Analysis risk of orthopedic implant failure using survival analysis and kernel estimation

Stanislav Katina, Iveta Selingerová, Andrea Kraus,
Ivana Horová, Jiří Zelinka

Department of Mathematics and Statistics
Faculty of Science, Masaryk University
Brno

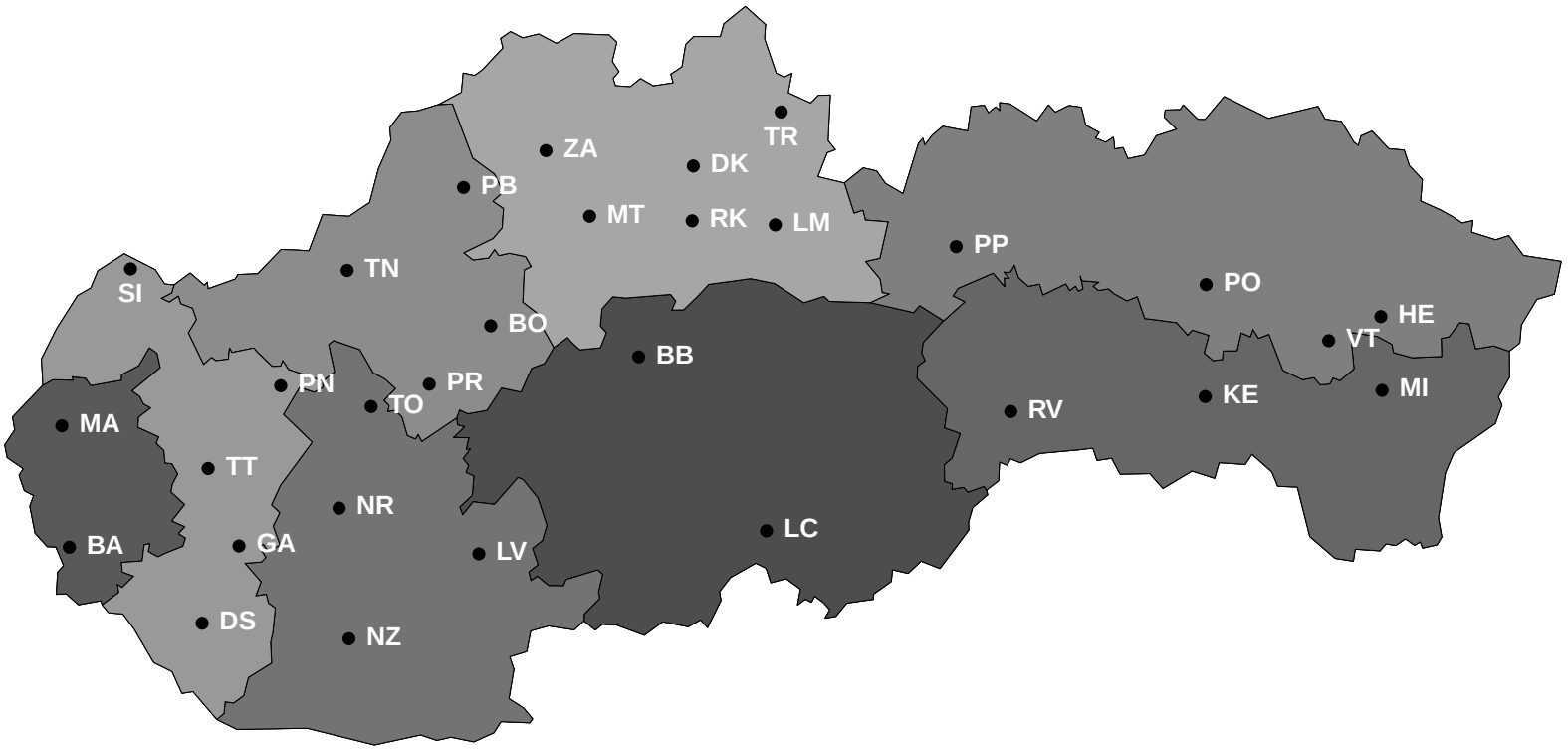
ROBUST 2016
11-16 September 2016

Outline

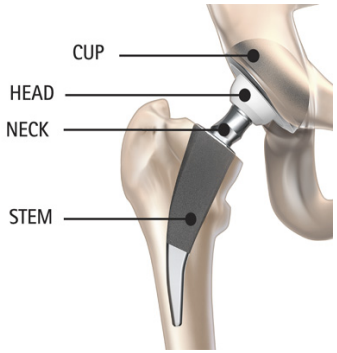
Slovak Arthroplasty Register (SAR)

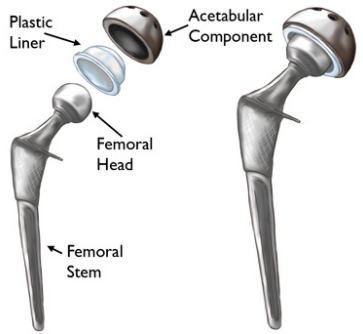
- One of the first national registries in Europe
  - Webpage: `http://sar.mfn.sk/.320.html`
  - Head: MUDr. Libor Nečas, Ph.D.
    (Head of Orthopedic Clinic, University Hospital Martin &
    Head of Jessenius Faculty of Medicine, Comenius University)
- Systematically collects data about arthoplasties since 2003
  (Law Nr. 576/2004)
- Maximum follow-up: 13 years (Jan 1 2003–Dec 31 2015)
- Implemented in 43 orthopedic and traumatology departments in 30 Slovak towns (99.9% coverage)

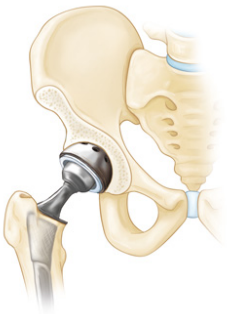
Orthopedic and traumatology departments



Prosthesis







- The implant may fail at some point after the operation . . .
- If it does, it needs to be replaced
  - A revision operation is performed . . . and recorded in the SAR
- Obvious questions
  - What is the risk of implant failure?
  - What influences the risk?

SAR data

- Outcome
  - 61 186 operations with 1 275 implant failures (2.1 %)
  - Time to implant failure $\approx$ the difference between
    - Date of primary operation
    - Date of (first) revision operation
  - Range of the difference: 2 days – 12.5 years
- Information on the patient
  - Gender: 59.9 % females, 40.1 % males
  - Age:

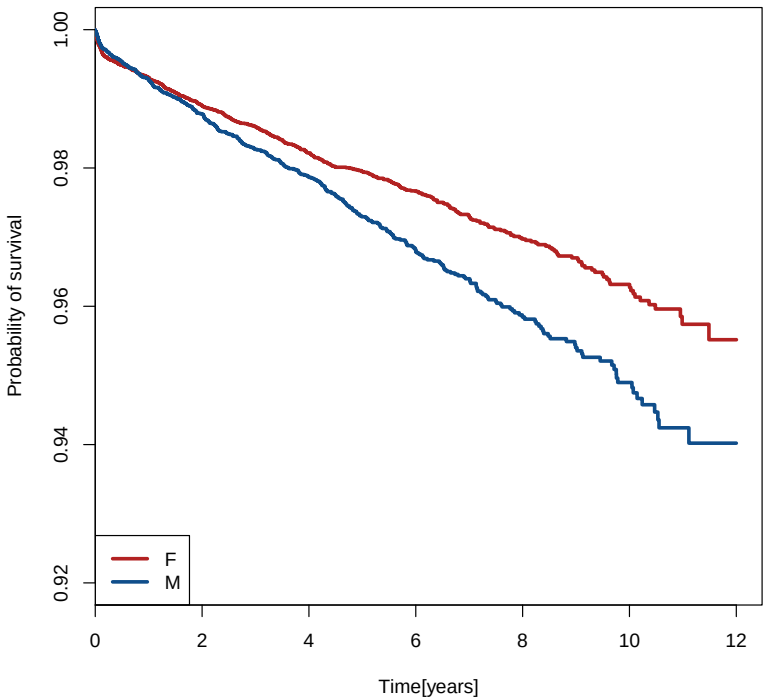
Min.	1st Qu.	Med.	3rd Qu.	Max.	IQR
8	57	66	74	104	17

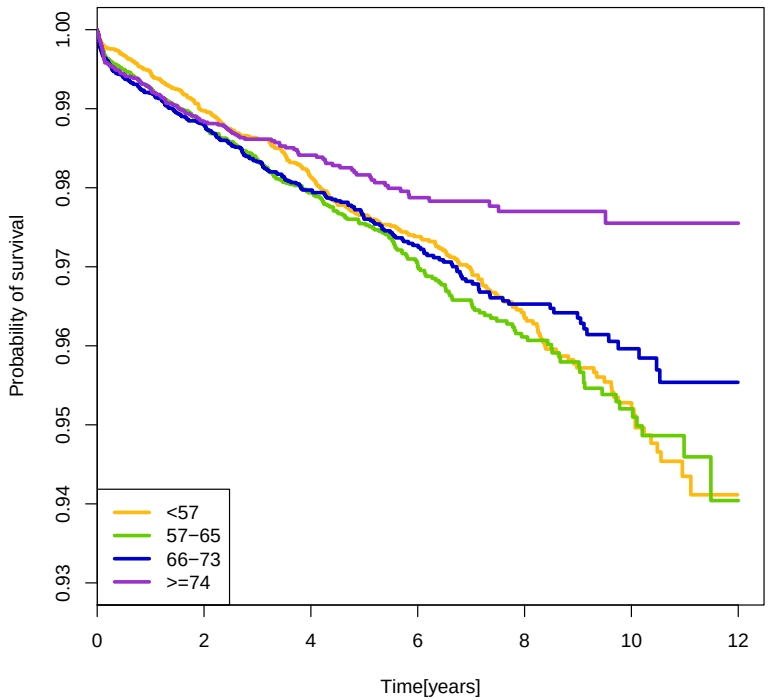
years
  - Diagnosis: primary coxathrosis (58.9 %), fracture of femoral neck (16.2 %), dysplastic coxathrosis (10.3 %), 5 other
- Information on the (primary) operation
  - Type of fixation and cementing technique chosen for the acetabular and femoral component
  - Year of the operation
  - Region of the operation (NUTS region, hospital, department)

Success/failure counts by diagnosis, fixation and gender

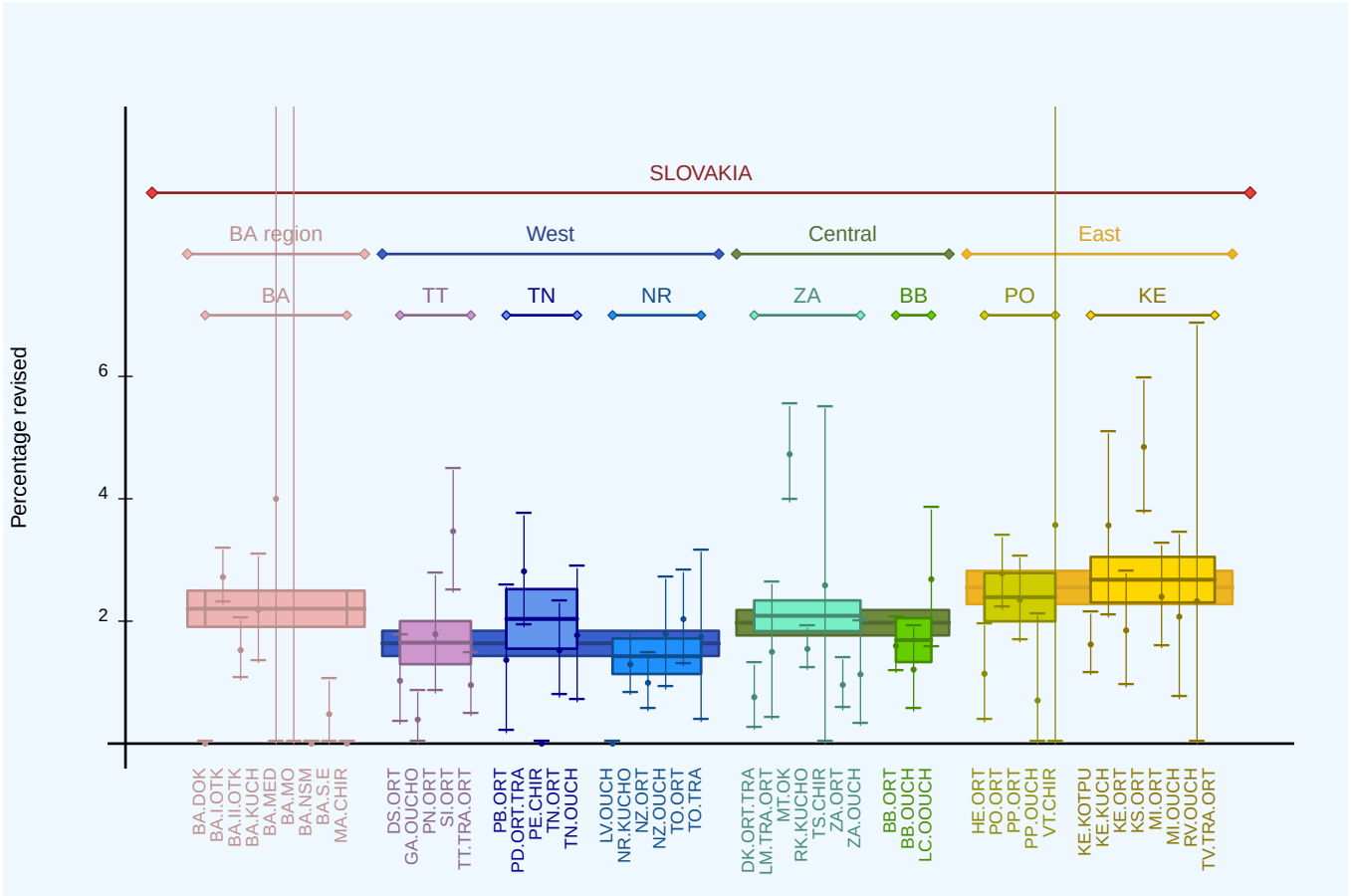
		diagnosis																								
		primary coxathrosis			dysplastic coxathrosis			posttraumatic coxathrosis			avascular necrosis			M.Perthes			rheumatoid arthritis			fractue of femoral neck			other			NA		
		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure	
			no	yes		no	yes		no	yes		no	yes		no	yes		no	yes		no	yes		no	yes		no	1
fixation		16044	15859	185	4670	4582	88	1050	1025	25	1830	1808	22	80	79	1	229	225	4	1115	1090	25	316	304	12	33		33
uncemented	ALL																											
	female	7895	7826	69	3688	3619	69	382	378	4	580	570	10	32	32		154	152	2	629	618	11	144	138	6	21		21
	male	8149	8033	116	982	963	19	668	647	21	1250	1238	12	48	47	1	75	73	2	486	472	14	172	166	6	12		12
cemented	ALL	9366	9147	219	410	400	10	448	435	13	591	568	23	6	6		93	89	4	1042	1017	25	237	221	16	36	1	35
	female	6343	6213	130	338	329	9	293	287	6	375	363	12	3	3		83	80	3	753	736	17	162	157	5	24	1	23
	male	3023	2934	89	72	71	1	155	148	7	216	205	11	3	3		10	9	1	289	281	8	75	64	11	12		12
hybrid	ALL	3787	3685	102	470	454	16	248	237	11	284	272	12	5	5		40	37	3	569	551	18	127	115	12	25	1	24
	female	2222	2175	47	365	350	15	126	121	5	135	129	6	4	4		25	24	1	384	372	12	75	71	4	16		16
	male	1565	1510	55	105	104	1	122	116	6	149	143	6	1	1		15	13	2	185	179	6	52	44	8	9	1	8
reverse hybrid	ALL	155	150	5	44	42	2	23	20	3	24	23	1	2	1	1	3	3		17	16	1	18	17	1	5		5
	female	90	88	2	41	39	2	10	10		14	14					2	2		10	10		12	12		5		5
	male	65	62	3	3	3		13	10	3	10	9	1	2	1	1	1	1		7	6	1	6	5	1			
cemented femo	ALL	21	21		1	1		353	350	3	8	8					2	2		2553	2524	29	247	243	4	10		10
	female	17	17		1	1		283	282	1	5	5					2	2		1947	1924	23	193	190	3	8		8
	male	4	4					70	68	2	3	3					.	.		606	600	6	54	53	1	2		2
uncemented femo	ALL	27	27		1	1		19	19		2	2					2	2		168	166	2	3	3				
	female	17	17		1	1		13	13		1	1					1	1		127	126	1	2	2				
	male	10	10					6	6		1	1					1	1		41	40	1	1	1				

Survival of implants by gender and age





Percentage of implant failures by hospital



- Total number of primary operations per hospital
  - 2 (TV.TRA.ORT) – 5 749 (BA.I.OTK)
- Total number of revision operations per hospital
  - 0 (several hospitals) – 197 (MT.OK)

Primary and revision operations and failure rates by year

- Number of operations by year

	2003	2004	2005	2006	2007	2008	2009
Primary	2117	3082	2974	3590	4246	4408	4753
Revision	6	28	52	66	92	124	122
Total	2123	3110	3026	3656	4338	4532	4875

	2010	2011	2012	2013	2014	2015
Primary	4953	5100	6026	6561	6737	6639
Revision	184	116	106	111	134	134
Total	5137	5216	6132	6672	6871	6773

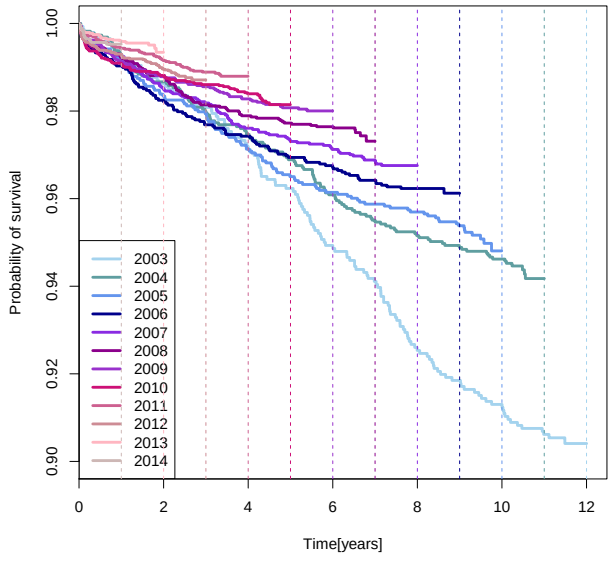
- Number of revised operations by the year of primary operation

	2003	2004	2005	2006	2007	2008	2009
Primary operations	2117	3082	2974	3590	4246	4408	4753
Revised by 2015	169	147	130	122	130	113	107
% censored	92.0	95.2	95.6	96.6	96.9	97.4	97.8

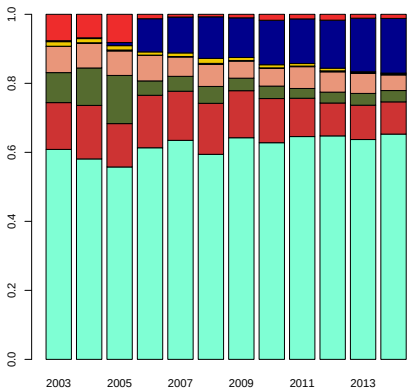
	2010	2011	2012	2013	2014	2015
Primary operations	4953	5100	6026	6561	6737	6639
Revised by 2015	92	67	82	47	41	28
% censored	98.1	98.7	98.6	99.3	99.4	99.6

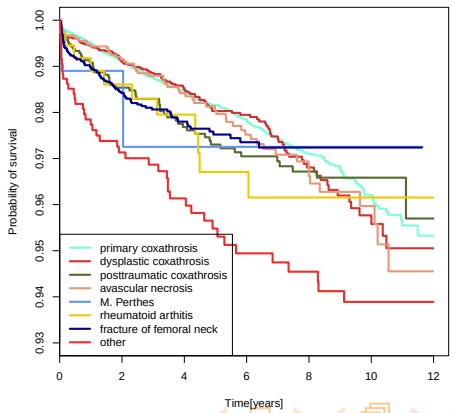
Differences due to the year of primary operation

- Time to implant failure



- Classification of diagnoses





Towards the model

- Outcome
  - Time to implant failure $\approx$ the difference between
    - Date of primary operation
    - Date of (first) revision operation
  - Censoring due to
    - End of the observation period (31 Dec 2015)
    - Death
- Covariate of interest
  - Region
    - At the level of NUTS2, NUTS3 or hospital depending on the number of events per category
- Adjusting for
  - Year of the operation
  - Age
  - Gender
  - Diagnosis
  - Type of fixation and cementing technique chosen for the acetabular and femoral component

Adjusting the model

- Inherent differences in the data and data collection in different **years** $\Rightarrow$ separate models for
  - Operations performed in 2003
  - Operations performed in 2004–2005
  - Operations performed in 2006–2015
    - And the operation year included as a covariate
- The continuous variable **age** included as a covariate
- The model stratified for the categorical variables
  - **Gender**
  - **Diagnosis**
  - Type of **fixation** and **cementing technique** chosen for the acetabular and femoral component

Model for the operations performed in 2003

- 2 117 patients with 169 implant failures, follow-up: 13 years
- Hazard rate modelled as

$$\begin{aligned}\lambda(t) \;=\; & \lambda_{0,h}(t) \times \exp\{ \\ & \beta_{\text{age}} \times \text{age at operation} + \\ & \beta_{\text{SK01}} \times \mathrm{I}\{\text{SK01}\} + \\ & \beta_{\text{SK02}} \times \mathrm{I}\{\text{SK02}\} + \\ & \beta_{\text{SK04}} \times \mathrm{I}\{\text{SK04}\} \;\}\end{aligned}$$

- $\lambda_{0,h}(t)$: different baseline hazards for different strata
- Results
  - Overall proportional hazards test based on Schoenfeld residuals
    - $p = 0.892$
  - Fitted hazard ratios $\exp\{\beta\}$

Region	Estimate	95 % Conf.Int.
SK01	0.64	(0.30, 1.34)
SK02	1.12	(0.49, 2.55)
SK04	0.99	(0.44, 2.22)

Model for the operations performed in 2004–2005

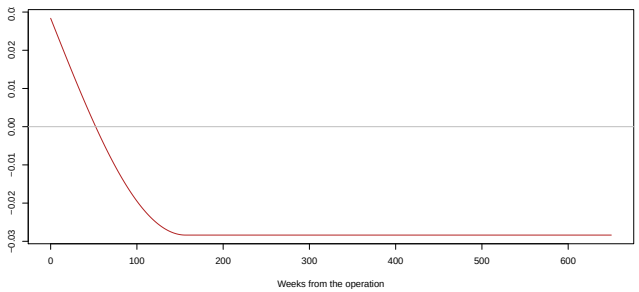
- 6 056 patients with 277 implant failures
- Follow-up: 11–12 years
- Hazard rate modelled as

$$\begin{aligned}\lambda(t) \;=\; & \lambda_{0,h}(t) \times \exp\{ \\ & \beta_{\text{age}} \times f(t) \times \text{age at operation} + \\ & \beta_{\text{SK01}} \times \mathrm{I}\{\text{SK01}\} + \\ & \beta_{\text{SK02}} \times \mathrm{I}\{\text{SK02}\} + \\ & \beta_{\text{SK04}} \times \mathrm{I}\{\text{SK04}\} \;\}\end{aligned}$$

- $\lambda_{0,h}(t)$: different baseline hazards for different strata

Results for the operations performed in 2004–2005

- $\hat{\beta}_{\text{age}} \times f(t)$



- Overall proportional hazards test based on Schoenfeld residuals
  - without $f(t)$: $p = 0.016$
  - with $f(t)$: $p = 0.108$

- Fitted hazard ratios $\exp\{\beta\}$

Region	Estimate	95 % Conf.Int.
SK01	0.97	(0.58, 1.64)
SK02	1.11	(0.66, 1.85)
SK04	1.40	(0.90, 2.18)

Model for the operations performed in 2006–2015

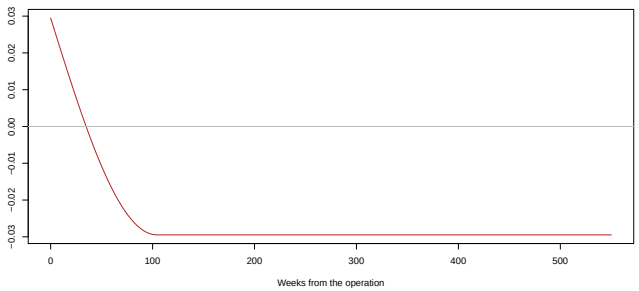
- 53 013 patients with 829 implant failures
- Follow-up: up to 10 years
- Hazard rate modelled as

$$\begin{aligned}\lambda(t) \;=\; \lambda_{0,h}(t) \times \exp\{ & \\ & \beta_{\text{op. year}} \times \text{year of operation} + \\ & \beta_{\text{age}} \times f(t) \times \text{age at operation} + \\ & \beta_{\text{SK010}} \times \mathrm{I}\{\text{SK010}\} + \\ & \beta_{\text{SK021}} \times \mathrm{I}\{\text{SK021}\} + \\ & \beta_{\text{SK022}} \times \mathrm{I}\{\text{SK022}\} + \\ & \beta_{\text{SK023}} \times \mathrm{I}\{\text{SK023}\} + \\ & \beta_{\text{SK032}} \times \mathrm{I}\{\text{SK032}\} + \\ & \beta_{\text{SK041}} \times \mathrm{I}\{\text{SK041}\} + \\ & \beta_{\text{SK042}} \times \mathrm{I}\{\text{SK042}\} \;\}\end{aligned}$$

- $\lambda_{0,h}(t)$: different baseline hazards for different strata

Results for the operations performed in 2006–2015

- $\hat{\beta}_{\text{age}} \times f(t)$



- Overall proportional hazards test based on Schoenfeld residuals
  - without $f(t)$: $p < 0.001$
  - with $f(t)$: $p = 0.123$

- Fitted hazard ratios $\exp\{\beta\}$

Region	Estimate	95 % Conf.Int.
SK010	0.91	(0.71, 1.17)
SK021	0.93	(0.69, 1.25)
SK022	1.28	(0.92, 1.77)
SK023	0.77	(0.57, 1.05)
SK032	**0.65**	**(0.46, 0.93)**
SK041	1.07	(0.82, 1.40)
SK042	**1.46**	**(1.13, 1.88)**

Conclusions

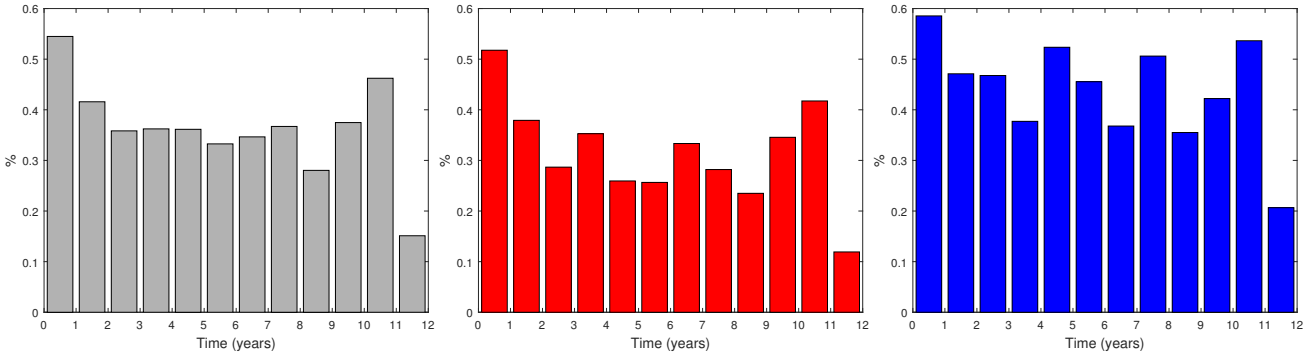
- We have shown:
  - Region where the operation was performed matters
    - There is a region that can teach and a region that should learn
- We have also learned:
  - Year when the operation was performed matters
    - In particular the initial years of the database
  - Age at the time of the operation matters
    - . . . in a non-trivial way

Summary table

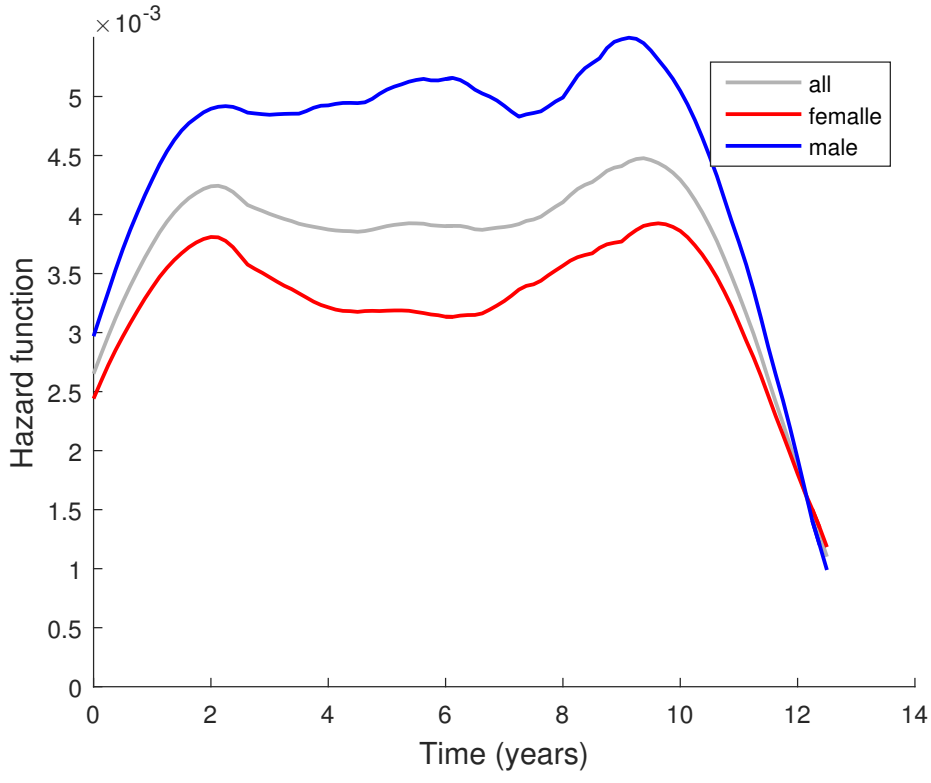
		diagnosis																										
		primary coxathrosis			dysplastic coxathrosis			posttraumatic coxathrosis			avascular necrosis			M.Perthes			rheumatoid arthritis			fractue of femoral neck			other			NA		
		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure		ALL	failure	
			no	yes		no	yes		no	yes		no	yes		no	yes		no	yes		no	yes		no	yes		no	1
fixation		16044	15859	185	4670	4582	88	1050	1025	25	1830	1808	22	80	79	1	229	225	4	1115	1090	25	316	304	12	33		33
uncemented	ALL																											
	female	7895	7826	69	3688	3619	69	382	378	4	580	570	10	32	32		154	152	2	629	618	11	144	138	6	21		21
	male	8149	8033	116	982	963	19	668	647	21	1250	1238	12	48	47	1	75	73	2	486	472	14	172	166	6	12		12
cemented	ALL	9366	9147	219	410	400	10	448	435	13	591	568	23	6	6		93	89	4	1042	1017	25	237	221	16	36	1	35
	female	6343	6213	130	338	329	9	293	287	6	375	363	12	3	3		83	80	3	753	736	17	162	157	5	24	1	23
	male	3023	2934	89	72	71	1	155	148	7	216	205	11	3	3		10	9	1	289	281	8	75	64	11	12		12
hybrid	ALL	3787	3685	102	470	454	16	248	237	11	284	272	12	5	5		40	37	3	569	551	18	127	115	12	25	1	24
	female	2222	2175	47	365	350	15	126	121	5	135	129	6	4	4		25	24	1	384	372	12	75	71	4	16		16
	male	1565	1510	55	105	104	1	122	116	6	149	143	6	1	1		15	13	2	185	179	6	52	44	8	9	1	8
reverse hybrid	ALL	155	150	5	44	42	2	23	20	3	24	23	1	2	1	1	3	3		17	16	1	18	17	1	5		5
	female	90	88	2	41	39	2	10	10		14	14					2	2		10	10		12	12		5		5
	male	65	62	3	3	3		13	10	3	10	9	1	2	1	1	1	1		7	6	1	6	5	1			
cemented femo	ALL	21	21		1	1		353	350	3	8	8					2	2		2553	2524	29	247	243	4	10		10
	female	17	17		1	1		283	282	1	5	5					2	2		1947	1924	23	193	190	3	8		8
	male	4	4					70	68	2	3	3					.	.		606	600	6	54	53	1	2		2
uncemented femo	ALL	27	27		1	1		19	19		2	2					2	2		168	166	2	3	3				
	female	17	17		1	1		13	13		1	1					1	1		127	126	1	2	2				
	male	10	10					6	6		1	1					1	1		41	40	1	1	1				

Modelling risk of failure – all patients

Failure rate



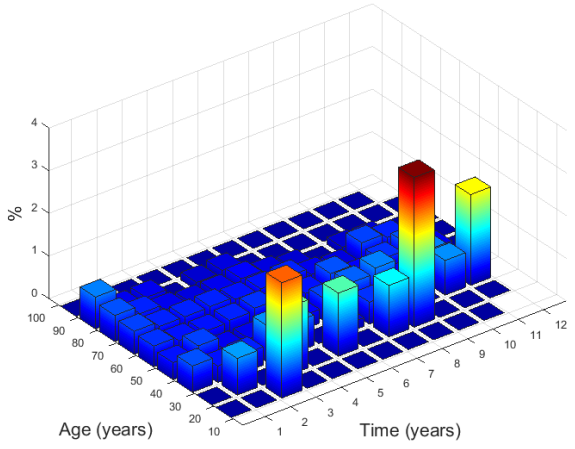
Risk of implant failure

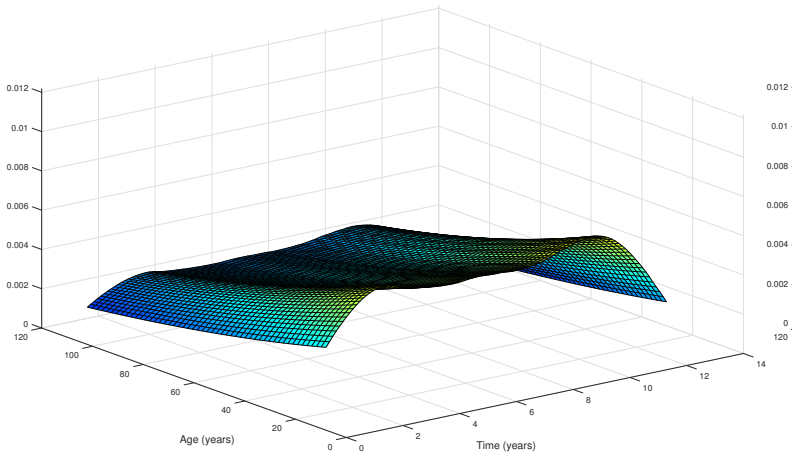


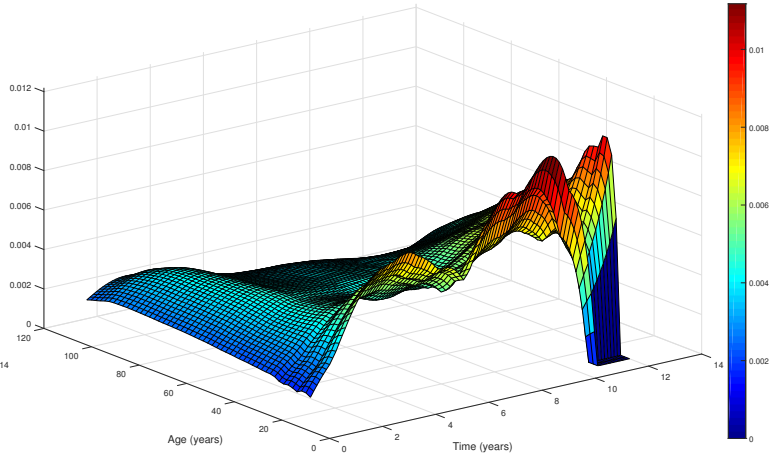
Modelling risk of failure – all patients

Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
0.9915	0.0020	< 0.0001





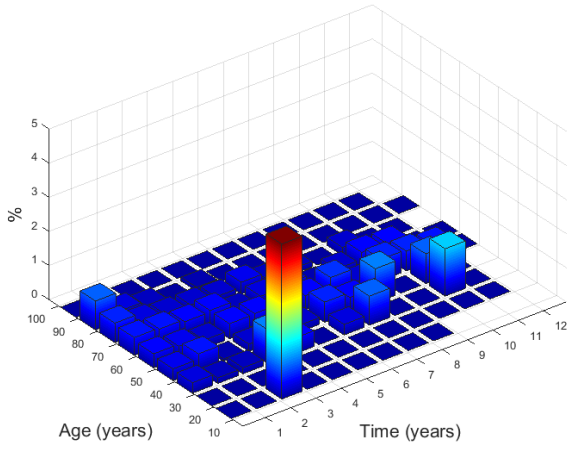


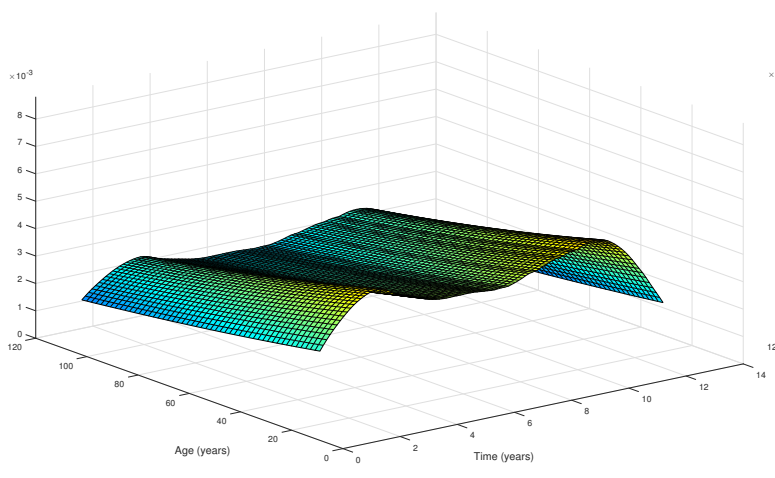
Cox model **Kernel estimate**

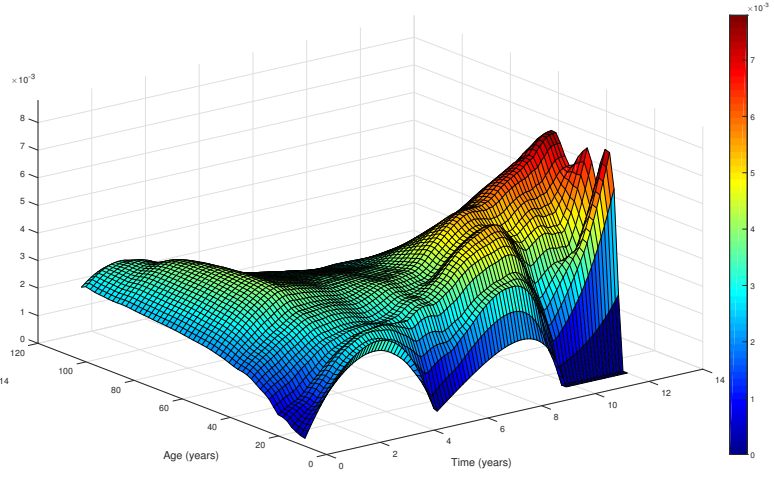
Modelling risk of failure – females

Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
0.9948	0.1574	< 0.0001





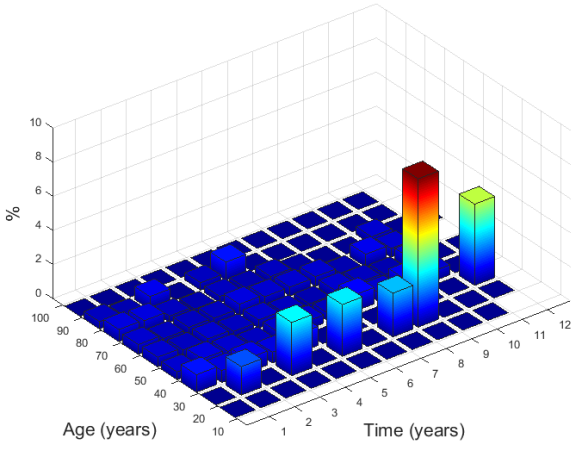


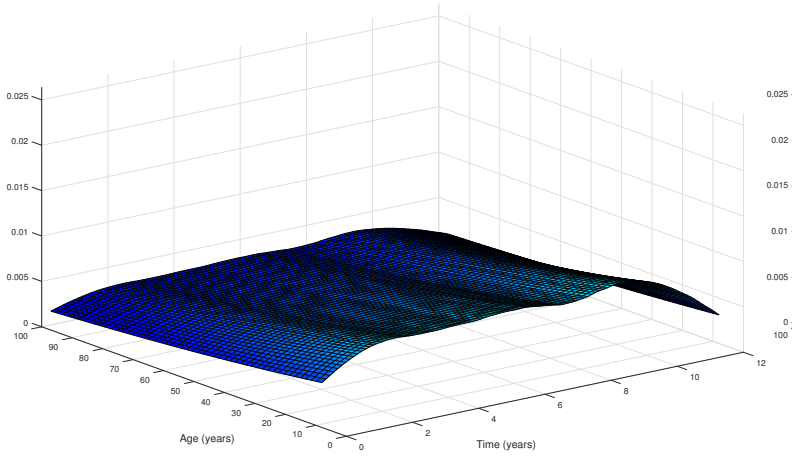
Cox model **Kernel estimate**

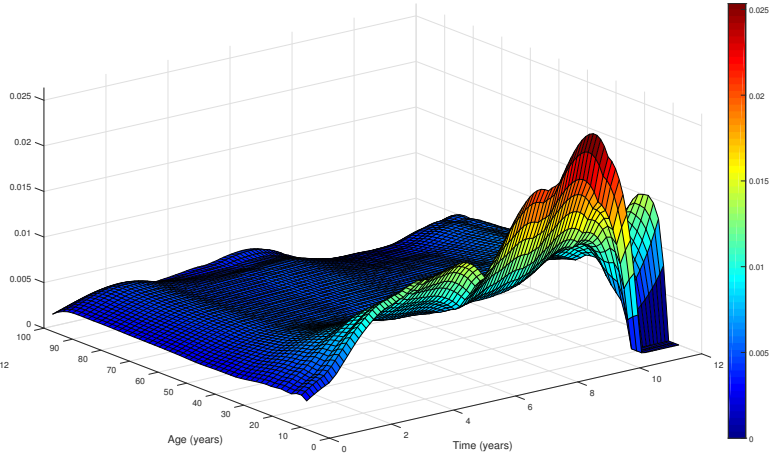
Modelling risk of failure – males

Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
0.9903	0.0229	0.0310



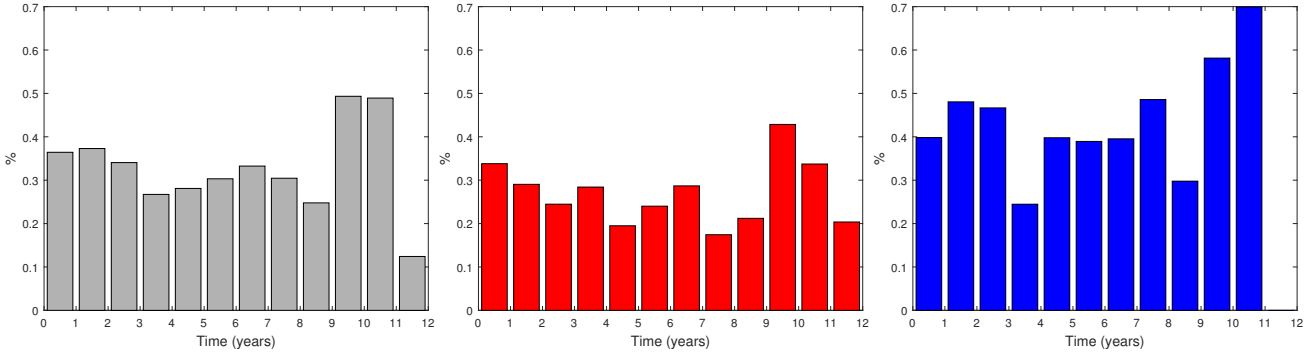




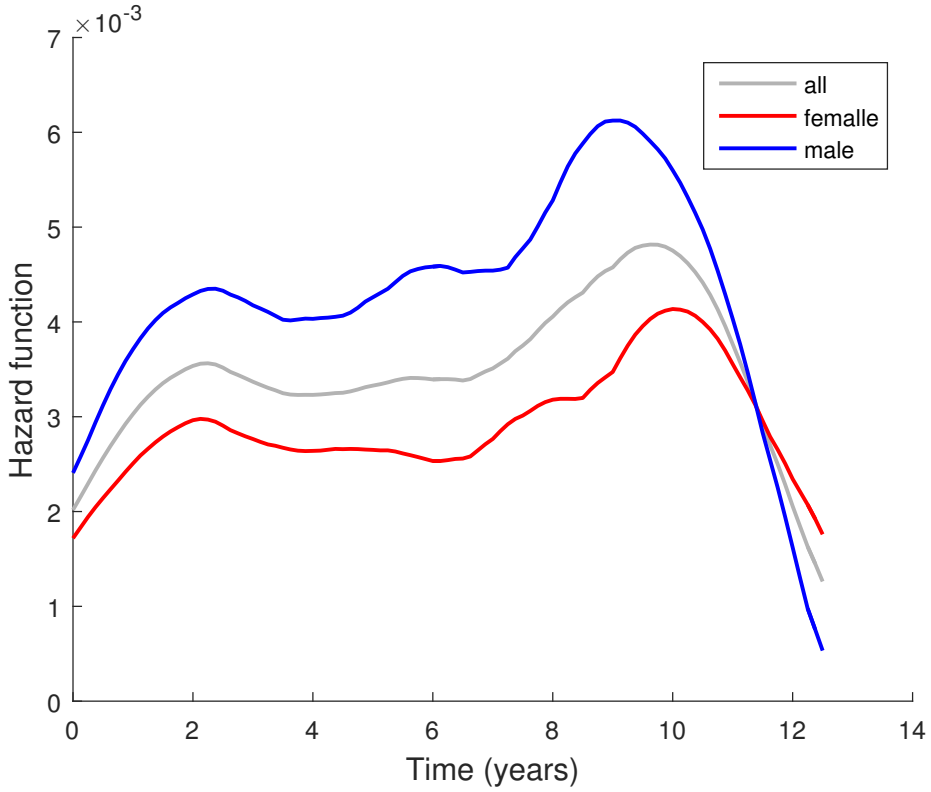
Cox model **Kernel estimate**

Modelling risk of failure – primary coxathrosis

Failure rate



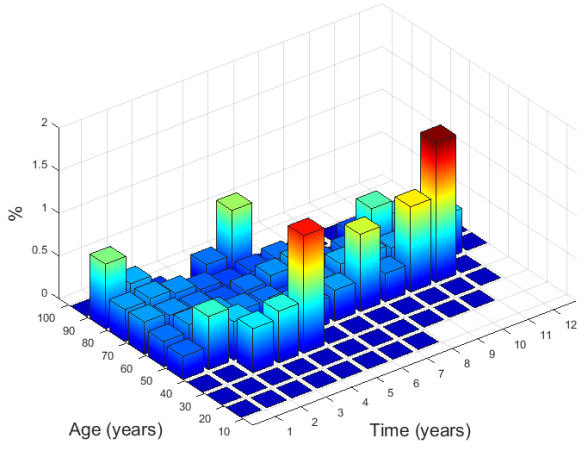
Risk of implant failure

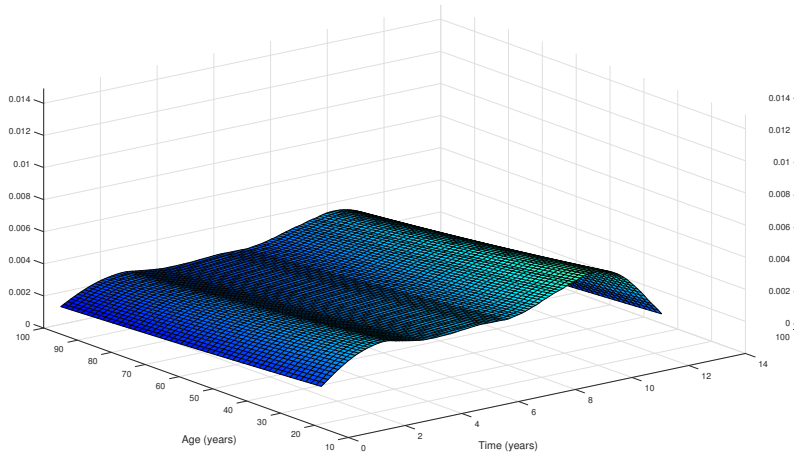


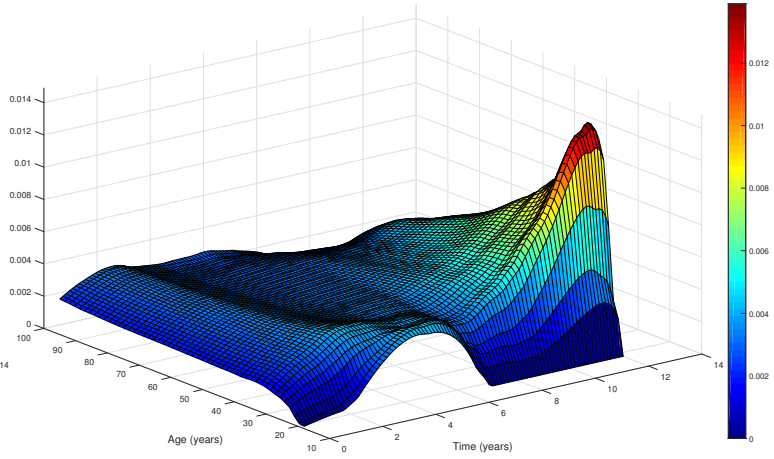
Modelling risk of failure – primary coxathrosis

Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
0.9947	0.2768	0.0029





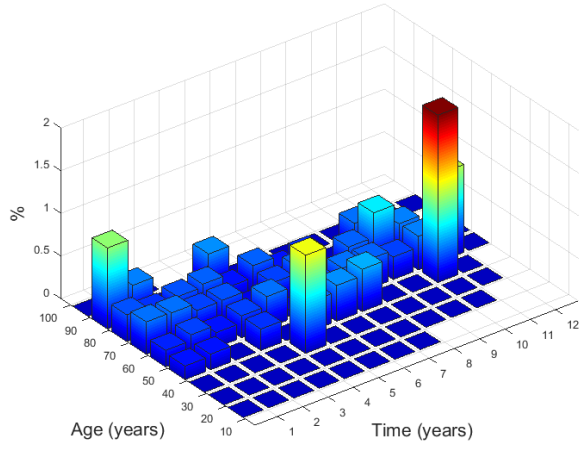


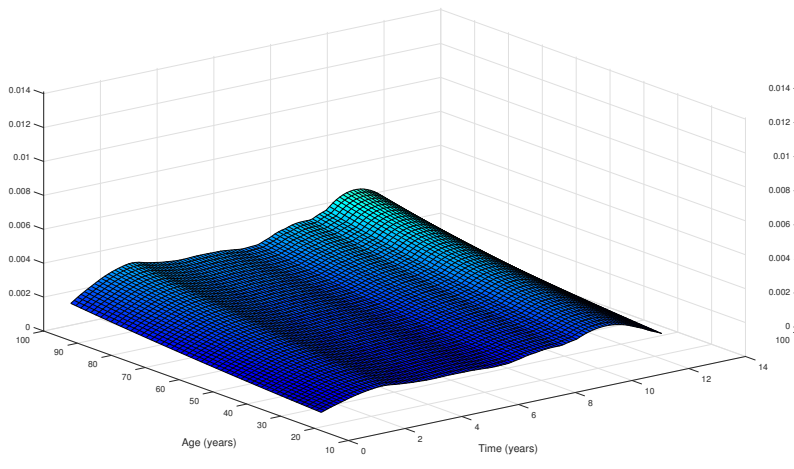
Cox model **Kernel estimate**

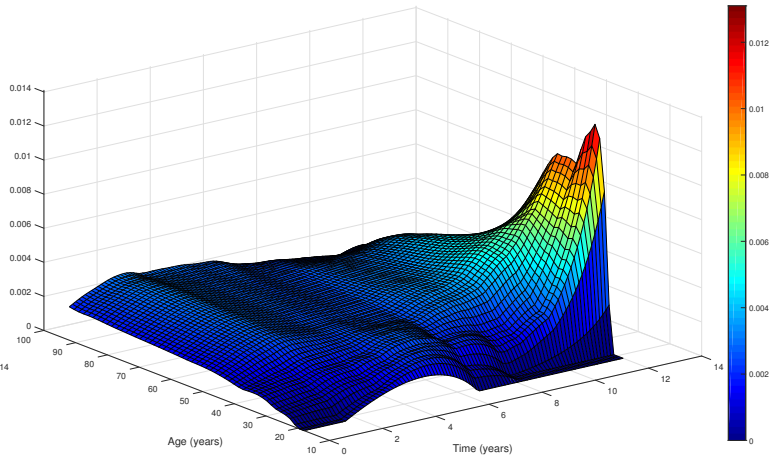
Modelling risk of failure – primary coxathrosis, females

Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
1.0096	0.1942	0.0081





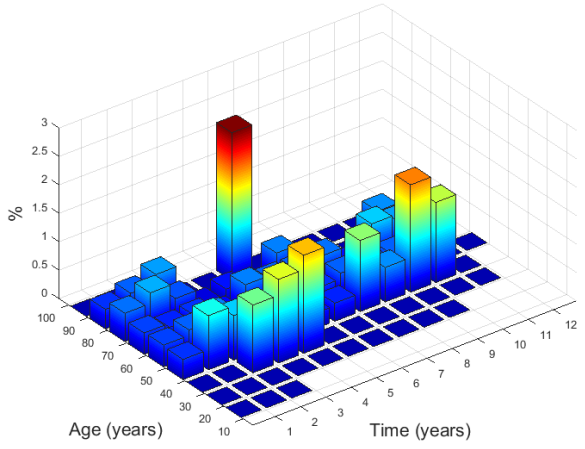


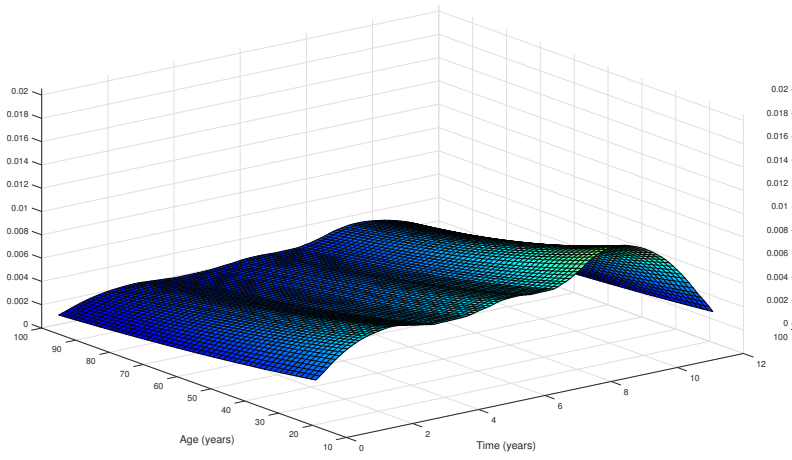
Cox model **Kernel estimate**

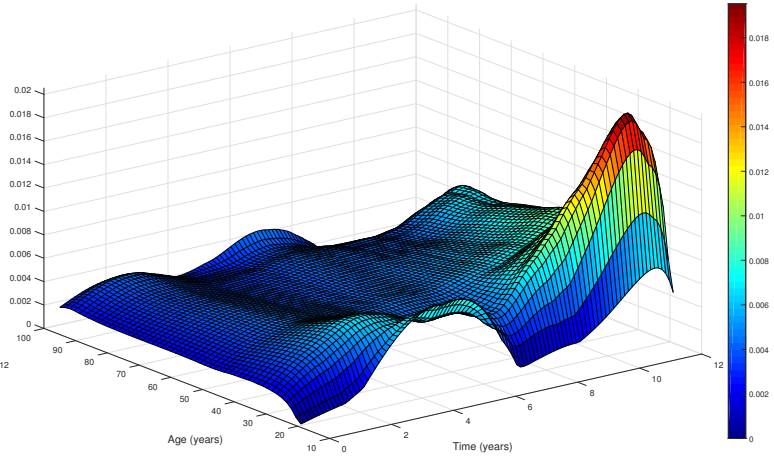
Modelling risk of failure – primary coxathrosis, males

Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
0.9884	0.0848	0.1574



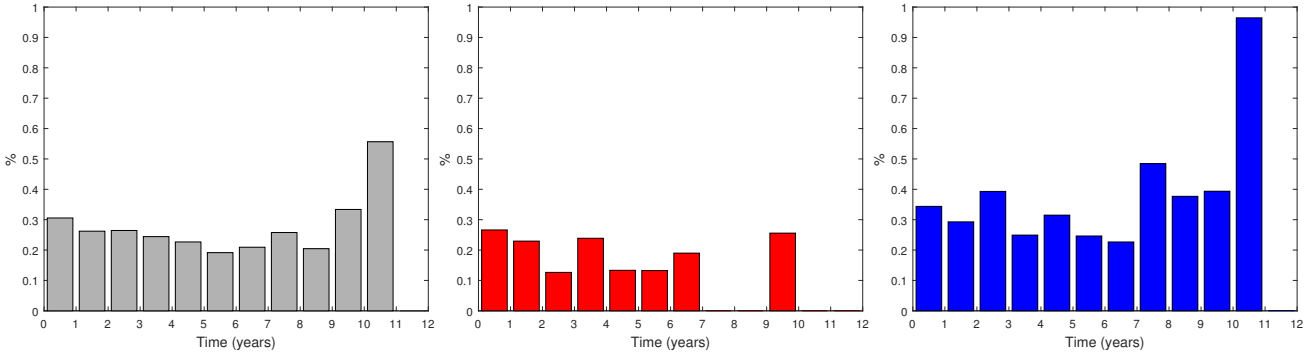




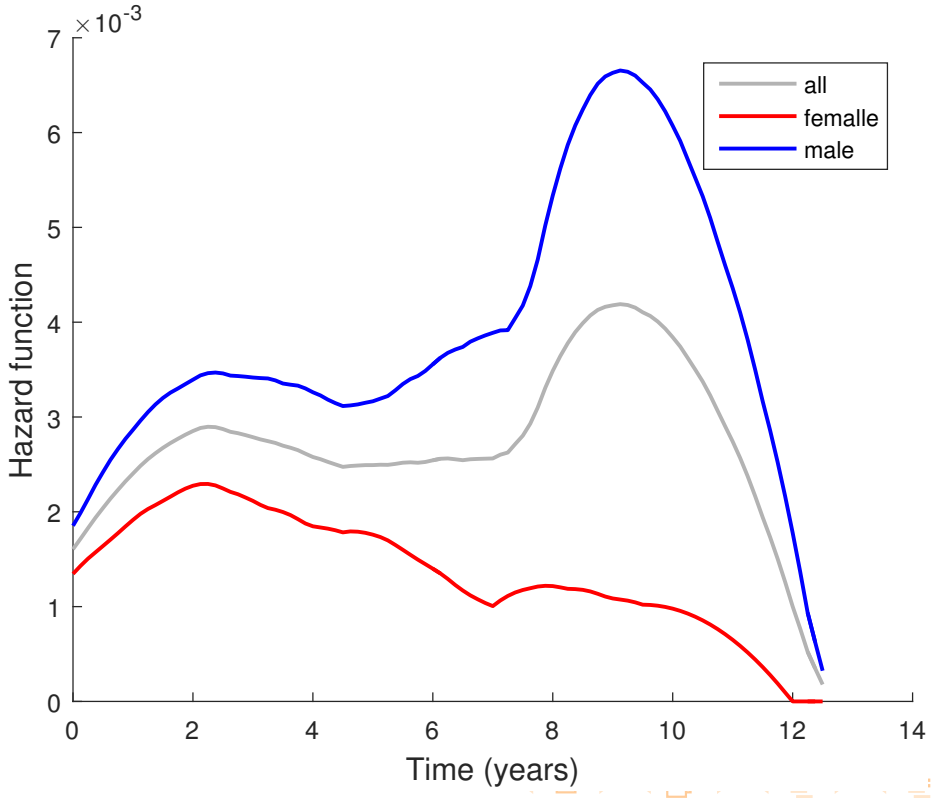
Cox model **Kernel estimate**

Modelling risk of failure – primary coxathrosis and uncemented fixation

Failure rate



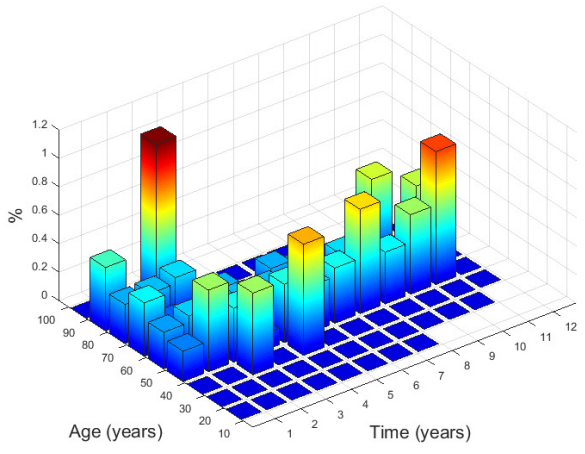
Risk of implant failure

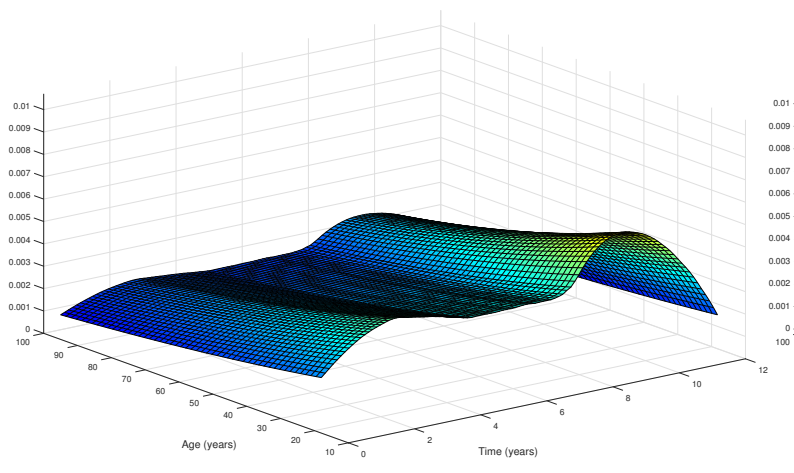


Modelling risk of failure – primary coxathrosis and uncemented fixation

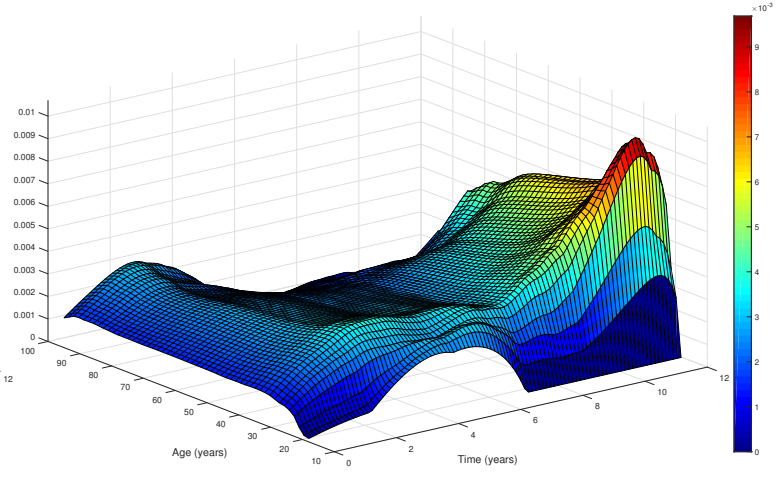
Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
0.9895	0.2291	0.0359





Cox model

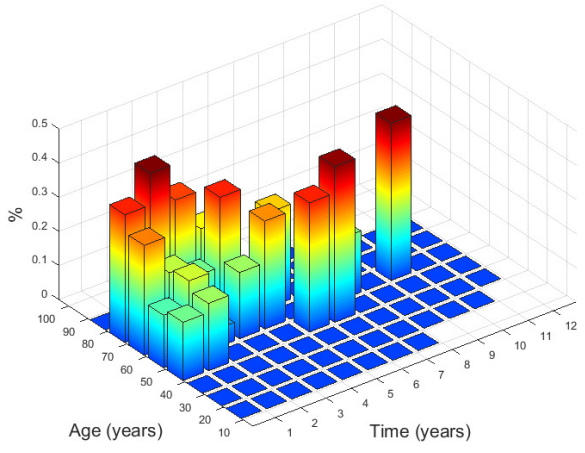


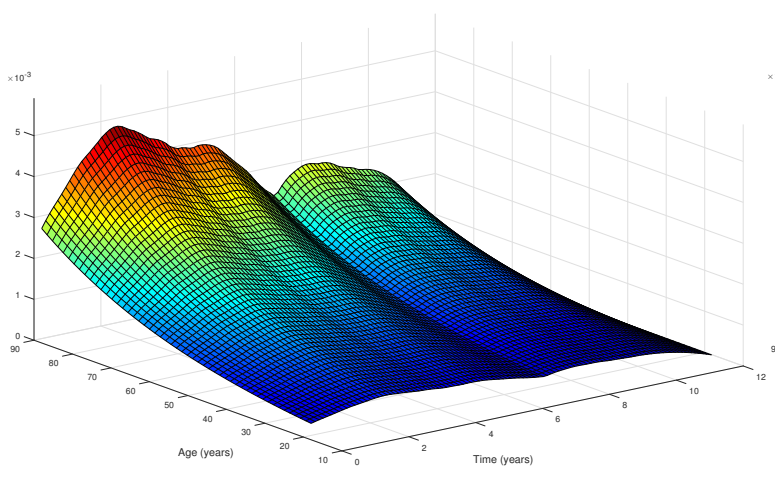
Kernel estimate

Modelling risk of failure – primary coxathrosis and uncemented fixation, females

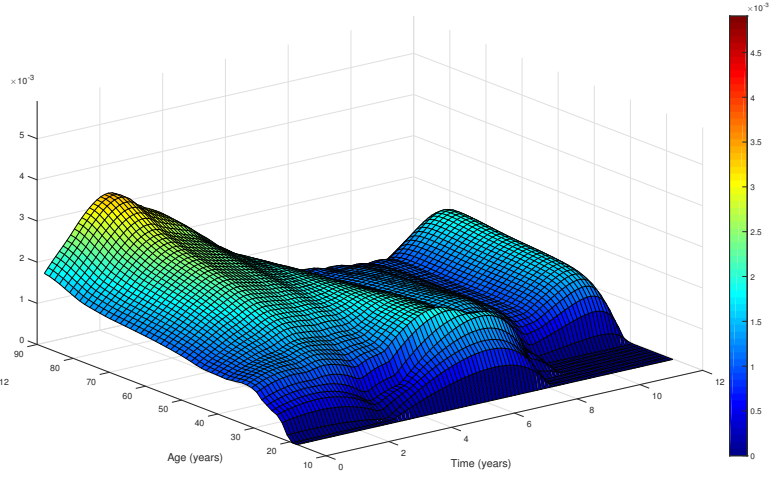
Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
1.0282	0.0548	0.2161





Cox model

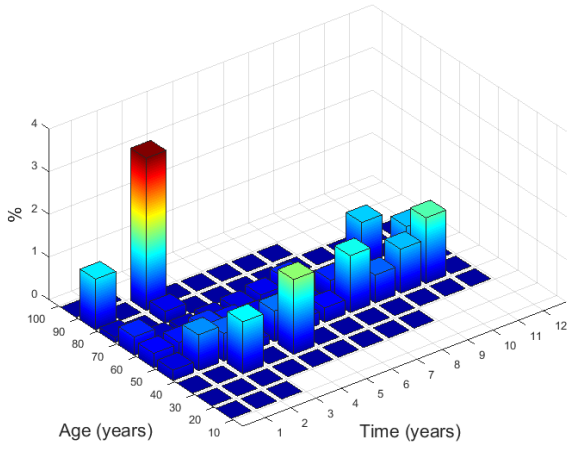


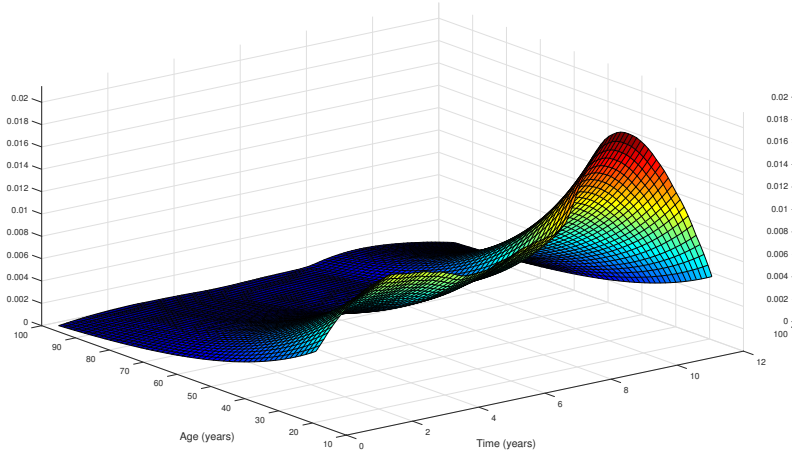
Kernel estimate

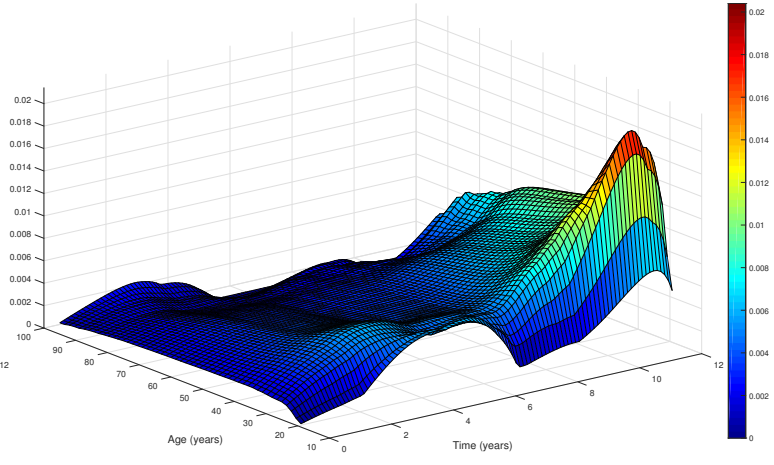
Modelling risk of failure – primary coxathrosis and uncemented fixation, males

Risk of implant failure conditioned on age

	p-value	
$\exp(\hat{\beta})$	β	PH
0.9679	0.0041	0.1707

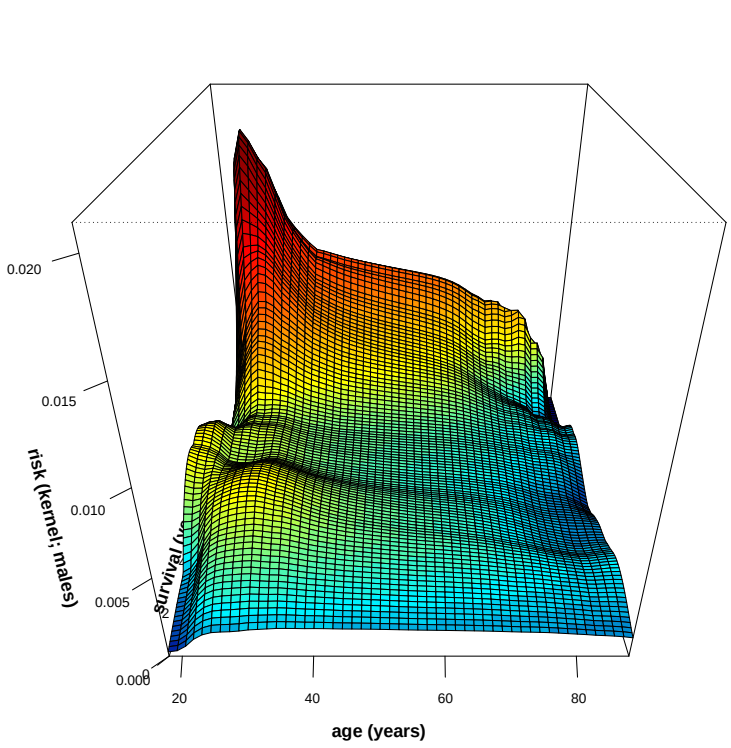




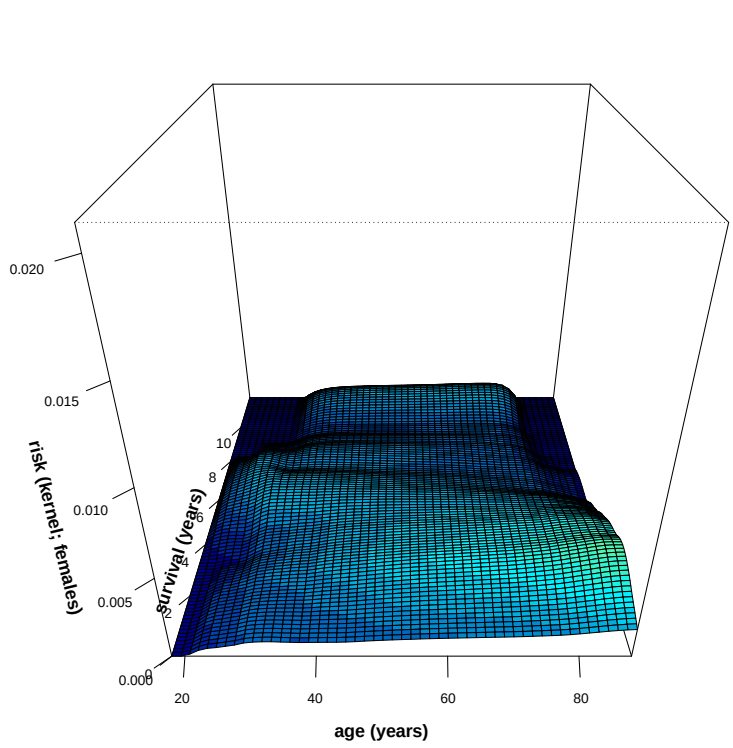


Cox model **Kernel estimate**

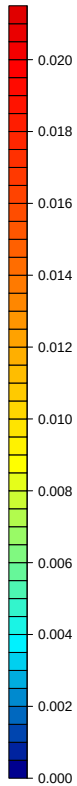
Animation



Male



Female



References

- L. Nečas, S. Katina a J. Uhlárová, *Survival analysis of total hip and knee replacement in Slovakia 2003-2011*, Acta Chirurgiae Orthopaedicae et Traumatologiae Cechoslovaca, Praha: Galen, 2013, roč. 80, 1, 1-85. ISSN 0001-5415 (`http://www.achot.cz/vydanacisla.php`)
- I. Selingerová, H. Doleželová, I. Horová, S. Katina, J. Zelinka, *Survival of Patients with Primary Brain Tumors: Comparison of Two Statistical Approaches*, PloS one **11**(2), 2016.
- T. R. Fleming and D. P. Harrington, *Counting processes and survival analysis*, John Wiley & Sons, 2011.
- P. K. Andersen, Ø. Borgan, R. D. Gill and N. Keiding, *Statistical Models Based on Counting Processes*, Springer, 1993.
- I. Horová, J. Koláček, J. Zelinka, *Kernel Smoothing in MATLAB: Theory and Practice of Kernel Smoothing*, World Scientific Publishing, 2012.
- L. Spierdijk, *Nonparametric Conditional Hazard Rate Estimation: A Local Linear Approach*, Computational Statistics & Data Analysis **52**, 2008, 2419–2434.

Thank you for your attention!