

# Mortality of Fertile and Subfertile Men: Associations between Sperm Counts and Causes-of-Death

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## **Abstract:**

Spermatogenesis is one of the few examples of non pathological cell proliferation in the adult mammal organism. Disorders in the spermatogenesis may indicate proliferation disorders in general. A previous study showed a higher mortality of men with subnormal sperm counts. Now we study associations between sperm parameters and - specific mortality. Two broad cause-of-death classes may have higher incidence among subfertile men: proliferation disorders and risky behavior which is more prevalent in childless men. We analyze death certificates of 391 men with normal and low sperm counts measured in the outpatient facility of the Department of Andrology at Marburg University Hospital from 1949 onwards. The first results show no differences between the fertility-groups regarding the prevalence of cancer, cardio vascular disease, outcome of risky behavior or any other cause of death.

## **Background:**

More is known about female as compared with male sex specific health risks, and, consequently, mortality risks. Such differences may nowhere be greater than in the field of reproductive health and reproductive disorders. In the present study we are looking for relations between the all over health status and the reproductive health. The spermatogenesis is one of a few examples of nonpathological continuous cell proliferation in a highly differentiated tissue of the human organism. Because of the fast reproduction and the high differentiation of the cells it is sensitive for noxious influences and stress factors. This knowledge goes well with the notion that spermatogenesis may be an indicator for the global state of health of the male organism. Any impairment of the spermatogenesis may indicate an exposure of the male organism with exogenous and/or endogenous noxae. The present study is part of a larger project working with data (medical records) from the outpatient facility of the Department of Andrology at Marburg University, Germany. In a previous study (Groos, 2006) - also part of this project - it could be demonstrated that men with subnormal sperm counts (sperm concentration  $<20 \times 10^6$  per mL) have a higher life time-

mortality risk than men with normal sperm counts (Wilcoxon (Gehan)-Test: 7,09;  $p=0,008$ ;  $n=296$ ). These differences in life time-mortality were found only in the older birth cohort (the whole sample – all patients born before January 1<sup>st</sup>, 1938 – was divided by the median of the birth date).

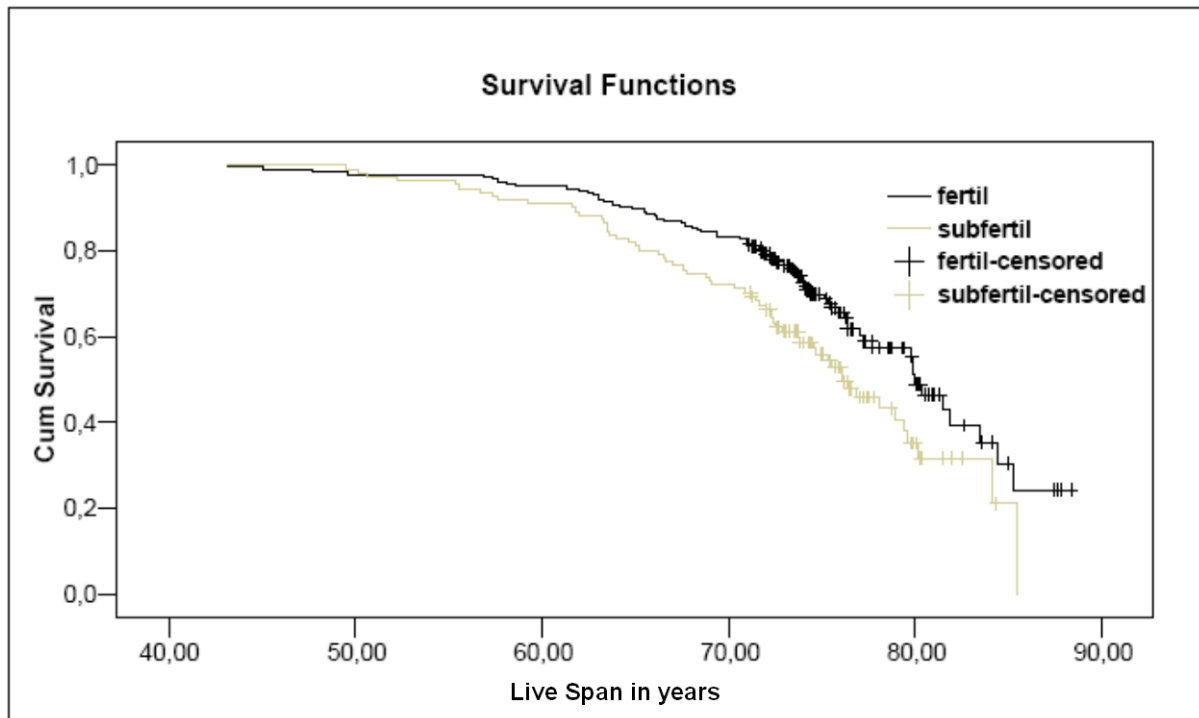


Figure 1: Survival functions of fertile and subfertile men; early natal-cohorts (In: Groos S: Lebenszeit-Mortalität von Männern mit normalen und subnormalen Spermienkonzentrationen. Diss., Marburg 2006 (p. 60))

We now want to proceed by looking in differences in specific mortality between subfertile and fertile men. Our research questions are: What are the causes of death and do they differentiate between the fertility groups (fertile/subfertile)? Is there any association between cause of death and fertility status? Various published studies show an increased mortality risk in men living without children: such men display a worse health behavior, a more risk taking attitude and they have fewer social contacts than men living together with their children. Differences in the distribution of causes of death may also be due to different conditions in utero or to genetic effects.

In another part of our project, a pretest is under way for interviewing former patients still alive or family members and other proxys of patients who already died to find out about which men had fathered children after the examination in the Department of Andrology or have adopted children.

### Material and Methods:

The basis of our present investigation are medical records of all men with normal and low sperm counts measured in the outpatient facility of the Department of Andrology at Marburg University Hospital from 1949 onwards. The data include sperm counts, the cause of

examination and anamnesis. Some documents also contain information about sexual behavior, the reproductive state of the wife, consume of tobacco and alcohol. Most men presented themselves for want of children. For this investigation we only include sperm counts. In the present study we were looking on the data of former patients born before January 1<sup>st</sup>, 1942 which accumulates in 2296 men. The vitality status of the former patients was checked via registration offices. For the actual investigation we include patients who have died until January 1<sup>st</sup>, 2007. Excluded are patients who had a vasectomy because it is an artificial way of becoming infertile. Until now we know the vitality status of 1387 men from whom 425 died before January 1<sup>st</sup>, 2007.

To find out about the causes of death we obtained death certificates from county public health agencies. Until now 391 death certificates were collected. The causes of death were coded by ICD-10 standards. We categorized men as fertile and subfertile according to the laboratory-guidelines of the WHO (1999) – subfertile men (including azoospermic – no sperms -and oligozoospermic men) have a sperm concentration of  $<20 \times 10^6$  per mL and fertile men (normozoospermic men) have a sperm concentration  $\geq 20 \times 10^6$  per mL. In our analysis we will control for age as a potential interacting factor for different causes of death.

### **Hypothesis:**

Two broad cause-of-death classes may have higher incidence among subfertile men: proliferation disorders and risky behavior which is known to be more prevalent in childless men. In particular

- We expect different incidence of cancer in general and of certain types of cancer between the fertility classes as measured by sperm counts. For example, we expect a higher rate of genital forms of cancer in subfertile subjects.
- We also expect higher rates of accidents, suicides and consequences of drug, alcohol and tobacco abuse within the group of subfertile men due to the increased likelihood of being childless.

### **Results:**

At first we compared the life time-mortality between the fertility groups (fertile/subfertile) to find out whether we can verify the results of Groos et al. (2006) in the extended study sample now including many younger birth cohorts, in addition to the prolonged observation of four more years. This is the case when dividing the whole sample by median of birth date for the first cohort (Breslow (Generalized Wilcoxon)-Test: 4,018; p=0,045).

The investigation of differences in the causes of death between the fertility groups shows no effect. There is no difference in the occurrence of cancer and other proliferating diseases nor cardiovascular disease between fertile and subfertile men. It is not possible to tell anything

about differences regarding to other diseases or injuries because in our sample they are represented in a small number.

Even without any results regarding the consequences of risky behavior we will drop the hypothesis that we expect higher rates of accidents, suicides and consequences of drug, alcohol and tobacco abuse within the group of subfertile men due to the increased likelihood of being childless. Because we don't know whether the fertile men became fathers after their examination it is difficult to compare fertile and subfertile men in this respect. Fertile men may have remained childless and subfertile men may have adopted children. These possibilities may distort the relation of fertility status and death because of risky behavior.

**Literature:**

Groos (2006) Lebenszeit-Mortalität von Männern mit normalen und subnormalen Spermienkonzentrationen, (Ph.D. dissertation available on the Dissertation Server of the University of Marburg)

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