Relationship of Gallbladder Disease to Parity, Obesity, and Age

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THE TYPICAL PATIENT with gallbladder disease has been alliteratively described as a "fat, fertile female of forty." This aphorism with four Fs implies a causal relationship between gallbladder disease in women and the "risk" factors of parity, obesity, and age. There has not been any large-scale study, however, in which these implied relationships in fat and fertile 40-year-old females have been examined. We therefore undertook to study the relationship between these three factors and gallbladder disease in 62,739 women.

The aphorism originated predominantly from clinical impressions and became inveterate before it could be tested conclusively. Several autopsy series (*1–3*) and hospital case studies (*4,5*) have evaluated one or two of the risk factors, but the investigation of several risk factors simultaneously has never been attempted.

A study of risk factors by Van der Linden in 1961 (*6*) differed from previous attempts in two respects: (*a*) all gallbladder disease cases (within a specific time interval and geographic area) were assumed to be included in the study and (*b*) matched controls were obtained for every woman with gallbladder disease. There were significantly more childless women in the control group than in the gallbladder group, but no differences were found between the groups with respect to the average number of children born. The author found that body weight and abdominal skinfold thickness were not significantly different between the two groups while subscapular and lateral thorax skinfold thicknesses did differ significantly. Van der Linden concluded that since all differences found were comparatively small, they were of little clinical value as risk factors.

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The first cohort study of risk factors for gallbladder disease was made in Framingham, Mass. (*7*). More than 5,200 persons in this community, considered to be somewhat representative of the general U.S. population, were followed for 10 years. Many risk factors were studied with the following conclusions: (*a*) a preponderance of gallbladder disease was found in women, (*b*) an increase in the disease occurred over the decades of life (from the 30s on) with no excess in the 40s, (*c*) an increase in weight seemed to be associated with an increased incidence, and (*d*) the number of pregnancies appeared related to incidence.

Following the initial estimates of the incidence of gallbladder disease from the Framingham study, other smaller population subgroups (*8–11*) were studied to estimate prevalence and evaluate risk factors. Not one of these studies was large enough, however, to permit subgroupings by age, sex, weight, and parity for specific comparisons of all possible risk factors at once. Table 1 summarizes the results of these studies with regard to the risk factors for gallbladder disease.

Sample Selection

In 1967 the TOPS (Take Off Pounds Sensibly) Club, Inc., a nonprofit organization, initiated a research program to investigate the etiology and consequences of obesity. TOPS members are considerably heavier and younger than the general U.S. population. There are, however, women of normal weight in this sample population. Entry into the TOPS program is voluntary and requires minimal dues. Women join TOPS not only because of their problems in controlling weight, but also because TOPS serves somewhat as a social organization, which has apparently caught on in many communities scattered throughout the country.

For our study, a questionnaire was carefully designed to cover a broad spectrum of related areas for future studies. Totaling 16 pages, it covered such areas as the respondent's family history, lifestyle, morbidity, and environmental conditions. These questionnaires were administered in a structured format in early 1969 throughout the United States and Canada to those TOPS members who volunteered to participate in the project. A total of 83,930 usable questionnaires were returned.

The questionnaires were edited, coded, and transferred in sections to computer storage. Initial studies of the respondents revealed that only a small number of males and nonwhites were included. Eliminating these subgroups and all those persons whose current height and weight were not reported resulted in a total sample size of 73,532 (*12*). For this particular study, only nondiabetic, nonpregnant women over 20 years of age (total of 62,739 women) were studied. Specific details of the study design and on the study sample are given elsewhere (*13*).

To handle such large data files effectively, a computer system—SCALPEL—was created (*14*). This system allows multiple statistical inquiries to be made of the large data files with a finite noncomputer language. Thus noncomputer-trained people can interrogate data directly without the need for computer-trained personnel.

Explanation of Variables

Obesity index. A separate study was conducted by our research group to determine the best index

Table 1. Summary of previous investigations of risk factors for gallbladder disease

Subjects and reference number	Number of subjects	Year of investigation	Factors found related to gallbladder disease			
			Sex [1]	Age [2]	Obesity [2]	Parity [2]
Autopsies (*1*)	31,311	1945	Yes	Yes	.....	.....
Autopsies (*2*)	26,895	1952	Yes	Yes	.....	.....
Gallstone patients (hospital records) (*24*)	783	1956	Yes	Yes	Yes [3]	Yes [4]
Pregnant females (*4*)	352	1959	.....	.....	.....	No
Ostersund, Sweden, females (*6*)	152	1961	.....	.....	?	?
Cholecystectomy patients (*5*)	1,756	1963	Yes	Yes	.....	.....
Framingham, Mass., whites (*7*)	5,209	1966	Yes	Yes	Yes	Yes
Pima Indians (*8*)	575	1967	Yes	.....	No	Yes
Pima Indians (review of medical records) (*9*)	596	1970	Yes	Yes	No	No
Southwest Indians (*10*)	101	1971	Yes	No	.....	?
Chippewa Indians (review of medical records) (*11*)	4,724	1971	Yes	Yes	.....	Yes

[1] Female predominance. [2] Increasing incidence of disease with increase in factor. [3] Only to age 50. [4] Only to age 40.

Table 2. Descriptive statistics for TOPS women at each obesity level

Factor	Level 1 (N=12,382)	Level 2 (N=13,039)	Level 3 (N=12,720)	Level 4 (N=12,324)	Level 5 (N=12,274)
Obesity index:[1]					
Minimum value	1.10	2.22	2.45	2.70	3.07
Maximum value	2.21	2.44	2.69	3.06	7.60
Age (years):					
Mean	39.3	40.8	41.1	41.1	39.9
Standard deviation	11.6	11.8	11.8	11.4	10.8
Height (inches):					
Mean	63.7	64.2	64.3	64.4	64.7
Standard deviation	2.5	2.4	2.4	2.5	2.6
Weight (pounds):					
Mean	132.4	149.7	165.2	184.7	227.7
Standard deviation	8.9	7.2	7.9	9.9	28.9
Percentage above desirable weight [2]	10.1	24.8	37.8	53.9	85.3

[1] Weight divided by height. [2] Percentage based on mean height and weight; desirable weight based on Metropolitan Life Insurance standard.

of obesity (or ponderosity) to use with the present data (*15*). Unfortunately, skinfold thickness was not available for this study. The index that had the highest correlation with weight and the lowest correlation with height was used. The index, weight ÷ height (W/H), met these criteria. The results of the correlation analysis are in agreement with another work (*16*) in which W/H is apparently a better index for females, whereas W/H^2 is more appropriate for males. The index was divided into five levels, each containing approximately 20 percent of the TOPS group. Each of these obesity levels and its descriptive statistics are shown in table 2. It should be noted that age and height are well matched within the levels of obesity contained in this table.

Number of live births. Parity was considered to be the number of live births at the time the respondent answered the questionnaire, and the women were divided into four groups: no live births, one birth, two births, and three or more. A range of 3 to 12 live births was found for this last group, with a mean of 4.1.

Age. Few women under 20 years of age completed the questionnaire; of those who did, very few reported a history of gallbladder disease. Reports of previous studies indicate a low incidence of gallbladder disease in females under 20 years old (*17–20*). For these reasons this study included only women over 19 years. These women were then grouped by decades of life.

History of diseases. In the TOPS questionnaire the history of 18 disease conditions was requested. For the present study of gallbladder disease, the specific question was: Has a doctor ever said that you had gallbladder disease? In other corroborating questions the respondent was specifically asked for the diagnosis, the duration of disease, and the treatment, based on her own knowledge. This question format has been used previously in a multiphasic screening program (General Medical History Questionnaire, Milwaukee County Health Department Multiphasic Screening Program). The accuracy (*21*) and reliability (*22*) of this kind of medical history question is reported to be high.

As part of the TOPS survey a questionnaire with a signed authorization was sent to a sample (20,000) of the members' physicians. Forty-two percent of the physicians answered the questionnaire. The physicians were asked if they had ever treated the patient for gallbladder disease. There was 87.3 percent agreement between the physicians and the TOPS women. Overreporting on the part of the TOPS women seemed to exist, but a large part of this excess may have been due to the mobility of the population; that is, the present physician might not be the one who had treated the woman for gallbladder disease. A further analysis showed that age and obesity levels were not related to the percentage agreement. Another important aspect of the interpretation of these data is that no mention was made of the type of gallbladder disease. These two misclassification problems, however, do not create a bias in studying the risk factors of gallbladder disease, for it is assumed that misclassification occurred in a random group of subjects, and consequently it would

tend to obscure existing relationships between the risk factors and gallbladder disease.

Occurrence of disease. In this kind of cross-sectional study the statistic used to reflect the disease rate is referred to as the occurrence rate and can be calculated as follows:

$$R = \frac{N_D}{N_T} \times 100 = \text{rate per 100 with history of disease condition}$$

when N_D = number of subjects reporting a history of the disease,

N_T = total number of subjects at risk.

This rate reflects a lifetime rate for the age-specific groups studied. For example, a rate of 10 for women between 30 and 39 years of age indicates that 10 women in 100 in this age group had a history of gallbladder disease sometime during their life. Consequently, with age-specific occurrence rates one would expect higher rates for the older groups since the rate reflects a lifetime or cumulative rate.

Incidence of disease. Techniques of the life table method were used to obtain estimated incidence rates for gallbladder disease. The cross-section life table (*23*) has been used when morbidity (or mortality) rates are determined for a specific period in a group of persons with a wide range of ages. In this approach the cohort is a hypothetical group of persons. The assumption is that if a cohort could be formed, it would follow the morbidity rates that occurred in the specific time interval observed for each age group. In our study the age-specific occurence rates were calculated for each level of each risk factor. Although these data were collected at one time, we assumed that the occurrence of gallbladder disease had remained uniform during the preceding years; that is, while the women presently in their 50s were in their 20s gallbladder disease would have been diagnosed at the same rate as that found in women in their 20s now. Although diagnostic criteria and techniques may have changed in the past 30 years, for example, the introduction of cholecystograms, no appreciable differences have been found for women in whom gallbladder disease was diagnosed in the 1950s versus those in whom it was diagnosed in the past decade.

Furthermore, we assumed that women in the cohort were not selectively removed from this group. This assumption is supported by results (*7*) showing that the mortality rate for women with gallbladder disease is not higher than that for women without the disease. With the life table method the assumption is that before age 60 there are no losses due to death. We also assumed that women who had had gallbladder disease were not any less likely to join or leave the TOPS organization than women who were free of it. Of course, the presence or the diagnosis of gallbladder disease may have preceded the onset of the risk factors being studied. A further investigation of this problem is now in progress.

Table 3 is an example of the method of calculation of incidence. A hypothetical cohort of 100 women in their 20s was formed to estimate incidence rates, and this group was "followed" for four decades of life. It is assumed that at age 20 none had had gallbladder disease diagnosed. Therefore, 100 women are at risk at the beginning of their 20s. The number of new cases expected to occur in these women between 20 and 29 years of age is estimated by using the observed occurrence rate per 100. The ratio of the number

Table 3. Determination of incidence of gallbladder disease in TOPS women and in a theoretical female cohort, by age group

Present age group	TOPS women		Theoretical cohort of women		
	Sample size	Occurence rate	Number at risk	Estimated number of new cases in decade	Incidence per 100 for decade of life
20–29	12,321	7.27	100.0	7.27	7.27
30–39	19,367	13.63	92.73	6.36	6.86
40–49	16,900	17.96	86.37	4.33	5.01
50–59	10,149	21.81	82.04	3.85	4.69
60 and over	4,002	26.79	78.19	4.98	6.37

Table 4. Mean obesity index and number of live births in TOPS women with and without gallbladder disease, by age group

Present age group (years)	Obesity index		Number of live births	
	No gallbladder disease	Gallbladder disease	No gallbladder disease	Gallbladder disease
Number 20–29	11,425	896	11,425	896
Mean	2.61	[1] 2.79	1.85	[1] 2.28
Standard deviation	.53	.59	1.27	1.27
Number 30–39	16,728	2,639	16,728	2,639
Mean	2.65	[1] 2.89	3.16	[1] 3.39
Standard deviation	.54	.61	1.63	1.71
Number 40–49	13,865	3,035	13,865	3,035
Mean	2.66	[1] 2.87	3.25	[1] 3.38
Standard deviation	.52	.61	1.86	1.91
Number 50–59	7,936	2,213	7,936	2,213
Mean	2.61	[1] 2.76	2.76	[1] 2.96
Standard deviation	.48	.53	1.84	1.87
Number 60 and over	2,930	1,072	2,930	1,072
Mean	2.58	[1] 2.70	2.46	[1] 2.71
Standard deviation	.43	.46	1.94	2.02
Number all age groups	52,884	9,855	52,884	9,855
Mean	2.63	[1] 2.82	2.80	[1] 3.12
Standard deviation	.52	.58	1.76	1.85

[1] Significantly different from that of women with normal gallbladders ($P < .01$).

of new cases to the number of women at risk, 7.27, is the estimated incidence per 100 for women 20–29 years in the TOPS sample. At age 30 the hypothetical cohort contains 92.37 women (100—7.27) still at risk of gallbladder disease. In the TOPS group 18,540 women between 30 and 39 had an occurrence rate of gallbladder disease of 13.60 per 100. Assuming that these women had had gallbladder disease diagnosed in their 20s at the same rate as women presently in their 20s, we would expect only 6.36 new cases (13.63—7.27) to occur during their 30s. The estimated incidence per 100 is the ratio of the number of new cases to the number at risk in the hypothetical cohort—6.86. Incidence rates are likewise estimated for each decade of life. The formula for the incidence rate of the *k*th age group is:

$$I_K = \frac{R_K - R_{K-1}}{100 - R_{K-1}} = \text{incidence rate per hundred per decade}$$

where R_K = occurrence rate in the k^{th} age group.

Results

From the questionnaires completed by the TOPS members we determined that 9,855 of the 62,739 women had had gallbladder disease sometime during their lives. Thus, the overall occurrence rate for the disease was calculated to be 15.7 per hundred for the entire sample. This rate is dependent upon the age structure of our sample.

Mean obesity index and live births. The mean obesity level and the mean number of live births were calculated for each age group and gallbladder status subgroup formed (table 4). This method of analysis of means is a conventional approach to determining the significance of a risk factor. For every decade of life there is a statistically significant increase ($P < .01$) in the obesity index for women with a history of gallbladder disease as compared with women having no history of the disease. Women with a history of the disease also have more live births ($P < .01$) than women without the disease for every decade of life studied. A second method of analysis, in which parity and obesity are broken down into categories of possible clinical distinction, was used to investigate detectable trends in the data.

Parity appears to decrease for the oldest group. One would expect the number of live births to remain constant in the post-menopausal group if our original assumptions concerning similarity of cohorts were completely true. The cohorts were admittedly not similar in that women living now have different concepts of ideal family size, birth

control, population control, and so forth than women of earlier generations. Previous studies have demonstrated that cohorts of women born around the turn of the century have larger families. This fact is not reflected by the present study and may be related to the self-selection of our study group.

Incidence by age, obesity, and live births. Eighty subgroups were formed by stratifying the sample according to age (four decades), obesity (five levels), and number of live births (four groups). These subgroups were chosen so that each contained at least 100 women, while a majority had more than 400. Table 5 displays the estimated incidence rates for each subgroup. The highest estimated incidence was 15.77 per hundred, found in the 20–29 year olds, who had three or more live births and an obesity level of 5. There appeared to be a slight trend for a fat, multiparous woman in her 20s to have had gallbladder disease. The trend for a higher incidence with increasing obesity seems to remain for the 30–39 year old group. For the 40–49 and 50–59 year old groups, however, it is not easy to discern any noticeable relationship between incidence rates and number of live births or obesity.

Incidence rates by age. Table 3 gives the estimated incidence rates per 100 for gallbladder disease in the TOPS sample for each decade of life. The oldest group (60 to 82 years) is included in these calculations because we believed that its size (4,002 women) was large enough for an accurate estimate of the occurrence rate. When further breakdowns by obesity, number of live births, or both, were made, this group was excluded because of the small sample sizes. The incidence rate for the 40–49 year olds, 5.10 per hundred, is one of the lowest rates for any decade and indicates that no special tendency existed for these women to have gallbladder disease diagnosed in their 40s.

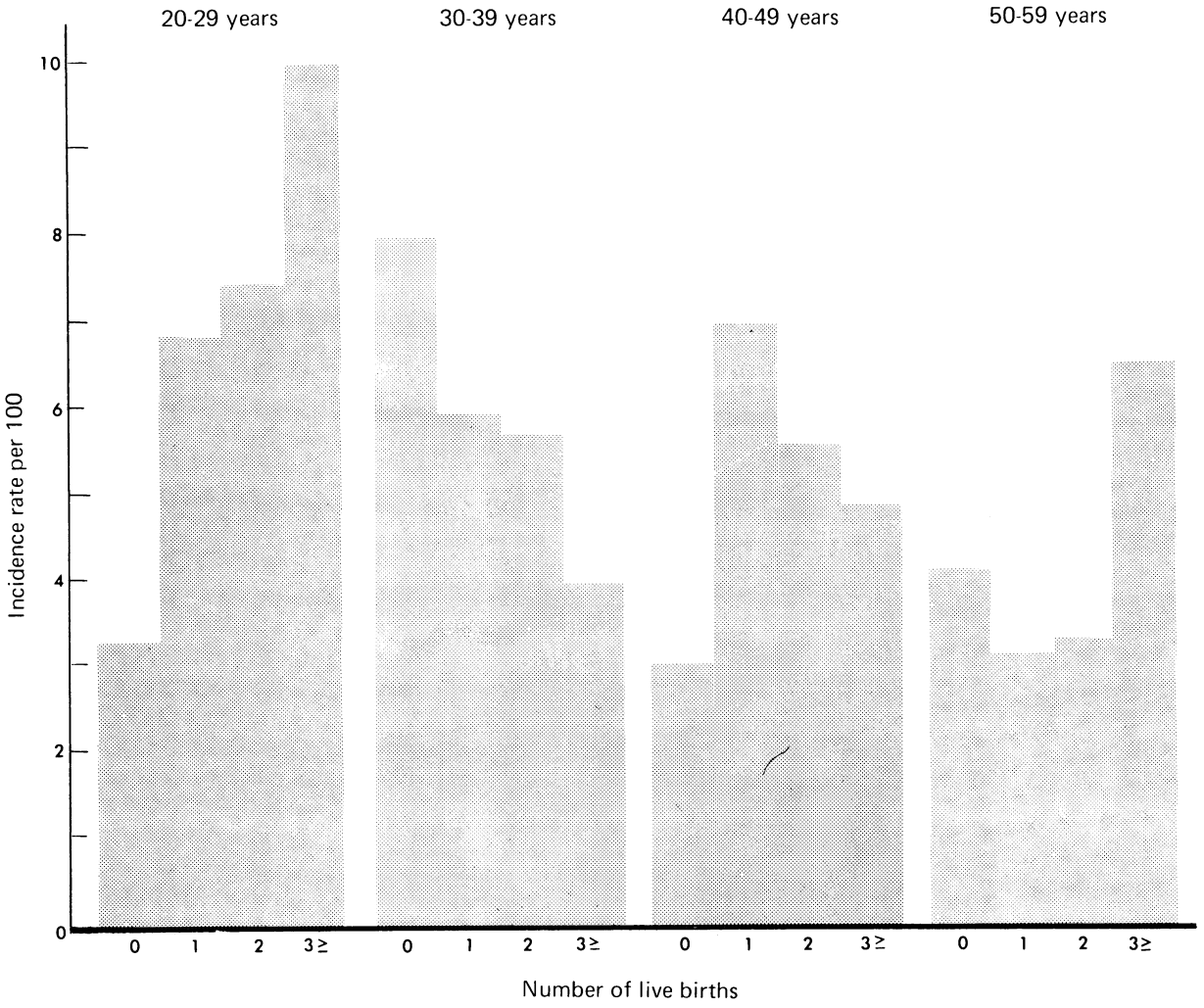
Incidence rates by age and live births. Incidence rates were also estimated for each subgroup when the TOPS sample was stratified by age and number of live births. Figure 1 shows the results of these calculations. The incidence increases as the number of live births increases only for women in their 20s. For women in their 30s this trend apparently reverses—as the number of live births increases, the incidence decreases. The age groups 40–49 and 50–59 exhibit no obvious trends.

Incidence rates by age and obesity level. Figure 2 shows the estimated incidence rates of gallbladder disease at the five obesity levels for each decade of life studied. The increasing incidence of

Table 5. Estimated incidence rates per 100 TOPS women for gallbladder disease, by age, number of live births, and obesity level

Age group and live births	Present obesity level				
	1	2	3	4	5
20–29:					
0	2.58	1.31	2.11	4.61	5.08
1	4.42	4.82	8.20	6.60	10.32
2	4.33	6.32	7.84	8.20	12.18
3 and over	5.30	9.54	9.65	10.61	15.77
30–39:					
0	.39	2.32	7.94	8.64	13.20
1	.32	−.08	3.80	8.75	11.46
2	1.47	3.62	3.54	6.71	12.08
3 and over	3.21	1.53	4.88	6.76	7.55
40–49:					
0	1.25	9.84	3.62	1.76	6.12
1	6.53	8.68	8.33	7.33	4.03
2	5.75	5.80	6.31	6.49	1.85
3 and over	3.68	3.91	2.47	3.73	9.00
50–59:					
0	6.14	3.16	3.66	8.49	4.59
1	2.82	6.74	1.09	4.25	6.81
2	2.43	4.32	3.29	3.01	6.72
3 and over	6.05	5.77	5.77	10.79	4.16

Figure 1. Estimated incidence of gallbladder disease among TOPS women according to age and number of live births



gallbladder disease with increasing obesity is apparent for the early decades, but it is less obvious for the 40- and 50-year-old women.

The incidence values show varying results for different decades of life. Although significant average differences were found for all decades, the actual trend for these variables is not distinguished for all decades.

Multiple variables analysis. The multiple linear regression technique was used to study the relationship between risk factors and incidence rates. This procedure showed a highly significant ($P < .01$) relationship between the incidence of gallbladder disease and obesity. This risk factor explained 24 percent of the variation in incidence rates. The only other statistically significant association with the incidence rates was the interaction of age and obesity, which accounted for an additional 11 percent of the variation in the rates. Figure 2 demonstrates this interaction by showing the increasing incidence rates for each obesity level between 20 and 39 years and by showing no relationship between the obesity level and incidence rates for the oldest age groups. Further analysis done by decades of life shows much more interesting and significant results.

Discussion

Although a member of the TOPS organization does not typify the average U.S. female, this study contains a larger number of subjects than any previous study of gallbladder disease. The size of

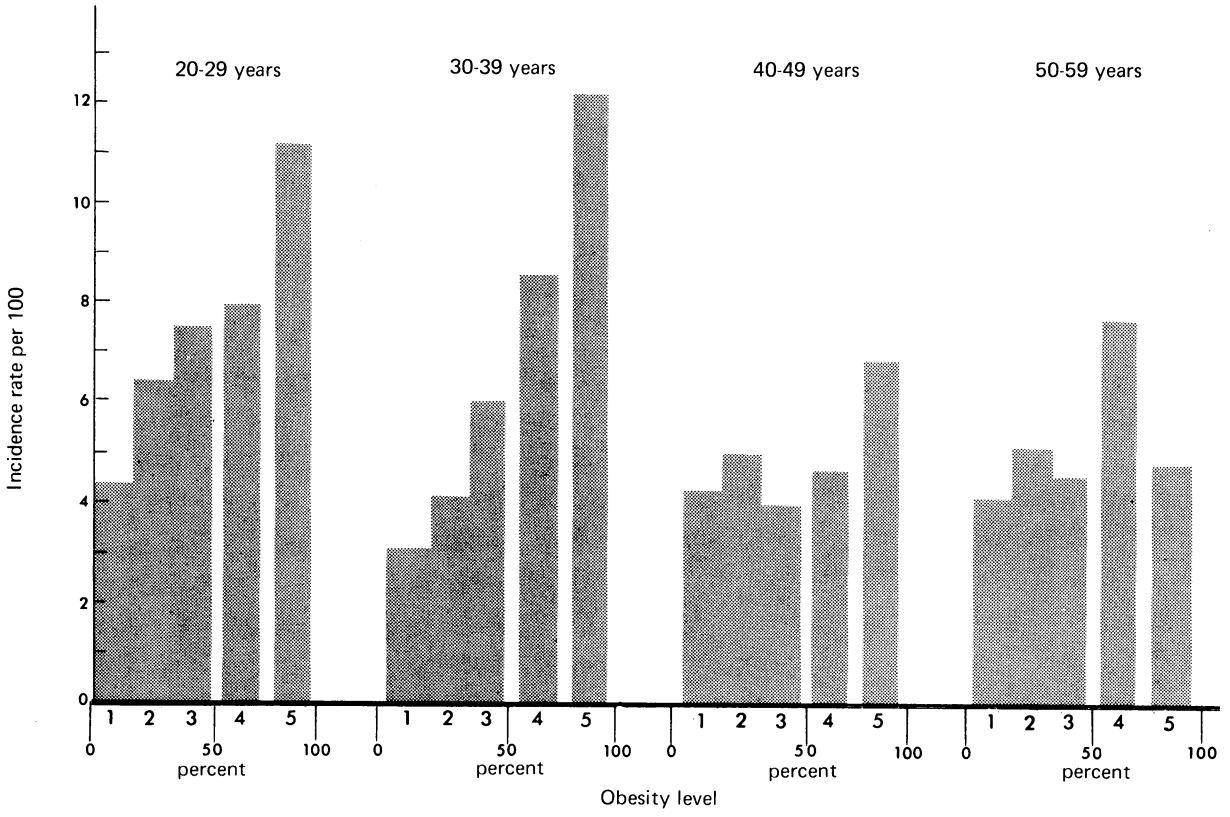
the sample permitted an assessment of all combinations of risk factors. Incidence rates were estimated by use of a theoretical cohort because it is unlikely that a prospective study of this disease will be undertaken among as large a group of women located throughout the continent.

Even though our data were obtained from a structured questionnaire, this approach offers a much more viable alternative to a longitudinal study than an educated opinion based on a very small number of patients. Those errors associated with use of a questionnaire that relate to recall, intelligence, and motivation should not be directed toward any particular subgroup. If these errors are considered to be random, their effect would be to obscure existing relationships, and any real associations between gallbladder disease and the risk factors would tend to be underestimated or become indistinguishable.

Much evidence already exists to support the higher prevalence of gallbladder disease in obese women. Obesity, an important health problem of epidemic proportions, has been associated with increased morbidity and mortality in general, yet the acknowledgment and definitive elucidation of its consequences is far from complete. This study confirms the relationship between obesity and gallbladder disease in women between the ages of 20–40 and evaluates age and parity as other risk factors.

The TOPS women were compared with Framingham whites and Pima and Chippewa Indians for age-specific prevalence rates of gallbladder disease (table 6). The prevalence of the disease among TOPS women was greater than among Framingham women; it was similar to that among the Chippewa Indians. Gallbladder disease was more prevalent, however, among the TOPS women than among the Pima Indians.

Figure 2. Estimated incidence of gallbladder disease among TOPS women according to age and obesity level



NOTE: Obesity level is expressed on a scale of percentage above ideal weight.

Table 6. Prevalence of gallbladder disease among TOPS women, Framingham whites, and Chippewa and Pima Indians

Study group	Age of women at time of study			
	30–39	40–49	50–62	Total 30–62
TOPS women at risk	19,367	16,900	11,728	47,995
Number positive	2,639	3,035	2,599	8,273
Percent positive	13.6	18.0	22.2	17.2
Chippewa Indians at risk	211	122	140	473
Number positive	21	33	41	95
Percent positive	10.0	27.1	29.3	20.1
Framingham whites at risk	1,037	963	873	2,873
Number positive	24	58	88	170
Percent positive	[1] 2.3	[1] 6.0	[1] 10.1	[1] 5.9
Pima Indians at risk	45	51	62	158
Number positive	16	20	21	57
Percent positive	[1] 35.6	[1] 39.2	33.8	[1] 36.0

[1] Significantly different ($P < .01$) from TOPS women.

The diagnostic criteria for gallbladder disease may at first appear to be an important factor in accounting for the differences in prevalence among these studies. In the Framingham study, cases were classified as definite based on the following nonclinical criteria: (*a*) patient's recall of a gallbladder operation with no hospital records available, (*b*) patient's recall of abnormal gallbladder X-ray results with no report available, and (*c*) patient's recall of a hospital diagnosis of gallbladder disease with no report available. Cases were also classified as doubtful on the basis of nonclinical evidence, such as (*d*) patient's recall of a physician's diagnosis of the disease made outside the hospital without hospitalization, X-ray, or surgery and (*e*) the patient's reporting of symptoms that could be related to gallbladder disease. In the Framingham study, category (*d*) cases could be distinguished from "definite" cases. (In our study, we could not. In the Pima study, evidence of gallbladder disease was classified in a similar way. The study of the Chippewa Indians was the most controlled in that only hospital records were used.) The extremely large differences in prevalence between the studies, shown in table 6, suggest that other factors may be involved besides the diagnostic selection of the Framingham group. Probably the most important is that the TOPS women were heavier than the women in the Framingham study.

A comparison of the mean number of live births among the Framingham, Pima Indian, and TOPS study subjects (table 7) shows for each study a statistically higher ($P < .01$) mean number of children for women with a history of gallbladder disease than those without. The TOPS women averaged more children than the Framingham women but less than the Pima Indian women. This result correlates well with the prevalence rates for gallbladder disease. In both the Framingham study and the Pima study the average number of children representing the number of live births at entry into the program was used, not the number at the time of diagnosis; thus, this information is comparable with the TOPS data. Obesity determinations for these populations unfortunately cannot be compared with TOPS data directly, since different measures of obesity are used. The Framingham group, however, has been assumed to be similar to the U.S. population; the TOPS group is heavier than that population. Overall, the TOPS group may be considered heavier than the Framingham subjects.

These differences in parity and obesity inherent in the two populations could account for the large differences found in table 6. If increasing obesity and parity are related to increased incidence of disease, the TOPS population would be expected to have higher occurrence rates than those reported in the Framingham study and lower than those reported in the Chippewa study. The estimated incidence rate for women in their thirties was twice as high for the TOPS population as that for the Framingham population (table 8). For the 40–49 year old group the rates for the two studies were similar, while in the oldest age

group the TOPS rates were somewhat lower. Apparently the TOPS women, who were considerably heavier than the general U.S. population, had a high incidence of disease at a young age.

The simultaneous evaluation of the three risk factors showed no consistent trend toward higher rates of gallbladder disease in fat, fertile, 40-year-old females. A multiple regression analysis for each decade of life showed that in the oldest group (50–59) only 13 percent of the variation in incidence values was explained by the two risk factors obesity and parity and their interaction (fig. 3). None of these factors, however, were statistically significant. Similar results were obtained for the 40-year-old women.

In the age group 30–39 obesity explained 83 percent of the variability in incidence rates. The obesity-parity interaction added 6 percent more. When the effect of parity was added, a total of 91 percent of the variation was explained. All these differences were statistically significant. For the 20 year olds, the obesity-parity interaction explained 83 percent of the variation in incidence rates. In young women pregnancy may have resulted in residual weight gain post partum, and therefore a compounding of the effects of parity and obesity may have existed. The effects of obesity and parity each added 3 percent more, so that a total of 89 percent of the variation is explained.

There may be several reasons why the effect of parity is more obvious in younger women:

1. It is possible that the spacing of children and not the number of children is related to the incidence of gallbladder disease. The number of live births may serve as a measure of the frequency of childbirth only for women in their 20s, as it is highly probable that more of these births occurred while the women were in their 20s. For women in their 30s and older, however, the frequency of childbirth is not as clearly related to the number of live births.

Table 7. Comparison of mean number of live births among TOPS women, Pima Indians, and Framingham whites 30-62 years old

Study group	Normal gallbladder		Gallbladder disease	
	Number of women	Mean live births	Number of women	Mean live births
Framingham whites ..	2,703	2.24	170	2.87
TOPS women	39,722	3.09	8,273	3.23
Pima Indians	101	4.40	57	5.83

NOTE: Study on Chippewa Indians does not include information on live births.

2. Throughout this study parity has been defined as the number of live births at the time of completing the questionnaire. Thus, the parity for older women may be an overestimate since it does not represent the number of births before the diagnosis of gallbladder disease. In spite of these weaknesses age-specific results in table 4 show that women who have a history of gallbladder disease also have a significantly higher average number of live births than women without such a history. This result was found for every age group.

It has also been suggested that it is not the number of children that is related to gallbladder disease but rather the difference between being nulliparous and having at least one child (7). This difference was significant for each population

Table 8. Comparison of prevalence of gallbladder disease per 100 women at entry into study and estimated incidence per 100 women between Framingham and TOPS women

Age group	Framingham women		TOPS women	
	Prevalence at entry	10-year incidence	Occurrence rate [1]	Estimated 10-year incidence
30–39.....	2.3	3.0	13.6	6.9
40–49.....	6.0	6.6	18.0	5.0
50–62.....	10.1	8.9	22.2	5.1

[1] Equivalent to prevalence among Framingham whites at time of entry into that study.

Figure 3. Percent of the variation in incidence of gallbladder disease explained by the risk factors of obesity and parity and their interaction, by decade of life

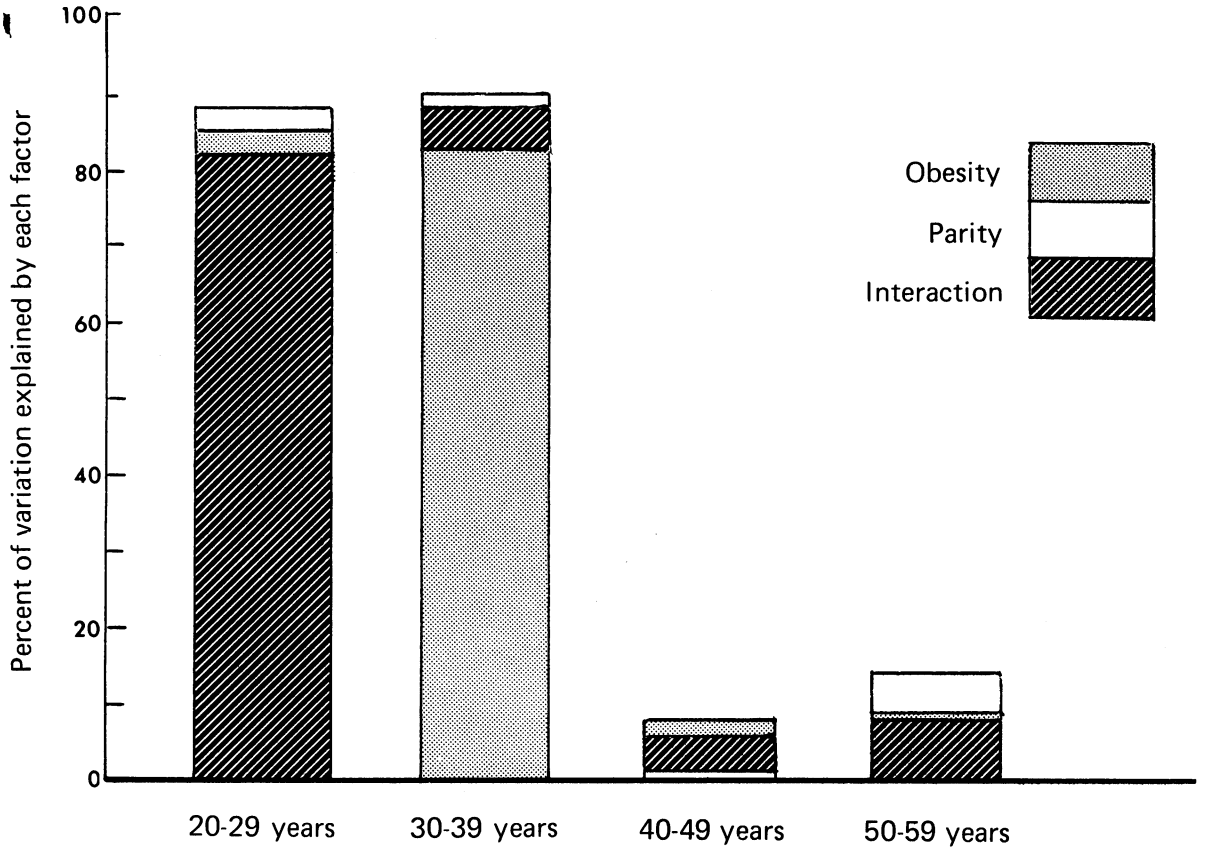


Table 9. Comparison of risk of gallbladder disease among nulliparous and parous Chippewa Indians, Framingham women, and TOPS women

Study group	Nulliparous women		Parous women	
	Total women	Percent with gallbladder disease	Total women	Percent with gallbladder disease
Chippewa Indians	756	1.8	635	20.0
Framingham whites	647	4.9	2,039	6.1
TOPS women[1]	5,499	11.0	57,240	16.1

[1] Women 30-59.

NOTE: Study on Pima Indians does not contain information on parity.

studied (table 9); nevertheless, in comparing these two categories for the TOPS population by size and obesity subgroups, this difference is not consistent.

Most studies of gallbladder disease unfortunately do not include women in their 20s—the period of its highest occurrence in the TOPS population. This study suggests that obesity and parity are important risk factors in this age group. Possibly the factors studied here, pregnancy and excess weight, create problems that result in morbidity earlier in life. Studies in which these factors have not been found to be important have probably not focused on younger women.

Our intention has been to examine the effects of obesity, age, and parity on the incidence of gallbladder disease in a large population of more than 62,000 white women. Unfortunately, inferences about all U.S. women cannot be drawn from this study because a random sample of U.S. women was not obtained.

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BERNSTEIN, RONALD A. (Medical College of Wisconsin), WERNER, LINDA H., and RIMM, ALFRED A.: *Relationship of gallbladder disease to parity, obesity, and age. A study of 62,739 weight-conscious women. Health Services Reports, Vol. 88, December 1973, pp. 925–936.*

A study was made of the interrelationships between gallbladder disease and obesity, age, and parity in more than 62,000 weight-conscious women who were members of TOPS (Take Off Pounds Sensibly). The results, based on perhaps the largest sample of its kind, show no support for the alliterative description of the typical gallbladder patient as a "fat, fertile female of forty". The overall occurrence rate of gallbladder disease was calculated to be 15.7 per hundred for the entire sample. This population showed a relatively constant incidence of this disease over the decades of life; no increase occurred during the forties. A trend toward increasing incidence with increasing obesity and parity was apparent only for the younger age groups. Obesity appeared to be the single factor having the greatest effect on the incidence of gallbladder disease. The results indicate that TOPS women with gallbladder disease were heavier and had more children than those women without disease. These women also had a high incidence of gallbladder disease at early ages.