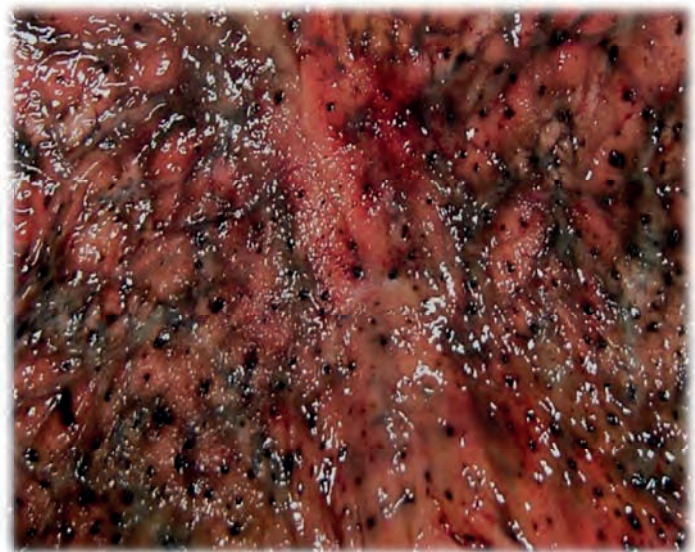
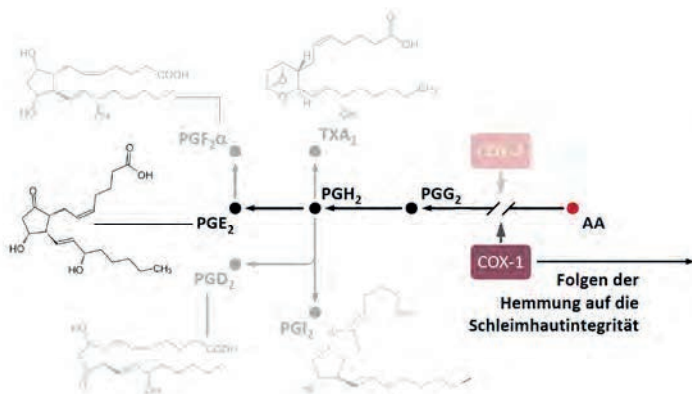
Folge der  
intermittierenden Anwendung von  
Ibuprofen (400-800mg 3xtgl.) für 8  
Wochen

Park K, Bavy AA. Risk of stroke associated with nonsteroidal anti-inflammatory drugs. *Vascular Health and Risk Management* 2014; 10: 25-32.  
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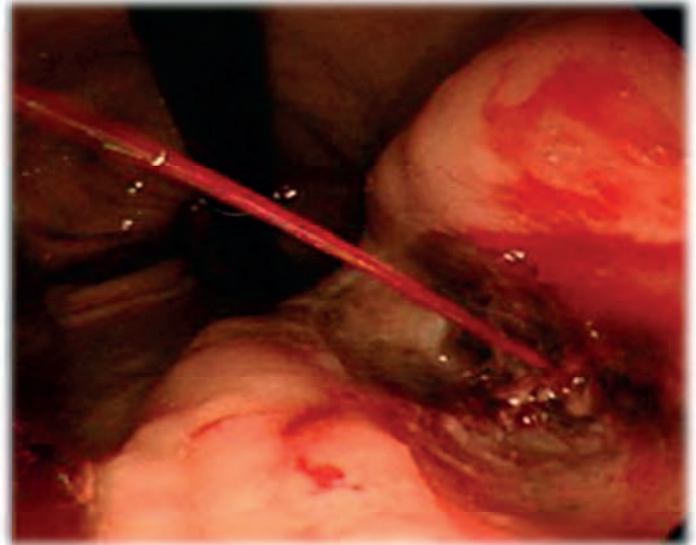
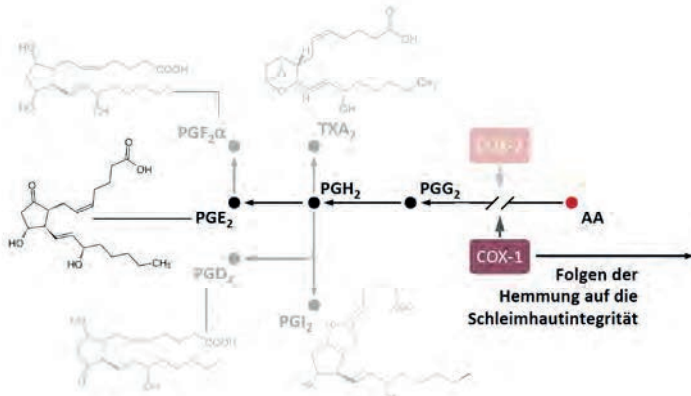


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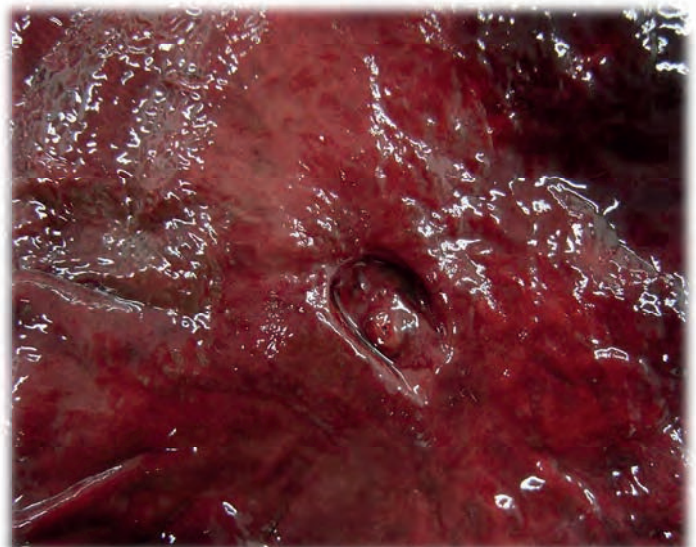
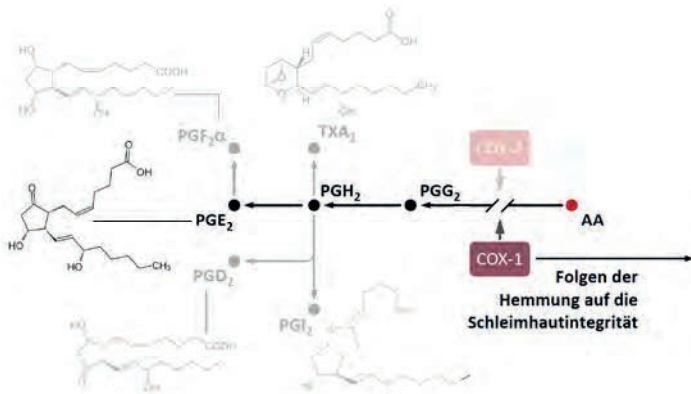


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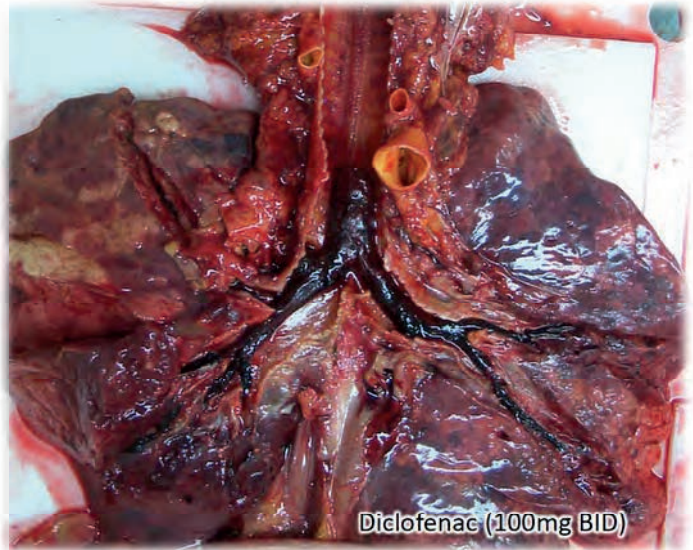
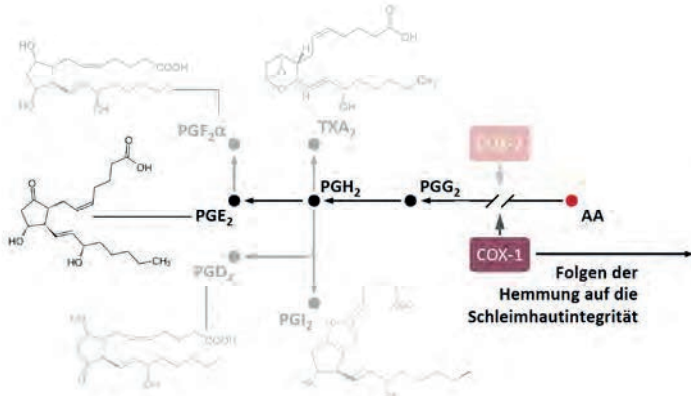
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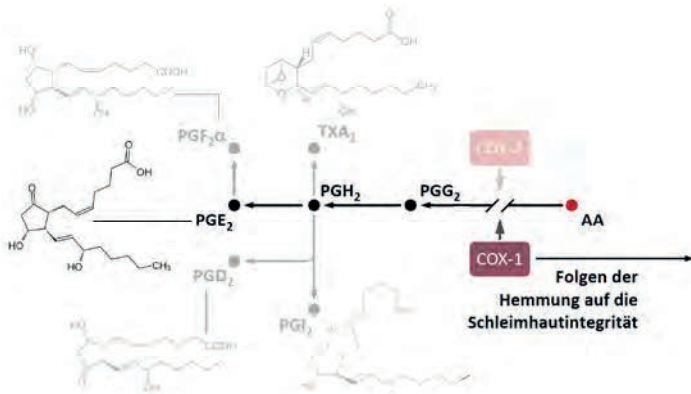


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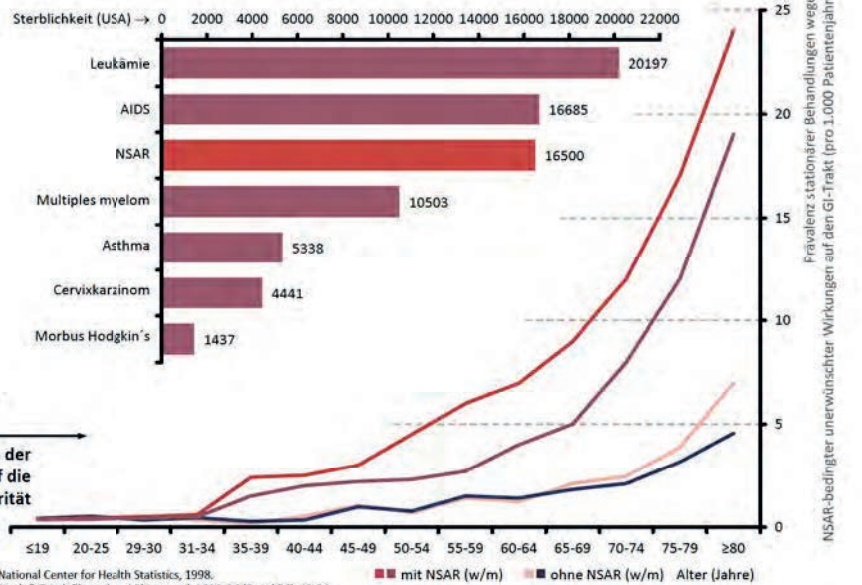
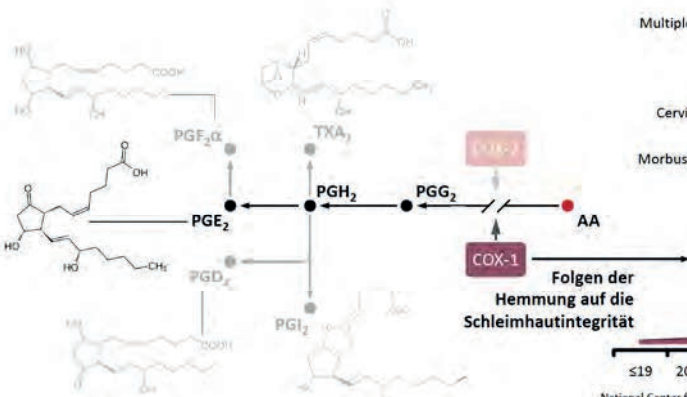
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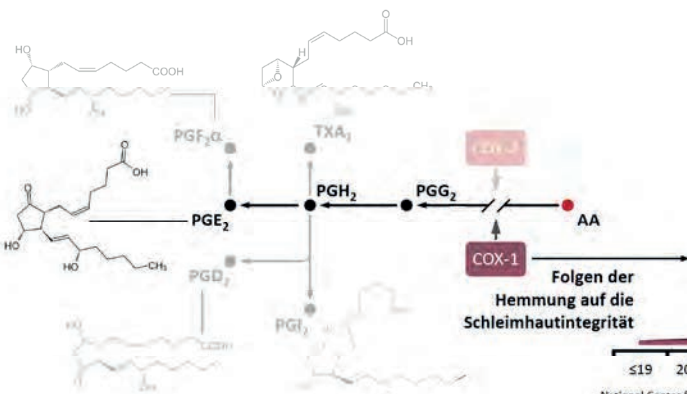


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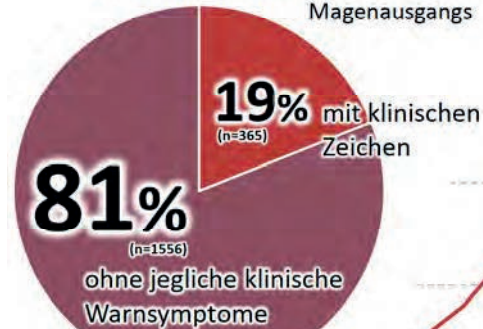
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Individual nonsteroidal anti-inflammatory drugs and other risk factors for upper gastrointestinal bleeding and perforation. *Epidemiology* 1997; 8: 18-24.  
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## NSAR: GI-SCHLEIMHAUTSCHÄDIGUNG



1992 Patienten mit nachgewiesener GI-Blutung, Perforation und/oder Vereengung des Magenausgangs



National Center for Health Statistics, 1998.  
Singh & Triadafilopoulos. *J Rheumatol*. 1999; 26 (Suppl 56): 18-24.  
Singh G, Ramey DR, Mcfeld D, Shi H, Hatoun HT, Fries JF. Gastrointestinal tract complications of nonsteroidal anti-inflammatory drug treatment in rheumatoid arthritis. *Arch Intern Med*. 1996 Jul 22; 156(14): 1530-1536.

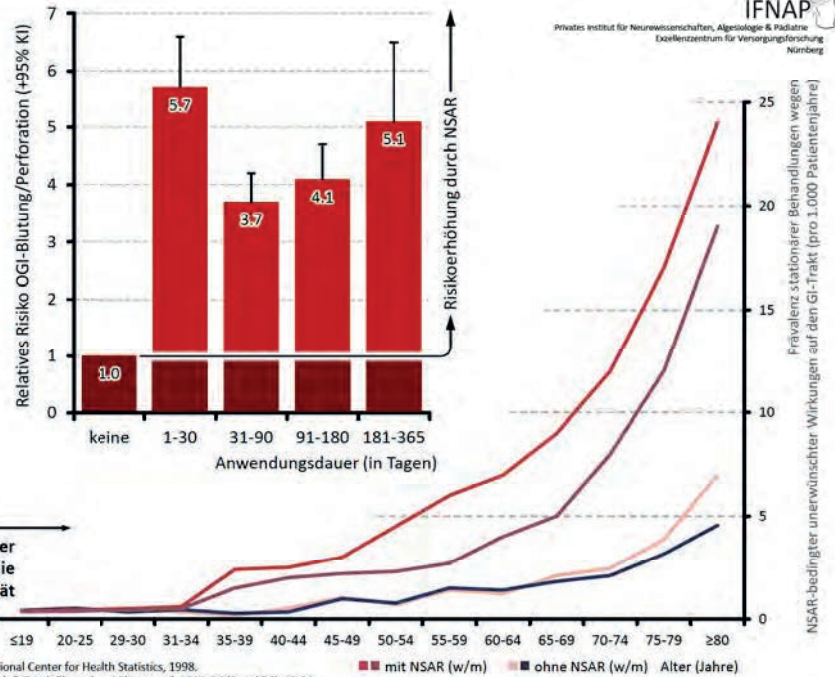
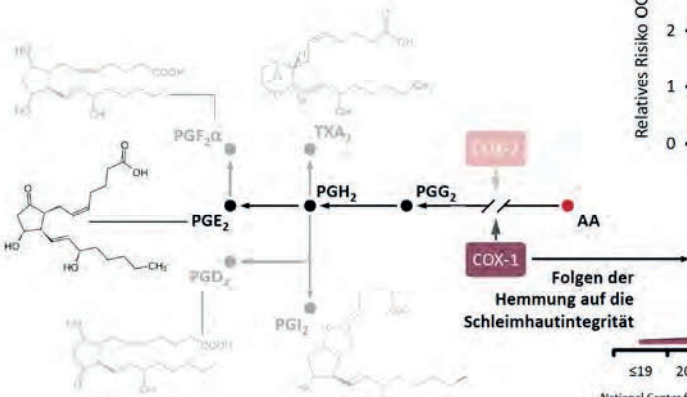
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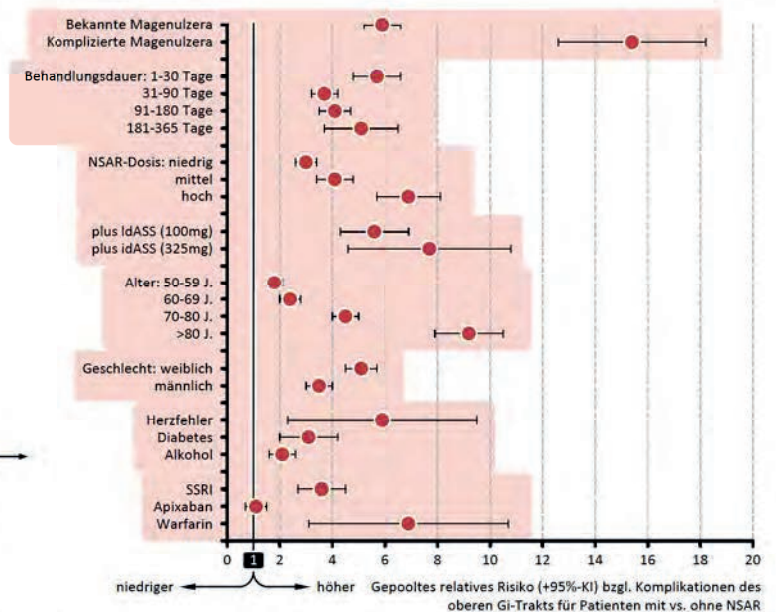
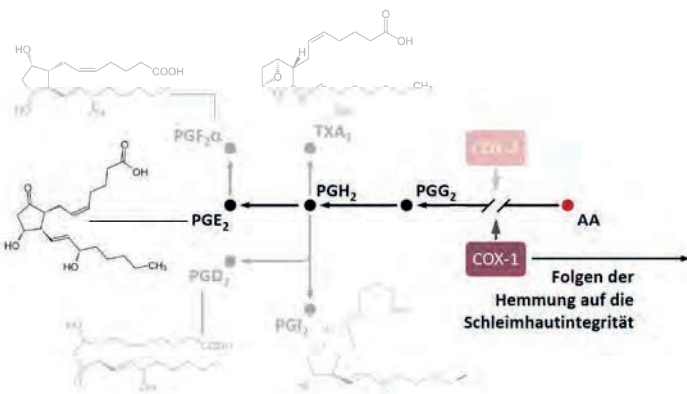
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Hernández-Díaz S, Rodríguez LA. Association between nonsteroidal anti-inflammatory drugs and upper gastrointestinal tract bleeding/perforation: an overview of epidemiologic studies published in the 1990s. Arch Intern Med 2000; 160(14): 2093-2099.  
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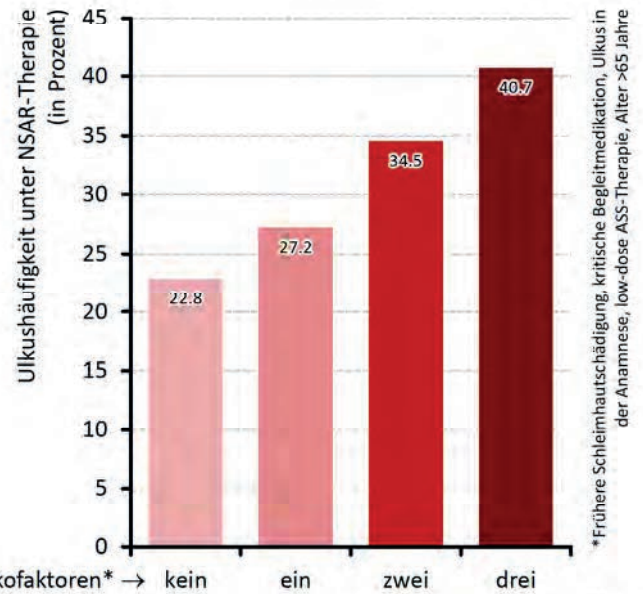
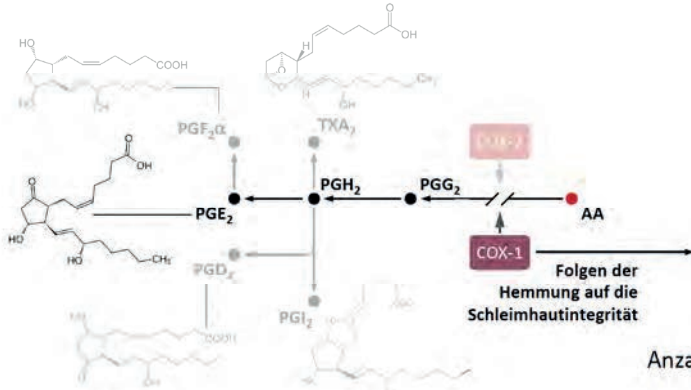


Dalgaard F, Mulder H, Wojdyla DM, Lopes RD, Held C, Alexander JH, De Caterina R, Washam JB, Hylek EM, Garcia DA, Gersh BJ, Wallentin L, Granger CB, Al-Khatib SM. Patients with atrial fibrillation taking nonsteroidal anti-inflammatory drugs and oral anticoagulants in the ARISTOTLE trial. Circulation 2020; 141(1): 10-20.  
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Lanas A, Garcia-Rodriguez LA, Arroyo MT, et al. Risk of upper gastrointestinal ulcer bleeding associated with selective cyclo-oxygenase-2 inhibitors, traditional non-aspirin non-steroidal anti-inflammatory drugs, aspirin and combinations. Gut 2006; 55: 1731-1738.  
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van de Laar MAFJ, Schöll R, Prevoo M, Jastorff J. Predictive value of gastrointestinal symptoms and patient risk factors for NSAID-associated gastrointestinal ulcers defined by endoscopy? Insights from a pooled analysis of two naproxen clinical trials. PLOS ONE 2023; 18(4): e0284358.

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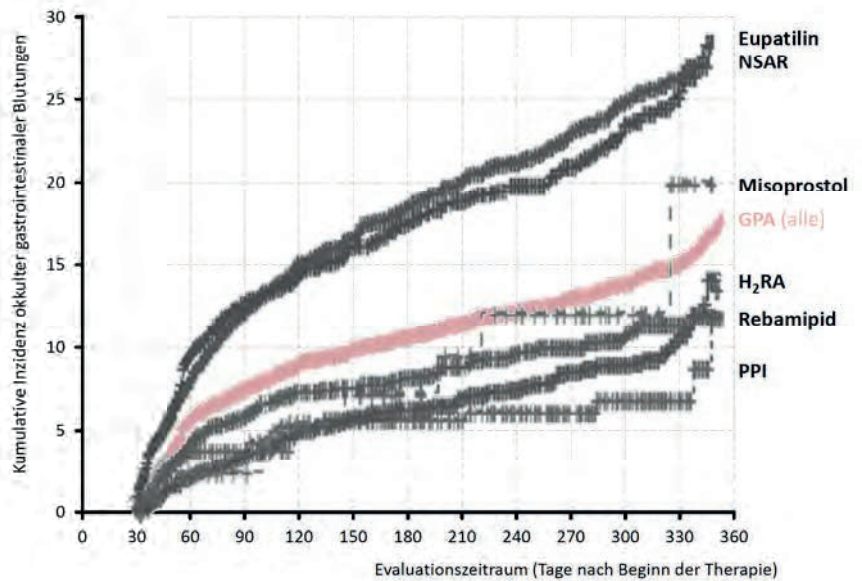
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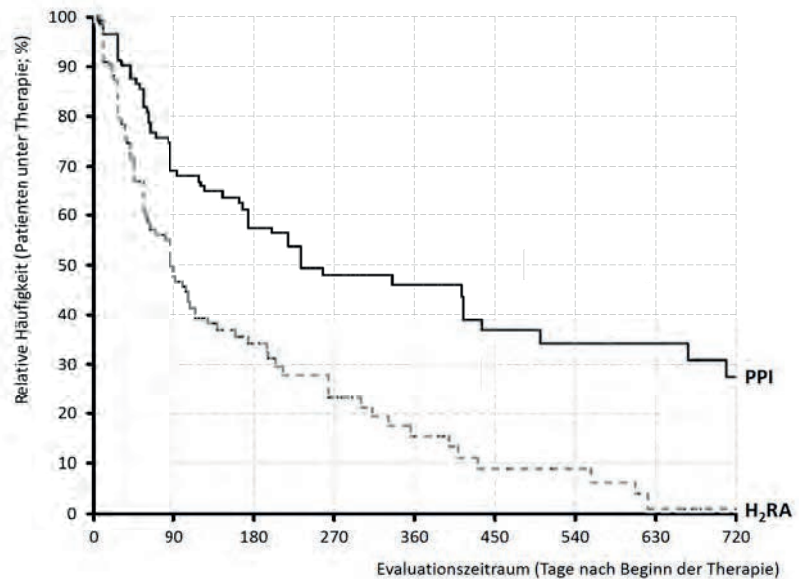
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## NSAR: WIRKSAMKEIT VON MAGENSCHUTZPRÄPARATEN?



## NSAR: KOMBINATION MIT PPI?

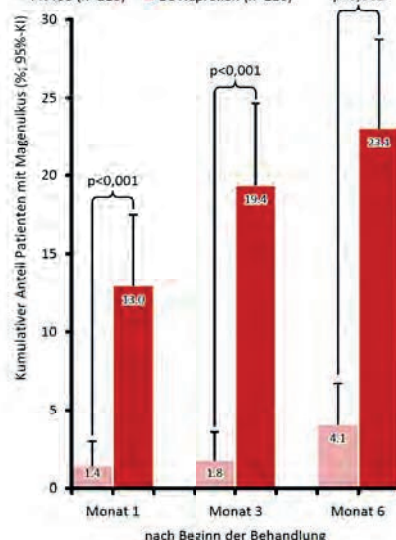


Sturkenboom MC, Burke TA, Tangelder MJ, Dieleman JP, Walton S, Goldstein JL. Adherence to proton pump inhibitors or H<sub>2</sub>-receptor antagonists during the use of non-steroidal anti-inflammatory drugs. Aliment Pharmacol Ther 2003; 18 (11-12): 1137-1147. doi: 10.1046/j.1365-2036.2003.01795.x.

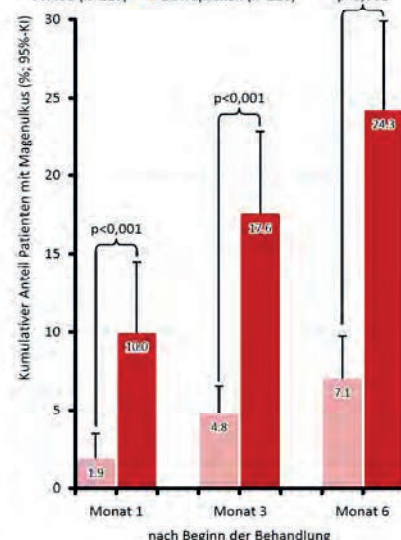
## NSAR: KOMBINATION MIT PPI?



Studie 301; ITT-Population  
PN400 (n=218) ■ EC Naproxen (n=216)



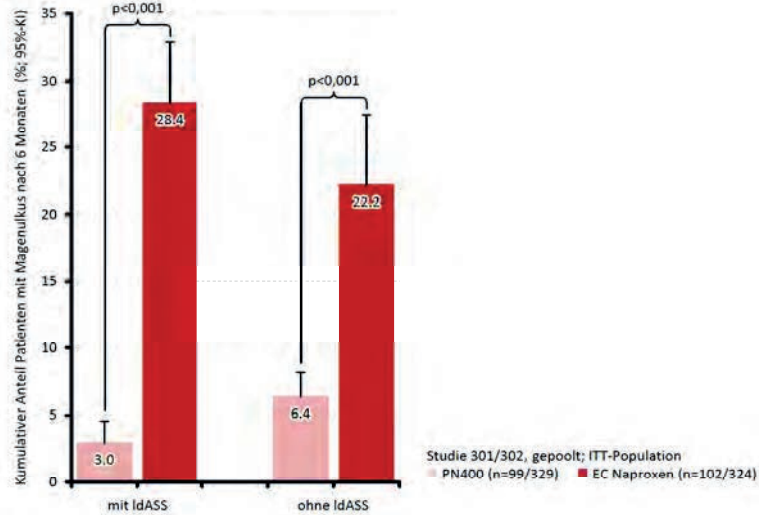
Studie 302; ITT-Population  
PN400 (n=210) ■ EC Naproxen (n=210)



Goldstein JL, Sturkenboom MC, Fort JG, Zhang JG, Sostek M. Clinical trial: the incidence of NSAID-associated endoscopic gastric ulcers in patients treated with PN 400 (naproxen plus esomeprazole magnesium) vs. enteric-coated naproxen alone. Aliment Pharmacol Ther 2010; 32: 401-413.



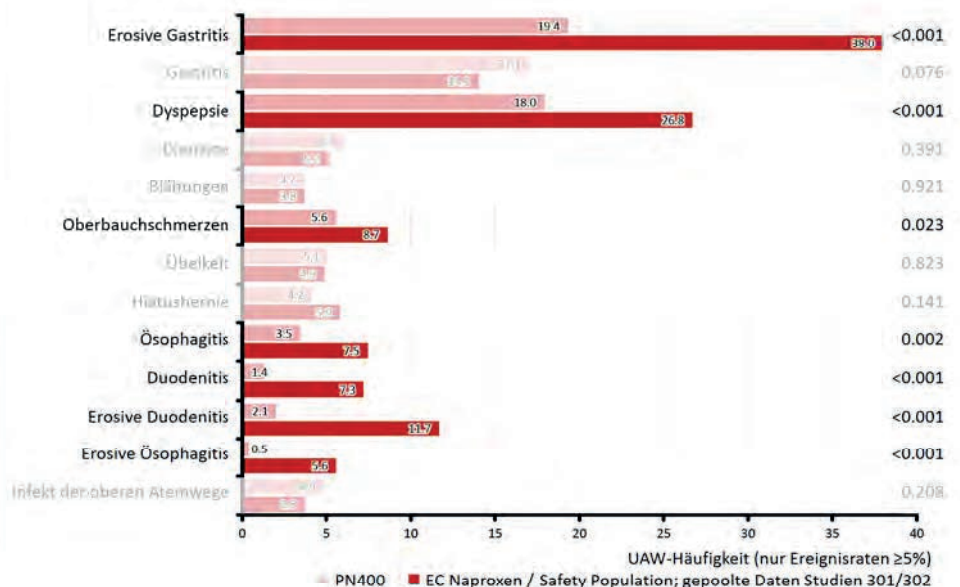
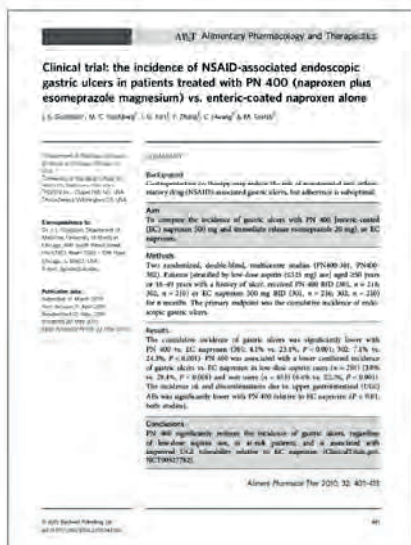
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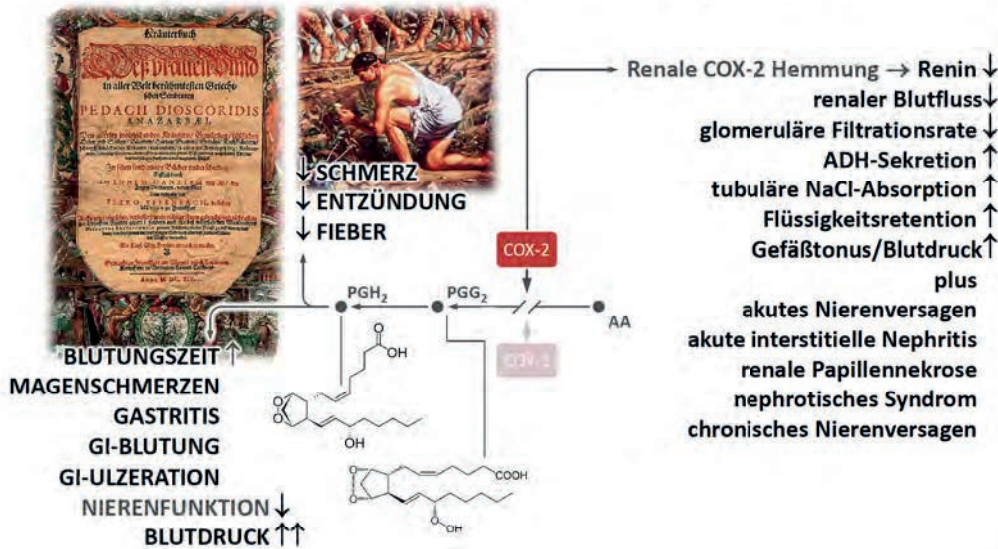
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## NSAR: NEBENWIRKUNGEN JENSEITS DES GI-TRAKTES

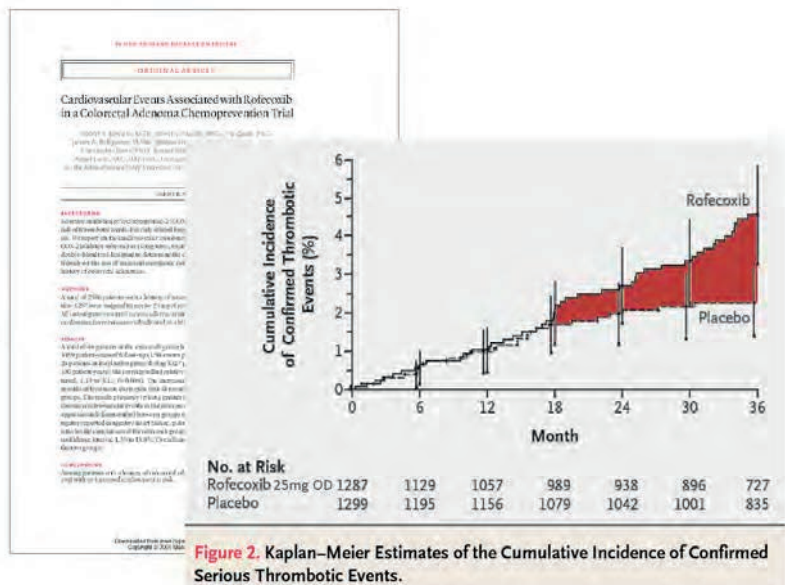
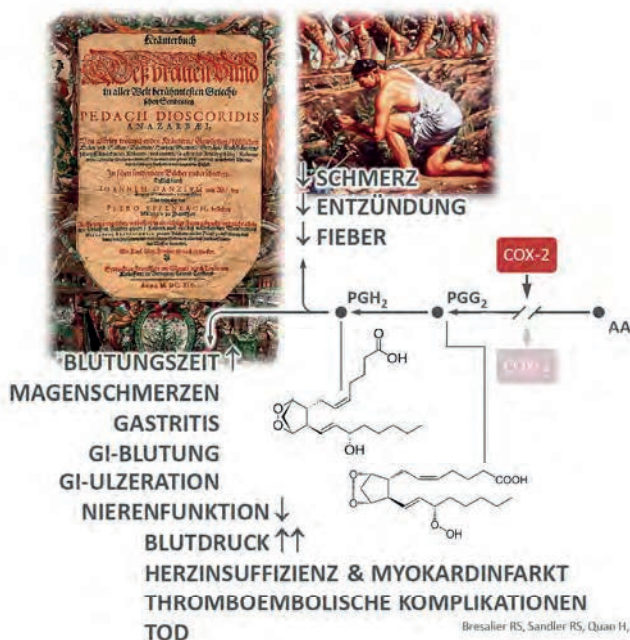


Cheng H-F, Harris RC. Cyclooxygenases, the kidney, and hypertension. Hypertension 2004; 43(3): 525-530.

Takayuki T, Togo K, Ebata N, Fujii K, Yonemoto N, Abraham L, Kikuchi S.

Burden of renal events associated with nonsteroidal anti-inflammatory drugs in patients with osteoarthritis and chronic low back pain: a retrospective database study. Pain Ther 2021; 10: 443-455.

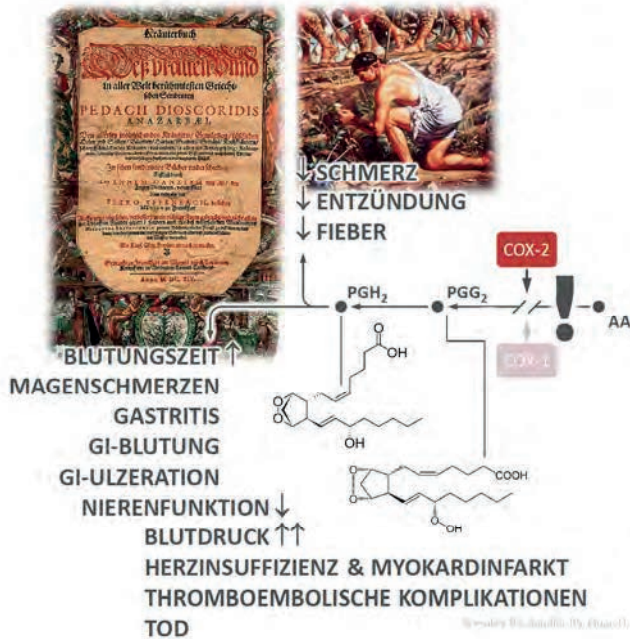
## NSAR: NEBENWIRKUNGEN JENSEITS DES GI-TRAKTES



Bresnall RS, Sandler RS, Quan H, Bolognese JA, Oxenius B, Horgan K, Lines C, Riddell R, Morton D, Lanus A, Konstam MA, Baron JA; Adenomatous Polyp Prevention on Vioxx (APPROVE) Trial Investigators. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. N Engl J Med 2005; 352(11): 1092-1102.



## NSAR: NEBENWIRKUNGEN JENSEITS DES GI-TRAKTES



## NSAR: NUTZEN-RISIKO OPTIMIERUNG



### Klinische Risikofaktoren

- Alter  $\geq 65$  Jahre
- Allgemeinerkrankungen (DM)
- aktuelle/frühere GI-Erkrankung
- Hypertonie
- kardiovaskuläre Erkrankungen
- renale Erkrankungen

### Pharmakologische Risikofaktoren (Ko-) Medikation mit...

- Glukokortikoiden
- low dose ASS
- Antikoagulantien
- SSRI
- Antihypertensiva

### NSAR-spezifische Risikofaktoren ( $\uparrow$ Dosis, $\uparrow$ HWZ, $\uparrow$ Dauer)

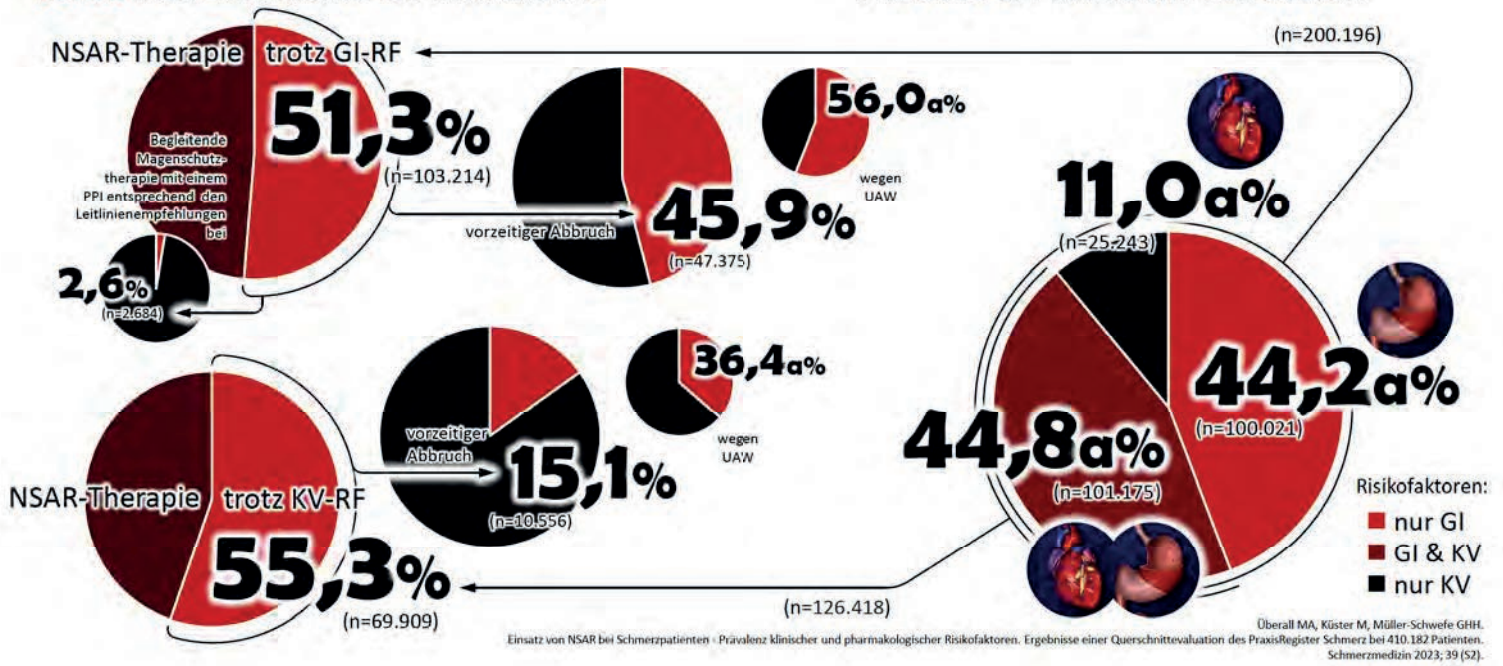


Einsatz von NSAR bei Schmerzpatienten - Prävalenz klinischer und pharmakologischer Risikofaktoren. Ergebnisse einer Querschnitterevaluation des PraxisRegister Schmerz bei 410.182 Patienten. Schmerzmedizin 2023; 39 (S2).

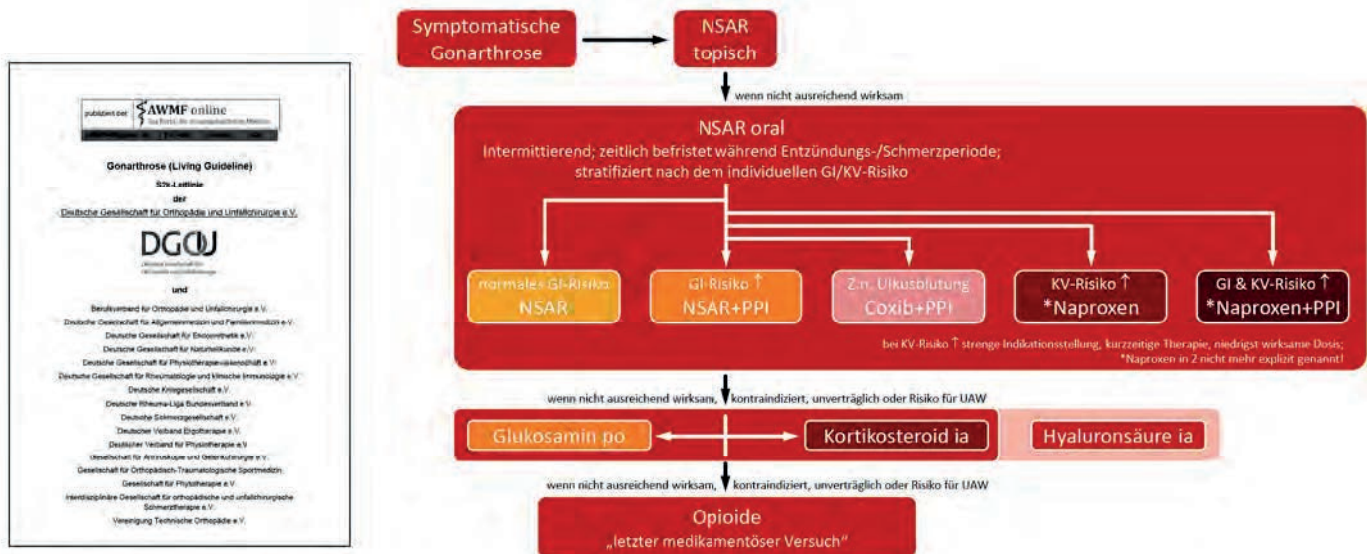


## NSAR: NUTZEN-RISIKO OPTIMIERUNG

## THEORIE & PRAXIS IM VERGLEICH



## NSAR: LEITLINIENEMPFEHLUNGEN ZUR BEHANDLUNG DER OSTEOARTHRITIS



Adaptiert und modifiziert nach:

- Stöve J et al., Gonarthrose, S2k-Leitlinie, Stand 18.01.2018, [https://www.awmf.org/uploads/tx\\_saletlinien/033-004f\\_S2k\\_Gonarthrose\\_2018-01\\_1.pdf](https://www.awmf.org/uploads/tx_saletlinien/033-004f_S2k_Gonarthrose_2018-01_1.pdf) (aufgerufen am 22.03.2022).
- Deutsche Gesellschaft für Orthopädie und Unfallchirurgie e.V., Gonarthrose S2k-Leitlinie, Version 4.0 vom 24.01.2024; <https://register.awmf.org/de/leitlinien/detail/033-004> (aufgerufen am 02.11.2024).
- Johns Hopkins University, Osteoarthritis, <https://www.hopkinsmedicine.org/health/conditions-and-diseases/arthritis/osteoarthritis>; aufgerufen am 22.03.2022.
- Kanno T, Moayyedi P. Who needs gastroprotection in 2020? Curr Treat Options Gastro 2020; 18: 557-573.

## NSAR: RATIONALISIERUNG DER INDIKATIONSSTELLUNG FÜR PPI-KOMBINATION

modifiziert nach Kanno et al. Curr Treat Options Gastro 2020; 18: 557-573.



### Punkte Risikofaktoren

- +2 Alter 70–79 Jahre
- +4 Alter >79 Jahre
- +6 Frühere peptische Ulkusblutung/-perforation
- +3 Früheres unkompliziertes peptisches Ulkus
- +6 Aktuelle Tumorerkrankung
- +5 Aktuelle Nierenerkrankung
- +4 Aktuelle Lebererkrankung
- +2 Aktuelle Atemwegserkrankung
- +2 Aktuelle Herz-Kreislaufkrankung
- +1 Diabetes mellitus
- +1 Einnahme selektiver Serotonin-Wiederaufnahmehemmer
- +1 Einnahme von Glukokortikoiden
- +4 Kombination von NSAR zu low-dose ASS
- +2 Kombination von low-dose ASS zu NSAR

SUMME ≥6 (für NSAR) bzw. ≥8 (für IdASS) → Kombination mit PPI!