Gut, 1991, 32, 316–320

Symptomatic and silent gall stones in the community

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Abstract

The prevalence of gall stone disease in a stratified random sample of 1896 British adults (72·2% of those approached) was established using real time ultrasound. The prevalence rose with age, except in women of 40–49 years, so that at 60–69 years, 22·4% of women and 11·5% of men had gall stones or had undergone cholecystectomy. The cholecystectomy rate of people with gall stone disease was higher in women than in men (43·5% *v* 24%, $p<0·05$). Very few subjects with gall stones had convincing biliary symptoms. In women, 10·4% had symptoms according to a questionnaire definition of biliary pain and 6·3% according to conventional history taking, while no men at all admitted to biliary pain. Nevertheless, cholecystectomy in men had nearly always been preceded by convincing biliary symptoms. The age at cholecystectomy was, on average, nine years less than the age at detection of silent gall stones in both sexes. It is concluded that either gall stones are especially prone to cause symptoms in younger people or that there are two kinds of cholelithiasis – symptomatic and silent. The lack of symptomatic gall stones in cross sectional surveys is probably due to their rapid diagnosis and treatment.

In the past, knowledge of gall stone prevalence has derived almost entirely from necropsy surveys, which is unsatisfactory because necropsy subjects are not representative of the living population. Population surveys are not practicable with cholecystography because of radiation exposure (though limited information was gained in this way in South Wales and Arizona in the early 1970s[1,2]) but have become safe and accurate with the advent of real time ultrasound. In the past few years ultrasound data on gall stone prevalence have been published from Italy,[3–6] Denmark,[7] Norway,[8] Japan,[9] Kashmir,[10] and the USA[11] but not from Britain, except in women aged 40–69 years.[12] In Sweden there have been small surveys of middle aged[13] and elderly[14] women. Only five surveys have involved a representative population of both sexes.[5,7–10]

These and other studies[15–19] have shown that gall bladder stones are asymptomatic in most people. Estimates of how often stones give rise to symptoms have varied, however, from under 10% to over 30%. This may be because definitions of biliary pain have varied and have not been based on clinical practice (it is universally agreed that gall stones do not cause flatulence, nausea, and other forms of dyspepsia).

Two of the aims of this study were to determine the prevalence of gall stone disease in a British population sample including men and younger women and to determine how often gall stones in the population are associated with convincing biliary symptoms.

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Accepted for publication
14 May 1990

Subjects and methods

A stratified random sample was drawn from patients on the lists of 19 general practitioners working at two health centres in East Bristol (where the population is almost entirely white). The size and composition of the sample were dictated by our wish to discover about 20 patients with gall stone disease in each of the three decades of men aged 40–69 years and each of the five decades of women aged 20–69 years so that useful age specific prevalence rates could be calculated for each decade. Younger and older people were not sampled for logistic reasons – younger ones because so many would have to be screened and older ones because we anticipated problems with eyesight, hearing, mobility, and transport to clinics. The initial sample had to be expanded twice because it was 'contaminated' by many incorrect entries on the family practitioner committee lists (people who had moved, were untraceable, had died, or had their birth date wrongly recorded).[20] Attempts to contact women aged 20–24 years were unrewarding since people of this age are so mobile, and after a few months it was decided to exclude them.

General practitioners were sent lists of the patients in our sample and asked to delete any they knew to be unavailable or unsuitable through physical or mental incapacity. Subjects were then sent letters signed by their own general practitioner which urged them to cooperate with a survey designed to throw light on the causes of gall stones using ultrasound scanning of the abdomen. A few days later a clerk telephoned the subject or, if telephone contact was impossible, a field worker visited their home to offer an appointment at a small local hospital. Non-attenders were telephoned or visited again. Most refusers were approached again after some months. Subjects were asked to fast for at least five hours before their appointment.

Ultrasonography was performed by one of two experienced radiographers with certificates in diagnostic ultrasound. A DSL 300 real time sector scanner with a 3·5 MHz probe was used in the supine, left lateral decubitus, and erect positions. Findings were classified as follows:

(1) Gall bladder normal;

(2) Gall bladder absent and scar of cholecystectomy present;

(3) Gall stones;

(4) Technically unsatisfactory.

Unsatisfactory scans were repeated on another day, if necessary, at the local district general hospital, so that a final conclusion about gall bladder status was always reached. Gall stones were diagnosed as mobile echoes in the gall

bladder lumen, usually throwing a shadow. Polyps and sludge were rarely seen and were ignored. Three subjects who had undergone cholecystectomy did not know the indication for it. All the others stated it was because of gall stones.

To determine the proportion of subjects in whom gall stones were causing symptoms, an experienced gastroenterologist (KWH or RAM) asked a series of questions before the subjects underwent ultrasonography:

(1) 'In the past year have you experienced any pain in the tummy or abdomen (other than with your monthly period)?' If yes

(2) 'Has the pain usually been in the upper part of the abdomen (above the umbilicus or belly button)?' If yes

(3) 'Has the pain occurred in distinct attacks or bouts each lasting at least half an hour?' If yes

(4) 'Has this pain forced you to stop what you were doing and lie down or take a pain killer?'

If the answer to the last question was 'Yes' the doctor took a brief informal history, asking in particular about clear cut, well remembered episodes of pain, and then wrote down his opinion as to whether this was biliary pain or not. The rationale for this sequence of questions was that, in the pioneering Italian studies,[3-5] biliary pain was defined as upper abdominal pain (central or right sided) lasting more than half an hour, but the specificity and predictive value of this pain for the presence of gall stones turned out to be very low. We hoped that stricter criteria would enable us to reach a definition of biliary pain with a better predictive value.

The survey began in October 1987 and was completed in March 1989.

Because convincing biliary symptoms were found to be completely absent in men with gall stones we investigated the indications for and results of the operation in men with previous cholecystectomy. To this end we examined the hospital discharge summaries and sent subjects a brief questionnaire on similar lines to the above, but relating to the 12 months before the operation, and including the question 'Did the pains stop after you had your operation?'

Hypotheses were tested using χ^2, Fisher's exact probability test, or Student's t test as appropriate; $p<0.05$ being taken as significant.

Results

Of 2627 subjects invited, 1896 attended – a response rate of 72·2%. The subjects invited represented 10% of the people registered as patients of the 19 general practitioners, but the sampling fraction varied from 3·6% of women aged 60–69 years to 15·5% of men aged 40–49 years.

Gall bladder disease was detected in 143 subjects – 51 who had undergone cholecystectomy and 92 who were found to have gall stones. Only three of the latter knew they had stones. Another three subjects claimed to have been diagnosed as having gall stones but had normal gall bladders on ultrasound.

The prevalence of gall stones, cholecystectomy, and gall stone disease – that is, combined gall stones and cholecystectomy – at different ages is shown in Table I. Prevalence rises with age in both sexes except that it is no higher in women in their 40s than in women in their 30s.

Figure 1 shows how the Bristol study compares with the 12 other published studies with regard to the number of subjects examined, the response rate, and the cholecystectomy rate. The Bristol study is roughly average in all respects. The cholecystectomy rate was nearly twice as high in women as in men, irrespective of age ($p<0.05$). The same was found in Copenhagen[7] and in US Mexicans,[11] whereas in Rome and Sirmione[3-5] the cholecystectomy rate was similar in the two sexes.

Figures 2 and 3 show how the age specific prevalence of gall stones in men and women compares between Bristol and the seven other European centres that have published their results from ultrasonography. The Bristol prevalence is similar to that in the other centres at the two youngest ages in women and at the youngest age in men but seems to be lower in the older age groups. Compared with women in Oxford,[12] the Bristol prevalence is significantly lower for the two decades 40–49 and 50–59 years ($p<0.001$ and <0.05 respectively).

The sensitivity, specificity, and positive predictive value of upper abdominal pain for the detection of gall stones are shown in Table II. In women, the predictive value of pain increased as the definition became more restrictive, especially at the level of conventional history taking. In men upper abdominal pain had no predictive value because no man with gall stones admitted to having this pain in attacks each lasting at least half an hour. The difference between men and women with gall stones, with regard to the proportion who admitted to attacks of pain lasting at least half an hour and severe enough to make the subject lie down or take an analgesic, was statistically significant (0 of 44 *v* 5 of 48, $p<0.05$). One man and two women with normal

TABLE I *Prevalence of gall stones, cholecystectomy, and gall stone disease in men and women at different ages (%)*

	Men				*Women*			
Age (yrs)	*No surveyed*	*Gall stones*	*Previous cholecystectomy*	*Gall stone disease*	*No surveyed*	*Gall stones*	*Previous cholecystectomy*	*Gall stone disease*
25–29					305	8 (2·62)	4 (1·31)	12 (3·93)
30–39					328	11 (3·35)	10 (3·05)	21 (6·40)
40–49	430	16 (3·72)	4 (0·93)	20 (4·65)	199	8 (4·02)	5 (2·51)	13 (6·53)
50–59	226	12 (5·29)	5 (2·20)	17 (7·49)	141	11 (7·80)	9 (6·38)	20 (14·18)
60–69	182	16 (8·79)	5 (2·75)	21 (11·54)	85	10 (11·76)	9 (10·59)	19 (22·35)
All ages	838	44	14	58	1058	48	37	85

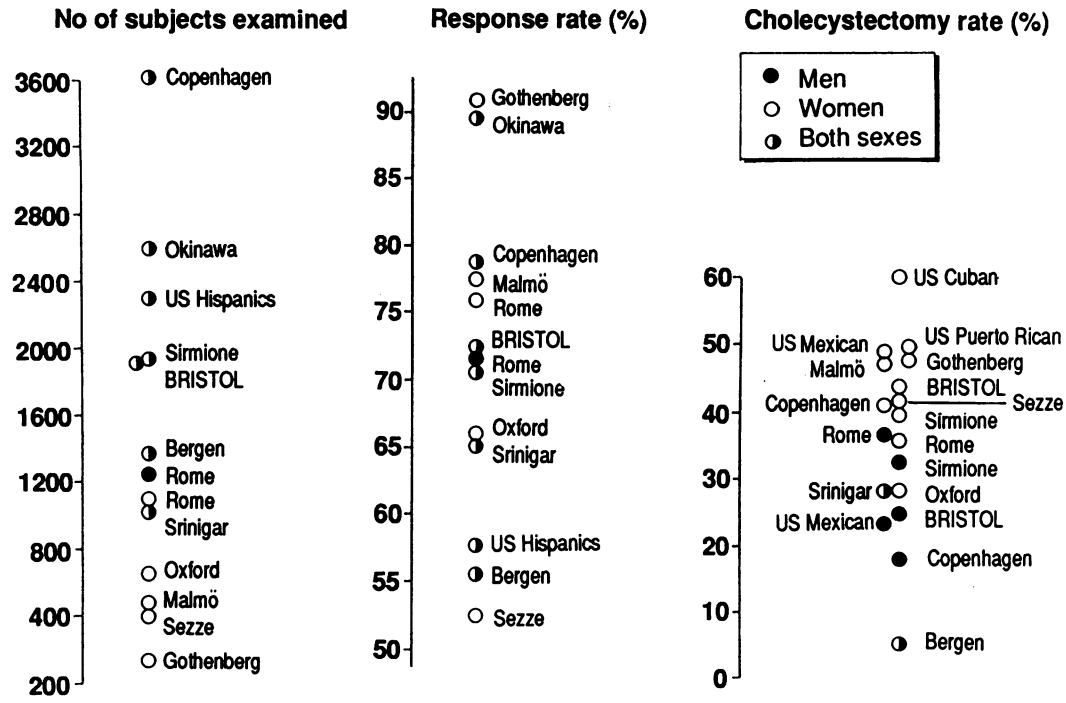

Figure 1: Summary data from the 12 ultrasonographic studies of gall stones in the general population hitherto published, plus the present one. Response rate is number of subjects examined divided by number of subjects invited. Cholecystectomy rate is number of subjects who had undergone cholecystectomy divided by total number with gall stone disease (cholecystectomy and gall stones combined) in the surveyed population.

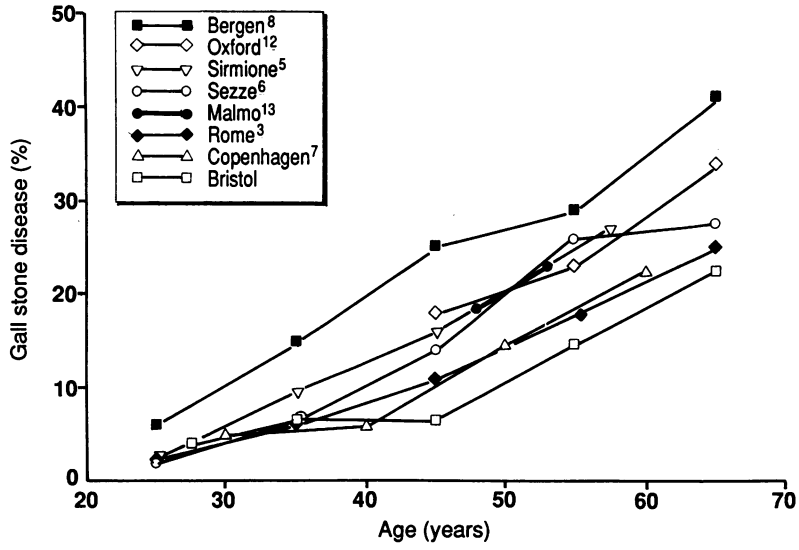

Figure 2: Age specific prevalence of gall stone disease (gall stones and cholecystectomy combined) in women in all European ultrasonographic studies including the present one.

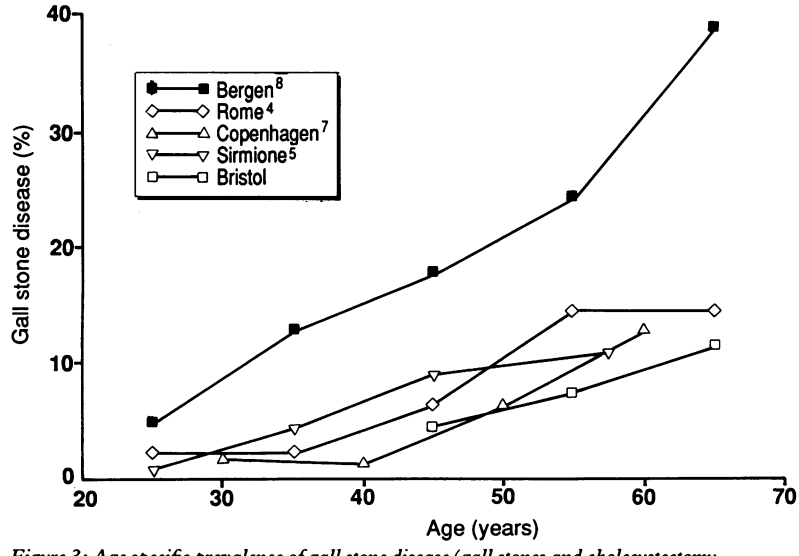

Figure 3: Age specific prevalence of gall stone disease (gall stones and cholecystectomy combined) in men in all European ultrasonographic studies including the present one.

gall bladders gave a convincing history of biliary 'colic' in the previous year, as did one woman who had undergone cholecystectomy.

Information about preoperative symptoms and gall bladder pathology was obtained in all 14 men who had undergone cholecystectomy. In one man silent gall stones were noticed incidentally during nephrectomy and the gall bladder was removed prophylactically. In the others there was a classic indication – typical biliary colic (occasional attacks of severe pain, usually with vomiting or radiation to the back), acute cholecystitis, or biliary obstruction. In one man the pains were less typical but, as in the others, his pains disappeared postoperatively.

The age at operation in cholecystectomised subjects was nine years lower than the age at ultrasonographic detection in subjects diagnosed in the survey (mean (SEM) – men 45·3 (2·9) *v* 54·2 (1·4) years, $p<0·05$; women 36·1 (2·0) *v* 45·2 (1·9) years, $p<0·01$).

Discussion

This is the first report of the prevalence of gall stones in a living adult population in this country that has included men and covered most age groups of women. The results should not be extrapolated to the whole of Britain because there may be regional variations. In a necropsy study there was a twofold variation in gall stone prevalence among nine towns of England and Wales,[21] but this needs to be confirmed by studies in the living population. The age and sex specific data for Bristol are close to the average English/Welsh necropsy data but, in women, tend to be lower than the ultrasonographic data from Oxford. These variations are unexplained but environmental factors are probably important in the aetiology of gall stones.[22]

This study confirms that most gall stones in the population are asymptomatic, especially in men. Indeed, not a single man with gall stones admitted to biliary type pain in the previous

TABLE II *Sensitivity, specificity, and positive predictive value of upper abdominal pain in the previous year for the detection of gall stones*

Symptom	Sensitivity* (%)		Specificity† (%)		Positive predictive value‡ (%)	
	M	W	M	W	M	W
Upper abdominal pain of any kind	13·6	20·8	89·3	91·1	6·7	10·3
Pain in distinct attacks each lasting longer than half an hour	0	14·6	96·5	94·8	0	12·1
Pain as above and forcing subject to lie down or take analgesic	0	10·4	99·0	97·9	0	20·0
Pain as above and in well remembered episodes	0	6·3	99·9	99·8	0	60·0

* Percentage of subjects with gall stones who had pain as defined.
† Percentage of subjects without gall stones who did not have pain.
‡ Proportion of subjects with pain as defined who had gall stones.
Subjects who had undergone cholecystectomy are excluded.
M=men; W=women.

year. Even in women the predictive value of upper abdominal pain for gall stones was poor but it improved greatly when a medical history that concentrated on clear cut, well remembered episodes was taken. In the Rome study only two of 65 men with gall stones admitted to upper abdominal pains lasting more than 30 minutes and severe enough to necessitate lying down or taking analgesics, compared with 12 of 66 women ($p<0·01$).[3 4] The same sex difference was present in Bristol and was recorded in Copenhagen but not commented on.[23]

The greater propensity of women to harbour symptomatic stones could be due to symptoms being less severe in them than in men, to greater tolerance of pain, or to reluctance to 'trouble the doctor'. Previous studies have failed to identify any feature of gall stones that favours the development of symptoms, such as stone size or number,[16 24 25] except that floating stones tend to be associated with prolonged attacks of pain.[16] It is not known whether floating stones are less common in women than in men. There is no evidence that the gall bladder contracts less strongly in women than in men, except during pregnancy.[26] The greater proportion of cholecystectomies in women could be due to a greater tendency of gall stones to cause symptoms in women but a more likely factor is diagnostic bias, doctors having a higher index of suspicion for gall bladder disease in women than in men.

Cholecystectomy rates in people with gall stone disease of 43% in women and 24% in men may seem surprisingly high when so few unoperated subjects had symptoms. The probable explanation is that when symptoms occur they are usually severe and are quickly treated so that at any one time few symptomatic cases are present in the community. This is supported by the finding that the men who had undergone cholecystectomy, with one or two exceptions, had severe symptoms preoperatively and clearly deserved surgery.

Occasional stone-free subjects admitted to convincing 'biliary pains'. Possible explanations include gall stones too small to be detected by ultrasound (the lower limit for detection probably being 1–2 mm[27 28]) spontaneous passage of stones before the examination, and mimicry by another condition such as acute pancreatitis or intestinal spasm. The last explanation is perhaps the most likely, since irritable bowel syndrome is so common and does mislead doctors into diagnosing biliary disease.[29]

A noteworthy finding was that in those who had undergone cholecystectomy the age at the time of the operation was substantially less than the age at the time of ultrasonography in people discovered to have gall stones. In the former, the stones were mostly symptomatic while in the latter they were mostly asymptomatic. Thus, in this population symptoms seem to be associated with youth. There are several possible explanations. One is that, in younger people, gall stones are smaller and so more likely to attempt passage out of the gall bladder. Certainly, gall stones usually grow as time passes.[30–32] There is, however, no difference in size between symptomatic and asymptomatic stones, either at necropsy[24] or in the living population.[23 25] A second possible explanation is that, irrespective of size, gall stones are more likely to cause symptoms in younger people, perhaps because they have stronger gall bladder contractions than older people. A third explanation is that our findings simply reflect the tendency of gall stone subjects to divide into two groups, those who get biliary pain and those who do not – a tendency which has been established in studies of the natural history of untreated gall stones.[16 19 33] In a cross sectional survey, those who get pain have been diagnosed and treated and appear as postcholecystectomy patients. Their operations have been done in past years and so, necessarily, at a younger age than the age of those people whose silent gall stones have been undisturbed, perhaps for many years, until discovered by the survey. To discover the true explanation requires knowledge of when gall stones form and when symptoms occur. This knowledge can come only from a prospective study in which, over many years, a large cohort of stone-free people is repeatedly subjected to ultrasonography and questioning about biliary symptoms.

This study depended on the help and advice of many people. We are especially indebted to David Bainton, Don Simpson, Alan Sanders, Julie Morris, and Peter Elwood who helped to launch it; to Judith Barber, Eileen Coleman, Janet Lloyd, Sue Moss, Subrata Ghosh, Jean Fairman, Jacqui Ryan, Eric Welsby, and Ben Fudge who helped to run it; and to the general practitioners of Fishponds and St George Health Centres who eased our path and allowed us access to their patients. Financial support was received from the South West Regional Health Authority, the Kellogg Company of Great Britain, and the British Digestive Foundation.

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