

# The Association of Cancer-Related Fatigue with All-Cause Mortality of Colorectal and Endometrial Cancer Survivors: a Population-Based Study

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## Background

- Cancer-related fatigue (CRF) can be described as a feeling of tiredness, reduced energy level, reduced muscle strength, and cognitive impairment. CRF is significant and prevalent problem for cancer survivors.<sup>1</sup> Studies show that around 40% of short-term (<5 years) cancer survivors experience CRF.<sup>2</sup>
- CRF is associated with outcomes such as depression and poorer health-related quality of life (HRQoL).<sup>3</sup> Depression has been associated with higher mortality among cancer survivors,<sup>4</sup> but the association of fatigue with mortality is still unclear.
- In this study, we aimed to investigate the association between CRF and overall mortality among cancer survivors.

## Data & Methods

- The study sample comprised of 2941 short-term (i.e. ≤5 years after diagnosis) cancer survivors from four PROFILES registry<sup>5</sup> studies conducted between 2008 and 2011. Survivors diagnosed with colorectal or endometrial cancer were identified from the Netherlands Cancer Registry.
- Fatigue was assessed with the *Fatigue Assessment Scale* (FAS) and depression with the *Hospital Anxiety and Depression Scale* (HADS). The FAS total score cut-off is: not fatigued (10-21), fatigued (22-34) and very fatigued (35-50).<sup>6</sup>
- Censoring date was February 1st 2017. Cox proportional hazards models were performed to assess the influence of CRF on all-cause mortality. These models were adjusted for age at study, tumor type, cancer stage, primary treatment, years since diagnosis, education and number of comorbidities, where appropriate. Additionally, we adjusted for survivorship bias by adding a variable with the left-truncation time (time between diagnosis and study invitation) and time of study invitation was set as entry time.

## Results

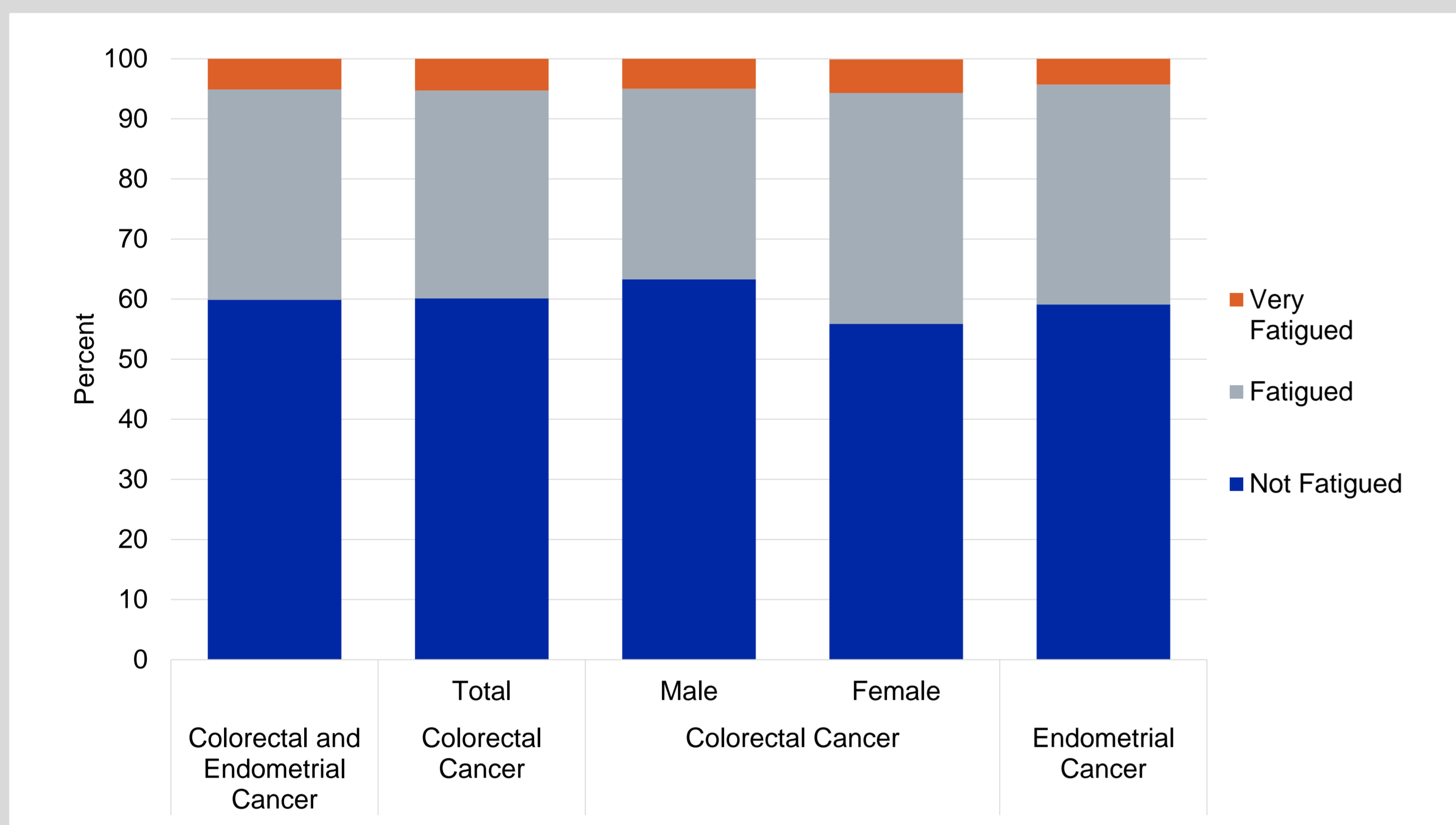


Fig. 1: % CRC (stratified by gender) and endometrial cancer survivors by fatigue levels

Table: Adjusted risk estimates of cancer survivors of different fatigue levels on all-cause mortality

Fatigue Level	Total, N	Deaths, N	Person-Years	HR	(95% CI)	P-value
<b>Colorectal and Endometrial Cancer Survivors</b>						
Not Fatigued	1762	377	11579.61	1.00	-	
Fatigued	1030	298	6569.42	1.40	[1.26 - 1.57]	<0.001
Very Fatigued	149	66	830.20	2.53	[2.26 - 2.85]	<0.001
<b>Colorectal Cancer Survivors</b>						
Not Fatigued	1386	318	8202.42	1.00	-	
Fatigued	797	249	4442.04	1.37	[1.23 - 1.53]	<0.001
Very Fatigued	122	56	571.29	2.33	[1.99 - 2.73]	<0.001
<b>Male Colorectal Cancer Survivors</b>						
Not Fatigued	830	215	4833.18	1.00	-	
Fatigued	415	147	2266.02	1.36	[1.17 - 1.58]	<0.001
Very Fatigued	66	38	262.72	2.99	[2.98 - 2.99]	<0.001
<b>Female Colorectal Cancer Survivors</b>						
Not Fatigued	556	103	3.369.25	1.00	-	
Fatigued	382	102	2176.02	1.42	[0.92 - 2.18]	0.112
Very Fatigued	56	18	308.57	1.45	[1.19 - 2.76]	<0.001
<b>Endometrial Cancer Survivors</b>						
Not Fatigued	376	59	2609.8	1.00	-	
Fatigued	233	49	1563.81	1.27	[1.12 - 1.43]	<0.001
Very Fatigued	27	10	163.77	2.43	[2.05 - 2.89]	<0.001

- Around 1/3 of CRC and endometrial cancer survivors are fatigued and around 5% are very fatigued, according to the FAS classification. The distribution of fatigue by tumor type and by gender (CRC survivors) do not differ significantly (all  $p > 0.05$ , Fig. 1).
- The median follow-up time was 9.03 years (range 0.4-14.3 years) in which 741 cancer patients died.
- Unadjusted (Fig. 2) and adjusted (Table) results showed that fatigued (HR=1.40,  $P < 0.001$ ) and very fatigued (HR=2.53,  $P < 0.001$ ) cancer survivors had a significant increased overall risk of death than not fatigued survivors. This association remained significant in adjusted stratified models for CRC and endometrial cancer patients. However, the association was less strong in female CRC survivors when compared to male CRC survivors.
- Among not-depressed CRC and endometrial cancer survivors, fatigue showed similar association with mortality. Fatigued (HR(adj)=1.42,  $p < 0.001$ ) and very fatigued (HR(adj)=2.38,  $P < 0.001$ ) cancer survivors had a significant increased risk of death than not fatigued survivors.

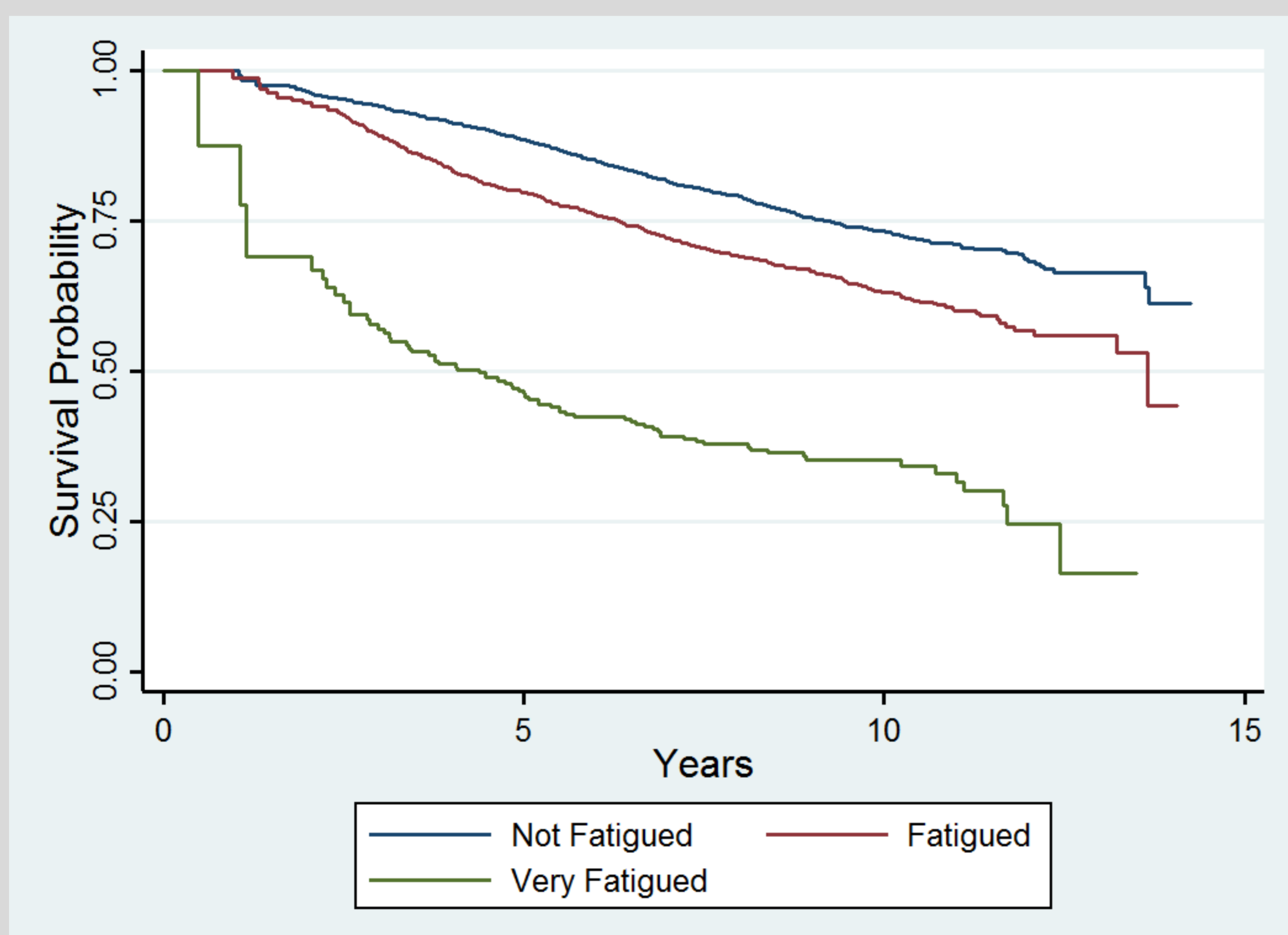


Fig. 2: Unadjusted Kaplan-Meier plot of colorectal and endometrial cancer survivors, stratified by fatigue levels

## Conclusion

- CRF is prevalent in CRC and endometrial cancer survivors.
- Our study found that CRF is a robust predictor for all-cause mortality in cancer survivors, irrespective of depression and other potential confounders.
- Current results suggest that further research into whether lowering burden of CRF in cancer survivors reduces mortality risk is recommended.

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## Selected References

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