Implementing disclosure controls in DataSHIELD demonstrated by the dsSurvival package

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Survival analysis

Rationale

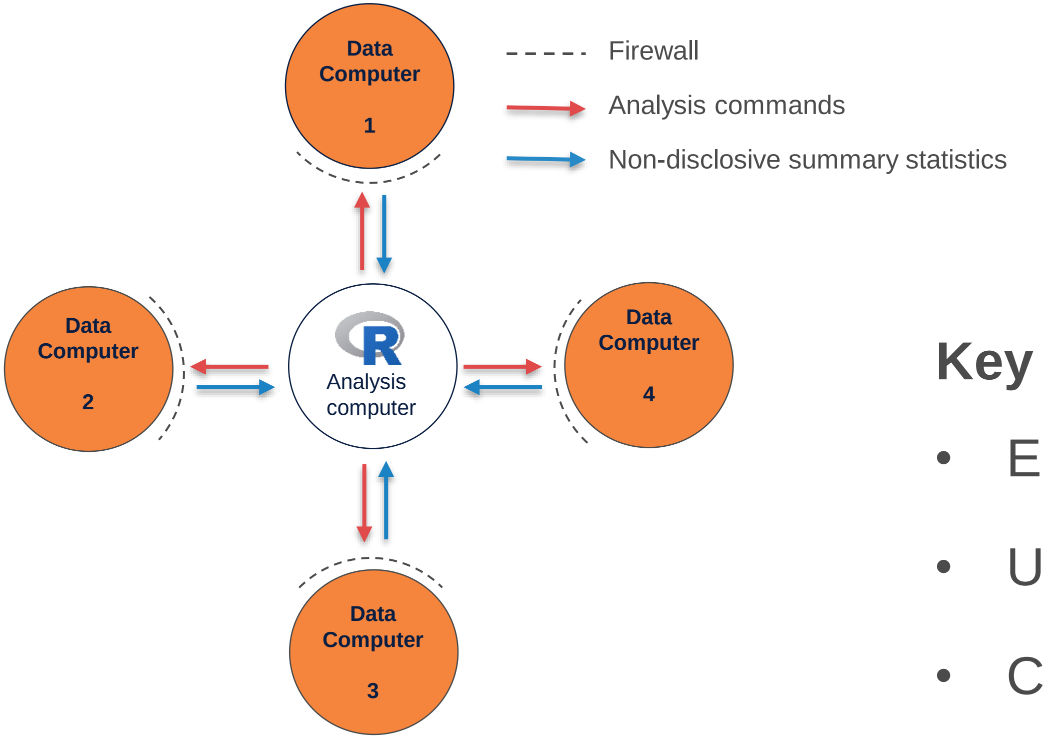
- Survival analysis is widely used in medical sciences to analyze the expected duration of time until some event of interest occurs
- The most frequently used model is the cox proportional hazard model (Cox, 1972)
- Performing meta-analysis of survival models requires large amount of data from different sites
  - General Data Protection Regulation
  - Physical size of data

Alternative: DataSHIELD

The DataSHIELD approach

Take “analysis to data” ….. not “data to analysis”

Data Aggregation Through Anonymous Summary-statistics from Harmonized Individual-levEL Databases



Key principles

- Enables federated analysis
- Uses client – server architecture
- Controls disclosure risks

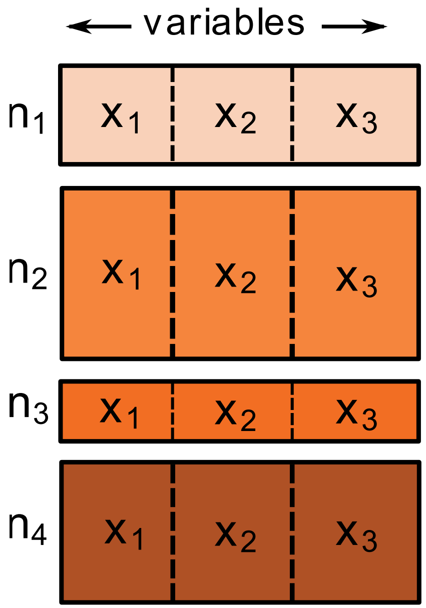
Gaye, Amadou, et al. "DataSHIELD: taking the analysis to the data, not the data to the analysis." International journal of epidemiology 43.6 (2014): 1929-1944.

https://www.datashield.org/

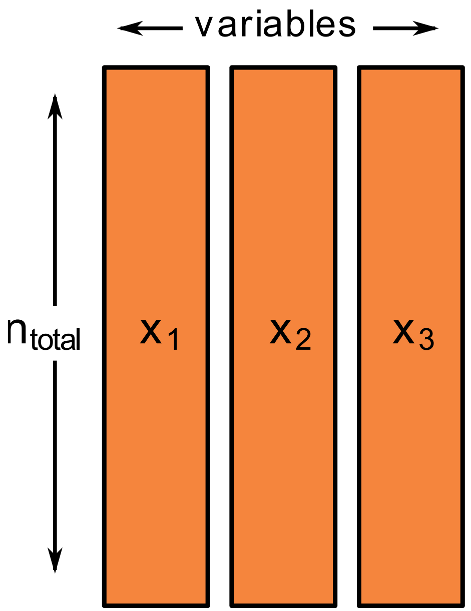
The DataSHIELD approach

Two classes of multi-score analysis

- **Horizontal partitioning**
  - meta-analysis setting



- Vertical partitioning
  - record linkage setting



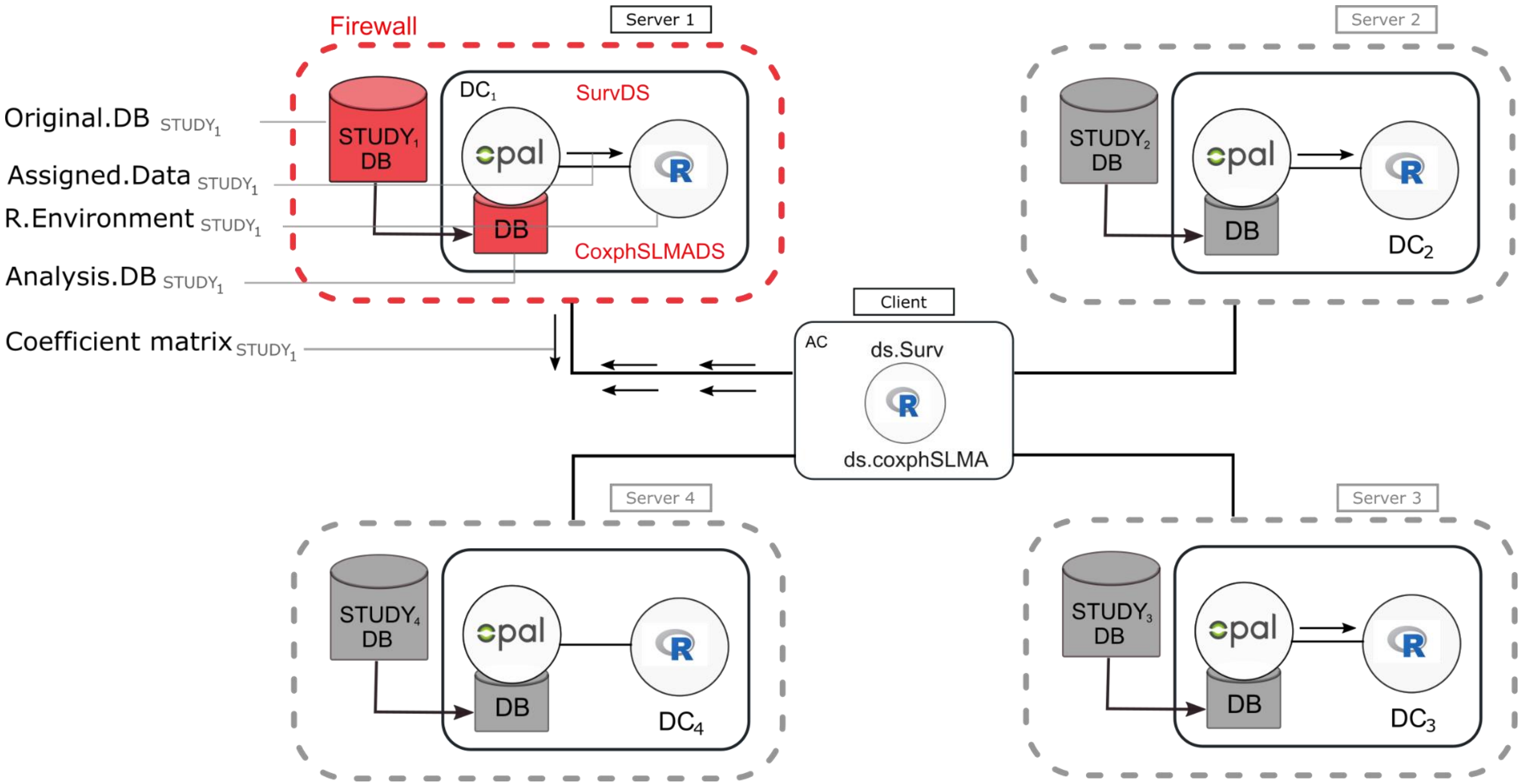
dsSurvival

Privacy preserving fitting of Cox models

- Allow Cox models to be fitted at each study, and then meta analyse the results
- Implementation is restricted to being study-level meta-analysis (SLMA) rather than full likelihood
- Server-side package: dsSurvival
  - SurvDS(…)
  - coxphSLMADS(…)
- Client-side package: dsSurvivalClient
  - ds.Surv(…) → assign function
  - ds.coxphSLMA(…) → aggregate function

dsSurvival Framework

Privacy preserving fitting of Cox models



AC: Analysis computer
DC: Data computer
DB: Database

Disclosure risks

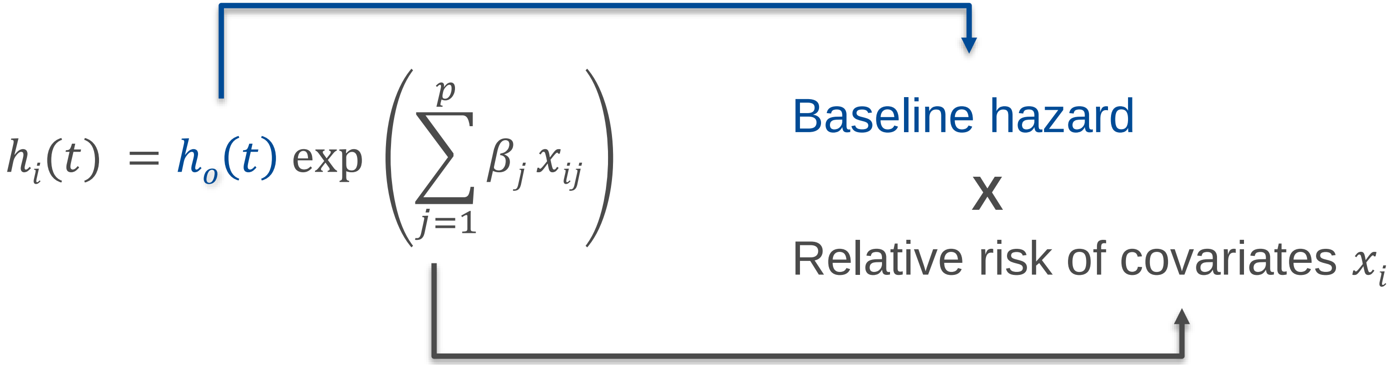
Survival analysis

- Controlling the risk that the data analyst can deliberately infer to the identity or to one of the key variables being analyzed.
- The results of a survival analysis are likely to be disclosive if:
  - Reveal identifying information, or exact values of variables, including dates, diagnoses, and comorbidities
  - Reveal status of observations

O'Keefe, Christine M., et al. "Confidentialising survival analysis output in a remote data access system." Journal of Privacy and Confidentiality 4.1 (2012).

Disclosure risks

Cox proportional hazard models



$$h_i(t) \ = h_o(t) \exp\left(\sum_{j=1}^{p} \beta_j \, x_{ij}\right)$$

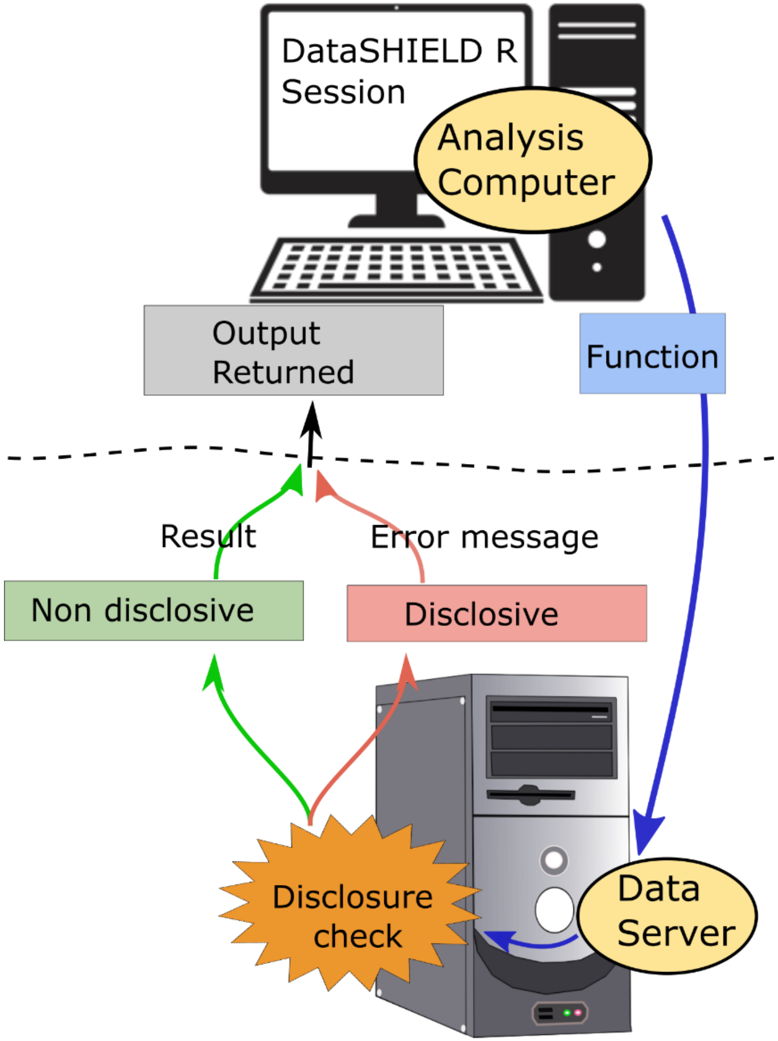
Baseline hazard

X

Relative risk of covariates x_i

- Interested in the coefficient estimates β rather than the baseline hazard $h_o(t)$
- Do not release the values of the covariates x_{ij} for each participant
- Do not reveal the hazard function $h_i(t)$ (survival objects) for each participant

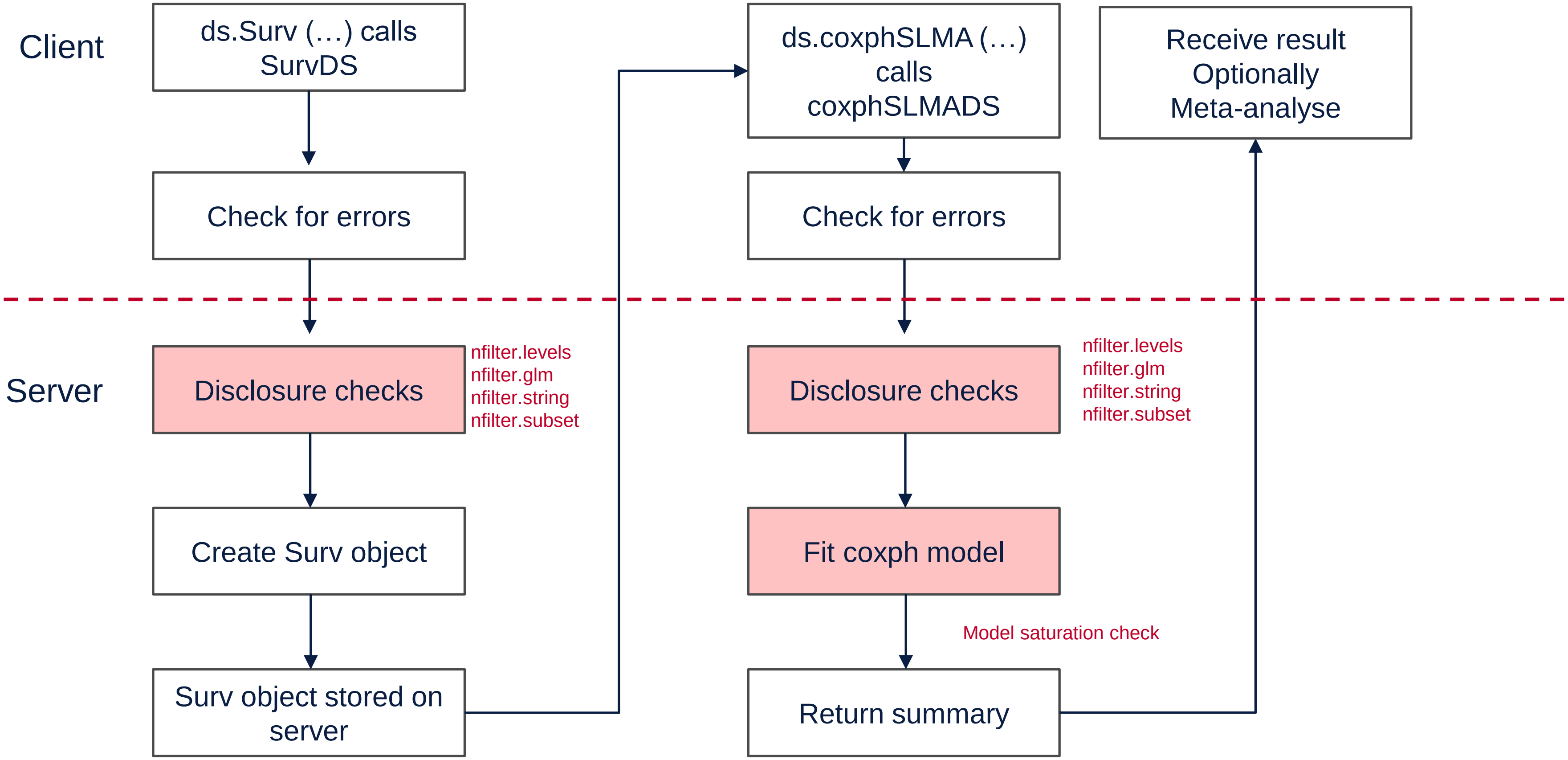
Disclosure control



Disclosure checks

- nfilter.levels
- nfilter.tab
- nfilter.glm
- nfilter.string
- nfilter.subset

Disclosure checks



- Number of parameters in Cox model as a proportion of the sample size
- Default : 20% of sample size
- Prevents model oversaturation

Output presentation

```
$study1

                     coef       exp(coef)   se(coef)   z        Pr(>|z|)
 D$age               0.00815    1.008191    0.001248   6.535    6.35e-11 ***
 D$bmi               0.00553    1.005551    0.030356   2.422    0.004245 **
 D$factor(sex)male   0.15224    1.164442    0.065621   0.215    0.000116 **

Signif. Codes: 0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1‘ ’ 1
```

```
$study2

                     coef       exp(coef)   se(coef)   z        Pr(>|z|)
 D$age               0.04067    1.04151     0.00416    9.776    < 2e-16  ***
 D$bmi               -0.62756   0.53389     0.11767    -5.333   9.66e-08 ***
 D$factor(sex)male   -0.66000   0.516850    0.099481   -6.634   3.26e-11 ***

Signif. Codes: 0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1‘ ’ 1
```

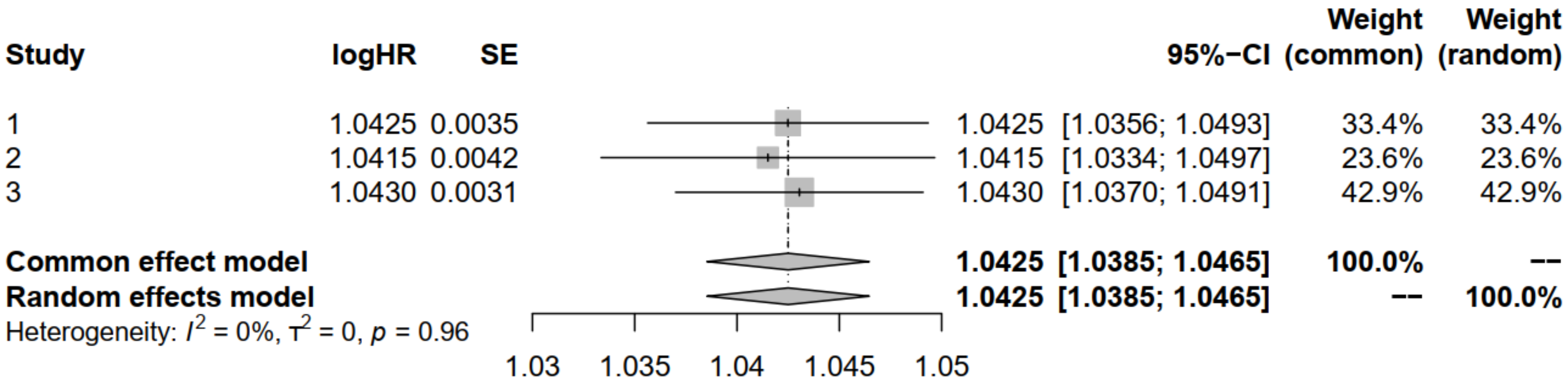
```
$study3

                     coef       exp(coef)   se(coef)   z        Pr(>|z|)
 D$age               0.042145   1.043045    0.003086   13.655   < 2e-16  ***
 D$bmi               0.006522   1.005551    0.03359    1.452    0.424513 ***
 D$factor(sex)male   -0.599238  0.549230    0.084305   -7.108   1.18e-12 ***

Signif. Codes: 0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1‘ ’ 1
```

Metafor R package

- Meta-analysis of the hazard ratios
- Forest plots of estimates from RE model



Study	logHR	SE		95%-CI	Weight (common)	Weight (random)
1	1.0425	0.0035	1.0425	[1.0356; 1.0493]	33.4%	33.4%
2	1.0415	0.0042	1.0415	[1.0334; 1.0497]	23.6%	23.6%
3	1.0430	0.0031	1.0430	[1.0370; 1.0491]	42.9%	42.9%
Common effect model			**1.0425**	**[1.0385; 1.0465]**	**100.0%**	**--**
Random effects model			**1.0425**	**[1.0385; 1.0465]**	**--**	**100.0%**

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.96$

http://www.metafor-project.org

Summary

- DataSHIELD enables federated analysis and tailored disclosure controls
- dsSurvival is a DataSHIELD package for privacy preserving meta-analysis of survival data distributed across different sites
- A tutorial in bookdown format with code, diagnostics, plots and synthetic data is available here:
- https://neelsoumya.github.io/dsSurvivalbookdown/
- All code is available from the following repositories:
- https://github.com/neelsoumya/dsSurvivalClient/
- https://github.com/neelsoumya/dsSurvival/

Thank you

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