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Tjagvad³, Birgitte Thylstrup³, Abdu Kedir Seid³, Marte Handal^{1,4,5},
Anne Bukten⁵, Thomas Clausen⁵, Svetlana Skurtveit^{4,5}

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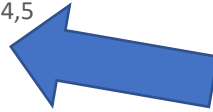


Department of Addictology

MORTALITY AND MORBIDITY IN PATIENTS IN OPIOID MAINTENANCE TREATMENT

Funding: Ministry of Health of the Czech Republic (grant no. NU20-09-00066); the institutional support programme (Progress no. Q06/LF1); Research Council of Norway (grant No. 320360).

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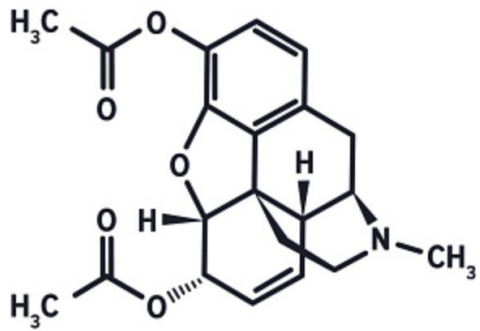
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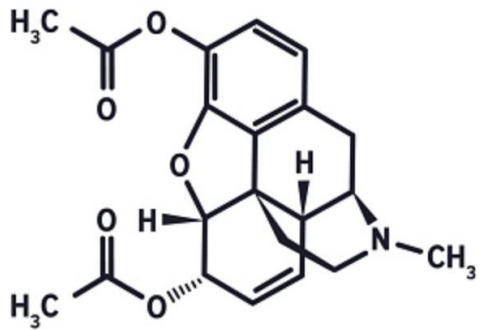
Disclosure

- RG is a shareholder of a company which is currently developing apps for treatment of addictions. Nevertheless, **no funding was related to this study** and the activities had no role in the study design or the collection, analysis, and interpretation of the data, writing of the manuscript, or the decision to submit the paper for publication.
- No other conflicts of interest.

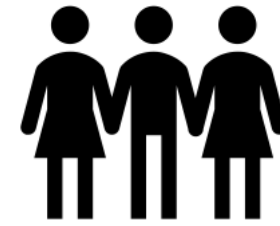


**Opioid
Maintenance
Treatment**

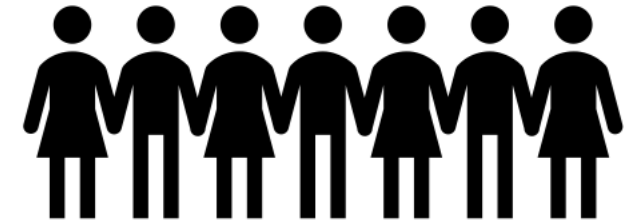




Opioid
Maintenance
Treatment



Mortality (all-cause, cause-specific...)

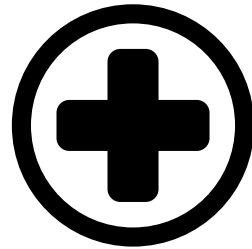
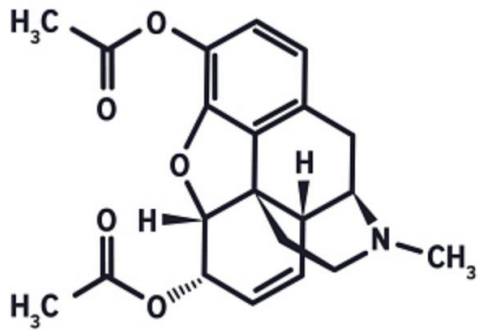


Morbidity - psychiatric

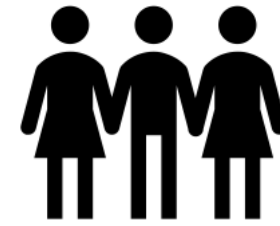


Morbidity - somatic

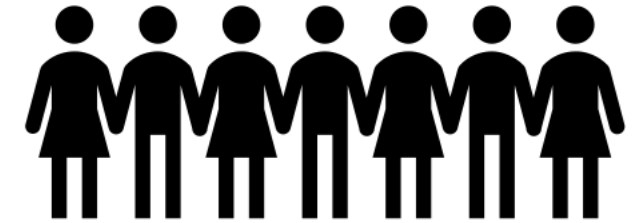




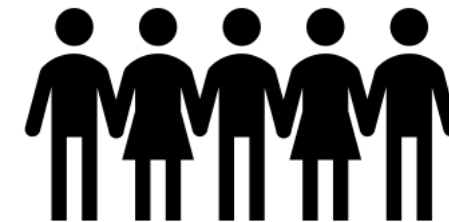
Opioid
Maintenance
Treatment



Mortality (all-cause, cause-specific...)

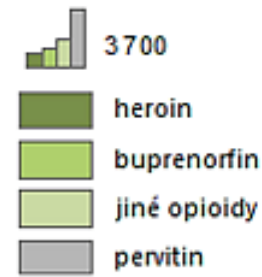
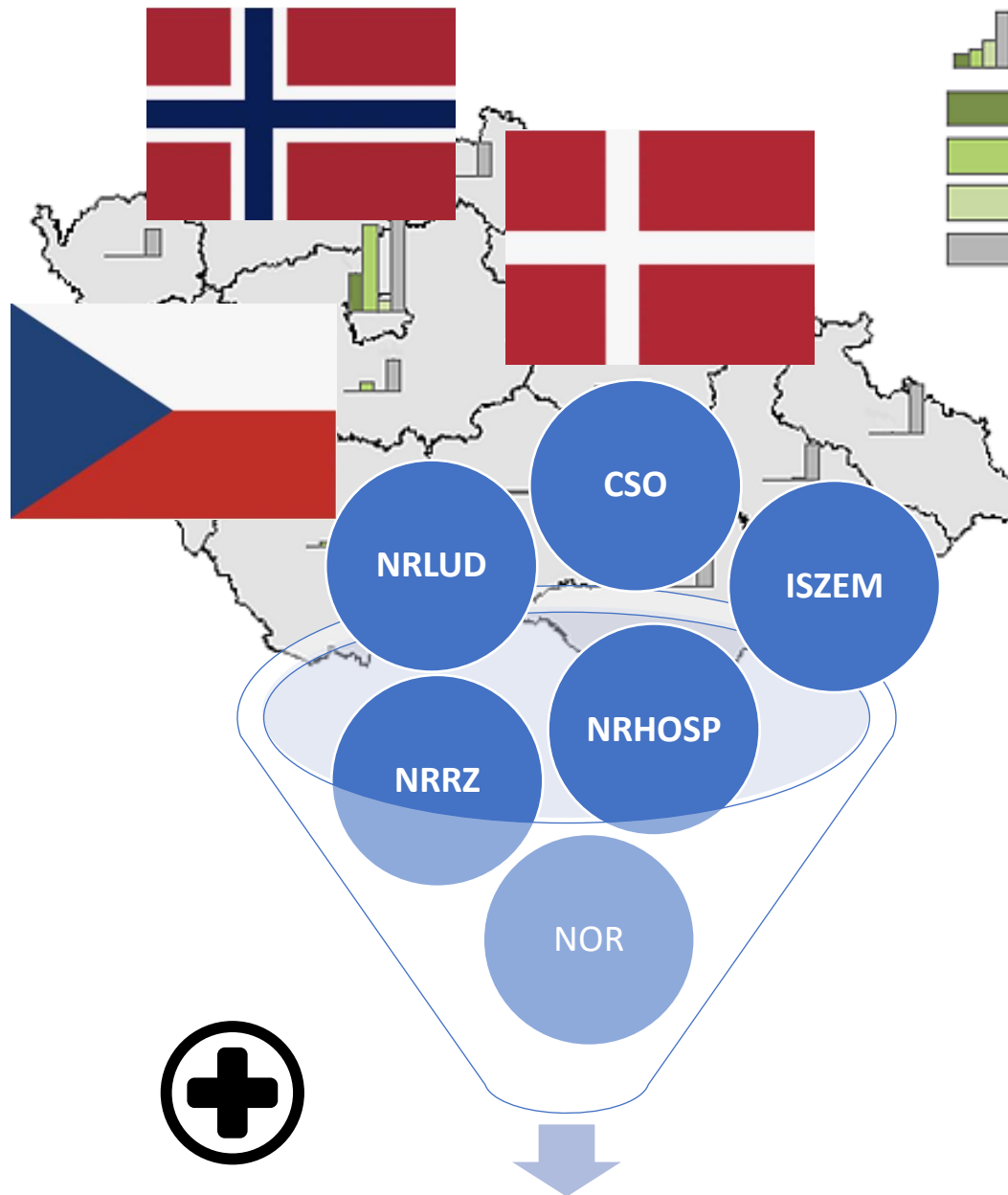
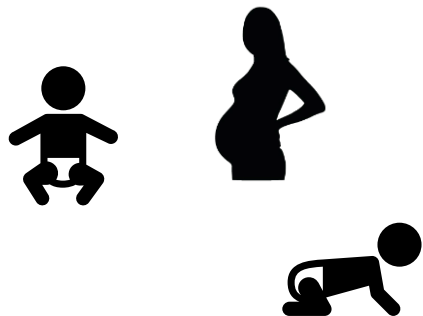
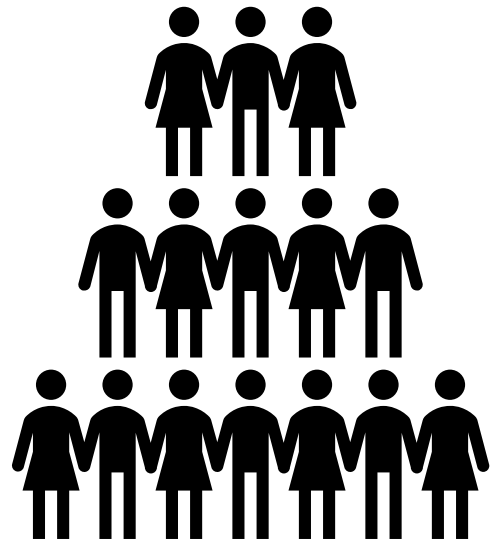
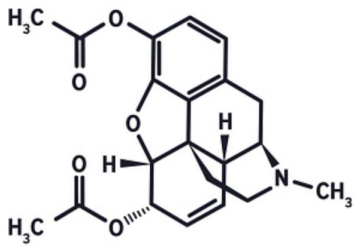


Morbidity - psychiatric



Morbidity - somatic

Our long-term goal is to further improve OMT and our understanding of key elements that will further increase the treatment outcomes.



Study protocol:

Gabrhelík R, Handal M, Mravčík V, Nechanská, B., Tjagvad, C., Thylstrup, B., Hesse, M., Minařík, J., Jarkovský, J., Bukten, A., Clausen, T., Skurtveit, S. (2021). Opioid maintenance treatment in the **Czech Republic, Norway and Denmark: a study protocol of a comparative registry linkage study. *BMJ Open*;11:e047028. doi: 10.1136/bmjopen-2020-047028**

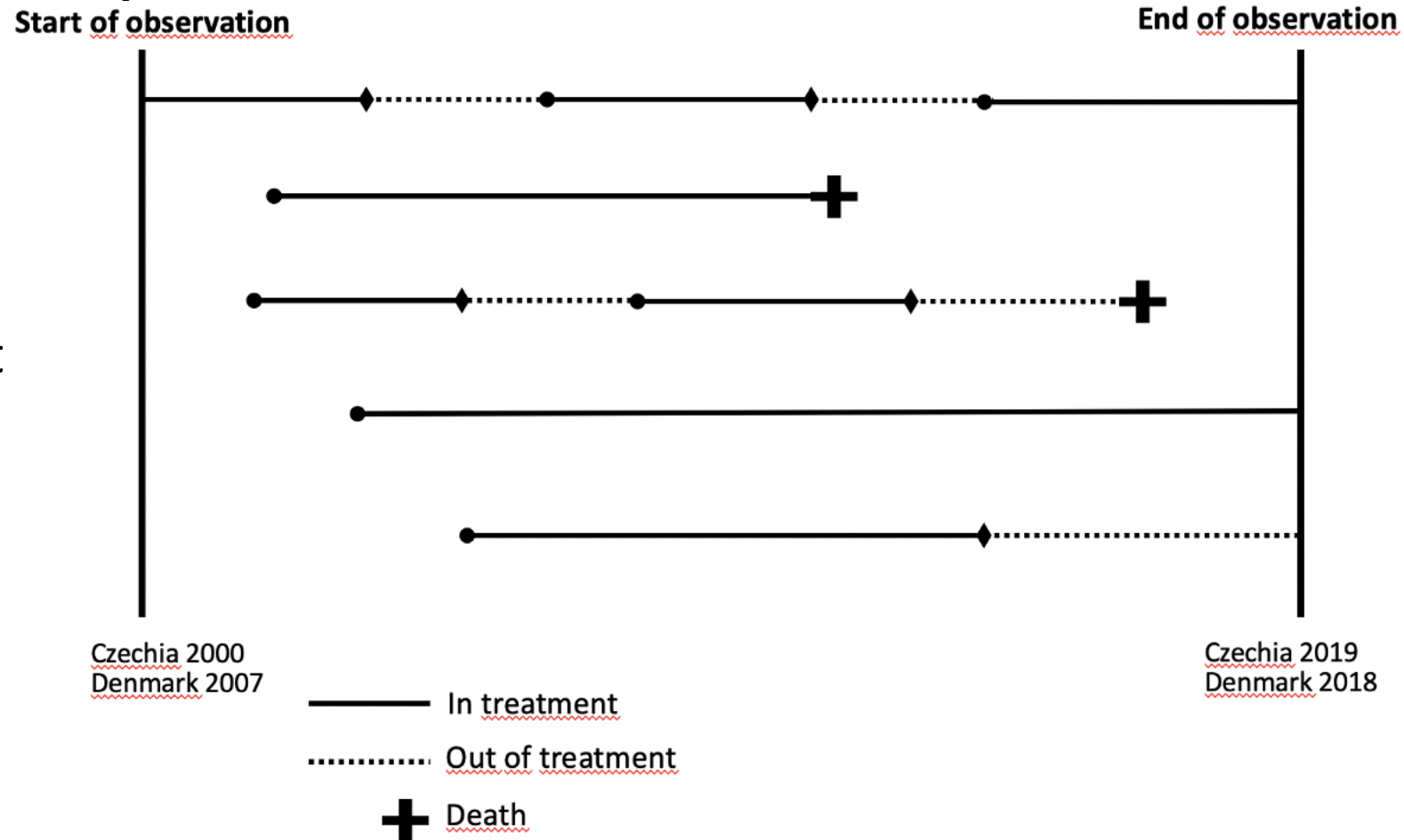
NATIONAL HEALTH REGISTERS

1) All-cause and overdose mortality in OMT patients

- **Aim:** To compare **all-cause and overdose mortality** among OMT patients while **in or out of OMT** in two different countries with different approaches to OMT.
- **Design:** Two nation-wide, registry-based cohort studies with identical analytical strategies.
- **Setting:** **Czechia** (2000–2019) and **Denmark** (2007-2018).
- **Participants:** A total of 3,637 men and 1,580 women enrolled in OMT in Czechia, and 6,387 men and 2,078 women enrolled in OMT in Denmark.

All-cause and overdose mortality in OMT patients

- **Measurements:** All-cause and overdose crude mortality rates (CMR) as number of deaths per 1000 person years (PY) in and out of OMT were calculated for all patients. **CMRs were stratified by gender and OMT medication** modality (methadone, buprenorphine, and buprenorphine with naloxone).



Characteristic of the study population. Opioid maintenance treatment (OMT) during 2000-2019 (N=5,219)^a in Czechia. OMT during 2007-2018 (N=8,465) in Denmark.

	Czechia	Denmark
Number of persons (who initiated OMT), n^a	5219	8465
Female, n (%)	1580 (30.3)	2078 (24.5)
Male, n (%)	3637 (69.7)	6387 (75.5)
Age at treatment start, mean median		
Female, mean, median	27.3, 26	40.2, 40
Male, mean, median	29.8, 29	39.8, 39
Medication at first admission		
methadone, n (%)	1362 (38.4)	6731 (79.5)
buprenorphine, n (%)	2020 (38.7)	1178 (13.9)
buprenorphine/naloxone, n (%)	1196 (22.9)	556 (6.6)
Multiple episode, n (%)	2687 (51.5)	3960 (46.8)

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Multiple episode, n (%)	2687 (51.5)	3960 (46.8)

Crude mortality rate (CMR) per 1000 person-years and 95% confidence interval (CI) in treatment and out of treatment in Czechia and in Denmark. All cause, overdose, and non-overdose death stratified on gender.

	Czechia						Denmark					
	In treatment			Out of treatment			In treatment			Out of treatment		
	n	PY	CMR (CI)	n	PY	CMR (CI)	n	PY	CMR (CI)	n	PY	CMR (CI)
Overdose	12	24 495	0.5 (0.2-0.8)	35	29 246	1.2 (0.8-1.6)	269	36886	7.3 (6.5-8.2)	130	18556	7.0 (5.9-8.3)
Non-overdose	94	24 495	3.8 (3.1-4.6)	280	29 246	9.6 (8.5-10.7)	712	36886	19.3 (18.0-20.8)	393	18556	21.2 (19.2-23.4)
All causes*	106	24 495	4.3 (3.5-5.2)	315	29 246	10.8 (9.6-12.0)	981	36886	26.6 (25.0-28.3)	523	18556	28.2 (25.9-30.7)
Female												
Overdose	N	-	-	5	9 048	0.6 (0.1-1.0)	61	9 636	6.3 (4.9-8.1)	20	4124	4.9 (3.1-7.5)
Non-overdose	N	-	2.9 (1.6-4.1)	56	9 048	6.2 (4.6-7.8)	182	9 636	18.9 (16.4-21.8)	94	4124	22.8 (18.7-27.8)
All causes	22	7 321	3.0 (1.7-4.3)	61	9 048	6.7 (5.0-8.4)	243	9 636	25.2 (22.3-28.5)	114	4124	27.6 (23.1-33.1)
Male												
Overdose	11	17 162	0.6 (0.3-1.0)	30	20 179	1.5 (1.0-2.0)	208	27 250	7.6 (6.7-8.7)	110	14432	7.6 (6.3-9.2)
Non-overdose	73	17 162	4.3 (3.3-5.2)	224	20 179	11.1 (9.6-12.6)	530	27 250	19.5 (17.9-21.2)	299	14432	20.7 (18.5-23.2)
All causes	84	17 162	4.9 (3.8-5.9)	254	20 179	12.6 (11.0-14.1)	738	27 250	27.1 (25.2-29.1)	409	14432	28.3 (25.8-31.2)



Crude mortality rate (CMR) per 1000 person-years and 95% confidence interval (CI) in treatment and out of treatment in Czechia and in Denmark. All cause, overdose, and non-overdose death stratified on gender.

	Czechia						Denmark					
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Crude mortality rate (CMR) per 1000 person-years and 95% confidence interval (CI) during treatment with methadone, buprenorphine, or buprenorphine with naloxone in Czechia and Denmark.

Czechia	Methadone			Buprenorphine			Buprenorphine/naloxone		
	n	PY	CMR (CI)	n	PY	CMR (CI)	n	PY	CMR (CI)
Overdose	E	-	-	8	10 289	0.8 (0.2-1.3)	E	-	-
Non-overdose	E	-	3.4 (2.2-4.6)	42	10 289	4.1 (2.8-5.3)	E	-	4.1 (2.3-5.8)
All causes	34	9 036	3.8 (2.5-5.0)	50	10 289	4.9 (3.5-6.2)	22	5 171	4.3 (2.5-6.0)
Denmark									
Overdose	255	31452	8.1 (7.2-9.2)	E	-	-	E	-	-
Non-overdose	676	31452	21.5 (20.0-23.2)	E	-	-	E	-	-
All causes	931	31452	29.6 (27.8-31.5)	28	3 404	8.2 (5.7-11.9)	22	2 030	10.8 (7.2-16.4)

Large variations in all-cause and overdose mortality among >13,000 patients in and out of opioid maintenance treatment in different settings

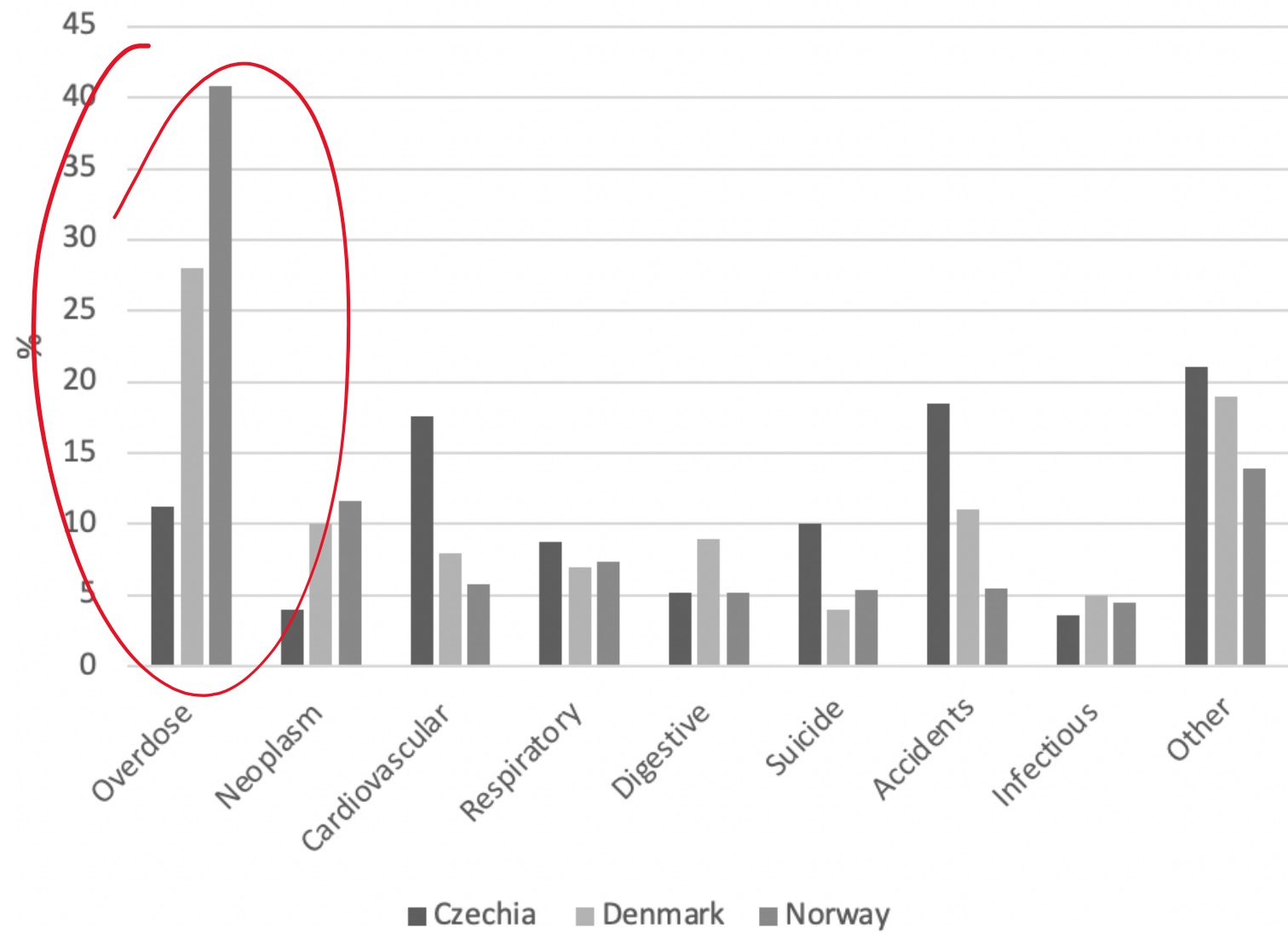
- Patients in Denmark are **10 years older** when starting OMT
- **Methadone** used the most in Denmark and linked to high CMR
- Lower CMR in Czechia not necessarily linked to better care...

- **Conclusion:**
- Country-specific differences in mortality while in and out of OMT **challenge the clinical practice in Czechia and Denmark.**
- One being overly restrictive? The other more liberal with loosen safety measures?

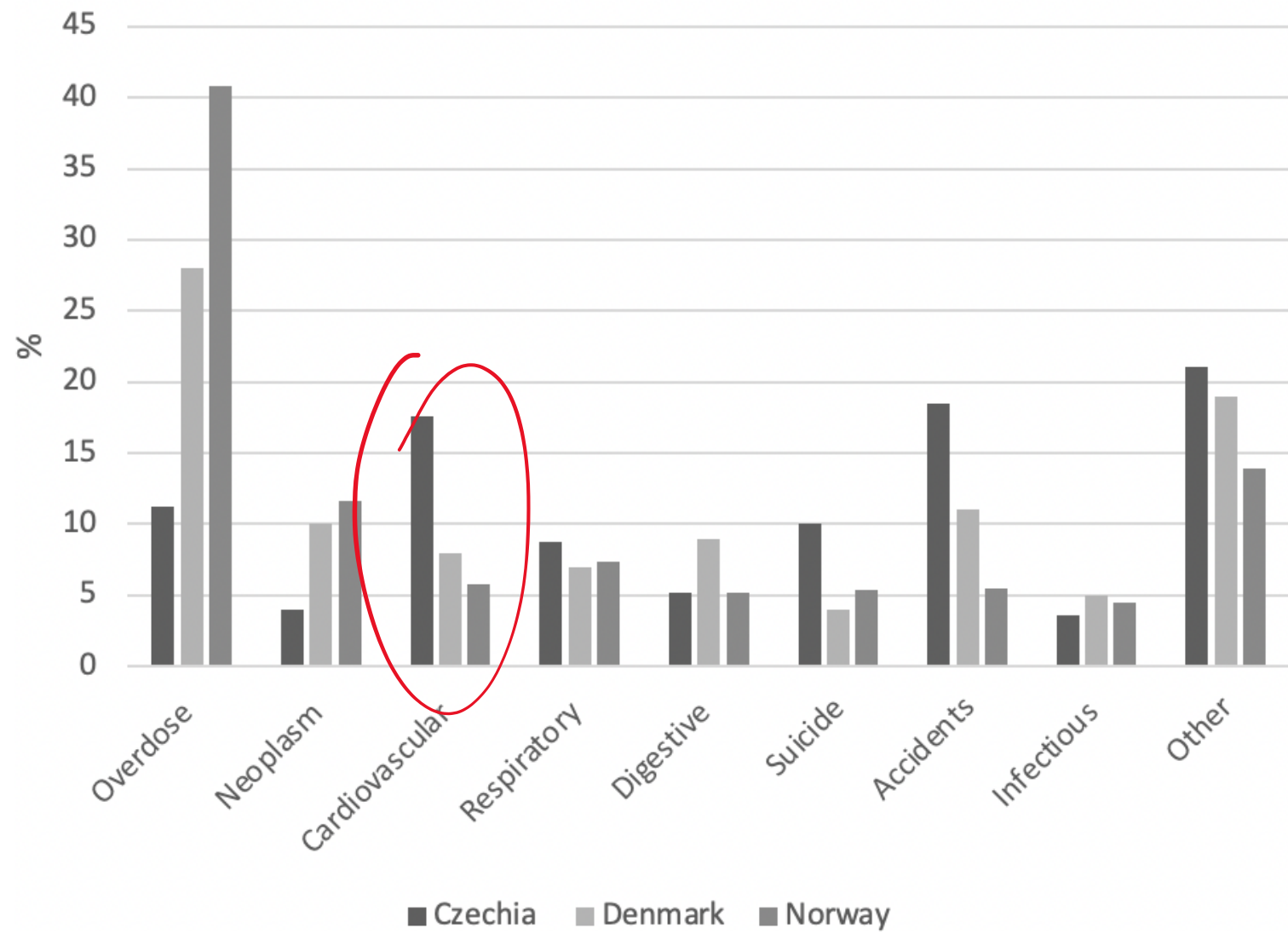
2) Cause-specific mortality among nearly 29,000 patients in treatment for opioid use disorder in multiple settings

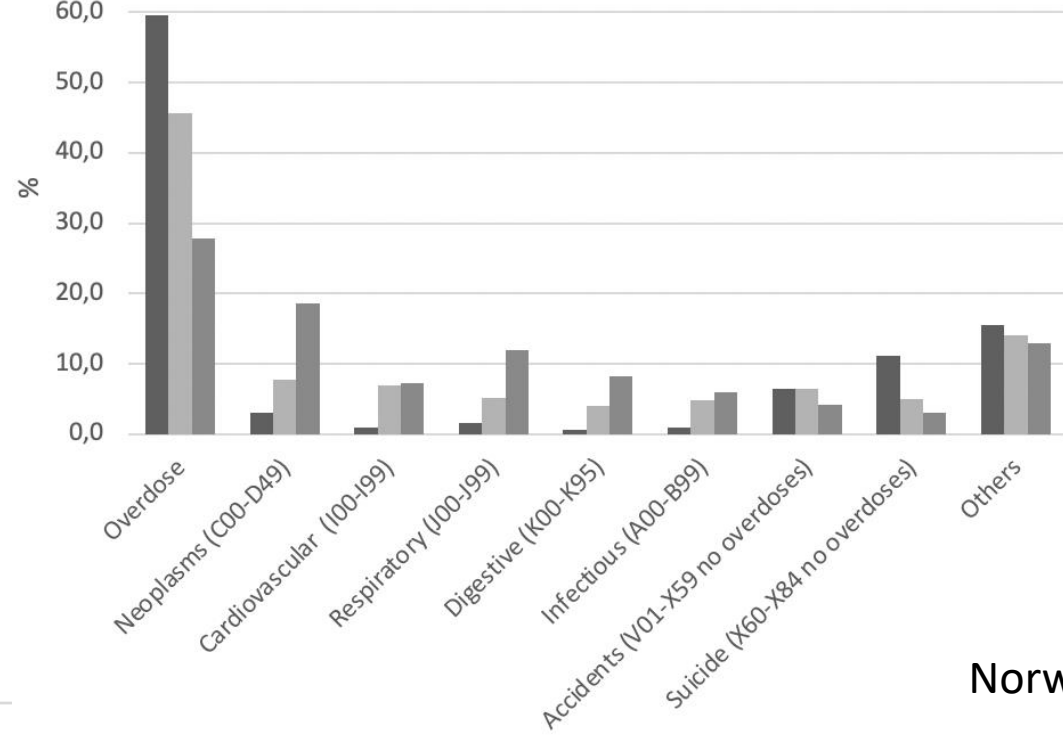
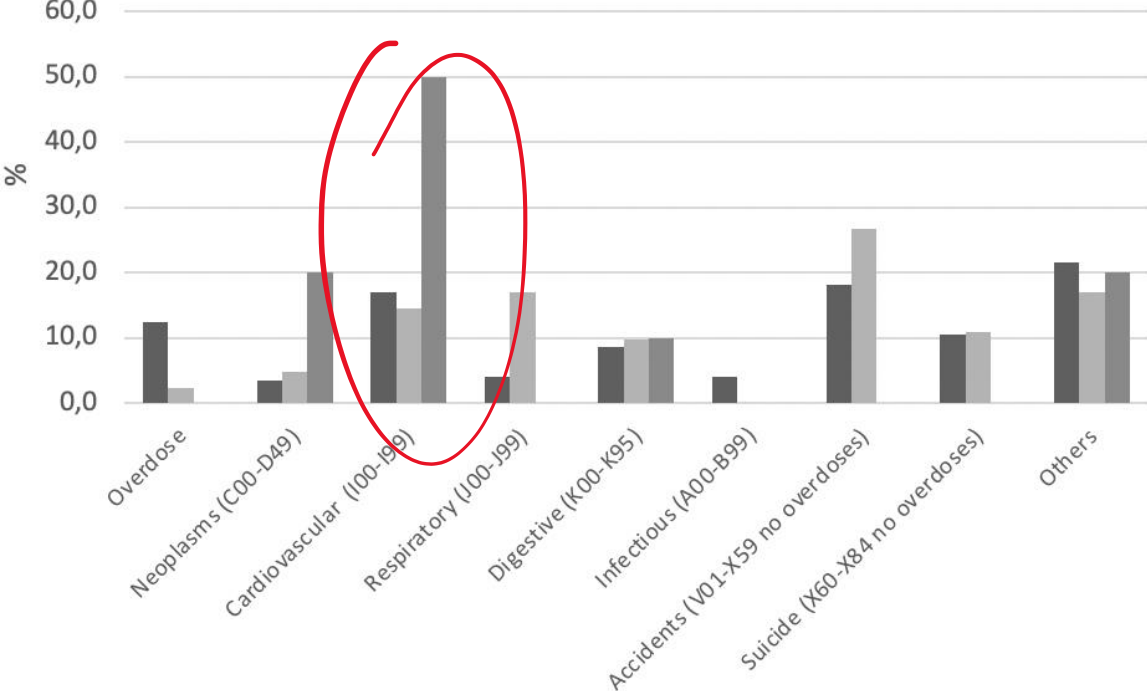
- **Aim:** To describe all non-overdose causes of death in three national cohorts among OMT patients and to **explore associations of non-overdose mortality with age and gender.**
- **Design and settings:** Prospective comparative cohort study using national mortality registry databases for OMT patients from **Czechia** (2000-2019), **Denmark** (2000-2018), and **Norway** (2010-2019).
- **Methods:** Crude mortality rates (**CMR**) were calculated as deaths per 1000 person years for cause-specific mortality.

Total causes of death by country



Total causes of death by country

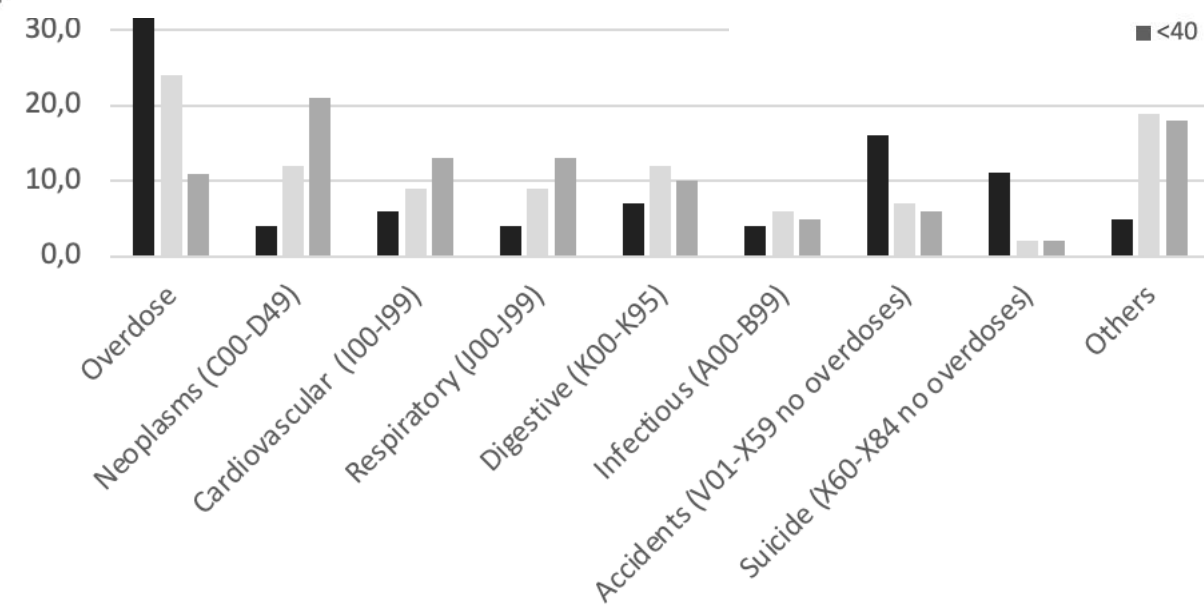




Norway

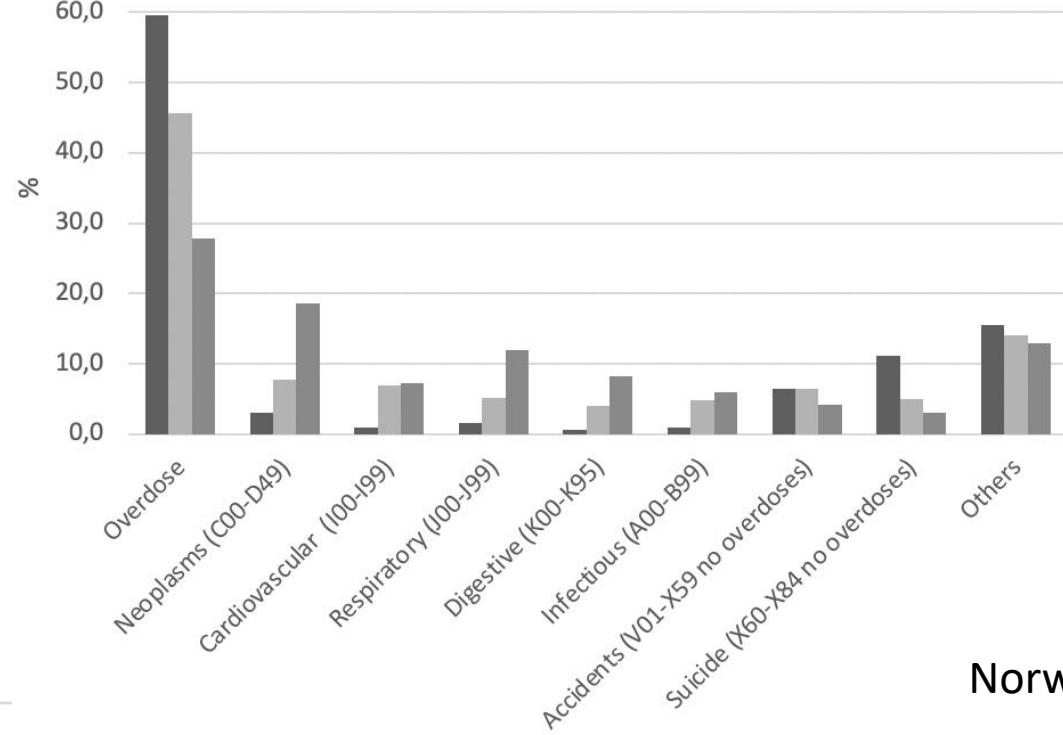
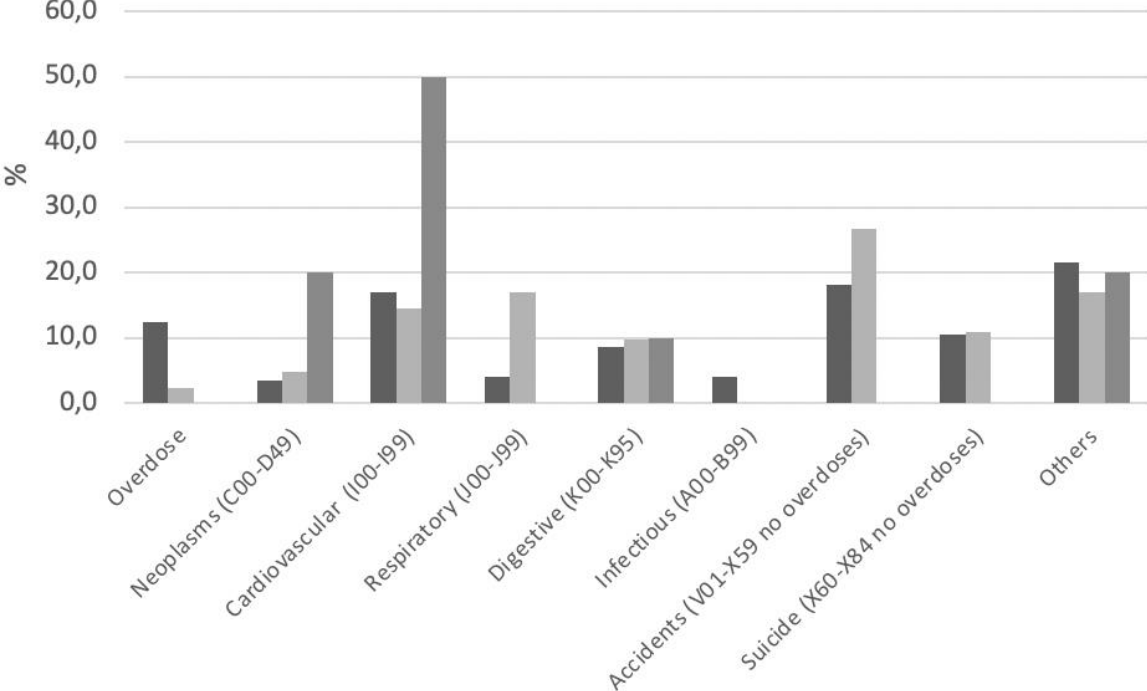
Czechia

■ <40 ■ 40-50 ■ 51+



Causes of death by age group in Denmark

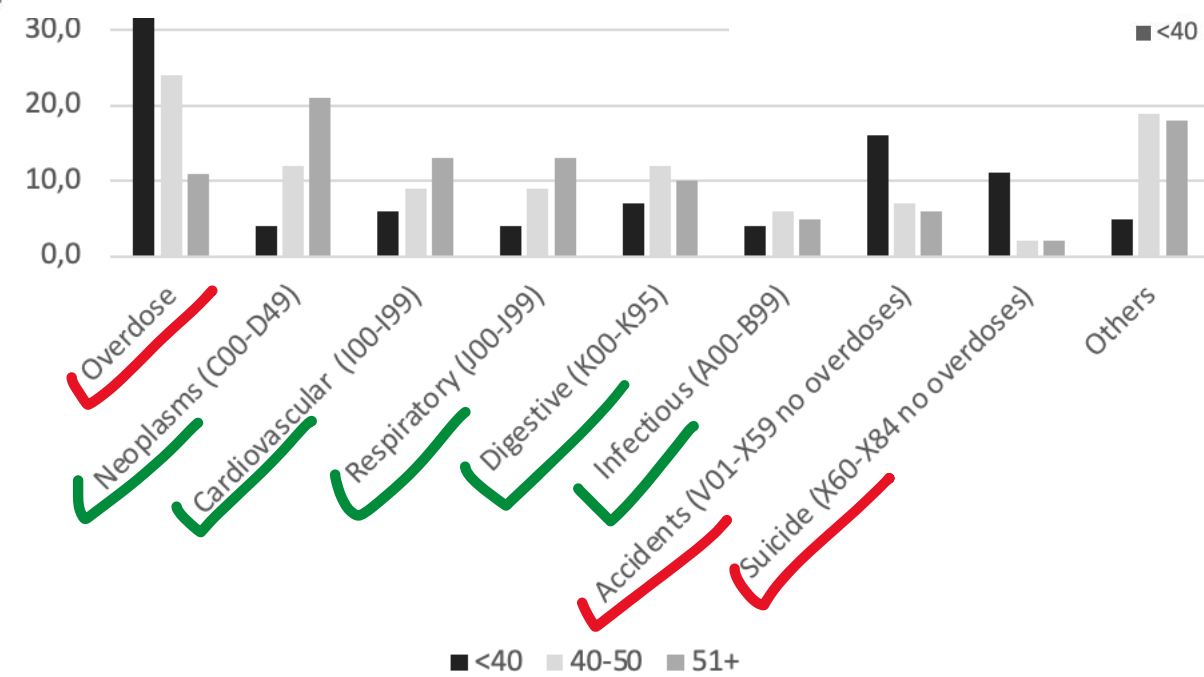
■ <40 ■ 40-50 ■ 51+



Norway

Czechia

■ <40 ■ 40-50 ■ 51+



■ <40 ■ 40-50 ■ 51+

Causes of death by age group in Denmark

Cause-specific mortality among nearly 29,000 patients in treatment for opioid use disorder in multiple settings

- **Results:**
- In total, 29,486 people were included, with 5322 deaths recorded (18%).
- The leading causes of death were accidents and cardiovascular disease in Czechia and overdoses in Norway and Denmark.
- **Unexpected deaths observed in the younger age group decreased in the older groups VS. somatic causes of death increased among the older age groups.**
- **Conclusion:** This study found high rates of preventable death among gender and age groups. The findings **support increased efforts towards screening and preventative health initiatives** among OMT patients specific to the demographic characteristics in different settings.

To conclude...

- Our findings **indicate potential for improvement in clinical practice** based on systematic evaluation and monitoring of mortality risk, more systematic involvement of psychosocial services, and enhanced safety measures to manage overdose and other health risks.
- The three main features in OMT; **(early) access, safety, and quality**, should not be perceived as inverse constructs, but as important dimensions of treatment that must be addressed and optimized.



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Thank you



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