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ASPECTS ON
DIVERTICULAR DISEASE

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ABSTRACT

Objective: The aims of this thesis were to evaluate the influence of ethnicity and other socio-demographic factors on the rate of diverticular disease (DD) (Paper I), to compare findings specific for DD and acceptance of CT Colonography (CTC) and conventional Colonoscopy (CC) in patients examined after diverticulitis (AD) (Paper II), to evaluate the value of antibiotics in conservative treatment of patients with mild AD (Paper III) and to study patients with diverticular fistulas to the female genital tract (Paper IV).

Methods: In paper I, Swedish national registers with information about health and socio-demographic indicators were used to study ethnicity and other socio-demographic factors and the risk of hospital admission due to DD in a national cohort (4.4 millions) followed prospectively over a period of ten years. Paper II was a prospective comparative study of 57 patients examined with CTC and CC respectively. Paper III was an observational study of 311 patients; all treated for AD and included mailed questionnaires. Paper IV reviewed evaluation, management, morbidity and outcome in 60 women treated for DD fistulas to the genital tract.

Results: In all 25,123 patients were hospitalized because of DD during 1991-2000. The risk ratio (RR) of DD, after adjustment for age, sex and socio-economic indicators, was lower in non-western immigrants (RRs 0.5-0.7) compared with indigenous patients. The risk increased with time after settlement in Sweden. Women had a higher risk compared with men (RR 1.50, CI 95% 1.46-1.54, p<0.001) and the difference increased with age. (Paper I) DD was found in 96 % of patients at CTC and in 90 % at colonoscopy. Eight suspected polyps sized ≥5 mm were found in six patients. Patients experienced colonoscopy more discomforting (p<0.03), painful (p<0.001) and difficult (p<0.01) than CTC. Seventy-four % of patients preferred CTC. (Paper II) During first hospitalisation, patients treated with antibiotics had a more pronounced inflammation compared with patients treated without antibiotics. If initially treated with antibiotics three patients (3 %) failed to respond to medical management and had surgery. Seven patients (4 %) treated without antibiotics failed to respond and antibiotics were then added. In all, 29 % of patients treated with antibiotics had further events (recurrent AD and/or subsequent surgery) during FU (mean 30 months, range 16-45), compared with 28 % (N.S.), if treated without antibiotics. In a multivariate analysis, antibiotics did not influence the risk for a further event (OR 1.03, CI 95 % 0.61-1.74). (Paper III) The most common presenting symptoms in women with a DD fistula to the genital tract were vaginal discharge of faeces or gas (95 %) and 75 % of them had previously had a hysterectomy. 57/60 patients had surgery, sigmoid resection and anastomosis was performed in 51 and a Hartmann's procedure with colostomy in six patients. In all, 26 % of the patients experienced morbidity after surgery, including anastomotic dehiscence (n=4) and ureteric injury (n=3). All operated patients were cured from their fistulas and outcome was satisfactory in 86 %. (Paper IV)

Conclusions: DD appears to be an acquired disorder and acculturation to a Western lifestyle has an impact on the risk for DD. Potential socio-demographic confounders, such as socio-economic status, residency and housing situation do not influence the risk. The diagnostic findings of CTC are comparable to colonoscopy in patients investigated after AD. CTC is less discomforting and preferred by a majority of patients. Thus, CTC seems to be a good alternative in the follow-up of patients after AD. To omit antibiotics in the treatment of mild AD appears safe and does not influence the rate of further events. DD fistulas to the female genital tract mostly occur in elderly patients with a prior hysterectomy. Sigmoid resection and primary anastomosis is done safely in the majority of patients.

LIST OF PUBLICATIONS

I. Diverticular Disease and Migration. The Influence of Acculturation to a Western Lifestyle on Diverticular Disease.
Hjern F, Johansson C, Mellgren A, Baxter NN, Hjern A.
Alimentary Pharmacology and Therapeutics, 2006:23, 797-805.

II. CT Colonography vs. Colonoscopy in the Follow up of Patients after Diverticulitis
- A Prospective Comparative Study.
Hjern F, Jonas E, Holmström B, Josephson T, Mellgren A, Johansson C.
Submitted.

III. Conservative Treatment of Acute Colonic Diverticulitis
- Are antibiotics always mandatory?
Hjern F, Josephson T, Altman D, Holmström B, Mellgren A, Pollack J, Johansson C.
Scandinavian Journal of Gastroenterology, In press.

IV. Management of Diverticular Fistulas to the Female Genital Tract.
Hjern F, Goldberg SM, Johansson C, Parker S, Mellgren A.
Colorectal Disease, In press.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AD   Acute Diverticulitis
BE   Barium Enema
CC   Conventional Colonoscopy
CRP   C-reactive Protein
CT   Computerised Tomography
CTC   Computerised Tomographic Colonography
DD   Diverticular Disease
DF   Diverticular Fistula
FU   Follow Up
IBD   Inflammatory Bowel Disease
ICD   International Classification of Diseases
I.V.   Intravenous
mSv   milliSievert
N.S.   Not Statistically Significant
OR   Odds Ratio
RCT   Randomised Controlled Trial
RR   Risk Ratio
SES   Socio Economic Status
SIR   Standardised Incidence Ratio
WBC   White Blood Cell Count
2D   Two Dimensional
3D   Three Dimensional

1   PREFACE

The clinical spectrum of diverticular disease (DD) varies from an asymptomatic condition, incidentally found when the colon is investigated for any reason, to symptomatic disease with potentially lethal complications. Diverticular disease is more common in the industrialised world compared with developing countries (Painter and Burkitt, 1971). Its incidence increases with age. Health expenses are significant and DD was recently ranked the fifth most costly digestive disease in the USA (Sandler et al., 2002). The rate of hospital admissions due to DD increased 23 % in Sweden between 1992 and 2002 (Centre for Epidemiology, 2002).

There are no generally accepted diagnostic criteria for DD. Usually, examination of the colon supports the clinical diagnosis and is performed either with a barium enema (BE) or with colonoscopy (CC). (Figure 1 a and b)

Figure 1. Diverticula (arrows) demonstrated on:

a) Barium Enema (X-ray)
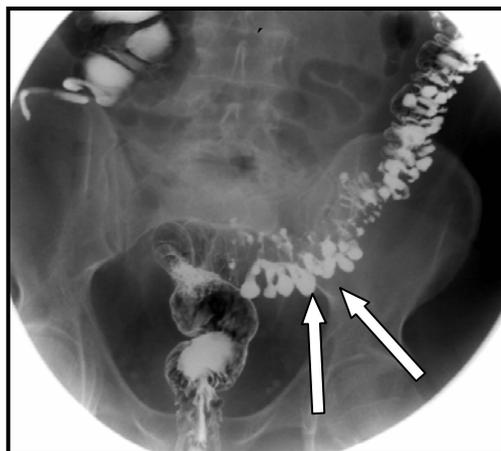
b) Intraluminal photo (Colonoscopy).
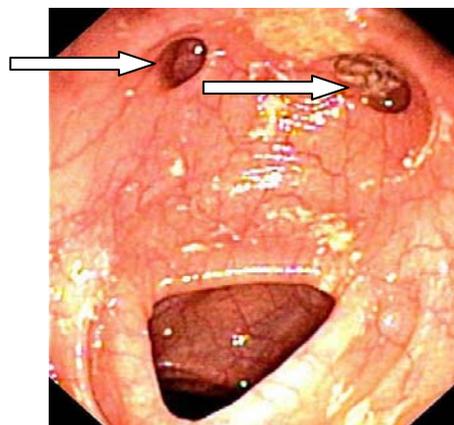
Most patients with DD are asymptomatic, but 10-25 % will develop complications, most commonly diverticulitis, an inflammation originating from one or more diverticula (Parks and Connell, 1969, Painter and Burkitt, 1971, Ferzoco et al., 1998, Stollman and Raskin, 2004). The inflammation is mostly mild, but complications sometimes occur, such as formation of abscesses, perforations, fistulas or obstructions.

This thesis is based on four papers, which study DD from epidemiological (Paper I), methodological (Paper II) and clinical (Paper III and IV) aspects (Table 1).

Table 1. Overview of the studies in the thesis.

Epidemiological Study	
I	Diverticular Disease and Migration. The Influence of Acculturation to a Western Lifestyle on Diverticular Disease
Methodological Study	
II	CT Colonography vs. Colonoscopy in the Follow up of Patients after Diverticulitis - A Prospective Comparative Study
Clinical Observational Studies	
III	Conservative Treatment of Acute Colonic Diverticulitis -Are antibiotics always mandatory?
IV	Management of Diverticular Fistulas to the Female Genital Tract

In **Paper I**, Swedish national registers, with information about health and socio-demographic indicators, were used to study ethnicity, sex, age, socio-economic status, housing, urban residency and the risk of hospital admission because of DD, in a prospectively followed national cohort over ten years.

In **Paper II,** patients were studied after Acute Diverticulitis (AD) examined with both CTC**,** a novel method of colon imaging, and CC, in order to compare DD specific findings and patient acceptance.

In **Paper III** the value of antibiotics in the conservative treatment of patients with mild AD was investigated.

Paper IV, finally, studied the management of patients with diverticular fistulas from the colon to the female genital tract.

2 BACKGROUND

2.1 ANATOMY AND PHYSIOLOGY

The colon wall consists of the mucosa surrounded by a submucosa, a muscularis mucosae and a muscularis propria. On the outer surface of the muscularis propria there are three interrupted bands of longitudinal muscle, taeniae coli, and the serosa. The tensile strength of the wall in the colon is provided by collagen. The ability to recoil after transient stretching is provided by elastic fibres, consisting of elastin (Rubin and Farber, 1988).

The arterial blood supply to the colon comes from the marginal artery along the mesenteric border where small branches, vasa recti, penetrate the circular muscle layer at the edge of the tenia and continue in the submucosa. The veins, lymphatic vessels and nodes follow the corresponding arteries (Gordon and Nivatvongs, 1999).

The colon is innervated by the sympathetic and parasympathetic systems, and the nerve distribution follows the distribution of the arteries. The peristalsis is stimulated by the parasympathetic nerves and is inhibited by sympathetic nerves (Gordon and Nivatvongs, 1999). The enteric nervous system plays a major role in the regulation of secretion, motility, activation of the immune system and regulation of inflammatory response. The intrinsic nervous system consists of a number of interconnected plexa. The Auerbach`s plexa are located between the longitudinal and circular muscle layers, and the Meissner`s plexa in the submucosa (Maximov and Bloom, 1949, Gordon and Nivatvongs, 1999).

The major functions of the colon are propulsion, storage and absorption of digested material. It absorbs mainly water and electrolytes. The propulsion and storage are the result of complex and poorly understood patterns of motility (Gordon and Nivatvongs, 1999). The colon motility can be divided in three different types:

1) **Segmental contractions** are the most commonly observed pattern and are simultaneous contractions of longitudinal and circular musculature that isolate short segments of the colon.

2) **Retrograde movements** originate in the transverse colon and travel towards the caecum.

3) **Mass movements** which are antegrade propulsive waves involving a long segment of colon and occur about three to four times daily.

Many factors affect motility, among them exercise, emotions, mechanical distension. Non-digestible polysaccharides, cellulose derivates and fatty acids have a greater effect on the motility than carbohydrate or protein meals (Schwartz, 1999).

2.2 DEFINITIONS

Diverticular disease (DD) is poorly defined in the literature. The presence of diverticula in the colon is called **diverticulosis** and is an acquired herniation of the mucosa through the muscular layers of the bowel wall.

DD is used to describe diverticula associated with symptoms of disease (Kohler et al., 1999, Simpson and Spiller, 2004). These symptoms commonly include abdominal pain and alteration in bowel habits. DD may be complicated by inflammation or haemorrhage.

Inflammation around diverticula is called **diverticulitis**, and its complications (perforation, abscess formation, fistula and obstruction) are included under the heading of DD.

Sometimes, especially in American literature, DD is used as a general term for both diverticulosis and diverticulitis (Arfwidsson, 1964, Rubin and Farber, 1988). A "prediverticular state" of mucosal out-pouching, still restricted to the muscular wall has been described (Spriggs and Marxer, 1925, Arfwidsson, 1964, Whiteway, 1985). A useful categorisation, based on radiological criteria, was made by Mendeloff (1986) and defined five types of DD.(Table 2).

Table 2. Types of diverticular disease based on radiological criteria (Mendeloff, 1986).

Prediverticulosis
Elastosis of taeniae coli
Mychosis (thickened muscular layer)
Diverticula still in bowel wall, not protruding
Diverticulosis, multiple (>2)
Simple massed diverticulosis
Diverticulosis of the right colon
Diverticulosis of the left colon and/or the sigmoid
With spasm
With history of irritable bowel syndrome
Diverticulosis, solitary
Of the right colon and/or caecum
Of the sigmoid giant type
Diverticulitis
With local inflammation
With generalised peritonitis and/or perforation
With penetration into adjacent structures; fistula formation
Generalised diverticulosis of small and large intestine

2.3 HISTORY

In the 18th century, the French surgeon Alexandre de Littre (Lauschke et al., 1999) was the first to describe diverticula as a pathologic entity. A detailed description of a diverticulum, as herniation of the colonic mucosa through gaps in the colonic wall, was given by another French surgeon, Jean Cruveilhier, from autopsy specimens in 1849. Haberschon described the thickening of the muscularis propria layer in the colonic wall in 1857. Graser (1899) and Beer (1904) were the first to point out the potential danger of the presence of diverticula and introduced the term peri-diverticulitis to describe the

relationship between lower abdominal pain, tenderness and colonic DD (Jun and Stollman, 2002). Graser also postulated that the point of weakness in the bowel wall that could promote protrusion of mucosa through the bowel wall was the penetration of the vasa recta (Jun and Stollman, 2002). In 1907 William Mayo reported his experience with diverticulitis, in which most cases were mild and resolved without operation (Stollman and Raskin, 1999).

2.4 EPIDEMIOLOGY

2.4.1 Incidence

The true incidence of DD is difficult to determine. Studies performed on findings of diverticula on x-rays, from subjects with miscellaneous gastrointestinal symptoms, must be clearly separated from studies performed to evaluate the occurrence of DD, mostly based on hospital discharge registers. However, no decisive physical signs exist and symptoms are neither sensitive nor specific. Furthermore, the incidence varies significantly in different studies from different parts of the world (Kyle et al., 1967) (Mendeloff, 1986).

There are indications that the prevalence of DD is increasing over time. In reports of autopsy and BE series, between 1910 and 1930, rates of 2-10 % were reported, but these rose significantly during the following decades (Painter and Burkitt, 1971, Parks, 1975).

Hospital discharge data are sometimes used to describe the prevalence of symptomatic DD, but do not include patients with mild symptoms, treated on an out-patient basis.

A study of hospital admissions in England found that between 1989/1990 and 1999/2000, the annual age-standardised hospital admission rates for DD increased by 16 % for males and 12 % for females (Kang et al., 2003).

The age standardised rates of hospital admissions because of DD in Sweden increased 23% from 1992 to 2002 and are presented in Figure 2 (Statistics Sweden, 1982, Centre for Epidemiology, 2002).

The life time risk of developing diverticulitis in subjects found to have diverticula has been estimated to be 10-25 % with an annual risk of 2% (Painter and Burkitt, 1971, Parks, 1975, Wong et al., 2000).

The prevalence of emergency surgery among patients admitted for DD has been estimated to be 10-30 % (Haglund et al., 1979, Makela et al., 1998, Ambrosetti, 2002). Reports of the incidence of DD and perforated diverticulitis based on hospital admission data are summarised in table 3.

Figure 2. Age-standardised rates of hospital admissions for DD in Sweden 1992 and 2002. (Statistics Sweden, 1982, Centre for Epidemiology, 2002)
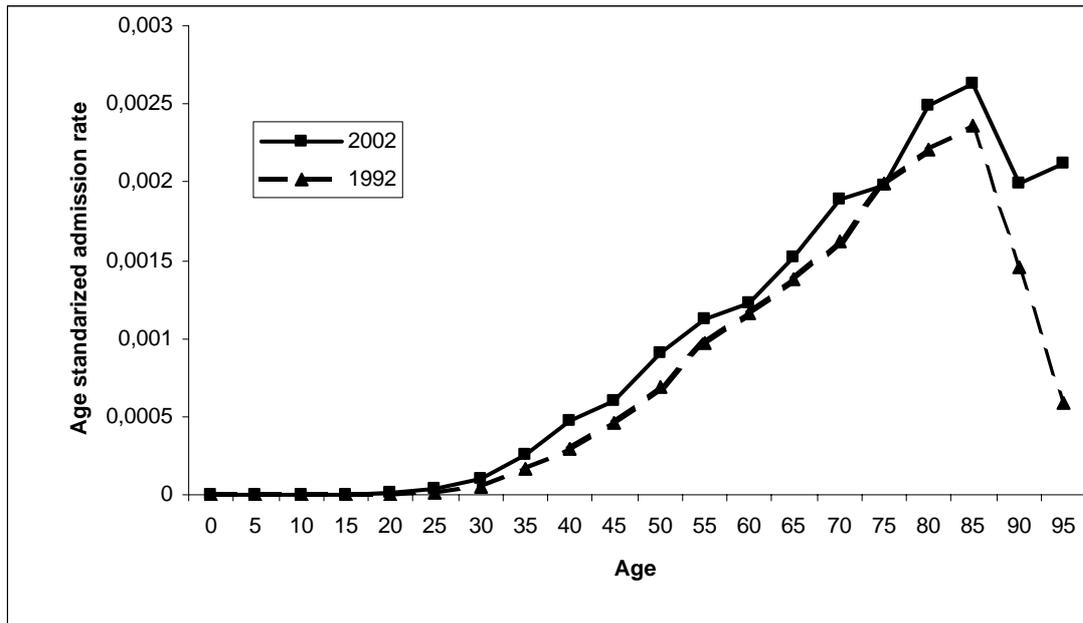
Table 3. Incidence of DD in various locations in Europe based on hospital admissions.

Reference, year	Incidence per 100,000/year	Geographic location, time period
Diverticular disease:		
Kyle and Davidson (1975)	23.5	North East Scotland 1968-71
Hjern (unpublished data)	53	Sweden 1992
Hjern (unpublished data)	65	Sweden 2002
Kang et al. (2003)	28	England 1999-2000
Perforated diverticulitis:		
Hart et al. (2003)	4	Norfolk, England, 1995-97
Makela et al. (2002)	3.8	Northern Finland, 1996

2.4.2   Age and sex distribution

Diverticular disease increases with age. The prevalence of asymptomatic DD in the general population, evaluated in a small series of symptom-free volunteers in Oxford, was 19 % in subjects 40-59 years, 29 % in subjects 60-79 years and 42 % in subjects about 80 years of age (Manousos et al., 1967).

There appears to be no difference in prevalence of diverticulosis among men and women (Manousos et al., 1967, Lee 1986, Jun and Stollman, 2002), but according to hospital admissions, the incidence of symptomatic DD is higher among women than

men (Kyle, 1975, Kang, 2003).´The female/male ratio is usually reported 1.5: /1 and with increasing age the female predominance is even more pronounced.

2.4.3   Geographical distribution

As DD is a relatively frequent in the Western world, it is uncommon in developing countries. This has been shown in prevalence studies, mainly based on BE examinations and autopsies performed in the mid 20th century. Diverticular disease was almost absent in rural African communities in Kenya, Nigeria, Ghana, Zaire, and South Africa (Kyle et al., 1967, Painter and Burkitt, 1971, Calder, 1979, Segal, 1988). Studies in USA, Europe and Australia have indicated a much higher prevalence in these westernised communities implicating that there was a close relationship between the lifestyle in a country and the incidence of DD (Painter and Burkitt, 1971, Kyle and Davidson, 1975, Kang et al., 2003).

Moreover, the incidence of DD can vary in ethnic groups within a given country (Kang et al., 2004, Loffeld, 2005). In an autopsy study of Japanese people, who migrated to Hawaii and adopted a Western lifestyle, diverticula were found in 52 %, compared with 0.5-1 % in Japan around the same time (Stemmermann and Yatani, 1973). In a retrospective evaluation of BE´s performed over five years in two hospitals in Israel (1979 to 1984), colon diverticula were found in 14.2 %. The prevalence among the mostly urban living Ashkenazi Jews was 19.7 %, compared with 16 % in Sephardi and Oriental Jews and 9.5 % in rural living Arabs (Levy et al., 1977, Levy et al., 1985).

2.4.4   Risk factors

Painter and Burkitt (1971) introduced the term "Westernisation" to describe lifestyle factors that alter the incidence of DD and they suggested a low content of dietary fibres being the key component. This hypothesis has then been supported by experimental, epidemiological, and treatment studies (Brodribb, 1977, Fisher et al., 1985, Manousos et al., 1985, Aldoori et al., 1994).

Moreover, different fibre types and the risk of DD was investigated in a prospective cohort study of 48 000 men. Fibres from fruit and vegetables appeared to be more protective than cereals (Aldoori et al., 1998). Other studies on the same cohort have found that physical activity was also protective, but high intake of red meat and fat increased the risk of DD. No relationships regarding alcohol intake, smoking or intake of caffeine and the risk of DD were found (Aldoori et al., 1995a, b).

2.4.5   Association with colon cancer

Similar epidemiological characteristics suggest a common aetiology for colon cancer and DD. Instead, in a study by Stefansson et al. (1993) an increased risk of left sided colon cancer was found both overall (SIR = 1.8; 95% CI 1.1-2.7) and consistently in men and women as well as in different age groups. These findings suggest a causal relationship between colon cancer and DD, possibly as a result of chronic inflammation (Stefansson et al. 1993, 1995, 2004).

2.5 AETIOLOGY AND PATHOGENESIS

2.5.1 Diverticular disease

Even though the specific cause of DD is not clearly defined, it is believed to be a disorder of bowel motility and structure (Golder et al., 2003). The elastin content of the taeniae coli is increased in patients with diverticula (Whiteway, 1985). Increased stiffness of the taeniae prevents the muscle layer from relaxing, which tends to produce intraluminal obstructive segments. The term "mychosis" describes the thickening of the circular muscular layer, shortening of taeniae coli and luminal narrowing (Whiteway and Morson, 1985, Mendeloff, 1986, Makela et al., 1998). The individual muscle cell nuclei in both the taeniae and the circular muscle layers are enlarged and these nuclei are found less frequently per area. Therefore the thickened sigmoid musculature in patients with DD can be designated hypertrophic (Arfwidsson, 1964).

With time, the inability of the circular muscle layer to relax promotes the protrusion of mucosa through connective tissue clefts in the circular muscle layer, sites where the vasa recti perforate, thus forming diverticular sacs (Figure 3). They are sometimes referred to as "false" diverticula as no muscular layer is included, only the mucosal and the serosal layers. Diverticula vary from solitary findings to many hundreds. They are typically 5-10 mm in diameter but can exceed 2 cm (Stollman and Raskin, 2004). The number and location of diverticula has no relationship with the severity of symptoms or complications.

Diverticula in the colon usually involve the sigmoid colon (>90 %), can occur in other locations, mostly in the descending colon, but also in other parts of the colon. Diverticula in the right colon occur more commonly in Japan and other parts of Asia (Lee, 1986, Miura et al., 2000).

Patients with diverticula have unusually high intraluminal pressure produced by increased motor activity causing the intestinal lumen to be divided into small, closed off segments (Arfwidsson, 1964). (Figure 4)

The decreased tensile strength of muscle fibres of the colon may explain the increase in diverticula formation with increasing age (Smith, 1986).

8

Figure 3. Formation of diverticula by protrusion of mucosa through holes in the muscularis propra, sites where the vasa recti penetrate.
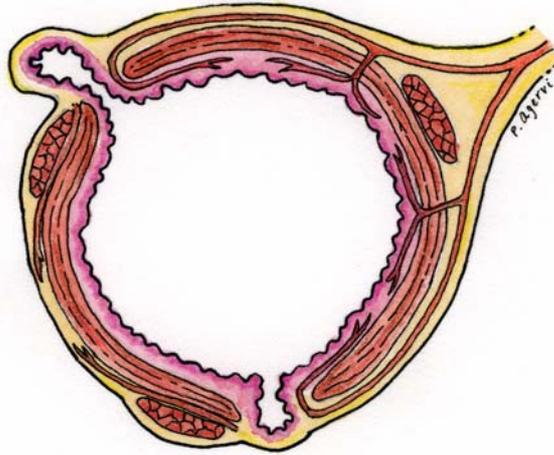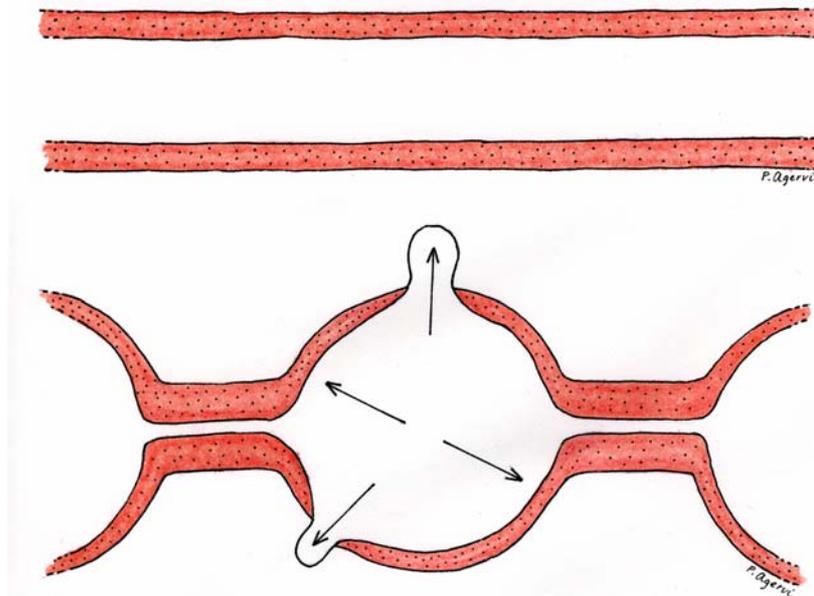

Figure 4. Longitudinal sections of the bowel wall:
Upper: normal bowel wall.
Lower: hypersegmentation caused by contraction rings thereby generating unusual high intraluminal pressure and thus promoting the formation of diverticula.

Based on measurements of transit time and stool weight from 1200 individuals in the UK and Uganda, Painter and Burkitt (1971) introduced the fibre hypothesis; lack of fibre residues causes longer transit times and smaller stool volumes, thus increases intraluminal pressure which predispose formation of diverticula. The elastin formation is secondary to sustained bowel contractions and raised intraluminal pressure. In addition, the defects in the bowel wall, where the diverticula protrude, can be promoted by degeneration of connective tissue. Ageing is associated with a decreased tensile strength of the muscle fibres of colon, (Smith, 1986) especially in the left colon (Watters and Smith, 1985). Patients with inherited connective tissue disorders such as Ehler-Danlos syndrome or Marfan´s syndrome often develop DD from early age (Simpson et al., 2002).

Lately, the dietary hypothesis has been challenged and questions have been raised regarding the methods used to measure colonic intraluminal pressure in earlier studies (Golder et al., 2003). Instead, a cholinergic denervation hypersensitivity-type occurrence in the sigmoid colon of patients with DD was demonstrated. An alternative hypothesis suggested recently (Yun et al., 2005); is that the formation of diverticula may be attributed to colonic smooth muscle dysfunction resulting from vagal attrition associated with ageing.

2.5.2   Diverticulitis

Diverticulitis is an inflammation originating from one or more diverticula, usually in the sigmoid colon. Common symptoms and signs include local pain and tenderness in the left lower abdomen, sometimes with a palpable mass. (Simpson and Spiller, 2004). General symptoms and signs of infection are common. The left colon is affected in more than 90 %. The apex of a diverticulum is mostly the primary origin of the inflammation and the reason is usually impaction of faeces within the diverticulum (Hultén et al., 1999). The inflammation is typically phlegmonous and engages a part of the adjacent bowel and mesenteric fat in close proximity, but can also spread diffusely along the peritoneal surface, form abscesses and/or involve neighbouring organs. Sometimes a large inflammatory mass develops with only minimal formation of pus, which macroscopically can be difficult to distinguish from cancer or IBD. Most inflammations are mild and resolve with conservative treatment (Parks and Connell, 1969, Haglund et al., 1979). However, a diverticulum can also perforate into the peritoneal cavity and lead to a rapidly spreading purulent or faecal peritonitis. Based on the findings in 95 operated patients, Hinchey et al (1978) classified four distinct stages of perforated diverticulitis (Table 4).

Table 4. Classification of perforated diverticulitis according to Hinchey et al, (1978).

Stage	Description
I	A *pericolic abscess* confined to the mesentery of the colon. It may enlarge by spreading either deeper into the mesentery or along the outer layer of the bowel wall.
II	A *pelvic abscess* resulting from local perforation of a pericolic abscess. The abscess may be walled off by colon, mesocolon, omentum, small bowel, uterus, Fallopian tubes, ovaries and pelvic peritoneum.
III	*Generalised peritonitis* resulting from the rupture of either a pericolic or pelvic abscess into the general peritoneal cavity. Free communication between the abscess and the lumen of the bowel does not exist because of obliteration of the neck of the diverticulum by the inflammatory process.
IV	*Faecal peritonitis* results from the free perforation of a diverticulum. Its evolution is usually rapid and faeces escape from the lumen of the colon through the perforated diverticulum and are present in the free peritoneal cavity.

The inflammation can involve other pelvic organs and lead to the formation of fistulas, engaging for example the bladder or vagina. In women, fistula formation to the bladder or to the vagina occur predominately in patients who have previously undergone hysterectomy (Wychulis and Pratt, 1966, Woods et al., 1988).

Sometimes the inflammation will result in the formation of a scar tissue with collagen formation, causing a stricture of the affected bowel segment, and the patient will develop obstructive symptoms.

Inflammation in a diverticulum may erode the arterial wall of the vasa recti, and thereby cause gastrointestinal bleeding (Arfwidsson, 1964, Jensen et al., 2000).

2.5.3 Microbiological aspects

The bacteria involved in abscesses and peritonitis secondary to diverticulitis come from the normal bacterial flora in the colon. Anaerobes are the predominant organisms and form at least 99 % of the normal flora. Bacteroides fragilis, Escherchia coli, Kleibsella enterobacteria and Enterococcus species are bacteria seen frequently (Duma and Kellum, 1991, Elsakr et al., 1998, Vedantam and Hecht, 2003).

2.6   DIAGNOSTIC MODALITIES

Traditionally, the two most common ways to examine the colon in patients with suspected DD has been BE or CC. (Figure 1/Page 1) Even though BE has been the first choice in many settings, it has limitations in patients with DD (Baker et al, 1985, Stefansson et al 1994) and CC has also been generally regarded as a more accurate diagnostic modality regarding polyps and tumours. However, endoscopy is sometimes painful, discomforting and have a higher failure rate in patients with DD, because of pericolic adhesions fixating bowel loops and muscular wall hypertrophy narrowing the bowel lumen (Stefansson et al, 1994, Anderson et al., 2001). Computed tomography colonography (CTC) has been introduced as a novel and promising method for imaging of the colon, but has not yet been thoroughly evaluated in patients with DD (Lefere et al. 2003, Gollub et al., 2005).

2.7   TREATMENT

2.7.1   Uncomplicated diverticular disease

As mentioned above, lack of dietary fibres is believed to be the most important factor in the formation of diverticula. Therefore, all patients with symptomatic DD should be advised to increase their ingestion of fibre. Even though one small cross-over RCT found relief of symptoms for three months, with fibre supplement as compared to placebo (Brodribb, 1977), there is no overwhelming evidence to support long term fibre supplement therapy to reduce symptoms related to DD.

In a placebo controlled RCT (Ewerth et al., 1980), nine patients complaining of constipation and having colonic diverticula on BE were examined with regard to transit-time, bowel movements and subjective symptoms. They were treated with placebo and a bulking agent (Vi-Siblin®), using a double- blind cross-over technique. The subjective symptoms were significantly reduced in patients treated with fibres.

However, another report demonstrated conflicting results. A cross-over RCT study (Ornstein et al., 1981) compared fibre supplements versus placebo in 76 subjects with uncomplicated DD. Three treatments were compared: bran crisp bread, ispaghula husk drink and placebo. No significant difference in symptom relief was found between these regiments.

Peristalsis regulators (lactulose), antibiotics (rifaximin) and anti-inflammatory agents (mesalazine) have been suggested to reduce symptoms and prevent complications in patients with DD. Lactulose has not been proven to be more effective than placebo (Papi et al 1992, Simpson and Spiller, 2004). So far, two RCTs from Italy have evaluated long term treatment of Rifamixin, a poorly absorbed aminoglycoside, together with fibre supplements compared with placebo. The rationales for this treatment is that the colonic micro flora should be involved in determine the symptoms of DD. Symptoms improved after twelve months of treatment (Papi et al., 1992, Latella et al., 2003). Finally, it has been suggested that Mesalazine might relief symptoms and prevent recurrences but its role is not yet been clarified (Simpson and Spiller, 2004, Di Mario et al., 2005).

12

2.7.2 Uncomplicated acute diverticulitis

2.7.2.1 Medical treatment

Medical treatment is often effective in the management of uncomplicated AD and includes; analgesics, low residue diet and, sometimes antibiotics. However, no systematic review or RCTs has evaluated medical treatment vs. placebo in patients with AD (Simpson and Spiller, 2004).

The use of antibiotics are often advocated but have not been thoroughly evaluated.

If symptoms are severe including inability to tolerate oral feeding or if systemic signs are present, inpatient treatment with bowel rest, i.v. fluids and careful observation is recommended (Wong et al., 2000, Murphy et al., 2003, Stollman and Raskin, 2004).

Advices to consume a high fibre diet or a dietary fibre supplementation to prevent complications after medically resolved AD seems reasonable (see above) but it has never been systematically investigated (Simpson and Spiller, 2004).

Rates of recurrences after one attack of medically managed AD have been reported to be 7-42 % (Anya and Flum, 2005, Parks and Connell, 1969, Haglund et al., 1979). In one study fifty percent occurred within one year and 90 % within five years (Parks and Connell, 1969).

It also appears that severe complications of AD (perforation, obstruction and fistula) occur as the primary event in the vast majority of patients (Larson et al., 1976, Lorimer, 1997, Anaya and Flum, 2005, Salem et al., 2006).

2.7.2.2 Surgical treatment

Generally, surgical treatment in uncomplicated AD is indicated either *acutely* when medically management have failed or *electively* to prevent recurrences and further complications. Surgical treatment usually includes sigmoid colectomy with anastomosis or sometimes a stoma.

When an elective operation is indicated has been debated widely. Even though expert panels have advocated elective colon resection after two episodes of medically treated diverticulitis, (Stollman and Raskin, 1999, Wong et al., 2000, Murphy et al., 2003) there is no evidence in the literature to support such an algorithm (Janes et al., 2005). An early elective resection might be justified after a well documented (CT positive) conservatively managed episode of AD, especially in young patients (Chautems et al, 2002). In old patients after a mild episode of AD recurrences appear to be less frequent and these patients have a higher risk of morbidity after surgery (Broderick-Villa et al., 2005). Moreover, elective surgery for DD is associated with a significant rate (0-15%) of mortality, but reported rates have improved during the last decades and are especially low (0-1%) in young patients (Janes et. al, 2005, Bokey et al., 1981, Chodak, 1981, Oomen et al., 2006).

A RCT have found that preservation of the inferior mesenteric artery is of importance to prevent leakage of the colorectal anastomosis in resection of sigmoid DD (Tocci et al, 2001).

Lately, laparoscopic surgery has been introduced as an option in patients with DD. The Laparoscopic Colorectal Surgery Study Group (Kockerling et al., 1999) has stated that the conversion, complication, and mortality rates associated with laparoscopic surgery in patients with uncomplicated DD are acceptable. A French prospective comparative study (Alves et al., 2005) found that electively laparoscopic surgery may be associated with reduced postoperative morbidity and shorter hospital stay than open approach but patients were not randomised.

About 7 % of patients who undergo surgery resections for DD later suffer from recurrent disease. The distal resection margin seems to be of importance for a better outcome according to a retrospective study of 501 patients from the Mayo Clinic (Benn et al., 1986). Recurrent AD developed in 12.5 % of the patients in whom the sigmoid colon had been used for the distal margin of anastomosis and in 6.7 % of those in whom the rectum had been used (p = 0.03). These findings were recently confirmed in a study of 236 patients and it was found that the anastomosis level (colorectal over colosigmoid) was the only predictor of recurrence in a regression analysis (p = 0.03) (Thaler et al., 2003).

2.7.3 Complications to diverticulitis

Surgical treatment is indicated in most cases when complications to DD occur, such as acute perforation, obstruction, abscess or fistula formation and bleeding. In patients with generalised purulent (Hinchey III) or faecal (Hinchey IV) peritonitis surgery must be performed urgently. Traditionally, the three stage operation was used; an initial diversion with a proximal colostomy and drainage, followed by resection of the involved segment of colon with end-to-end anastomosis, and finally the stoma was reversed. More recently, and still the treatment of choice in many institutions, the two-stage procedure (resection and proximal colostomy, i.e. Hartmann) have been used (Belmonte et al., 1996).

Data from randomised trials in surgery of DD are sparse and are mainly observational. However, two RCT trials have studied acute surgery in perforated disease. One RCT found no significant difference in mortality and complication rates between acute sigmoid resection, colostomy (Hartmann) compared with transverse colostomy and suture (Kronborg, 1993). Another multicentre RCT studied primary and secondary sigmoid colonic resection in generalised peritonitis and found no significant difference in mortality and rates of wound or extra-abdominal complications (Zeiton et al, 2000). Primary resection reduced rates of postoperative peritonitis and emergency re-operations. During the past decade, primary resection and anastomosis have been advocated in selected patients. Notably mortality rates are significant in surgery of perforated disease and patients are often old and have major comorbidities (Salem and Flum, 2004).

Surgery is mostly indicated when acute obstructive symptoms because of chronic inflammation and stenosis occur. Recently the use of endoscopic stents has been introduced (Tamim et al., 2000, Forshaw et al., 2006) as a possible bridge to definitive surgery. Resection, primary anastomosis and intra-operative lavage have been shown to be safe in acute obstruction of the left colon (Pollock et al., 1987, Stewart et al., 1993,

Kressner et al., 1994), but still the Hartmann procedure is used by several surgeons (Salem and Flum, 2004).

Diverticular fistulas, predominantly to the bladder or vagina, are mostly an indication for elective surgery. Conservative treatment might be an option if symptoms are mild and severe comorbidities exist. Hartmann procedures or resection and primary anastomosis have usually been favoured and reported in observational series (Woods et al., 1988, Grissom and Snyder, 1991, Vasilevsky et al., 1998).

Historically, abscesses secondary to DD were treated with exploration and open drainage. Today, treatment including antibiotics and sometimes percutaneous drainage, the latter preferably performed with the help of CT or ultrasound, are effective in most cases and exploratory surgery is rarely needed (Rothenberger, 1993).

Gastrointestinal bleeding in patients with DD stops spontaneously in 70-80 % of cases and most patients can therefore be treated conservatively (Murphy et al., 2003). Endoscopy is an important tool for correct diagnosis, and this technique has also a therapeutic role (Jensen et al., 2000). Angiography with embolisation has also been used. Urgent surgery is restricted to patients that are hemodynamical unstable and when considerable transfusion of blood is needed or if recurrent massive haemorrhage occur.

3 AIMS

The overall aim of this thesis was to increase the knowledge of diverticular disease by exploring the epidemiological, diagnostic and clinical aspects of the disease, especially diverticulitis.

Specific aims:

1. Evaluate the influence of ethnicity and other socio-demographic factors (age, sex, socioeconomic status, housing, urban residency) on the rate of DD. (Paper I)

2. Compare the findings specific for DD and acceptance when imaged by CT Colonography and Colonoscopy respectively in patients after acute diverticulitis. (Paper II)

3. Evaluate if antibiotics will change the outcome in patients with mild acute diverticulitis. (Paper III)

4. Review evaluation, surgical management, morbidity and outcome in patients with internal fistulas to the female genital tract secondary to DD. (Paper IV)

4 PATIENTS

The patients in the thesis were derived from four separate patient cohorts. The number of patients, their origin and the time period during which they were recruited are summarised in table 5.

Table 5. Number, origin and time period during which patients for this thesis were recruited.

	Papers	n	Patients origin	Time Period
I	DD and Migration	25,123	Swedish National Cohort	1990 (followed 1991-2000)
II	CT Colonography and Colonoscopy in DD	50 (57)	Division of Surgery, Danderyd Hospital, Sweden	Aug. 2002-Dec. 2004
III	Antibiotics and AD	311 (448)	Division of Surgery, Danderyd Hospital, Sweden.	Jan. 2000-June 2002
IV	Diverticular fistulas to the female genital tract	60	Division of Colon and Rectal Surgery, Department of Surgery, University of Minnesota, Minneapolis, USA	Aug. 1992 – July 2004

4.1 PAPER I

The study population consisted of all 4,426,260 Swedish residents aged between 25 and 64 years in Sweden in 1990. This population was followed from January 1991 until December 2000. Of the study population, 3,889,315 were indigenous Swedes and 536,945 were immigrants, with a mean age of 43.5 years. From the national cohort there were 25,123 patients were hospitalised due to DD during the study period of which, 9,846 were men (39.2 %) and 15,277 were women (60.8 %). The population's ethnicity is presented in table 6.

Table 6. Ethnicity of patients in the study group, Paper I.

Category	n	Country of birth	% of group
Indigenous	3 889 315	Sweden	100%
Western Europe, Australia, New Zealand, Northern America	303 883	Finland	59%
		Norway	10%
		Denmark	10%
		Germany	9%
		Other	12%
Eastern Europe	59 819	Poland	41%
		Hungary	19%
		Other	40%
The Balkans	48 062	Yugoslavia	76%
		Greece	24%
		Other	0.1%
Middle East	71 202	Iran	34%
		Turkey	23%
		Iraq	10%
		Other	33%
Asia	17 603	Far East	64%
		South Asia	36%
Central, South America	29 391	Chile	51%
		Other	49%
Africa	6 985	Africa	100%
All	**4 426 260**		

4.2   PAPER II

All patients eligible for the study had recently been admitted to Danderyd hospital for treatment of AD. According to the routine, the attending surgeon made a decision whether a follow-up (FU) colon examination was indicated. During the study period (July 2002 through August 2004) 57 patients listed for a colon examination gave consent to participate in the study and were prospectively examined. During the initial hospitalisation the diagnosis was based on clinical signs only (n=3), supported by CT imaging (n=51) or by findings when operated for peritonitis (n=3). The characteristics of the patients are presented in table 7.

Table 7. Patient characteristics, Paper II.

	n=57
Age mean (years)	56 (29-79)
Female	31 (54%)
Previous history of DD	8 (16%)

4.3   PAPER III

In all 311 patients were evaluated in Paper III. Between January 2000 and June 2002 all patients hospitalised with a diagnosis of AD at The Department of Surgery, Danderyd hospital, Stockholm, Sweden were identified from the hospital computerised registry. Of 448 eligible patients, 137 were excluded. In these patients, diagnoses were based on clinical findings only (n=131), or they were operated on immediately following admission (n=6). The characteristics of the patients are presented in table 8.

Table 8. Patient characteristics, Paper III.

	All patients **n=311**	**Antibiotics**	
		(-)(n=193)	**(+)(n=118)**
Age mean (years)	59.3	59	60
Female	130 (64%)	126 (65%)	74 (63%)
Previous history of DD	87 (28%)	57 (30%)	30 (25%)
Co-morbidity	108 (35%)	62 (32%)	46 (39%)

4.4   PAPER IV

In all, 60 consecutive women with colo-genital fistulas caused of DD were treated by The Division of Colon and Rectal Surgery Faculty at the University of Minnesota-affiliated hospitals from August 1992 to July 2004. Mean age at surgery was 70 (range, 36-90) years and mean FU time after surgery was 12 (range, 1-77) months. The characteristics of the patients are presented in table 9.

Table 9. Patient characteristics, Paper IV.

	n=60
Age mean (years)	70 (36-90)
Previous history of DD	15 (25%)
Co-morbidity	39 (65%)

5 METHODS

5.1 PAPER I

In Paper I the design was observational and prospective since the data regarding the national cohort were collected prospectively.

5.1.1 Swedish national registers

Sweden has a long tradition of national registers with information about health and socio-demographic indicators of the entire population. This paper was based on data from national registers held by the Swedish National Board of Health and Welfare and by Statistics Sweden.

The study population was followed from January 1991 until December 2000 in the National Patient Discharge Register, the National Cause of Death Register and (yearly) in the Total Enumeration Income Survey (Centre for Epidemiology, 2004).

5.1.2 Socio-demographic variables

Year of birth, sex, year of the latest immigration, country and socio-economic status of the household (SES), urban residency (metropolitan, town, rural) and housing situation (rent apartment/owns apartment, owns house) were documented and added to the dataset through linkage to the Swedish Population and Housing Census 1990. Socio-economic groups were defined according to a classification used by Statistics Sweden which is based on occupation but also takes into account the educational level, type of work and position of the head of the household into the statistics (Statistics Sweden, 1982). The Total Enumeration Income Survey for 1990 was used to identify members in households that received social welfare benefits in 1990 (Centre for Epidemiology, 2002). Eight different geographical groups of origin were created by birth countries: Sweden, Western Europe including Australia, New Zealand and Northern America, Eastern Europe, the Balkans, Middle East, Asia, Central and South America and Africa according to the major groups of immigrants which came to Sweden during the last decades. The category of 'Western Europe including Australia, New Zealand and Northern America' incorporated northern and southern Europe west of the Balkans. (Table 10).

Table 10. Categorisation of Western and non-Western societies in the study.

Western societies	Non-Western Societies
Western Europe *(including northern and southern Europe west of the Balkans)*	Eastern Europe The Balkans Middle East Asia
Australia	Central and South America
New Zealand	Africa
Northern America	

5.1.3 Outcome variables

Dichotomised outcome variables (at least once/never) were obtained through individual record linkage to the National Hospital Discharge Register (Centre for Epidemiology, 2002). This register covers 99 % of all hospital discharges in Sweden.

Variables were defined in accordance with the WHO International classification of diseases (ICD) (WHO, 1989, WHO, 1992). Diverticular disease (DD) was defined by primary ICD-9 diagnosis of 562 in 1991 through 1996 and K572-9, 1997 through 2000 (ICD-10). Acute diverticulitis (AD) was defined by a primary diagnosis of K572 (WHO, 1992) 1997 through 2000. Deaths because of DD were identified if the diagnosis was identified as the primary underlying cause of death in the National Cause of Death Register 1991 through 2000 (Centre for Epidemiology, 2004).

5.2 PAPER II

Paper II was prospective and comparative in its design.

In all, 57 patients underwent CTC followed immediately the same day by CC at median 85 (range, 29-153) days after discharge from hospital. Preparation for the examinations included a clear liquid diet for 48 hours prior to the examination and 2 doses of 250 ml each of sodium phosphate (Phosforal™, Ferring, Limhamn, Sweden) at twelve hours interval the day prior to the investigation.

5.2.1 CT Colonography

After injection of 20 mg buthylscopolamine i.v., to minimise smooth-muscle spasm and peristalsis, the colon was gently insufflated with air, taking into account patient tolerance. Dual scanning (prone and supine positioning) was performed on a multidetector CT scanner. For evaluation Advantage Workstation (version AW 4.0, General Electric Medical System), including the Navigator 1, (General Electric Medical System) a system for three-dimensional (3D) rendering was used. Axial two-dimensional prone and supine CT images and endoluminal 3D reconstructions were reviewed by an experienced gastro-intestinal radiologist unaware of the CC results.

5.2.2 Colonoscopy

Conventional colonoscopy (CC) followed immediately after CTC. A standard video colonoscope was used. The examinations were performed by one of two experienced endoscopists, unaware of the results of CTC.

Morphine and Midazolam were given i.v. on demand immediately before or during the procedure. Fluoroscopy was used mainly for determination of the position of a diverticulum or polyp. The location of each lesion was documented and polyps retrieved for histological examination.

5.2.3 Comparison

Findings of DD (absence, presence of 1-10 or >10 diverticula, with or without either focal wall thickening or reduced luminal diameter), polypoid lesions ≥five mm at CTC and CC respectively and dose of irradiation administered were noted in a study protocol. To determine location, the colon was divided into segments: Each examiner graded the effect of bowel preparation, the overall ability of the colon to distend and the overall quality respectively on a scale from one (poor) to four (excellent). The amount of retained fluid was ranked on a scale from one (large amount retained fluid) to four (no retained fluid).

Patient acceptance was evaluated with three written questionnaires (see Appendix). A first questionnaire was completed directly after CTC and before CC. A second questionnaire was completed directly after CC. These two identical questionnaires included questions regarding discomfort (no/mild/moderate/severe), pain and the overall impression of difficulty for each modality. In a third questionnaire, answered after completion of CTC and CC, patients were asked to compare the two examinations ("which examination was the most discomforting, painful and difficult?") and to note preference (which examination would you prefer if you would have to undergo one of the examinations again?). To minimise bias due to the effects of sedation and pain medication, an exact copy of the third questionnaire was distributed and completed by each patient the day after the examinations and returned by mail.

5.3 PAPER III

Paper III was observational in its design and was performed in retrospect. Hospital records were reviewed and data concerning the first hospitalisation were collected: (age at first presentation, sex, co-morbidity, history of DD, previous abdominal surgery, CT findings, temperature, levels of WBC and CRP on admission, length of hospital stay and treatment regime (conservative or operative). For conservatively treated patients, specified data regarding antibiotic therapy were gathered. In patients who had surgery, the collected data also included indications, procedures performed and complications ≤30 days.

5.3.1 First hospitalisation

In all, 311 patients were initially managed conservatively, and treatment included careful observation, i.v. fluids and restriction of oral intake. In 118 patients, conservative treatment also included antibiotics, while in 193 patients no antibiotics were given initially. The decision to add, or not add, antibiotics was made by the attending surgeon, taking into account clinical findings, results of CT images, laboratory parameters, presence or absence of fever and co-morbidity.

The most common antibiotics, used in 83 % of patients, were a combination of a cephalosporine and metronidazol given i.v.. This was usually followed (88 %) by an orally administered quinolone together with metronidazol. The course of antibiotic treatment was usually 10-14 days.

Failures of conservative treatment during first hospitalisation were registered. A failure was classified as a need for immediate surgery (in a patient treated with/without antibiotics) or an addition of antibiotics because of aggravating symptoms and clinical signs in patients initially treated without antibiotics. Patient flow is illustrated in figure 5.

Figure 5. Patient flow in Paper III.
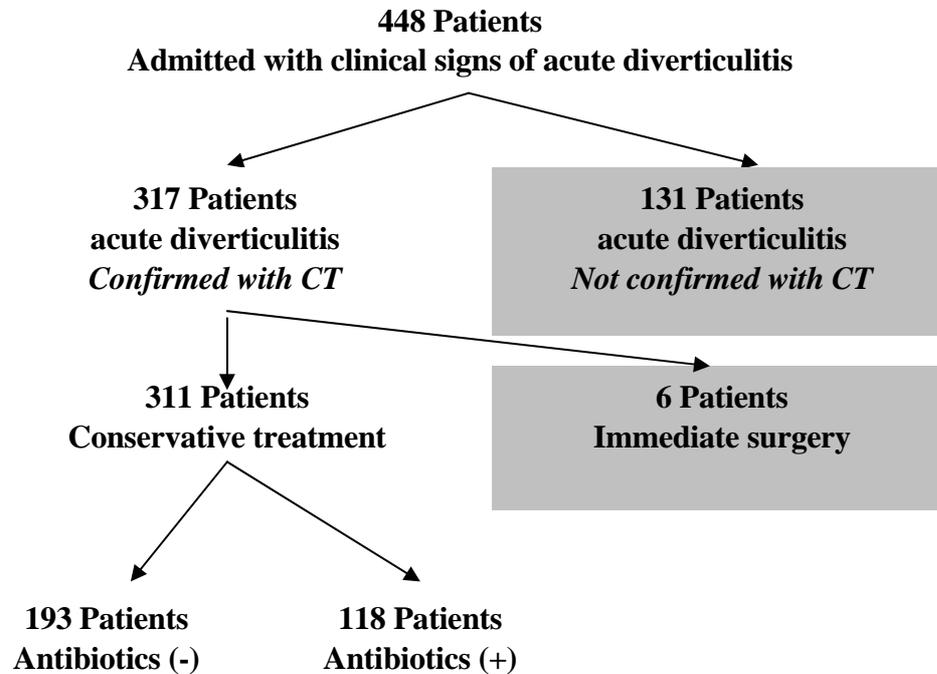
5.3.2 Follow Up

All patients were followed after discharge and further events (recurrent AD with readmission to hospital and/or subsequent surgery) were noted. Mean FU-time was 30 (range, 16-45) months.

5.3.3 Questionnaire

In order to collect data also directly from patients, a standardised questionnaire was created and sent by mail to all 309 patients that were alive at FU. Questions concerned previous history of DD, colon examinations, recovery time after discharge from hospital (<1week, 1-4 weeks, >4 weeks), admissions to other hospitals for recurrent AD or subsequent surgery for DD. A total of 248 patients (80 %) answered and returned the questionnaire.

5.3.4 Confirmation

Results of the CT examinations were recorded and all CT images were re-evaluated by an experienced radiologist. The grade of AD was classified as mild or severe according to a classification proposed by Ambrosetti et al. (1997) (Table 11/Figure 6a-6b).

Additional examinations of the colon, (including BE, CC or CTC) to evaluate the presence of DD, were reviewed.

Table 11. Computed Tomography criteria to assess severity of AD (Ambrosetti, 1997).

Mild	Severe
Localised wall thickening >5 mm	Localised wall thickening >5 mm
Inflammation of pericolic fat	Inflammation of pericolic fat:
	and at least one of the following:
	Abscess
	Extraluminal air
	Extraluminal contrast

Figure 6a. CT image demonstrating *mild* diverticulitis (localised wall thickening and inflammation of pericolic fat (arrow)).
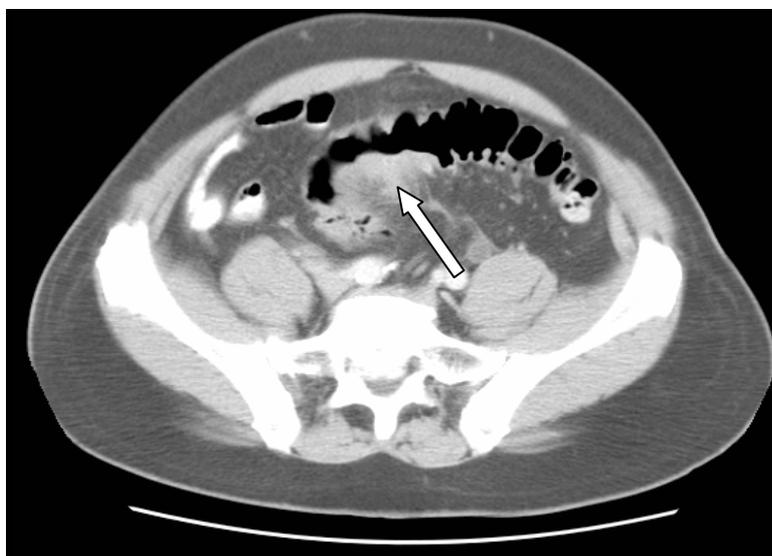
Figure 6b. CT image demonstrating *severe* diverticulitis (abscesses in the pouch of Douglas (arrows)).

5.4   PAPER IV

Paper IV was performed in retrospect. In the 60 patients, hospital records were reviewed and data were collected regarding patient demographics, co-morbidity, history of symptomatic DD, previous surgery, presenting signs, results from examinations of the colon and the fistula tract (enema, endoscopy, CT, vaginography), indication and type of operation performed, blood loss, details of the operative procedure, pathoanatomical report, length of hospital stay, surgical complication and outcome.

5.5   STATISTICAL ANALYSES

In *Paper I* the influence of immigration status and socio-economic status on hospital admission for DD and AD was calculated using *Cox proportional hazards regression models* with DD and AD (as defined above) as the outcome variables. The rates of DD and AD were calculated for each geographical group. Hazard ratios produced by Cox regression can be interpreted as risk ratios (RR) and this term was used. Person time in the study was calculated from January 1, 1991 to the date of first hospital admission due to DD from the National Patient Discharge Register, the date of deaths from the National Cause of Death Register, or the last date of FU (December 31, 2000). Disposable income was checked yearly in the Total Enumeration Income Survey as an indicator of residency in Sweden. To minimise bias because of unrecorded emigration, time in the study was censored if no household income related to employment or social benefits were reported as suggested by Ringbäck-Weitoft et al (Weitoft et al., 1999). Birth year was entered as a continuous variable in the regression models. Other socio-demographic confounders were entered as dichotomised or dummy variables into the models. In order to increase the specificity of the diagnosis of DD, a separate analysis was also performed where each subject (n=188) registered with a diagnosis of gastrointestinal cancer (C15-C26, ICD 10) (WHO, 1992) in the Swedish Cancer Registry during the study period was excluded. The SPSS software package, version 11.5, was used in all statistical analyses in Paper I.

In *Paper II* findings of CTC and CC were compared. Polyp detection was assessed on a per-polyp basis. To assess differences in examiners´ ratings, the *Wilcoxon matched pair test* was used and differences in patients' experiences and preferences between CTC and CC were assessed with *the Sign test.*

In *Paper III* data of patient groups treated with or without antibiotics were compared using univariate analysis and variables that may possibly influence the risk of further events (recurrent AD and/or subsequent surgery) during FU were then analysed using a *multivariate logistic regression model*. Variables included in the analysis included treatment with antibiotics, age, sex, history of DD, severity of inflammation according to CT, CRP, WBC, temperature on admission and co-morbidity. *Chi square test* was used for dichotomous data, *Students t-test* was used for numerical data assuming normal distribution and *Mann Whitney U* test was used for comparisons of non-parametric ordinal data.

In *Paper IV* data of patient groups were compared to evaluate if morbidity after surgery depended on duration of symptoms at time of surgical repair (<6 weeks), patients age (>60 years) or (presence of) co-morbidity. *Chi-squared test* was used.

In Paper II-IV, STATISTICA 6.0 software (Statsoft Inc. Tulsa, Oklahoma, USA) was used for all statistical analyses and a p-value <0.05 was considered significant.

5.6 ETHICS

Papers I-III were approved by the Karolinska Institutet Ethics Committee North, Stockholm, Sweden. In **Paper IV**, the study protocol was approved by the Institutional Review Board at the University of Minnesota, Minneapolis, USA.

6   RESULTS

6.1   PAPER I

There were 25,123 subjects hospitalised due to DD between 1991 and 2000 (9,846 men and 15,277 women), yielding a ten year cumulated incidence of 0.44 % for men and 0.70 % for women. During the study period 140 individuals in the study group died because of DD, which represents a cumulated mortality rate of 0.03 % (Table 12).

The incidence of DD increased in a linear fashion with age. The adjusted risk of hospital admissions related to DD was higher for women compared to men with a RR of 1.50 (Table 13/Figure 7).

The risk of DD in immigrants of different origins was analysed in a multivariate model adjusted for age, sex and available socio-economic confounders. The age and sex-adjusted risks of DD in immigrants from Western societies was similar to the Swedish majority population (RR 0.99), while immigrants with a non-Western origin (Table 10/Page 22) had a significantly lower risk. (Table 13; Model 1). Adjusting the model for the socio-economic variables had minimal to small effect on the risk estimates in the non-Western immigrant study groups (Table 13; Model 2).

The model was further adjusted by excluding all subjects (n=188), that were also registered with gastrointestinal cancer (C15-C26, ICD 10) (WHO, 1992) from the group hospitalised with DD, during the study period, in order to increase the specificity of the diagnosis of DD and reduce the problem with confounding by misclassification. The risks estimated were only minimally affected (Table 13; Model 3).

The risk for hospital admissions with a diagnosis of AD was calculated using the same multivariate model. Cases of AD were collected from 1997-2000 when coding became more specific. There were 2,907 subjects hospitalised due to AD (59 % women). Patterns were similar as seen for DD over the whole study period. Ethnicity outside Western societies had a significantly lower risk of hospital admission for AD (RR 0.35, CI 95 % 0.22-0.54) compared with indigenous Swedes. The risk for AD for immigrants originating from Western societies was 0.94 (CI 95 % 0.89-1.09).

The number of years the immigrant had spent in Sweden when the study started was used a proxy for acculturation. In a multivariate analysis including immigrants of non-western origin only, adjusted for age, sex and geographical categories, RR was 0.75 (CI 95 % 0.57-0.97) in non-western immigrants that had lived less than five years in Sweden, 0.74 (CI 95 % 0.54-0.99) 5-10 years and 0.87 (CI 95 % 0.69-1.09) 10-20 years compared to non-western immigrants with more than 20 years of residency.

Subjects receiving social welfare during 1990 and subjects with a low SES had elevated risks for DD. Moreover, subjects living outside metropolitan areas had slightly elevated risks (Table 13). The risk patterns for DD and AD were similar.

Table 12. Socioeconomic and demographic indicators for patients admitted because of diverticular disease and mortality because of diverticular disease 1991-2000.

		Admissions because of DD 1991-2000				Mortality because of DD 1991-2000	
		Men	*per 10 000*	Women	*per 10 000*	Total	*per 10 000*
Mean age (yrs) 1990		49.2		51.4		58.3	
		n		*n*			
All		9846	44.0	15277	69.8	140	0.32
Ethnicity	Sweden	9011	45.7	13658	71.2	131	0.34
	Western Europe including Australia, New Zealand and Northern America	563	39.3	1242	77.4	8	0.26
	Eastern Europe	92	35.4	146	43.1	1	0.17
	The Balkans	62	23.4	64	29.6	0	0
	Middle East	69	24.5	92	12.9	0	0
	Asia	8	7.5	22	31.5	0	0
	Central and South America	30	22.7	52	32.2	0	0
	Africa	11	21.3	1	5.5	0	0
SES	Manual workers	1630	38.7	3787	68.5	24	0. 25
	Skilled workers	1483	37.0	1098	59.6	7	0.12
	White Collar 1	900	48.3	2436	63.7	10	0.18
	White Collar 2	1477	43.9	1894	55.7	12	0.18
	White Collar 3	1192	42.3	830	54.2	7	0.16
	Unclassified	3164	51.7	5232	91.0	80	0.67
Received social welfare 1990	Yes	436	35.6	702	60.3	5	0.21
	No	9410	44.5	14575	70.4	135	0.32
Housing	Rents apartment	2743	39.7	4723	67.3	58	0.42
	Owns apartment	1010	39.2	1940	71.3	20	0.38
	Owns house	5662	49.2	8253	73.0	54	0.24
	Missing	431	30.9	361	43.5	8	0.36
Urban residency	Metropolitan area	2833	40.5	4294	61.4	45	0.32
	Smaller city	4972	45.0	7890	73.2	62	0.28
	Rural	2041	46.9	3093	75.4	33	0.39

SES groups were classified according to Statistics Sweden 1982)

Table 13. Cox regression models of socio-demographic determinants of hospital admissions for diverticular disease. (n=4 426 260).

		Model 1 RR (95 % C.I.)	Model 2 RR (95 % C.I.)	Model 3 RR (95 % C.I.)
Sex	Male	1	1	1
	Female	1.50 (1.46-1.54)	1.49 (1.45-1.53)	1.48 (1.44-1.52)
Ethnicity	Sweden	1	1	1
	Western societies	0.99 (0.92-1.04)	0.99 (0.94-1.04)	0.99 (.94-1.04)
	Eastern Europe	0.66 (0.58-0.75)	0.65 (0.57-0.74)	0.64 (0.56-0.73)
	The Balkans	0.54 (0.45-0.64)	0.52 (0.44-0.62)	0.52 (0.44-0.62)
	Middle East	0.64 (0.55-0.75)	0.55 (0.47-0.63)	0.56 (0.47-0.65)
	Asia	0.56 (0.39-0.80)	0.51 (0.36-0.73)	0.51 (0.36-0.73)
	Central and South America	0.77 (0.62-0.95)	0.70 (0.56-0.87)	0.69 (0.56-0.86)
	Africa	0.56 (0.32-0.99)	0.52 (0.29-0.91)	0.52 (0.29-0.91)
SES	Manual workers	1.10 (1.05-1.16)	1.08 (1.03-1.14)	1.08 (1.03-1.14)
	Skilled workers	1.11 (1.05-1.18)	1.10 (1.03-1.16)	1.10 (1.03-1.16)
	White Collar 1	1.10 (1.04-1.16)	1.09 (1.03-1.15)	1.09 (1.03-1.15)
	White Collar 2	1.07 (1.01-1.28)	1.06 (1.00-1.12)	1.06 (1.00-1.12)
	White Collar 3	1	1	1
	Unclassified	1.17 (1.12-1.23)	1.16 (1.10-1.21)	1.16 (1.10-1.21)
Received social welfare	Yes	1.23 (1.16-1.30)	1.29 (1.22-1.38)	1.29 (1.22-1.38)
	No	1	1	1
Housing	Rents apartment	1.02 (0.99-1.05)	1.03 (1.00-1.06)	1.03 (1.00-1.06)
	Owns apartment	0.93 (0.90-0.97)	0.95 (0.91-0.99)	0.95 (0.91-0.99)
	Owns house	1	1	1
	Missing	1.01 (0.94-1.09)	0.97 (0.90-1.05)	0.97 (0.90-1.05)
Urban residency	Metropolitan area	1	1	1
	Smaller city	1.08 (1.05-1.12)	1.06 (1.03-1.10)	1.06 (1.03-1.10)
	Rural	1.09 (1.05-1.13)	1.05 (1.01-1.09)	1.05 (1.01-1.09)

Model 1. Variables adjusted for year of birth and sex

Model 2. All variables in the model

Model 3. All variables in the model excluding individuals (n=188) registered with gastrointestinal cancer

Figure 7. Ten year cumulated incidence of hospitalisation because of diverticular disease.
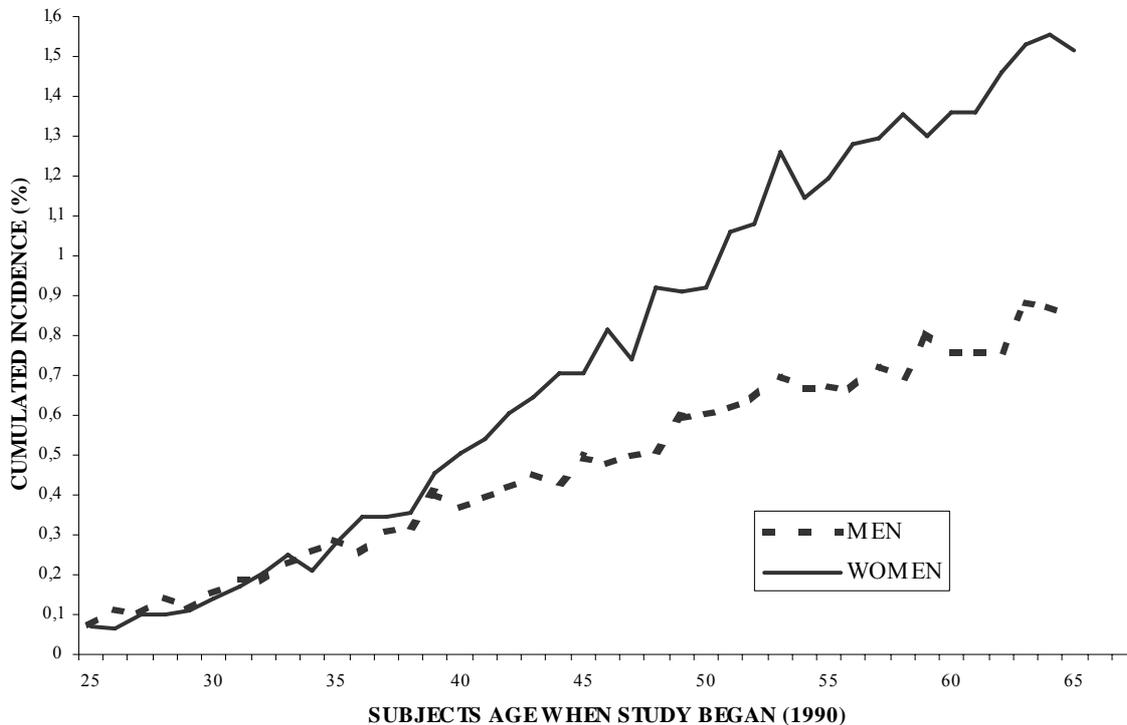
6.2 PAPER II

Of the 57 patients included in the study 50 patients were completely examined by both CTC and CC. In seven patients CC was incomplete (88 % success rate) due to pain and discomfort and they were excluded from further analysis.

The radiologist and the endoscopists rated the bowel preparation to be excellent in the majority of patients (CTC: mean 3.60; CC mean 3.50, p=0.59, N.S.).

The ability of the colon to distend was regarded as excellent in the majority of patients and did not differ between the two modalities (CTC mean 3.86; CC mean 3.80, p=0.50, N.S.). Fluid retention was not experienced in the majority of patients (CTC mean 3.70; CC mean 3.72, p=0.89, N.S.), and the overall quality was rated excellent in the majority of patients (CTC mean 3.52; CC mean 3.64, p=0.35, N.S.).

Irradiation dose administered at CTC was mean 5.37 (range, 2.8-6.5) mSv. No complications were seen, neither at CTC nor CC.

6.2.1 Findings of diverticular disease

DD was found in 48 of 50 patients (96 %) at CTC and in 45 of 50 patients (90 %) at CC. The number of diverticula found (caecal/ascending/transverse and/or descending/sigmoid colon respectively) in the patients are summarised in figure 8.

Figure 8 a –b: Number of diverticula in descending/sigmoid colon (a) and caecum/ascending/transverse colon (b) for CTC and CC respectively.

a) Descending/sigmoid
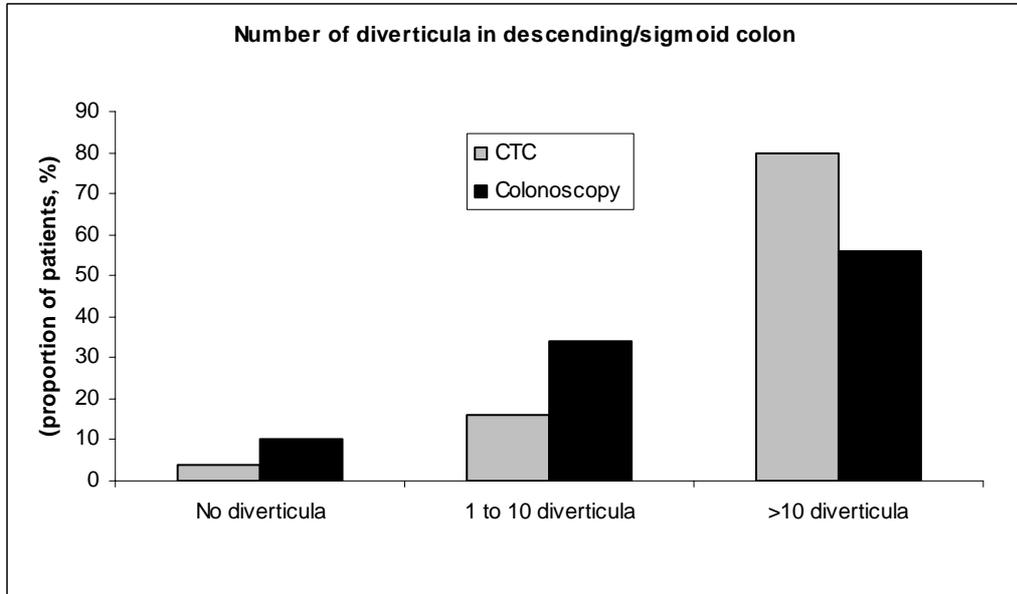
b) Caecum/ascending/transverse
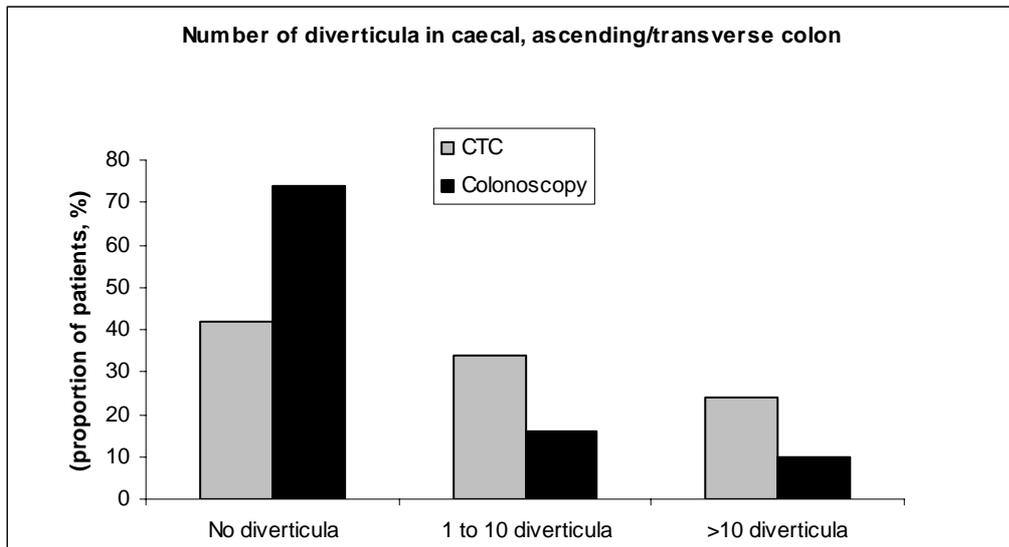
Reduced lumen diameter in the sigmoid colon (compared with adjacent parts of colon) was found in 21/50 patients at CTC and in seven patients at CC. Four patients had such findings at both CTC and CC. The agreements between these findings were poor between the two modalities.

Focal wall thickening, in the sigmoid colon, was found in 16 patients (32 %) at CTC. Twelve of these 16 patients also had reduced lumen diameter but there was no difference in the overall quality of the examinations (mean 3.56 vs. 3.52, N.S.) or grade of fluid retention (3.94 vs. 3.79, N.S.) compared with patients without focal wall thickening.

6.2.2 Polyps

Eight polyps between five and eight mm in size were found. Polyp findings and histopathology are summarised in Table 14.

Table 14. Location, size and type of the eight suspected polyps found in six patients, examined by both CT Colonography and CC.

Pt nr	Location	CT Colonography	Colonoscopy	Size (mm)	Pathology
1	Rectum	X	X	5	Hyperplastic
1	Sigmoid	X		6	
1	Descending	X		8	
2	Rectum	X		6	
3	Sigmoid	X		5	
4	Sigmoid		X	5	Hyperplastic
5	Ascending		X	5	Hyperplastic
6	Caecum		X	5	Adenoma

Suspected polyp findings at CTC were all<10 mm and were not regarded an indication to repeat CC.

6.2.3 Patient acceptance

All 50 patients completed the questionnaires evaluating patient acceptance after each examination. During CTC, patients experienced less discomfort (p<0.025), less pain (p<0.001) and less difficulty (p<0.009) than during CC. When the patients were asked to compare the two examinations, CC was reported to be the most discomforting (p<0.001), most painful (p<0.001) and most difficult (p<0.001) examination.

Of the 38 patients who favoured one examination, 28 patients (74 %) would prefer CTC if they were to undergo an examination again.

6.3 PAPER III

The characteristics of patients (age, sex, co-morbidity and history of DD) were presented in Table 8/Page 22) and did not significantly differ between patients treated with or without antibiotics.

6.3.1 First hospitalisation

When comparing patients treated with or without antibiotics, fever on admission was more common, inflammatory parameters were higher and hospitalisation was longer in patients treated with antibiotics (Table 15). According to the initial CT report, AD was

classified as mild in all patients treated without antibiotics and in 85 % of patients treated with antibiotics (Table 15). Patient's time to symptomatic recovery, reported in the questionnaire, did not differ significantly between the two groups (Table 16).

Table 15. Findings during first hospitalisation.

	Antibiotics (-) n=193	Antibiotics (+) n=118	p-value
Temperature on admission			
<37,9°C	86%	64%	<0.001[††]
≥38°C	14%	36%	
CRP on admission (mg/L)	87 (4-231)	119 (7-421)	<0.01[††]
WBC on admission (x 10^9)	10.2 (4.3-19.6)	11.7 (5.8-28.1)	<0.001[††]
CT mild/severe (initial report)	193/0	99/19	<0.001[†]
Treatment failure			
Antibiotics added	7 (4%)	-	-
Emergency surgery	0	3 (3%)	-
Hospital stay, days (mean, range)	3 (1-15)	5 (1-22)	<0.001[††]

†=Chi square test, ††= Mann Whitney U test

Table 16. Time to recovery reported in questionnaire for patients successfully treated during first admission (p=0.18, N.S.).

	Antibiotics	
	(-) n=193	(+) n=115
Answered the questionnaire	*n=153*	*n=83*
<1week	51%	41%
1-4 weeks	34%	40%
>4 weeks	15%	19%

In patients treated without antibiotics 186 patients of 193 (96 %) were successfully treated without failures. Seven patients (4 %) failed the treatment and antibiotics were added because of aggravating symptoms and clinical signs (Figure 9). None of the patients initially treated without antibiotics required surgery during the first hospitalisation.

In patients treated with antibiotics 115 patients of 118 (97 %) were successfully treated without failures. Three patients (3 %) failed conservative treatment and underwent surgery on days three, six and nine, respectively, after admission because of worsening of symptoms (Figure 9).

Operative findings in all three patients were consistent with Hinchey stage III (Hinchey et al., 1978), and the patients were operated with sigmoidectomy and primary anastomosis (n=2) or a Hartmann procedure (n=1). The latter patient developed a stoma

necrosis requiring additional surgery. No other major post operative complications (≤30 days) were seen.

6.3.2 Follow-up

Of the 186 patients treated successfully without antibiotics during the first hospitalisation, 53 had further events during FU. (Figure 9-10) Fifty-one patients were readmitted and treated conservatively for at least one episode of recurrent AD and two patients had surgery. One of these patients was operated with an elective sigmoid resection because of recurrent episodes of AD and one patient was readmitted seven months after first hospitalisation and had an emergency operation with a sigmoid resection because of colonic obstruction.

Of the 115 patients treated successfully with antibiotics during the first hospitalisation, 33 had further events during FU (Figure 9-10). Thirty-two patients were re-admitted and treated for at least one episode of recurrent AD and fourteen patients were operated, of which ten patients had an elective sigmoid resection performed because of recurrent episodes of AD. Two patients had emergency operations because of colonic obstruction (one patient with a Hartmann procedure and one with a diverting transverse colostomy). One patient was operated with a sigmoid resection because of a colovaginal fistula and one patient had a sigmoid resection prior to a renal transplant.

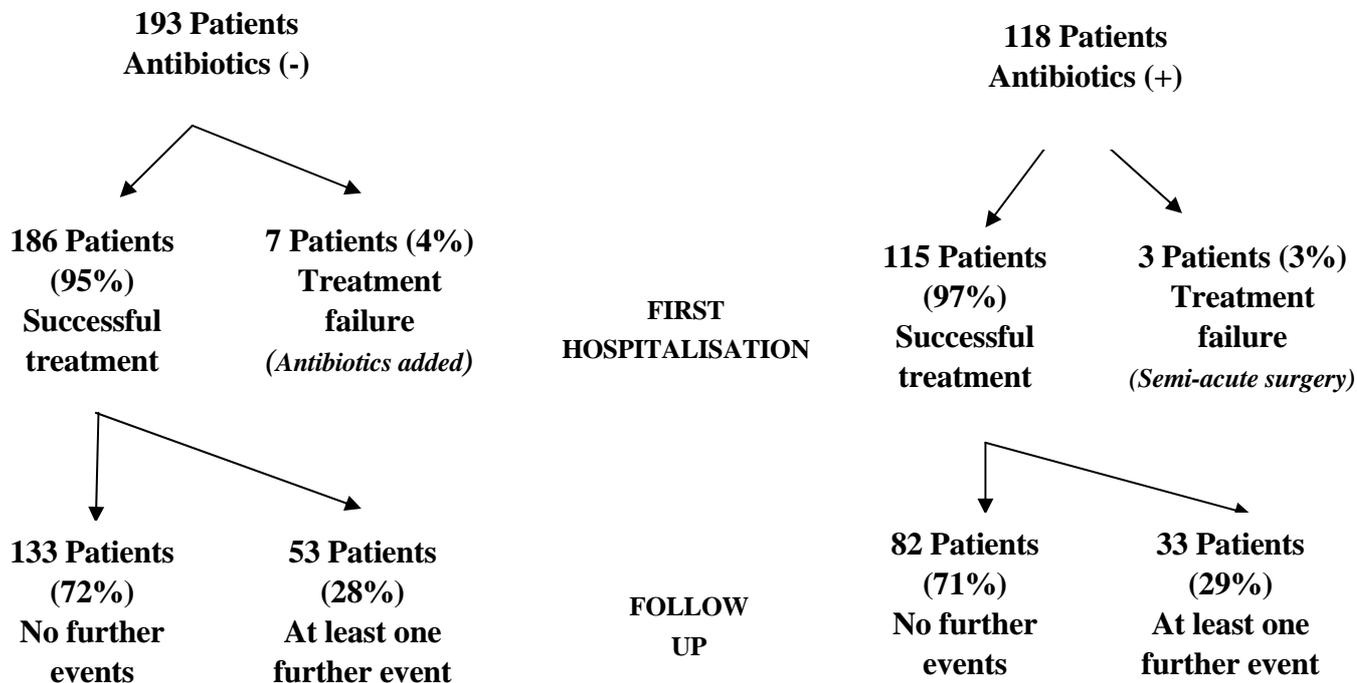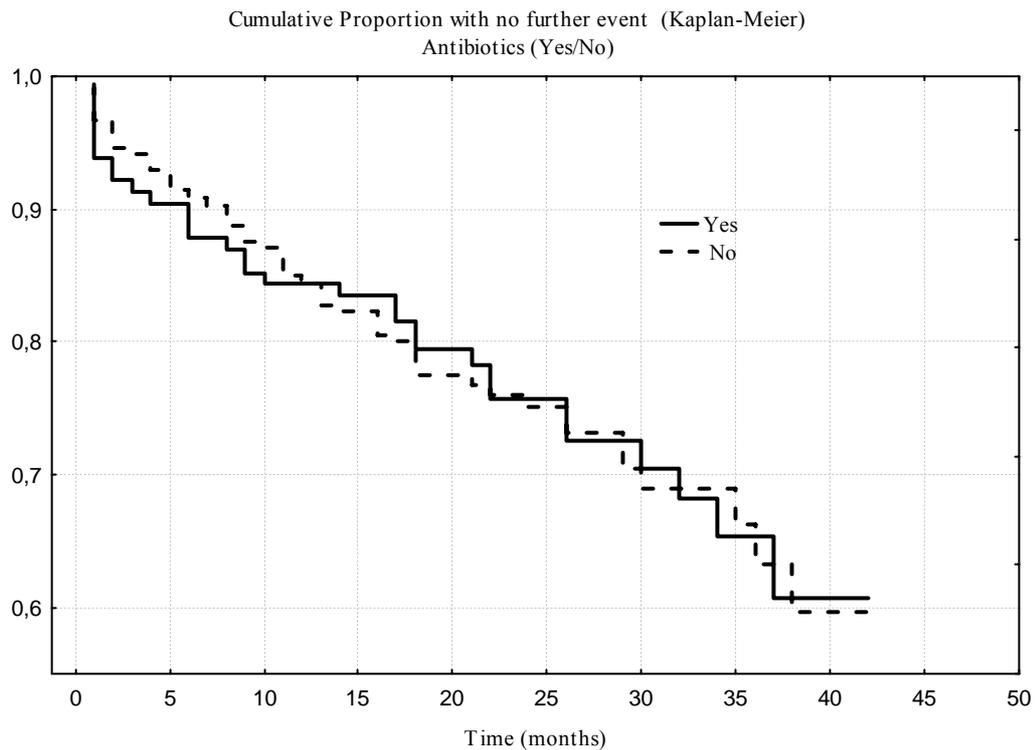**Figure 9.** Patient flow during first hospitalisation and follow up.

Figure 10. Further events in patients treated with or without antibiotics.

Cumulative Proportion with no further event (Kaplan-Meier)
Antibiotics (Yes/No)

The rate of further events for patients successfully treated without antibiotics during first hospitalisation (53/186, 28 %) (Figure 9-10) were compared with patients treated with antibiotics (33/115, 29 %) and did not differ significantly (p=0.97, N.S.).

Furthermore, factors possibly influencing the risk for a further event were analysed using logistic regression. Of the variables considered only a previous history of DD increased the risk for recurrent episodes of AD (Odds Ratio 2.63, CI 95 % 1.55-4.47). Neither antibiotic treatment (Odds Ratio 1.03, CI 95 % 0.61-1.74) nor the other factors (age, sex, severity of inflammation according at CT, CRP, WBC, temperature on admission or co-morbidity) influenced the risk for a further event.

6.3.3 Confirmation

Re-evaluation of the initial CT images resulted in changes of the initial report in 14 patients (4 %). The classification of AD was changed from mild to severe in 13 patients and from severe to mild in one patient.

During the FU-period 272 of the patients (84 %) had at least one colon examination with a BE (242 patients), CC (19 patients) or CT colonography (eight patients). The diagnosis of DD was confirmed in 266 patients (98 %) and in six patients the FU-examination could not confirm DD. Colorectal cancer was not found in any patient.

6.4   PAPER IV

Mean FU time after surgery was 12 (range, 1-77) months. Twenty-five % of the patients had a previous history of symptomatic DD. In all, 45 patients (75 %) were previously hysterectomised.

6.4.1   Symptoms

Fifty-seven patients (95 %) reported discharge of faeces or gas from vagina and 26 patients (43 %) reported abdominal pain. Median duration of symptoms at the time of surgical repair was 3 (range, 0.2 - 84) months.

6.4.2   Evaluation

Preoperative evaluation usually included clinical examination, endoscopy and radiological evaluation (enema, vaginography and/or CT).

The vaginal fistula opening, mostly in the apex of the vagina, was found at clinical examination in 18 patients (30 %). In some patients, vaginal examination was performed using a flexible sigmoideoscope.

Positive findings in different preoperative x-ray examinations (gastrografin or BEs, vaginography and/or CT) are shown in Table 17. In total, radiological evaluation was used in 56/60 patients and a fistula was demonstrated in 45 (80 %) of these patients.

Table 17. Positive findings with different radiological methods.

Examination	n	Fistula tract	Pelvic abscess
Gastrografin enema	24	20 (83%)	
BE	22	18 (82%)	
Vaginography	4	2 (50%)	
CT	29	11 (38%)	5

6.4.3   Surgical treatment

Fifty-seven patients (95 %) were operated. Two patients had minor symptoms and one was regarded as a major surgical risk and they were therefore they were not operated. The types of fistulas found at surgery are summarised in Table 18.

Table 18. Types of fistulas in the studied patients (n=60).
All fistulas originated from the sigmoid colon.

	n
Single fistulas	**52**
Fistula to vagina	50
Fistula to uterus	2
Multiple fistulas	**8**
Fistulas to vagina & urinary bladder	5
Fistulas to vagina & tube	1
Fistulas to vagina & ileum	1
Fistulas to vagina & urinary bladder & skin	1

Sigmoid resection and takedown of the fistulas was performed in all operated patients. In patients with a single fistula from the sigmoid colon to the vagina (n=49), the external opening of the fistula in the vagina was managed in three different ways: suture closure of the opening (n=7), use of an omental flap for covering (n=15), leaving the hole open (n=13) or not described in the procedure note (n=14). Ureteric stents were inserted prior to surgery in 32 patients (56 %). Estimated blood loss was mean 384 (range, 0-1600) ml. Mean postoperative hospital stay was 8.5 (range, 4-19) days.

A primary anastomosis was performed in 51 patients (89 %). The anastomosis was protected with a loop ileostomy in two patients. Six patients underwent a Hartmann procedure with colostomy (11 %). Reasons for a Hartmann procedure with colostomy, instead of an end-to-end anastomosis, included a frosen pelvis because of chronic inflammation (n=4), chemotherapy and malnutrition secondary to lung cancer (n=1) and history of faecal incontinence (n=1).

In the 51 patients who had a primary anastomosis, the resection involved the sigmoid and upper rectum in 47 patients and included a left hemicolectomy in an additional four more patients. Four patients had a concomitant hysterectomy and bilateral salpingoophorectomy as part of the procedure. Two of these patients had a colo-uterine fistula, one patient had a fistula involving the ovarian tube, and one patient was found to have an ovarian cyst at surgery.

6.4.4   Pathology

Pathology reports were reviewed in all 57 patients having surgery and all confirmed the diagnosis of DD. One patient had an ovarian cyst removed as part of the procedure and pathoanatomical investigation demonstrated a radically removed ovarian cancer. The average length of the removed colon specimen was 19 (range, 8-35) cm.

6.4.5   Complications

Surgical complications occurred in 15 patients (26 %/Table 19). Four patients developed anastomotic dehiscence. Two of them were re-operated with resection of the anastomosis and colostomy and two were managed conservatively (of which one

already had a covering loop ileostomy done at the primary operation). Three patients had an ureteric injury that was diagnosed and managed during the primary procedure. Two of them had ureteric stents in place at the time of the injury. One patient was re-explored because of bleeding. Three patients developed wound infections requiring surgical drainage. Morbidity after surgery was not influenced by patient age >60 years (p=0.11, N.S.), presence of co-morbidity (p=0.35, N.S.) or duration of symptoms <6 weeks (p=0.93, N.S.).

Table 19. Complications after surgery in 15/57 patients (26 %).

Complication	n
Anastomotic dehiscence	4
Ureteral injury	3
Wound infection requiring surgical evacuation	3
Cardiopulmonary complication	3
Bleeding (re-operation)	1
Transient renal failure	1

6.4.6 Outcome

There was no mortality. The fistula tract healed promptly in all but one patient in whom vaginal discharge persisted for three months but the fistula then healed spontaneously. In this patient, the external fistula opening in the vagina was covered by an omental flap. No patient had recurrent episodes of diverticulitis or signs of a recurrent fistula during FU.

One of the six patients initially operated with a Hartmann procedure had the colostomy reversed. One of the two patients initially operated with a covering loop ileostomy had the stoma reversed. The colostomies were not reversed in the two patients operated because of anastomotic dehiscence. In total, 8 of 57 operated patients (14 %) had a persistent stoma.

7   DISCUSSION

In this thesis, DD was studied from different perspectives. Epidemiological (*incidence in relation to ethnicity and other socio-demographic factors*) and methodological (*CT Colonography and CC in the FU after AD*) aspects of the disease were addressed as well as treatment; conservative; (*role of antibiotics in management of AD*) and surgical (*female genital fistulas*).

7.1   INCIDENCE OF DIVERTICULAR DISEASE – SOCIODEMOGRAPHIC DIFFERENCES

7.1.1   Ethnicity

In Paper I, a considerably lower risk for hospital admissions because of DD and AD for Non-Western immigrants than for indigenous Swedes and immigrants from westernised countries was found. These results suggest that after a fairly short period of acculturation in Sweden, there is an increasing risk for DD in subjects with origin outside the westernised world.

The results are consistent with findings reported previously from Israel by Levy (1977, 1985). Prevalence of DD increased only slightly among urban living Jews origining from Europe and America (16.2 % to 17.3 %), but a sevenfold increase was seen in rural Arabs (0.7 % to 5.4 %). In two recent cross-sectional studies from the Netherlands and United Kingdom, immigrants (mostly originating from Turkey and India) had low rates of DD findings compared with indigenous population, when investigated with endoscopy because of gastrointestinal symptoms (Kang, 2004, Loffeld, 2005).

Paper I is the first *population based* evaluation of the rate of DD in immigrants moving from low risk countries to a high risk country and also the first to evaluate the change in incidence with time and acculturation. Painter and Burkitt (1971) suggested that a low content of dietary fibres was a key component among lifestyle factors that affect the incidence of DD in different societies. They introduced the term "westernisation" to describe the increased risk of DD in Western countries. The fibre deficiency hypothesis has been confronted as too simple to explain the difference in incidence between societies and a concept of multifactor causation is probably more reasonable (Mendeloff, 1986). Yet, other factors proposed such as red meat and physical activity have been shown to alter the risk of DD (Aldoori, 1994 and 1995, Tonnesen, 1999).

7.1.2   Sex

In the present study women had a higher risk for developing DD than men and with increasing age the female predominance became increasingly obvious. This has been shown in previous reports of hospital admission data (Kyle et al., 1975, Kang et al., 2003). Hormonal factors have been proposed to explain the female predominance, but have not been clearly demonstrated.

7.1.3   Age

The incidence of DD increases with age, especially from the fifth decade of life and onwards (Figure 7/Page 32). The time of risk exposure (low intake of dietary fibres) might be the most attractive explanation but it has also been demonstrated that the tensile muscle strength of the colon wall decreases with age (Smith, 1986). Moreover, recently it was suggested that colonic smooth muscle dysfunction resulting from slow destruction of vagal innervation associated with ageing could play a role in the formation of diverticula ´s (Yun et al., 2005).

7.1.4   SES, housing, urban residency

SES, housing or residency did not influence the rate of DD in this study. As far as we know, this was the first population-based study to evaluate the impact of these factors on the rate of DD. A small case-control study from Greece (Manousos et al., 1985) suggested that patients with DD had higher SES than controls.

7.2   IMAGING OF DIVERTICULAR DISEASE

Examination of the colon in a patient with probable DD, as performed in *Paper II*, is important for confirmation and assessment of the severity of DD and for the exclusion of polyps and colorectal tumours. CT examinations to confirm the diagnosis of acute AD, as done in *Paper III*, are also of great value and have direct impact on the management of the patient. In addition the specificity of the diagnosis made on clinical features only is often poor. Moreover, a systematic evaluation is essential for planning of surgical management in patients with internal diverticular fistulas (*Paper IV*).

7.2.1   CTC and Colonoscopy in diverticular disease

Paper II is a comparative study evaluating CTC and CC in patients with symptomatic DD. Our results demonstrate that the diagnostic findings, specific of DD at CTC and CC, show a good rate of agreement. Thus, CTC can image manifestations of DD with at least similar sensitivity as CC.

CTC can, unlike CC, also provide additional important information when evaluating DD, such as imaging of focal wall thickening and pericolic inflammatory changes involving adjacent organs. Over all, findings of DD were more pronounced in CTC compared with CC in this study.

Incomplete examinations are a shortcoming of CC. In DD the failure rate is expected to be particularly high, as CC appears to be more painful and discomforting for patients with DD (Church, 1994, Cirocco and Rusin, 1995, Anderson et al., 2001). In the present study, two senior endoscopists achieved a success rate of 88 %. However, CC has obvious advantages compared with CTC. Lesions can be biopsed or removed at the same procedure and irradiation is usually not administered (unless when fluoroscopy is used). It is noteworthy that findings of reduced luminal diameter diverged considerably between CTC and CC. CTC is probably more accurate than CC in evaluating the lumen diameter, since x-ray films give the possibility of measuring the actual diameter in each segment of the colon. The grade of distension also depends on how much air is filled in

the lumen both in CTC and CC. This was, however routinely evaluated in CTC on a scout image before the actual scanning began in each patient.

In a previous pictorial review, (Lefere et al., 2003), evaluating CTC findings in 89 patients with DD, the authors suggested that findings associated with DD, such as a faecal impaction or inverted diverticulum and non-specific focal thickening of the wall could be difficult to differentiate from adenomas or neoplastic lesions. Concerns were also raised that muscular hypertrophy and reduced luminal distension could decrease visibility. Another study demonstrated that the presence of DD with associated muscular abnormality (myochosis) compromised the quality of distension of the sigmoid colon during CTC and recommended further work up to securely exclude polyps and cancer in these patients (Gollub et al., 2005). Focal wall thickening was strongly associated with reduced luminal diameter (12 of 16 patients) in the present study, but neither CTC nor CC in these patients revealed any polyp and therefore this issue could not be addressed.

Most studies comparing CTC and CC have been performed in patients with high risk for colorectal polyps or cancers. The reported accuracy for polyp detection ranges widely and sensitivity improves with increasing polyp size. The clinical relevance has been questioned for flat adenomas and for small polyps (<10 mm) (Rex et al., 1997, Fenlon et al., 1999, Fletcher et al., 2000, Miao et al., 2000, Hara et al., 2001, Yee et al., 2001, Gluecker and Fletcher, 2002, Johnson et al., 2003, Pickhardt et al., 2003, Cotton et al., 2004). No malignant tumours were found in Paper II. All suspected polyps diagnosed were only five to eight mm in diameter and the correlation between the two modalities was low.

Traditionally BE has been the method of choice when evaluating DD (Halligan and Saunders, 2002) and especially the double contrast technique, introduced by Welin (1974) has been shown to be especially useful. No trials have compared BE with CTC when evaluating DD findings, since most reports have focused on the detection of cancer and polyps, and also used CC for comparison.

In the present study the anticipated doses of irradiation together with the advantages of biopsies were the reasons why CC was preferred over BE. However, CTC has most likely advantages over BE due to its capability to *directly* display thickening of the bowel wall and also for the visualisation of peri-colic changes.

Where BE has been compared with CTC, it also appears to be less sensitive in detecting malignant tumours and polyps than CTC and also less reproducible (Winawer et al., 2000, Johnson et al., 2004).

When diagnosing strictures, which sometimes are the result of inflammation secondary to DD, the role of CTC to exclude cancer tumours is yet to be demonstrated.

7.2.1.1 Patient acceptance

The majority of patients favoured CTC if they had to undergo a colon examination again. This is in accordance with previous reports (Gluecker and Fletcher, 2002, van Gelder et al., 2004). In a study comparing CTC, CC and BE, CTC caused less discomfort than BE and similar discomfort as to CC (Gluecker and Fletcher, 2002). A recent study from St Mark's hospital (Taylor et al., 2005) evaluated patient acceptance

for CTC and BE in 78 subjects and CTC caused significantly less physical discomfort and was overwhelmingly preferred.

7.2.1.2 *Radiation*

The administered irradiation might be a concern, especially in young patients, when evaluating CTC for routine clinical practice. The mean effective dose administered to patients in this study (5.37 mSv/range, 2.8-6.5) was lower than doses reported for BE (6.4± 2.1 mSv) (Kemerink et al., 2001). Also, recent experiences suggest that the irradiation dose in CTC can be reduced without significantly compromising diagnostic accuracy (Cohnen et al., 2004).

7.2.2   Evaluation of acute diverticulitis

In Paper III a CT examination positive for AD was mandatory for entering the study. The grading of inflammation appeared accurate and the results from the preliminary report were only changed in a limited number of patients (4 %), when re-evaluated. Thus, all patients in the present study treated without antibiotics were classified to have a mild inflammation according to the initial CT report.

A diagnosis of AD based on clinical features only has a poor accuracy (Rao et al., 1998). CT is an important tool in confirming the diagnosis of AD and to grade the extent of the inflammation when tailoring the optimal treatment for the patient. Advantages of CT are the non-invasiveness, the ability to visualise the bowel wall and pericolic tissues and to exclude the presence of other intra-abdominal pathological conditions. When compared with contrast enemas, the reported sensitivity for CT has been 93-98 % and the specificity 75-100 % (Hulnick et al., 1984, Ambrosetti et al., 2000).

Ultrasonography is another proposed tool when diagnosing AD. Even though it is non-invasive and also offers therapeutic options (drainage of abscesses), its operator dependence, inability to visualise free air and often poor image quality in obese patients limits its use (Schwerk et al., 1992, Zielke et al., 1997).

Other studies have ranked CT ahead of other diagnostic modalities when imaging AD (Hulnick et al., 1984, Ambrosetti, 1997, Eggesbo et al., 1998, Halligan and Saunders, 2002)

Moreover, the rate of further events during FU, were not influenced by the severity of inflammation, graded on CT. Other studies have been contradictive, especially in young patients (Ambrosetti et al., 2002, Chautems et al., 2002, Kaiser et al., 2005). In the present study all patients having emergency surgery were excluded from further analyses and there were few conservatively treated patients with CT-findings of severe AD (n=19/Table 15/Page 34), making the validity of this finding questionable.

7.2.3   Evaluation of female genital fistulas

The majority of patients in Paper IV underwent radiological studies prior to surgery. In all, 20/24 (82 %) of barium studies and 18/22 (83 %) of gastrografin studies visualised the fistula preoperatively (Table 17/Page 38). These findings are in accordance with

Abcarian and Udezue, (1978) who found that BE visualised the fistula in eleven of twelve patients. However, other studies have reported a lower sensitivity using contrast enema techniques. In a study by Wychulis and Pratt (1966) only 48 % of DFs were visualised. Woods et al. (1988) visualised a fistula in 34 % of patients with colovaginal fistulas examined with BE.

According to our results, CT imaging seems to be of limited value in demonstrating a cologenital fistula. In the present study, only 11 of 28 CT images were positive. However, as seen in Paper III, and discussed above, CT is as an important tool to diagnose additional complications of diverticulitis, such as intra-abdominal abscesses (Hulnick et al., 1984, Labs et al., 1988, Rothenberger and Wiltz, 1993, Ambrosetti et al., 2002), which, if present, should preferably be managed before definite surgery of the fistula. Five patients in this study had an abscess adjacent to the sigmoid colon diagnosed on CT. Ahead of definitive surgery, two of the patients with abscesses were drained percutaneously and all were treated with antibiotics.

To summarise, it is reasonable to evaluate the patient before surgery with a vaginal examination and to perform a contrast medium enema. If clinical signs of an abscess are present, CT imaging is most likely justified.

7.3 TREATMENT OF ACUTE DIVERTICULITIS

Most patients with symptoms and signs of AD can be managed conservatively. Acute surgery is indicated if signs of obstruction or peritonitis secondary to perforation are present and semi-acutely if conservative management fails and the patient's condition deteriorates.

7.3.1 The role of antibiotics

Conservative treatment of AD usually includes careful observation, restriction of oral intake, i.v. fluids, and most patients receive antibiotic therapy. It is, however, not certain whether all patients with AD benefit from antibiotics. In Danderyd hospital, antibiotics have not been routinely used in patients with mild AD for more than 30 years.

Moreover, problems associated with antibiotic resistance and side-effects are well documented (Ibrahim et al., 2000, Kollef, 2003, Vedantam and Hecht, 2003, Goossens et al., 2005).

In the case of AD, antibiotics have usually been included in medical management regiments. In a (small) RCT treatment two antibiotics (i.v. gentamycin versus i.v. clindamycin) were compared but no significant difference in clinical cure was found (Kellum et al., 1992). However, toxicity, probably antibiotic related, occurred in 10 %. Numerous panels of experts have proposed antibiotics to be mandatory in the management of AD (Ferzoco et al., 1998, Stollman and Raskin, 1999, Wong et al., 2000, Mazuski et al., 2002, Murphy et al., 2003). Our data, however, indicate that antibiotics can be omitted for the majority of, but not for all, patients with mild AD. Once the infection is established, the host immune response is often sufficient to wall off the inflammation adjacent to the affected diverticulum and inhibit further bacterial spread in the peritoneal cavity (Cheadle and Spain, 2003).

Thus, in some patients, antibiotics should probably be mandatory when managing AD, such as in immune-suppressed patients and when significant co-morbidity is present.

As AD can present itself with very different clinical pictures, it is important to establish in which patients antibiotics may be omitted. Diagnostic imaging, laboratory parameters (WBC, CRP), temperature, abdominal tenderness and the patient's general condition are probably parameters which should be considered when defining criteria for the selection of patients who would benefit or not from antibiotics.

Laboratory parameters (WBC, CRP) on admission might also be of value, but the time from onset of symptoms is crucial and probably a major difficulty when deciding the proper cut-off level. In this study, laboratory values were significantly higher in the group treated with antibiotics (Table 15/Page 34, but there was considerable overlapping between the groups.

Notably, in 86 % of patients treated without antibiotics temperature was below 38° on admission (Table 15/Page 34), indicating that the temperature seems to have been of importance in the selection of treatment. Nevertheless, 2/3 of patients treated with antibiotics had no fever on admission. Abdominal tenderness is probably another important clinical finding, when assessing a patient with AD, but the observational design of this study prevented us from drawing any conclusions regarding its potential impact.

To conclude, among the group of patients, where antibiotics were omitted (the vast majority), observation and supportive care only appeared safe and did not influence patient's recovery, the rate of recurrence or subsequent surgery, findings that have never been reported previously, as far as we know.

7.4   SURGICAL MANAGEMENT OF FEMALE GENITAL FISTULAS

Management of DF to the female genital tract represents a challenge for the surgeon. Colon resection combined with primary anastomosis and excision of the fistula resulted in satisfactory outcome in the majority of patients, however a significant rate of morbidity was demonstrated and 14 % of patients had to accept a permanent stoma. Evaluation of patients with a suspected DF has been discussed above (see 7.2.3/Page 44).

In all, 44/57 patients were previously hysterectomised which may have facilitated the creation of a colo-vaginal fistula, as the inflammation will be close to the vagina without a protecting uterus in place (Grissom and Snyder, 1991). Previous series have reported a similar high incidence of prior hysterectomy (Table 20).

Table 20. Summary of surgical findings in women with diverticular genital fistulas from the present and previous studies.

Study	n	Fistula to			Prior hysterectomy
		Vagina	**Uterus**	**Tube**	
Wychulis and Pratt (1966)	11	11			6 (54%)
Woods et al. (1988)	26	23	3		19 (83%)
Grisson and Snyder (1991)	9	9			7 (78%)
Tancer and Veridiano (1996)	12	10	1	1	10 (100%)
Vasilevsky et al. (1998)	21	20		1	20 (95%)
Hjern et al (present study)	60	57	2	1	44 (77%)
Total	**139**	**130**	**6**	**3**	**106 (82%)**

7.4.1   Indication and timing of surgery

A patient with discharge of faeces or gas from vagina and verified DD most probably needs an operation, but sometimes the decision to operate has to be taken in spite of lack of radiological confirmation of the fistula tract. In the present study 15 patients were operated on despite lack of radiological confirmation. For these patients, the history and signs together with the presence of DD were regarded sufficient to proceed with surgery.

Patients with fistulas because of DD should preferably be managed electively. Median duration from first symptom to surgery in the present study was 13 weeks, reflecting that the majority of patients were managed in an elective manner.

7.4.2   Surgical procedures

In all, 89 % of patients in this study were operated with colon resection and a primary anastomosis. The concept of resection and primary anastomosis in patients with complications of diverticulitis has been debated. Previous studies on DF have been retrospective and only a limited number of patients have been reported in each study (Wychulis and Pratt, 1966, Abcarian and Udezue, 1978, Woods et al., 1988, Tancer and Veridiano, 1996). Patients identified with a high risk of dehiscence of the anastomosis may need a Hartmann procedure. In some cases an alternative approach may be to perform a primary anastomosis and to protect this anastomosis with a proximal loop-ileostomy (Williams et al., 1986). This approach was used in two patients in this study, of which one developed an anastomotic leak that was treated conservatively. The covering ileostomy was never reversed.

Three patients in the present series were treated conservatively. Non-surgical management of a colo-vaginal fistula is sometimes a reasonable alternative to surgery, especially in elderly patients with minor symptoms or poor surgical risk.

The management of the fistula opening in the vagina varied in the present series. The hole was sutured, left open or covered by an omental patch. All openings healed and

only one patient had prolonged discharge from the vagina. Vasilevsky et al. (1998) reported 21 patients in which the fistula opening in the vagina was not closed and no patient developed a recurrent fistula.

7.4.3   Complications

The complication rate was 26 % and similar or lower than previous series reported by Vasilevsky et al. (1998) and Woods et al. (1988). In a study from the University of Minnesota (Belmonte et al., 1996) on surgery for DD, 200/ 227 (88 %) patients had a primary resection and anastomosis with a morbidity rate of 23 %. In the same study, colostomy closure was associated with significant prolonged hospital stay and one third of colostomy patients did not have their colostomies reversed. In the present study a successful primary resection was achieved in 49/57 (86 %) patients.

Ureteric stents facilitate the localisation of the ureters and are important adjuncts to minimise ureteric injuries at surgery. However, ureteric stents are no a guarantee against ureteric injuries and it is noteworthy that two of the three ureteric injuries in this study occurred in patients despite the use of stents. Thus, in these patients, the stents most likely helped to identify the injury at the time of surgery. This is important, as the prognosis is better when the injury is diagnosed and managed during the primary procedure (Dorairajan, 2004).

7.5   METHODOLOGICAL CONSIDERATIONS

7.5.1   Paper I

An obvious strength in this study was the large study population, made possible by the high quality and coverage of Swedish National Registers. However, the classification of DD might have been a shortcoming, the diagnosis of DD or AD were set by each clinician and stated in the discharge summary and subsequently reported to the National Hospital Discharge Register. No strict diagnostic criteria exist, but the diagnosis was most probably based primarily upon clinical features together with radiology, endoscopic or surgical findings consistent with DD. According to the FU-examinations usually done in patients in our hospital after an episode of AD, (reported in Paper III) 70 % of 311 patients had their diagnosis confirmed on CT images performed in close proximity to admission. Further, in 85 % of patients DD was confirmed with barium contrast enema or CC during FU.

The model was adjusted further to increase the specificity of the registered diagnosis of DD (Table 13, model 3/Page 30). In this model, all individuals recorded with gastrointestinal cancer were excluded but the risks estimated were only minimally affected. Finally, the risk estimated for the diagnosis of AD during 1997-2000 was similar to the risk for DD during the whole study period, implying an acceptable specificity for the DD diagnose in Swedish National Patient Discharge Register.

Discrimination between immigrants and the indigenous population with regard toaccess to health care might be confer a significant risk of bias in studies of this kind. A recent study from the Netherlands, investigated DD findings amongst Turkish immigrants examined with endoscopy because of gastrointestinal symptoms. The number of immigrants undergoing endoscopy reflected the proportion of this group of immigrants

in the region where the study was done (Loffeld, 2005). Recent studies in Sweden on access to primary health care and hospital care have found that ethnic minorities have a fairly equal access, compared to the indigenous population (Hjern et al., 2001, Robertsson E, 2003).

The size of the immigrant population reported sometimes tends to be overestimated in population statistics according to previous reports (Weitoft et al., 1999), as of foreign-born emigration from Sweden is less often reported to authorities compared to native residents. This tendency is particularly important for residents born in countries outside Northern Europe. In order to minimise the effect of this problem in the present study, years period where there was no income from work or social welfare in the household were excluded from the study.

7.5.2   Paper II

The study design required CTC to be completed prior to CC, which may have introduced a response bias favouring CTC. Residual gas from CTC could have contributed to technical difficulty or greater discomfort during the subsequent CC. The given sedation may have masked the patients' recollection of the examinations. In an effort to minimise bias, the examiners were blinded to the results of the other examination and the final questionnaire was sent home to patients to be answered once more. CTC was compared with CC as the reference method and not BE, which in many institutions has been the method of choice when diagnosing DD. This issue was discussed earlier (7.2.1/Page 42).

7.5.3   Paper III

Primarily, the study was observational and patients were not randomised. Therefore, the risk of selection bias was apparent since criteria for the use of antibiotics were not clearly stated; the attending surgeon decided on the use of antibiotics. The group of patients treated with antibiotics presented in a higher proportion with signs of systemic reaction (Table 15/Page 34).

In order to render the patients´ groups (+/- antibiotics) more comparable, it could be argued that patients with CT findings of severe AD, all of whom received antibiotics-Table 15/Page 34), should have been excluded from the study, (. However, findings on CT images were only one of the parameters considered when the decision to add or omit antibiotics (i.e. grade the severity of the acute inflammation) was made. We therefore believed that it was more correct to include all conservatively treated patients.

7.5.4   Paper IV

This study was observational and in retrospect. The most apparent methodological issue in studies of this kind is selection bias in this study, patients were not randomised to surgical management with resection and primary anastomosis or colostomy. Instead, each surgeon decided the surgical procedure. However, since colovaginal fistulas caused of DD are such an infrequent condition, it is virtually impossible to perform prospective randomised trials. This study collected patients over a twelve year period

and only included 60 patients. Thus, this figure is more than twice as large as the larges series reported previously (Table 20/Page 47). When RCT:s are not available or impossible to conduct observational studies are the best available source of data (Benson, 2000).

It is noteworthy that patients may have been missed if they had negative radiological studies and therefore not classified as having a colovaginal fistula.

8 CONCLUSIONS

For the reader's convenience, *the aims* are repeated with the conclusions.

Aims	**Conclusions**
1. Evaluate the influence of ethnicity, and other socio-demographic factors (age, sex, socioeconomic status, housing, urban residency), on the rate of diverticular disease.	Immigrants from Non Westernised countries have lower risk ratios for hospitalisation because of diverticular disease than indigenous Swedes, but the risk increases with time after settlement in Sweden. Diverticular disease appears to be an acquired disorder and acculturation to a Western lifestyle has an impact on the risk. Moreover, this appears to occur during a relatively short period of time in adulthood. Potential socio-demographic confounders, such as socio-economic status, residency and housing situation does not influence the risk.
2. Compare the findings specific for DD and acceptance when imaged by CT Colonography and Colonoscopy respectively in patients after acute diverticulitis.	The diagnostic findings of CT Colonography are comparable to colonoscopy in patients investigated after diverticulitis in this limited study of CT Colonography in routine clinical practice. CT Colonography appears to have a better diagnostic potential for imaging of findings specific to diverticular disease (focal wall thickening, peri-inflammatory changes), when compared with colonoscopy. Irradiation and no possibility of biopsies are disadvantages of CT Colonography. CT Colonography is less discomforting and is preferred by a majority of patients and seems to be a good alternative in the follow-up of patients with acute diverticulitis.

3. Evaluate if antibiotics will change the outcome in patients with mild acute diverticulitis.

To omit antibiotics in the treatment of mild acute diverticulitis appears safe and does not influence the rate of further events (recurrent acute diverticulitis and/or subsequent surgery).

4. Review evaluation, surgical management, morbidity and outcome in patients with fistulas to the female genital tract secondary to diverticular disease.

Diverticular fistulas to the female genital tract most often occur in elderly patients with a prior hysterectomy. The most common presenting symptom is faecal discharge from the vagina. Radiological studies with contrast medium demonstrate the fistulous tract in the majority of cases. Sigmoid resection and primary anastomosis are done safely in the majority of patients. Complications included anastomotic dehiscence, ureteral injuries and wound infections. There was no mortality and all operated patients were cured from their fistulas.

9   SWEDISH SUMMARY FOR LAYMEN

Avhandling för avläggande av medicine doktorsgrad vid Karolinska Institutet, Institutionen för Kliniska Vetenskaper, Danderyds sjukhus, 2006.

ASPEKTER PÅ DIVERTIKELSJUKDOM

Förekomsten av divertikelsjukdom (fickbildning) i tjocktarmen varierar mellan olika delar av världen. Sjukdomen är ovanlig i u-länder, men är en av de vanligaste mag-tarmsjukdomarna i den industrialiserade världen. Divertikelsjukdom är ovanlig före 40 års ålder, men förekomsten ökar sedan med åldern, ses hos mer än hälften av alla 70-80 åringar och är vanligare hos kvinnor än hos män. Den kliniska bilden spänner från ett helt symptomfritt tillstånd, till inflammation i det drabbade tarmsegmentet, som kan leda till förträngning eller fistelbildningar (onormala förbindelser mellan tjocktarmen och intilliggande organ, t.ex. urinblåsan eller slidan), men kan leda till livshotande tillstånd till följd av akut tarmbristning och bukhinneinflammation. I nio av tio fall är det den sista (vänstra) delen av tjocktarmen som är drabbad.

Avhandlingen studerar i fyra delarbeten epidemiologiska (sjukdomens förekomst/delarbete I), metodologiska (undersökningsmetoder för att fastställa sjukdomen/delarbete II), samt kliniska (behandling av inflammation och fistelkomplikationer/delarbete III och IV) aspekter på divertikelsjukdom.

Delarbete I

Epidemiologiska studier i befolkningsgrupper som flyttar från en del av världen till en annan har varit viktiga för att öka kunskapen om livsstilsfaktorers inverkan på flera sjukdomar i mag-tarmkanalen. I delarbete I användes nationella vårdregister, bl.a. Socialstyrelsens slutenvårdsregister, för att göra en befolkningsbaserad studie om riskfaktorer för divertikelsjukdomen. Studiegruppen bestod av 4,4 miljoner individer i Sverige 1990, som följdes under de nästkommande tio åren. 25 000 av dem blev vårdade på sjukhus för divertikelsjukdom. Vi studerade följande faktorer: Etnicitet (svenskfödda jämfört med invandrare från olika delar av världen), ålder, kön, socialgrupp, boendeort, boendeform och dessa faktorers inverkan på risken för individen att utveckla divertikelsjukdom.

Risken var lägre för invandrare från länder utanför västvärlden, jämfört med personer födda i Sverige eller i industrialiserade delar av världen, men risken ökade med tiden som förflutit efter invandringstillfället. Sjukdomen var också vanligare hos kvinnor, framför allt i högre åldrar. Boendeform, socialgrupp och boendeort påverkade endast marginellt risken.

Delarbete II

Undersökning av tjocktarmen är ofta nödvändigt för patienter som behandlats för akut inflammation (divertikulit) i tjocktarmen orsakad av tarmfickor. Detta för att kartlägga utbredningen av sjukdomen samt för att utesluta cancer eller polyper. Förekommande metoder har varit koloskopi (kameraundersökning) eller kontraströntgen, men båda dessa metoder har nackdelar som begränsar användbarhet och diagnostisk kvalitet vid fickbildning. CT kolografi ("Virtuell koloskopi") är en relativt ny metod för avbildning av kolon, vars användbarhet inte specifikt utvärderats för divertikelsjukdomen. Genom att vanlig tvådimensionell skivröntgen kombineras med tredimensionell

bildbearbetning skapas virtuella avbildningar av tjocktarmen. 57 individer undersöktes på Danderyds sjukhus både med CT kolografi och, som referensmetod, traditionell koloskopi. Undersökningarna jämfördes med tonvikt på fynd specifika för divertikelsjukdom samt patienternas upplevelse.

Den diagnostiska kvaliteten för CT kolografi vid divertikelsjukdom var jämförbar med vanlig koloskopi och undersökningen upplevdes som mindre obehaglig och smärtsam än koloskopi samt föredrogs av en majoritet av patienterna.

Delarbete III

Upp till var fjärde av alla individer som har konstaterade tarmfickor får någon gång behandling för inflammation (divertikulit), vanligen med tarmvila och ibland antibiotika. Akut operation behövs i enstaka fall. Värdet av antibiotika har ifrågasatts, men aldrig studerats i kliniska studier. Därför efterundersöktes 311 patienter som behandlats vid Danderyds sjukhus för akut divertikulit och utfallet av behandlingen för de patienter som fick antibiotika jämfördes med dem som behandlades utan antibiotika.

Antibiotikabehandling inverkade inte på vare sig graden av återinsjuknande eller på den av patienterna själva, genom frågeformulär, rapporterade tiden till tillfrisknandet.

Delarbete IV

En ovanlig komplikation till inflammation i tarmfickor är fistelbildning från det sjuka tarmsegmentet i tjocktarmen, till angränsande organ, oftast urinblåsa, eller, hos kvinnor, till underlivet. Symtomen är besvärande och i allmänhet behövs en operation för att bota patienten. I delarbete IV undersöktes 60 kvinnor som behandlats vid Minnesotauniversitet i Minneapolis, USA för, en av tarmfickor orsakad, fistel mellan tjocktarmen och underlivet 3/4 av kvinnorna hade tidigare fått livmodern bortopererad. 57/60 opererades och den vanligaste operationen var borttagande av den del av tjocktarmen där tarmfickorna satt, varefter tarmen kopplades ihop igen. Sex patienter fick en tarmstomi. Ungefär en fjärdedel utvecklade en komplikation, varav fyra tarmskarvar som inte läkte och hos tre patienter fick man reparera skadade urinledare. Slutresultatet blev acceptabelt hos 86 % av patienterna trots att de ofta var gamla och hade andra sjukdomar.

Slutsatser

- Förekomst av divertikelsjukdom påverkas av anpassning till ett västerländskt levnadssätt och denna anpassning kan ske relativt snabbt och i vuxen ålder.

- CT kolografi bör övervägas vid undersökning av tjocktarmen hos patienter med divertikelsjukdom.

- Antibiotikabehandling är inte nödvändigt vid milda former av divertikelinflammation.

- Kirurgisk behandling med tarmresektion och ihopkoppling leder till ett gott resultat hos de flesta patienter med divertikelorsakad fistel till de kvinnliga könsorganen.

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12 APPENDIX

The Swedish questionnaires used in Paper II here translated to English.

QUESTIONNAIRE 1
(AFTER EXAMINATION WITH
COLONOSCOPY)

Mark the alternative that most correctly reflects your experience.

1. Did you experience the examination as strenuous?

☐ Not strenuous at all ☐ A little strenuous ☐ Very strenuous ☐Extremely strenuous

2. Did you experience the examination as painful?

☐ Not painful at all ☐ A little painful ☐ Very painful ☐ Extremely painful

3. Did you experience the examination as discomforting?

☐ Not discomforting at all ☐ A little discomforting ☐ Very discomforting
☐Extremely discomforting

4. Did you experience the examination as embarrassing?

☐ Not embarrassing at all ☐A little embarrassing ☐ Very embarrassing
☐ Extremely embarrassing

Name:_____

Social security number:_____

Date:_____

THANK YOU FOR YOUR COOPERATION

QUESTIONNAIRE 2
(AFTER EXAMINATION WITH
CT COLONOGRAPHY)

Mark the alternative that most correctly reflects your experience.

1. Did you experience the examination as strenuous?

☐ Not strenuous at all   ☐ A little strenuous   ☐ Very strenuous ☐Extremely strenuous

2. Did you experience the examination as painful?

☐ Not painful at all   ☐ A little painful ☐ Very painful ☐ Extremely painful

3. Did you experience the examination as discomforting?

☐ Not discomforting at all ☐ A little discomforting ☐ Very discomforting
☐Extremely discomforting

4. Did you experience the examination as embarrassing?

☐ Not embarrassing at all   ☐A little embarrassing ☐ Very embarrassing
☐ Extremely embarrassing

Name:_____

Social security number:_____

Date:_____

THANK YOU FOR YOUR COOPERATION

QUESTIONNAIRES 3 AND 4 (identical)
(AFTER EXAMINATION WITH BOTH CT COLONOGRAPHY AND COLONOSCOPY)

Mark the alternative that most correctly reflects your experience.

1. Which of the two examinations did you experience as the most strenuous?

☐ CT Colonography ☐ Colonoscopy ☐ No difference ☐ Don't know

2. Which of the two examinations did you experience as the most discomforting?

☐ CT Colonography ☐ Colonoscopy ☐ No difference ☐ Don't know

3. Which of the two examinations did you experience as the most painful?

☐ CT Colonography ☐ Colonoscopy ☐ No difference ☐ Don't know

4. Which of the two examinations did you experience as the most embarrassing?

☐ CT Colonography ☐ Colonoscopy ☐ No difference ☐ Don't know

5. Which one of the two examinations would you prefer if you had to undergo one of them again?

☐ CT Colonography ☐ Colonoscopy ☐ No preference ☐ Don't know

Name:_____

Social security number:_____

Date:_____

THANK YOU FOR YOUR COOPERATION