

## Benign gynecological tumors: estimated incidence Results of the German Cohort Study on Women's Health

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### Abstract

**Objective:** To analyze the lifetime incidence of benign gynecological tumors. **Study design:** The German Cohort Study on Women's Health was launched in 1998 as historic cohort study with prospective follow up. The study ascertained self-reported information on tumors by calendar time. The incidence of benign gynecological tumors was calculated from the data of the first cohort period. **Results:** The cohort comprised 396,000 women-years of observation and 1676 benign tumors were observed. This lead to incidence estimates of 27.0, 18.6, and 23.3 per 100,000 women-years of observation for all benign tumors of the uterus, ovary, and breast respectively. **Conclusion:** In absence of other data, it is reasonable to use incidence rates generated by a large cohort of German women as a best estimate for the population up to 65 years of age.

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### 1. Introduction

There are no reliable data available on the incidence of benign gynecological tumors for the German population. International data are similarly scarce, because this needs cohort studies designed to collect this information. This is different for malignant tumors, where valid registries are operating in most of the developed countries. Cancer registries, however, do not usually collect information about benign tumors in a systematic way.

A classical cohort study as well a historic lifetime history in a group of volunteers are appropriate methodological approaches to estimate the incidence of diseases. This applies both for cohort studies with historic and concurrent ascertainment of data. The German Cohort Study on Women's Health was launched in 1998 [1]. This study ascertains—among other variables—lifetime information on medical conditions, such as benign gynecological tumors

and their time of occurrence. Estimates of disease incidence can be generated both in historical and concurrent cohort studies under two conditions: there should be reason to assume that the event can be reliably documented and the cohort should be as compatible as possible with the general population. The first can be generally assumed for tumors, which are usually perceived as a life threatening event until the diagnosis is definitely benign, and good evidence for the latter was recently published [2].

This short paper reports incidence estimates generated with a lifetime analysis of the participants of the German Cohort Study on Women's Health accrued by the end of December 2000.

### 2. Methods

#### 2.1. Design and objectives

The protocol of the German Cohort Study on Women's Health was published elsewhere [1]. In brief, this is a cohort study on women up to 65 years of age at entry into the study who volunteered to supply historic (lifetime) and concurrent

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information on steroid hormone use, medical conditions and other important events. The study began with the inclusion of the first cohort members in 1998. Participants were accrued by approaching women directly via address lists, with the assistance of physicians and pharmacists, as well as by announcements in newspapers and other media. All analyses are therefore based on data from volunteers, not from a random sample of the general population. The main objective of the study was to analyze associations between use of sex steroids and occurrence of medical conditions, particularly malignant tumors.

The study is coordinated by the Centre for Epidemiology & Health Research in Berlin, Germany. A network of university-based and other collaborators helped to improve the execution of the study, their analyses and publication of first results.

### 2.2. Data collection, variables and database

Time-dependent data on hormone use, reproductive history, lifestyle, diseases/conditions, symptoms were obtained in a self-administered postal baseline questionnaire. Questions were to be answered concerning the lifetime history of above parameters, what enabled us to construct a type of calendar. In case of problems or queries emerging from the questionnaire, telephone interviews were done to improve data quality. Annual follow up is part of the study.

Benign tumors of the uterus, ovary and the breast were recorded as women recalled names used by their physicians. Even if the localization of the benign tumor was clear, often unspecific information about the exact type of the tumor could not be further clarified. Validation with doctors' notes or histological findings have not been feasible before this publication, but are under preparation now. This analysis therefore focuses on tumor sites (e.g. all benign breast tumor) rather than specific types (e.g. fibroadenomas, fibrocystic tumor). Any sub-classifications of benign tumors in this publication should be understood as preliminary.

Due to the importance of temporal relationship of exposures and outcomes for the main study objectives, a periodic database was created to accommodate both concurrent as well as time-dependent variables.

### 2.3. Analysis

The focus of this analysis is the occurrence of benign tumors over time. This permits calculations of incidence rates per 100,000 years of observation in women aged up to 65 years.

Because more than one tumor could occur in each participant (e.g. a benign tumor of the uterus followed by one or more benign breast tumors), the sum of all subtypes is greater than the total sum in a certain tumor site.

The statistical package STATA 6.0 was used for this descriptive analysis.

## 3. Results

At the conclusion of the first phase of this ongoing study 10,077 datasets were ready for a first analysis (396,000 women-years of observation).

Table 1 shows the baseline characteristics of our cohort of volunteers. The age ranged between 18 and 65 years at the time of baseline survey. Number of children, education, marital and employment status as well as body mass index and smoking status showed a similar distribution as that in the general population, as was published elsewhere in detail [2].

Altogether, benign tumors in 1676 women were observed in this first cohort analysis. There were 1042 benign tumors of the uterus, including 498 uterine fibroids and 583 other (or unspecified) benign tumors. A total of 725 cases of benign tumors of the ovary were reported, with 655 ovarian cysts and 77 other (or unspecified) tumors. Regarding benign

Table 1  
Description of the 10,241 participants of the German Cohort Study on Women's Health at the time when this analysis was performed

	Mean (S.D.)
Age (years)	39.6 (12.9)
Number of children	1.4 (1.1)
Body mass index	24.4 (4.9)
Education (%)	
Abitur <sup>a</sup>	12.7
University <sup>b</sup>	26.2
Employment: yes (including part-time) (%)	59.7
Smoking: yes, current smoker (%)	24.4
OC use: yes, current use (%)	20.1

Some characteristics at the time of baseline survey.

<sup>a</sup> Examination that certifies maturity for university.

<sup>b</sup> University (classical), technical universities and education with an equivalent diploma or master degree.

Table 2  
Lifetime incidence of benign gynecological tumors that occurred within 396,000 years of observation in women up to the age of 65 years

	N <sup>a</sup>	Women-years of observation	Age at diagnosis (median, 25–75%)	Incidence per 100,000 women-years
Uterus all	1042	385,341	38.2 (31–45)	27.0
Fibroids	498	391,725	39.7 (34–45)	12.7
Others <sup>b</sup>	583	396,598	37.1 (29–45)	14.7
Ovary all	725	389,596	28.5 (22–38)	18.6
Cysts	655	391,723	28.1 (22–37)	16.7
Others <sup>b</sup>	77	396,498	30.9 (23–41)	1.9
Breast all	898	385,789	35.7 (26–44)	23.3
More cystic	609	391,186	34.5 (25–44)	15.6
More solid	317	393,300	37.9 (30–44)	8.1

If several benign tumors occurred at different times and sites these were counted all. The age at diagnosis of a tumor is listed as median (50% percentile). The variation of 25–75% is provided in parenthesis.

<sup>a</sup> N: number of tumors documented in each site.

<sup>b</sup> Other benign or unspecified tumors of the same site.

breast tumors, 898 observations were reported by our cohort members, 609 were preliminary classified to be more of cystic nature (fibrocysts or mastopathy) and 314 as predominantly solid (fibroadenomas, nodules, fibromas, adenomas).

Table 2 shows the frequency of these benign tumors, the age at diagnosis (median, 25–75% percentile), the number of women-years of observation (WYO), and the incidence per 100,000 WYO. The calculation is based on the time span from birth to occurrence of the benign tumor.

The incidence was highest for benign uterine tumors, followed by breast tumors, and tumors of the ovary.

#### 4. Discussion

There are no publications concerning incidence of benign gynecological tumors in Germany that we are aware of. The results of the German cohort study provides important data on whether the observed incidence of benign tumors under certain exposures or conditions is within the range expected for the general population.

These results quantitatively underscore the common experience of gynecologists: benign tumors are fairly frequent in the age under 65 years, i.e. in the uterus (27 per 100,000), breast (23 per 100,000) and the ovary (19 per 100,000). Moreover, they demonstrate that about 50% of the benign gynecological tumors have been diagnosed before the age of 35 years. This is partly due to the easy diagnosis with non-invasive diagnostic techniques but might be also related to the increasing awareness and health consciousness of women. Considering the impact of a suspicion of “a tumor” in a young women, even tumors finally proven to be benign are an important life event if not personally perceived as life threatening in the beginning.

There are limitations of this study approach: the lifetime history based on one survey with additional telephone queries, the self-reported nature of the data with the potential of recall bias, and the compatibility of the self-selected sample of volunteers with the general population.

The lifetime history of events that are perceived as life threatening—at least in the phase of ‘tumor suspicion’ is less likely to be biased (recall or detection bias) than for other conditions, although we have no data to demonstrate this. Of course, data from a prospective cohort study would be preferable, but it would possibly take decades to collect sufficient material, not to mention the monetary implications. Moreover, we are confident that our information on aggregates of benign tumors are sufficiently robust and reliable to estimate incidence rates.

The self-reported nature of the data is another concern. This may lead to a lack of diagnostic accuracy, if no

validation of the ‘diagnosis’ with the treating physician was feasible. This process is still ongoing for our study. It is rather unlikely that histological findings will become available for all cases, like in other cohort studies, i.e. a certain proportion will remain ‘unspecified’. Because of this, we focused mainly on tumor aggregates rather than on specific tumor types. We doubt that these aggregated analyses of self-reported tumors are materially biased, but have no data yet to assess the magnitude of a potential misclassification bias. We also doubt that recall bias plays a substantial role, since tumors in general might be particularly good recalled because of their potentially life threatening nature as discussed before.

Furthermore, we were worried about the selection bias, because women might volunteer to participate in a study either because they are particularly health conscious, because they have had a tumor, or for some other reason which might lead to differences in the volunteer group when compared with the general population. We have shown in a previous paper that the available characteristics of this cohort (see above) correspond very well with those of the general population [2]. This means that our volunteer cohort is satisfactorily similar to the general population of women up to 65 years of age with regard to parameters of our concern and interest.

We conclude that the incidence rates of aggregated benign gynecological tumors estimated by the German Cohort Study on Women’s Health largely reflect the situation in the general population of Germany under the age of 65 years. This provides data for comparisons with incident tumors occurring under suspected exposures.

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#### References

- [1] Heinemann LAJ, Garbe E, Winkler U, Rabe T. Die Deutsche Kohortenstudie zur Frauengesundheit: Zum Nutzen von oralen Kontrazeptiva. Ausführungen zum Studienprotokoll. *Zentralbl Gynaekol* 2000;122:112–5.
- [2] Heinemann LAJ, Assmann A, Lewis MA. How representative can be a cohort of volunteers for the general population? The German Cohort Study on Women’ Health. *Life and Medical Science Online* [www.lamso.com], 2001;2:DOI:10.1072/LO203322 (11 pages).