

# CARING

# Cancer Incidence

Preliminary Results

Odense 13-11-2015

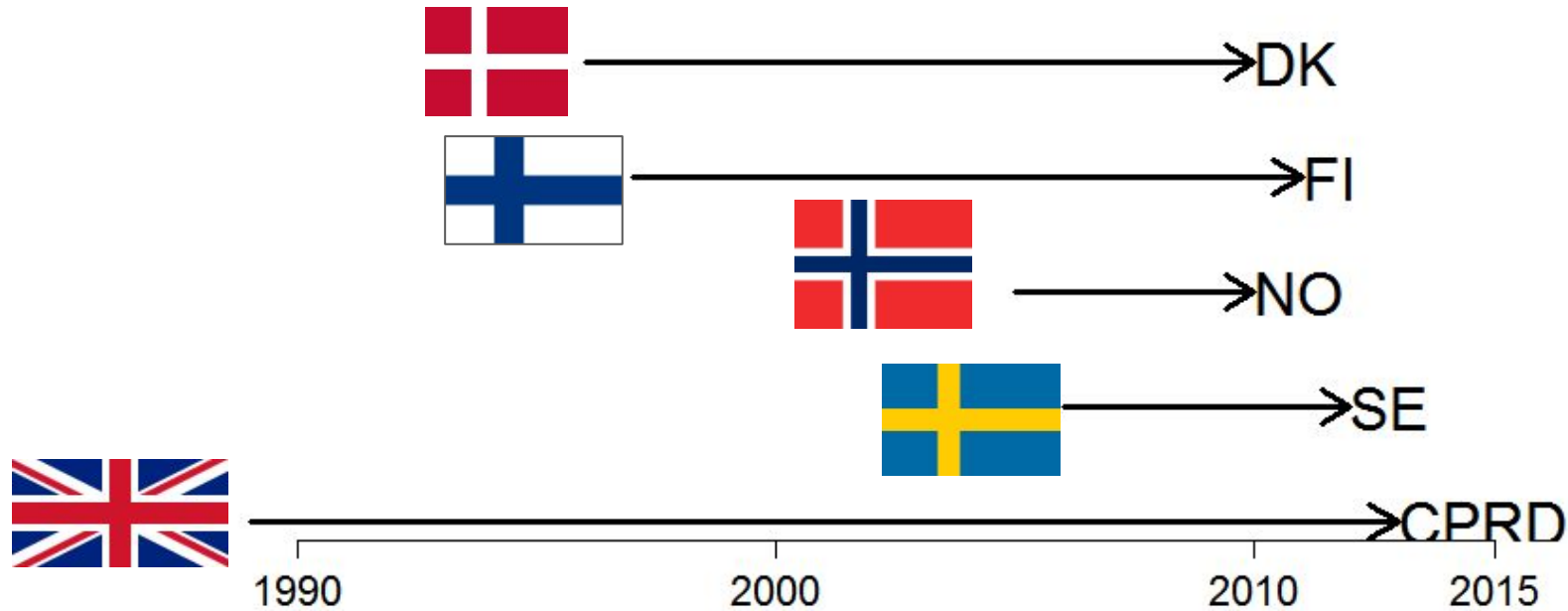
Jari Haukka, Anna But and CARING Group

# CARING

- The **CARING** (**C**Ancer **R**isks and **I**Nsulin analogues) project obtained precise data on the incidence of cancer in diabetic patients
- Determine if there is **any link with use of various insulin and insulin analogues and cancer.**
- <http://www.caring-diabetes.eu/>



# Data sources and coverages



# Study Population

- Start of follow-up (SOF) **at first insulin prescription**
- 1 year wash-out period without insulin before SOF required
- End of follow-up (EOF):
  - first cancer (not NMSC)
  - death (censoring)
  - end of data coverage (censoring)
- Excluded:
  - any cancer before SOF (not NMSC)
  - age<18 at SOF

# Cancer Types

- Any cancer
- **Liver cancer**
- Pancreatic cancer
- Lung cancer
- **Bladder cancer**
- Colorectal cancer
- Non Hodgkin lymphoma
- Breast cancer
- Cancer of corpus uteri
- Prostate cancer

# Explanatory variables (1)

- Time fixed:
  - Sex
  - Usage of oral antidiabetic medication (OAD)(other than insulins) in one year before SOF
  - Usage of NSAID in one year before SOF
  - Usage of HRT in one year before SOF
  - Usage of statins in one year before SOF

## Explanatory variables (2)

- Time varying:
  - Age
  - Time since start of follow-up
  - Calendar year
  - **Cumulative time exposed to any insulin**
  - **Cumulative time exposed to human insulin**
  - **Cumulative time exposed to glargine (ATC A10AE04)**
  - **Cumulative time exposed to detemir (ATC A10AE05)**

# Modeling (1)

- **Poisson regression model**
- Data arrange in **Lexis** structure
  - Age
  - Calendar year
- Outcome: any cancer or cancer types
- log-person-years as offset
- R language:
  - “**Epi**”-package
  - exposures calculate with function “**gen.exp**”



## Modeling (2)

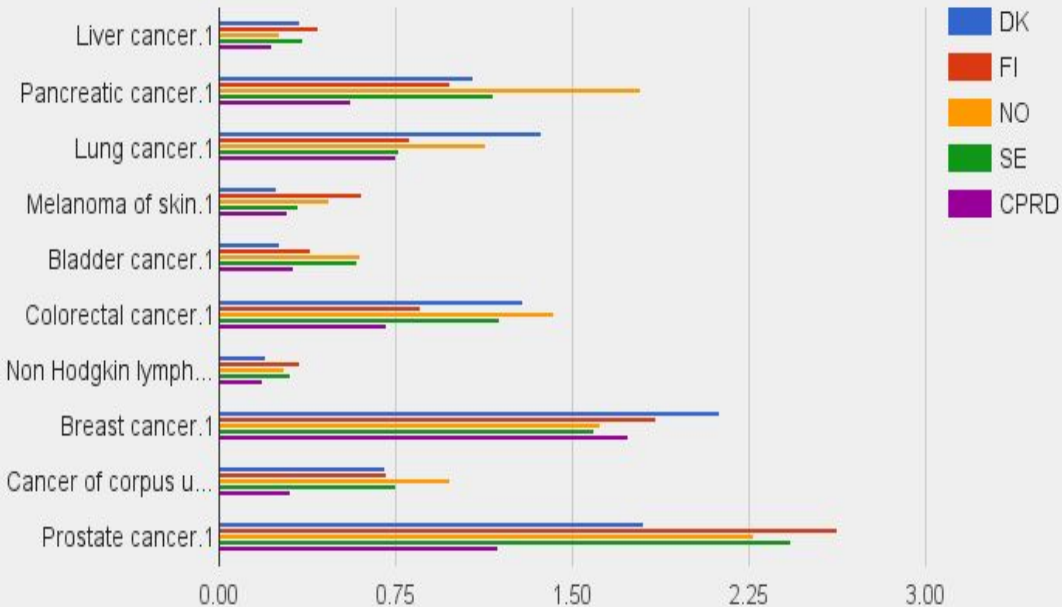
- Model, simple
  - Age, sex, time since SOF, calendar year
  - Country
  - time exposed to human insulin (discrete)
  - time exposed to glargine (A10AE04)(discrete)
  - time exposed to detemir (A10AE05)(discrete)

# Baseline characteristics

	Denmark (N=63,252)	Finland (N=105,945)	Norway (N=21,309)	Sweden (N=88,038)	CPRD (N=47,537)
Study period	1996 – 2010	1996 – 2011	2005 – 2010	2007 – 2012	1987 – 2012
Males, N ( %)	38,292 (57%)	57,691 (55%)	11,913 (56%)	50,254 (57%)	25,570 (54%)
Follow-up time, mean (SD)	5.3 (3.9)	5.6 (3.9)	2.7 (1.8)	2.7 (1.7)	5.6 (4.4)



### Standardized rates

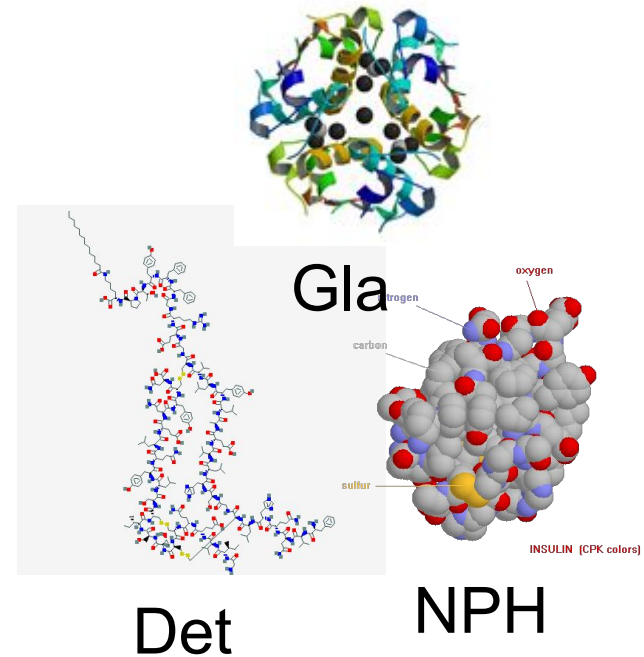


## Large population

- 1.47 million person-years
- 21,368 cancer cases

# Insulin type comparisons

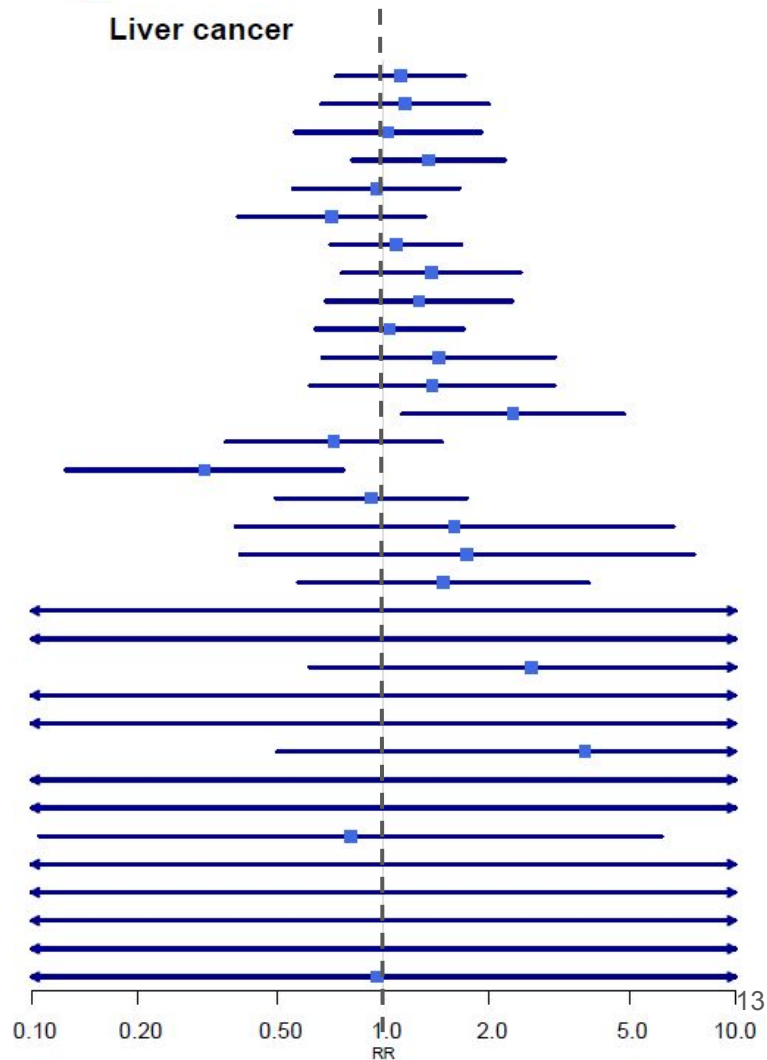
- We compared three insulin types with same cumulative exposure lengths in years for each cancer type
- Results of liver and bladder cancer



# Liver cancer

- Adjusted multi-country results
- No consistent differences

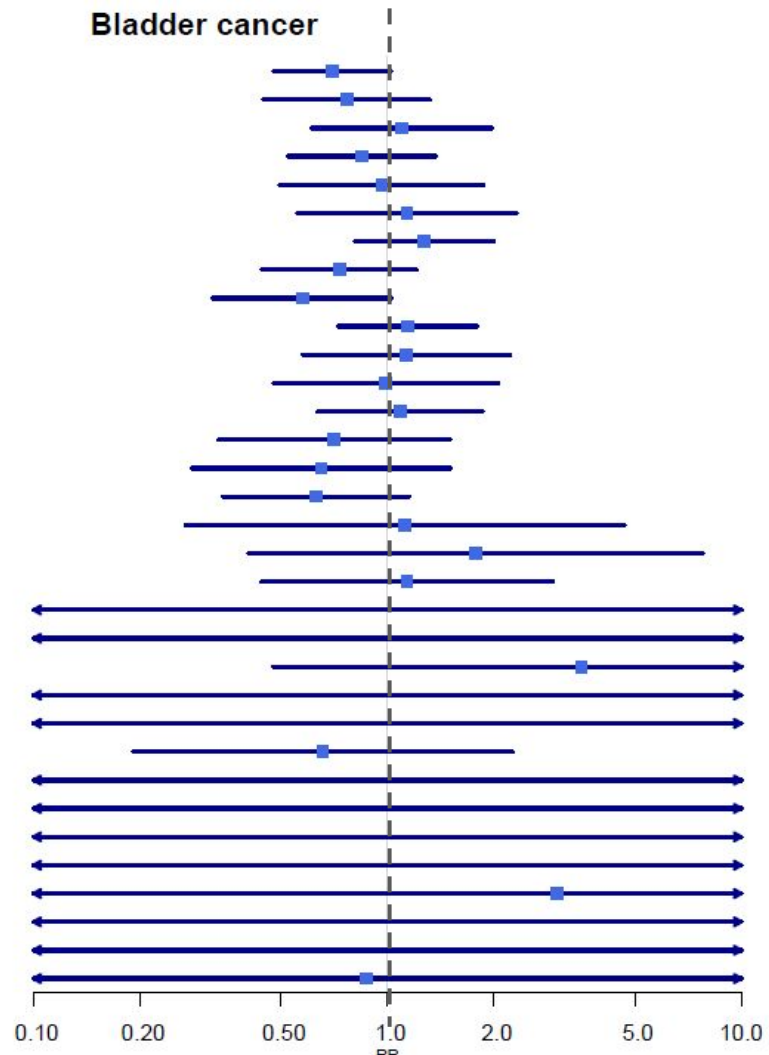
NPH(0,0.5] vs. Gla(0,0.5]  
 NPH(0,0.5] vs. Det(0,0.5]  
 Gla(0,0.5] vs. Det(0,0.5]  
 NPH(0.5,1] vs. Gla(0.5,1]  
 NPH(0.5,1] vs. Det(0.5,1]  
 Gla(0.5,1] vs. Det(0.5,1]  
 NPH(1,2] vs. Gla(1,2]  
 NPH(1,2] vs. Det(1,2]  
 Gla(1,2] vs. Det(1,2]  
 NPH(2,3] vs. Gla(2,3]  
 NPH(2,3] vs. Det(2,3]  
 Gla(2,3] vs. Det(2,3]  
 NPH(3,4] vs. Gla(3,4]  
 NPH(3,4] vs. Det(3,4]  
 Gla(3,4] vs. Det(3,4]  
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 Gla(4,5] vs. Det(4,5]  
 NPH(5,6] vs. Gla(5,6]  
 NPH(5,6] vs. Det(5,6]  
 Gla(5,6] vs. Det(5,6]  
 NPH(6,7] vs. Gla(6,7]  
 NPH(6,7] vs. Det(6,7]  
 Gla(6,7] vs. Det(6,7]  
 NPH(7,8] vs. Gla(7,8]  
 NPH(7,8] vs. Det(7,8]  
 Gla(7,8] vs. Det(7,8]  
 NPH(8,9] vs. Gla(8,9]  
 NPH(8,9] vs. Det(8,9]  
 Gla(8,9] vs. Det(8,9]  
 NPH(9,10] vs. Gla(9,10]  
 NPH(9,10] vs. Det(9,10]  
 Gla(9,10] vs. Det(9,10]



# Bladder cancer

- Adjusted multi-country results
- No consistent differences

NPH(0,0.5] vs. Gla(0,0.5]  
 NPH(0,0.5] vs. Det(0,0.5]  
 Gla(0,0.5] vs. Det(0,0.5]  
 NPH(0.5,1] vs. Gla(0.5,1]  
 NPH(0.5,1] vs. Det(0.5,1]  
 Gla(0.5,1] vs. Det(0.5,1]  
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 NPH(2,3] vs. Gla(2,3]  
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 Gla(2,3] vs. Det(2,3]  
 NPH(3,4] vs. Gla(3,4]  
 NPH(3,4] vs. Det(3,4]  
 Gla(3,4] vs. Det(3,4]  
 NPH(4,5] vs. Gla(4,5]  
 NPH(4,5] vs. Det(4,5]  
 Gla(4,5] vs. Det(4,5]  
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 NPH(8,9] vs. Det(8,9]  
 Gla(8,9] vs. Det(8,9]  
 NPH(9,10] vs. Gla(9,10]  
 NPH(9,10] vs. Det(9,10]  
 Gla(9,10] vs. Det(9,10]



# Conclusion

- No alarming results of excess risk was detected when comparing three insulin types
- Limited set of covariates shared by all data sources
  - Data sources with more covariates (DK, NO, SWE, CPRD) will model with more complete set of covariates
- More sensitivity analyses will be carried out





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NETHERLANDS  
CANCER  
INSTITUTE  
ANTONI VAN LEEUWENHOEK



SEVENTH FRAMEWORK  
PROGRAMME



Aarhus University Hospital



UNIVERSITY  
OF TAMPERE



Karolinska  
Institutet



UNIVERSITY OF HELSINKI



Thank you for your attention!