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ORIGINAL SCIENTIFIC PAPER

**Self-reported Antenatal Adherence to medical treatment among Pregnant Women with
Crohn's Disease**

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Short running title: Adherence in pregnant women with Crohn's disease.

Keywords: Crohns disease, Adherence, Compliance, Medical treatment, Pregnancy, Reproduction, Treatment refusal, Epidemiology, Outcomes research.

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7 BACKGROUND: Adherence to medical treatment among women with Crohn's disease (CD) prior
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9 to and during pregnancy has never been investigated.

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11 METHODS: A total of 132 women with CD who had given birth during 2000-2005 were drawn
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13 from a study population of 1.6 million inhabitants. Questionnaires were used to investigate
14
15 predictors and extent of adherence. The validity of self-reported use of medication was assessed
16
17 using data from the Danish Prescription Database. We used logistic regression to estimate
18
19 prevalence odds ratios for non-adherence according to smoking status and other predictors.
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23 RESULTS: 80% returned the questionnaire. A total of 58 (54%) women reported to have been in
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25 medical treatment, 50 of whom had fulfilled a prescription on relevant medication. Adherence to
26
27 medical treatment was 72%. Fear of a negative effect on fertility/fetus was a reason for non-
28
29 adherence by 18.8% prior to and 45.5% during pregnancy. Among smokers, 30.8% were non-
30
31 adherent compared with 11.5% among non-smokers (prevalence odds ratio 3.41, 95% CI 0.8-14.7).
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35 CONCLUSION: Despite fear of a negative effect on fertility/the fetus, adherence to medical
36
37 treatment was high in women with CD. We observed no substantial variation in adherence prior to
38
39 and during pregnancy. Smoking prior to pregnancy was a predictor of non-adherence.
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44 INTRODUCTION

45
46 Crohn's disease (CD) is an idiopathic, chronic inflammatory disease of the intestine seen among
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48 women of reproductive age. The incidence of this disease has risen substantially from 4.1 in 1978-
49
50 1982 to 10.7 per 100,000 person-years in 1998-2002 (1). Clinical remission is regarded as important
51
52 for the outcome of pregnancy in women with CD (2-4). In order to induce and maintain remission
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54 medical treatment is often needed during both asymptomatic and symptomatic stages of the disease
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59 (5-10).
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4 Lack of adherence to medical treatment is arbitrarily defined as less than 80% intake of the daily
5 prescribed dose of medicine (11). To our knowledge no studies have so far investigated predictors
6 or prevalence rates of non-adherence to medical treatment among pregnant women with CD. Data
7 on non-pregnant patients with ulcerative colitis (UC), however, have demonstrated much variation
8 in non-adherence rates of maintenance therapy, ranging from 20% for short-term to more than 50%
9 for long-term therapy (12-16), and predictors of non-adherence in this group have been shown to
10 include short disease duration, psychiatric comorbidity, and a history of more than four drugs,
11 among others (13;17). These data may therefore serve as clues to the predictors and adherence rates
12 in CD whose incidence seems to be rising. To fill this gap in current knowledge about CD, the aim
13 of the present study was to examine both the predictors and prevalence rates of non-adherence to
14 maintenance medical treatment among women with CD prior to and during pregnancy. We also
15 wanted to validate self-reported adherence prior to and during pregnancy among CD patients by
16 comparing the information they gave with data obtained from an official prescription database.
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37 MATERIALS AND METHODS

38 *Study population*

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40 We conducted this prevalence study in four Danish counties whose total population approximates
41 1.6 million inhabitants. The study included all women having given birth to a singleton between 1
42 January 2000 and 31 December 2005, and who were diagnosed with CD more than one year prior to
43 their date of conception. Multiple births were not included, since women who are pregnant with
44 multiple births may have more complicated pregnancies than singleton mothers (18). Therefore,
45 compliance in these women may be different because of the pregnancy itself. If a woman had given
46 birth more than once during the study period, only the first birth was included.
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4 In August 2006, all the eligible women were asked to fill in a postage prepaid 14-page
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6 questionnaire on medical adherence. Only women returning the questionnaire were included in the
7
8 final study.
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11 12 13 ***Identification of women with CD***

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16 Women with CD were identified through the Regional Patient Administrative System. Established
17
18 in 1977, this registry transfers data to the National Patient Registry which covers 99.4% of all
19
20 discharges from Danish medical hospitals. Outpatient visits at hospitals have been included since
21
22 1995. The data include dates of admission and discharge, surgical procedures performed, and up to
23
24 20 discharge diagnoses which are classified according to the International Classification of Diseases
25
26 10th revision (ICD-10) (19). The code K 50 was used to identify patients with CD. The diagnosis
27
28 was confirmed by review of each patient's medical record.
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34 35 ***Identification of pregnant women***

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37 We identified all singletons born by women with CD through the Danish Medical Birth Registry
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39 which contains information on all births, including homebirths, in Denmark since 1 January 1973;
40
41 the data are recorded by the midwives or doctors responsible for the deliveries (20). The main
42
43 variables in the registry are maternal age, smoking status, birth weight, birth length, parity,
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45 gestational age, sex of child, and stillbirth.
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51 52 ***Self-reported data from women with CD***

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54 The authors developed a questionnaire specifically for the present study to obtain information on
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56 adherence. The questionnaire was tested in twenty randomly chosen women with CD from the
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study-population in May 2006. Answers and comments were evaluated by the authors, which led to only minor changes in the final design.

All study participants received the questionnaire in August 2006. Reminders, including pre-stamped return envelopes and a new questionnaire, were sent twice.

The questionnaire was divided into two sections with identical questions for the two periods: six months prior to conception and from conception to birth. Details concerning birth, weight, length and sex of the offspring were obtained from the Danish Medical Birth Registry and printed in the individual questionnaire to confirm the relevant pregnancy and for the women to confirm the correctness of the data.

The women were asked to evaluate their average daily intake of prescribed medication during the two investigation periods (0-49%, 50-80%, or >80% of the recommended daily dose).

We defined good adherence as a reported consumption of more than 80% of prescribed medications (11). The participants stated one or more reasons for taking less than 80%, such as fear of negative effect on fertility/fetus, quiescence in CD, or forgetfulness were stated. Each participant was asked whether the pregnancy had been planned, and whether experience from a previous pregnancy had influenced her acceptance of medical treatment.

Detailed questions were asked about number and types of drugs prescribed, the administration form, and any inconvenience when rectal administration was applied.

The participant was instructed to state number of flares, which were defined as need for increased medical treatment, and what kind of medical counseling she had received and by whom. Lifestyle factors such as smoking status and alcohol intake were stated. The question about smoking had four categories: on a daily basis, occasionally, former smoker, and non-smoker. Alcohol intake was stated as average number of standard drinks per week. The principal investigator's e-mail address

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4 and private cell phone number was given and participants were told that they could contact the
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6 investigator if they had any questions.
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9 All women signed a written declaration allowing the first and the last author to obtain information
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11 from their hospital records. All questionnaires were converted to a datasheet by double entry
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13 verification.
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18 *The Prescription Database at Aarhus University*

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20 To assess the validity of self-reported use of medication, we retrieved data from the population-
21
22 based Pharmaco-Epidemiological Prescription Database of the four Danish counties covered by the
23
24 present study. In Denmark, the National Health Service provides tax-supported health care for all
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26 inhabitants. Apart from guaranteeing free access to general practitioners, hospitals, and public
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28 clinics, the insurance program refunds part of the costs associated with the purchase of most
29
30 prescribed drugs. The four counties are served by pharmacies equipped with electronic accounting
31
32 systems that track data on all prescriptions on reimbursable medicines. Data tracked include the
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34 patient's Civil Personal Registration (CPR) number (which incorporates date of birth), the type of
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36 drug prescribed according to the anatomical therapeutical chemical (ATC) classification system,
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38 and the date of prescription. From these accounting systems data are transferred to the prescription
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40 database at Aarhus University.
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47 For each pregnant woman with CD, we identified all prescriptions for drugs used to treat CD from
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49 1August 1999 to 31July 2006. The following ATC-codes were used for medicine redeemed in the
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51 period six months prior to and during pregnancy: A07EC01 - 04, L04AX01, L01BB02, A07EA01 –
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53 02, A07EA06, H02AB06 - 07, P01AB01, and J01MA02.
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The unique 10-digit CPR number, which is assigned to all Danish citizens shortly after birth, was used to link prescription records with the Danish Medical Birth Registry and the county hospital discharge registry.

Statistical analysis

The redemption of a prescription of CD-specific medication registered in the prescription database was used as reference standard in the validity analysis. We computed the positive predictive value (PPV) as the proportion of women reporting to receive medical treatment who were also registered with a prescription in the prescription database, *i.e.*, the numerator was the number of women who reported use of medication and who fulfilled a prescription and the denominator was the number of women who reported to receive medication.

For the two pregnancy periods, we constructed frequency tables of major study variables.

We cross-tabulated planned pregnancy, previous pregnancy with the CD diagnosis, counseling and smoking status by non-adherence status and estimated prevalence odds ratios using logistic regression models, and calculated exact 95% confidence intervals (CI) for a binomial distribution.

All analysis was done using Stata version 9.2 (StataCorp LP, Texas, USA).

The study was approved by the National Board of Health, by the University of Aarhus Institutional Review Board and by the Danish Data Protection Agency before any patients were recruited. No approval from the Danish Ethical Committee was needed according to the Danish law.

RESULTS

We identified a total of 154 women diagnosed with CD who gave birth to a singleton during our study period. No stillbirths among women with CD were identified. We excluded 21 (14%) women

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4 since review of their medical records could not confirm a CD diagnosis. One woman had passed
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6 away for reasons unrelated to CD, leaving a study-population of 132 women.
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9 Among these 132 women, 105 (80%) returned filled-in questionnaires. Patient characteristics are
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11 shown in Table 1. The majority of pregnancies (78%) were planned. A total of 58 (54%) women
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13 had received medical treatment prior to and/or during their pregnancy. According to the Regional
14
15 Patient Administrative System, 17 (63%) of the non-responders had redeemed a prescription of a
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17 drug used to treat CD.
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23 **Validity of self-reported data**

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25 Overall, 58 women stated to be in medical treatment prior to and/or during pregnancy, among
26
27 whom 50 had fulfilled a prescription on relevant medication according to the Prescription Data
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29 Base, which yielded a PPV of 86.2% (95% CI 74.6-93.9). We observed no substantial difference
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31 between the PPVs for the period six months prior to pregnancy (85.2% (95% CI 72.9-93.4) and the
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33 PPVs during pregnancy (and 87.3% (95% CI 75.5-94.7)).
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40 **Use of medical treatment**

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42 Among the participants, 40% of those who received medical treatment for CD had been pregnant
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44 before knowing that they had CD. In approximately half of these pregnancies (44%), the women
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46 stated that the previous pregnancy had influenced their choice of medical treatment during their
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48 current pregnancy.
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52 The different drugs used prior to and during pregnancy are shown in Table 2: 54% were taking 5-
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54 ASA drugs. The proportion of women in medical treatment using immunosuppressants
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56 (thiopurines) was higher prior to pregnancy (38%) than during pregnancy (30%). 51 women (49%)
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4 received medical treatment in both periods of investigation. The characteristics on those women
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6 who received medical treatment are shown in Table 3.
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9 *Six months prior to pregnancy*

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11 Six months prior to the pregnancy 54 (51.4%) women reported that they were in medical treatment
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13 and 41 (75.9%) (95% CI 62.4-86.5) reported that they were adherent to medical treatment. **The type**
14
15 **of medication had no impact on adherence.** Among non-adherent women, 72.7% (95% CI 39.0-
16
17 94.0) stated that the main reason for their non-adherence was quiescence in CD, while 18.8% (95%
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19 CI 2.3-51.8) stated fear of negative effect on fertility as their main reason. One woman (9.1%) (95%
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21 CI 0.2-41.3) stated forgetfulness as a reason for non-adherence. A majority of the women (72%)
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23 were in remission six months prior to pregnancy. Five of the seven women who experienced a flare
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25 were either non-adherent to medical treatment or smokers.
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29 The form of administration (i.e. tablets, enema, or suppositories) had no influence on adherence in
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31 89% (95% CI 77.4-95.8). Approximately 60% (95% CI 45.0-72.4) of the women had received
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33 counseling on medical treatment; most often by a gastroenterologist. More than 70% (95% CI 53.3-
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35 86.3) were advised to continue their current medical treatment, whereas nearly 20% (95% CI 7.2-
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37 36.4) were advised to stop medical treatment. **Of the six patients who were advised to stop medical**
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39 **treatment three stated adherence and three stated non-adherence to medical treatment.**
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45 *During pregnancy*

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47 During pregnancy, 55 (52.4%) women reported that they were in medical treatment and 37 (67%)
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49 (95% CI 53.3-79.3) reported that they were adherent to medical treatment. **The type of medication**
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51 **had no impact on adherence.** The main reason for being non-adherent was stated to be quiescent CD
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53 (72.7%) (95% CI 39.0-94.0). Non-adherence was ascribed by 45% (95% CI 16.8-76.6) to fear of
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55 negative effects on the fetus. Non-adherence was ascribed to forgetfulness by one woman (9.1%)
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4 (95% CI 0.2-41.3). Remission during pregnancy was seen in 64% (95% CI 49.6-76.2). Four of the
5
6 five women who experienced a flare were either non-adherent to medical treatment or smokers.
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9 The administration form of medical treatment, i.e. tablets, enema or suppositories, was reported by
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11 82% of the patients (95% CI 63.0-86.8) to have had no influence on their adherence. A total of 80%
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13 (95% CI 67.0-89.5) of the patients had received counseling concerning medical treatment during
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15 pregnancy which was offered in most cases by a gastroenterologist, and 75% (95% CI 59.7-86.8)
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17 were advised to continue their current medical treatment. Close to 10% (95% CI 2.5-21.7) had been
18
19 advised to stop medical treatment, whereas five women (95% CI 3.8-24.6) had been advised to
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21 modify their current treatment. Of the four patients who were advised to stop medical treatment one
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23 stated adherence and one stated non-adherence to medical treatment. Two women did not state their
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25 adherence-status.
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33 **Lifestyle factors**

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35 According to the women's responses, a total of 48 (46%) smoked prior to their pregnancy (Table 4).
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37 In comparison, 32 (31%) were recorded as smokers in the Danish Medical Birth Registry. Among
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39 non-responder, ten (37%) were registered as smokers in the Danish Medical Birth Registry of
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41 whom eight (80%) (95% CI 44.4-97.5) were in medical treatment according to the Prescription
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43 Database.
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46 Prior to pregnancy, 50% of those who were in medical treatment and 37% of those who were not in
47
48 medical treatment were total abstainers. Irrespective of medical treatment, 35-40% had one to two
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50 standard drinks pr week and approximately 10% had more than three standard drinks per week.
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53 During pregnancy, no one reported to have had more than one to two standard drinks per week.
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58 **Predictors for non-adherence prior to pregnancy**

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4 Among women who reported to be smokers, 58.3% were in medical treatment among whom 30.8%
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6 reported to be non-adherent to their medical treatment compared with 11.5% among non-smoking
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8 women. Non-adherence was thus almost three times higher among smokers than among non-
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10 smokers (prevalence odds ratio [POR] 3.41, 95% CI 0.8-14.7).
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14 We found that women who received counseling regarding medical treatment were less likely to be
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16 non-adherent than women received no such counseling (POR 0.69, 95% CI 0.2-2.9). This was also
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18 the case if the woman had been pregnant before while knowing that she had CD compared with
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20 primiparous CD women (POR 0.52, 95% CI 0.1-2.3) and if the pregnancy had been planned (POR
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22 0.58, 95% CI 0.1-2.8).
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28 **Predictors for non-adherence during pregnancy**

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30 The prevalence of smokers decreased during pregnancy. Among women who reported to be
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32 smokers, 57.1% were in medical treatment of whom 21.4% reported to be non-adherent to their
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34 medical treatment compared with 22.9% among non-smoking women (POR 0.89, 95% CI 0.2-4.0).
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38 We found that counseling about medical treatment did not change the likelihood of being non-
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40 adherent to medical treatment (POR 0.97, 95% CI 0.1-10.4). However, the women were less likely
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42 to be non-adherent to medical treatment if they had been pregnant before while knowing that they
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44 had CD compared with primiparous CD women (POR 0.75, 95% CI 0.2-3.0), and if the pregnancy
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46 had been planned (POR 0.55, 95% CI 0.1-2.7).
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51 **DISCUSSION**

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53 This study is the first population-based study on adherence to medical treatment among pregnant
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55 women with CD. A major strength of the study is its 80% response rate and a high concordance
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57 between self-reported medical treatment and the prescription database.
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4 Overall adherence to medical treatment was 72%, which is higher than reported among non-
5 pregnant women (13;21;22). We found that the type of medication had no impact on adherence. The
6 majority of non-adherent women cited quiescence in CD as a primary reason for non-adherence.
7
8 The percentage who stated fear of negative effect on fertility/fetus as their reason for non-adherence
9
10 was higher during pregnancy than prior to pregnancy. Data regarding forgetfulness as a reason for
11 non-adherence were conflicting. In accordance with Ediger et al., we found that forgetfulness had
12 no impact on adherence (21), whereas Kane et al. and D'Incá et al. found that 50% and 61%
13 reported forgetfulness as a reason for being non-adherent to medical treatment among non-pregnant
14 and pregnant women, respectively (16;23).
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28 Smoking was associated with non-adherence prior to pregnancy. Information on smoking status was
29 self-reported and could be confirmed by data from the first antenatal care among two thirds of the
30 women. The prevalence of smokers among CD women having their first antenatal care consultation
31 was lower in the present study than in a previous Danish study by Nørgaard et al. (24), which
32 reflects a decrease in the prevalence of smokers among Danish pregnant women. During a period of
33 seven years (1989-1996), the prevalence of smoking among pregnant women dropped from 34% to
34 21% (25). Still, we cannot rule out that we may have classified some smokers as non-smokers
35 which could cause underestimation of the association between smoking and non-adherence. In
36 accordance with two other studies, the prevalence of smokers among patients with CD was
37 markedly reduced during pregnancy (26;27), and an association between smoking status and non-
38 adherence could not be detected during pregnancy.
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56 A high proportion of women received counseling on medical treatment prior to and during
57 pregnancy, which was mostly provided by gastroenterologists. It was anticipated that counseling
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4 would affect adherence to medical treatment, but the results of our study only supported this
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6 assumption for the period prior to pregnancy. Our questionnaire did not specifically ask questions
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8 regarding the patient-physician relationship, but Nguyen et al. found that patient-physician
9
10 relationship in general, and patients' trust in physicians in particular, was a significant, positive
11
12 predictor of adherence to medical treatment in patients with inflammatory bowel disease (IBD)
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14 (28). **How accurate women remember medical counselling may differ according to time since**
15
16 **pregnancy and also according to compliance. We anticipated that women with poor compliance to a**
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18 **higher degree reported that their gastroenterologist had advised them to discontinue their treatment.**
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20 **Yet, our results did not support any clear conclusions regarding this aspect.**
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28 A novel finding in the adherence literature and of particular interest in this context is that the
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30 present study found that non-adherence to medical treatment was less likely both prior to and during
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32 pregnancy if the woman had been pregnant before while knowing that she had CD compared with
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34 primiparous CD women, and if the pregnancy had been planned. **Unfortunately, we did not ask the**
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36 **women whether they had experienced a flare during a previous pregnancy so we were unable to**
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38 **examine whether this aspect influenced adherence to medical treatment in a following pregnancy.**
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45 Among women who experienced a flare, more than 50% were either smokers or non-adherent to
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47 medical treatment; however, the numbers were small. The importance of adherence to maintain
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49 remission was also demonstrated by Kane et al., who found that adherent patients with UC had an
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51 89% chance of maintaining remission compared with only 39% in those who were non-adherent
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53 (16). We found a decrease in the number of flares during pregnancy which may be explained by the
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55 low number of smokers, since smoking leads to a more severe disease course as well as an
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57 increased use of medical treatment (29;30). Agret et al. found a reduction in tobacco consumption, a
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4 lower CD activity, and a significant decrease in medical treatment during pregnancy compared with
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6 prior to pregnancy (26).
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11 In the present study, more than half of the women were in medical treatment prior to and during
12 pregnancy. This correlates well with a European study by Riis et al. of a cohort of 266 IBD patients
13 diagnosed with CD or UC in 1991-93 and followed for 10 years, where 177 pregnancies occurred
14 after IBD diagnosis was settled (31), even if we found a higher frequency of thiopurine use than did
15 Riis et al. This difference probably reflects the increased use of thiopurines in CD in response to the
16 international recommendations and guidelines (32).
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28 There are no safe methods for detecting non-adherent behavior. We used a measure of self-reported
29 non-adherence to medication (33) since previous studies have shown that this method correlates
30 well with pill counts (34), electronic monitoring, and pharmacy refill records (35). In addition, more
31 elaborate and less practical methods have not yet obtained the sophistication to disclose attempts to
32 conceal non-adherence (36).
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42 Conducting an investigation using questionnaires has previously been shown to be difficult because
43 response rates tend to be low. Thus, the response rate obtained in the present study was much higher
44 than rates obtained in three recently published IBD studies on aspects of adherence to medical
45 treatment (32%), voluntary childlessness (20%), and reproductive behaviour (59%) (37-39). The
46 high response rate in the present study may be explained by the importance women with CD ascribe
47 to medical treatment during their pregnancy. Furthermore, the use of a pre-stamped return envelope
48 enclosed with the questionnaire in combination with the repeated contacts to the patients may also
49 have had a positive effect on the response rate.
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7 Recall bias cannot be ruled out when conducting a questionnaire survey. In the present study, we
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9 found an approximately 14% discrepancy between self-reported medical treatment and the Danish
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11 prescription database. We therefore hardly expect recall bias to play a substantial role in the present
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13 study.
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18 Bias due to differential recruitment was avoided owing to the population-based design. Further
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20 design strength was gained owing to the highly organized nature of the Danish Health Care system.
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22 Thus, a previous study found that the quality of the diagnosis of CD in the Regional Patient
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24 Administrative System reached 97% (40). The quality of the data in the Danish Medical Birth
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26 Registry is also reported to be high (41;42). In the present study, participants found all data from the
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28 Danish medical Birth Registry to be correct. Furthermore, in order to minimize the influence of
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30 short disease duration on adherence, the diagnosis had to be established at least a year prior to
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32 pregnancy (43).
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40 Information from the prescription database shows that the proportion of women in medical
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42 treatment was the same in the group included in our study and in the group that did not return the
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44 questionnaire. However, we do not know whether non-participants were more or less likely to be
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46 non-adherent than were the participants.
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51 In conclusion: Adherence to medical treatment among pregnant women with CD was high, and self-
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53 reported adherence is a useful data source when studying these women. We found that women who
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55 received professional counseling were less likely to be non-adherent to medical treatment prior to
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57 pregnancy than women who received no counseling. Moreover, smoking was associated with non-
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4 adherence prior to pregnancy. Experience from a previous pregnancy influenced the women's
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6 behaviour in regard to medical treatment during the pregnancy. These aspects should be taken into
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8 account in the consultation prior to pregnancy with a view to reducing the risk of complications that
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10 may spring from patient-related attitudes.
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Table 1: Characteristics of 105 women with Crohn's disease who gave birth to a singleton between 2000-2005 with and without medical treatment prior to and/or during pregnancy

	Medical treatment prior and/or during the pregnancy N=58 ^A	No medical treatment prior and during the pregnancy N=47
Demographic	Median (Range)	Median (Range)
Years since diagnosed	7.9 (3.3-12.9)	7.5 (4.1-12.9)
Age at the time of delivery, yr	30.1 (22.3-39.1)	30.5 (24.0-39.8)
Height (cm)	168.0 (152.0-181.0)	168.0 (154.0-180.0)
Weight (kg)	61.5 (47.0-98.0)	63.5 (43.0-110.0)
Body mass index (kg/m ²)	22.2 (17.2-31.6)	22.7 (15.1-39.9)
Gestational age (week)	39.0 (34.1-42.3)	39.9 (34.4-42.0)
Clinical	N (%)	N (%)
Planned pregnancy	45 (77.6)	43 (91.5)
Weight gain during the pregnancy (kg)	(11-15) (43.8)	(11-15) (42.6)
Cesarean section	24 (41.4)	16 (34.0)
Had been pregnant before while diagnosed with CD	23 (39.7)	17 (36.2)
Stated their phone number	54 (93.1)	44 (95.7)

^A 51 women received medical treatment prior to and during pregnancy. Three women only received medical treatment prior to their pregnancy, whereas four women only received medical treatment during their pregnancy. In total, 58 women received medical treatment.

^B Answer given on a 5 kg interval scale from 5kg - >30kg

^C Women were asked for contact information in the case the investigators needed to clarify their answers in the questionnaire

Table 2: Self-reported use of medical treatment among women with Crohn's disease prior to and during pregnancy

Drug	Prior to pregnancy	During pregnancy
	N (%)	N (%)
5-ASA (5 Aminosalicylates)	31 (53.4)	28 (52.8)
Thiopurines (Azathioprine & 6-MP)	22 (38.0)	16 (30.2)
Systemic glucocorticoid	5 (8.6)	8 (15.1)
Local glucocorticoid	0 (0.0)	1 (1.9)
Antibiotics (Metronidazole or Ciprofloxacin)	0 (0.0)	0 (0.0)
Total number of women treated within the group ^A	58 (100.0)	53 (100.0)

^ASome women are listed more than once due to a combination of several drugs in their daily treatment. No recollection of exact medication prior to their pregnancy was reported by approximately 2% of the women, and no recollection during pregnancy was reported by approximately 10%. Fifty women (49%) took no medication prior to pregnancy, 50 women (48%) took no medication during pregnancy.

Table 3: Characteristics of women with Crohn's disease in medical treatment who gave birth to a singleton between 2000-2005.

Characteristics	Prior to pregnancy N = 54 ^A	During pregnancy N=55 ^A
	N (%)	N (%)
Remission according to the patients	39 (72.2)	35 (63.6)
Flare which resulted in increased medical treatment	7 (13.0)	5 (9.1)
Received medical treatment counseling	32 (59.3)	44 (80.0)
The counselors profession:		
Gastroenterologist	31 (96.9)	41 (93.2)
General practitioner	0 (0.0)	1 (2.3)
Gynecologist	1 (3.1)	2 (4.6)
The advice from the counselor:		
Increase medical treatment/drug intake	0 (0.0)	1 (2.3)
No changes in medical treatment	23 (71.9)	33 (75.0)
Decrease in medical treatment	1 (3.1)	1 (2.3)
Stop medical treatment	6 (18.8)	4 (9.1)
Another kind of advice	2 (6.3)	5 (11.4)
Adherence to medical treatment ^B	41 (75.9)	37 (67.3)
Non-adherent to medical treatment	11 (20.4)	11 (20.0)
Reasons for non-adherence:		
Quiescent Crohn's disease	8 (72.7)	8 (72.7)
Fear of negative effect on fertility/the fetus	2 (18.8)	5 (45.5)
Forgetfulness	1 (9.1)	1 (9.1)
Another reason	2 (18.8)	1 (9.1)
Did administration form influence on adherence:		
Yes	1 (1.9)	3 (5.5)
No	48 (88.9)	42 (81.8)

^A 51 women received medical treatment 6 months prior to and during pregnancy.

^B Intake of >80% of daily prescribed dose

Table 4: Lifestyle factors among women with Crohn's disease who gave birth to a singleton between 2000-2005.

	Six months prior to pregnancy		During pregnancy	
	Medical treatment N = 54	No medical treatment N = 51	Medical treatment N = 55	No medical treatment N = 50
Smoking	N (%)	N (%)	N (%)	N (%)
Smoker	28 (51.9)	20 (39.2)	16 (29.1)	12 (24.0)
Non-smoker	26 (48.1)	31 (60.8)	39 (70.9)	38 (76.0)
Alcohol intake pr. week				
No weekly intake	27 (50.0)	19 (37.3)	46 (83.6)	32 (64.0)
1-2 standard drinks	19 (35.2)	21 (41.2)	9 (16.4)	14 (28.0)
3-4 standard drinks	4 (7.4)	3 (5.9)	0 (0.0)	0 (0.0)
> 4 standard drinks	1 (1.9)	4 (7.8)	0 (0.0)	0 (0.0)
Missing	3 (5.5)	4 (7.8)	0 (0.0)	4 (8.0)

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7 **ACKNOWLEDGMENTS**
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DECLARATION OF INTERESTS

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