The unique Nordic health registries: Challenges

ISPOR, Copenhagen 2-6 November 2019

Workshop W19:

NORDIC REGISTRIES IN SAFETY STUDIES AND OUTCOME RESEARCH: USING REAL WORLD EVIDENCE. ADVANTAGES AND CHALLENGES OF POOLING REGISTER DATA FROM DENMARK, SWEDEN, FINLAND AND NORWAY.

6 November 2019

INTRODUCTION

- The Nordic health registers represent unique opportunities for provision of RWE in an unmatched setting
- Yet, there are challenges when using these data for research purposes
- We here give some examples of such challenges
- Subsequently, we can discuss
  - How to cope with these challenges
  - What is needed to improve the source registers to eliminate these challenges

Institute of Applied Economics & Health Research ApHER

Your ENCePP partner enepp

Points for review

1	**Pitfalls in registration of treatments in hospital activity registers**
2	**Challenges when using cancer register data, exemplified with the Danish Cancer Registry**
3	**The NORDCAN database: What is going on?**
4	**Conclusions and discussion**

Points for review

1	**Pitfalls in registration of treatment in hospital activity registers** • **Registration of treatment given as part of clinicl trial???** • **Medical treatments administered at hospitals in Sweden (like infusions) underreported** • **The Danish National Patient Register: New treatments administered at hospitals**
2	**Challenges when using cancer register data, exemplified with the Danish Cancer Registry**
3	**The NORDCAN database: What is going on?**
4	**Conclusions and discussions**

Points for review

1	**Pitfalls in registration of treatment in hospital activity registers** • **Registration of treatment given as part of clinical trial???** • **Medical treatments administered at hospitals in Sweden (like infusions) underreported** • **The Danish National Patient Register: New treatments administered at hospitals**
2	Challenges when using cancer register data, exemplified with the Danish Cancer Registry
3	The NORDCAN database: What is going on?
4	Conclusions and discussions

Case example, the Danish National Patient Register: Introduction of new immunotherapies

- Increasingly more new (and expensive!) immunotherapies are introduced
- There is a need for post-authorization safety studies (PASS) based on RWE and to monitor their use as part of 'personalized medicine'
- An ATC (Anatomical Theraputical Chemical Classification) code is assigned to *all* drugs

In general, no persons treated with these drugs can be identified in the Danish Prescription Registry ---->

- The drug is administered at specialist hospital departments
- Patients treated with these drug should be identifiable in the National Patient Register

However:

- For registration as the **principal** treatment of a drug in the National Patient Register, a special Danish code (other than ATC) is needed
- For such new treatments, the special Danish codes
  - may not be assigned at all
  - may be assigned with a substantial delay (years)

Challenge: Which options to use for registration of such treatment?

- Avoiding the registration
- *Using registration with the ATC code as a **supplementary** treatment code (not used very much)*
- Using a higher level treatment code
- Using a treatment code for a 'similar drug'

Points for review

1	Pitfalls in registration of treatment in hospital activity registers
2	**Challenges when using cancer register data, exemplified with the Danish Cancer Registry:** • **Can we trust morphology data?** • **Can we trust TNM/stage data?**
3	The NORDCAN database: What is going on?
4	Conclusions and discussion

Institute of Applied Economics & Health Research ApHER Your ENCePP partner enepp

Danish Cancer Registry (CAR): Morphology codes for selected cancers

Status	Breast	C67	Lung	Ovary	Prostate
No data/no conclusion	448	197	4,099	308	1,328
Plausible classification	47,009	8,601	40,457	5,201	42,117
Wrong tumor	194	9	158	49	183
Total	47,651	8,807	44,714	5,558	43,628
% distribution					
No data/no conclusion	0.9%	2.2%	9.2%	5.5%	3.0%
Plausible classification	98.7%	97.7%	90.5%	93.6%	96.5%
Wrong tumor	0.4%	0.1%	0.4%	0.9%	0.4%
Total	100.0%	100.0%	100.0%	100.0%	100.0%

Unpublished results

Why is it possible to publish morphology codes that according to pathologists do not apply to the cancer concerned?

In many of these cases the patient has a history of more than one cancer form

Danish Cancer Registry (CAR): Staging via TNM codes for selected cancers

Status	Breast	C67	Lung	Ovary	Prostate
No data	2,069	621	1,536	376	6,579
Classifiable	40,776	3,863	41,082	5,127	15,456
Unclassifiable	4,806	4,323	2,096	55	21,593
Total	47,651	8,807	44,714	5,558	43,628
% distribution					
No data	4.3%	7.1%	3.4%	6.8%	15.1%
Classifiable	85.6%	43.9%	91.9%	92.2%	35.4%
Unclassifiable	10.1%	49.1%	4.7%	1.0%	49.5%
Total	100.0%	100.0%	100.0%	100.0%	100.0%

Unpublished results

Why is it impossible to infer stage for so many cases?

- *The M stage may be clinically irrelevant and therefore not reported*
- *Some departments report T stage to pathology register and not cancer registry*

Points for review

1. Pitfalls in registration of treatment in hospital activity registers
2. Challenges when using cancer register data, exemplified with the Danish Cancer Registry
3. **The NORDCAN database: What is going on?**
4. Conclusions and discussion

The NORDCAN database

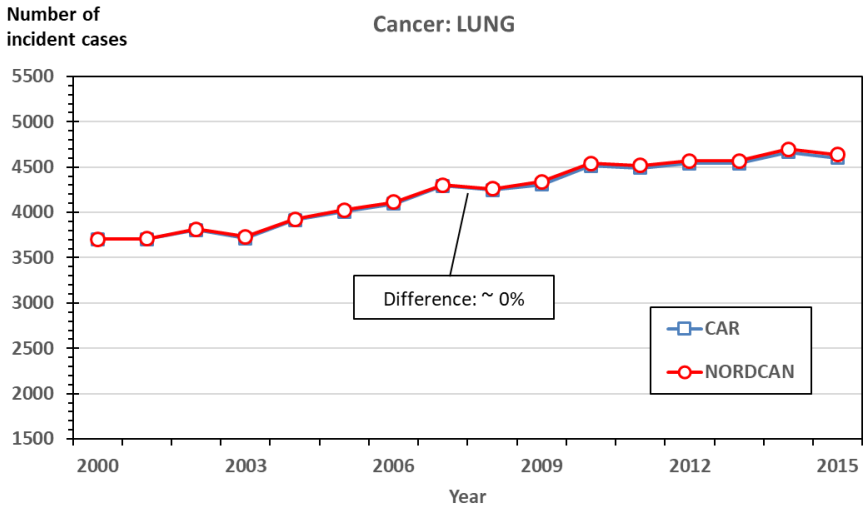
http://www-dep.iarc.fr/NORDCAN/English/frame.asp

NORDCAN is a database of cancer statistics for the Nordic countries: Denmark, Finland, Iceland, Norway, Sweden, Faroe Islands and Greenland.

Tabulated data are put to your disposal by the Association of Nordic Cancer Registries (ANCR) and *data are delivered from each national Cancer Registry and Cause of Death registry. Population registers makes it possible to follow each cancer patient for death and emigration when we calculate prevalence and relative survival.*

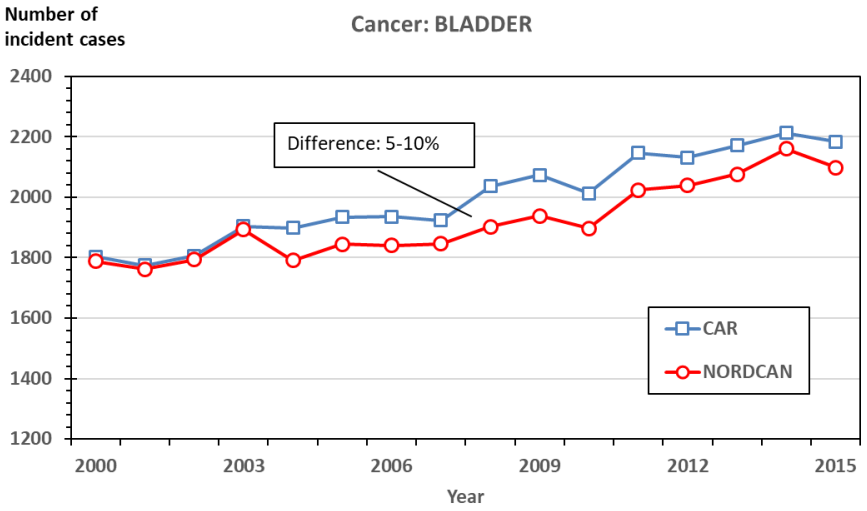
The number of cancer cases might differ slightly from the numbers found in the national reports. This is because we follow international rules to make statistics more comparable between countries (Pukkala et al, 2018). The methods we use to convert data and exceptions to comparability of data are described in "The NORDCAN database", which you find in the menu. A detailed presentation from the Norwegian Cancer Registry including examples of use can be found in a special_issue-NORDCAN.pdf

Comparison of incidence: Danish CAR versus NORDCAN



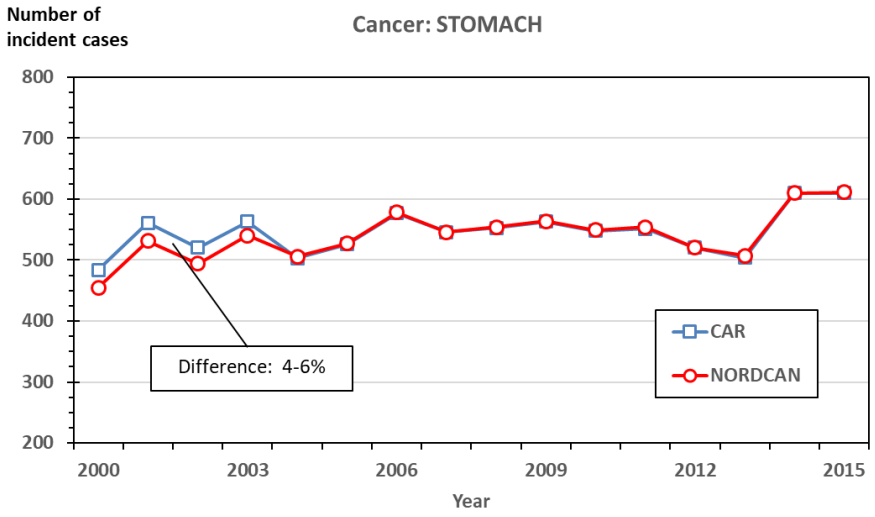
CAR: Danish Cancer Registry

Comparison of incidence: Danish CAR versus NORDCAN



CAR: Danish Cancer Registry

Comparison of incidence: Danish CAR versus NORDCAN



CAR: Danish Cancer Registry

The NORDCAN database: Checking the validity of mortality data

Principle:

Migrations are negligible after the diagnosis of cancer, at least for severe cancer forms with incidence in higher age groups. Therefore, the following should hold true as a first order approximation:

Prevalence end of year t-1:	N(t-1)
New cases (incidence) in year t:	I(t)
Deaths (regardless of cause) in year t:	D(t)
Prevalence end of year t:	P(t) = P(t-1) + I(t) – (D(t)

Comparison of Mortality: Danish CAR versus NORDCAN

PANCREAS CANCER in DENMARK

Extract from Danish Cancer Registry (2017)

Year	Incidence	Deaths	Prevalence	Prevalence Expected	Prevalence Deviation
1999			419		
2000	729	744	404	404	0
2001	783	727	460	460	0
2002	767	733	494	494	0
2003	775	753	516	516	0
2004	849	810	555	555	0
2005	849	794	610	610	0
2006	872	829	653	653	0
2007	920	880	693	693	0
2008	916	888	721	721	0
2009	984	862	843	843	0
2010	964	915	892	892	0
2011	996	898	990	990	0
2012	986	961	1015	1015	0
2013	945	898	1062	1062	0
2014	973	892	1143	1143	0
2015	984	889	1238	1238	0

Comparison of Mortality: Danish CAR versus NORDCAN

LUNG CANCER in DENMARK

Extract from Danish Cancer Registry (2017)

Year	Incidence	Deaths	Prevalence	Prevalence Expected	Prevalence Deviation
1999			4404		
2000	3704	3378	4730	4730	0
2001	3706	3443	4993	4993	0
2002	3806	3549	5250	5250	0
2003	3715	3629	5336	5336	0
2004	3915	3598	5653	5653	0
2005	4009	3695	5967	5967	0
2006	4097	3910	6154	6154	0
2007	4291	3820	6625	6625	0
2008	4247	3927	6945	6945	0
2009	4305	3974	7276	7276	0
2010	4512	4033	7755	7755	0
2011	4491	3951	8295	8295	0
2012	4541	4020	8816	8816	0
2013	4541	4001	9356	9356	0
2014	4664	4128	9892	9892	0
2015	4602	4099	10395	10395	0

Points for review

1. Pitfalls in registration of treatment in hospital activity registers
2. Challenges when using cancer register data, exemplified with the Danish Cancer Registry
3. The NORDCAN database: What is going on?
4. **Conclusions and discussion**

CONCLUSIONS

- The Nordic health registers are indeed unique but not without challenges when using their data for research purposes
- Challenges may relate to
  - Data models and coding schemes
  - Inappropriate coding practice
  - Lack of validation
- Researchers using health register data should be observant to such challenges and handle them appropriately

Institute of Applied Economics & Health Research ApHER
Your ENCePP partner enepp

EXTRA SLIDE

T stage reporting: Danish Cancer Registry (CAR) versus Danish Pathology Register

Bladder cancer (C67) in the CEDAR project (unpublished results)

		PATOBANK							
		No data	**T0/Ta/Tis**	**T1**	**T2**	**T3**	**T4**	**Total**	Agreement:
CAR	**No data**	332	33	166	174	64	20	**789**	332/789 = 42.1%
	T0/Ta/Tis	<5	<5	13	<5	0	0	**18**	<5/18 = 11.1%
	T1	296	42	2596	193	37	8	**3172**	2596/3172 = 81.8%
	T2	221	16	102	2302	175	30	**2846**	2302/2846 = 80.9%
	T3	193	6	62	403	342	13	**1019**	342/1019 = 33.6%
	T4	258	5	64	463	46	127	**963**	127/963 = 13.2%
	Total	**1302**	**104**	**3003**	**3536**	**664**	**198**	**8807**	
	Agreement:	332/1302 = 25.5%	<5/104 = 1.9%	2596/3003 = 86.4%	2302/3536 = 65.1%	342/664 = 51.5%	127/198 = 64.1%		

Overall agreement: 5701/8807 = 64.7%

- *Note the substantial general disagreement*
- *Why are T stage registrations in the pathology register not identifiable in the cancer registry?*

Institute of Applied Economics & Health Research ApHER
Your ENCePP partner enepp

Comparison of Mortality: Different extracts from CAR

LUNG CANCER	CanEpid/CEDAR datasæt, 24JUL2013					CanEpid/CEDAR datasæt, 16FEB2017					Deviation: Datasæt2017 - Datasæt 2013		
Year	Incidence	Deaths	Prevalence	Prevalence Expected	Prevalence Deviation	Incidence	Deaths	Prevalence	Prevalence Expected	Prevalence Deviation	Incidence	Deaths	Prevalence
1999			4396					4404					8
2000	3700	3371	4725	4725	0	3704	3378	4730	4730	0	4	7	5
2001	3701	3443	4983	4983	0	3706	3443	4993	4993	0	5	0	10
2002	3793	3541	5235	5235	0	3806	3549	5250	5250	0	13	8	15
2003	3711	3623	5323	5323	0	3715	3629	5336	5336	0	4	6	13
2004	3904	3594	5633	5633	0	3915	3598	5653	5653	0	11	4	20
2005	3995	3684	5944	5944	0	4009	3695	5967	5967	0	14	11	23
2006	4061	3868	6137	6137	0	4097	3910	6154	6154	0	36	42	17
2007	4273	3809	6601	6601	0	4291	3820	6625	6625	0	18	11	24
2008	4202	3887	6916	6916	0	4247	3927	6945	6945	0	45	40	29
2009	4274	3950	7240	7240	0	4305	3974	7276	7276	0	31	24	36
2010	4448	3973	7715	7715	0	4512	4033	7755	7755	0	64	60	40
2011	4398	3889	8224	8224	0	4491	3951	8295	8295	0	93	62	71

GENERAL DISCUSSION

Institute of Applied Economics & Health Research ApHER
Your ENCePP partner enepp

POINTS FOR INTERACTIVE DISCUSSION

- Possibilities with rare diseases or natural experiments?
- Do you have any need for pooled data?
- Have you experienced these or similar challenges?
  - How did you handle these challenges?
- What can be done to improve the registers to reduce or maybe even eliminate these challenges?