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Citation for the published paper:

Carlsson, S; Sandin, F; Fall, K; Lambe, M; Adolfsson, J; Stattin, P; Bill-Axelsson, A

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European journal of cancer, 49 (7) s. 1588–1599

<http://dx.doi.org/10.1016/j.ejca.2012.12.018>

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1 **Risk of Suicide in Men with Low-risk Prostate Cancer**

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Running title: Prostate cancer and suicide risk

Key words: *prostatic neoplasms, suicide, mass screening*

Funding

This study was supported by funding from Swedish Research Council 825-2010-5950, the Swedish Cancer Society and the Prostate Cancer Foundation.

S.C. is supported by grants from the Swedish Cancer Society, the Sweden America Foundation, the Swedish Council for Working Life and Social Research and the Swedish Society for Medical Research.

Conflict of interest

None of the co-authors have any conflict of interest to declare.

List of where and when the study has been presented in part elsewhere:

Oct 4, 2012, annual meeting of Swedish Urology Association

Ethics/human subjects statement

The study was approved by the Umeå Research Ethics committee Umeå university dnr 2010 234 31M

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1 **Abstract**

2

3 **Purpose:** Risk of suicide is increased among men with prostate cancer. We
4 investigated this association among men with low-risk cancer, usually detected by
5 prostate specific antigen (PSA)-testing.

6 **Patients and Methods:** Relative risk (RR) of suicide was calculated by use of
7 Poisson regression analysis within the Prostate Cancer data Base Sweden
8 (PCBaSe) 2.0, a nationwide, population-based database, comparing 105,736 men
9 diagnosed with prostate cancer between 1997-2009 to 528,658 matched prostate
10 cancer-free men.

11 **Results:** During the first six months after diagnosis, there were 38 suicides among
12 men with prostate cancer; incidence rate 0.73 per 1,000 person-years (PY) and 30
13 suicides in the comparison cohort; 0.11 per 1,000 PY, corresponding to a RR of
14 suicide of 6.5 (95% CI 4.0-10). Risk was highest among men with distant
15 metastases, incidence rate 1.25 per 1,000 PY, RR 10 (95% CI 5.1-21) but risk was
16 also increased for men with low-risk tumors, incidence rate difference 0.45 per 1,000
17 PY and RR 5.2 (95% CI 2.3-12) and across categories of socioeconomic status and
18 comorbidity. Eighteen months after diagnosis, risk of suicide had decreased to 0.27
19 per 1,000 PY, RR 1.0 (95% CI 0.68-1.5) for low-risk prostate cancer but remained
20 increased among men with metastases, 0.57 per 1,000 PY, RR 1.8 (95% CI 1.1-2.9).

21 **Conclusion:** Although the increase in absolute risk of suicide was modest, our
22 findings reflect the severe psychological stress that prostate cancer patients may
23 experience after diagnosis. The increased risk of suicide observed in men with
24 prostate cancer, including low-risk, calls for increased awareness.

1 **Introduction**

2 Cancer is often perceived as a life-threatening disease, even though many cancers
3 are currently diagnosed in an early and curable stage(1). Men diagnosed with
4 prostate cancer are at increased risk of suicide and also of anxiety, depression, post-
5 traumatic stress disorder, psychiatric hospitalization and treatment(2-4). An
6 increased risk of suicide and cardiovascular events shortly after the date of cancer
7 diagnosis was recently reported, highlighting that a cancer diagnosis *per se* may
8 evoke severe stress and trigger these events(3-8).

9 Prostate cancer has an extremely variable prognosis ranging from a 10-year
10 risk of cancer death of 3% for low-risk prostate cancer, (cT1-T2, GS 2-6, serum
11 levels of Prostate-Specific Antigen, PSA, below 10 ng/mL)(9) to 70% among men
12 with metastatic disease.(10, 11) Since the introduction of PSA testing for early
13 detection of prostate cancer, there has been a sharp rise in the number of men
14 diagnosed with low-risk prostate cancer(12, 13). If these men also have an increased
15 risk of suicide is unknown.

16 The aim of the present study was therefore to assess the risk of suicide in
17 men with prostate cancer with special reference to time after diagnosis and disease
18 risk category. We further aimed to explore the influence of co-morbidity and
19 socioeconomic status on the risk of suicide among men newly diagnosed with
20 prostate cancer.

21

1 **Materials and methods**

2 This is a prospective study of two cohorts within the Prostate Cancer data Base
3 Sweden (PCBaSe) 2.0, a database that has been described in detail previously(14).
4 In brief, the prostate cancer cohort consisted of men diagnosed with prostate cancer
5 between January 1, 1997 and December 31, 2009 in the National Prostate Cancer
6 Register (NPCR), which captures more than 96% of incident prostate cancer cases
7 compared to the Swedish Cancer Register to which registration is compulsory and
8 mandated by law. Data available in NPCR include diagnostic unit, date of diagnosis,
9 serum level of PSA at diagnosis, tumor stage (TNM), tumor grade and primary
10 treatment performed or decided within 6 months after date of diagnosis. Since 2000,
11 details on the evaluation leading to the diagnosis are also recorded (symptoms of
12 disease, health control, i.e. unorganized screening or other reasons). We used a
13 modification of the National Comprehensive Cancer Network risk group classification
14 (Table 1)(9).

15 For each case, PCBaSe 2.0 includes five randomly selected men that were
16 prostate cancer-free at the time of the case's diagnosis, matched to the index case
17 on year of birth (+/- 1 year) and county of residence. These men formed our
18 comparison cohort.

19 By use of the individually unique personal identity number assigned to all
20 residents in Sweden, NPCR was linked to a number of other nation-wide population-
21 based health care registers and demographic databases.(14)

22 The Cause of Death Register was used to identify suicide as defined by
23 International Classification of Diseases [ICD]-10 code recorded as "certain suicide"
24 (ICD-10 code X60.84). The Swedish Longitudinal integration database for health
25 insurance and labor market studies (LISA) provided information on socioeconomic
26 status and marital status.

1 We classified comorbidity for the prostate cancer patients and men in the
2 comparison cohort according to Charlson's co-morbidity index (CCI)(15): 0=no co-
3 morbidity, 1= mild, 2+ =severe co-morbidity based on data in the National Patient
4 Register according to ICD-9 or ICD-10.

5 Follow-up started on the date of diagnosis of the index case and ended on
6 the date of death, emigration, or December 31, 2010, whichever came first.

7 Psychiatric disease as indicated by medication may modify the risk of suicide
8 and therefore, we assessed patterns of filings of drug prescriptions (antidepressants
9 ATC code N06A, neuroleptics ATC code N05A, sedatives and ataractics ATC code
10 N05B and sleep medications and sedatives ATC code N05C) through linkage with
11 the Prescribed Drug Register. In a sub-analysis, we assessed the exposure
12 (psychiatric medication use never/ever) in the pre-diagnosis period July 2005 (when
13 the Prescribed Drug Register started) to Dec 31, 2006 and assessed the outcome
14 suicide during the period 2007-2009.

15

16 *Statistics*

17 Age during follow-up was divided into five-year categories and the number of
18 suicides along with person-time at risk was calculated separately for the two cohorts.
19 In order to study the effect of time since diagnosis, the data were further divided into
20 three categories of follow-up time (0-6 months, 6-18 months, and >18 months since
21 date of diagnosis of the index case). Poisson regression models were used with the
22 observed number of events as response and the logarithm of person-time at risk as
23 offset. The covariates included in the model were age (as natural cubic splines with
24 two internal knots), calendar time since inclusion, an indicator of cohort, and the
25 interaction between this indicator and the time since inclusion. The relative risks of

1 suicide in the three follow-up intervals, along with 95% confidence limits, were
2 calculated.

3 Relative risks were also estimated with flexible parametric models(17), using
4 an indicator of cohort and age at diagnosis (as natural cubic splines) as covariates.
5 This allowed for the relative risks to be plotted as a continuous function of time since
6 diagnosis.

7 A p-value less than 0.05 was considered statistically significant. Statistical
8 analyses were performed with the Stata statistical software v.11.0 (Stata Corp 2009,
9 College Station, TX, U.S.A.) and the R statistical software package v.2.12.2.(18)

10

1 **Results**

2 During the entire follow-up time, mean time 4.9 (SD 3.2) years for men with prostate
3 cancer and 5.4 (SD 3.3) years for the comparison cohort (**Table 1 & 2**), we observed
4 an overall increased relative risk of suicide of 1.5 (95% CI 1.3-1.8) (**Table 3**) based
5 on 211 suicides among men with prostate cancer and 785 suicides in the
6 comparison cohort. Over the entire study period, the incidence rate was 0.41/1,000
7 person-years (PY) among prostate cancer cases and 0.27/1,000 PY in the
8 comparison cohort.

9 The median age at date of diagnosis among men with prostate cancer was 72
10 years (IQR 65-79.5). The median age at suicide for men with prostate cancer was 75
11 years (67-83) and 76 (69-83) in the comparison cohort. (**Table 1**) There was an
12 almost equal distribution in socioeconomic status in the cohort of men with prostate
13 cancer and the comparison cohort and the majority was married and had no co-
14 morbid conditions. (**Table 1&2**)

15

16 Risk of suicide by time since diagnosis

17 Within the first six month after date of diagnosis, we observed an increased
18 relative risk of suicide of 6.5 (95% CI 4.0-10) (**Table 3**); with 38 suicides among men
19 with prostate cancer; incidence rate 0.73 per 1,000 PY and 30 suicides in the
20 comparison cohort; 0.11 per 1,000 PY (**Table 4**), i.e. an excess of 0.62
21 suicides/1,000 PY among men with prostate cancer.

22 This risk decreased to RR 2.1 (95% CI 1.5-2.9) 6-18 months after date of
23 diagnosis and was lower and not statistically significant, RR 1.2 (95% CI 0.96-1.4)
24 beyond 18 months after diagnosis (**Table 3**).

25

26

1 Risk of suicide by risk category

2 There was an increasing relative risk of suicide within 6 months with higher risk
3 category; men with low-risk tumors relative the comparison cohort had a RR of 5.2
4 (95% CI 2.3-12), incidence rate difference 0.45 per 1,000 PY and men with distant
5 metastases had an RR 10 (95% CI 5.1-21), incidence rate 1.25 per 1,000 PY, (**Table**
6 **3,4**). Eighteen months after diagnosis, risk of suicide had decreased to 0.27 per
7 1,000 PY, RR 1.0 (95% CI 0.68-1.5) for low-risk prostate cancer but remained
8 increased among men with metastases 0.57 per 1,000 person-years, RR 1.8
9 (95%CI 1.1-2.9). (**Table 3,4**)

10 The absolute risk of suicide increased with increasing risk category,
11 particularly among older men (**Figure 1**). Risk remained elevated over time for men
12 with distant metastases whereas for men with localized disease it decreased to the
13 same level as among controls 3 years after diagnosis (**Figure 2**).

14 We also observed increased RR's in the first 6 months among men
15 diagnosed with T1c tumors (RR 8.2; 95% CI 4.4-15), in men with low or slightly
16 elevated PSA levels, in men with intermediate risk tumors, and in asymptomatic men
17 who were diagnosed as a result of PSA testing (**Table 3**).

18

19 Risk of suicide by treatment modality

20 The risk of suicide within 6 months was increased among all treatment
21 strategies. This risk was somewhat lower (RR 2.0, 95% CI 0.6-6.4) for men managed
22 expectantly as compared to those treated with curative intent (RR 2.7, 95% CI 1.1-
23 7.0) or with hormonal therapy (RR 6.0, 95% CI 3.2-11). (**Table 3**)

24

25 Risk of suicide by history of filed prescriptions

26 Prostate cancer cases with no filed prescriptions of antidepressants,
27 antipsychotic medication or sleeping pills, "never users", had a lower absolute risk of

1 suicide (0.37 per 1,000 PY) than cases on psychiatric medication, “ever users”, (0.87
2 per 1,000 PY) and “never user” cases also had a lower absolute increase in risk of
3 suicide than “ever user” cases (**Appendix 1**). However, the relative risk was higher
4 among never user cases (RR 2.7, 95% CI 1.6-4.7) than ever user cases (RR 1.9,
5 95% CI 0.94-3.7).

6

7 Risk of suicide by socioeconomic status and comorbidity burden

8 The same relationship was seen for cases with high socioeconomic status
9 (SES) and low comorbidity (CCI), i.e. a lower absolute increase of suicide than cases
10 with low SES and high CCI, but a higher increase in relative risk (Table 1). The risk
11 of suicide among men with prostate cancer was increased during the first six months
12 among men with high (RR 8.1, 95% CI 3.7-18), and low socioeconomic status (RR
13 5.4, 95% CI 2.9-10) and severe comorbidity (RR 6.0, 95% CI 2.4-15) and no
14 recorded comorbidity (RR 11, 95% CI 5.7-22), compared with men in the comparison
15 cohort with the same socioeconomic status and comorbidity index (**Table 3**).

16

1 **Discussion**

2 In this population-based, nation-wide cohort study of prostate cancer in Sweden, we
3 found an increased risk of suicide following a prostate cancer diagnosis. The relative
4 risk was highest during the first six months after diagnosis among all prostate cancer
5 cases. The risk increased with more advanced disease from a five-fold increase
6 among men with low-risk disease to a ten-fold increase among men with metastatic
7 disease.

8 Risk estimates were stratified on comorbidity, socioeconomic status and
9 previous psychiatric morbidity and we found an increased risk of suicide among
10 prostate cancer cases with and without comorbidity, with low and high
11 socioeconomic status and with and without previous psychiatric morbidity. Although
12 we cannot exclude confounding by unknown factors we consider it highly unlikely
13 that an unknown confounder would have resulted in a peak of suicides during the
14 first 6 months after diagnosis and thereafter a gradual decline.

15 There was an increased risk of suicide also among men with low-risk tumors
16 most often diagnosed as a result of opportunistic screening. Given that there has
17 been a considerable uptake of PSA-testing with ensuing increase in incidence of low-
18 risk prostate cancer in Europe and many other countries in the Western world our
19 findings are relevant outside of Sweden. For example, in the Nordic countries of
20 Finland, Sweden, Iceland, and Norway, prostate cancer incidence rates are amongst
21 the highest in Europe.(19)

22 Our interpretation of these findings has clear clinical relevance. First, there
23 was an increased risk of suicide also among men with low-risk tumors following early
24 detection. Our data thus underline the importance of an awareness of the increased
25 suicide risk among men with newly diagnosed prostate cancer – in all risk categories.
26 It has been estimated that more than one third of Swedish men aged 50-75 years
27 underwent PSA-testing between 2000 and 2007(13, 20) even though no systematic
28 PSA-screening has been, or is, in operation(21) (apart from in a screening trial in

1 Göteborg(22)). Given that many low-risk cancers would not have been diagnosed if
2 PSA-testing had not been performed, an increase in suicide risk is a concern.
3 Vigilance concerning suicide risk and appropriate counseling and treatment when
4 indicated is therefore important in the management of men with newly diagnosed
5 prostate cancer.(23)

6 Secondly, although repeated PSA-screening decreased prostate cancer
7 mortality in two large well-designed randomized screening trials(22, 24), the balance
8 between the harms and benefits remains debated. Our current study adds some
9 further data to be included in the trade-off calculation. Whereas the observation of a
10 substantially increased relative risk of suicide among all prostate cancer patients
11 warrants caution as discussed above, this potential harm of PSA-testing was low in
12 absolute terms (approximately 1 extra suicide per 2000 person-years). Further,
13 PSA-testing may speculatively affect suicide risk in two opposite ways; increasing the
14 number low-risk prostate cancers with modestly increased risk of suicide, but at the
15 same time reducing the risk of metastatic disease(22, 24, 25), which is associated
16 with a larger increase in risk(3, 4).

17 Fang and colleagues recently reported that a cancer diagnosis increases risk
18 of suicide across all tumor stages: regional, localized and metastasized prostate
19 cancer.(3) Our findings in a data set with higher precision in tumor and patient
20 characterization corroborate these results.

21 In a previous publication, based on data from the PCBaSe linkage 1.0
22 including 77,439 men diagnosed with prostate cancer between 1997 to 2006 with
23 128 suicides, we found no increased risk of suicide among men diagnosed with T1c
24 tumors, whereas the risk was twice as high among men with locally advanced and
25 metastatic disease compared to an age-matched background population.(4) In our
26 present study, we compared the relative risk of men with prostate cancer with that of
27 prostate cancer- free men matched for age and residency with information on
28 socioeconomic status and comorbidity. Therefore, with an increased number of

1 events (n=211) and additional data on cases and comparison men, we were able to
2 assess the risk of suicide with increased precision also allowing for stratification for
3 time after diagnosis.

4 Regarding treatment, there was an increased risk of suicide within the first 6
5 months for all treatment categories. This risk was lower for men managed with
6 expectancy or active surveillance in comparison with men receiving curative or
7 palliative treatment. This finding is line with findings from a study where men on
8 active surveillance reported lower short-term levels of anxiety and distress as
9 compared to data in the literature for men on other treatments.(26)

10

11 **Conclusions**

12 Men diagnosed with prostate cancer, also low-risk prostate cancer, had an increased
13 risk of suicide, especially shortly after diagnosis. Our data underline the importance
14 of an awareness of the risk of suicide among men with newly diagnosed prostate
15 cancer.

1 **Acknowledgement**

2 This project was made possible by the continuous work of the National Prostate
3 Cancer Register of Sweden (NPCR) steering group: Pär Stattin (chairman), Anders
4 Widmark, Lars Egevad, Magnus Törnblom, Stefan Carlsson, Jan Adolfsson, Anna
5 Bill-Axelson, Jan-Erik Johansson, Ove Andrén, Mats Lambe, Erik Holmberg, David
6 Robinson, Bill Pettersson, Jonas Hugosson, Jan-Erik Damber, Ola Bratt, Göran
7 Ahlgren, Karin Hellström, and Maria Nyberg.

8

9 **Author contributions**

10 A.B-A. and P.S. had full access to all of the data in the study and takes responsibility
11 for the integrity of the data and the accuracy of the data analysis. P.S. created and
12 financed the database, conceived statistical analyses together with A.B.A. and F.S.,
13 participated in drafting and writing of manuscript.

14 S.C. performed the literature search, contributed to the concept of the study, to the
15 analysis and interpretation of data and important intellectual revisions, drafted and
16 coordinated the revisions and finalized the manuscript.

17 J.A. and K.F. contributed to the data analysis and interpretation of data and in the
18 manuscript writing.

19 F.S. and M.L. carried out the statistical analyses, interpreted the results and
20 participated in writing and revising the manuscript.

21 All authors approved the final version of the manuscript to be published.

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22

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Table 1. Baseline characteristics of men with **prostate cancer** in Prostate Cancer data Base Sweden (PCBaSe) 2.0 who committed early suicide, suicide and full cohort.

	Death due to ICD10 X60-84 (n = 211)	Death due to ICD10 X60-84 within 6 months from prostate cancer diagnosis (n = 38)	All men with prostate cancer (n = 105 736)
Follow-up, yr, mean (sd)	2.7 (2.5)	0.3 (0.2)	4.9 (3.2)
Age, yr, median (IQR)	72 (65-79.5)	72.5 (64.5-80)	71 (64-78)
Age, yr, No (%)			
<65	51 (24)	10 (26)	28197 (27)
65-74	70 (33)	11 (29)	38914 (37)
≥75	90 (43)	17 (45)	38625 (37)
Year of PC diagnosis, No (%)			
1997-1999	45 (21)	3 (8)	18162 (17)
2000-2002	71 (34)	8 (21)	22305 (21)
2003-2005	53 (25)	9 (24)	28304 (27)
2006-2009	42 (20)	18 (47)	36965 (35)
Mode of detection ¹ , No (%)			
Symptoms	113 (68)	26 (74)	51231 (59)
Health control	22 (13)	5 (14)	24349 (28)
Other reason	15 (9)	1 (3)	6009 (7)
Missing	16 (10)	3 (9)	5985 (7)
T stage, No (%)			
T1c	56 (27)	15 (39)	34551 (33)
T0	0 (0)	0 (0)	496 (<1)
T1ab	13 (6)	2 (5)	6625 (6)
T2	61 (29)	6 (16)	33352 (32)
T3-4	75 (36)	15 (39)	28708 (27)
Missing	6 (3)	0 (0)	2004 (2)
M stage, No (%)			
M0	48 (23)	5 (13)	28886 (27)
M1	22 (10)	6 (16)	10350 (10)
MX	140 (66)	27 (71)	65483 (62)
Missing	1 (<1)	0 (0)	1017 (<1)
PSA ng/mL, No (%)			
PSA <4	9 (4)	2 (5)	6933 (7)
PSA ≥4 - <10	62 (29)	10 (26)	34222 (32)
PSA ≥10 - <20	41 (19)	10 (26)	22414 (21)
PSA ≥20 - <100	68 (32)	9 (24)	26602 (25)
PSA ≥100	25 (12)	7 (18)	12879 (12)
Missing	6 (3)	0 (0)	2686 (3)
Gleason score ² , No (%)			
2-6	100 (47)	16 (42)	47189 (45)
7	59 (28)	9 (24)	34850 (33)
8-10	45 (21)	10 (26)	21275 (20)
Missing	7 (3)	3 (8)	2422 (2)
Risk group ³ , No (%)			
Low risk	49 (23)	7 (18)	25297 (24)
Intermediate risk	35 (17)	8 (21)	24692 (23)
High risk	59 (28)	10 (26)	26986 (26)
Regionally metastatic	27 (13)	2 (5)	8980 (8)
Distant metastases	34 (16)	10 (26)	17012 (16)
Missing	7 (3)	1 (3)	2769 (3)
Planned initial treatment, No (%)			
Expectancy	49 (23)	3 (8)	27502 (26)
Treatment with curative intent	46 (22)	5 (13)	34826 (33)
Treatment with hormonal therapy	92 (44)	14 (37)	40387 (38)
Missing	24 (11)	16 (42)	3021 (3)
Charlson comorbidity index, No (%)			
0	135 (64)	27 (71)	68706 (65)
1	28 (13)	1 (3)	19161 (18)
2+	48 (23)	10 (26)	17869 (17)
Socioeconomic status, No (%)			
High	95 (45)	17 (45)	51731 (49)
Low	114 (54)	20 (53)	52531 (50)
Not gainfully employed	1 (<1)	0 (0)	396 (<1)
Unclassified/Missing	1 (<1)	1 (3)	1078 (1)
Marital status, No (%)			
Unmarried	30 (14)	8 (21)	9308 (9)
Married	111 (53)	18 (47)	71907 (68)

Table

Table 2. Baseline characteristics of **prostate-cancer free men** in Prostate Cancer data Base Sweden (PCBaSe) 2.0 who committed early suicide, suicide and full cohort.

	Death due to ICD10 X60-84 (n = 785)	All prostate cancer-free men (n = 528 658)
Follow-up, yr, mean (sd)	4.1 (2.8)	5.4 (3.3)
Age, yr, median (IQR)	73 (65-79)	71 (65-78)
Age, yr, No (%)		
<65	188 (24)	132087 (25)
65-74	259 (33)	194022 (37)
≥75	338 (43)	202549 (38)
Charlson comorbidity index, No (%)		
0	506 (64)	339708 (64)
1	152 (19)	96214 (18)
2+	127 (16)	92736 (18)
Socioeconomic status, No (%)		
High	306 (39)	237227 (45)
Low	461 (59)	276426 (52)
Not gainfully employed	6 (<1)	3521 (<1)
Unclassified/Missing	12 (2)	11484 (2)
Marital status, No (%)		
Unmarried	162 (21)	60326 (11)
Married	384 (49)	339433 (64)
Divorced	140 (18)	70777 (13)
Widower	99 (13)	58122 (11)
Missing	0 (0)	0 (0)

Table

Table 4. Number of events (death due to ICD10 X60-84), person-years at risk, and number of events per 1000 py.

	Number of events	Person-years at risk	Number of events per 1000 py
Prostate cancer-free men in comparison cohort			
0-6 months after inclusion	30	263653	0.11
6-18 months after inclusion	121	507589	0.24
>18 months after inclusion	634	2100308	0.30
Men with prostate cancer			
0-6 months after diagnosis	38	51947	0.73
6-18 months after diagnosis	48	97546	0.49
>18 months after diagnosis	125	368461	0.34
Early detection features:			
Men with prostate cancer - T1c			
0-6 months after diagnosis	15	17163	0.87
6-18 months after diagnosis	14	33122	0.42
>18 months after diagnosis	27	125366	0.22
Men with prostate cancer - Mode of detection¹ - Health control			
0-6 months after diagnosis	5	12140	0.41
6-18 months after diagnosis	7	23445	0.30
>18 months after diagnosis	10	76840	0.13
Men with prostate cancer - Low risk			
0-6 months after diagnosis	7	12612	0.56
6-18 months after diagnosis	14	24612	0.57
>18 months after diagnosis	28	103557	0.27
Men with prostate cancer - Intermediate risk			
0-6 months after diagnosis	8	12274	0.65
6-18 months after diagnosis	10	23688	0.42
>18 months after diagnosis	17	95989	0.18
Men with prostate cancer - Treatment with curative intent			
0-6 months after diagnosis	5	17392	0.29
6-18 months after diagnosis	13	34003	0.38
>18 months after diagnosis	28	144349	0.19

¹ Presented for subcohort with PC diagnosis after January 1, 2000.

Table 3. Relative risk of suicide after prostate cancer diagnosis according to time after diagnosis.

	0-6 months after diagnosis		6-18 months after diagnosis		>18 months after diagnosis		Overall, disregarding time since diagnosis	
	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
Full cohort	6.5	(4.0-10)	2.1	(1.5-2.9)	1.2	(0.96-1.4)	1.5	(1.3-1.8)
Age, yr ¹								
<65	4.7	(1.9-11)	2.4	(1.3-4.7)	0.90	(0.60-1.4)	1.3	(0.99-1.8)
65-74	6.9	(2.8-17)	2.0	(1.1-3.6)	1.1	(0.82-1.6)	1.5	(1.1-1.9)
≥75	7.8	(3.7-16)	2.0	(1.2-3.4)	1.4	(1.0-1.8)	1.7	(1.4-2.2)
Year of PC diagnosis								
1997-1999	3.0	(0.90-9.7)	2.8	(1.5-5.2)	1.0	(0.72-1.5)	1.3	(0.97-1.8)
2000-2002	6.4	(2.9-14)	2.0	(1.1-3.9)	1.6	(1.2-2.1)	1.8	(1.4-2.3)
2003-2005	5.8	(2.7-12)	2.1	(1.2-3.7)	1.0	(0.70-1.4)	1.4	(1.0-1.8)
2006-2009	8.8	(4.9-16)	1.8	(1.0-3.1)	0.75	(0.40-1.4)	1.6	(1.2-2.3)
Mode of detection								
Symptoms	8.9	(5.1-15)	1.8	(1.2-3.0)	1.5	(1.2-2.0)	2.0	(1.6-2.4)
Health control	3.8	(1.5-10)	1.3	(0.61-2.8)	0.49	(0.26-0.91)	0.81	(0.53-1.2)
Other reason	3.0	(0.41-22)	3.8	(1.5-9.3)	1.3	(0.65-2.4)	1.7	(1.0-2.9)
T stage								
T1c	8.2	(4.4-15)	1.9	(1.1-3.3)	0.79	(0.53-1.2)	1.3	(0.98-1.7)
T0	-	-	-	-	-	-	-	-
T1ab	5.3	(1.3-22)	1.3	(0.33-5.4)	1.0	(0.54-2.0)	1.2	(0.72-2.1)
T2	3.2	(1.4-7.8)	1.9	(1.1-3.3)	1.1	(0.79-1.5)	1.3	(1.0-1.7)
T3-4	9.1	(4.9-17)	2.3	(1.3-4.0)	1.9	(1.4-2.6)	2.3	(1.8-2.9)
M stage								
M0	3.2	(1.3-8.3)	1.1	(0.52-2.4)	0.91	(0.65-1.3)	1.0	(0.77-1.4)
M1	11	(4.4-25)	1.6	(0.50-4.9)	2.6	(1.5-4.5)	2.8	(1.8-4.2)
MX	7.3	(4.4-12)	2.6	(1.8-3.8)	1.2	(0.95-1.5)	1.7	(1.4-2.1)
PSA ng/mL								
PSA <4	5.3	(1.3-22)	3.3	(1.4-8.2)	0.28	(0.07-1.1)	0.99	(0.51-1.9)
PSA ≥4 - <10	5.5	(2.7-11)	2.5	(1.5-4.0)	0.95	(0.67-1.3)	1.4	(1.1-1.8)
PSA ≥10 - <20	8.1	(4.0-17)	1.2	(0.54-2.8)	0.95	(0.64-1.4)	1.3	(0.93-1.7)
PSA ≥20 - <100	5.8	(2.8-12)	1.8	(0.99-3.4)	1.7	(1.3-2.3)	1.9	(1.5-2.4)
PSA ≥100	9.4	(4.1-21)	1.9	(0.78-4.7)	1.7	(0.98-3.0)	2.1	(1.4-3.2)
Gleason score								
2-6	6.3	(3.4-12)	2.3	(1.4-3.5)	1.1	(0.84-1.4)	1.5	(1.2-1.8)
7	4.6	(2.2-9.7)	2.4	(1.4-3.9)	0.92	(0.65-1.3)	1.3	(1.0-1.7)
8-10	8.2	(4.0-17)	1.1	(0.46-2.7)	2.0	(1.4-2.9)	2.1	(1.5-2.8)
Risk group								
Low risk	5.2	(2.3-12)	2.6	(1.5-4.5)	1.0	(0.68-1.5)	1.4	(1.1-1.9)
Intermediate risk	6.0	(2.8-13)	1.9	(0.98-3.5)	0.62	(0.38-1.0)	1.0	(0.73-1.4)
High risk	6.5	(3.2-13)	1.6	(0.86-3.1)	1.3	(0.93-1.8)	1.5	(1.2-2.0)
Regionally metastatic	3.8	(0.91-16)	2.0	(0.73-5.4)	2.4	(1.5-3.7)	2.3	(1.6-3.4)
Distant metastases	10	(5.1-21)	1.8	(0.78-4.0)	1.8	(1.1-2.9)	2.2	(1.6-3.2)
Planned initial treatment								
Expectancy	2.0	(0.60-6.4)	2.3	(1.3-4.0)	0.96	(0.67-1.4)	1.2	(0.89-1.6)
Trt w curative intent	2.7	(1.1-7.0)	1.7	(0.98-3.1)	0.74	(0.51-1.1)	1.0	(0.74-1.4)
Trt w hormonal therapy	6.0	(3.2-11)	1.9	(1.2-3.2)	1.8	(1.4-2.3)	1.9	(1.6-2.4)
Charlson comorbidity index ²								
0	11	(5.7-22)	2.2	(1.4-3.4)	1.1	(0.86-1.4)	1.5	(1.3-1.8)
1	0.57	(0.07-4.5)	1.7	(0.76-3.8)	0.94	(0.58-1.5)	1.0	(0.70-1.6)
2+	6.0	(2.4-15)	2.3	(1.2-4.5)	1.8	(1.2-2.8)	2.2	(1.6-3.1)
Socioeconomic status ³								
High	8.1	(3.7-18)	3.1	(1.9-5.0)	1.1	(0.80-1.5)	1.6	(1.3-2.0)
Low	5.4	(2.9-10)	1.5	(0.92-2.5)	1.3	(0.99-1.6)	1.5	(1.2-1.9)
Not gainfully employed	-	-	-	-	-	-	-	-
Marital status ⁴								
Unmarried	9.0	(3.1-26)	2.4	(1.0-5.5)	0.91	(0.53-1.6)	1.5	(0.98-2.1)
Married	7.9	(3.7-17)	1.9	(1.1-3.1)	1.3	(0.97-1.6)	1.6	(1.3-1.9)
Divorced	5.5	(1.8-17)	2.1	(0.99-4.6)	1.1	(0.70-1.8)	1.5	(1.0-2.2)
Widower	4.6	(1.5-14)	3.0	(1.4-6.2)	1.6	(0.97-2.7)	2.2	(1.5-3.2)

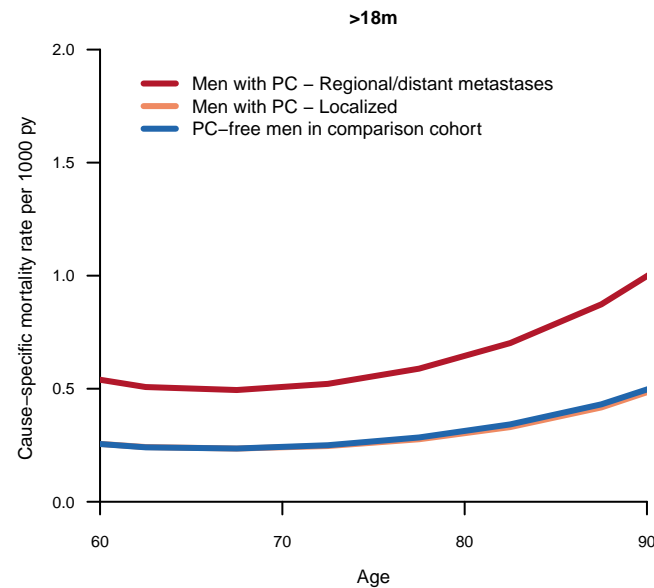
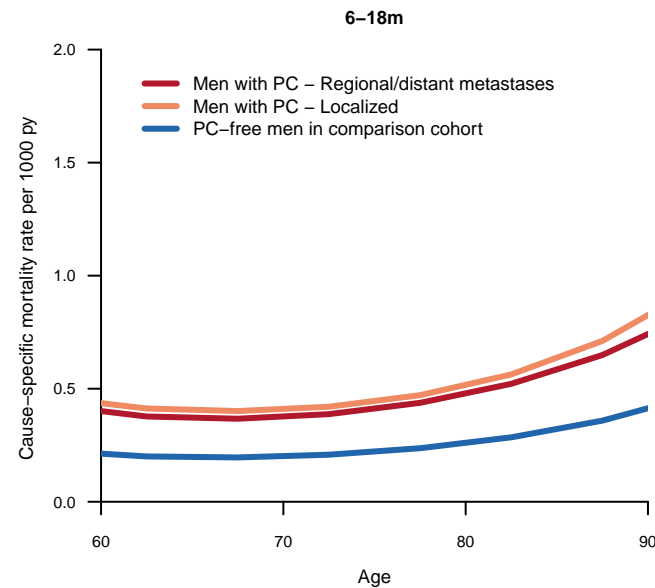
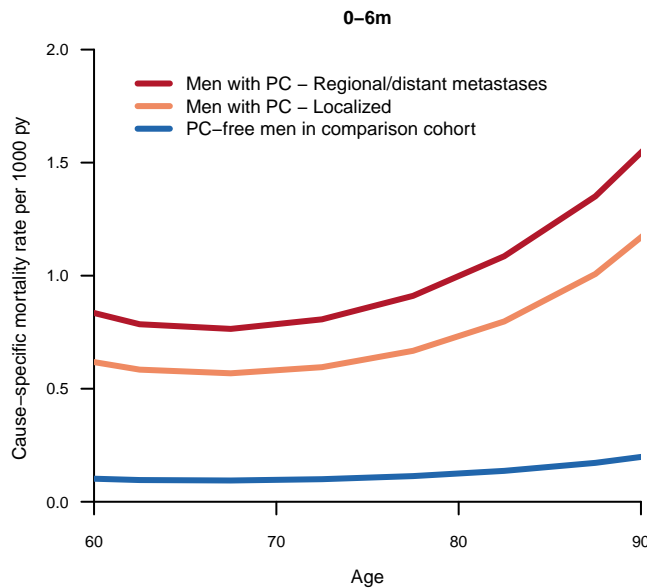
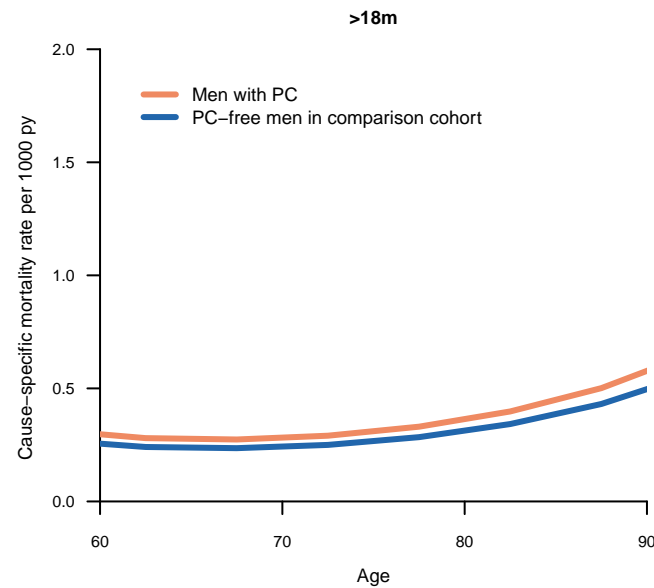
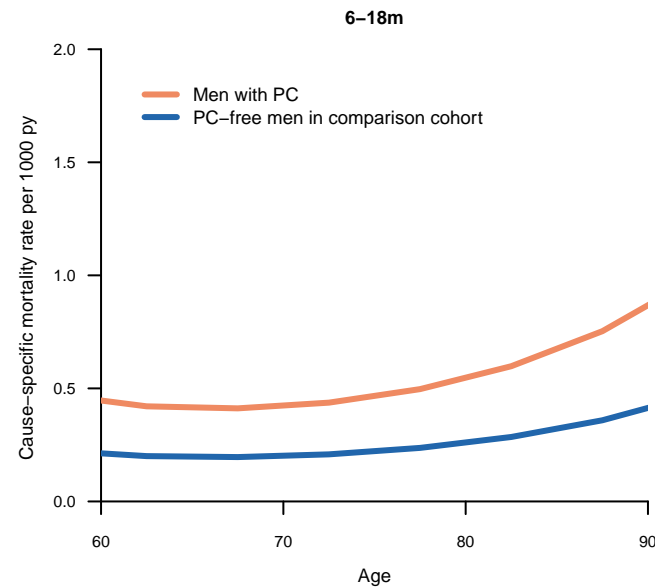
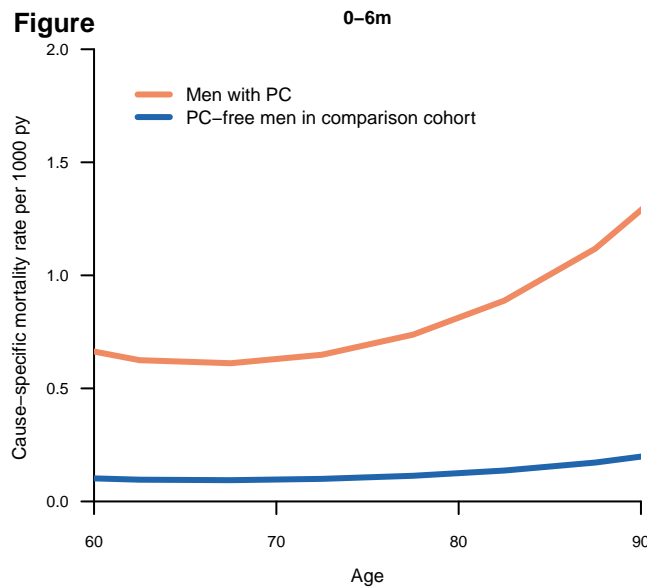
¹ Men with prostate cancer compared to prostate cancer-free men in comparison cohort of the same age group at inclusion.² Men with prostate cancer compared to prostate cancer-free men in comparison cohort of the same CCI at inclusion.³ Men with prostate cancer compared to prostate cancer-free men in comparison cohort of the same SES at inclusion.⁴ Men with prostate cancer compared to prostate cancer-free men in comparison cohort of the same marital status at inclusion.

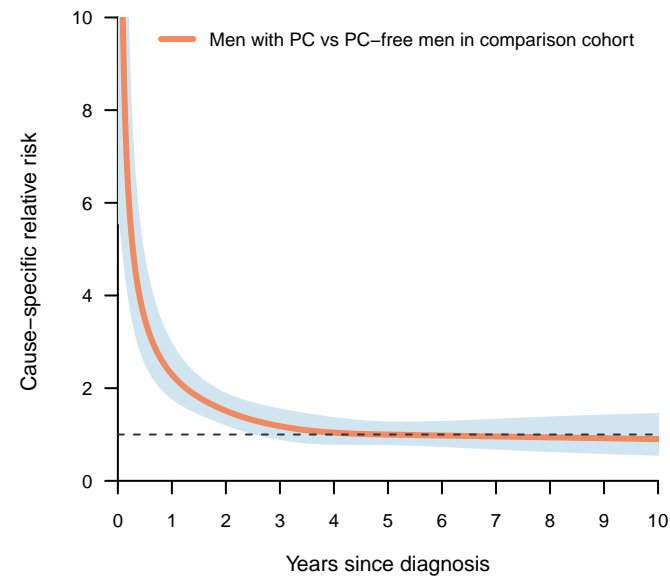
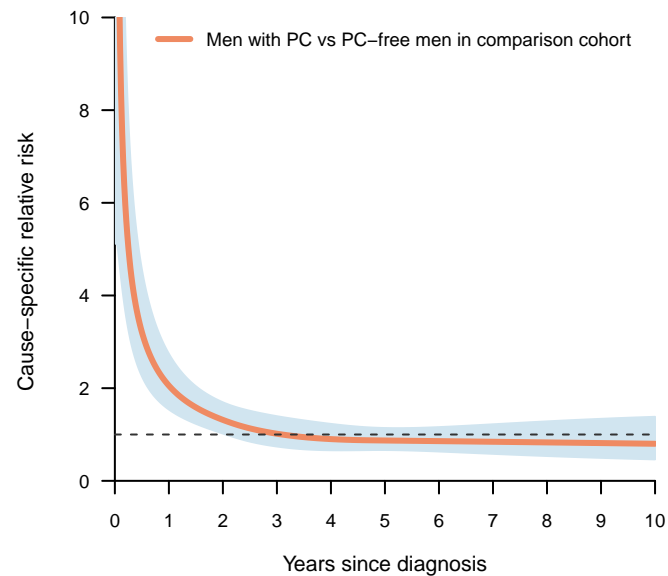
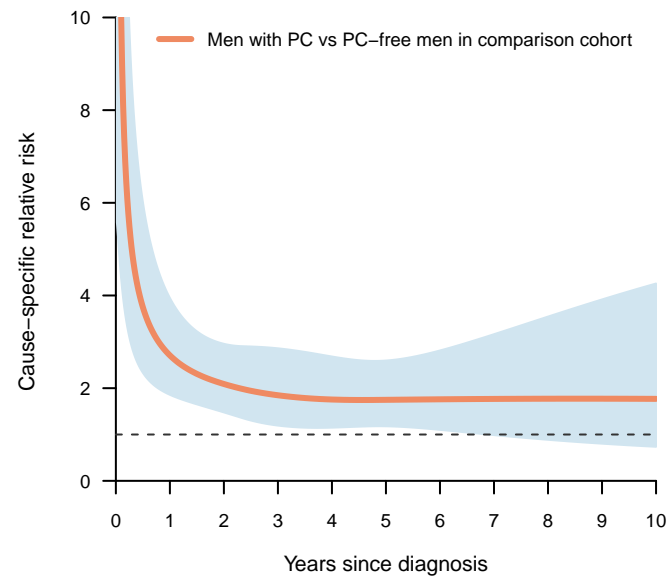
Table

Appendix 1. Risk of suicide in relation to psychiatric medication usage.

	Overall, disregarding time since diagnosis		Men with prostate cancer			Prostate-cancer free men in the comparison cohort		
	RR	(95% CI)	Number of events	Person-years at risk	Number of events per 1000 py	Number of events	Person-years at risk	Number of events per 1000 py
Men with prostate cancer compared to prostate-cancer free men in the same category in respect to ever/never users								
Ever users								
Prostate-cancer free men in the comparison cohort	1.0							
Men with prostate cancer	1.9	(0.94-3.7)	11	12628	0.87	32	70225	0.46
Never users								
Prostate-cancer free men in the comparison cohort	1.0							
Men with prostate cancer	2.7	(1.6-4.7)	19	50863	0.37	36	258357	0.14

Inclusion 2007-2009, follow-up until end of 2010. Ever users are those on drugs (N05A, N05B, N05C, N06A) within 18 months before inclusion.



Figure**ALL****LOCALIZED****METASTASES**

Conflict of Interest

Authors declare no conflict of interest