



An.Sgpl Symposium
14.11.2024

ANDERS PH KARLSEN
PERNILLE B SUNDE

PERIOPERATIVE OPIOID ALGORITHMS FOR INDIVIDUALISED DOSING



 Bispebjerg and Frederiksberg Hospital

 Zealand University Hospital

 IT University of Copenhagen

 Copenhagen Trial Unit



Bispebjerg and Frederiksberg Hospital



Zealand University Hospital



IT University of Copenhagen



Copenhagen Trial Unit



CEPRA

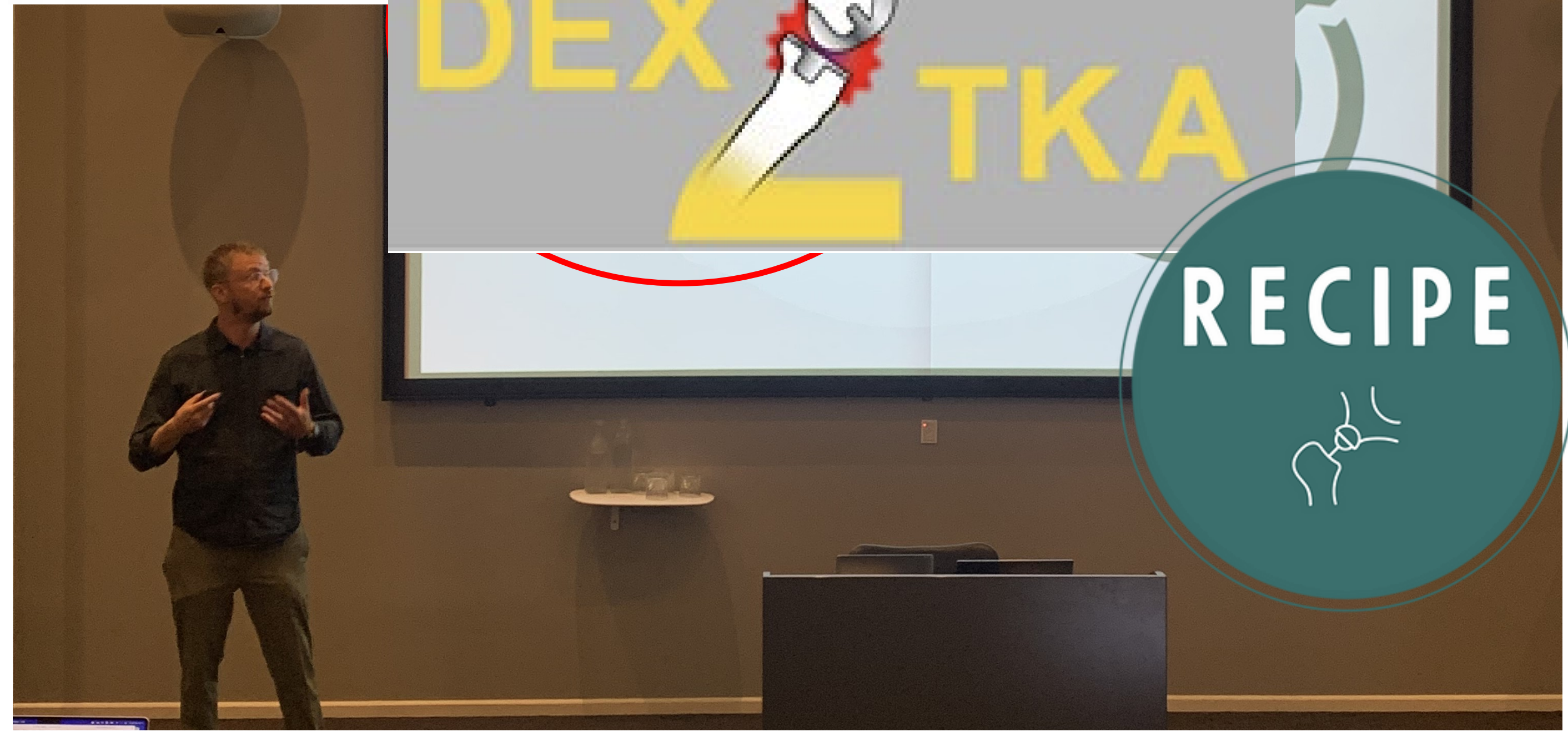
En programoversigt

- Om OPIAID
- Kendte prædiktorer
- Litteraturens prædiktionsmodeller (*Pernille*)
- Nuværende dansk praksis (*Trang*)
- OPIAID databasen (*Markus*)
- Udvikling af algoritmen
- TripleA



OPIAID algoritmen skal, for den enkelte patient, prædiktere den intraoperative afslutningsvise opioiddosis, som giver det samlet set bedste forløb i timerne efter operation.

Algoritmen skal fungere som et software der kan implementeres i fx Sundhedsplatformen.



AIM

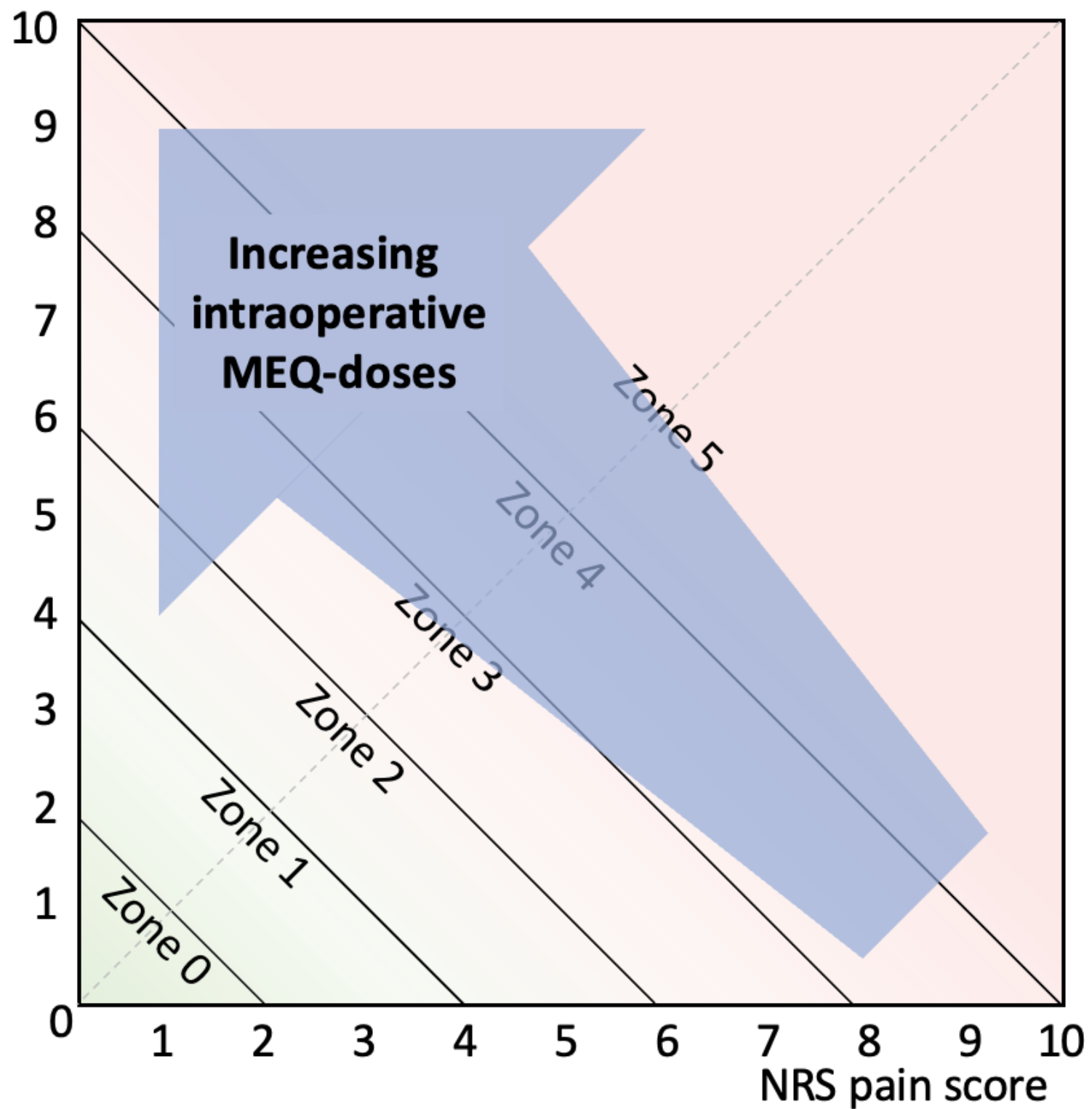
Investigate the relative benefits
and harms of different
combinations of paracetamol,
ibuprofen and dexamethasone
following THA

RECIPE

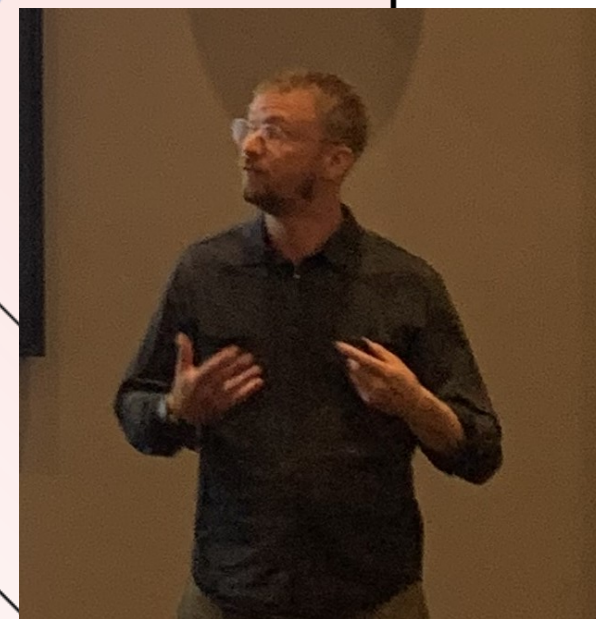
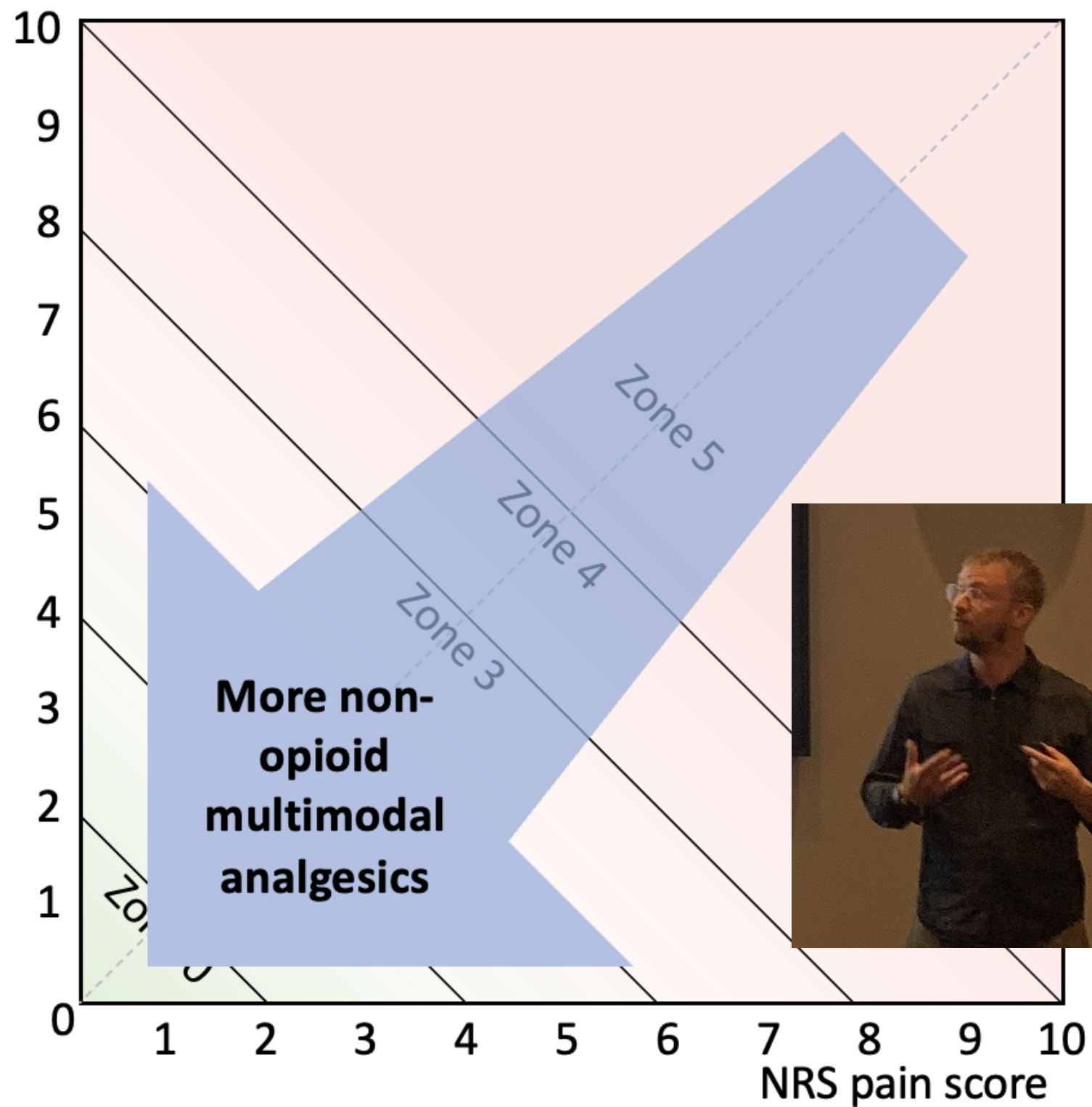


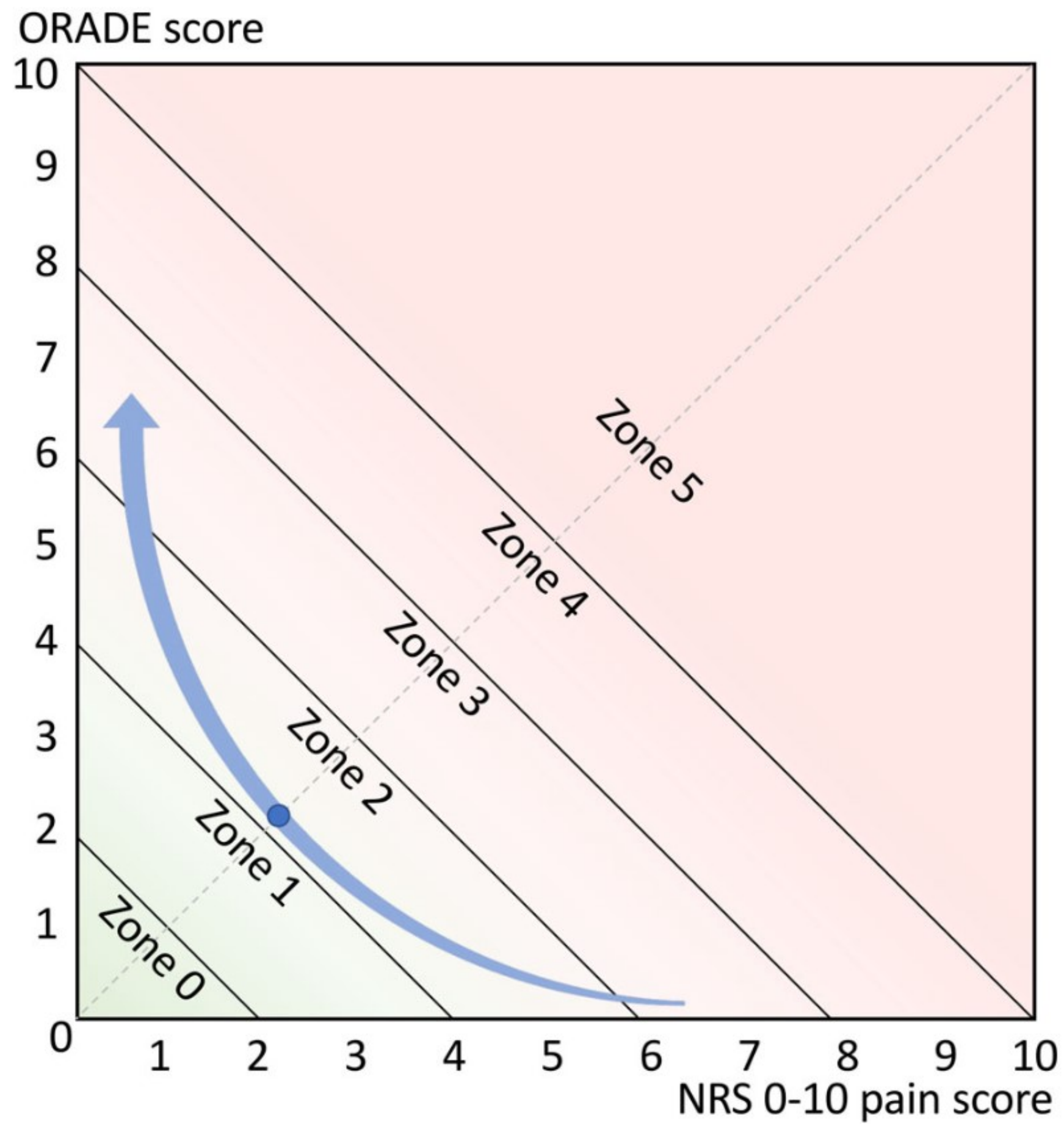
**Non-opioid systemisk
behandling er
optimeret, så hvad nu?**

OPIOID ADVERSE EVENT SCORE



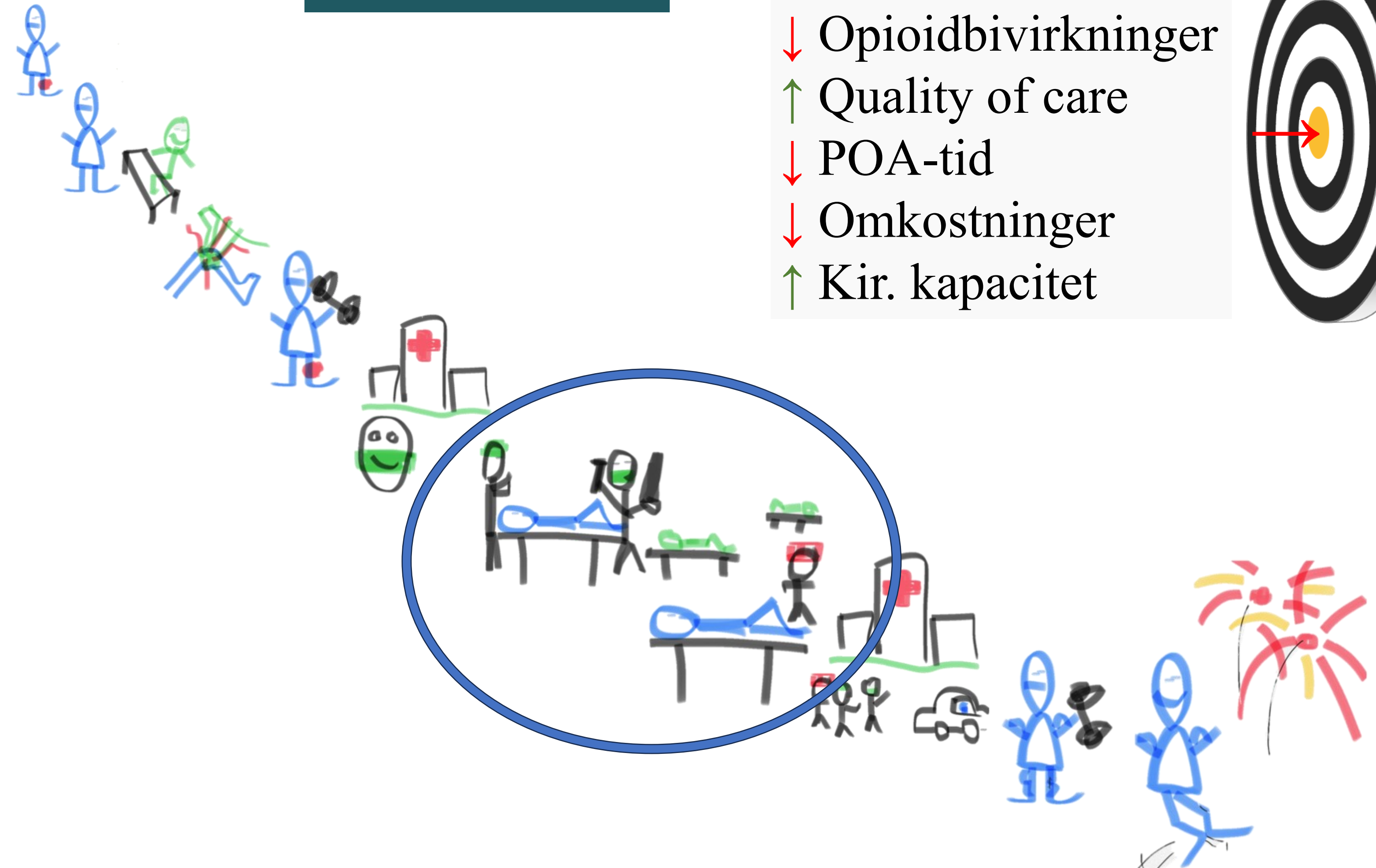
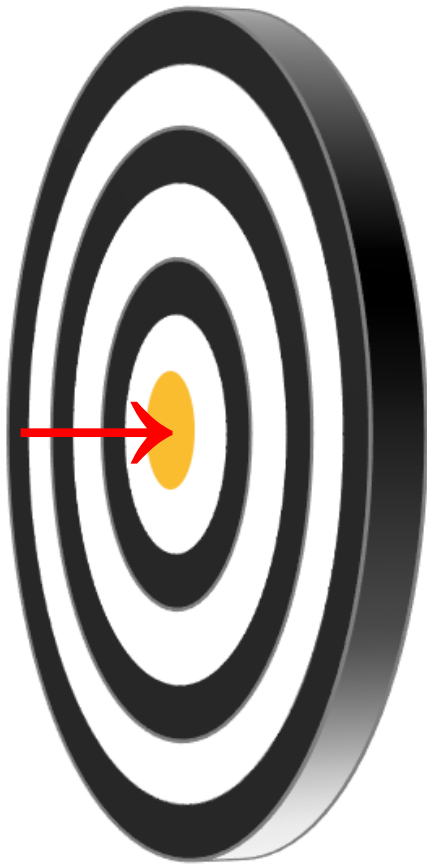
OPIOID ADVERSE EVENT SCORE





MÅL

- ↓ Smerte
- ↓ Opioidbivirkninger
- ↑ Quality of care
- ↓ POA-tid
- ↓ Omkostninger
- ↑ Kir. kapasitet



HVORDAN OG HVORNÅR?



Phase 1: Evidence & practice

Reviews: Prediction models, prediction factors, choice of opioid, opioid minimal difference

Phase 3: External validation

Prospective, observational study, 700 patients, multicenter. Model accuracy, performance and safety.

Phase 5: Clinical implementation

“5.5 in-house rule”; medical device
Retraining after actual clinical use of the algorithm → improved algorithm



International validation
Postoperative prediction

Phase 2: Algorithm development

Retrospective cohort study: Data from 895,000 surgeries into optimized machine learning model

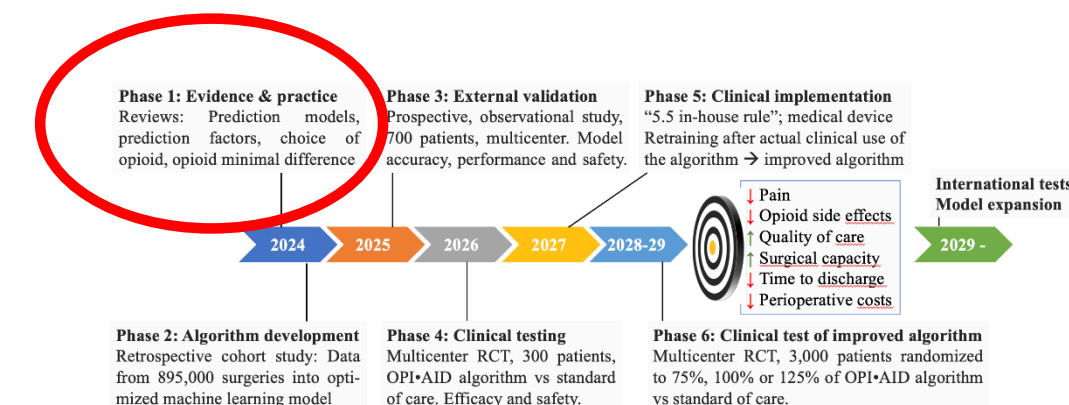
Phase 4: Clinical testing

Multicenter RCT, 300 patients, OPI•AID algorithm vs standard of care. Efficacy and safety.

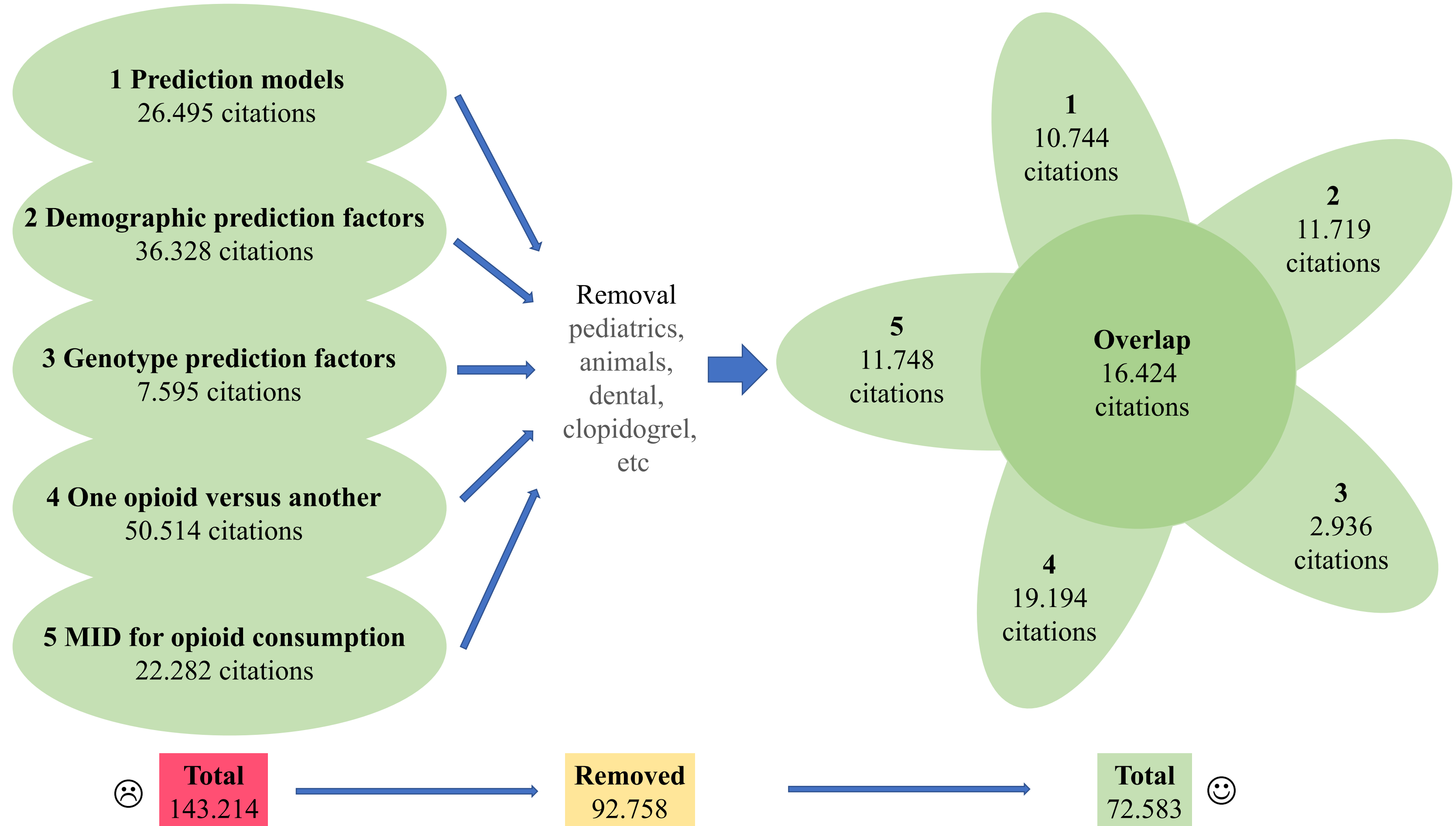
Phase 6: Clinical test of improved algorithm

Multicenter RCT, 3,000 patients randomized to 75%, 100% or 125% of OPI•AID algorithm vs standard of care.

Fase 1: evidens og nuværende praksis for intra- og postoperative opioider



Evidens: 5 systematiske reviews



Evidens: 5 systematiske reviews

1 Prediction models

26.495 citations

2 Demographic prediction factors

36.328 citations

3 Genotype prediction factors

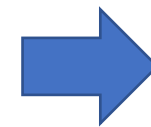
7.595 citations

4 One opioid versus another

50.514 citations

5 MID for opioid consumption

22.282 citations



1 Prediction models

21 included studies

2 Demographic prediction factors

35 included studies

3 Genotype prediction factors

48 included studies

4 One opioid versus another

100ish included studies

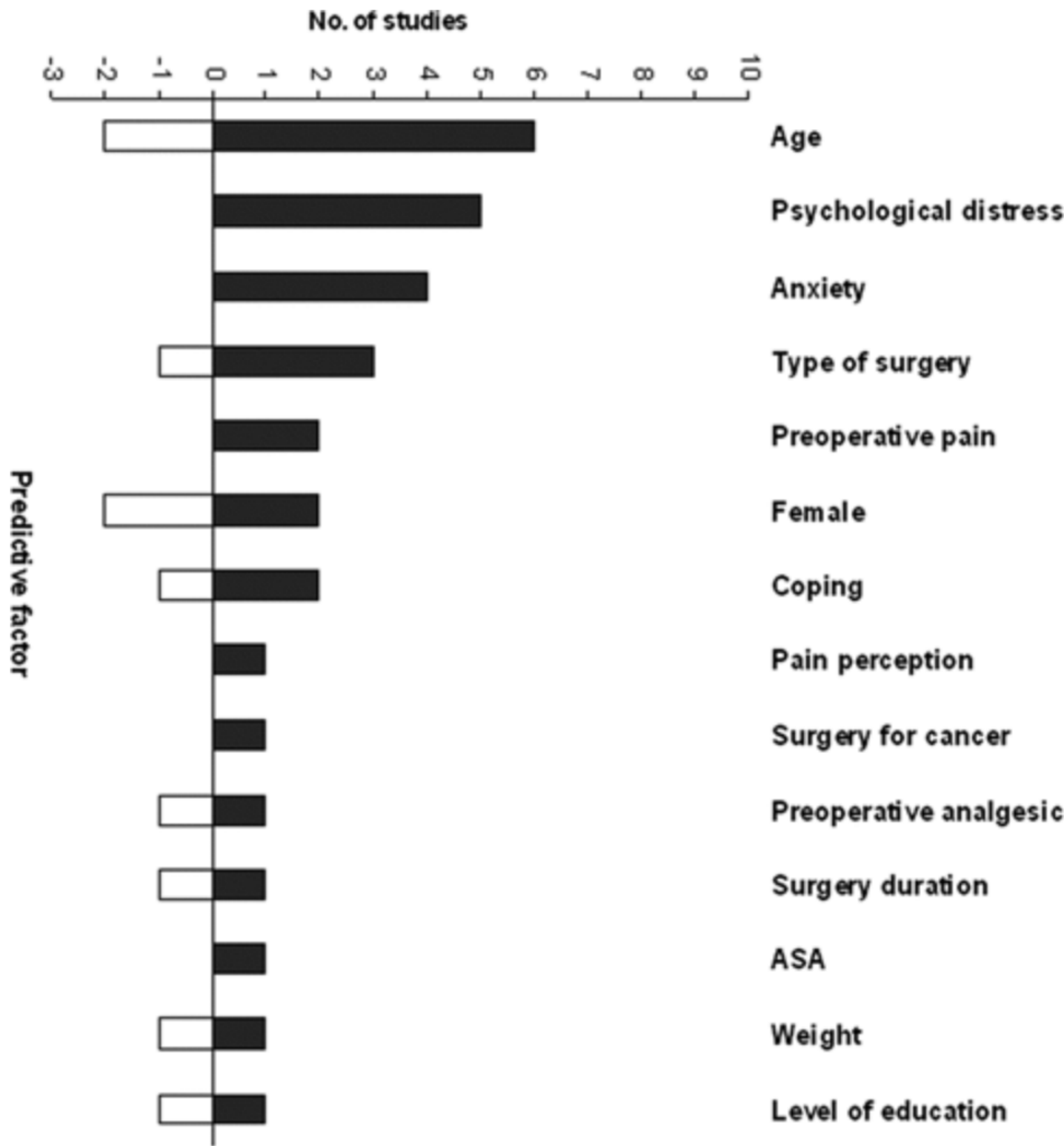
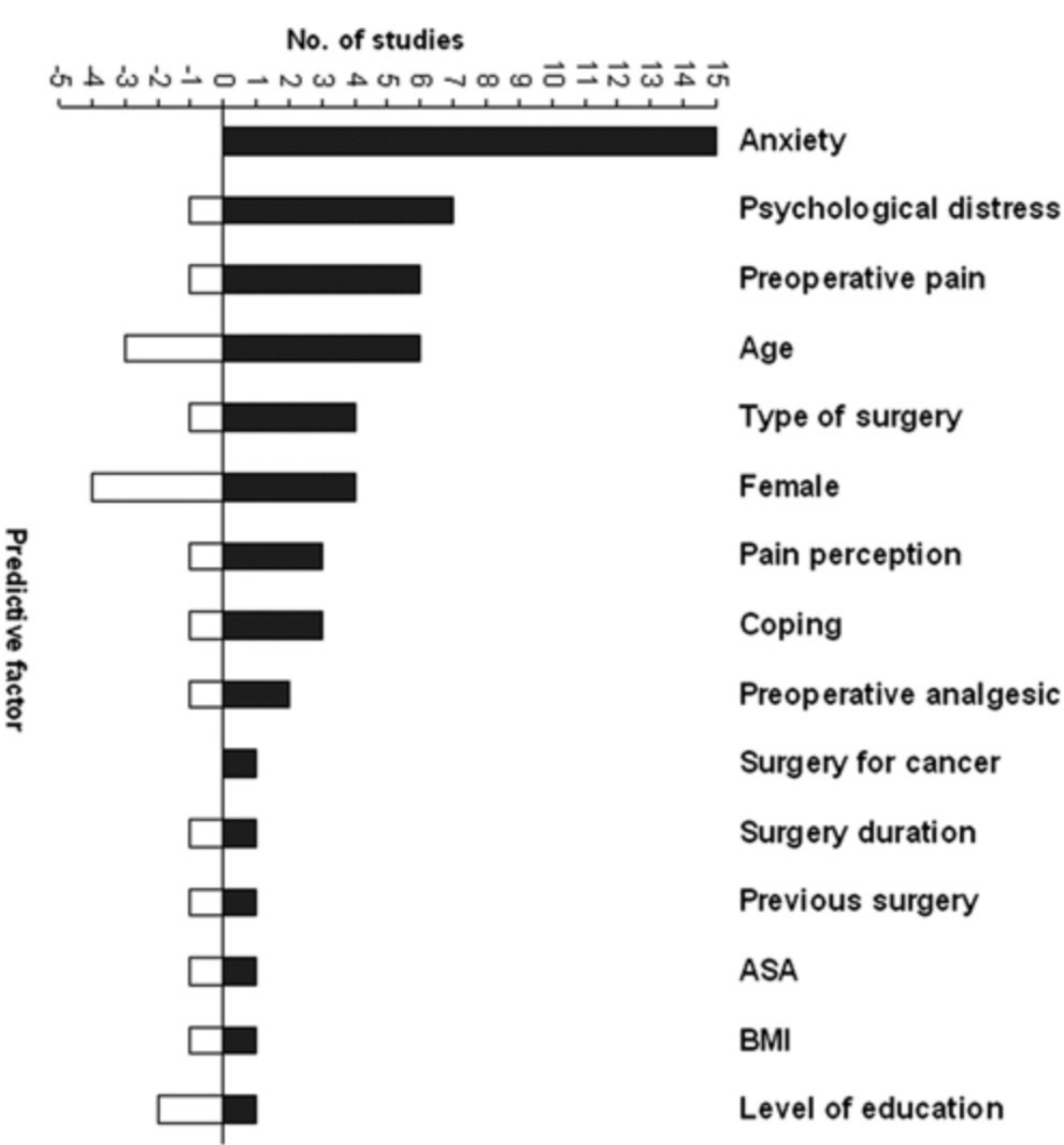
5 MID for opioid consumption

13 included studies

Prædiktorer for postop.

Smerte

Opioidbehov



Preoperative predictors of poor acute postoperative pain control: a systematic review and meta-analysis

Michael M H Yang^{1, 2}, Rebecca L Hartley^{2, 3}, Alexander A Leung⁴, Paul E Ronksley², Nathalie Jetté⁵, Steven Casha¹, Jay Riva-Cambrin^{1, 2}

Smerte

Younger age (n=14)

Female sex (n=20)

Smoking (n=9)

History of depressive symptoms (n=8)

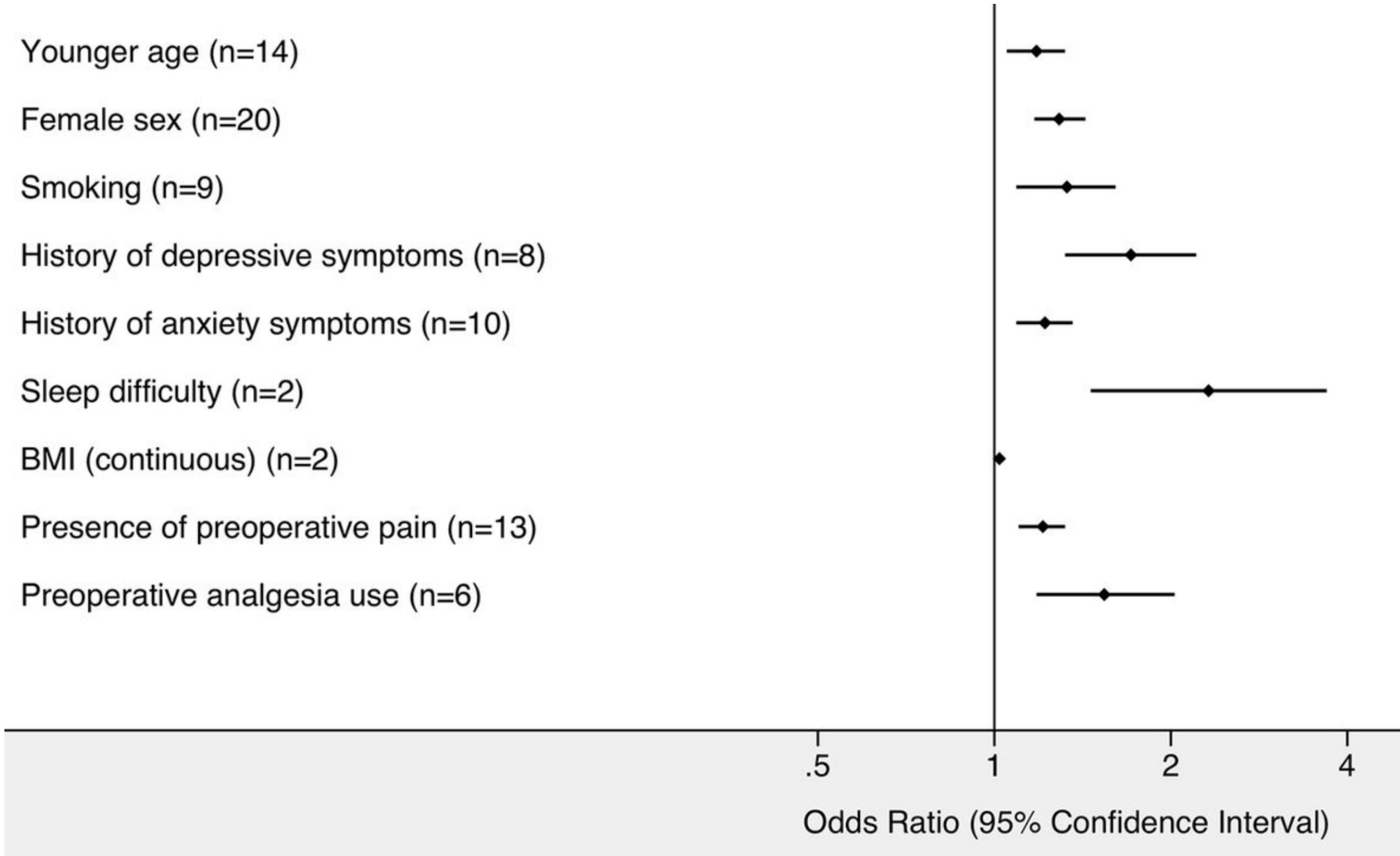
History of anxiety symptoms (n=10)

Sleep difficulty (n=2)

BMI (continuous) (n=2)

Presence of preoperative pain (n=13)

Preoperative analgesia use (n=6)



Pain sensitivity som prædikator

PAIN

Preoperative pain sensitivity and its correlation with postoperative acute and chronic pain: a systematic review and meta-analysis

Fan Wu^{1,†}, Jiehui Liu^{1,†}, Liang Zheng^{2,†}, Changqi Chen¹, Diksha Basnet¹, Jingya Zhang¹, Chaonan Shen², Xuanran Feng¹, Yiyang Sun¹, Xue Du¹, Jialin C. Zheng^{3,4,*} and Jianhui Liu^{1,*}

Konklusion; afhænger af testværktøjet (eller er drevet af tilfældigheder)

Postoperative pain was **negatively** associated with **pressure pain** threshold and **electrical pain** threshold

Postoperative pain was **positively** correlated with **temporal pain summation** and **Pain Sensitivity Questionnaire**

Nuværende prædiktionsmodeller

Personalized perioperative pain management: a systematic review

Formål:

To review developed or tested personalized systems for perioperative systemic analgesic management and their potential effect on perioperative pain outcomes

Population:

Voksne kirurgiske patienter

Intervention:

1) Algoritmebaseret behandling:

- Intraoperativt
- 0-24 timer postoperativt

2) Risikostratificering:

- Prædiktionsmodeller for postoperativ opioidforbrug
- Prædiktionsmodeller for moderat til svær smerte (inkluderes ikke i review)

Outcomes

- Smerte
- Opioidforbrug
- Opioid bivirkninger
- Serious adverse events
- Indlæggelsestid

v/ ph.d.-studerende Pernille Sunde,

Nuværende prædiktionsmodeller

Hvad fandt vi?

Algoritmebaseret behandling:

- Intraoperative nociception monitoring

Risikostratificering:

- Prædiktionsmodeller for postoperativ opioidforbrug

Vi har ikke fundet

- Individualiseret algoritmer for smertestillende behandling

Nuværende prædiktionsmodeller

NOCICEPTION monitoring

- Bruger objektive, fysiologiske data til at vurdere smerte og behovet for smertestillende medicin under og efter operationer.
- Metoder
 - Nociception Level Index (NOL)
 - Analgesia Nociception Index (ANI)
 - Surgical Pleth Index (SPI)
 - Pupillary Pain Index (PPI)

Author (publication year)	Model type	Overall bias	# Partici-pants	Surgery type	Postoperative pain	Postoperative opioid use	ORADEs
Espitalier (2021)	NOL	High	70	Gynecology laparoscopic surgery	No effect	Decreased (not significant)	Sedation: No effect
Fuica (2023)	NOL	Unclear	75	Major abdominal surgery	Less pain 0-2h, p <0.05	No effect	N/A
Meijer (2020)	NOL	Low	50	Abdominal surgery	Less pain 0-2h, p <0.05	No effect	Nausea: No effect
Ruetzler (2023)	NOL	High	72	Major abdominal surgery	No effect	No effect	Nausea: No effect
Funcke (2020)	SPI, PPI, NOL	Low	48	Radical retropubic prostatectomy	No effect	No effect	N/A
Won (2016)	SPI	Unclear	45	Thyroidectomy	No effect	N/A	Nausea: No effect Sedation: No effect
Dostalova (2019)	ANI, SPI	High	72	Spinal surgery	No effect	N/A	N/A
Szentai (2015)	ANI	Low	120	Laparoscopic cholecystectomy	No effect	No effect	Nausea: No effect

Nuværende prædiktionsmodeller

Prædiktionsmodeller for 0-24 timers postoperativt opioidforbrug

Hvad er en prædiktionsmodel?

Et værktøj, der anvender data og statistiske metoder eller algoritmer til at forudsige specifikke udfald.

Hvad skal modellen fortælle os?

Forventet opioidbehov, risiko for ORADEs, optimering af smertelindring

Hvordan bliver den lavet?

Dataindsamling, identifikation af variabler/prædiktorer, statistisk analyse, modeludvikling

Hvad er det næste?

Evaluering/validering → implementering → kontinuerlig overvågning

Hvad findes der?

- Ingen prædiktionsmodeller som fortæller os hvad vi skal gøre
- Prædiktionsmodeller: moderat til højt opioidforbrug
- Prædiktionsmodeller: moderate til svære smerter

Author, Year, Operation/setting	Modelling method	Sample size	No predictors		Selection of candidate predictors	Selection of final predictors	Model performance	PROBAST SUMMARY	
			Cand.	Final				RoB	Applicability
Nair, 2020 Ambulatory surgery	Machine learning techniques	10960 (80% dataset)	32	32	Based on prior knowledge	Unclear	Accuracy 72%	-	-
Kumar, 2023 Major breast surgery	Machine learning techniques	206 (80% of dataset)	21	8	Based on prior knowledge	Stepwise selection	R-squared: 0.313	-	-
Yoshida, 2015 Development Mandibular osteotomy	Multiple linear regression	354	10	6	Based on prior knowledge	Stepwise selection	R-squared: 0.185	-	-
Yoshida, 2015 External validation Open abdominal surgery	Multiple linear regression	354	10	6	Based on prior knowledge	Stepwise selection	R-squared: 0.100	-	-
Tsuboi, 2022 Open abdominal surgery	Multiple linear regression	179	42	9	Based on prior knowledge	Stepwise selection	R-squared: 0.302	-	-
Dolendo, 2022 Elective mastectomy	Multivariable logistic regression	148	27	11	All available predictors	Stepwise selection	R-squared: 0.777	-	-
Hu, 2018 Several different surgeries	Machine learning techniques	3.052	15	15	All available predictors	No information	RMSE: 2.97 mg	-	-
Pan, 2006 Cesarean section	Multiple linear regression	34	5	2	Other	Stepwise selection	R-squared: 0.270	-	-

1

Baggrund

OPIAID Survey

**Danish perioperative opioid administration and clinician-
perceived factors for dose adjustments in adults:
a nationwide survey**

Trang Xuan Minh Tran, Mik Wetterslev, Anders Kehlet Nørskov,
Christian Sylvest Meyhoff, Markus Harboe Olsen, Theis Skovsgaard Itenov,
Ole Mathiesen, Anders Peder Højer Karlsen, and OPI•AID Collaborators



CEPRA



Bispebjerg og Frederiksberg
Hospital

v/ Trang Xuan Minh Tran, stud.med
Anæstesiologisk Forskningsenhed

1

Baggrund

2

Metode

3

Resultater

4

Hoved
budskaber

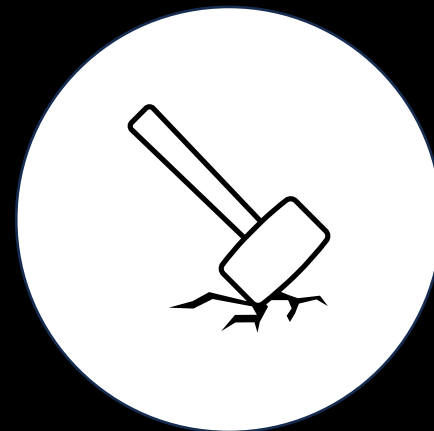
OPIOID PRAKSIS

Hvad er kontekst?



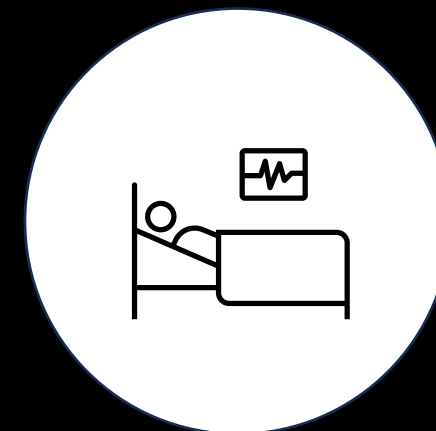
300 MILLIONER

Årlige operationer globalt



30-60% PATIENTER

Moderate til svære akutte
postoperative smerter
el. bivirkninger

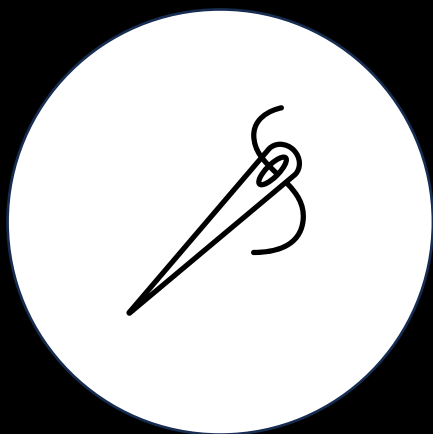


FORBEDRINGER

Ressourcer, recovery, risici

OPIOID PRAKSIS

Hvilken evidens?



PRÆDIKTORER

Begrænset viden om demografiske og kirurgiske faktorer



GUIDELINES

Ingen evidensbaserede guidelines vedr. faktorerers indflydelse

Variation?

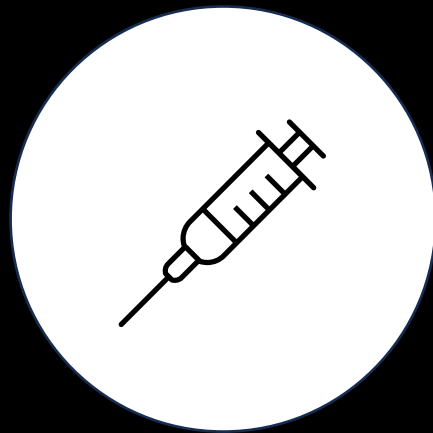


TILTAG

Ekspert-vejledninger, klinisk erfaring, lokale guidelines

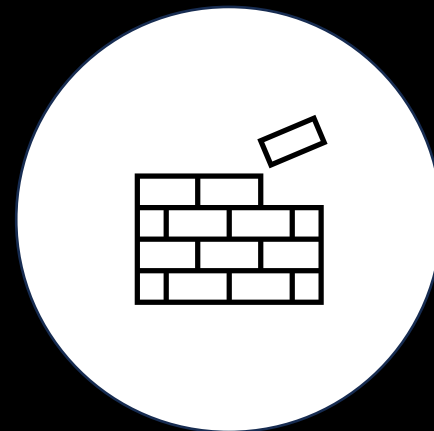
OPIOID PRAKSIS

Forskningsspørgsmål



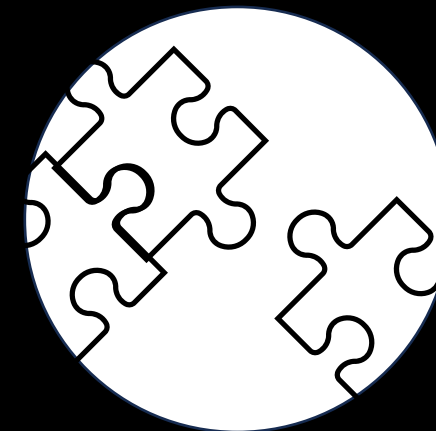
HVILKE OPIOIDER?

Hvad er de foretrukne?



HVOR MEGET?

Hvor meget? Variation?



HVILKE FAKTORER?

Inddrages i doseringsvalg?

METODE

POPULATION

Anæstesilæger



Demografi
Intra- og postoperativ fase

Anæstesisygeplejersker



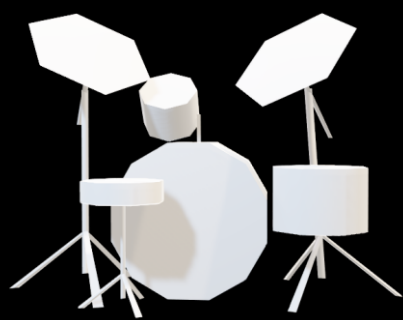
Demografi
Intraoperativ fase

Opvågningssygeplejersker

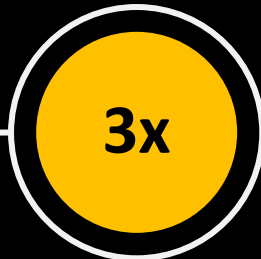


Demografi
Postoperativ fase +
bivirkninger

TIDSLINJE

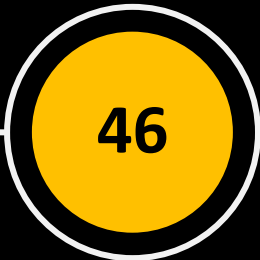
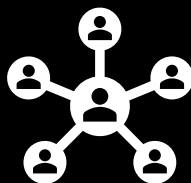


okt 2023 – jan 2024



dec 2023 - jan 2024

jan – feb 2024



METODE

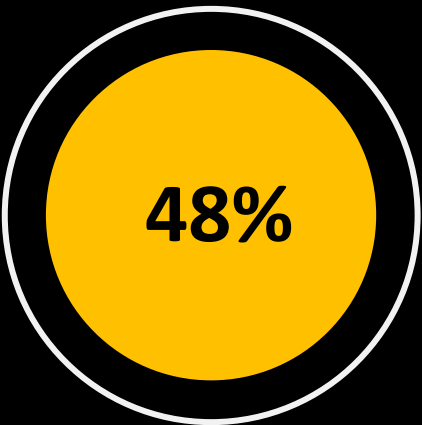
Løbende svarprocenter



05 februar 2024

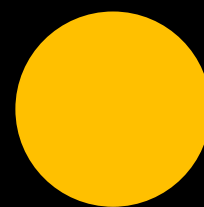


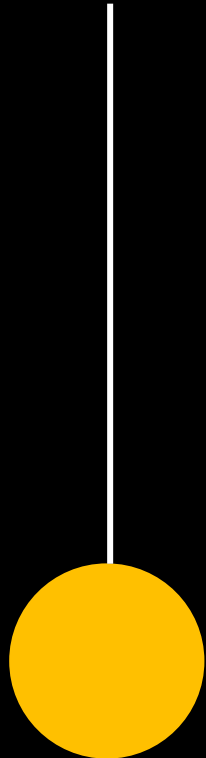
30 april 2024



RESULTATER

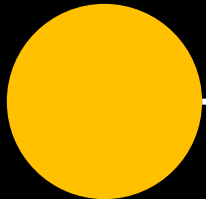
HOVEDBUDSKABER





VARIATION: FORETRUKKET OPIOID OG DOSIS

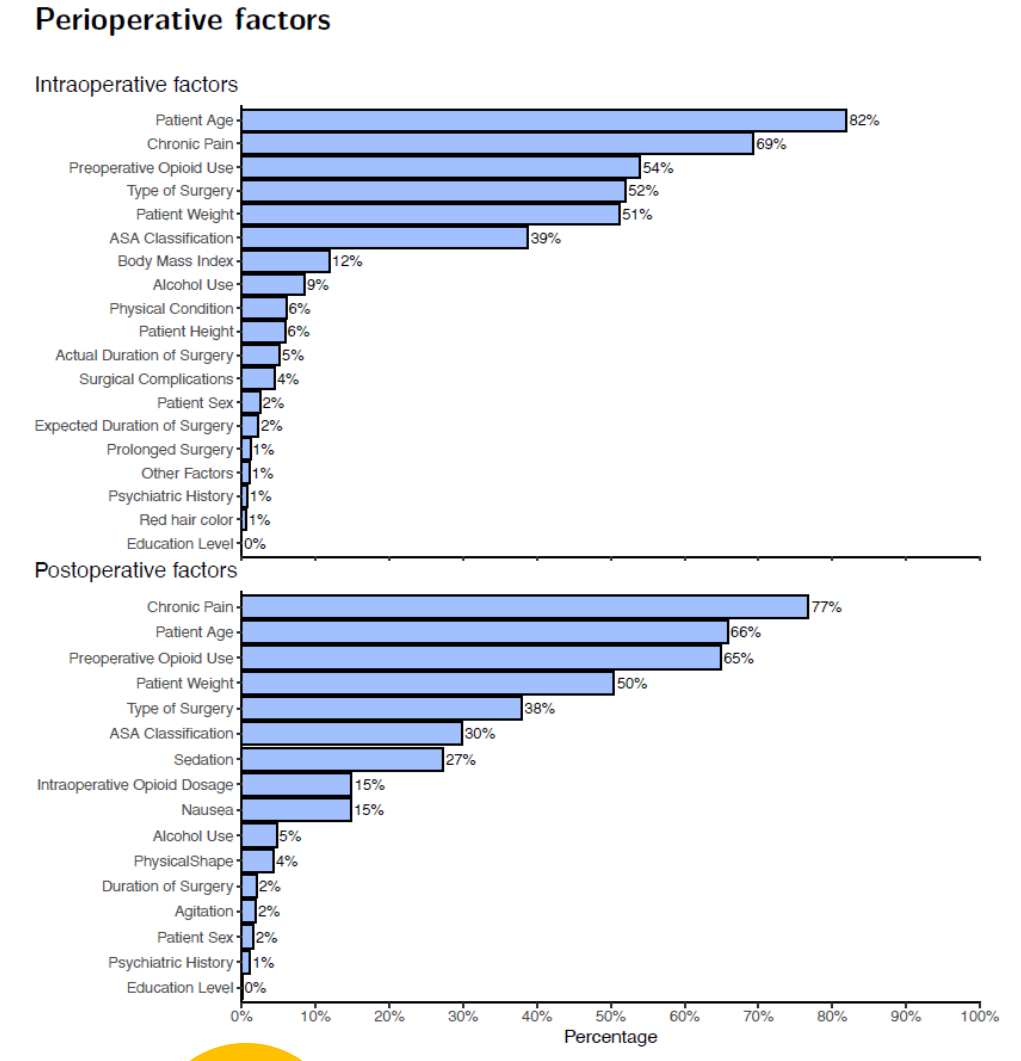
Behandlingsvariation for ensartede patientpopulationer

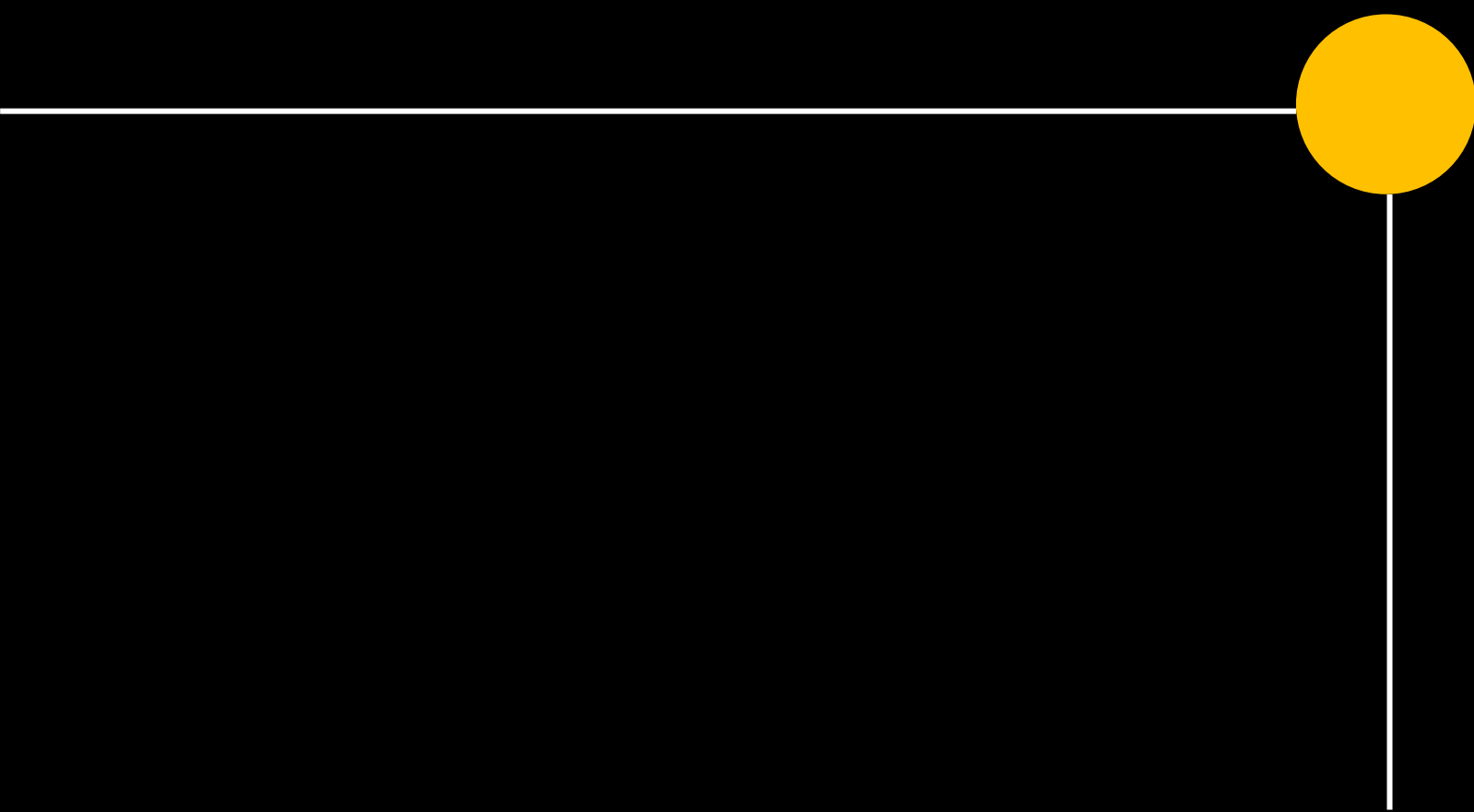


RESULTATER

FAKTORER

Alder, vægt, kroniske smerter, præoperativ opioid, type kirurgi





GUIDELINES

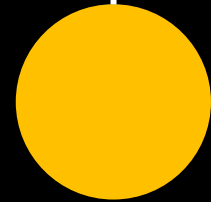
84-89 %

Guidelines var tilgængelige
Fulgte guidelines i høj grad

RESULTATER

FORETRUKKET INTRAOPERATIV OPIOID

Fentanyl, morfin, oxycodon

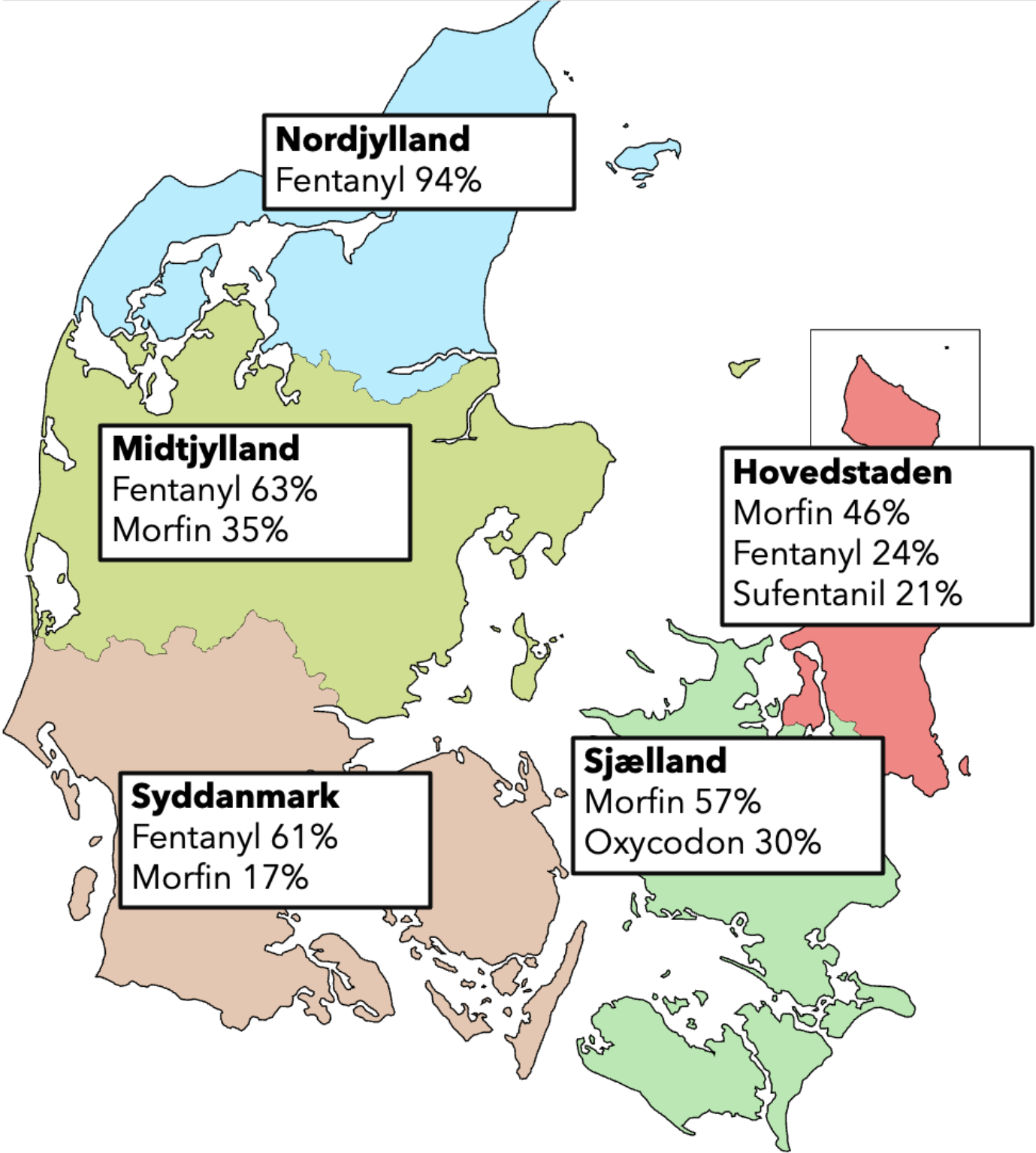


FORETRUKKET POSTOPERATIV OPIOID

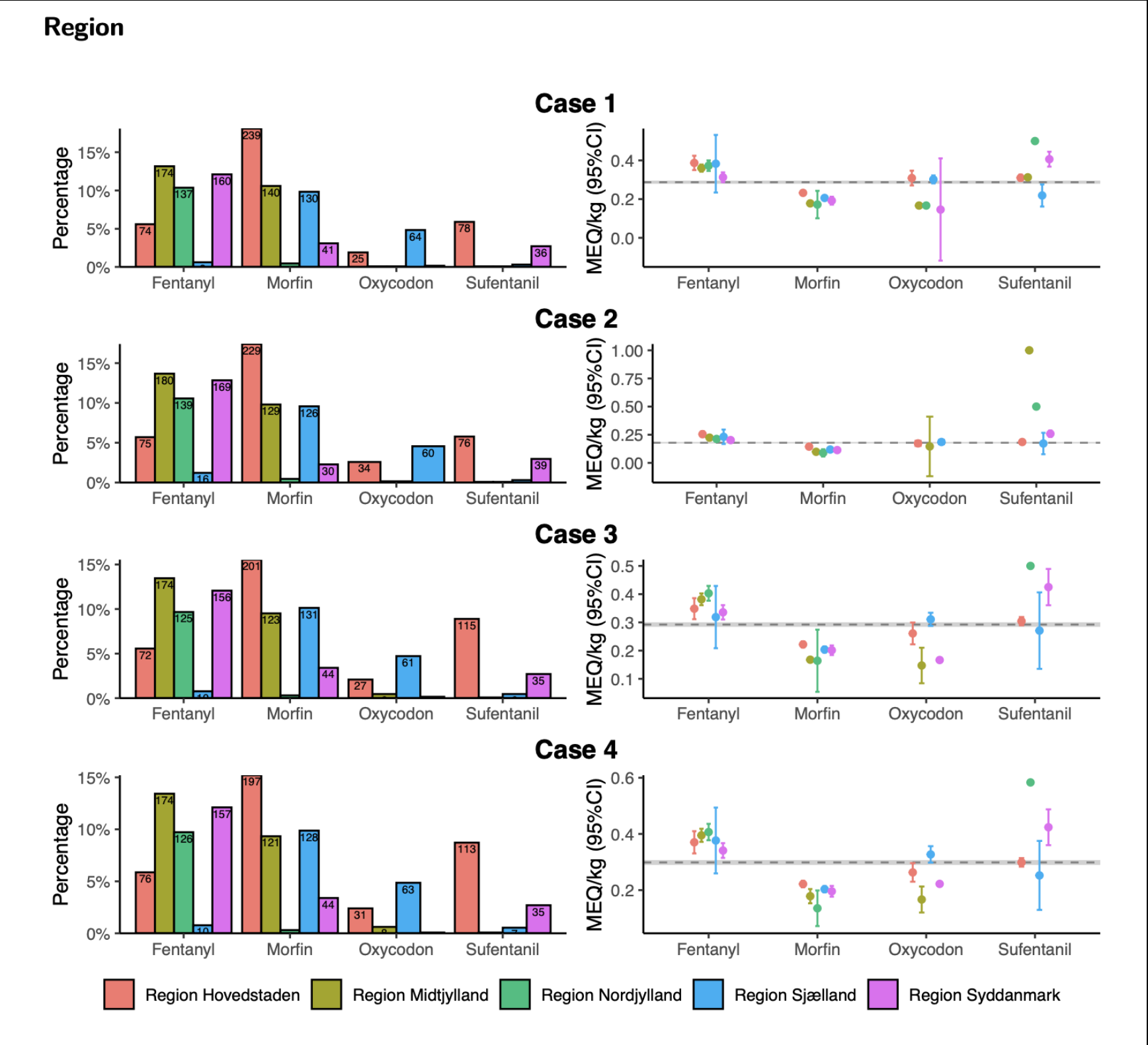
Morfin i.v. (moderate smerter)
Fentanyl i.v. / morfin i.v. (svære smerter)
Fentanyl i.v. / oxycodon i.v.
(svære smerter + bivirkninger)

Regionale forskelle

Foretrukne førstevalgsopioider



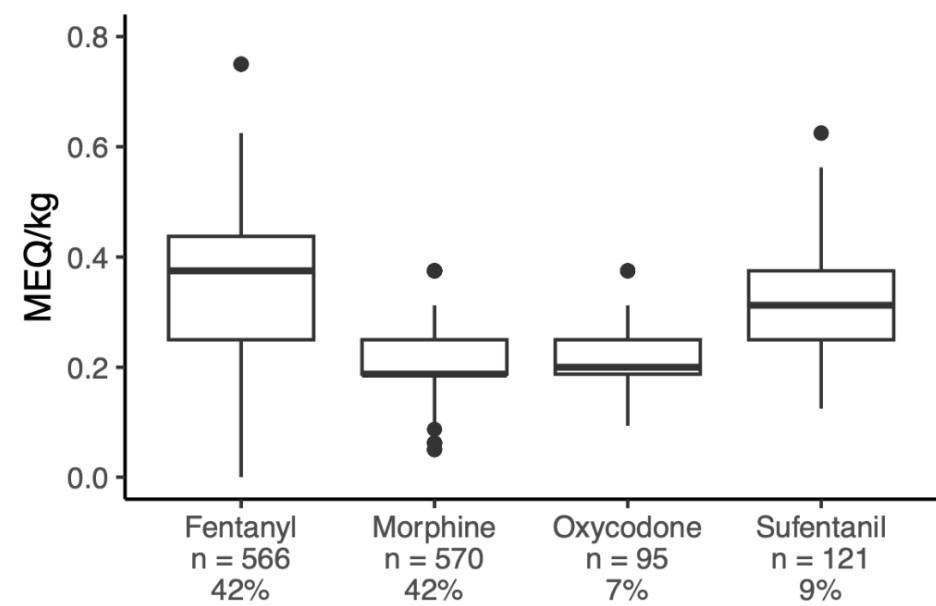
Regionale forskelle: Intraoperative cases



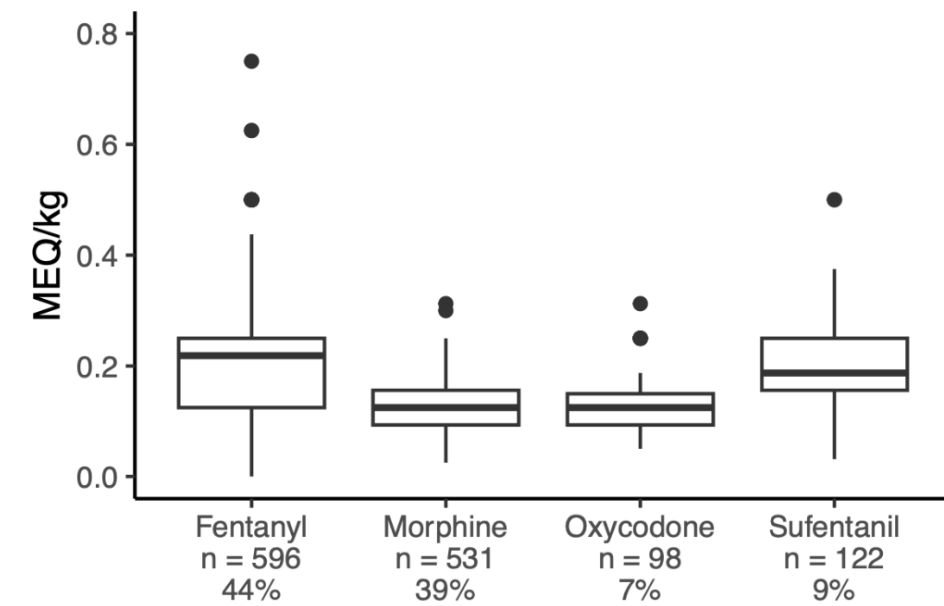
INTRAOPERATIVE CASES

Median spænd: 0.2-0.4 mg/kg i.v. MEQ

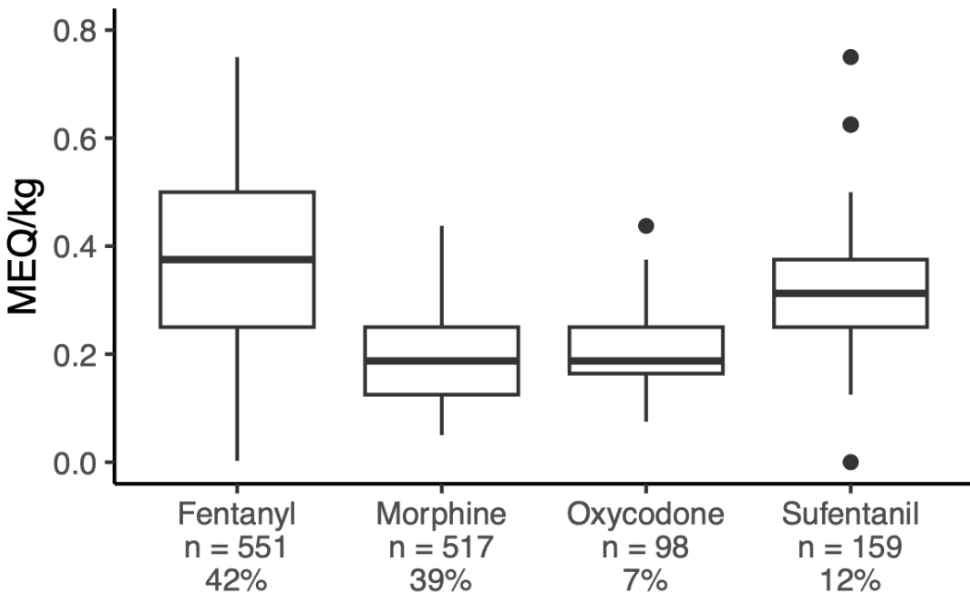
CASE 1 | 30 years old male, 180 cm, 80 kg, ASA 1, anterior cruciate ligament reconstruction



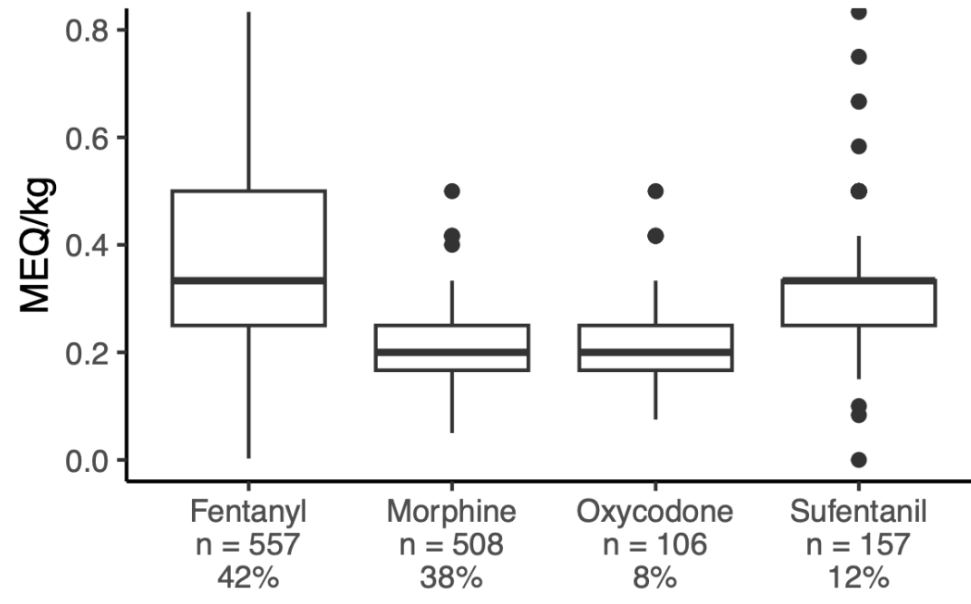
CASE 2 | 80 years old male, 180 cm, 80 kg, ASA 3, anterior cruciate ligament reconstruction



CASE 3 | 30 years old male, 180 cm, 80 kg, ASA 1, laparoscopic cholecystectomy

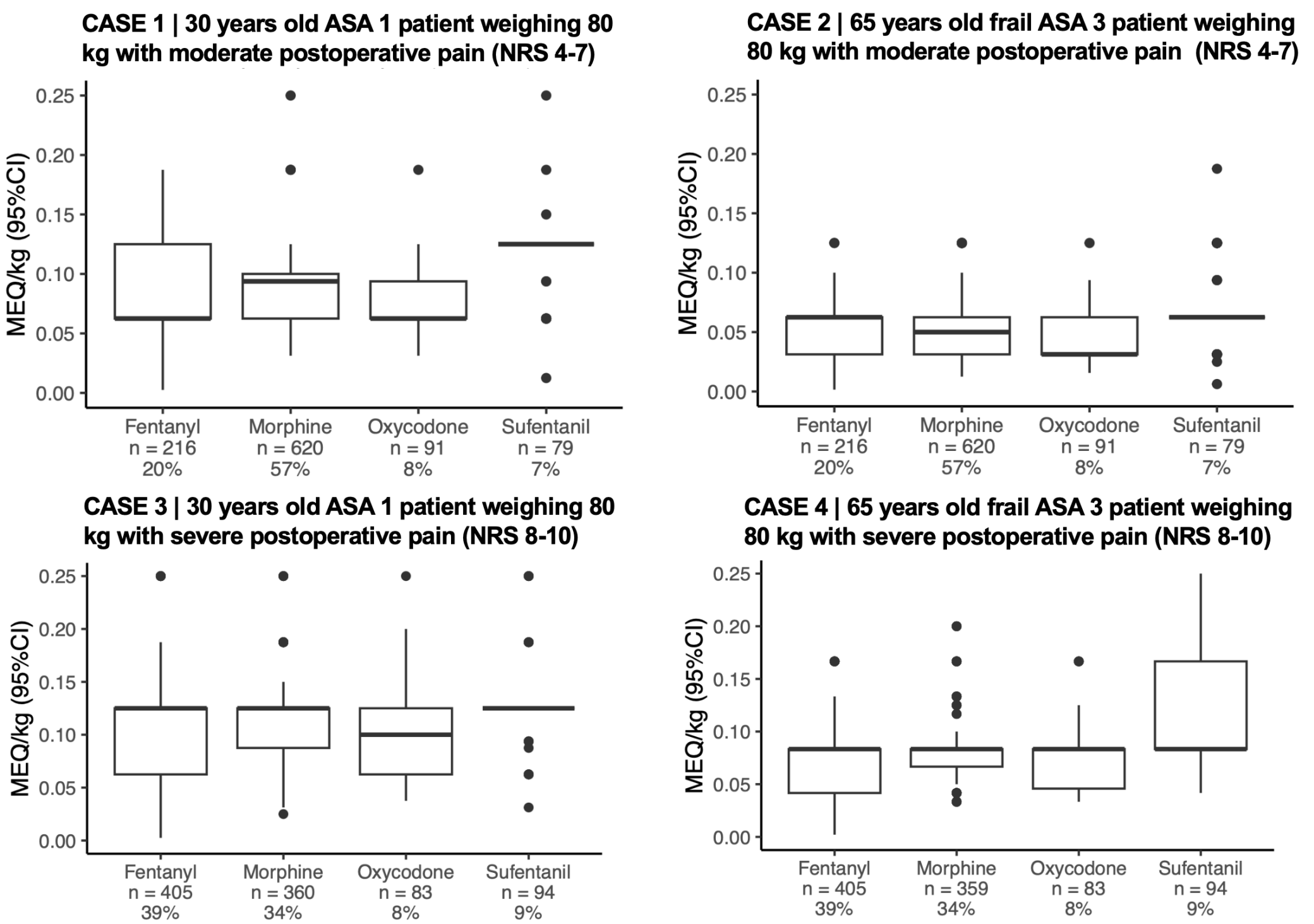


CASE 4 | 30 years old female, 180 cm, 60 kg, ASA 1, laparoscopic cholecystectomy



POSTOPERATIVE CASES

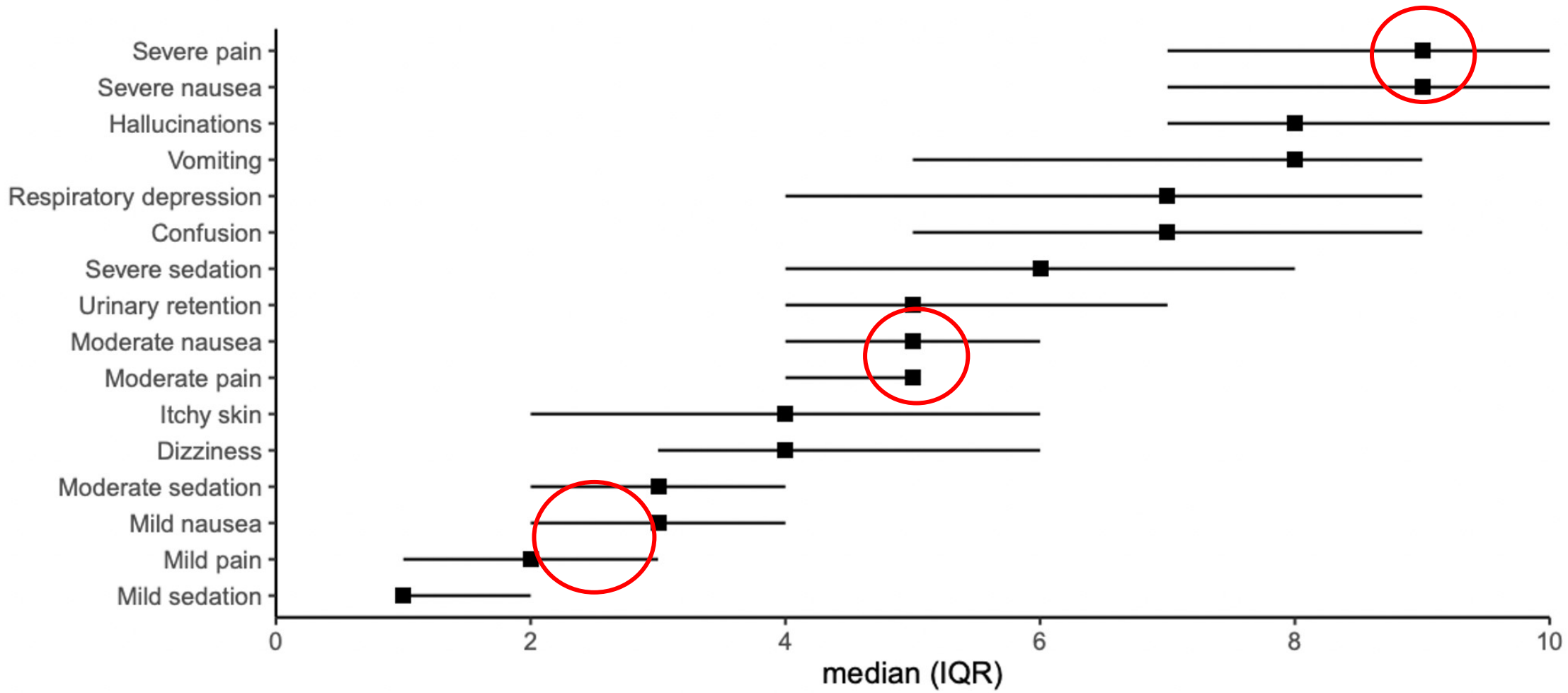
Median spænd: 0.06-0.12 mg/kg i.v. MEQ



ORADES

Hvad mener opvåkningssygeplejersker?

Figure 4: Perceived impact of postoperative pain and ORADEs on patient recovery



DATABASEN



DATABASEN

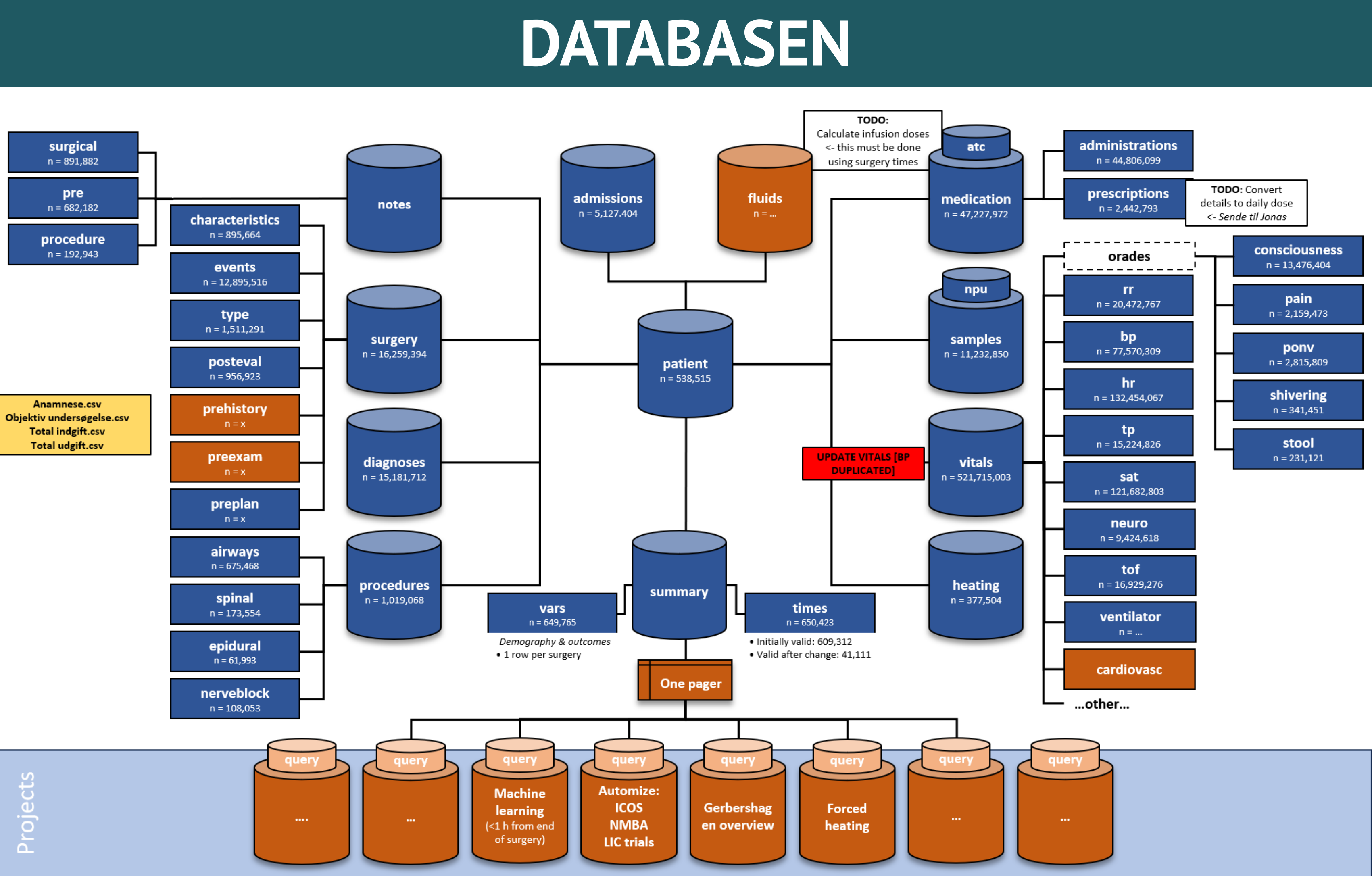
The diagram illustrates a complex database schema for a medical database, centered around a **patient** table (n = 538,515). The schema is organized into several main categories:

- Administrative and Patient Information:**
 - admissions** (n = 5,127,404)
 - fluids** (n = ...)
 - medication** (n = 47,227,972) with sub-tables **atc** and **npu**
 - samples** (n = 11,232,850)
 - vitals** (n = 521,715,003) with a red box indicating **UPDATE VITALS [BP DUPLICATED]**
 - heating** (n = 377,504)
 - vars** (n = 649,765) with a note: *Demography & outcomes*, 1 row per surgery
 - times** (n = 650,423) with notes:
 - Initially valid: 609,312
 - Valid after change: 41,111
- Medical History and Procedures:**
 - notes** (n = 16,259,394)
 - surgery** (n = 16,259,394)
 - diagnoses** (n = 15,181,712)
 - procedures** (n = 1,019,068)
 - characteristics** (n = 895,664)
 - events** (n = 12,895,516)
 - type** (n = 1,511,291)
 - posteval** (n = 956,923)
 - prehistory** (n = x)
 - preexam** (n = x)
 - preplan** (n = x)
 - airways** (n = 675,468)
 - spinal** (n = 173,554)
 - epidural** (n = 61,993)
 - nerveblock** (n = 108,053)
- Administrations and Prescriptions:**
 - administrations** (n = 44,806,099)
 - prescriptions** (n = 2,442,793) with a red box indicating **TODO: Convert details to daily dose** and a note: *Sende til Jonas*
 - orades** (n = 13,476,404)
 - consciousness** (n = 13,476,404)
 - pain** (n = 2,159,473)
 - ponv** (n = 2,815,809)
 - shivering** (n = 341,451)
 - stool** (n = 231,121)
 - cardiovasc** (n = ...)
 - ...other...**
- Summary and Reporting:**
 - summary** (n = 649,765)
 - One pager**
- Projects and Analytics:**
 - query** (n = ...)
 - Machine learning** (<1 h from end of surgery)
 - Automize: ICOS NMBA LIC trials**
 - Gerbershag en overview**
 - Forced heating**
 - ...**

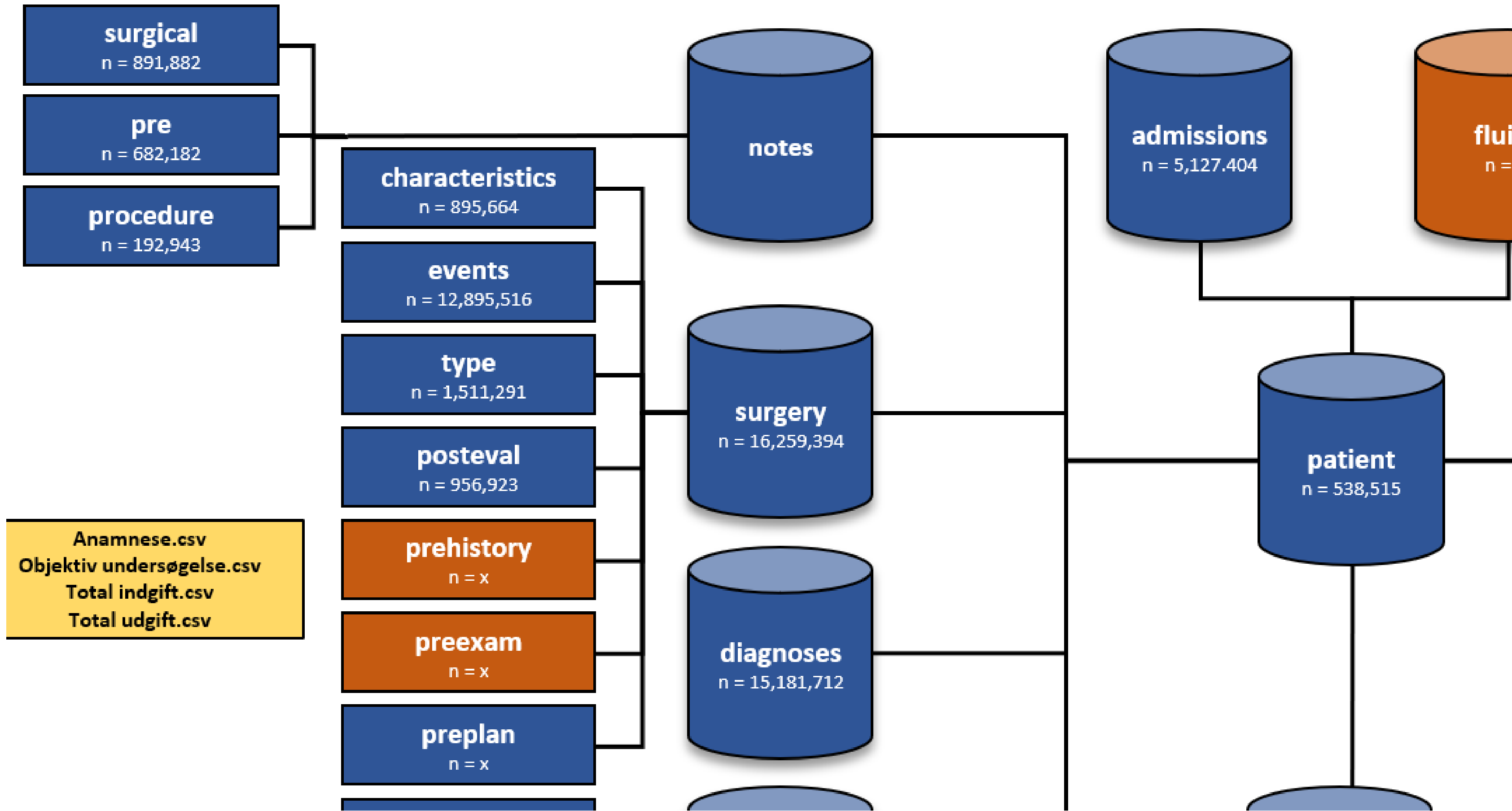
Additional Information:

- TODO:** Calculate infusion doses <- this must be done using surgery times
- TODO:** Convert details to daily dose <- Sende til Jonas
- UPDATE VITALS [BP DUPLICATED]**
- cardiovasc** (n = ...)
- ...other...**

The diagram shows a hierarchical structure where the **patient** table is the central entity, with various other tables branching out to store detailed medical and administrative data. The **query** table is used for data retrieval, and the **Projects** section lists specific analytical tasks and reports.



DATABASEN

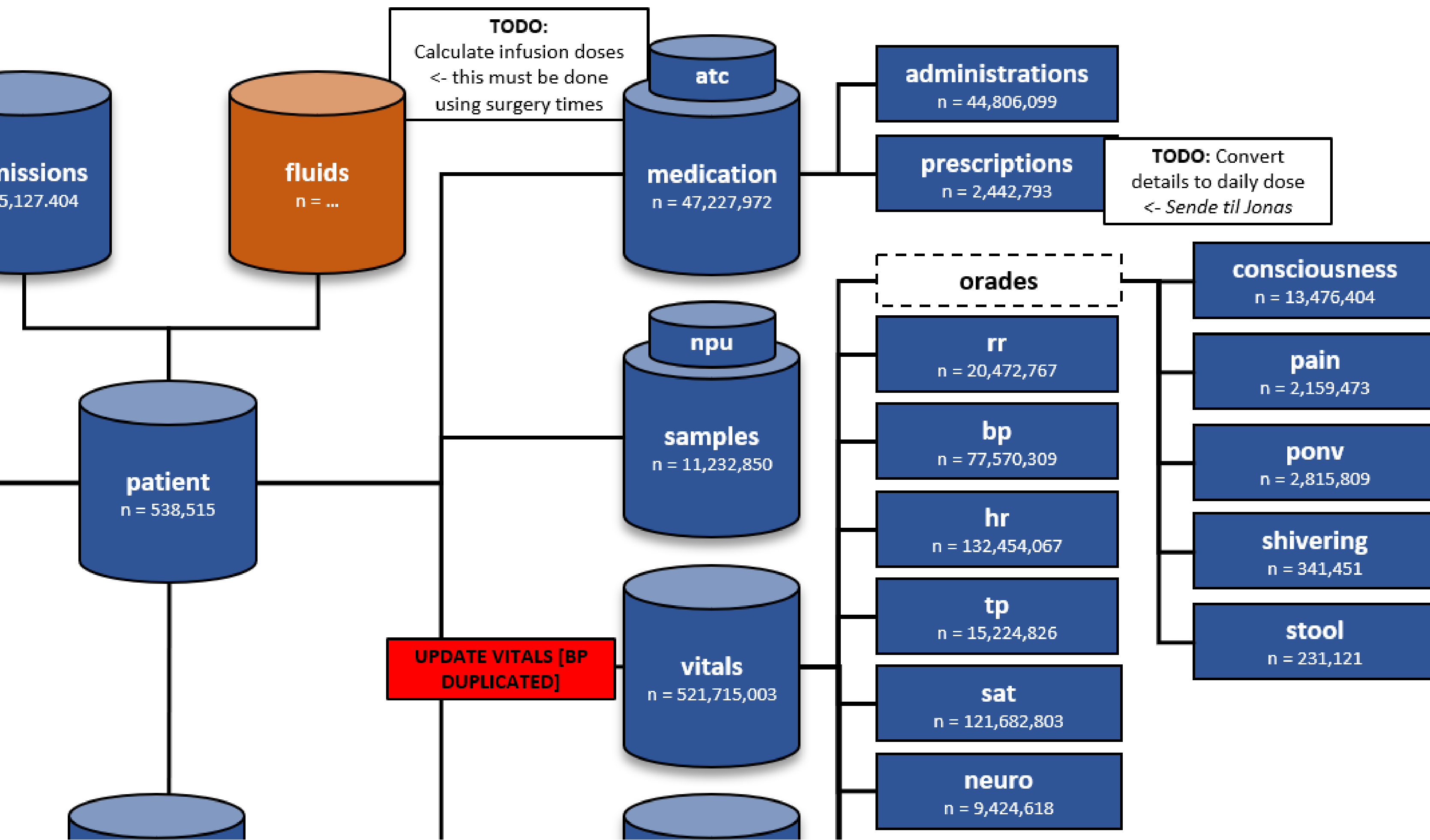




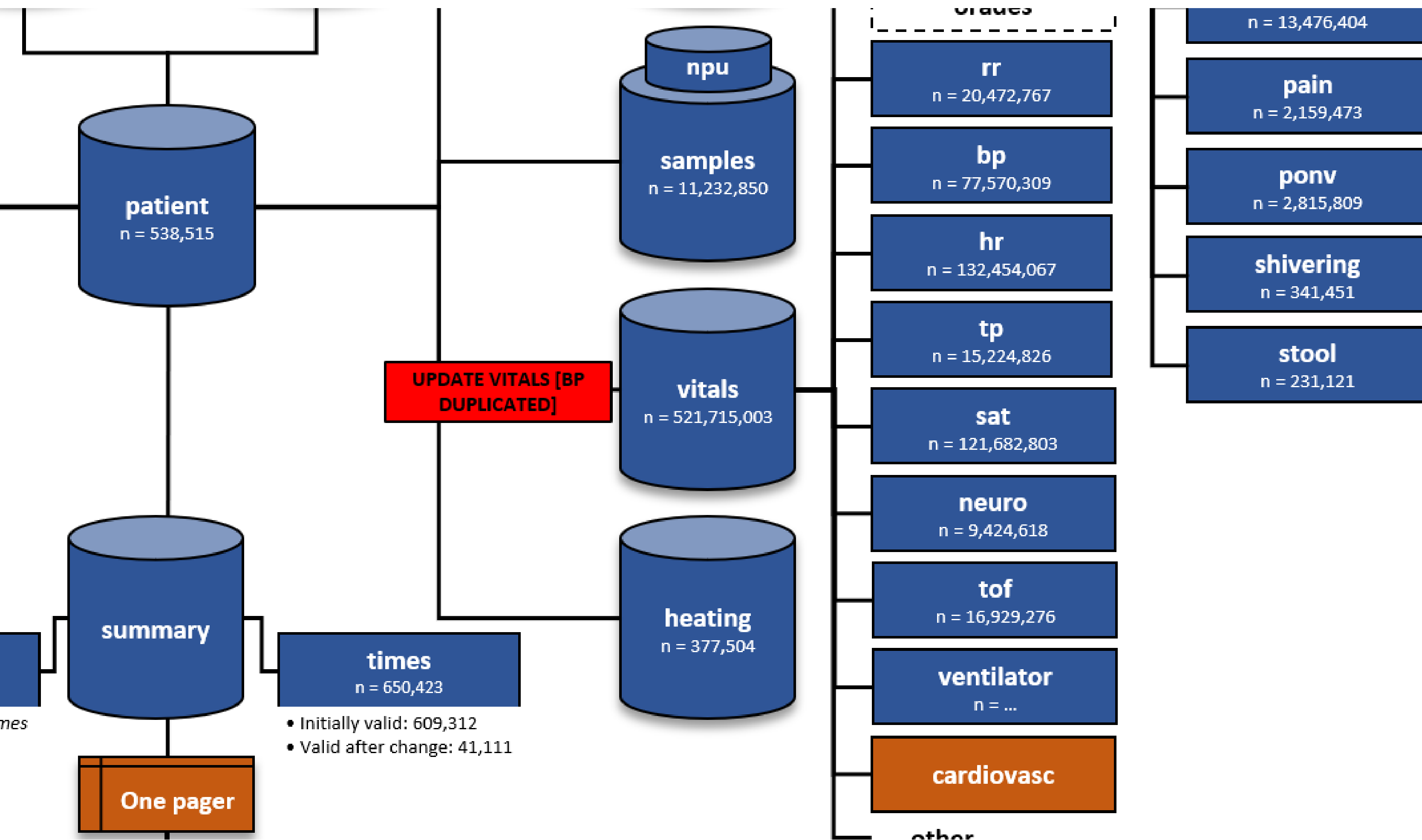
INDGREBSOPRYDNING

	A	B	C	D	E	F	G
1	original operationsbooking	SKSkode	SKSkodenavn	FREKVEN	SPECIAL/ANATOMISK PLACER	et udfø	Udført operation
8253	TOTAL THYREOIDECTOMI + NECK	KBAA60, KBBA70, KPJ	IMPLANT. EL. TRANSPLANTATION AF BISKJOLDBRUSKKIR	22	ØNH HALS	THYROIDE	THYROIDEKTOMI TOTAL
8254	TOTAL THYREOIDECTOMI + NECK	KBAA60, KPJD51	RADIKAL EXCISION AF CERVIKALE LYMFEKNUDER, TOTAL	141	ØNH HALS	THYROIDE	THYROIDEKTOMI TOTAL
8255	TOTAL THYREOIDECTOMI + NECK	KBAA60, KPJD51, KUD	FLEKSIBEL LARYNGOSKOPI, RADIKAL EXCISION AF CERVIK	48	ØNH HALS	THYROIDE	THYROIDEKTOMI TOTAL
8256	TOTAL THYREOIDECTOMI + NECK	KBAA60, KUDQ12	FLEKSIBEL LARYNGOSKOPI, TOTAL THYROIDEKTOMI	28	ØNH HALS	THYROIDE	THYROIDEKTOMI TOTAL
8257	ATTUNE KNÆ	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	141	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8258	ATTUNE KNÆ	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	149	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8259	PRIMÆR TKA TC3/NOILES	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	27	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8260	TKA	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	170	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8261	TKA	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	45	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8262	TKA - AGC	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	137	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8263	TKA - HÅ PERSONA MC POLY	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	52	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8264	TKA - LCCK	KNGC40	SEK. INDSÆT. AF ALLE KOMP. AF CEMENT. TOTALPROT.	91	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8265	TKA - LPS	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	83	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8266	TKA - NEXGEN	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	624	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8267	TKA - PERSONA BILATERAL	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	42	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8268	TKA - PERSONA MC VS. CR	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	68	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8269	TKA - PFC	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	1030	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8270	TKA - POST STABIL SIGMA	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	20	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8271	TKA - PRIMÆR CEMENTERET	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	348	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8272	TKA - PRIMÆR CEMENTERET	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	160	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8273	TKA - SIGMA CEMENTERET	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	1163	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8274	TKA - SIGMA CEMENTERET	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	29	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8275	TKA - SIGMA CEMENTERET	KNGC40	SEK. INDSÆT. AF ALLE KOMP. AF CEMENT. TOTALPROT.	23	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8276	TKA - SIGMA HYBRID	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	27	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8277	TKA - VE PERSONA MC POLY	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	110	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8278	TKA - FB - CR	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	2155	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8279	TKA - FB - CR	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	254	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8280	TKA - FB - PS	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	50	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8281	TKA - MBT - PS	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	89	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8282	TKA - NEXGEN + PATELLA	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	529	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8283	TKA - NEXGEN + PATELLA	KNGB40, KWAA01	IMPLANTAT INDSAT, PRIMÆR INDSÆTTELSE AF CEMEN	25	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET
8284	TKA - PERSONA VS NEXGEN	KNGB40	PRIMÆR INDSÆTTELSE AF CEMENTERET TOTALPROTESE	83	ORTOPÆD KNÆ/UNDERBEN	TKA	TKA CEMENTERET

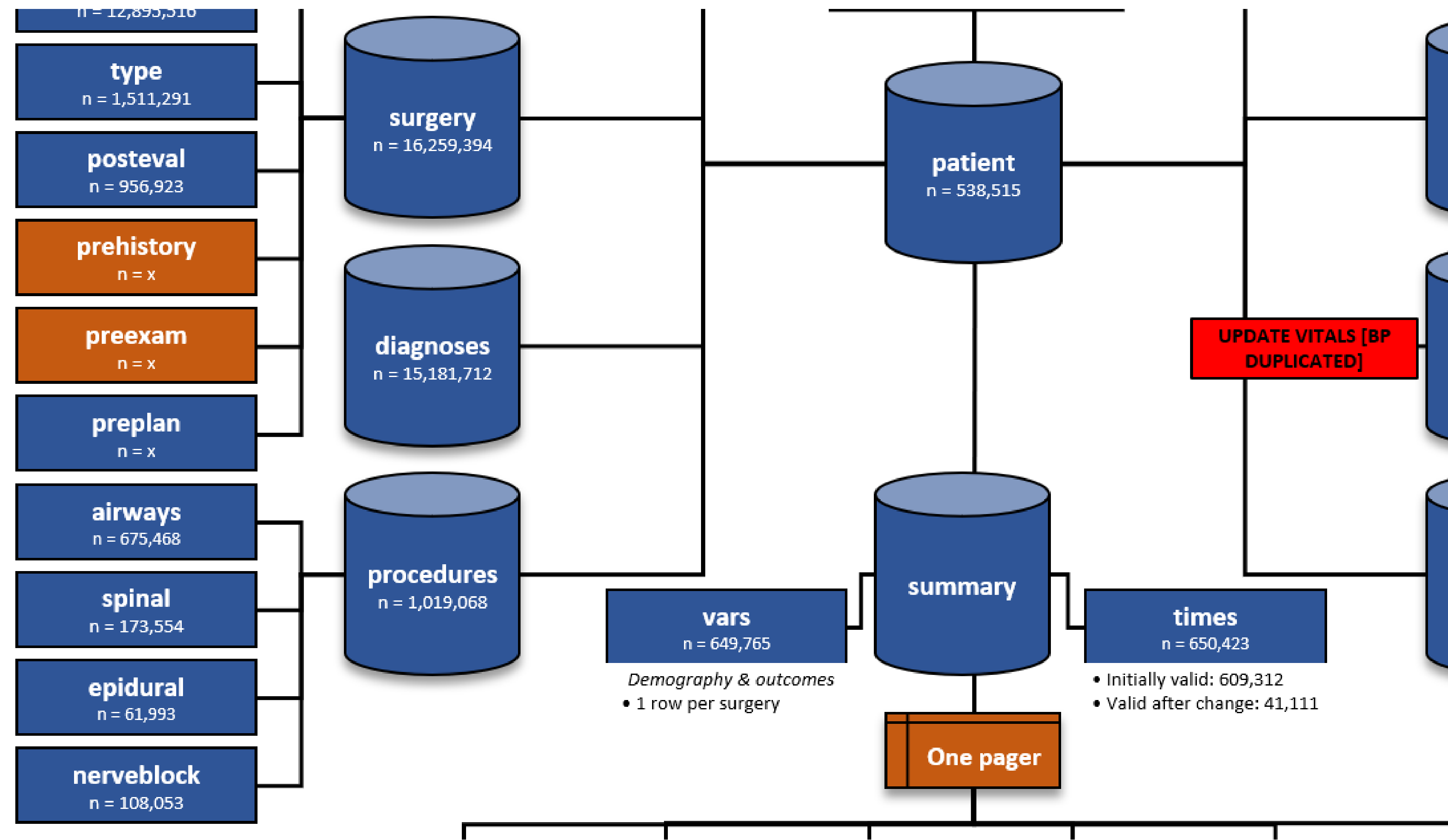
DATABASEN



DATABASES



DATABASEN





VALIDERING

The OPI•AID Retrospective Cohort study, patient data

Patient ID EXAMPLE

Data completeness: 90%

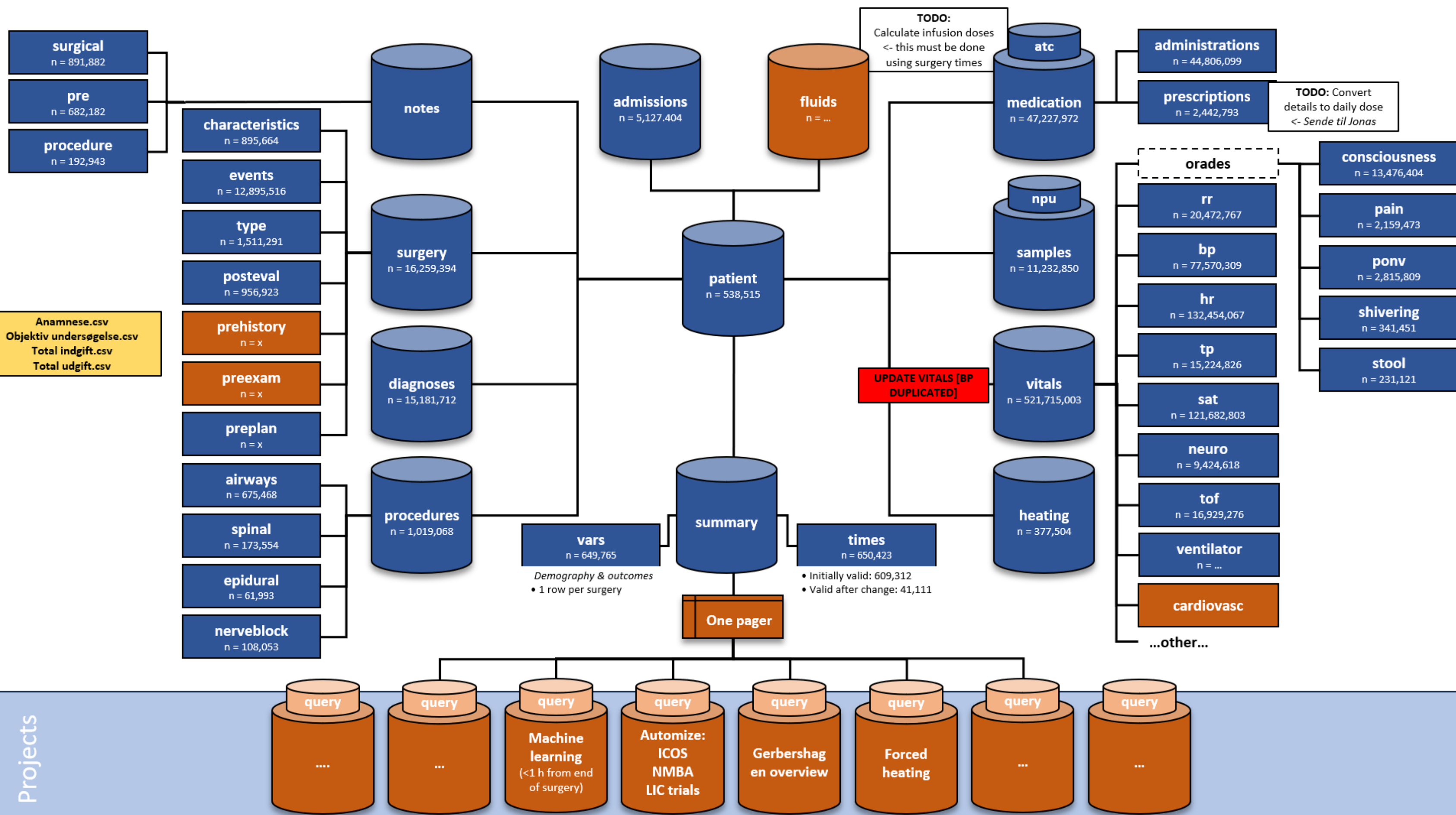
Bispebjerg 17.10.2023 08:30	Anaesthesia General anaesthesia	Procedure Total hip arthroplasty
Patient characteristics	Intraoperative anaesthesia [minutes from end surgery]	Surgery and vitals
ASA 1	Paracetamol [180min]	Duration 90min
Psychiatric diagnosis	Ibuprofene [180min]	500ml bloodloss
Age 60	Dexamethasone 16 mg [150min]	Preop EWS 5 [240min]
Male	LIA ropi 0,25% 10ml [20min]	Preop CRP 40 [1200min]
BMI 25, H 180cm, W 82kg	Ondansetron 4 mg [60min]	Preop Kreatinin 120 [1200min]
Smoking N/A	Remifentanil mean 2.5mg/h	Preop pain: NRS 2 [230min]
Preop opioid: 30 oral MEQ Prior surgery x3: - High opioid requirement - PONV	Propofol mean 40ml/h Fluid balance +1100ml, no blood	
Opioid during surgery	PACU stay	Time to discharge
Oxycodon iv 15mg [60min]	150 minutes	2.2 days

MEQ	Pain	OAE
ΔPACU stay 5mg iv MEQ 2.5mg iv morph	PACU NRS 3 [+0min] NRS 6 [+20min]	PACU Nausea none [+0min] Nausea moderate [+50min]
Δ0-24h 10mg iv MEQ Above doses and 2.5mg iv morph	Δ0-24h NRS 5 [+300min] NRS 3 [+600min]	Δ0-24h Resp. depression [+520min]
ΔHospital 22mg	ΔHospital NRS 6 Worst	ΔHospital PONV: severe Worst Sedation: mild
Postoperative non-opioid analgesic administrations		
6h, 13h, 18h, 24h, Paracetamol: 32h	Ibuprofene: 8h, 17h	Other: N/A
Reoperation	Readmission	ICU during admission
None 6h, 12h, 18h, 24h	None	None
Kidney injury	Infection	Death up to 1 year post-surgery
Kreatinin 190 [30h]	CRP 140 [30h]	No

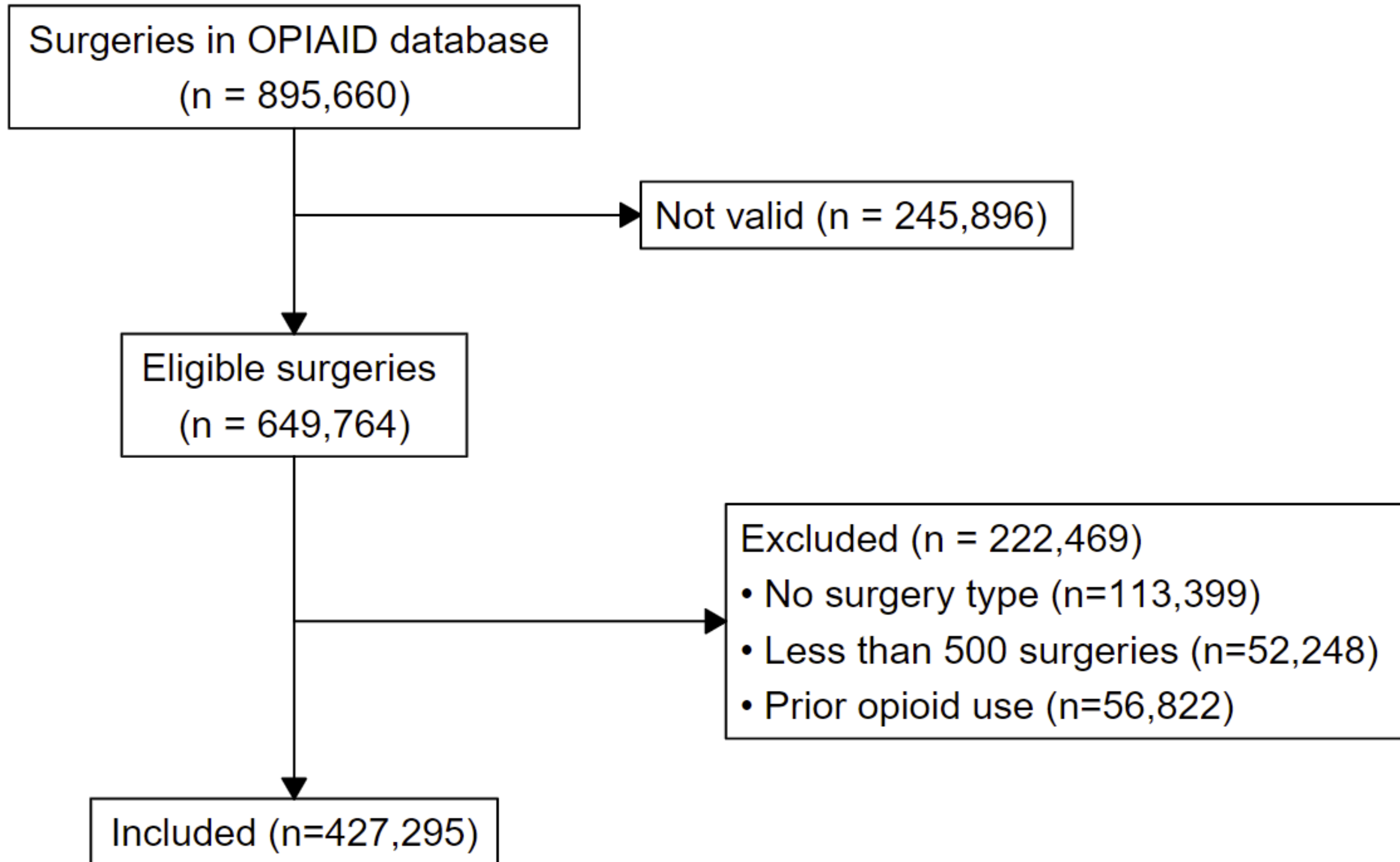
Surgical procedure description

FULL TEXT DESCRIPTION

DATABASEN



SMERTER



SMERTER

Frequency	Procedure
24093	THA (Total Hip Arthroplasty)
20381	Uterine Evacuation
19039	TKA (Total Knee Arthroplasty)
18934	Osteosynthesis Near Hip Fracture
16964	Esophago/Gastro/Duodenoscopy
14912	Cholecystectomy
14877	Emergency C-section
13731	Elective C-section
12710	Laparoscopic Appendectomy
10928	TUR-B (Transurethral Resection of the Bladder)
	...

SMERTER										
Surgery	Age	Female	BMI	ASA				Smokers	Alcohol	Exluded due
	median [IQR]		median [IQR]	1	2	3	4+		abuse	to prior opioids use
		n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n/N (%)
All (n=427674)	56 [36;71]	257156 (60.1%)	26 [23;30]	112186 (27.4%)	215155 (52.6%)	76253 (18.6%)	5280 (1.3%)	70378 (19.9%)	8368 (6%)	56884/484558 (11.7%)
.										
Surgery	Age	Female	BMI	ASA				Smokers	Alcohol	Exluded due
	median [IQR]		median [IQR]	1	2	3	4+		abuse	to prior opioids use
		n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n/N (%)
OSTEOSYNTSE	81	7677	23	642	5262	5392	346	2016	410 (11%)	2481/14201
HOFTENÆR	[73;87]	(65.5%)	[21;26]	(5.5%)	(45.2%)	(46.3%)	(3%)	(23.2%)		(17.5%)
FRAKTUR (n=11720)										
THA	71	7530	26	2485	7682	2248	22	1415	366 (5.1%)	3685/16147
(n=12462)	[63;77]	(60.4%)	[24;30]	(20%)	(61.8%)	(18.1%)	(0.2%)	(12.2%)		(22.8%)
TKA	71	6126	29	1347	6754	2238	15	968	273 (4.8%)	2381/12753
(n=10372)	[64;76]	(59.1%)	[26;33]	(13%)	(65.2%)	(21.6%)	(0.1%)	(9.9%)		(18.7%)

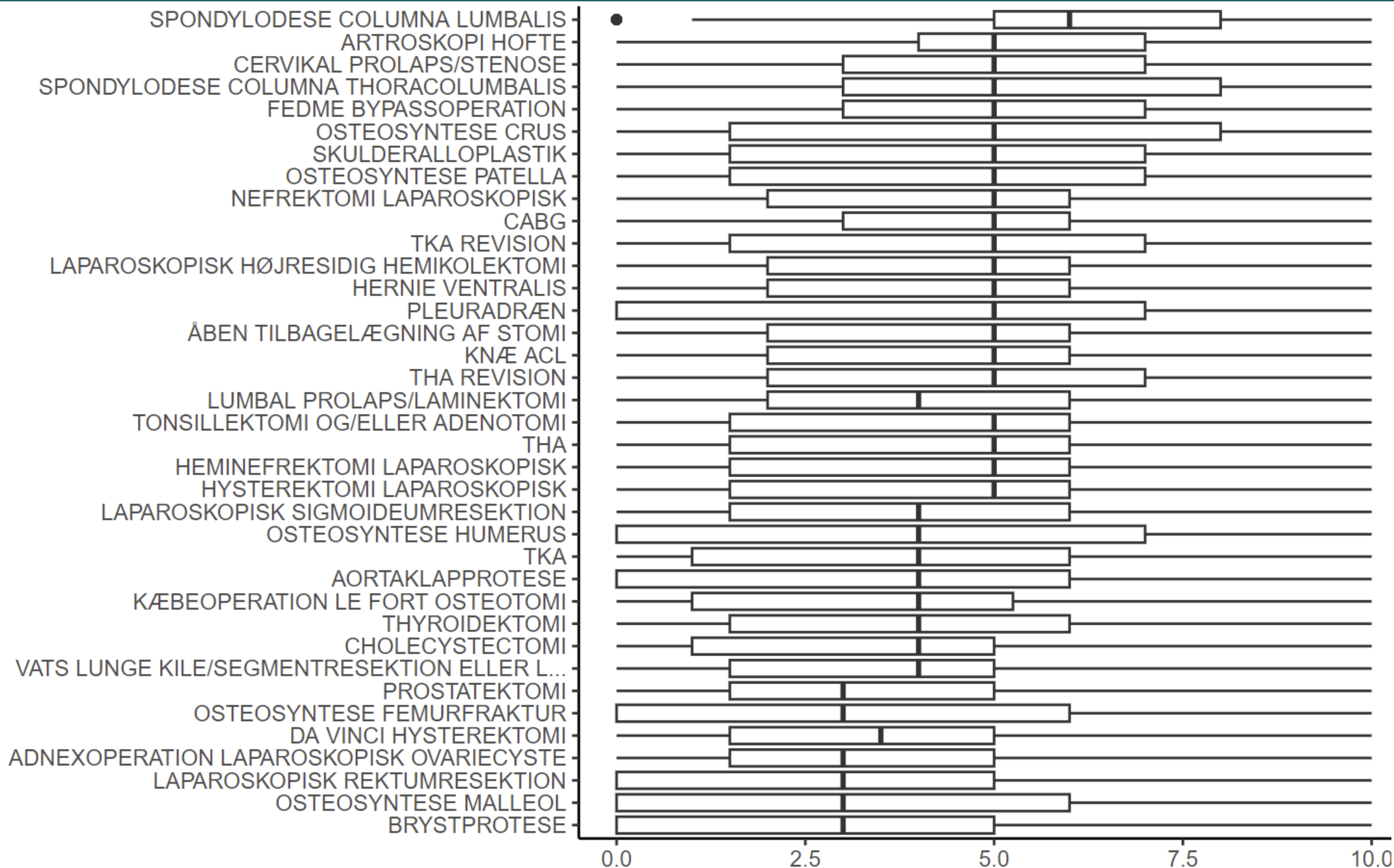
SMERTER										
Surgery	Anesthesia					Intraoperative		Postoperative		1 year mortality
	UA n (%)	Spinal n (%)	Epidural n (%)	Regional n (%)	MEQ n (%)	Minutes of surgery median [IQR]	PACU n (%)	Minutes in PACU median [IQR]	Days to discharge median [IQR]	
All (n=427674)	219630 (51.4%)	53846 (12.6%)	18885 (4.4%)	78812 (18.4%)	13 [10;20]	42 [22;71]	311123 (72.7%)	100 [69;150]	0 [0;2]	15373 (3.6%)
Fracture of the hip										
Surgery	Anesthesia					Intraoperative		Postoperative		1 year mortality
	UA n (%)	Spinal n (%)	Epidural n (%)	Regional n (%)	MEQ n (%)	Minutes of surgery median [IQR]	PACU n (%)	Minutes in PACU median [IQR]	Days to discharge median [IQR]	
OSTEOSYNTESIS OF FEMORAL NECK FRACTURE (n=11720)	9058 (77.3%)	2119 (18.1%)	5346 (45.6%)	3056 (26.1%)	20 [10;30]	68 [51;89]	10649 (90.9%)	153 [112;222]	6 [4;8]	2675 (22.8%)
THA (n=12462)	7818 (62.7%)	9662 (77.5%)	260 (2.1%)	8046 (64.6%)	20 [10;30]	54 [45;67]	11609 (93.2%)	132 [94;191]	1 [1;2]	140 (1.1%)
TKA (n=10372)	6732 (64.9%)	8109 (78.2%)	51 (0.5%)	8155 (78.6%)	15 [10;27]	67 [59;79]	9626 (92.8%)	111 [84;150]	1 [1;2]	96 (0.9%)

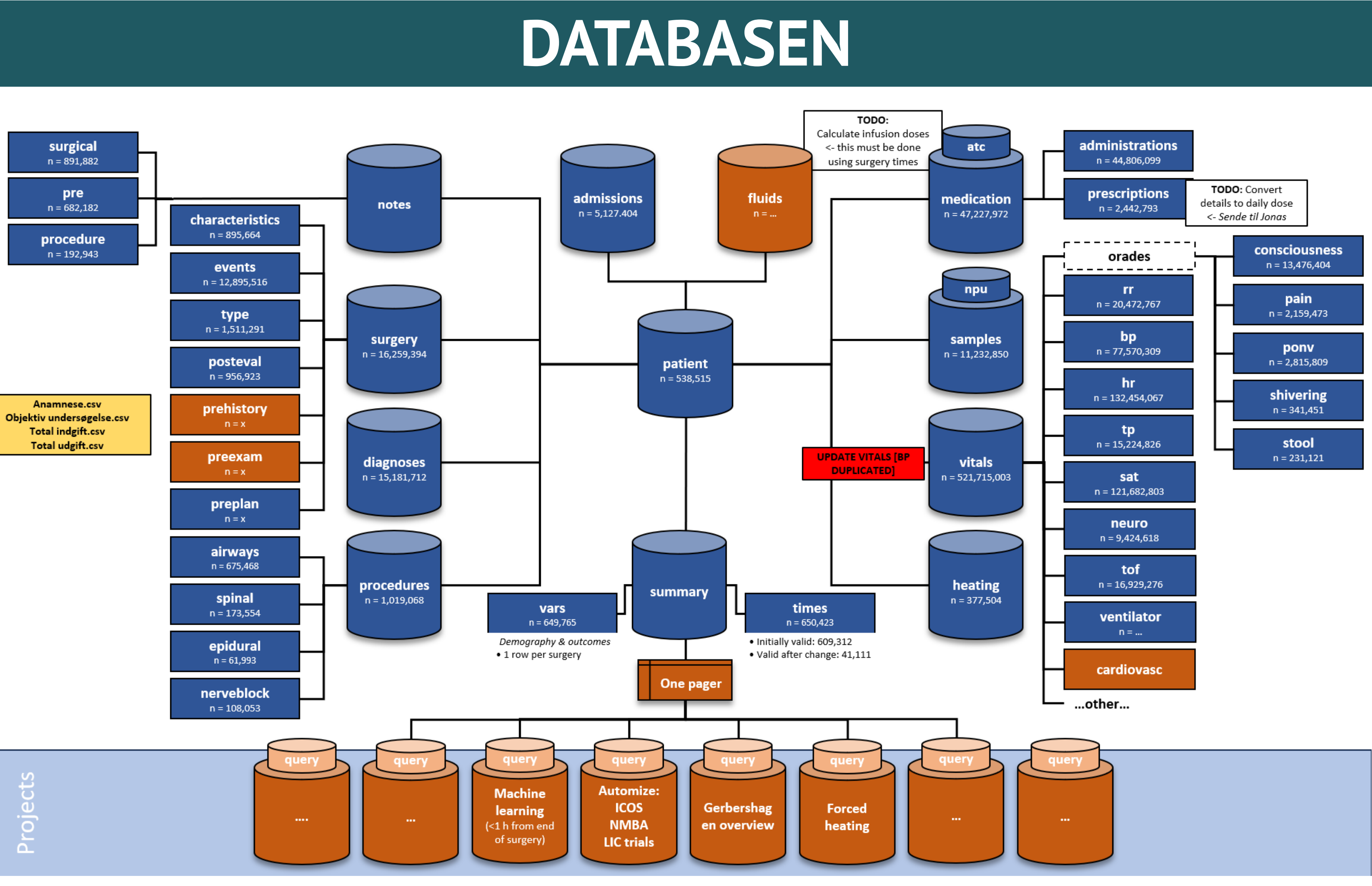
SMERTER

	First 0-2h median [IQR]	Worst 0-2h median [IQR]	Missing 0-2h n (%)	Mean 0-24h median [IQR]	Worst 0-24h median [IQR]	Missing 0-24h n (%)	0-24h MEQ median [IQR]
Surgery							
All (n=427674)	0 [0;2]	0 [0;3]	27701 (6.5%)	0 [0;2]	2 [0;5]	21491 (5%)	28 [19;42]

	First 0-2h median [IQR]	Worst 0-2h median [IQR]	Missing 0-2h n (%)	Mean 0-24h median [IQR]	Worst 0-24h median [IQR]	Missing 0-24h n (%)	0-24h MEQ median [IQR]
Surgery							
OSTEOSYNTSE HOFTENÆR FRAKTUR (n=11720)	0 [0;0]	0 [0;2]	483 (4.1%)	0 [0;2]	2 [0;5]	140 (1.2%)	28 [19;40]
THA (n=12462)	0 [0;0]	0 [0;3]	520 (4.2%)	2 [0;3]	5 [2;6]	105 (0.8%)	34 [20;51]
TKA (n=10372)	0 [0;0]	0 [0;2]	351 (3.4%)	1 [0;3]	4 [1;6]	78 (0.8%)	34 [21;50]

SMERTER



[illegible]

Data til algoritmer

OPIAID-databasen



Renses og omkodes til:

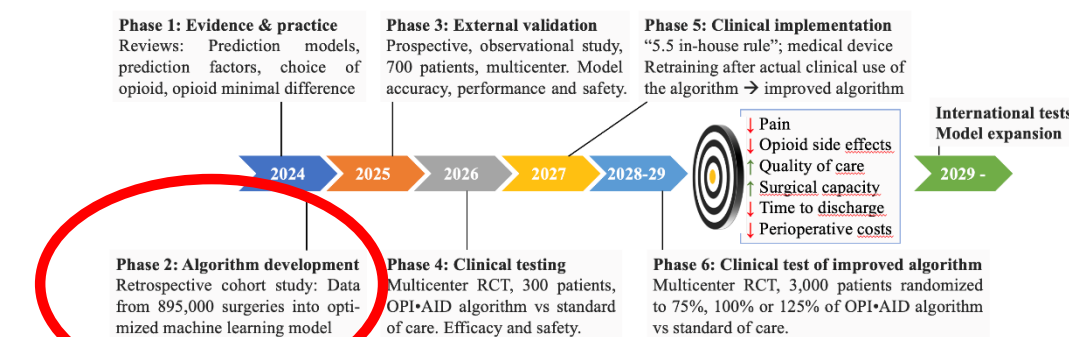
Prædiktorer

- 80-100 potentielle prædiktorer

Outcomes

- Smerter
- Opioidbivirkninger
- Komplikationer
- Length of stay/phase

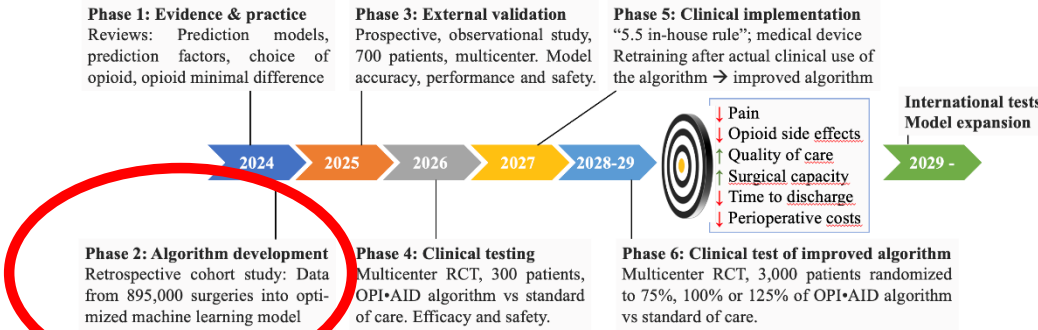
(Nej tak til unsupervised ML...)



Appendix 1: Procedures in the OPIAID database (as per June 2024)

Frequency	Procedure	Frequency	Procedure
24093	THA (Total Hip Arthroplasty)	2342	Laparoscopic Right-Sided Hemicolectomy
20381	Uterine Evacuation	2276	TKA Revision
19039	TKA (Total Knee Arthroplasty)	2275	Eye Muscle Surgery
18934	Osteosynthesis Near Hip Fracture	2224	Lymph Node Excision Head/Neck
16964	Esophago/Gastro/Duodenoscopy	2204	Osteotomy Calcaneus/Metatarsal/Foot Unspecified
14912	Cholecystectomy	2178	Hand Osteosynthesis
14877	Emergency C-section	2045	FESS (Functional Endoscopic Sinus Surgery)
13731	Elective C-section	1982	Breast Biopsy/Tumor Excision
12710	Laparoscopic Appendectomy	1943	Crus Osteosynthesis (Tibia/Fibula)
10928	TUR-B (Transurethral Resection of the Bladder)	1940	Dupuytren Fasciectomy
9686	Breast Resection	1920	Parathyroid Resection
9415	Sigmoidoscopy/Colonoscopy	1896	Trunk Skin Tumor Removal
8130	Lumbar Disk Prolapse/Laminectomy	1830	Laparoscopic Sigmoid Resection
7815	Knee Arthroscopy: Cartilage and/or Meniscus Resection	1811	Laparoscopic Adnexal Surgery BSO
7811	Inguinal Hernia Repair	1806	Lumbar Spine Fusion (Spondylodesis)
7112	Diagnostic Laparoscopy	1772	Forearm/Olecranon Osteosynthesis
6780	JJ Catheter	1767	THA Revision
6435	Distal Forearm Osteosynthesis	1759	Hematoma Removal Epidural/Intracranial/Subdural
6074	Perianal Abscess	1758	Thrombendarterectomy/Percutaneous Angioplasty
6025	Manual Exploration/Placenta Removal/Perineal Suturing	1745	Hysteroscopy with Endometrial Curettage
5866	Cystoscopy	1669	Cervical Prolapse/Stenosis
5586	Bronchoscopy	1631	Laryngoscopy
5567	Retrograde Intrarenal Stone Removal (RIRS)	1581	Conization
5513	UKA (Unicompartmental Knee Arthroplasty)	1577	Laparoscopic Adnexal Surgery for Ovarian Cyst
5310	JJ Catheter Removal/Replacement	1576	Wound Revision Lower Extremity
5048	Closed Hip Dislocation	1523	Urethrocystopexy (TVT - Tension-Free Vaginal Tape)
5034	Open Ventral Hernia Repair	1480	Rectocele and/or Enterocoele
4978	Anal Fistula	1456	Ventral Hernia Repair
4754	Hysteroscopic Polyp Resection or Fibroid Resection	1449	Ankle/Foot Arthrodesis
4668	Pilonidal Cyst	1427	Ureteronephroscopy
4610	Malleolar Osteosynthesis	1400	Hand Tendon Surgery
4379	Open Inguinal Hernia Repair	1398	Tympanoplasty
4261	Shoulder Arthroscopy	1389	Vulvar Resection
4135	Hysteroscopy	1371	Femoral Amputation
4010	Explorative Laparotomy	1313	Carpal Tunnel Nerve Decompression
3925	VATSLung Wedge/Segmental Resection or Lobectomy	1279	Shoulder Rotator Cuff Tendon Reinsertion/Exostosis
3831	Hysteroscopic Endometrial Resection	1246	Female Sterilization Laparoscopic
3661	Tonsillectomy and/or Adenoidectomy	1213	Oro/Pharyngo/Laryngoscopy Tumor Biopsy
3548	Adenoidectomy	1205	Upper and Lower Endoscopy
3504	AA Ankle/Foot/Lower Leg	1174	Laparoscopic Rectal Resection
3501	Knee Arthroscopy	1166	Humerus Osteosynthesis
3453	Brain Tumor	1161	Soft Tissue Revision Lower Extremity
3162	CABG (Coronary Artery Bypass Grafting)	1131	Cystoscopic Bladder Stone Removal
3156	Hemithyroidectomy	1122	Femur Fracture Osteosynthesis
3114	Mastectomy	1093	Testicular Biopsy
3076	ERCP	1074	Marsupialization
2999	Laparoscopic Hysterectomy	1071	Aortic Valve Prosthesis
2925	Anoscopy	1066	Vulvar/Vaginal Abscess
2756	Prostate Resection	1066	Manchester Operation
2732	Soft Tissue Revision/Tumor Trunk/Spine	1058	Radical Mastectomy or with Axillary Dissection
2724	Shoulder Arthroplasty	1053	Parotid Gland Resection
2686	Abscess of Trunk	1052	Urethrotomy
2614	Ureteroscopic Stone Removal	1034	Jaw Surgery
2510	Laparoscopic Adnexal Surgery USO	1027	Open Reversal of Stoma
2484	Cystocele with/without Rectocele and Vulvoplasty	1026	Toe/Forefoot Amputation
2439	Knee ACL (Anterior Cruciate Ligament)	1015	Retrograde Ureteroscopy
2396	Prostatectomy	1012	Thyroidectomy
2375	Hemorrhoidectomy	1004	Intracranial thrombectomy

Operationer



Prædiktorer

80 predictor variables (up to dosing)

Binary^{Bi} Categorical^{Cat} Continuous^{Con} Done

Demographics

Age^{Con}
Gender^{Bi}
Weight^{Con}, height^{Con}, BMI^{Con}
Smoking status^{Cat}, Weekly alcohol intake^{Cat}
ASA score^{Cat}
Prior opioid^{Bi} use incl. daily dose^{Cat}
Chronic pain^{Bi}
Prior surgery registered in database^{Bi}
Prior [large postoperative MEQ] in database^{Bi}
Prior [PONV] registered in database^{Bi}

Comorbidity^{All Bi}

IHD, Aorta stenosis, AFLI, COPD, CKD, Diabetes, IBD,
Liver disease, Cancer, sleep apnea, rheum. arthritis
Anxiety, Depression, Schizophrenia, other psychiatry

Surgery

Surgical specialty^{Cat}
Overall type^{Cat}
Specific type^{Cat}
Acute/elective^{Cat}

Anaesthesia/intraoperative analgesia management

Type of anaesthesia^{Cat}
Mean infusion rate propofol^{Con}
Mean infusion rate remifentanyl^{Con}
MAC value sevoflurane^{Con}
Spinal anaesthesia^{Bi} (drug^{Cat}, dose^{Con})
Epidural anaesthesia^{Bi} (drug^{Cat}, dose^{Con})
Peripheral nerve block^{Bi} (block^{Cat}, drug^{Cat})
Local infiltration analgesia^{Bi}
Paracetamol^{Bi}
NSAID^{Bi}
High-dose glucocorticoid^{Bi}
Gabapentinoids^{Bi}
Other administered opioids before end-dose^{Con}
Type of airway^{Cat}
Vasopressor^{Bi} (drug^{Cat}, mean infusion rate^{Con})
Antibiotic administration^{Cat}

Ventilator

Mean compliance^{Con}
ETCO2^{Con}

Vital signs (intraoperative)

Mean systolic blood pressure^{Con} (+ variability^{Con})
Mean diastolic blood pressure^{Con}
Mean heart rate^{Con} (+ variability^{Con})
Mean saturation^{Con}
Mean perfusion index^{Con} (+ variability^{Con})
Mean temperature^{Con}
TOF^{Bi}
Use of BIS^{Bi} (+ mean^{Con})

Blood samples

Creatinine^{Cat}
Leukocytes^{Cat}, CRP^{Cat}
Arterial blood-gas^{Bi}
Hemoglobin^{Cat}
Lactate^{Cat}
Albumin^{Cat}
Glucose^{Cat}

Acute symptoms

Preoperative pain^{Cat}
Preoperative nausea/vomiting^{Bi}

Limitations

Lacking predictors

Ethnicity

Socioeconomic status

Pain perception tests

Pain catastrophizing

Genotypes; COMT, OPRM1, CYP2D6, ABCB1

Issues with outcomes

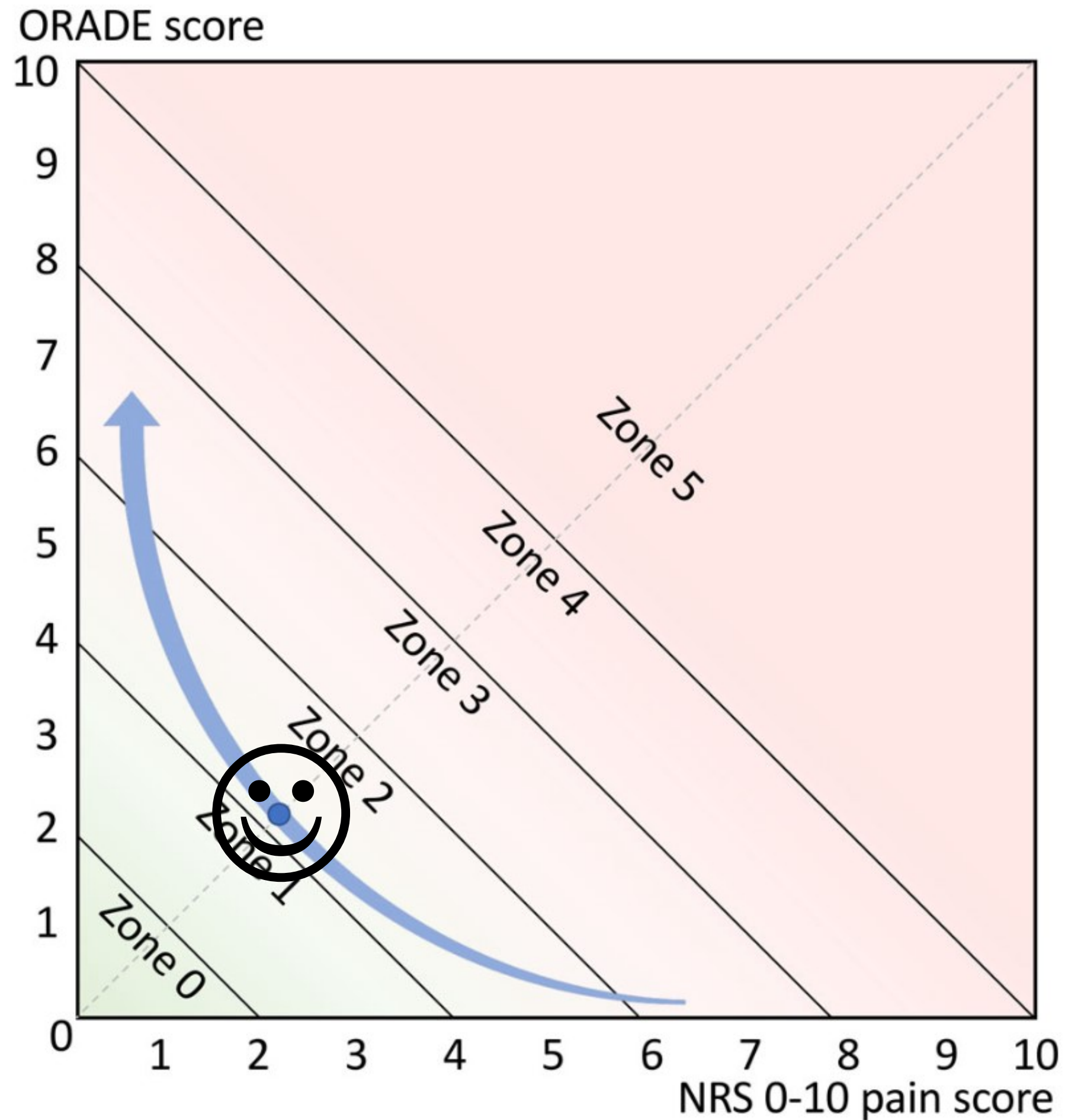
Underreported outcomes - ORADEs

Misclassification

Overfitted models

Other overseen predictors

OPIAID ALGORITMEN



ALGORITMEN

7 machine-learning modeller; accuracy, model performance

Træning 80% -> test 15% -> intern validering 5%

Cholecystektomi

60 år

Mand

80 kg

ASA 3

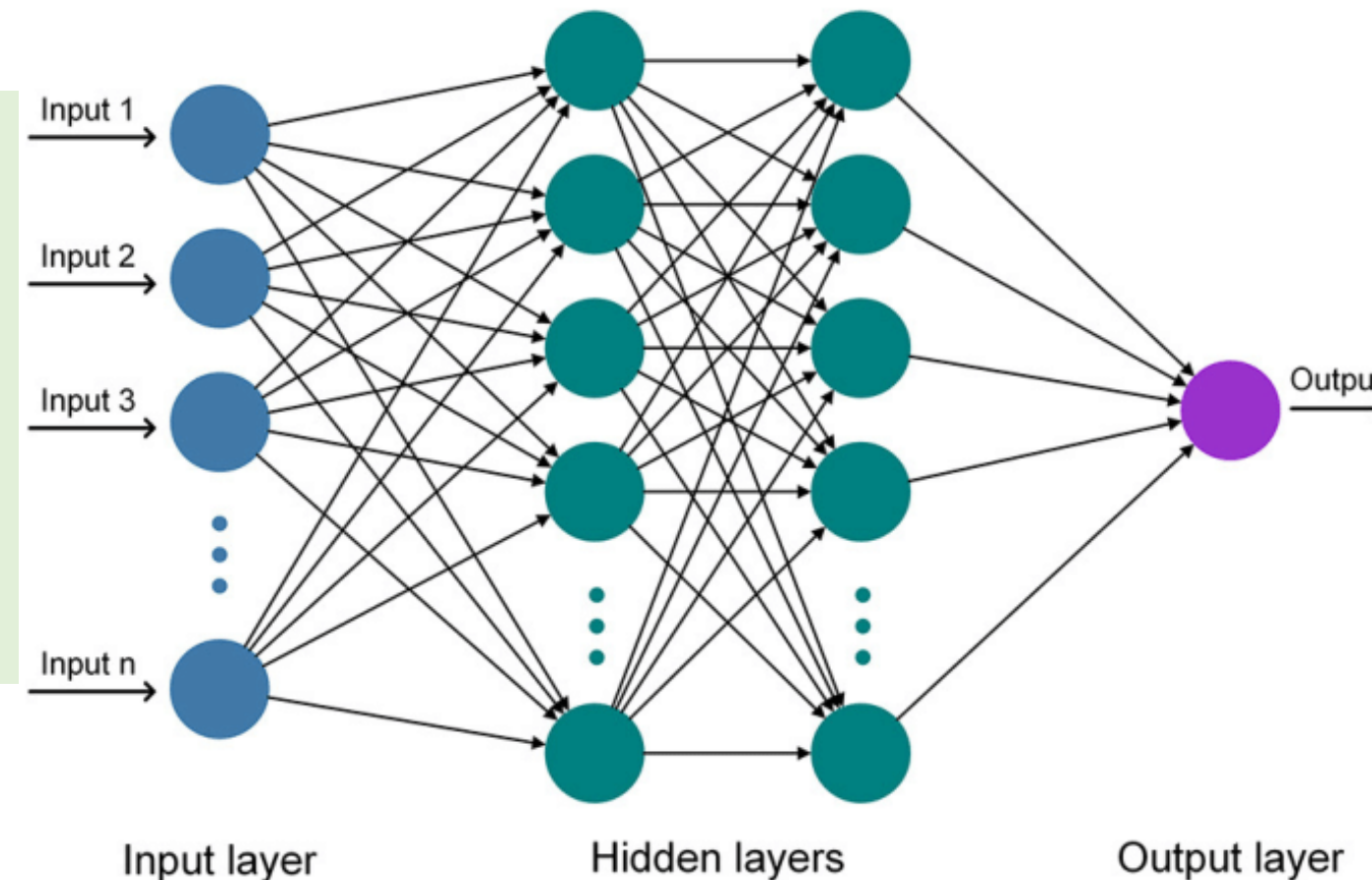
Fravær af kroniske smerter

HT, KKI, KOL

Pamol, Iprel, Dexamethason

Højt P/U intraoperativt

Høj puls intraoperativt



17,5 mg
OXYNORM

IT-UNIVERSITETET I KØBENHAVN

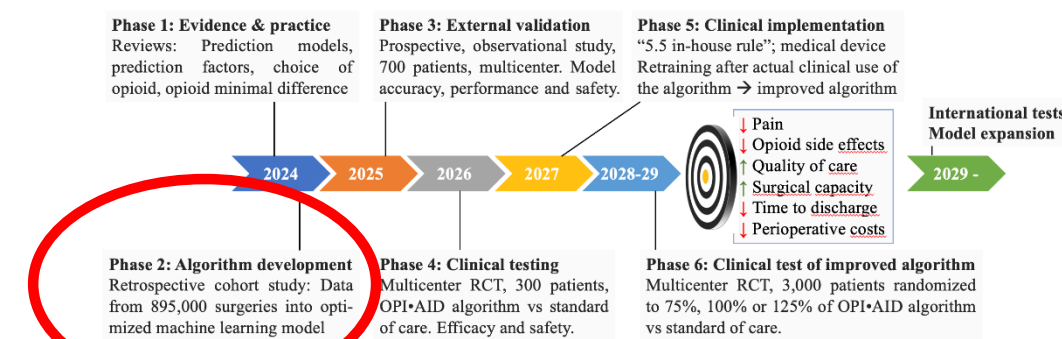


Jonas Valbjørn Andersen

Associate Professor, Business IT

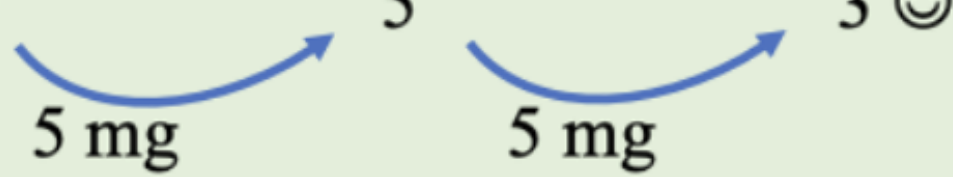
Information Systems and Digital Innovation (ISDI)

European Blockchain Center (EBC)



1: Klinikersuperviseret outcome

Algorithm development

		Intraoperative dose	Postoperative pain and rescue doses
Case 1	Standard treatment	Iv morphine 20 mg	Pain (NRS) NRS 7 ☹️ 
	Algorithm	<u>30 mg</u> →	NRS 3 😊
		Intraoperative dose	Postoperative pain and rescue doses
Case 2	Standard treatment	Iv morphine 20 mg	NRS 7 ☹️ 
	Algorithm	<u>25 mg</u> →	NRS 5 (still better than before)
		Intraoperative dose	Postoperative pain and rescue doses
Case 3	Standard treatment	Iv morphine 30 mg	NRS 2 and respiratory depression ☹️
	Algorithm	<u>20 mg</u> →	NRS 4 but no ORADEs

Phase 2: Algorithm development
Retrospective cohort study: Data from 895,000 surgeries into optimized machine learning model

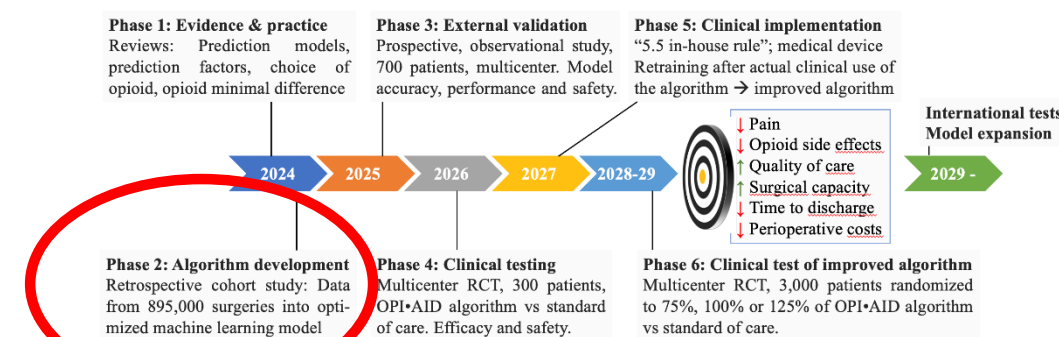
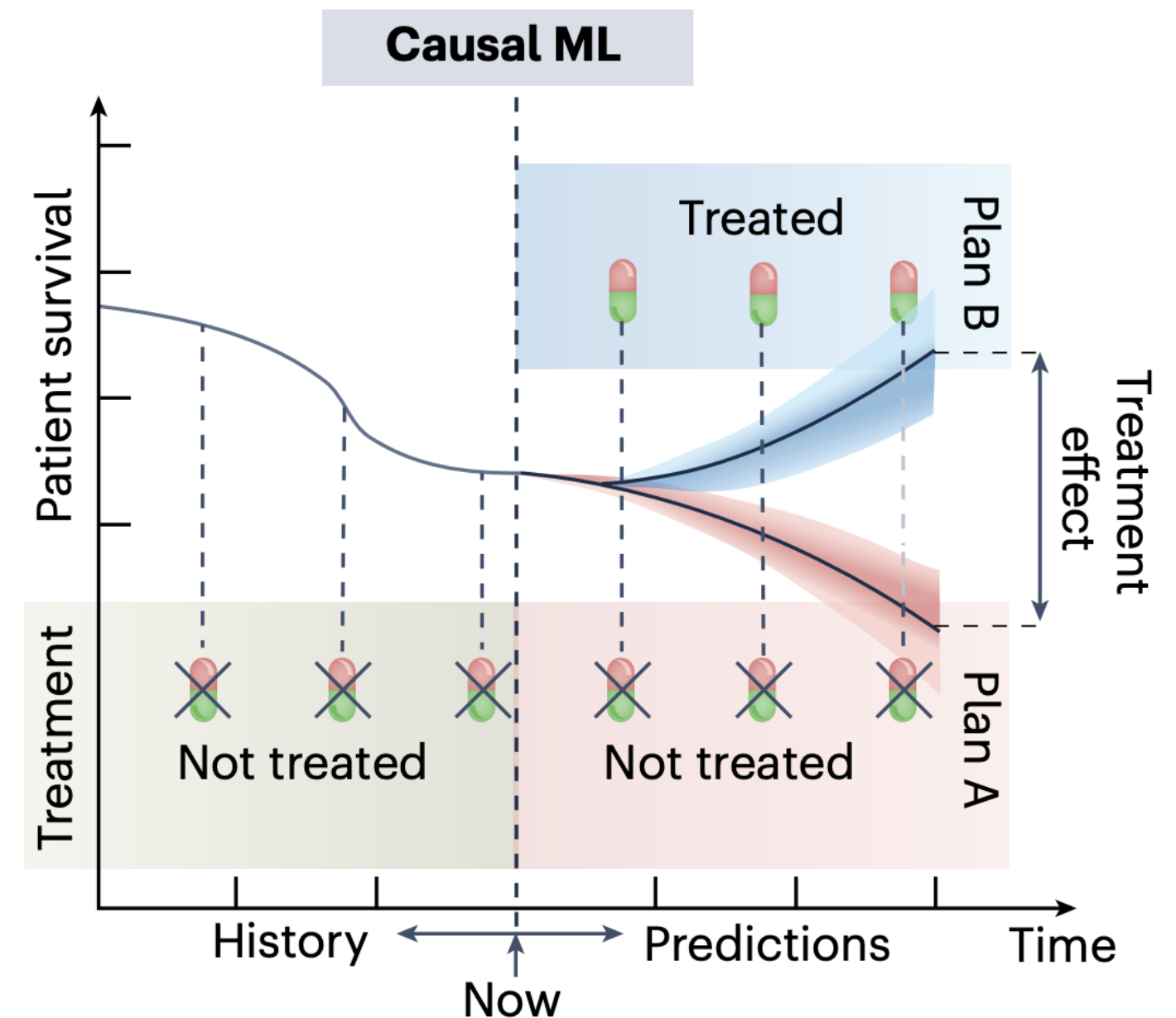
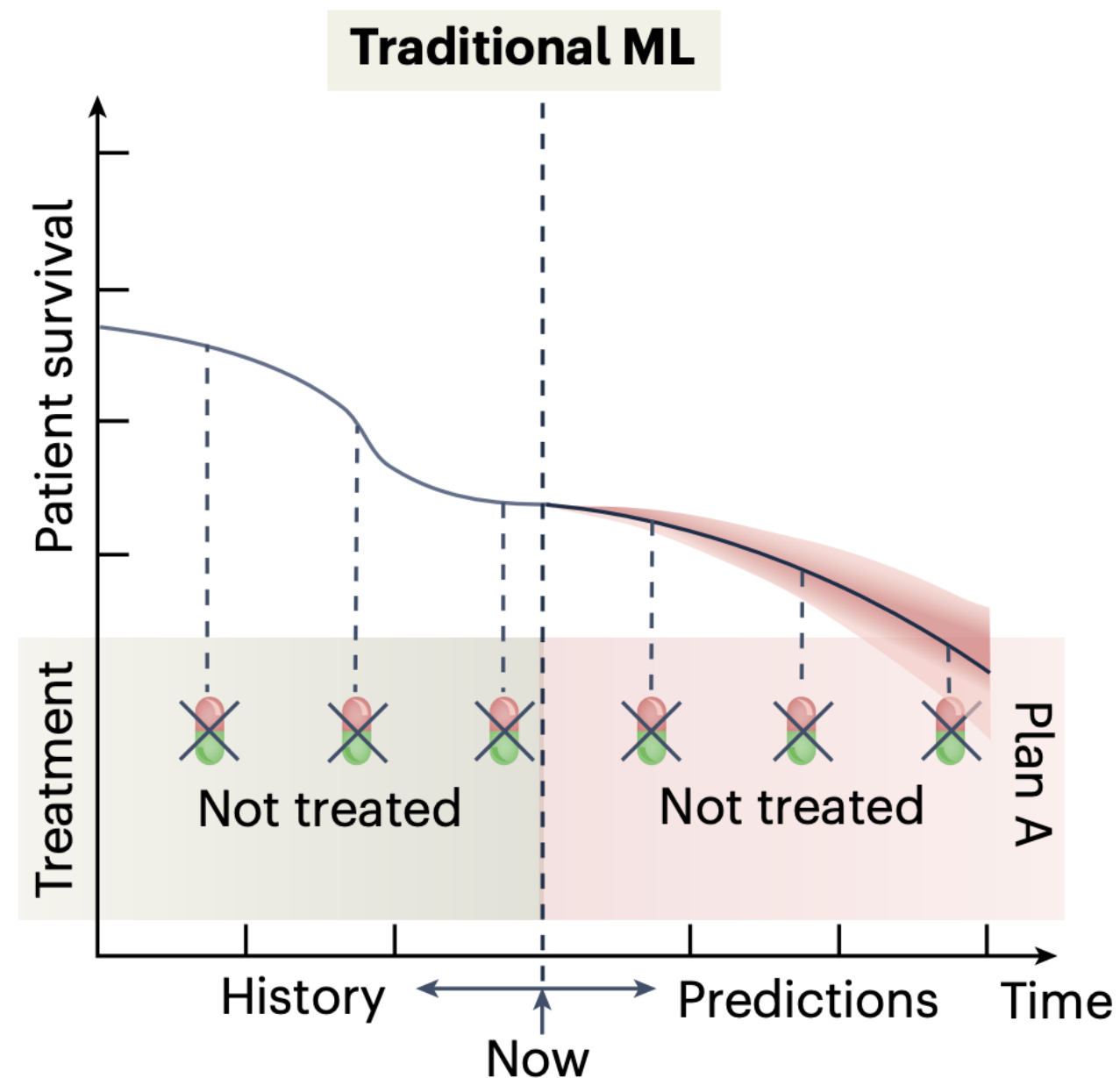
Phase 4: Clinical testing
Multicenter RCT, 300 patients, OPI•AID algorithm vs standard of care. Efficacy and safety.

Phase 6: Clinical test of improved algorithm
Multicenter RCT, 3,000 patients randomized to 75%, 100% or 125% of OPI•AID algorithm vs standard of care.

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pansion

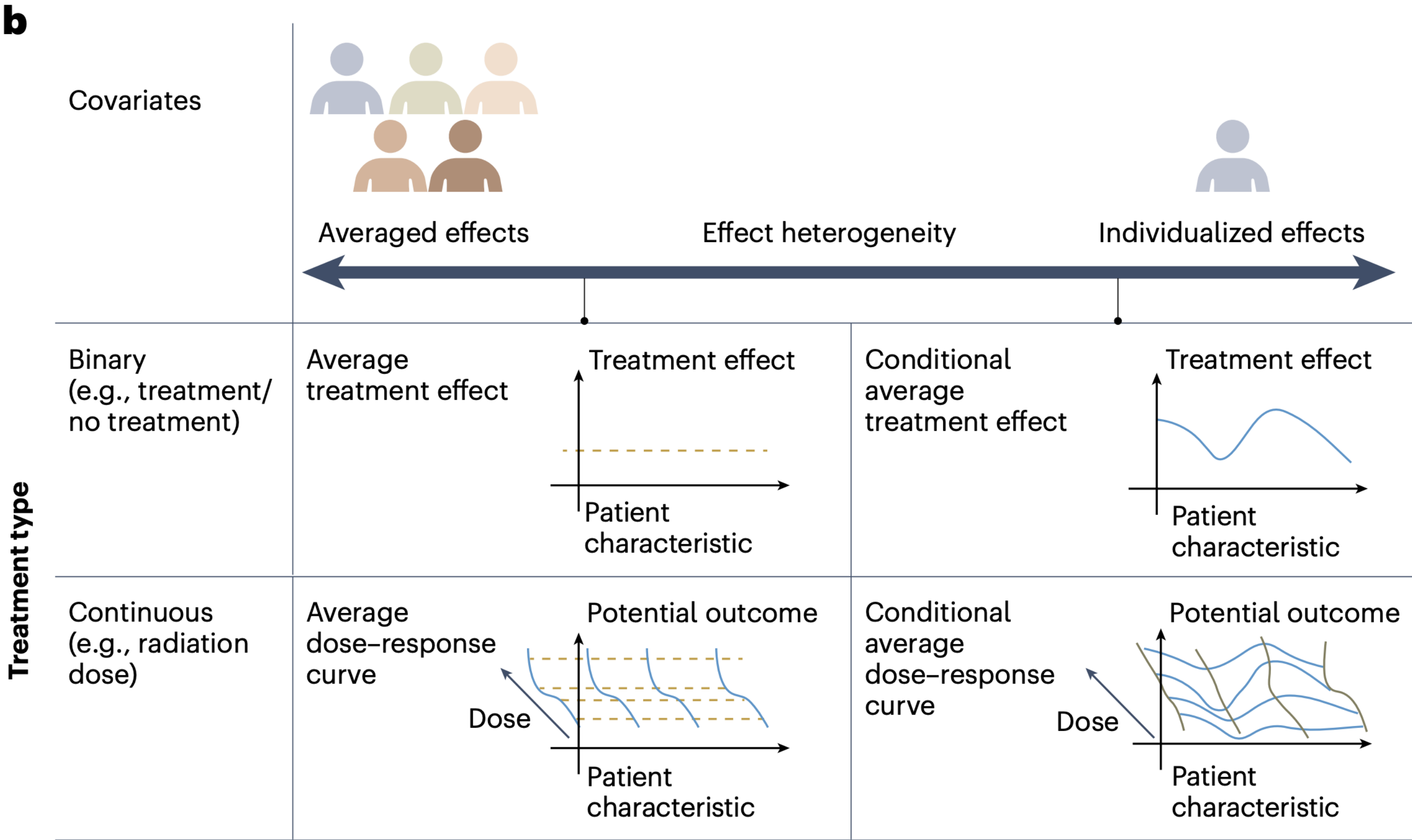
2: Konditionelt gennemsnitligt dosis-respons

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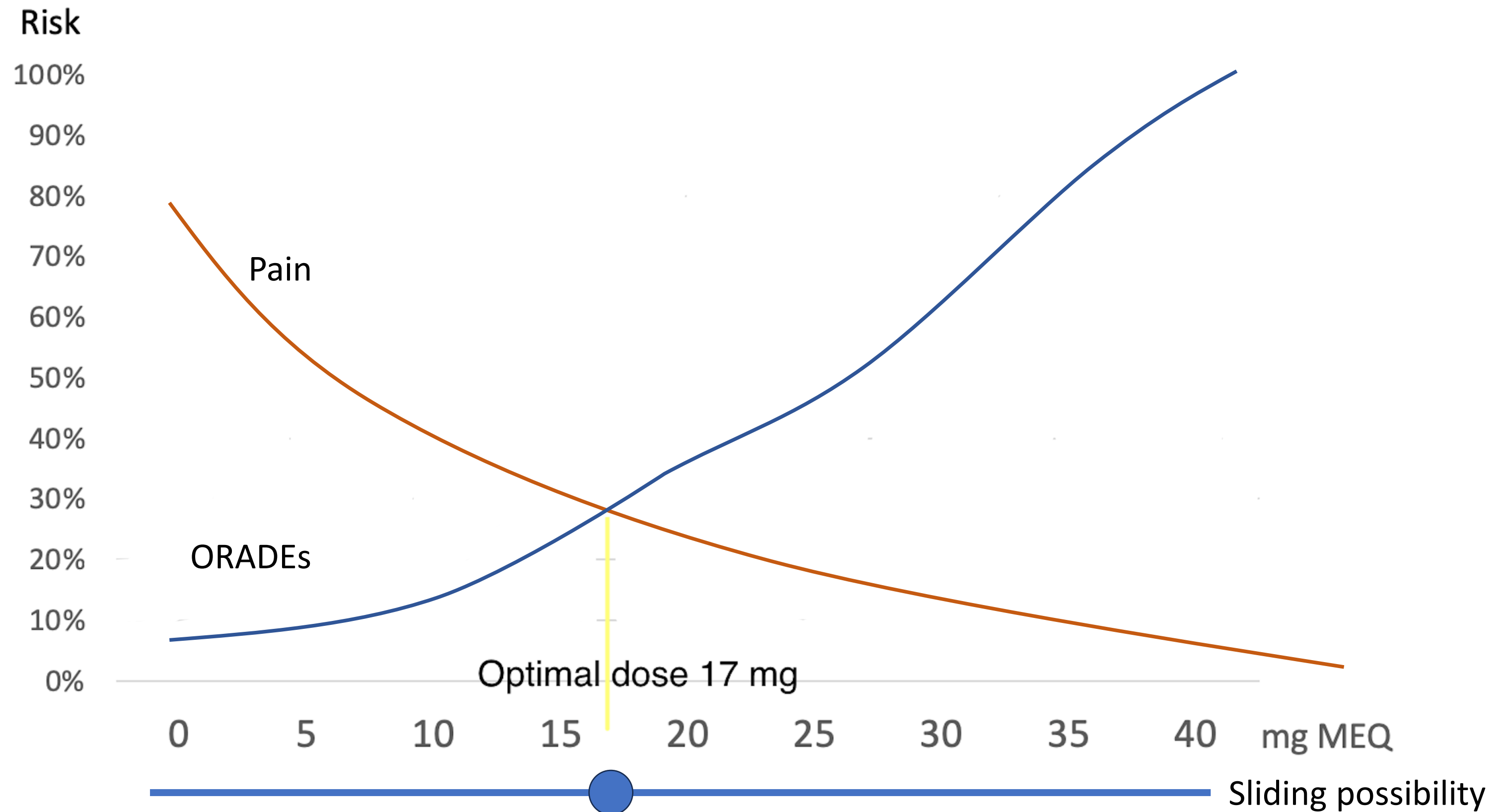
2: Konditionelt gennemsnitligt dosis-respons

Conditional average dose-response model with utility function



2: Konditionelt gennemsnitligt dosis-respons

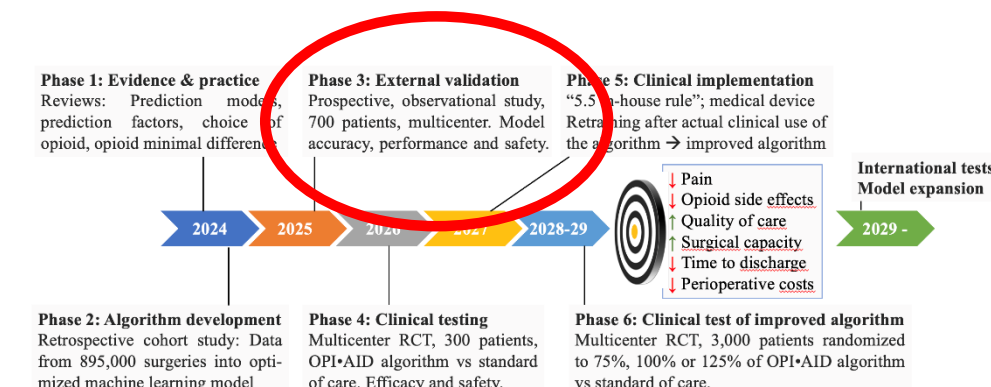
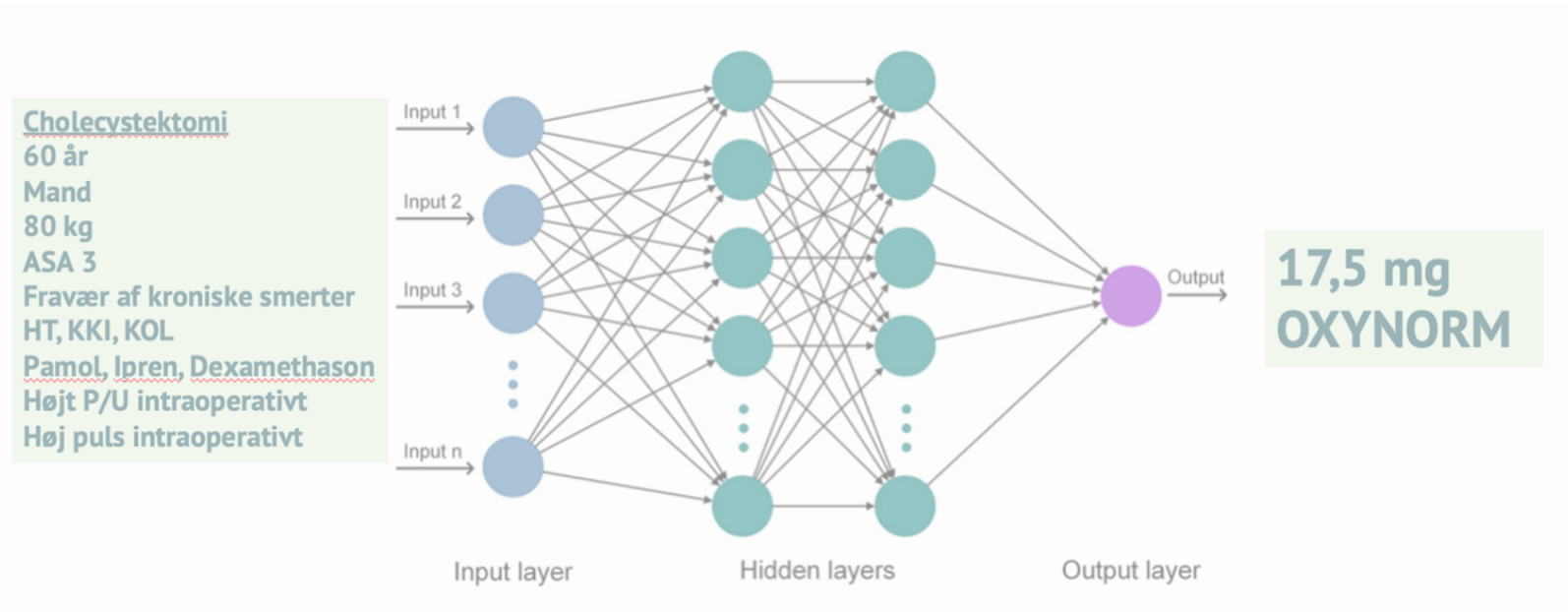
Cholecystektomi, 60 år, mand, ASA 3, etc etc etc



ALGORITME-VALG

7 modeller;

Accuracy, model performance → 2 bedste modeller i intern validering videre til ekstern validering



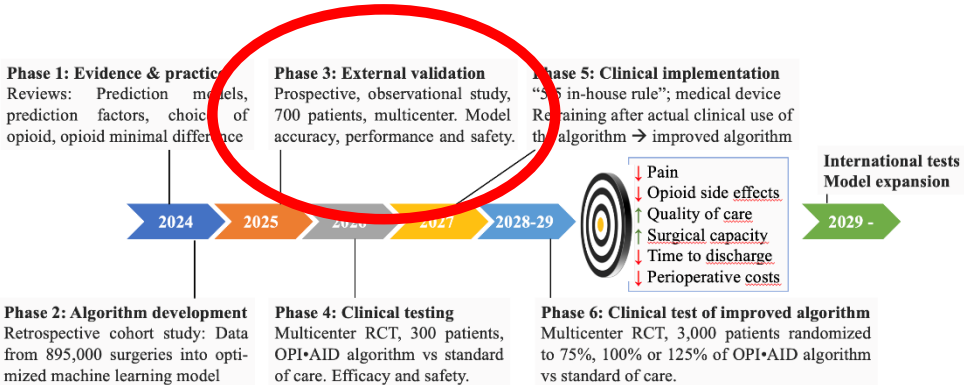
Fase 3: Ekstern validering

Pilotstudie done:
145 patienter

The OPI•AID Zone Tool as a composite outcome for
postoperative pain management quality—A protocol for an
observational pilot study

ACTA

Anders Peder Højer Karlsen¹ | Trang Xuan Minh Tran¹ | Ole Mathiesen^{2,3} |
Janus Christian Jakobsen^{4,5} | Christian S. Meyhoff^{1,3} | Troels Haxholdt Lunn^{1,3} |
Markus Harboe Olsen^{2,4,6}



Fase 3: Ekstern validering 2025 feb-jun

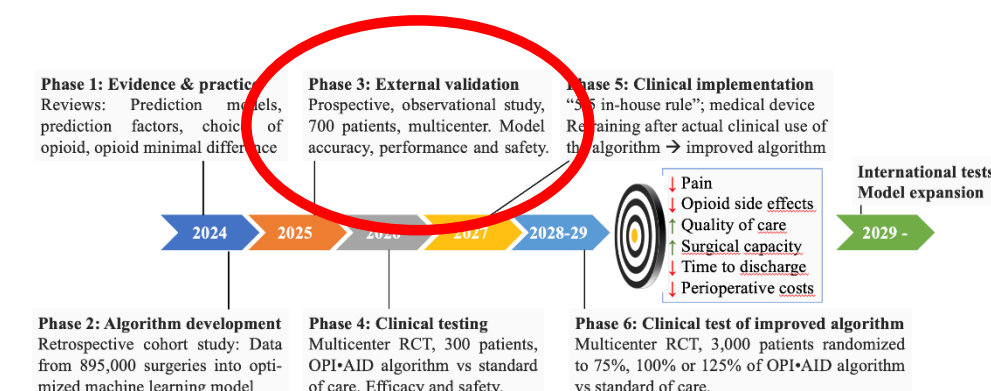
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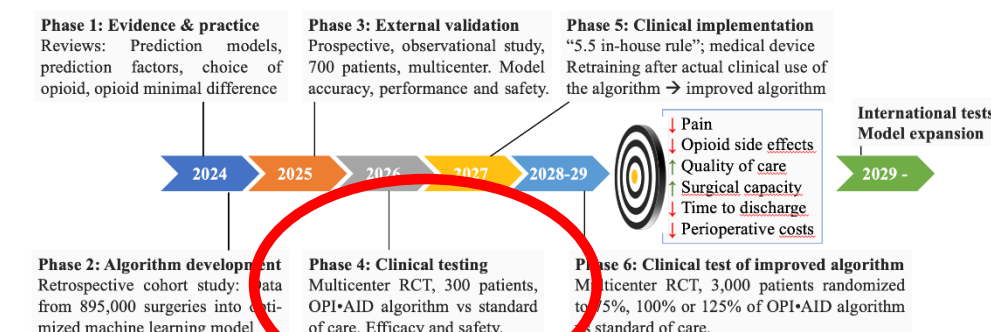
Anders Peder Højer Karlsen¹ | Trang Xuan Minh Tran¹ | Ole Mathiesen^{2,3} |
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Markus Harboe Olsen^{2,4,6}

- Protokol næsten færdig
- Grundig smerte/ORADE registrering
- 500-700 kirurgiske patienter i GA
- Sites
 - BFH
 - Køge
 - Hillerød?
 - Herlev?
 - Hvidovre?



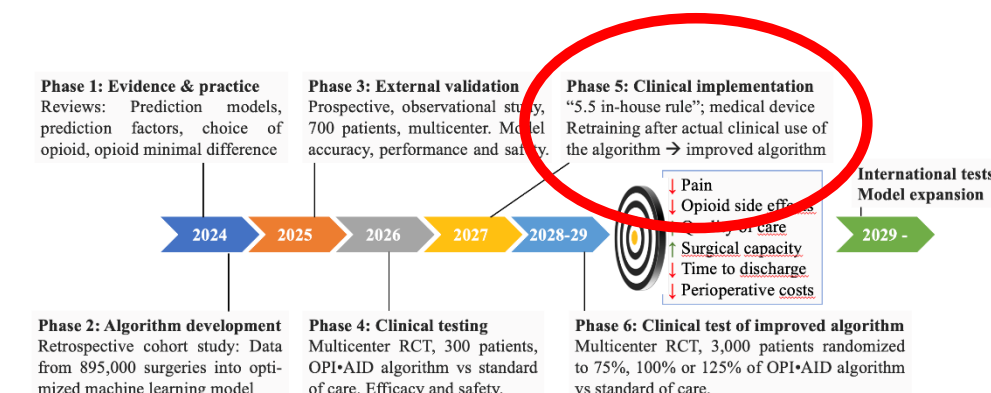
Fase 4: Klinisk afprøvning 2026 feb-jun

- OPIAID-algoritme vs standard of care
- 330 kirurgiske patienter i GA
- Sites
 - BBH
 - Køge
 - Hillerød
 - Herlev
 - Hvidovre
 - ...?



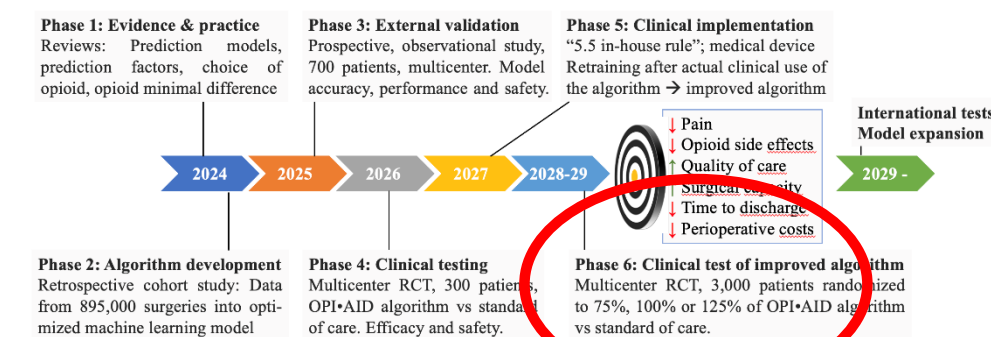
Fase 5: Implementering

- In-house reglen i CIMT!
- 330 patienter
- 01.01.2027→
- Samme sites og operationer som i RCT
- Forventer >10.000 algoritme-assisterede opioiddoseringer
 - Gentræning med 'rigtig' data -> **algoritme 2.0**

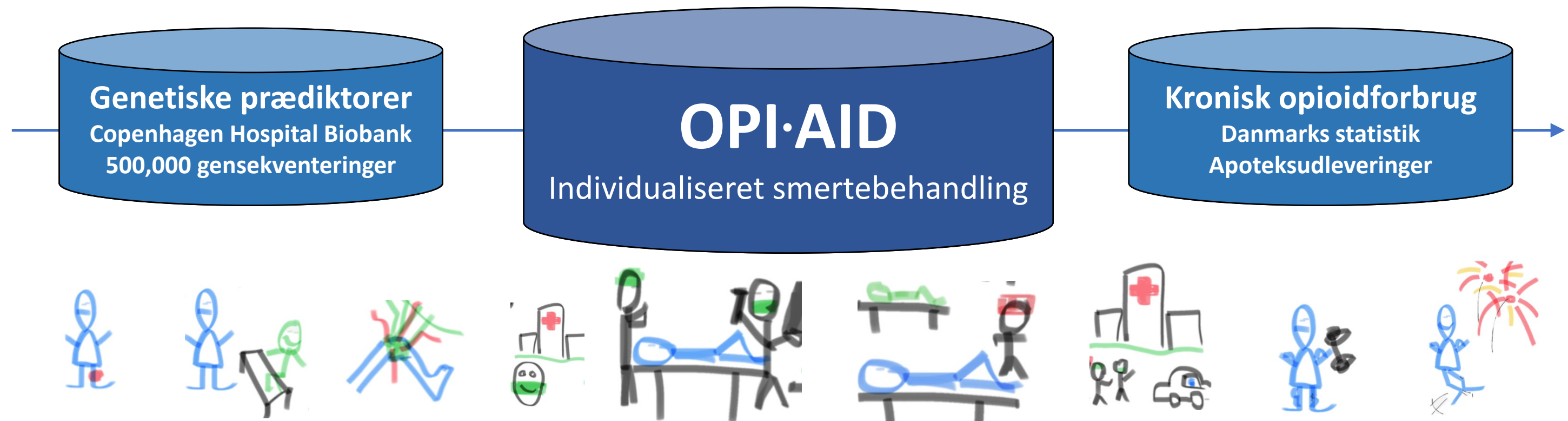


Fase 6: Upscale klinisk afprøvning

- Algoritme 2.0 vs standard of care
- 3000 patienter
- 2028→



”EXPANSION PACK”



Når vi nu alligevel var i gang...

AI and Automated CRFs in Anesthesia



CEPRA



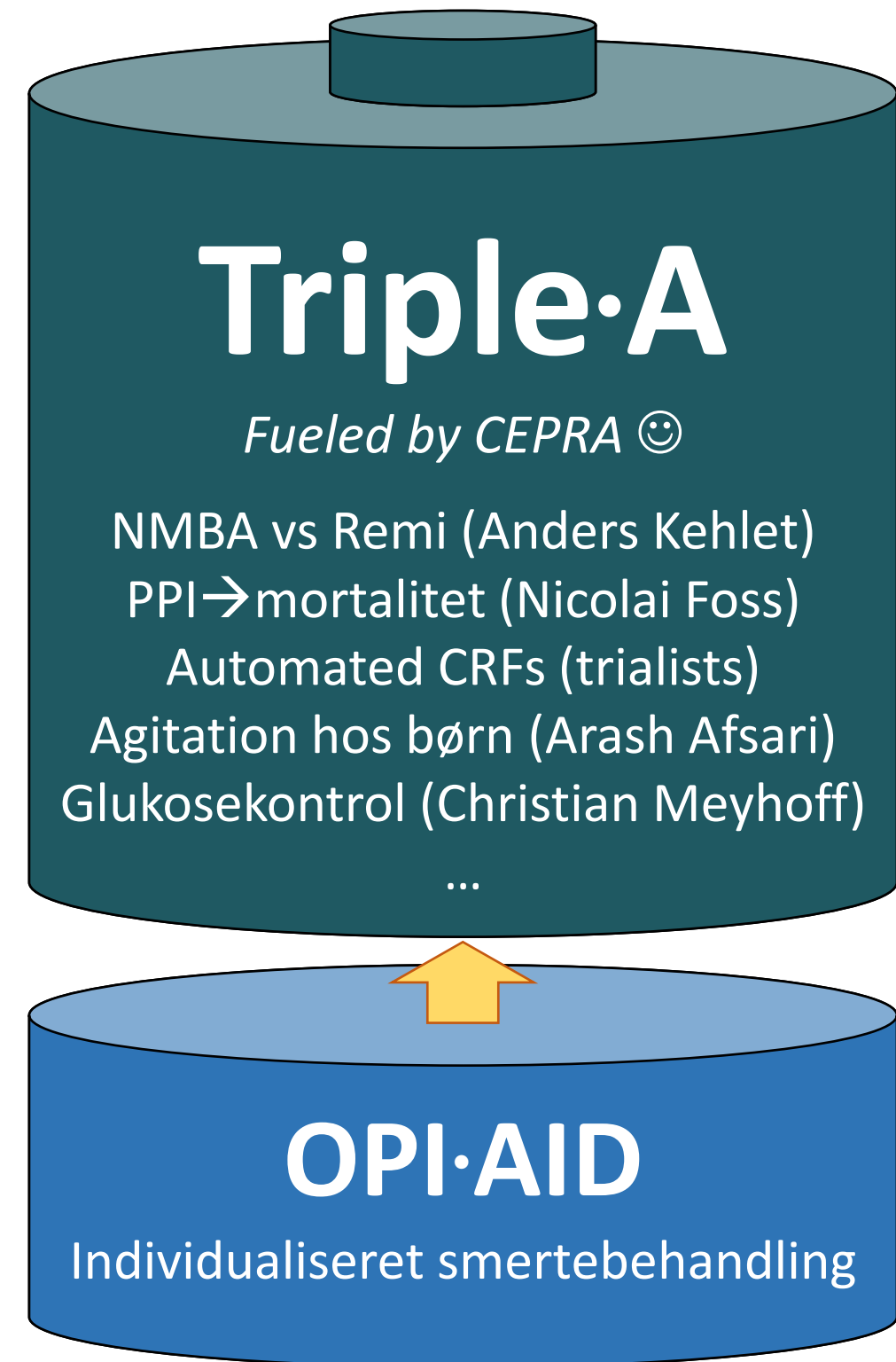
?



Genbrug OPIAID scripts til:

- Standardiseret datarensning
- Epidemiologiske studier
- Automated CRF i RCTer

Anders Karlsen og Markus Harboe Olsen



TAK!



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