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## How Representative Can be a Cohort of Volunteers for the General Population? The German Cohort Study on Women' Health

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**ABSTRACT:** *Background:* The representativeness of epidemiological studies becomes important when a cohort is also used for cross-sectional comparisons at any time during the observational period. We examine the parameters for representativeness of the German Cohort Study on Women's Health. *Method:* The data of a volunteer cohort of over 10,000 women were collected 1998–1999 through a standardized self-administered questionnaire and compared with 8,700 women pooled from the four representative random sample National Health Surveys performed from 1986–1992. Methods of descriptive statistics were used to assess the comparability of our cohort with the general population. *Results:* The comparison between our volunteer cohort and data from the general population are in good agreement. The social markers were almost identical. The distribution of the number of children was similar as was the prevalence of current oral contraceptive (OC) use. The members of the cohort seem to have a slightly better health behaviour with regard to smoking and alcohol, at least in the age group under 40. The satisfaction with various aspects of life, including health is also similar in the cohort of volunteers and the population health surveys as is the prevalence of medical conditions. *Conclusions:* The comparison between our volunteer cohort with the representative population surveys shows good agreement. This indicates an acceptable level of generalizability of cross-sectional results from our cohort for the general population. Because small differences could be important for specific research questions, the representativeness of each cross-sectional sub-study needs to be examined individually.

**KEY WORDS:** Representativeness, Methods, Cohort Study

### INTRODUCTION

The applicability of results from epidemiological and clinical studies to the general population is often questioned on the basis of representativeness. In addition, it is often asked whether all features of the results obtained will be representative.

The representativeness of cross-sectional epidemiological studies is usually determined by the response rate. Response rates in turn are determined by circumstances such as general attitude of the population. Selection becomes a problem if in observational studies the exposure is highly associated with the response rate (1). The issue of participation or response as an indicator for representativeness can be even more complex if one distinguishes between contact, cooperation and response (2). Studies based on volunteers are sometime not avoidable for cohort studies, and random sampling from the population is less feasible, more

costly and associated with less motivation to participate (3), as they require high motivation to cooperate over long periods of time. Apart from evaluation the participation rate, the comparison of variables within the study with an outside population standard (like a representative population survey) can serve as indicator for representativeness.

Representativeness is also defined by the objectives of the research done. While a cross sectional study describes the current status of a defined population or group, a longitudinal study shows the development of one or more phenomena over time. In the first instance the sample should reflect the current situation in the population at the time of the survey. In a cohort, the comprehensive monitoring of development of conditions and exposures during follow-up takes precedence over the comparability with the general population at baseline or any other point in time. This means that prospective cohort studies can be and are conducted with groups of volunteers. This also applies for clinical trials and follow-up studies. Nonetheless, it is interesting to know how close a cohort of volunteers could be to the general population at a certain point in time, particularly if cross-sectional sub-studies are also planned. This is the case for the German Cohort Study on Women's Health.

This paper reports on the comparison of a long-term volunteer cohort of women with the general population. We particularly focused on the question whether this cohort of volunteers is comprised of women who differ substantially in health status, social affluence and age from the general population, i.e. whether this cohort is 'representative' with regard to these factors.

## METHODS

We report about a comparison of the first 10,000 women of the German Cohort Study on Women' Health with the women included in the representative German Health Interview and Examination Surveys. The protocol of our cohort study was published elsewhere (4). Briefly, the study was designed to analyse benefits of oral contraceptives (OCs) of any formulation, particularly with regard to long-term effects such as development of medical conditions (e.g. tumors). The results should permit conclusions for the general population, i.e. the impact of OC use on public health. Secondary aims are to study other aspects of women's health such as psychosocial features, sexuality, and associated patterns. The participants were volunteers aged up to 65 years of age recruited through cooperating physicians, drug stores, announcements in newspapers, magazines, brochures of health insurances, and through contacts to friends or relatives of a respondent. A lifetime history of hormone use, variables of the reproductive life, lifestyle pattern, conditions/diseases, symptoms, and many other factors were documented using a self-administered postal questionnaire. An annual follow-up form has to be completed by the participants as well as occasional questionnaires from optional sub-studies. Both historic analyses based on past exposures and medical conditions as well as prospective analyses were planned.

The first phase from 1998 to 2001 planned to accrue 400,000 women-years of observation of historic and concurrent exposures and conditions. At present, data on about 15,000 women were obtained, and the first 10,000 women of the cohort are included in the analyses. These compare the age-specific data of our cohort study with the pooled information of more than 8,700 women from three cross-sectional, national population surveys performed between 1984 and 1992 in the former West-Germany and one in East-Germany. These surveys were

designed to generate health related data representative for the German population. The following data from the health surveys were used:

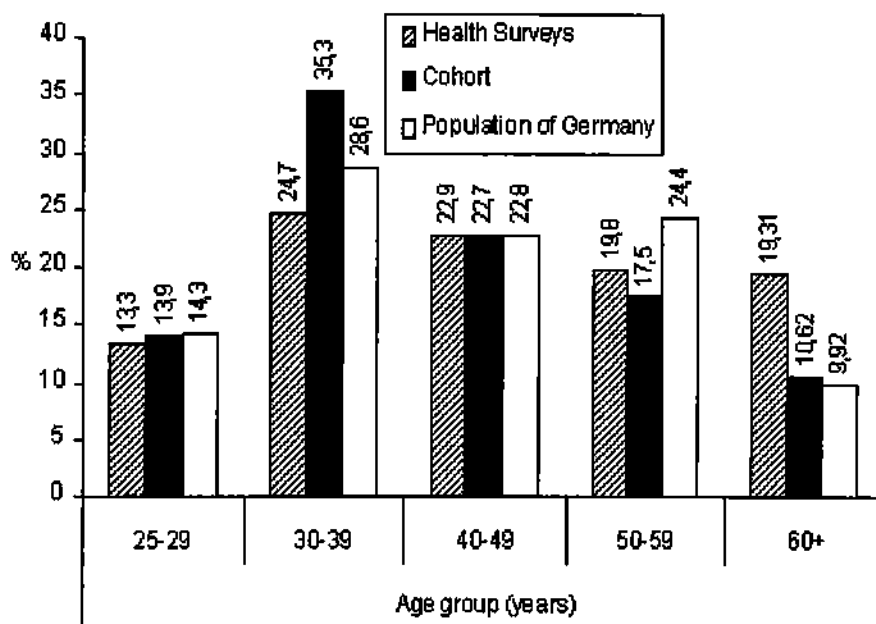
- the public use file of the German Interview and Examination Survey 1984–1991 (5), provided by the Robert Koch Institute Berlin 1995: over 7,300 female participants (25–69 years of age);
- the East German Health Interview and Examination Survey 1991–1992 (5, 6): public use file with over 1300 females (aged 18–79).

Methods of descriptive statistics were used in this analysis which addresses the question of generalizing the specific information generated by cross-sectional analyses of our volunteer cohort. Because the objective of this exercise was the determination of similarities between our volunteer cohort and a representative random population sample, no formal statistical testing was considered necessary.

There are a few methodological shortcomings in this comparison: Although the cohort study started with recruitment of women almost 10 years later, there are no other representative data for German women available for comparisons. Another methodological problem is, that direct information about the women that did not participate cannot be obtained, because the source population is not clearly defined. Therefore data from external source (and previous time) have to be used as a best available comparator. A third problem for consideration is the fact that about 15 % of the participants of the pooled representative health surveys came from East Germany (with its different socialization), but about 50 % of the volunteers of our cohort study.

## RESULTS AND DISCUSSION

Figure 1 shows the age structures of the volunteer cohort, women included in the Health Surveys, and the age structure of the general population. It is found that the volunteer cohort slightly oversamples women of younger age (35 % aged 30–39 years versus 29 % in the general population) as compared with the population health surveys, which in turn oversamples the group of women 60 years old and above (19.3 % versus about 10 % in our cohort and the general population) due to differences in study design.



**Figure 1:** Comparison of the age distribution between the pooled health surveys and the cohort of volunteers (aged 25–60+). Percentage (%) of the total group. The captured age range within the Health Survey was 25 to 79 years, that within the women's cohort was 25 to 64 years.

This age difference in one age group should be considered when comparing other variables between the two databases, particularly age related ones such as family status, number of children, body mass index.

### Social Markers

With regard to social markers, Table 1 shows that the proportion of women with university maturity (Abitur) and completed university or other tertiary education is similar in the two studies, being slightly less prevalent in the cohort in the age group under 40 and more common in the age group over 40. The percentage of married women (or living in stable unions) is identical with the proportion found in the population health surveys. Between 50–60 % of the women in the cohort and the pooled survey population are employed (including part-time employment), with a slightly higher proportion in the cohort in the age group over 40, and somewhat lower under age 40.

**Table 1:** Comparison of education, family status, and employment between the cohort and pooled population surveys in percent (%)

	Cohort (%)		Pooled surveys (%)	
	<40	40+	<40	40+
Education				
Abitur	13.2	5.0	19.8	7.8
University or comparable education	29.8	28.7	30.7	19.6
Married	73.7	76.3	73.5	76.7
Working (including part-time)	56.4	53.8	62.4	48.6

It is unfortunate that this comparison does not include regional differences, because of the large component of East German women in the cohort, who might differ significantly in employment or social status from their West German counterparts. However, the notion that a volunteer cohort would recruit itself largely from individuals of higher socioeconomic status than a representative sample is unfounded.

## Reproductive History

### *Number of Children*

The distribution of the number of children is similar in the cohort of volunteers aged 25–64 and the pooled population surveys (Figure 2). The proportion of women with three and more children is remarkable for a cohort of volunteers. The proportion of women without children, however, is higher in the cohort than the population surveys in the age group 20–29 (data not shown).

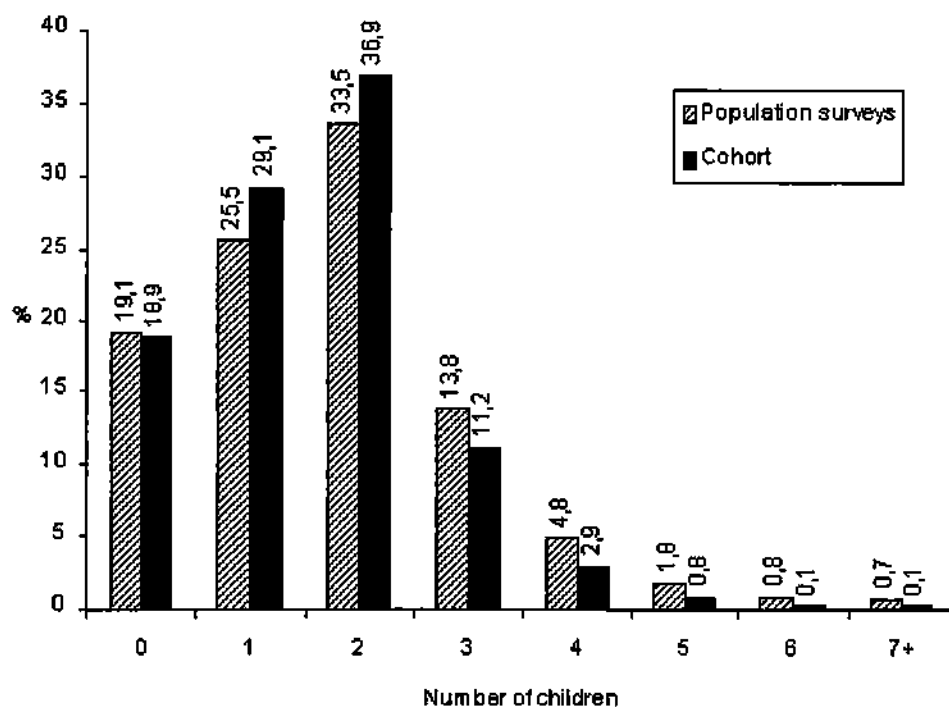


Figure 2: Number of children; comparison between the percentage in the cohort of volunteers aged 25–64 and the percentage within the pooled representative health surveys.

### *Use of Hormones*

Use of *oral contraceptives* (OC) is quite similar between the cohort and representative population health surveys (Table 2). There was also no important time trend in the about ten years elapsing between the health surveys and accrual of volunteers of the cohort.

However, the prevalence of use of *hormone replacement therapy* (HRT) increased in the recent decade. This found its reflection in the comparison between the cohort and pooled health surveys. There is a much larger proportion of users in the cohort sample.

	Age groups (years)				
<b>OC use</b>	25-29	30-34	35-39	40-44	45-49
Pooled Health Surveys	52.7	41.3	34.2	22.2	16.0
Cohort	49.2	37.0	30.0	22.8	21.9
<b>HRT use</b>	25-29	30-39	40-49	50-59	60+
Pooled Health Surveys			0.5	13.5	4.2
Cohort		0.5	14.0	46.4	38.5

A preliminary analysis of the 'One-Million-Women' cohort in the UK showed an increase of current HRT user from less than 5 % in the early 1980s to 33 % in 1998 (7). Our own prevalence rates from the 'German Cohort study on Women's Health' are similar: 4-5 % in 1979-1983 and 32 % in 1998.

## Lifestyle Indicators

### *Smoking Status*

The crude comparison of smoking status also showed no substantial overall differences between the volunteer cohort and the representative population surveys. Slightly more than half of the women in each group were never-smokers and a quarter were current smokers (Table 3). However, in the age group under 40 there is a higher proportion of never-smokers and lower proportion of current smokers in the cohort than in the population health surveys. Moreover, the cohort has a higher prevalence of ex-smokers and less current smokers than the population sample. Because this is unlikely to be explained by time trends alone, it appears that the women in the cohort are a more health conscious group.

Age (years)	<40	40+	Total
<b>Never smoker</b>			
Health Surveys	38.9	64.3	53.7
Cohort	49.4	63.4	56.2
<b>Ex-smoker</b>			
Health Surveys	21.6	15.5	18.0
Cohort	21.2	19.8	19.4
<b>Current smoker</b>			
Health Surveys	39.5	20.2	28.2
Cohort	29.4	16.9	24.4

### Alcohol Use

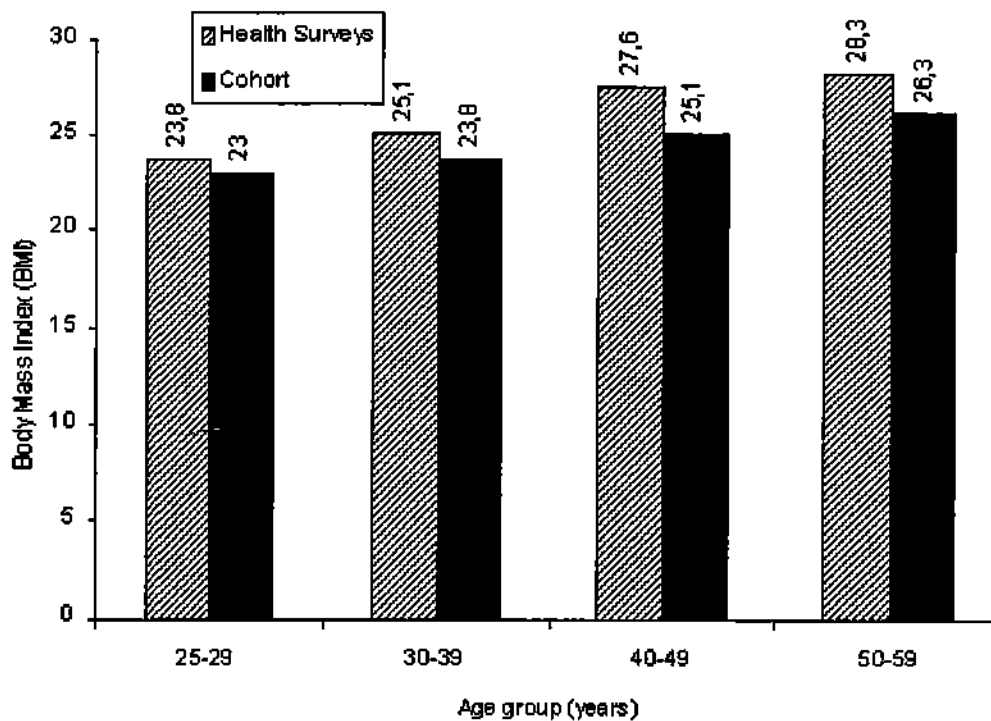
Compatible data on alcohol use were only available in the East German Health Survey 1991–1992 (n=1373 women). The comparison with women of the cohort again showed similarities. The frequency of never use seems to be a bit less common in the cohort and for rare use more frequent in aggregate (Table 4). Regular and frequent alcohol consumption is less common in younger age group of the cohort than in the population sample. This could be again an indicator of a better health behaviour as discussed for smoking. However, the questions were phrased differently in the two studies so that these differences might be explained methodologically.

**Table 4: Crude comparison of the frequency of alcohol use (irrespective of amount) between the cohort and the East German Health Survey (aged 25–60+). Prevalence (%) in two age groups**

Age (years)	<40		40+ years		Total	
Frequency of alcohol consumption	Survey	Cohort	Survey	Cohort	Survey	Cohort
Never	7.4	6.1	13.5	8.4	12.5	7.5
Rare	60.5	72.8	63.0	68.7	61.4	71.5
Up to 3x per week	25.8	16.6	17.9	16.2	20.0	15.5
More than 3x per week	6.3	4.7	5.5	6.7	6.1	5.5

### Body Mass Index (BMI)

The body mass index (BMI) is a complex expression of many influencing factors, particular dietary habits. A problem of a comparison between the pooled population health surveys and the cohort of volunteers is that in the latter weight and height is self-reported, whereas it is measured in a standardized way in the health surveys by trained personnel. The experience from other studies shows that BMI based on self-reported values is systematically lower compared with measured values. The age-specific BMI values accordingly differ systematically in favor of lower values in the cohort (Figure 3), which is compatible with the above hypothesis of self-reported weight/height.



**Figure 3: Mean values for body mass index (BMI) in the national health surveys (measured) and the women's cohort (self-reported).**

This is also reflected in the BMI categories: Normal BMI (<25) was found to be similarly frequent among cohort members and population survey participants (51 % vs. 50 %), what applies also for mild overweight (BMI 25–29: 32 % vs. 32 %). However, severe obesity is more frequent in the survey population (BMI≥30: 17 % vs. 19 %). It cannot be excluded that the differences in BMI are entirely due to different methods used.

**Table 5: Comparison of three BMI categories between voluntary participants of the cohort (aged 25–64) and the pooled population health surveys in percent (%)**

	BMI <25	BMI 25–30	BMI >30
Health Surveys	49.5	31.8	18.7
Cohort	51.1	32.1	16.9

**Satisfaction with Different Aspects of Life**

The subjective impression regarding various facets of life can be used as an indicator for a general attitude towards life and health. The answers from participants of the population health surveys and the cohort members are very similar with regard to satisfaction with the circumstances of life in general, with working situation, accommodation, and with the family situation. Cohort members seem to be a bit less happy with their financial situation, but more satisfied with their health status (Table 6).

**Table 6: Satisfaction with general aspects of life between the pooled population random sample surveys and the self-selected cohort of women (aged 25–64). Percentage (%) of women who are quite happy with their situation**

	Survey	Cohort
Health	70.1	78.3
Family situation	85.0	86.2
Accommodation	86.1	88.4
Situation at work	77.7	77.3
Financial situation	73.6	68.9
Life in general	86.3	89.4

One could have expected that women who volunteered to participate in a long-term study with many questionnaires over the years have a more positive attitude towards life in general, but also less health problems. Although this comparison is very general and does not account for differences in sub-groups, it indicates that the cohort and the general population are similar. The self-selection of the cohort does not seem to affect generalizability.

### **Prevalence of Diseases**

The questions related to prevalence of diseases or conditions prior to the survey are worded very similarly in the two studies. Only self-reported morbidity without consideration of age differences was used in this comparison. The prevalences of various conditions are very similar (Figure 4).

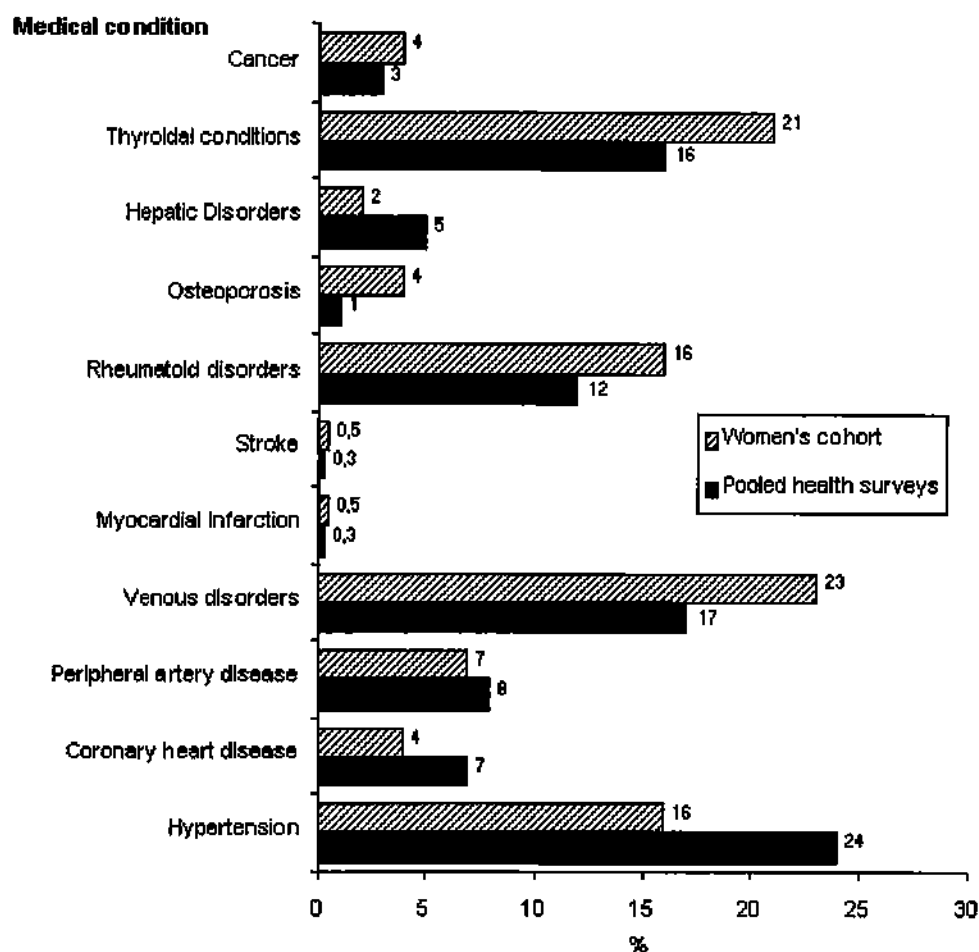


Figure 4: Overview self-reported conditions/diseases. Prevalence (%) in the cohort of volunteers and in the pooled population surveys.

The agreement in disease prevalences between the cohort and the pooled health surveys indicates that the results from cross-sectional comparisons within the cohort are applicable to the general population. Nonetheless, although the selection might be not great enough to alter representativeness in many regards, these factors need to be explored for each sub-analysis.

### Expected Incidence Values Based on Cohort Data

Because cancers are rare disease whose incidence can only be estimated when large populations are observed, and because there may be regional variations in cancer occurrence, an accurate population estimate is very difficult. Table 7 shows the population rates for various gynecological cancers from different cancer registries (8) and compares these estimates with the estimates based on the cases found in our cohort. Based on incidence rates reported from cancer registers we calculated expected values for cancers in our cohort with about 396,000 women-years of observation from 0 to 64 years. The expected numbers in our cohort were calculated using the average incidence rates (cf. Table 7).

**Table 7: Estimation of the magnitude of selection, i.e. missing cancer cases in the cohort due to various circumstances. Observed cases in about 396,000 women-years of observation in the age range of 0-64. Incidence rates from the IARC Monograph (8)**

Data source	Cancer Site				Population observed (million woman-yrs)
	Breast	Cervix	Corpus uteri	Ovary	
(crude rates per 100,000; 1988-1992)					
East Germany 1988-1989	50	25	14	12	17.38
Saarland (W. Germany)	70	15	12	9	2.76
Denmark	78	17	13	13	13.05
Netherlands	77	8	8	10	30.37
Switzerland (Basle)	80	6	11	10	2.76
Women's Cohort	45	15	15	9	0.40
Average observed incidence (registries)	71	14	12	11	
Number of cases in cohort	179	60	61	36	
Expected number of cases <sup>a</sup>	281	55	47	44	
Difference (Observed - Expected)	-102	5	14	-8	
Per cent difference	-36.3	9.1	29.8	-18.2	
<sup>a</sup> average observed incidence in registries multiplied by 396,000 women years of observation in our cohort					

A wide range for 50 per 100,000 to 80 per 100,000 is found for breast cancer in the registries, and the small Saarland cancer registry shows the lowest estimate, and seems in fact to be an outlier with an estimate of 50 per 100,000. The estimate from our cohort is yet lower, with 45 per 100,000 calculated from the 179 cases found, meaning that based on an incidence average from the registries included here there is an underascertainment of 102 cases, or an underestimate by 36 %. For cervical cancer, the cohort estimate of 15 per 100,000 is right within the range of 6 to 25 per 100,000 obtained in the registries, and no substantial over- or underascertainment is found. There seems to be overascertainment of cancer of the corpus uteri in the cohort by 30 % and a lesser underascertainment of ovarian cancer by about 18 %, though in both cases the cohort incidence estimate is within the range provided by the registries.

It is difficult to arrive at a final conclusion when evaluating these results. While for cervical and ovarian cancer, the women's cohort is within the range shown by the registries, there seems to be a comparative overestimate of cancer of the corpus uteri (where the cohort incidence is slightly higher than the highest registry estimate) and an underestimate of breast cancer incidence, where the cohort incidence is slightly lower than the lowest registry estimate. Despite the high proportionate differences, the cohort study results are within the range of variability provided by the registry estimates with the exception of breast cancer, where there is clear underascertainment. The main problem with our volunteer cohort and its historic analytic component is that there will be an underascertainment of cancers with high case fatality and a short-term course. These events will be missing in the cohort. However, given today's relatively good prognosis of breast cancer and the relatively poor prognosis of ovarian cancer, one would have expected underascertainment to be more extreme for ovarian

cancer and not as pronounced for breast cancer. For some cancers, therefore, we can conclude that only an undefined proportion of the events which occurred in the past could be recruited in this voluntary cohort. One therefore needs to carefully select the kind of cancer sites one will address in any cross-sectional analysis of cancer with this cohort. This further needs to be considered in the historic cohort analysis in the context of potentially biased exposure. Nonetheless, it is expected that this cohort will provide important information for women's health.

## CONCLUSION

The large degree of agreement of selected parameters of the women of the cohort and those from the representative population surveys indicates an acceptable generalizability of cross-sectional results within the cohort for the general population. However, this needs to be specifically explored for each cross-sectional sub-study, because small differences could be important for certain research questions.

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