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Gall stones in a Danish population. Relation to weight, physical activity, smoking, coffee consumption, and diabetes mellitus

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SUMMARY **The presence of gall stones diagnosed by ultrasonography in a cross sectional study was analysed in relation to relative weight, weight change since age 25, slimming treatment, physical activity, smoking, consumption of coffee, and diabetes mellitus. The random sample comprised 4581 men and women of Danish origin, aged 30, 40, 50, and 60 years, of whom 3608 (79%) attended the investigation. In women high body mass index, history of slimming treatment, and weight gain since the age of 25 of more than 5 body mass index units were each significantly associated with gall stones ($p<0.05$), while only body mass index was significant ($p<0.05$) in a multivariate analysis. In men history of slimming treatment was significantly associated ($p<0.05$) with gall stones in univariate and in multivariate analyses, where smoking also became significantly associated ($p<0.05$). No significant association was detected between gall stones and the other variables.**

Most studies, dealing with clinically diagnosed gall stones only, agree that there is an association in women between overweight and gall stone disease.[1-8] The fewer reports which exist on men show conflicting results.[1 2 6 7] Studies of clinically diagnosed gall stones are in risk of selection bias.[5 9] Some population studies, comprising the total prevalence of gall stone disease, show an increased prevalence of gall stones in those who are overweight,[10-12] but this is not found in all studies.[13] Nearly all those studies mentioned compare actual weight with the prevalence of gall stones, whereas weight history, which must be an important factor on which to focus when dealing with life prevalence of gall stone disease, has received little attention.[1 7]

Lack of physical activity, smoking, and coffee consumption are associated with changes in plasma lipids,[14-16] but evidence on the clinical implications in respect of any association with gall stones is either lacking or conflicting.[1 4 6-8 12] Clinical studies on the association between diabetes and gall stones likewise produce conflicting results.[2 8 11] This maybe because most studies include only those gall stones which are clinically diagnosed.

In this study, the prevalence of gall stone disease in a random sample of a Danish population was ascertained by ultrasonography.[9] For men and women estimates were made of possible associations between gall stone disease and relative weight, weight history, physical activity, smoking, consumption of coffee, and diabetes mellitus.

Methods

SAMPLING

An age and sex stratified random sample comprising 4807 men and women living in the western part of Copenhagen County and aged 30, 40, 50, and 60 years, was drawn from the National Person Register on 15 October 1982. Two hundred and twenty six people of foreign extraction were excluded, thereby reducing the sample to 4581. All received a standardised written invitation to a general health examination. Information about the project and a questionnaire to be completed in advance were enclosed. The examinations took place between

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November 1982 and February 1984 at the Glostrup Population Studies. The project was approved by the ethical committee for Copenhagen County.

EXAMINATION AND QUESTIONNAIRE

The upper abdomen was examined by ultrasonography using a Toshiba SAL 20A, real time, linear array scanner with a 2·4 MHz probe. Subjects were classified as having gall stone disease, when one of the following criteria was fulfilled: (1) Visible gall bladder lumen presenting echoes with an acoustic shadow. The echoes were required to move with gravity, except when obviously impeded by size, a septum, a fold, or wedging into the infundibulum. (2) Non-visualisation of the gall bladder lumen and high density echoes in the gall bladder fossa with an acoustic shadow. The echoes were required to have the same relation to the liver when the person was placed in different positions. (3) No gall bladder lumen in subjects with a history of cholecystectomy and a relevant scar.

Further details about material, non-participants, and ultrasonographic criteria have been reported elsewhere.[9]

Subjects with gall stone disease were compared with subjects with a normal gall bladder. History of gall stone disease was recorded. Participants, who had undergone cholecystectomy or had their history of gall stone disease confirmed ultrasonically, were classified as subjects with clinical gall stone disease. Participants, who had no history of gall stones and where they were detected ultrasonically were classified as subjects with non-clinical gall stone disease.

Height without shoes and weight without overcoat were recorded. Body mass index (kg/m^2) was used as an index of body fatness. Subjects with body mass index below 20 were regarded as underweight, between 20 and 25 normal, between 25 and 30 moderately obese, and over 30 unequivocally obese. Records were made of each subject's highest weight ever, the weight at age 25, and the number of slimming treatments undergone (defined as weight loss of more than 5 kg). Physical activity was registered for leisure time activity and work. Each of these physical activity variables had a four way classification, ranging from sedentary work and no spare time activities to heavy work and performance of competitive sports. Smoking habits were recorded as former and current smoking, amount of smoking and type (cigarettes, cheroots, cigars, and pipe). The consumption of tobacco was calculated as grams per day. The number of cups of coffee per day was recorded. A history of diabetes mellitus and the use of insulin were recorded.

Table 1 *Prevalence rates (%) of gall stone disease according to present body mass index (BMI). N= denominator*

Sex and age	BMI <20·00 %	N	20·00–24·99 %	N	25·00–29·99 %	N	>=30·00 %	N	Unknown
Men									
30	0·0	32	1·9	262	1·8	114	4·5	22	0
40	6·3	16	0·5	209	1·1	180	8·6	35	0
50	15·4	13	6·2	177	5·7	193	11·9	59	0
60	0·0	15	16·9	154	12·9	201	10·9	55	0
Mean	5·5		6·3		5·3		9·0		
Women									
30	2·5	120	4·5	266	8·5	47	27·3	11	0
40	8·0	50	4·1	268	8·4	83	19·4	31	1
50	8·3	36	15·1	232	13·3	113	26·7	45	1
60	12·0	25	20·3	177	23·4	128	41·7	48	0
Mean	7·5		10·6		13·0		28·4		

Men, (BMI >=25·00 *v* BMI <25·00):
M-H test=0·00, df=1, p>0·99, OR=0·98 (95% lim: 40·75–0·02).
(BMI >=30·00 *v* BMI <30·00):
M-H test=1·53, df=1, p>0·20, OR=1·46 (95% lim: 0·80–2·68).
Women, (BMI >=25·00 *v* BMI <25·00):
M-H test=11·47, df=1, p<0·001, OR=1·71 (95% lim: 1·25–2·33).
(BMI >=30·00 *v* BMI <30·00):
M-H test=26·02, df=1, p<0·0005, OR=2·87 (95% lim: 1·91–4.31).

STATISTICAL ANALYSIS

Each sex was analysed separately. A Mantel-Haenszel summary χ^2 test[17] was used as age was associated with the outcome variable and the determining variables. To account for associations between the independent variables, a multiple logistic regression analysis was carried out.[18] Confidence limits were 95%.

Results

Of 4581 subjects invited, 3608 (79%) attended the investigation. Aside from gall stone disease, 106 men and 84 women suffered other gall bladder pathology – mainly polyps.[9] In the ensuing analysis these subjects are omitted.

RELATIVE WEIGHT AND WEIGHT HISTORY

Prevalence of gall stone disease showed a significant positive association with present body mass index in women (Table 1). The most substantial association was found among women with a body mass index above 30. Men did not show the same association except for a non-significant trend towards higher prevalence among those with a body mass index above 30 (Table 1). When dealing with highest relative weight ever, the same pattern was observed. Change in body mass index from age 25 to present age (Table 2) showed in both sexes a non-significant tendency towards higher gall stone prevalence in

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Table 2 *Prevalence rates (%) of gall stone disease according to change in body mass index (BMI) from age 25 years to present age. N=denominator*

Sex and age	Present BMI as compared with BMI at age 25:* Reduced %	Reduced N	Stable %	Stable N	Increased %	Increased N	Unknown
Men							
30	0·0	44	2·5	198	1·6	187	1
40	2·8	36	1·7	120	1·4	284	0
50	9·8	51	1·4	71	7·5	319	1
60	15·6	45	9·8	82	14·5	297	1
Mean	7·0		3·8		6·2		
Women							
30	3·0	67	5·5	183	5·2	192	2
40	4·6	44	4·7	86	7·3	302	1
50	19·2	47	12·9	85	15·3	294	1
60	25·0	52	15·6	64	24·6	260	2
Mean	12·5		9·4		12·7		

*Stable BMI is here defined as same BMI at the age of 25 and now plus/minus 1 BMI. For subjects who could not remember their weight at the age of 25 a statement of 'less than now' was classified in the group with increased BMI, 'more than now' was classified in the group with decreased BMI, whereas 'about the same' was classified in the group with stable BMI.
Reduced >< stable: Men: M-H test=1·95, df=1, p>0·10, OR=1·92 (0·77–4·79).
Women: M-H test=0·66, df=1, p>0·40, OR=1·32 (0·68–2·57).
Increased >< stable: Men: M-H test=1·75, df=1, p>0·10, OR=1·55 (0·81–2·99).
Women: M-H test=1·97, df=1, p>0·10, OR=1·37 (0·88–2·11).
Increased >< stable or reduced: Men: M-H test=0·51, df=1, p>0·40, OR=1·22 (0·71–2·07).
Women: M-H test=1·09, df=1, p>0·20, OR=1·21 (0·85–1·73).

Table 3 *Prevalence rates (%) of gall stone disease according to number of slimming treatments. N= denominator*

Sex and age	Numbers of slimming treatments 0 %	0 N	1 %	1 N	>1 %	>1 N	Unknown
Men							
30	2·2	361	0·0	45	0·0	23	1
40	1·4	357	2·2	45	2·8	36	2
50	6·4	358	7·8	51	12·1	33	0
60	11·0	365	30·3	33	29·6	27	0
Mean	5·2		10·0		11·0		
Women							
30	4·3	301	1·1	87	14·5	55	1
40	5·2	288	1·6	64	14·8	81	0
50	13·6	294	23·1	65	15·2	66	2
60	19·3	274	37·3	59	28·6	42	3
Mean	10·2		14·9		17·9		

Slimming treatments, yes *v* no:
Men: M-H test=9·80, df=1, p<0·005, OR=2·15.
Women: M-H test=12·01, df=1, p<0·001, OR=1·76.

those, who had either increased or reduced their weight as compared with subjects with stable weight. Gall stone prevalence was 9·6% among men who had reduced their weight more than 3 units of body mass index and 8·5% among those who had increased it by more than 5 units of body mass index. In women the corresponding figures were 11·8% and 26·5% respectively. This last prevalence was significantly higher than gall stone prevalence among women who had not increased their weight by 5 units (M-H test= 10·23, df=1, p<0·005, OR=1·89 (1·28–2·78)). When highest body mass index ever was taken into account, the relationship ceased to be significant (log coeff=0·2588, SE=0·2350, OR=1·30, p=0·2708).

In both sexes, those who had been on a slimming treatment, had significantly higher prevalence of gall stone disease compared with those who had not (Table 3).

Among participants with gall stone disease the proportion aware of having gall stones was significantly higher in obese than in non-obese women. The same trend, but not significant, was observed among men (Table 4). Likewise, the proportion aware of having gall stones was significantly higher in women with increase in body mass index since age 25 exceeding 5 units than in the rest of women. No trend was seen among men.

PHYSICAL ACTIVITY

The level of physical activity (Table 5) showed no association with gall stone disease in women, but a non-significant trend towards higher prevalence in men with low activity.

SMOKING AND COFFEE CONSUMPTION

Smoking showed a non-significant positive association with the presence of gall stone disease in both

Table 4 *Proportion of clinical gall stones/total gall stones according to actual body mass index (BMI)*

Sex	Age	BMI <25·00 %	BMI <25·00 N	BMI >=25.00 %	BMI >=25.00 N
Men	30	40·0	5	33·3	3
	40	0·0	2	40·0	5
	50	7·7	13	22·2	18
	60	34·6	26	25·0	32
Mean		24·7		25·8	
Women	30	20·0	15	28·6	7
	40	26·7	15	61·5	13
	50	44·7	38	66·7	27
	60	46·2	39	54·0	50
Mean		40·2		56·3	

BMI >=25·00 >< BMI <25·00:
Men: M-H test=0·02, df=1, p>0·80, OR=1·04 (0·66–1·62).
Women: M-H test=4·64, df=1, p<0·05, OR=1·95 (1·06–3·59).

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Table 5 *Prevalence rates (%) of gall stone disease according to physical activity at work or as exercise in leisure time. N=denominator*

Sex and age	Level of physical activity: Sedentary %	Sedentary N	Moderate active %	Moderate active N	Active %	Active N	Heavy/competitive sport %	Heavy/competitive sport N	Unknown
Men									
30	2·9	35	3·1	163	0·6	166	1·6	64	2
40	3·3	30	0·5	189	2·4	166	1·9	52	3
50	12·1	33	8·1	209	4·7	169	3·7	27	4
60	20·4	49	13·8	232	11·4	123	5·9	17	4
Mean	9·6		6·3		4·7		3·3		
Women									
30	4·3	70	5·5	273	3·8	78	5·3	19	4
40	8·2	73	6·5	245	5·7	105	0·0	6	4
50	15·9	69	14·6	260	15·7	89	40·0	5	4
60	25·3	91	22·0	227	28·6	56	0·0	1	3
Mean	13·0		11·8		12·9		11·5		

Sedentary and mod active >< active and heavy/competitive sport: Men: M-H test=3·04, df=1, p>0·05, OR=1·51.
Women: M-H test=0·09, df=1, p>0·70, OR=0·93.
Sedentary >< other groups: Men: M-H test=3·71, df=1, p>0·05, OR=1·85.
Women: M-H test=0·16, df=1, p>0·60, OR=1·19.

sexes (Table 6). There was no substantial dose-response effect. Type of smoking (cigarette, cheroot, cigar, pipe) was not found to be important. There was no significant association between intake of coffee and the presence of gall stones. The trend was towards higher prevalence among non-drinkers. No dose-response relationship was noticed.

DIABETES MELLITUS

In men gall stone prevalence was 9·0% among diabetics and 5·9% among non-diabetics. Corresponding figures among women were 23·8% and 12·4% respectively. Because there being few subjects with diabetes (45 men and 22 women), these differences were not significant. The trends were the same in insulin dependent and non-insulin dependent diabetes.

LOGISTIC REGRESSION ANALYSIS

The variables were included in a multiple logistic regression analysis for each sex separately. As the study was dealing with life prevalence of gall stone disease, highest body mass index ever was used in the present model instead of actual body mass index. The

Table 6 *Prevalence rates (%) of gall stone disease according to smoking habits. N=denominator*

Sex and age	Never smoked %	Never smoked N	Previously smoked %	Previously smoked N	Actual smoking (g): <14·9 g %	<14·9 g N	15–24·9 g %	15–24·9 g N	>=25 g %	>=25 g N	Unknown
Men											
30	0·0	103	1·8	57	3·2	94	2·9	136	0·0	40	0
40	0·0	94	3·5	85	2·0	101	0·0	112	4·2	48	0
50	4·1	49	7·9	101	6·4	110	6·6	137	11·1	45	0
60	11·4	35	14·6	137	8·8	113	18·6	113	11·1	27	0
Mean	3·8		6·9		5·1		6·9		6·6		
Women											
30	2·5	121	1·7	58	4·9	123	8·7	126	6·3	16	0
40	3·5	173	11·1	45	11·2	107	3·1	98	20·0	10	0
50	12·1	116	10·0	70	16·9	124	18·9	106	30·0	10	1
60	27·4	124	23·6	89	20·4	108	22·6	53	0·0	4	0
Mean	10·8		11·1		13·0		13·0		14·4		

Smokers (previous or present) >< non-smokers: Men: M-H test=2·21, df=1, p>0·10, OR=1·92
Women: M-H test=1·19, df=1, p>0·20, OR=1·22.

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following variables, which in this study had previously been shown to be associated with gall stone disease, were also included: age[9] and familial occurrence of clinically diagnosed gall stones[19] in both sexes; school education, cohabitation, and number of years resident in the Municipality of Copenhagen, for men;[19] pregnancies, age at menarche, and use of oral contraceptives, for women.[20] Variables with a p-value of more than 0·30 in the logistic regression analysis were omitted from the model (Table 7). Among men, smoking became and reducing treatment remained, significantly related to gall stone disease, whereas body mass index, weight change since the age of 25, lack of physical activity, consumption of coffee, and diabetes mellitus did not become significantly associated with gall stone disease. Among women body mass index remained significantly related to gall stone disease, whereas slimming treatments lost their association with gall stones. Weight change since the age of 25, lack of physical activity, consumption of coffee, smoking, and diabetes mellitus did not become significantly associated with gall stone disease (Table 7).

Table 7 *Results of the logistic regression analysis of each sex separately*

Variables	*Log coeff*	*SE*	*OR*	*p-value*	χ^{2}*
Men					
Slimming treatment (yes >< no)	0·6596	0·2534	1·93	0·0092	6·78
Physical exercise (no >< yes)	0·2925	0·2374	1·34	0·2179	1·52
Ever smoked (yes >< no)	1·1029	0·4788	3·01	0·0212	5·31
Coffee (no >< yes)	0·5633	0·4051	1·76	0·1644	1·93
Women					
Highest BMI ever	0·0757	0·0171	1·08	0·0000	19·60
Ever smoked (yes >< no)	0·2138	0·1798	1·24	0·2345	1·41

BMI is entered as a continuous variable.
*Change in χ^{2} if the variable is removed from the model.

Of the variables earlier shown to be associated with gall stones,[9 19 20] the relationship regarding the age at menarche changed substantially. After body mass index was included, the significant negative association with gall stone disease[20] became insignificant (log coeff=−0·0678, SE=0·0525, OR=0·93, p=0·1960), probably because of the relationship between weight and age at menarche.[21] With inclusion of body mass index, the use of oral contraceptives[20] became significantly associated with gall stones (log coeff=0·4192, SE=0·1965, OR=1·52, p=0·0329).

Discussion

WEIGHT AND WEIGHT HISTORY

In the present study there was a positive association between gall stone disease and body mass index among women. This confirms results from several studies comprising clinically diagnosed gall stones.[1-7] These may be in danger of overestimating the positive association, however, because of diagnostic suspicion bias.[5 9] Population studies estimating the total prevalence of gall stone disease disagree on the subject. Some[10-12] find an association between obesity and gall stone disease, whereas others[13] do not. The lack of any significant association between body mass index and gall stone disease among men in this study, can only be compared with the few studies on clinically diagnosed gall stones, some showing an association with obesity,[2 6] whereas others do not.[1 7] One explanation for this sex difference could be that body mass index may not be as good an indicator of obesity in men as in women, an issue which has not been closely investigated.[22] The index could be the same in a subject who is fat and a subject who is heavily muscled. For further clarification we need more direct measurements of body fatness. Another explanation of the sex difference could be that gall stone disease is only associated to any great extent with morbid obesity. Gall stone prevalence in morbidly obese subjects who were scheduled for gastric bypass surgery was high in women and men.[23 24] As men have less body fat than women,[25] the proportion of men with sufficiently high body fat may be too low in a random population study to yield adequate numbers. It may be noted that men with body mass index beyond 30 show a trend towards higher gall stone prevalence in this study.

Obesity might also be defined as being present when an individual decides to go on a slimming diet. This factor was positively associated with gall stone disease in both sexes in the univariate analysis, and could be taken as evidence that gall stone disease among men, too, is associated with fatness. Another explanation could be that gall stones were caused by weight loss itself. During weight loss the saturation of gall bladder bile increases.[26] The high incidence of gall stone formation during weight loss after gastric bypass surgery[27] supports this, but it can be questioned whether gall stone formation under these conditions is a stable phenomenon, as stones, which were not treated, disappeared spontaneously shortly after weight stabilisation.[27] It is also noteworthy that no association between slimming treatments and gall stones among women was observed in this study when body mass index was taken into consideration.

Weight change over longer periods was not substantially associated with gall stone disease in this study, a finding which is supported by others.[1 7] The significant higher gall stone prevalence in women

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with large weight increase disappeared when body mass index was taken into account, showing that body mass index itself rather than weight changes is the important factor. In these calculations weight at age 25 was chosen as a baseline, which of course means that nothing can be said about the relationship between gall stones and weight changes before this age.

The demonstration of higher body mass index and a larger weight increase in those women aware of their disease could be due to changes in weight after the diagnosis of gall stones was made, but could also represent an example of diagnostic suspicion bias.[5 9]

PHYSICAL ACTIVITY

No significant association between the level of physical activity and gall stone disease was shown in this study. This confirms others' findings,[1 6 7] although one earlier study showed a relationship between gall stone disease and low physical activity in rural Caucasian women.[12] Low physical activity has been shown to be associated with low plasma high density lipoprotein cholesterol independently of body mass index and smoking.[14 15] The demonstration of the association between low plasma high density lipoprotein cholesterol and both high lithogenic index of bile[28] and occurrence of gall stones[29] could, therefore, support an association between low physical activity and gall stones. Current clinical results suggest that this association may exist, but it does not seem to be of much import.

SMOKING AND CONSUMPTION OF COFFEE

In this study smoking showed a significant association with gall stone disease among men when weight parameters were included in the multivariate analysis. A positive trend was seen among women. Two other studies did not find any relationship.[1 8] Layde[4] found a significant association in women, however, but – as in this study – no dose response relationship. Previous smoking was added to current smoking in the analysis, because we are dealing with the life prevalence of gall stone disease. Smoking is associated with low plasma high density lipoprotein cholesterol,[14 15] which is shown to be associated with gall stone disease.[29] The lack of any dose response relationship could be interpreted as meaning that smoking itself is not a risk factor but an indirect measure of some other risk factor. Coffee consumption was not significantly associated with gall stones. No other reports have dealt with this subject. Intake of coffee is related to changes in serum lipids[16] and may influence the enterohepatic circulation of bile acid. More evidence is needed on this but it is unlikely that any association with gall stone prevalence is substantial.

DIABETES MELLITUS

Diabetes was not significantly associated with gall stone disease in the present study. Former studies disagree, some finding an association,[2 8] whereas others do not.[1 3 30 31] These reports are either studies comprising clinically diagnosed gall stones or autopsy studies. Gall bladder function is impared among diabetics as compared with non-diabetics,[32–34] and it seems to be related to diabetic neuropathy.[34] Bile lithogenic index was higher in maturity onset diabetes as compared with non-diabetic individuals in one study,[35] but not in another.[36] Regulation of hyperglycaemia with insulin seems to raise the lithogenic index as compared with non-regulated hyperglycaemia.[37] Relationships therefore are complex, which may imply that only some diabetics are at risk. This may be the reason for finding no substantial association in this study. At least diabetes does not contribute substantially to the total prevalence of gall stone disease in a random population.

Obesity seems to be associated with gall stone disease at least in women but probably also in men. Physical activity, coffee consumption, and diabetes are not, or at least not substantially, associated with the prevalence of gall stone disease. Smoking is related to gall stone disease in men but not in women, and may be an indirect measure of some other risk factor.

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References

1 Friedman GD, Kannel WB, Dawber TR. The epidemiology of gallbladder disease: Observations in the Framingham study. *J Chronic Dis* 1966; **19:** 273–92.
2 Hanis CL, Ferrell RE, Tulloch BR, Schull WL. Gallbladder disease epidemiology in Mexican Americans in Starr County, Texas. *Am J Epidemiol* 1985; **122:** 820–9.
3 Honore LH. The lack of a positive association between symptomatic cholesterol cholelithiasis and clinical diabetes mellitus: A retrospective study. *J Chronic Dis* 1979; **33:** 465–9.
4 Layde PM, Vessey MP, Yeates D. Risk factors for gallbladder disease: A cohort study of young women attending family planning clinics. *J Epidemiol Comm Health* 1982; **36:** 274–8.

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5 van der Linden W. Some biological traits in female gallstone-disease patients. *Acta Chir Scand* 1961; [suppl 269].
6 Wheeler M, Hills LL, Laby B. Cholelithiasis: a clinical and dietary survey. *Gut* 1970; **11:** 430–7.
7 Scragg RKR, McMichael AJ, Baghurst PA. Diet alcohol and relative weight in gall stone disease: A case-control study. *Br Med J* 1984; **288:** 1113–9.
8 Diehl AK, Stern MP, Ostrower VS, Friedman PC. Prevalence of clinical gallbladder disease in Mexican-American, Anglo, and Black women. *South Med J* 1980; **73:** 438–43.
9 Jørgensen T. Prevalence of gallstones in a Danish population. *Am J Epidemiol* 1987; **126:** 912–21.
10 GREPCO. Prevalence of gallstone disease in an Italian adult female population. *Am J Epidemiol* 1984; **119:** 796–805.
11 Barbara L, Sama C, Labate AMM, *et al*. A population study on the prevalence of gall stone disease: the Sirmione study. *Hepatology* 1987; **7:** 913–7.
12 Williams CN, Johnston JL. Prevalence of gallstones and risk factors in Caucasian women in a rural Canadian community. *Can Med Assoc J* 1980; **120:** 664–8.
13 Janzon L, Aspelin P, Eriksson S, *et al*. Ultrasonographic screening for gallstone disease in middle-aged women. *Scand J Gastroenterol* 1985; **20:** 706–10.
14 Criqui MH, Wallace RB, Heiss G, Mishkel M, Schonfeld G, Jones GTL. Cigarette smoking and plasma high-density lipoprotein cholesterol. The lipid research clinics program prevalence study. *Circulation* 1980; **62** [Suppl IV]: 70–6.
15 Stamford BA, Matter S, Fell RD, Sady S, Cresanta MK, Papanek P. Cigarette smoking, physical activity, and alcohol consumption: Relationship to blood lipids and lipoproteins in premenopausal females. *Metabolism* 1984; **33:** 585–90.
16 Williams PT, Wood PD, Vranizan KM, Albers JJ, Garay SC, Taylor CB. Coffee intake and elevated cholesterol and apolipoprotein B levels in men. *JAMA* 1985; **253:** 1407–11.
17 Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959; **22:** 719–48.
18 Breslow NE, Day NE. *Statistical methods in cancer research. Vol 1 – The analysis of case-control studies*. Lyon: IARC, 1980.
19 Jørgensen T. Gallstones in a Danish population: Familial occurrence and social factors. *J Biosoc Sci* 1988; **20:** 111–20.
20 Jørgensen T. Gallstones in a Danish population: Fertility period, pregnancies, and exogenous female sex hormones. *Gut* 1988; **29:** 433–9.
21 Garn SM, LaVelle M, Rosenberg KR, Hawthorne VM. Maturational timing as a factor in female fatness and obesity. *Am J Clin Nutr* 1986; **43:** 879–83.
22 Sjostrom L, Kvist H, Lapidus L, Bengtsson C, Tylen U. Weight-height indices and adipose tissue distribution: Measurements and health consequences. In: Norgan NG, ed. *Human body composition and fat distribution*. Euro nut – report 8, 1985: 189–98.
23 Amaral JF, Thompson WR. Gallbladder disease in the morbidly obese. *Am J Surg* 1985; **149:** 551–7.
24 Thiet MD, Mittelstaedt CA, Herbst Jr CA, Buckwalter JA. Cholelithiasis in morbid obesity. South Med J 1984; **77:** 415–7.
25 Krotkiewski M, Bjorntorp P, Sjostrom L, Smith U. Impact of obesity on metabolism in men and women – importance of regional adipose tissue distribution. *J Clin Invest* 1983; **72:** 1150–62.
26 Lefkof IR, Marks JW, Schoenfield LJ. Diet in the formation and treatment of cholesterol gallstones. In: Cohen S, Soloway RD, eds. *Gallstones. Contemporary issues in gastroenterology*. New York: Churchill Livingstone, 1985: **4:** 114.
27 Wattchow DA, Hall JC, Whiting MJ, Bradley B, Iannos J, Watts JMcK. Prevalence and treatment of gall stones after gastric bypass surgery for morbid obesity. *Br Med J* 1983; **286:** 763.
28 Thornton JR, Heaton KW, MacFarlane DG. A relation between high-density-lipoprotein cholesterol and bile cholesterol saturation. *Br Med J* 1981; **283:** 1352–4.
29 Scragg RKR, Calvert GD, Oliver JR. Plasma lipids and insulin in gall stone disease: A case-control study. *Br Med J* 1984; **289:** 521–5.
30 Diehl AK, Elford J. Gallstone disease in diabetics: Analysis using multiple-cause mortality tables. *Public Health* 1981; **95:** 261–3.
31 Zahor Z, Sternby NH, Kagan A, Uemura K, Vanecek R, Vichert AM. Frequency of cholelithiasis in Prague and Malmo. An autopsy study. *Scand J Gastroenterol* 1974; **9:** 3–7.
32 Braverman DZ. The lack of effect of metoclopramide on gall-bladder volume and contraction in diabetic cholecystoparesis. *Am J Gastroenterol* 1986; **81:** 960–2.
33 Shreiner DP, Sarva RP, Van Thiel D, Yingvorpant N. Gallbladder function in diabetic patients. *J Nucl Med* 1986; **27:** 357–60.
34 Gitelson S, Schwartz A, Fraenkel M, Chowers I. Gallbladder dysfunction in diabetes mellitus. The diabetic neurogenic gall bladder. *Diabetes* 1963; **12:** 308–12.
35 Ponz de Leon M, Ferenderes R, Carulli N. Bile lipid composition and bile acid pool size in diabetes. *Dig Dis* 1978; **23:** 710–6.
36 Haber GB, Heaton KW. Lipid composition of bile in diabetics and obesity-matched controls. *Gut* 1979; **20:** 518–22.
37 Bennion LJ, Grundy SM. Effects of diabetes mellitus on cholesterol metabolism in man. *N Engl J Med* 1977; **296:** 1365–71.

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