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## **Tibial plateau fractures are associated with a long-lasting increased risk of total knee arthroplasty a matched cohort study of 7,950 tibial plateau fractures**

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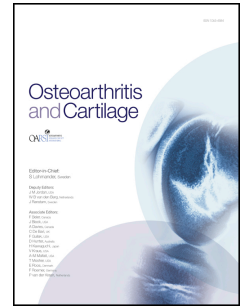
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# Accepted Manuscript

Tibial plateau fractures are associated with a long-lasting increased risk of total knee arthroplasty a matched cohort study of 7,950 tibial plateau fractures

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**Tibial plateau fractures are associated with a long-lasting increased risk of total knee arthroplasty***a matched cohort study of 7,950 tibial plateau fractures**Rasmus Elsoe (RE), MD, PhD<sup>1</sup>, Martin B. Johansen (MBJ), MSc<sup>2</sup>,**Peter Larsen (PL), PT, PhD<sup>3</sup>*

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**Objective:** This study aims to investigate the risk of total knee replacement (TKR) following tibial plateau fractures. Secondary the study aims to investigate the risk of knee arthroscopy following tibial plateau fractures.

**Method:** The study was designed as a matched cohort study. All patients who sustained a tibial plateau fracture in Denmark between January 1, 1996, and December 31, 2000, were included and followed until December 31, 2015. For each patient with a tibial plateau fracture, 10 matched citizens without a tibial plateau fracture were included as a reference group.

**Results:** 7,950 patients sustained a tibial plateau fracture in Denmark during the study period. The median age of patients was 52.6 (IQR: 32.4-71.5) years. The mean observational period was 13.9 years. 5.7% were treated with a TKR (N=452), and 2.0% of patients from the reference group were treated with a TKR (N=1,623). Patients with a tibial plateau fracture had a 3.5 (95%CI: 3.1-3.9) times higher hazard ratio (HR) compared to patients from the reference group. 7.6% of patients with a tibial plateau fracture were treated with a secondary knee arthroscopy (N=603) and 2.0% of patients from the reference group were treated with a knee arthroscopy (N=1,565). Patients with a

tibial plateau fracture presented with a 5.0 (95%CI: 4.5-5.6) times higher hazard ratio compared to patients in the reference group.

**Conclusions:** Tibial plateau fractures are associated with a 3.5 times increased risk of TKR compared with an age- and gender-matched reference group with a mean follow-up of 13.9 years.

Running title: Increased risk of TKR following tibial plateau fractures

*Keywords: tibial plateau fracture; total knee replacement; knee arthroplasty, knee arthroscopy; long-term follow-up*

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The manuscript including related data, figures, and tables has not been submitted or is not simultaneously being submitted elsewhere, and no portion of the data has been or will be published in proceedings or transactions of meetings or symposium volumes.

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, acquisition of data, analysis, and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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4

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28

29

30 **INTRODUCTION**31 Fractures of the tibial plateau are reported with an incidence of 10.3/100,000/year<sup>1</sup>.

32 Surgical treatment of displaced tibial plateau fractures has become the treatment of

33 choice<sup>2</sup>. The surgical procedure is challenging due to the majority of patients

34 presenting with multi-fragmented bones in combination with cartilage damage and

35 intra-articular soft tissue lesions<sup>3</sup>.

36

37 A common and well-known complication following tibial plateau fractures is an

38 increased risk of post-traumatic knee osteoarthritis<sup>2,4-8</sup>. The incidence of knee

39 osteoarthritis following tibial plateau fractures has been reported between 13% and

40 83%, indicating a wide range in severity of osteoarthritis and follow-up time<sup>2,6,9-19</sup>.

41 Increasing fracture comminution, comorbidity, and patients age are commonly

42 reported to increase the risk of early onset of post-traumatic knee osteoarthritis<sup>7</sup>.

43

44 Total knee replacement as a salvage procedure in the treatment of patients with end-

45 stage knee osteoarthritis is widely accepted<sup>8</sup>. Treatment with TKR following tibial46 plateau fractures has been less reported and with different frequencies<sup>2,7,18,20</sup>.

47 However, most studies available included only small patient groups and/or short

48 follow-up periods. Recently, a study by Wasserstein et al.<sup>7</sup> with a 10-year follow-up

49 period reporting on 8,426 tibial plateau fractures suggests a 5.3 times increase in the

50 likelihood of TKR compared to a matched reference group, corresponding to 7.3% of

51 patients in the 10-year period. However, only adult patients treated by open reduction

52 internal fixation (ORIF) were included, excluding young patients and patients

53 managed by conservative means or external fixation.

54

55 Intra-articular soft tissue lesions and restrictions in knee joint motion following tibial  
56 plateau fractures are commonly reported<sup>21-23</sup>. Secondary treatment with knee  
57 arthroscopy is indicated for some patients<sup>24</sup>. However, the incidence of secondary  
58 knee arthroscopy following tibial plateau fractures has not been previously reported.

59

60 The primary question is: What is the national risk of TKR following tibia plateau  
61 fractures regardless of treatment modalities compared to an age- and gender-matched  
62 reference group without a prior tibial plateau fracture?

63

64 The secondary questions were to investigate the incidence of secondary knee  
65 arthroscopy following a tibial plateau fracture and compare this to an age- and  
66 gender-matched reference group without a prior tibial plateau fracture. A further  
67 secondary question was to compare the time to TKR and secondary arthroscopy  
68 following a tibial plateau fracture compared to that of the age- and gender-matched  
69 reference group.

70

## 71 ***PATIENTS AND METHODS***

### 72 ***Study design***

73 The study was designed as a matched cohort study. Prospectively obtained registry  
74 data including all citizens of Denmark were used.

75

76 All patients who sustained a tibial plateau fracture in Denmark between January 1,  
77 1996, and December 31, 2000, were included and followed until December 31, 2015,  
78 regarding treatment with TKR and/or secondary knee arthroscopy.

79

80 Secondary knee arthroscopy was defined as all knee arthroscopy procedures  
81 performed at least 30 days after the primary operation. Arthroscopic procedures  
82 performed during primary operative treatment of the tibial plateau fracture were  
83 excluded from this analysis.

84

85 Danish law requires that all patient contacts with hospital and outpatient clinics in  
86 Denmark are registered in the Danish National Patient Register<sup>25</sup>. Hospital  
87 identification, date and time of activity, and the patient's municipality (among other  
88 characteristics) are registered. A civil registration number (CPR) is given to all  
89 residents of Denmark and registered in the Civil Registration System, and information  
90 on emigration and death is recorded in this registry<sup>26</sup>. This enables researchers to have  
91 a complete and valid registration of all health-related issues on an individual level in  
92 the entire Danish population<sup>27</sup>.

93

94 The Danish Data Protection Agency approved the study (J. nr. 2008-58-0028, Id:  
95 2016-176). A full study protocol and study analysis plan was published online before  
96 the start of the study<sup>28</sup>. The reporting of the study complies with the Strengthening the  
97 Reporting of Observational Studies in Epidemiology (STROBE) Statement<sup>29</sup>.

98

#### 99 ***Study population and data***

100 The group of patients with a tibial plateau fracture was identified through a  
101 retrospective review in the Danish National Patient Register. All Danish citizens  
102 registered with a tibial plateau fracture between January 1, 1996, and December 31,  
103 2000, were included. Information regarding gender and age at the time of fracture was  
104 registered. Patients with prior tibial plateau fractures and TKR were excluded from



105 the study. All patients were followed with regard to surgery with TKR and/or  
106 secondary arthroscopic surgery of the knees throughout the observational period.

107

108 The matched reference group consisted of individuals identified from the Civil  
109 Registration System matched to the tibial plateau patient group on age and gender.  
110 For each patient with a tibial plateau fracture, 10 matched citizens were included.

111

112 Both groups were censored in case of emigration from the country or at the end of  
113 follow-up. Death was considered a competing event as was receiving a TKR when  
114 considering secondary knee arthroscopy as the outcome.

115

116 The primary outcome was treatment with a TKR. The secondary outcome was  
117 treatment with secondary knee arthroscopy.

118

### 119 *Statistical methods*

120 The risk of experiencing a TKR was assessed using cumulative incidence proportions  
121 which were calculated using the Aalen-Johansen estimator<sup>30</sup>.

122

123 The effect of tibial plateau fracture on the incidence of TKR was performed using a  
124 Cox proportional hazards regression model comparing the group of patients with  
125 tibial plateau fractures and the matched reference group. The effect estimate was  
126 reported as a hazard ratio with a corresponding 95% confidence interval to estimate  
127 the incidence rate ratio. Results from the crude analysis without adjustments were  
128 reported. Furthermore, we repeated the analysis stratified by age groups (0-50, 51+)

129 and gender. To investigate the assumption of proportional hazards, the follow-up time  
130 is divided into five-year periods.

131

132 Additional analyses were performed to investigate the effect of tibial plateau fracture  
133 on the secondary outcome (secondary knee arthroscopy) following the same methods  
134 as for the main analysis except that TKR, in addition to death, was considered a  
135 competing event for secondary arthroscopy.

136

137 All analyses were performed using Stata statistical software (StataCorp LP), and the  
138 significance level for analyses ( $\alpha$ ) was set to 0.05.

139

## 140 **RESULTS**

141 A total of 7,950 patients sustained a tibial plateau fracture in Denmark during the  
142 study period. The matched reference group consists of 79,300 citizens. Only 13  
143 patients with a tibial plateau fracture were matched by age and gender with less than 9  
144 citizens from the reference group (0.16%).

145

146 The median age of patients was 52.6 (IQR: 32.4-71.5) years. The gender distribution  
147 was 56.4% women and 43.6% men. The mean observational period was 13.9 years.

148

### 149 **Primary outcome**

150 The analysis showed that 5.7% of patients with a tibial plateau fracture were treated  
151 with a TKR (N=452) and that 2.0% of patients from the reference group were treated  
152 with a TKR (N=1623) during the observational period. The distribution of  
153 arthroplasties procedures for both groups is presented in Table 1.

154

155 Patients with a tibial plateau fracture had a 3.5 (95%CI: 3.1-3.9) times higher hazard

156 ratio (HR) compared to patients from the reference group. The effect was highest

157 during the first five years after the fracture (HR: 8.6 (95%CI: 7.1-10.3)) (Table 2).

158 The cumulative incidence of TKR during the entire observational period expressed for

159 the two groups is shown in Figure 1. The figure shows a significantly increased risk

160 of TKR in patients with a tibial plateau fracture compared to patients from the

161 reference group throughout the observational period.

162

163 *Analyses of age and gender difference on TKR*

164 Both men and women presented with a significantly increased incidence of TKR in

165 patients with a tibial plateau fracture compared with the reference group. Compared to

166 men, women presented with an increased incidence of TKR throughout the

167 observational period. The incidence of TKR for women showed a substantial increase

168 during the first five years compared to men. The age group above 50 years presented

169 with a substantially increased risk of TKR compared to the age group below 50 years.

170 (Supplemental figure 1-4).

171

172 *Secondary outcomes—secondary knee arthroscopy*

173 The analysis showed that 7.6% of patients with a tibial plateau fracture were treated

174 with a secondary knee arthroscopy (N=603) and 2.0% of patients from the reference

175 group were treated with a knee arthroscopy (N=1,565). The distribution of knee

176 arthroscopy procedures in both groups is presented in Table 3.

177 Patients with a tibial plateau fracture presented with a 5.0 (95%CI: 4.5-5.6) times

178 higher hazard ratio compared to patients in the reference group. As for TKR, the

179 effect was highest during the first five years after the tibial plateau fracture. (HR: 9.7  
180 (95%CI: 8.5-11.0)) (Table 4).

181

182 The cumulative incidence of secondary knee arthroscopy throughout the observational  
183 period is shown in Figure 2. The figure shows a significantly increased risk of  
184 secondary knee arthroscopy within the first five years following the tibial plateau  
185 fracture compared to the reference group. After the first five years, patients with a  
186 tibial plateau fracture and the reference group presented with almost equal risk of  
187 receiving a TKR.

188

189 The analyses of age and gender differences in the incidence of knee arthroscopy show  
190 that men presented with increased risk during the first five years compared to women,  
191 with almost equal risk of receiving a knee arthroscopy past five years. The analysis  
192 of age differences showed that the age group below 50 years of age presented with  
193 considerably increased risk compared to the age group above 50 years of age.  
194 (Supplemental Figure 5-8).

195

## 196 ***DISCUSSION***

197 This large-scale matched cohort study based on high-quality data showed that patients  
198 following a tibial plateau fracture increase the likelihood of TKR 3.5 times and knee  
199 arthroscopy 5.0 times. By a mean of 13.9 years follow-up, 5.7% of patients were  
200 treated with a TKR, and 7.9% with knee arthroscopy. The incidence of TKR and knee  
201 arthroscopy was highest during the first five years following the tibial plateau  
202 fracture. These findings indicated a long-lasting elevated risk of knee pain and  
203 decreased knee function in patients following a tibial plateau fracture.

204

205 The association between tibial plateaus fracture and TKR have been discussed  
206 extensively in the literature. However, most available studies are limited by small  
207 samples, short follow-up periods, and methodological quality. Recently, a study by  
208 Wasserstein et al.<sup>7</sup> with a 10-year follow-up period reported a 5.3 times increase in  
209 the likelihood of TKR, corresponding to 7.3% of patients treated with a TKR. The  
210 difference between the two studies may be explained by the present study including  
211 patients managed by all treatment modalities (ORIF, conservative means, and external  
212 fixation) in contrast to the study by Wasserstein et al., including only patients treated  
213 by ORIF. By including non-operative tibial plateau fractures in the present study, we  
214 included a cohort of patients who most likely had lower energy and less severe  
215 fractures compared to the Wasserstein<sup>7</sup> study, which is likely the major reason for the  
216 observed differences. Moreover, the increased risk of TKR in the study by  
217 Wasserstein may be partly explained by younger age. Moreover, conservative  
218 treatment of tibial plateau fracture may be more likely in older patients with a higher  
219 degree of comorbidity and decreased physical performance. Unfortunately, the  
220 present study did not include data on comorbidity and distribution between treatment  
221 modalities, which is an interesting research question for further studies. The need for  
222 long observational periods to investigate the increased risk of TKR following a tibial  
223 plateau fracture is evident as the 15-20 year hazard ratio is 1.86, indication a  
224 continually increased risk and hence the need for long follow-up periods.

225

226 This study showed that patients following a tibial plateau fracture presented with an  
227 increased likelihood of TKR throughout life. However, end-stage osteoarthritis and  
228 treatment with TKR are rare. In the present study, 5.7% of patients were treated with

229 TKR by a mean of 13.9 years follow-up. Investigating the association between a tibial  
230 plateau fracture and subsequent treatment with TKR is challenging due to the rarity  
231 and the long-term follow-up needed to capture the development of end-stage  
232 osteoarthritis. To the author's knowledge, the present study presented the largest  
233 cohort and longest follow-up of patients following a tibial plateau fracture.

234

235 Although the incidence of knee arthroscopy in patients with knee osteoarthritis is  
236 decreasing, the operative procedure is still common before treatment with TKR<sup>31</sup>.

237 Moreover, intra-articular soft tissue lesions and restrictions in knee joint motion  
238 following a fracture of the tibial plateau are common, which may lead to secondary  
239 knee arthroscopy in some patients. The present study showed that patients with a  
240 previous tibial plateau fracture had a five times higher incidence of a knee

241 arthroscopy compared to the matched control group. During the first five years after  
242 the fracture, the likelihood of knee arthroscopy was increased almost 10 times. The

243 subgroup analyses showed that especially younger men were treated with knee

244 arthroscopy. In the authors opinion, younger patients are much more likely to be

245 offered knee arthroscopy for continued knee pain following a tibial plateau fracture in

246 an effort to preserve the knee joint and are less likely to be offered knee replacement.

247 The converse is true for older patients. A single non-matched cohort study by Mehin

248 et al.<sup>6</sup> supported these findings, reporting that 16% of patients (N=311) following a

249 tibial plateau fracture at 10 years follow-up had an elective operative procedure

250 (arthroscopic procedure or intra-articular injection). This study suggested that many

251 patients experience knee pain and decreased knee function, especially in the first

252 years following a tibial plateau fracture. However, this study did not include clinical

253 information regarding the underlying causes leading to arthroscopic surgery and the

254 outcomes following the procedures. Further research is needed to address specific  
255 indications and outcomes of secondary knee arthroscopy in patients with a prior tibial  
256 plateau fracture.

257

258 Nevertheless, the present study included the entire Danish population of patients with  
259 tibial plateau fractures and compared this to a 10-fold non-exposed age- and gender-  
260 matched control group; some important limitations may be addressed. Information  
261 regarding laterality of tibial plateau fracture, TKR, and secondary arthroscopy is  
262 missing as side-specific information was not mandatory in the Danish National  
263 Patient Register. This is a limitation, and as a result, the ipsilateral risk of TKR and  
264 arthroscopy is likely higher than the risk estimates reported in the present study.  
265 Moreover, clinical information regarding comorbidity, fracture severity, treatment  
266 methods, and outcomes is not available from the register. It is likely that such clinical  
267 factors may affect secondary treatment with TKR and knee arthroscopy in  
268 subgroups<sup>7</sup>. Finally, shortcomings related to health registers may be addressed. Since  
269 1978, reporting to the Danish National Patient Register was required by Danish  
270 national law. Moreover, the allocation of payment to health care providers is partly  
271 based on this reporting. However, a small private activity, especially regarding  
272 arthroscopy, might have eluded the registry until mandatory registration by private  
273 hospitals was introduced in 2003. Although this might have had some effect on the  
274 crude incidence of surgery, this effect would have been present in both groups.

275 In conclusion, tibial plateau fractures are associated with a 3.5 times increased risk of  
276 total knee replacement and a 5.0 times increased risk of secondary knee arthroscopy

277 compared with an age- and gender-matched reference group with a mean follow-up of  
278 13.9 years.

279 Author contributions

280 Larsen, Elsoe and Johansen contributed all to the conception and design of this work. Larsen,  
281 Elsoe and Johansen contributed to analysis and interpretation of the data. Johansen  
282 contributed the data analysis. All authors were involved in drafting the article or revising it  
283 critically for important intellectual content, and granted final approval of the manuscript.

284 Conflict of interest

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*Legends:*

Table 1— The distribution of arthroplastic procedures for patients with a tibial plateau fracture and patients from the matched reference group.

Table 2— Cox proportional hazards regression model of TKR comparing patients with a tibial plateau fracture with the matched reference group.

Table 3— The distribution of secondary knee arthroscopy procedures for patients with a tibial plateau fracture and patients from the matched reference group.

Table 4— Cox proportional hazards regression model of secondary knee arthroscopy comparing patients with a tibial plateau fracture with the matched reference group.

Figure 1— Cumulative incidence of TKR

Legends: -- tibial plateau fracture group, -- reference group

Figure 2— Cumulative incidence of arthroscopy

Legends: -- tibial plateau fracture group, -- reference group

Supplemental figures:

Figure 1— Cumulative incidence of TKR, Women

Legends: -- tibial plateau fracture group, -- reference group

Figure 2— Cumulative incidence of TKR, Men

Legends: -- tibial plateau fracture group, -- reference group

Figure 3— Cumulative incidence of TKR, below 50 years of age

Legends: -- tibial plateau fracture group, -- reference group

Figure 4— Cumulative incidence of TKR, above 50 years of age

Legends: -- tibial plateau fracture group, -- reference group

Figure 5—Cumulative incidence of arthroscopy, Women

Legends: -- tibial plateau fracture group, -- reference group

Figure 6—Cumulative incidence of arthroscopy, Men

Legends: -- tibial plateau fracture group, -- reference group

Figure 7—Cumulative incidence of arthroscopy, below 50 years of age

Legends: -- tibial plateau fracture group, -- reference group

Figure 8—Cumulative incidence of arthroscopy, above 50 years of age

Legends: -- tibial plateau fracture group, -- reference group

Table 1—Cox proportional hazards regression model of TKR and knee arthroscopy comparing patients 0-50 years with a tibial plateau fracture with the matched reference group.

Table 2—Cox proportional hazards regression model of TKR and knee arthroscopy comparing patients 50+ years with a tibial plateau fracture with the matched reference group.

Table 3—Cox proportional hazards regression model of TKR and knee arthroscopy comparing men with a tibial plateau fracture with the matched reference group.

Table 4—Cox proportional hazards regression model of TKR and knee arthroscopy comparing women with a tibial plateau fracture with the matched reference group.

Table 1:

	<b>Tibial plateau fractures</b>		<b>Reference group</b>	
Procedure:				
Cemented TKR	335	74%	1160	71%
Hybrid TKR	48	11%	246	15%
Uncemented TKR	43	10%	90	6%
Medial arthroplasty	5	1%	66	4%
Other	21	5%	61	4%
Total arthroscopies	452	100%	1623	100%

**Table 2:**

Follow-up time N at beginning of interval # events in interval HR (95% CI)

0-5 years	87248	509 8.55 [7.12 - 10.27]
5-10 years	74510	588 2.41 [1.92 - 3.02]
10-15 years	65279	659 2.15 [1.72 - 2.70]
15-20 years	57484	318 1.86 [1.31 - 2.66]
0-20 years	87248	2074 3.50 [3.14 - 3.91]

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Table 3:

	Tibial plateau fractures				Reference group			
	Knee Arthroplasty		No Knee Arthroplasty		Knee Arthroplasty		No Knee Arthroplasty	
Diagnostic arthroscopy	75	61%	458	65%	167	62%	1381	63%
Synovectomy	16	13%	96	14%	26	10%	243	11%
Miniscal resection	17	14%	81	12%	57	21%	424	19%
Cartilage resection	7	6%	33	5%	12	4%	95	4%
Other	8	7%	33	5%	6	2%	43	2%
Total arthroscopies	123	100%	701	100%	268	100%	2186	100%
One arthroscopy	71	76%	353	69%	97	57%	739	53%
> 1 arthroscopy	23	24%	156	31%	74	43%	655	47%
Total	94	100%	509	100%	171	100%	1394	100%
Total	603				1565			

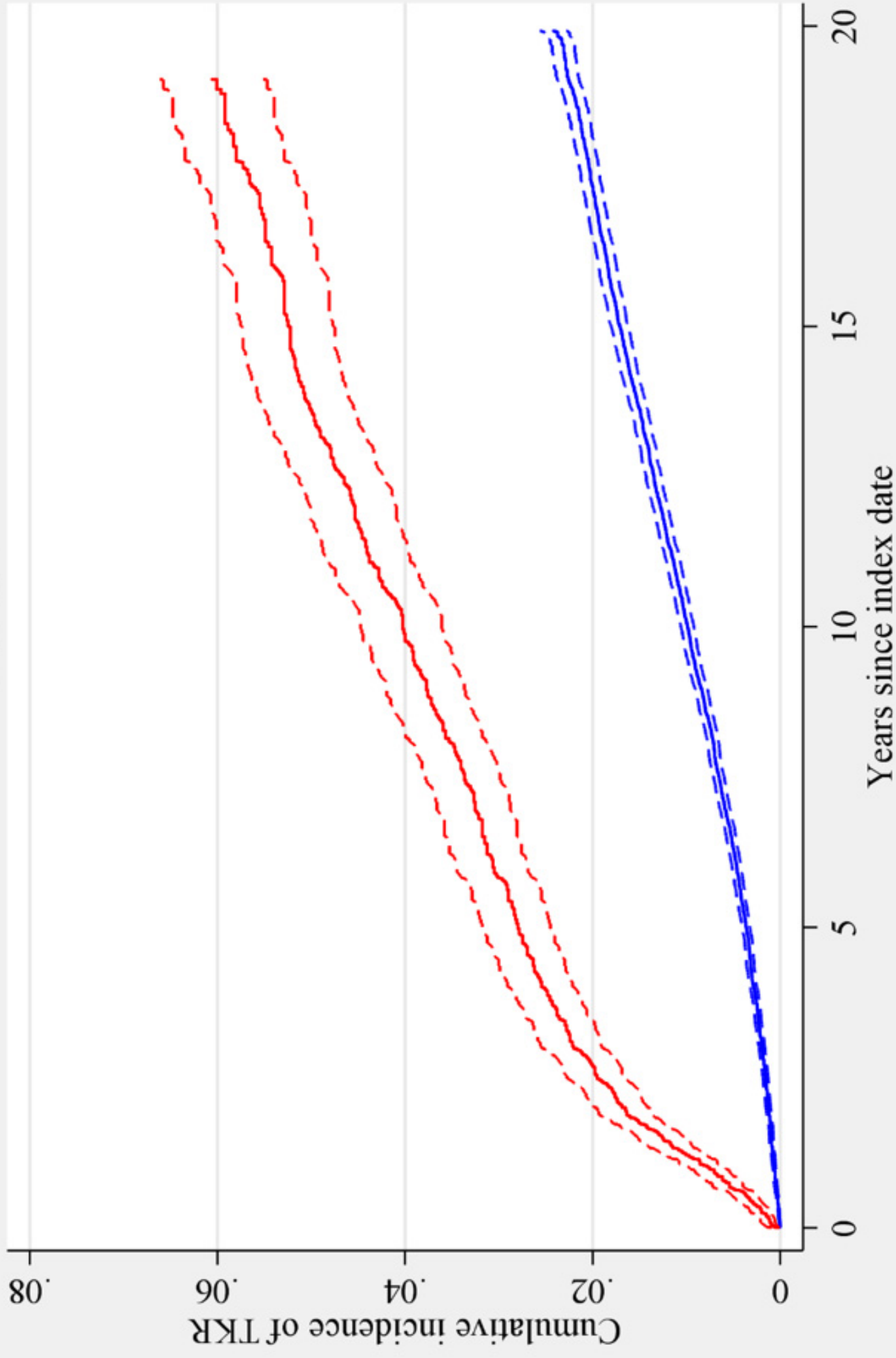


**Table 4:**

Follow-up time	N at beginning of interval	# events in interval	HR (95% CI)
0-5 years	86927	936	9.66 [8.45 - 11.03]
5-10 years	73347	482	1.87 [1.43 - 2.44]
10-15 years	63743	322	1.63 [1.15 - 2.31]
15-20 years	55779	91	1.05 [0.48 - 2.30]
0-20 years	86927	1831	5.02 [4.52 - 5.57]

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# Overall



# Overall

