Body Mass and the Risk of Endometrial Cancer

by

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CONTENTS

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PAPERS INCLUDED IN THIS THESIS

Paper I: Lindemann K, Vatten LJ, Ellstrøm-Engh M, Eskild A. **Body mass, diabetes and smoking, and endometrial cancer risk: a follow-up study.** Br J Cancer. 2008 May 6;98(9):1582-5.

Paper II: Lindemann K, Vatten LJ, Ellstrøm-Engh M, Eskild A. **Serum lipids and endometrial cancer risk: Results from the HUNT-II study.** Int J Cancer. 2009 Jun 15;124(12):2938-41

Paper III: Lindemann K, Vatten LJ, Ellstrøm-Engh M, Eskild A. **The impact of BMI on subgroups of uterine cancer.** Br J Cancer. 2009 Aug 4;101 (3):534-6.

Paper IV: Lindemann K, Eskild A, Vatten LJ, Bray F. **Endometrial cancer incidence trends in Norway during 1953-2007 and predictions for 2008-2027**. Int J Cancer. 2010 Feb. In press.

ABBREVIATIONS

APC	Adenomatous polyposis coli
Bcl-2	B-cell lymphoma 2
BMI	Body mass index
COCs	Combined oral contraceptives
E_1	Estrone
E_2	Estradiol
FIGO	International Federation of Gynecology and Obstetrics
GOG	Gynecologic Oncology Group
HDL	High-density lipoprotein
HER-2/neu	Human epidermal growth factor receptor
HNPCC	Hereditary nonpolyposis colorectal carcinoma syndrome
HRT	Hormone replacement therapy
HUNT	Nord-Trøndelag Health Study
ICD	International Classification of Diseases
IGF-1	Insulin-like growth factor 1
IGFBP-1	Insulin-like growth factor binding protein 1
IL-6	Interleukin 6
K-ras	Kirsten rat sarcoma viral oncogene
LDL	Low-density lipoprotein
MAPK/ERK	Mitogen-activated protein kinase/extracellular signal-regulated kinase
MMR	Mismatch repair genes
MSI	Microsatellite instability
MOTNAC	Manual of Tumour Nomenclature and Coding
MVD	Microvessel density
PCOS	Polycystic ovary syndrome
PIK3CA	Phosphatidylinositol-3-kinase, catalytic, alpha polypeptide
PPAR	Peroxisome proliferator-activated receptor
PTEN	Phosphatase and tensin homolog
PI3K/AKT	Phosphatidylinositol-3-kinase/serine/thyreonine kinase Akt
SHBG	Sex-hormone binding globulin
TNF-α	Tumour necrosis factor alpha
VEGF-A	Vascular endothelial growth factor A
15d-PGJ_2	15-deoxy-Δ-prostaglandin J_2

FIGURES AND TABLES

Figures

Tables

1. INTRODUCTION

1.1 Epidemiology of uterine cancer

Uterine cancer accounted for 233,300 new cases and 61,400 deaths worldwide in 2005 [1]. It is the most common cancer of the female genital tract in developed countries, but there is more than 14-fold variation in the incidence between countries (Figure I) [2]. In Norway, the reported rate is about 16 cases per 100,000 women per year, whereas rates in developing countries are generally lower than 5 per 100,000 [1,3]. Temporal incidence trends appear to differ by the timing of menopause. In Norway, the increasing incidence of postmenopausal uterine cancer contrasts with the declining rates observed in premenopausal women from 1953 to 1997 [4].

Uterine cancer refers to different types of carcinomas of the uterine corpus. Epithelial, mesenchymal, mixed epithelial and mesenchymal and trophoblastic tumours can be distinguished according to the cells they originate from (Table I). Epithelial tumours originate from the cells of the endometrium, the inner lining of the uterus, and account for ca. 90% of all uterine cancers.

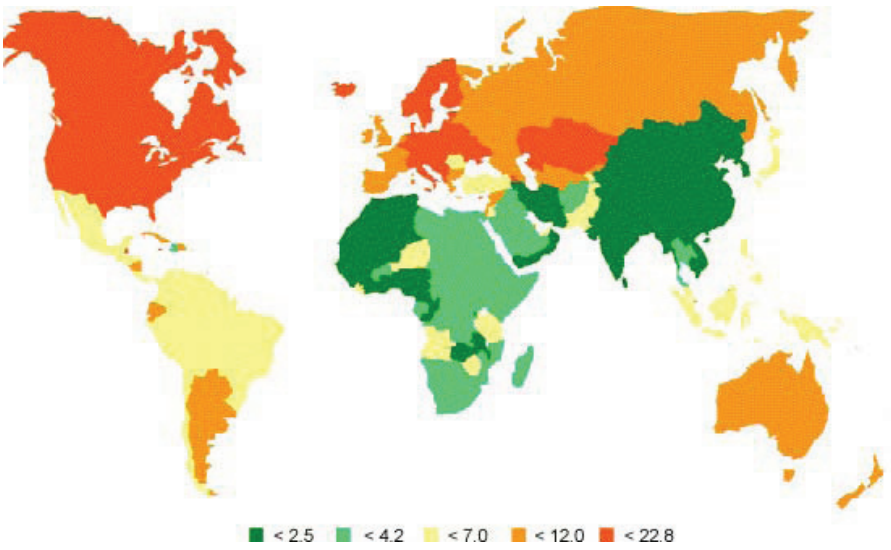


Figure I: Incidence of cancer of the uterine corpus:
Age-standardized rates (world) per 100,000 (all ages) [5]

Table I: Histological classification of malignant tumours of the uterine corpus [6]

1. Epithelial tumours/ Endometrial carcinoma	Type I/Endometrioid adenocarcinoma	• Typical • Villoglandular • Variant with squamous differentiation • Secretory variant • Ciliated variant
	Type II	• Papillary serous • Clear-cell
	Mixed pattern cancers	• Mixed adenocarcinoma
	Rare subtypes	• Mucinous adenocarcinoma • Squamous cell carcinoma • Transitional cell carcinoma • Small cell carcinoma • Undifferentiated carcinoma
2. Mesenchymal tumours	Endometrial stromal tumours	• Endometrial stromal sarcoma, low grade • Endometrial stromal nodule • Undifferentiated endometrial sarcoma
	Smooth muscle tumours	• Leiomyosarcoma • Smooth muscle tumour of uncertain malignant potential
	Miscellaneous mesenchymal tumours	
3. Mixed epithelial and mesenchymal tumours	Carcinosarcoma	
	Adenosarcoma	
	Carcinofibroma	
4. Gestational trophoplastic disease	Trophoplastic neoplasms	• Choriocarcinoma • Placental site trophoplastic tumours • Epithelioid trophoplastic tumours
	Molar pregnancies	• Partial • Complete • Invasive • Metastatic

As the vast majority of cancers of the uterine corpus are endometrial adenocarcinomas, we will hereafter refer to the disease as endometrial cancer.

1.2 Established risk factors of endometrial cancer

Age: The majority of endometrial cancers are diagnosed in postmenopausal women. In 2007 the highest incidence rates in Norway were observed in the age group 70-74 years (89 per 100,000).

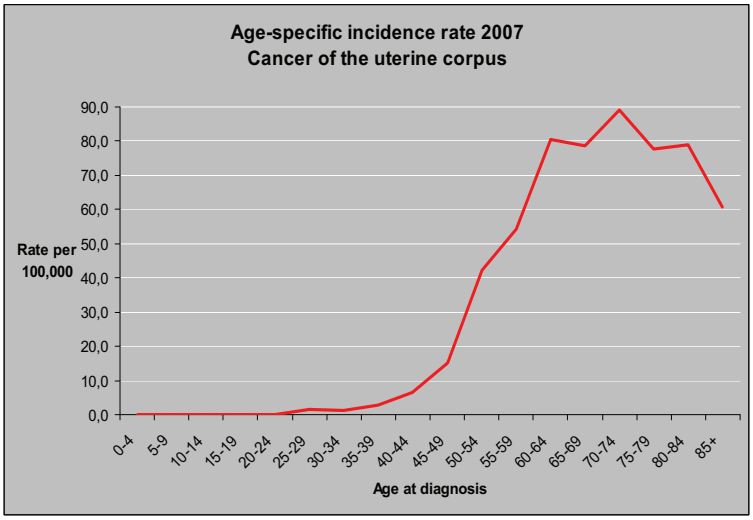


Figure II: Age-specific incidence rates for cancer of the uterine corpus (2007) [7]

Reproductive factors: Early menarche and late menopause have consistently been associated with increased risk, probably due to a longer lifetime exposure to endogenous estrogen [8-11]. Nulliparity is associated with increased risk. Risk decreases with increasing parity, with the most pronounced risk reduction following the first birth [12-15]. However, studies of the impact of age at first or last birth have shown conflicting results [9-11;13;15]. Endocrine disorders like the polycystic ovary syndrome (PCOS) are also associated with an increased risk of endometrial cancer. Chronic anovulation in those women leads to a lack of progesterone secretion normally present in the luteal phase. This constant estrogenic stimulation of the endometrium may cause endometrial hyperplasia and ultimately endometrial cancer [16].

Exogenous hormone use

Hormone replacement therapy (HRT): The main hypothesis in the development of endometrial cancer is exposure to unopposed estrogen (lack of progesterone) leading to increased mitotic activity, DNA replication and somatic mutations in endometrial cells [17]. Menopausal treatment using estrogen unopposed by progesterone increases the risk of subsequent endometrial cancer in a dose-risk manner [18], and combined

regimens of estrogen and progesterone were introduced to prevent this side effect. Nevertheless, minor increases in risk have also been reported for the combined treatment [19;20].

Combined oral contraceptives (COCs): The use of combined oral contraceptives has consistently been found to reduce the risk for endometrial cancer. Ever use is reported to be associated with a 30% lower risk with an approximately 10% decrease in risk per each year of use. The protective effect of COCs appears to last over several years after cessation [21-23].

Tamoxifen: Clinical trials such as the National Surgical Adjuvant Breast and Bowel Project (NSABP) and British Tamoxifen Second Cancer Study Group have provided evidence that endometrial cancer risk is increased in women with breast cancer treated with Tamoxifen [24;25]. Tamoxifen use has been associated with a two-fold increased risk for endometrial cancer that was also dependent on duration of the use [26].

Obesity: Endometrial cancer was the first cancer that was related to obesity [27]. Several cohort [28-34] and case-control studies [35-42] have confirmed a positive association of obesity with endometrial cancer risk.

Diabetes mellitus: Diabetes type 2 has also been related to increased risk of endometrial cancer in both cohort [29;43;44] and case-control studies [40;45-51].

Smoking: Smoking has been reported to reduce risk in many studies [52-55]. The underlying mechanisms for the reduced risk associated with cigarette smoking are poorly understood and are probably not exclusively caused by lower body weight among smokers.

Heredity: Approximately 5% of all endometrial cancers are caused by inherited susceptibility. The Lynch syndrome (hereditary nonpolyposis colorectal carcinoma syndrome, HNPCC) accounts for most hereditary cases. Women with HNPCC have a lifetime risk of 42% for endometrial carcinoma [56].

1.3 Symptoms and diagnosis

Endometrial cancer is often detected early, since bleeding is a symptom in the early stage of the disease. Abnormal bleeding is present in approximately 90% of the cases [57]. Among postmenopausal women, any bleeding is considered a possible

symptom of endometrial cancer and should lead to diagnostic testing. The probability of endometrial cancer in postmenopausal women with vaginal bleeding is 5-10%, but the chances increase with age and risk factors [58]. Pre- and perimenopausal women with abnormal bleeding should also be examined for endometrial cancer, particularly if they have other risk factors (obesity, hormone-replacement therapy, tamoxifen use). Vaginal discharge without bleeding may be another symptom, whereas abdominal pain and distension occur later, at an advanced stage of the disease. Diagnostic approaches include gynaecological examination, vaginal ultrasound and endometrial sampling by either a Pipelle de Cornier sampling device or curettage in order to obtain tissue for a histological diagnosis. A pelvic magnetic resonance imaging is best in order to evaluate the size of the tumour, myometrial invasion and involvement of the cervix. Intra-abdominal spread is assessed by an abdominal computer tomography scan (CT). A thoracic x-ray or CT is performed to assess extra-abdominal spread.

1.4 Molecular basis of endometrial cancer

The understanding of the molecular pathogenesis of endometrial cancer is still far from complete, although various molecular alterations have been identified. These advances in molecular biology have reinforced that malignant tumours seem to arise from an accumulation of inherited and somatic alterations in oncogenes, tumour suppressor genes and DNA repair genes.

Oncogenes: Oncogenes are usually inactive, and activation stimulates cell division. Among proto-oncogenes, the k-ras gene has been extensively studied in endometrial cancer, with a reported frequency of point mutations in 10-37% [59]. There is further evidence for k-ras mutations being an early event in the development of endometrial cancer as the mutation is also reported in endometrial hyperplasia.

Another proto-oncogene, Her-2/neu, a member of the tyrosine kinase family, is considered to play a role in cellular transformation and tumourigenesis. Over-expression of Her-2/neu is reported in 10-20% of the cases, being more frequent in non-endometrioid tumours [59].

Mutations in PIK3CA, a catalytic subunit of PI3K, have been identified in 24-36% of endometrial carcinomas and are coexisting with PTEN mutations [60].

Tumour suppressor genes: Tumour suppressor genes code for proteins inhibiting tumour growth. When mutated, they become inactive and growth is allowed. The tumour suppressor gene PTEN is the most frequently mutated gene in endometrial carcinoma and is an early event in carcinogenesis. Loss of PTEN activates the PI3K/AKT pathway leading to up-regulation of several factors involved in cell proliferation, cell survival and angiogenesis [61]. Absence of functional PTEN leads to activation of the MAPK/ERK (mitogen-activated protein kinase/extracellular signal-regulated kinase) pathway that is stimulated by growth factors [62].

The tumour suppressor gene p53 encodes a protein that contributes to cell cycle arrest by binding to transcriptional elements in DNA. Nuclear p53 induces cell cycle arrest at the G1/S checkpoint prior to DNA replication and at the G2/M checkpoint prior to mitosis. These arrests enable time for DNA damage repair and prevent accumulation of mutations. In cases where the DNA damage is beyond repair, it also promotes apoptosis [63]. Cells with mutated p53 that have damaged DNA, will continue directly to the S-phase leading to further accumulation of mutations, ultimately leading to tumorigenesis [64]. P53 mutations have been found in 10-20% of endometrial carcinomas [65], while overexpression is present in about 15-30% [66].

The tumour suppressor gene CDKN2A/p16 encodes the p16 protein which acts by blocking cell cycle progression through inhibition of the CyclinD-CDK4 complex formation [67]. In endometrial cancer, loss of protein expression varies from 14-74% [68].

Microsatellite instability (MSI): Microsatellites are simple repetitive DNA sequences distributed widely throughout the genome. Microsatellite instability is a result of an accumulation of mutations caused by defects in the mismatch repair genes (MMR) during replication. MSI was first detected in tumours from patients with HNPCC, but has also been found in sporadic endometrial cancer [69].

Cell cycle regulation and proliferation: In endometrial carcinoma, both cell cycle stimulating and cell cycle inhibitory proteins show altered expression. The most frequent disruption of the cell cycle is at the G1/S restriction point before DNA replication. The G1/S regulators are oncogenes like cyclin D1, D2 and E, CDK4/6 and tumour suppressor genes like p16, p21, p27 and the retinoblastoma protein.

Apoptosis: The normal cyclic variation in endometrial tissue seems to be regulated by apoptotic stimuli. In endometrial carcinoma, mutations in the apoptosis inhibitory gene Bax cause concomitant loss of Bax expression [70]. The oncogene Bcl-2 encodes a protein that inhibits apoptosis, and its expression is reduced in endometrial carcinoma [70].

Cell adhesion and invasion: The ability of cancer cells to invade the surrounding tissue and to establish growth of tumour cells in distant organs represents the final step of tumour progression and is dependant on the interaction of their cell surface with the microenvironment. Specific genetic alterations in cellular adhesion molecules, among them cadherins and catenins, have been shown to be important for tumour-stroma and tumour-vascular interactions. The β-catenin gene product is involved in two biological pathways. One involves E-cadherin that takes part in cell-cell adhesion and the transmission of anti-growth signals. In the second pathway, β-catenin is released from its association with APC (adenomatous polyposis coli) tumour suppressor protein allowing its translocation to the nucleus, where it acts as a cofactor to induce expression of cyclin D1 and other genes involved in cell cycle progression [71].

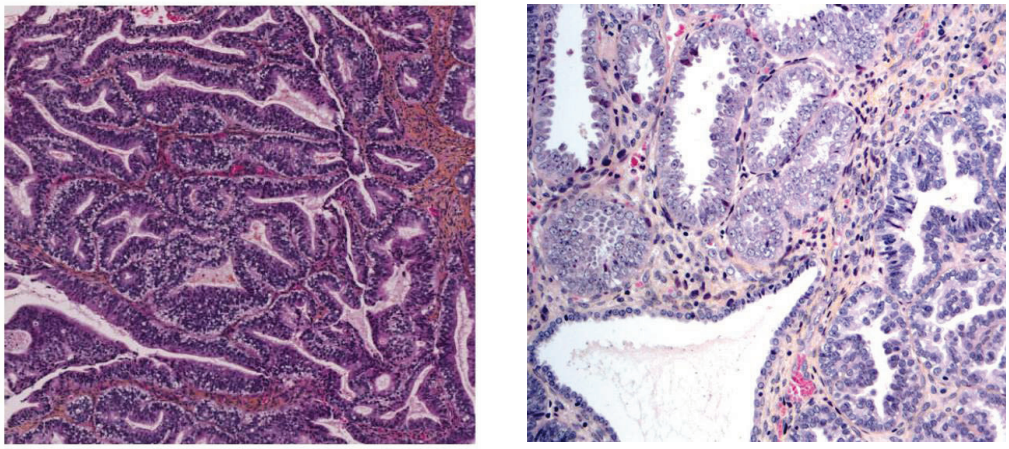
Steroid receptors: The endometrium contains estrogen and progesterone receptors. Estrogen induces endometrial cell proliferation and differentiation, and progesterone can antagonize this effect [72].

Angiogenesis: Angiogenesis estimated by intra-tumour microvessel density (MVD) is a critical factor for the growth and spread of malignant tumours. Vascular endothelial growth factors (VEGF) are important regulators, where VEGF-A stimulates endometrial proliferation and tumour progression [73].

1.5 Dualistic model of sporadic endometrial cancer

A dualistic model of two types of endometrial carcinomas with distinctive histological and clinical features and molecular alterations has been established [74;75] (Figure III). Type I accounts for 80-90% of all endometrial cancers and have endometrioid (typical, villoglandular, with squamous differentiation, secretory or ciliated) features. These tumours develop from endometrial hyperplasia and are mostly well or moderately differentiated. Type II cancers represent 10-20% of all cases and have

serous or clear-cell features. They develop from atrophic endometrium and show no or very little estrogen and progesterone receptor expression. There are several other histological subtypes of endometrial cancers, but they are rare (Table I). The clinico-pathologic differences between type I and type II cancers are paralleled by specific gene alterations, despite some overlap. Inactivation of the PTEN tumour suppressor gene is the most common genetic defect in type I carcinomas. Other genetic mechanisms involved in type I include microsatellite instability, mutations of k-ras, PIK3CA and the β1-catenin gene. Conversely, genetic abnormalities in type II include p53 mutation, Her-2/neu amplification and inactivation of p16 [76].



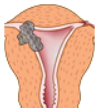
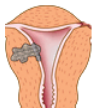
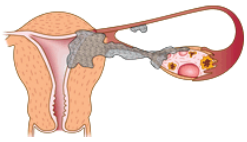
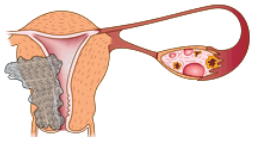
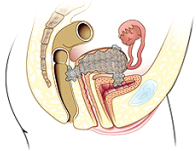
A **B**

Figure III: The prototypes of the dualistic model of endometrial carcinoma. A: Endometrioid adenocarcinoma (type I). B: Serous papillary adenocarcinoma (type II). Adapted from Alfsen C., Neoplasier I Uterus. Kurs O-23558

1.6 Staging of endometrial cancer

Endometrial cancer is surgically staged according to The International Federation of Gynecology and Obstetrics (FIGO). Recently, a new staging system for endometrial cancer was published [77]. Surgical staging is based on total hysterectomy, bilateral salpingo-oophorectomy, peritoneal cytology and lymph node sampling.

Table II: Staging of endometrial cancer (FIGO)

Stage	Features	
I	Tumour confined to the uterine corpus, not involving the uterine serosa	
IA	No or ≤ 50% myometrial invasion	
IB	Myometrial invasion > 50%	
II	Tumour invasion of cervical stroma but no extension beyond the uterus	
III	Local and/or regional spread of the tumour	
IIIA	Tumour invasion of the uterine serosa and/or the adnexae	
IIIB	Vaginal and /or parametrial involvement	
IIIC	Metastases to the pelvic and/or para-aortic lymph nodes	
IIIC1	Positive pelvic nodes	
IIIC2	Positive para-aortic nodes with or without positive pelvic nodes	
IV	Tumour involvement of the bowel and/or bladder mucosa and/or distant organs	
IVA	Tumour involvement of the mucosa of the bowel and/or bladder	
IVB	Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes	

The purpose of surgical treatment is i) to remove malignant tissue for therapeutic purposes and ii) to determine the presence of extrauterine disease for treatment decisions. Positive peritoneal cytological findings are no longer a criterion for disease upstaging, but the procedure is still recommended due to the independent prognostic value when combined with other poor prognostic factors. The depth of myometrial invasion and the extent of extrauterine disease have all been incorporated into the FIGO staging system. However, preoperative assessment is important in order to tailor treatment and to choose the optimal institution for treatment.

1.7 Treatment

Hysterectomy with bilateral salpingo-oophorectomy is the first step in the treatment of endometrial cancer. There is an ongoing debate with regard to the most appropriate surgical approach (laparotomy, laparoscopy or robotic techniques). The most debated issue in endometrial cancer management, however, is the lymph node dissection in women with low grade and early stage disease. Based on FIGO stage and histological grade of the tumour, patients are classified as being at low, intermediate or high risk for extrauterine spread, lymphatic metastasis and recurrence (Table III). Two randomized studies trials could not report a survival benefit for intermediate risk patients undergoing lymphadenectomy [78;79]. However, the percentage of nodal positivity was low in both studies, and nodal dissection was restricted to the pelvis. There also remains controversy regarding the extent of retroperitoneal lymph node dissection. In patients with positive pelvic nodes 40-57% will also have para-aortic metastasis [80;81]. However, in GOG (Gynecologic Oncology Group) #33, 35% of the patients showed positive para-aortic spread without the presence of pelvic node involvement [82]. Thus, lymphadenectomy should include para-aortic nodes. In Norway, sampling of lymph nodes and evaluation of DNA ploidy are recommended for intermediate risk patients. In high risk patients, a thorough lymphadenectomy of the pelvic and para-aortic region is performed. Different surgical management is needed for type II endometrial cancers. Given the high likelihood of extrauterine disease, a thorough lymphatic dissection and omentectomy is recommended in women with such tumours [83]. Still, evidence from randomized trials regarding a benefit from this more extensive treatment of type II cancers is lacking.

Indications for radiotherapy are generally in the adjuvant setting with the goal to treat the pelvic lymph node regions that might contain microscopic disease, as well

as the central pelvic region including the upper vagina. There is general consensus that adjuvant radiation therapy can be omitted in low risk women with FIGO stage 1A and grade 1 or 2 tumours. However, more recent large, randomized trials (PORTEC, GOG-99, ASTEC/EN.5) [84-86] failed to show a survival benefit of adjuvant pelvic radiotherapy for all intermediate or high-risk patients with stage I endometrial cancer. Most women with intermediate risk will therefore not receive adjuvant treatment on the condition that they are appropriately staged. In cases of advanced disease, chemotherapy is now the standard therapy as many high risk patients will have extrapelvic disease at the time of diagnosis. The combination of paclitaxel, epirubicin and carboplatin (TEC) or carboplatin and paclitaxel (TC) are the most commonly used regimes. The role of the combination of adjuvant chemotherapy alone, the combination of chemotherapy and radiotherapy, the best chemotherapeutic regimen and the identification of subgroups of patients that may benefit from adjuvant therapy still deserve further research.

Primary hormone therapy can be considered in patients with advanced disease who are not eligible for other treatment options or with relapse with distant metastasis. Important positive predictive factor for response is the presence of estrogen and progesterone receptors with 72% response rate in receptor positive tumours. Progestagens have been the cornerstone of the hormone therapy for endometrial cancer, and the ideal dose considered is 200 mg of medroxyprogesterone acetate [87].

Table III: Risk stratification of early stage endometrial cancer [83]

Risk	Stages	Risk and localisation of relapse
Low risk	Stage IA (grade 1,2)	5-7%; mostly local
Intermediate risk	Stage IA (grade 3)	10%; mostly local
	Stage IB (grade 1,2)	
High risk	IB (grade 3)	25%; pelvis and distant disease
	Papillary serous or clear-cell histology	

1.8 Prognosis

Diagnosis of endometrial cancer at an early stage of disease is usual due to the presence of symptoms at an early stage. Overall, the five year survival rate is around 83%. The prognostic impact of age, histological subtype, histological grade and

surgical FIGO stage is well-established [83]. The FIGO stage reflects the 5-year survival around 85% for stage I, 75% for stage II, 45% for stage III and 25% for stage IV [88-90]. The favourable survival in early stage cancers may also reflect the problem of onset confounding as tumours diagnosed at early stage may not be likely to progress. Survival in patients with type II cancers is decreased compared to patients with well-differentiated adenocarcinomas of the type I category.

1.9 Prognostic tumour markers

In order to further improve treatment and follow-up, ploidy, hormone receptor status and a wide range of other molecular markers have been extensively studied for prognostic impact [91]. Diploid tumours are often well-differentiated and have been shown to correlate with longer median survival. Still, only a few reports have included other prognostic factors and the true clinical value of this method remains to be validated. Expression of p53 and alteration of p16 seem to be associated with unfavourable prognosis, and there are other potentially prognostic factors like steroid receptor expression, PTEN alterations, Her2/neu-, Ki-67- and E-cadherin expression. Angiogenesis is a critical factor for tumour growth and spread. Thus, increased intra-tumour microvessel density (MVD) and overexpression of VEGF-A (vascular endothelial growth factor) are markers for tumour proliferation and progression and can result in vessel defects and hematogenous spread. Lymphatic vessel invasion and blood vessel invasion seems to be associated with an aggressive phenotype and a worsened prognosis even in the absence of documented lymph node metastasis [92;93]. However, studies of the prognostic impact of these biologic markers, and their utility in routine diagnostic remain to be settled.

2. OBJECTIVES OF THIS THESIS

The major objective of this thesis was to study different aspects of the association of obesity with endometrial cancer. It is still not clear whether the effect of body mass index (BMI) on endometrial cancer risk displays a linear relation or if there is a threshold effect leading to higher risk for obese women (BMI ≥30 kg/m^2) only [94]. The relative impact of high BMI categories has not been extensively studied, and in most cohort studies calculation of BMI was based on self-reported weight and height. Only few studies have addressed a possible differential impact of BMI on endometrial cancer risk before and after menopause, with conflicting results [30;32-34]. We have therefore studied the association of increments of body mass index with the risk of endometrial cancer in all women and separately in women younger than or older than 55 years of age.

Despite the growing evidence that the metabolic syndrome, including obesity and obesity-related insulin resistance, is implicated in endometrial carcinogenesis, it is not known whether related factors, such as serum lipids and lipoprotein levels, are associated with the risk of this cancer. A number of risk factors (e.g. obesity and exogenous estrogen exposure) appear to interact with the metabolism of lipids. Only two prior epidemiological studies of sufficient size have assessed the association of serum lipids with endometrial cancer risk [95;96] and they showed conflicting results. We therefore studied whether the obesity-related factors, serum lipids and lipoprotein levels, were associated with subsequent risk of endometrial cancer.

The impact of BMI may vary across different histological subtypes of endometrial cancer, and it has been hypothesized that the positive association of obesity may be restricted to estrogen dependent type I cancers. The development of clear-cell and serous tumours (type II) seems not to be related to estrogen exposure [74]. Three population-based studies have addressed whether obesity is differentially associated with histological subtypes of uterine cancer, but with inconsistent results [28;32;97]. We compared the association of BMI with the risk of uterine cancer as a single entity, with all endometrial cancers and with the risk of endometrioid adenocarcinomas.

The incidence rates of endometrial cancer have constantly increased over the last decades. In Norway, repeated health surveys have documented an increase in both mean BMI and in the prevalence of obesity in the female population (Figure IV).

By analyzing period and cohort related patterns, we wished to describe the endometrial cancer epidemic and evaluate which factors may have had an impact on the incidence trends. Monitoring the incidence is important for healthcare planning purposes and is an integral component of cancer control programmes. Surveillance of incidence may also provide indicators of risk factors of the disease. Prediction of the future number of cases is therefore of great interest to society, also in order to develop preventive strategies. Based on the observed trends in Norway we provided two scenarios of the future burden of endometrial cancer and predicted the number of new cases and incidence rates in 2015 and 2025 by using these models.

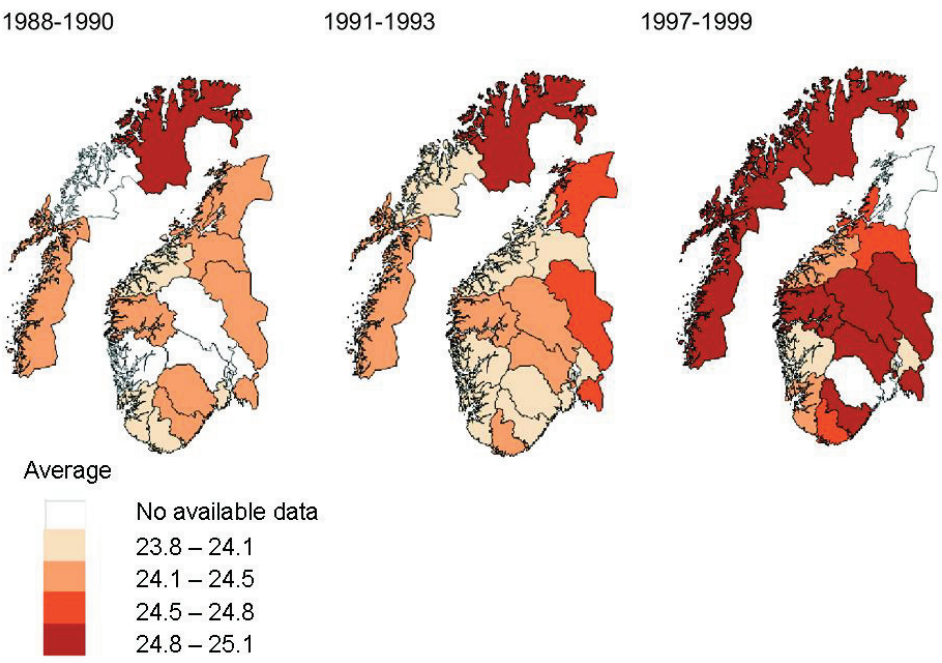


Figure IV: Changes in body mass index in 40 year old women, Norway 1989-1999. Adapted from Norwegian Institute of Public Health, www.fhi.no

More specifically, we aimed at the following:

Paper I: To study the impact of increments of BMI, diabetes and smoking on the risk of endometrial cancer

Paper II: To study the association of serum lipids and lipoprotein levels with subsequent risk of endometrial cancer

Paper III: To study the impact of BMI on subgroups of uterine cancer

Paper IV: To study endometrial cancer incidence trends in Norway during 1953-2007 according to calendar period and birth cohort and to predict future trends in incidence rates until 2027

3. MATERIAL AND METHODS

3.1 Study design and study population

Paper I-III: Nord-Trøndelag Health Study (HUNT)

In our studies we used data from the Nord-Trøndelag Health Study 1 (HUNT 1) and 2 (HUNT 2). In both surveys every individual resident in the county at the age of 20 and older was invited to participate.

HUNT 1 was conducted between 1984 and 1986 and was the largest health survey ever performed in Norway. It was primarily designed to cover studies on hypertension, diabetes, lung disease and quality of life. The invitation letter and a questionnaire were mailed to each participant (appendix). At the examination the participants received a second questionnaire that included items on physical activity, alcohol use, diabetes and smoking (appendix). The second questionnaire was to be filled in at home and returned in a pre-stamped envelope.

The second Nord-Trøndelag Health Study in 1995-97 (HUNT 2) was partly a follow-up study of HUNT 1. HUNT 2 comprised, however, a larger scientific program and aimed at the large public health issues like cardiovascular disease, diabetes, obstructive lung disease, osteoporosis and mental health. The invitation letter was sent by mail, attached to a three-page questionnaire (appendix) and an information folder. The questionnaire was to be completed prior to the examination and returned at attendance to the examination site. A second questionnaire (appendix) was handed out at the screening site and should be completed and returned in a pre-stamped envelope. A wide range of topics was addressed in questionnaire 1 and 2 covering health issues, personal environment, personal habits like food intake and drug use, family medical histories and health services consumption.

A detailed description of the study populations used in paper I-III is given in figures V-VII.

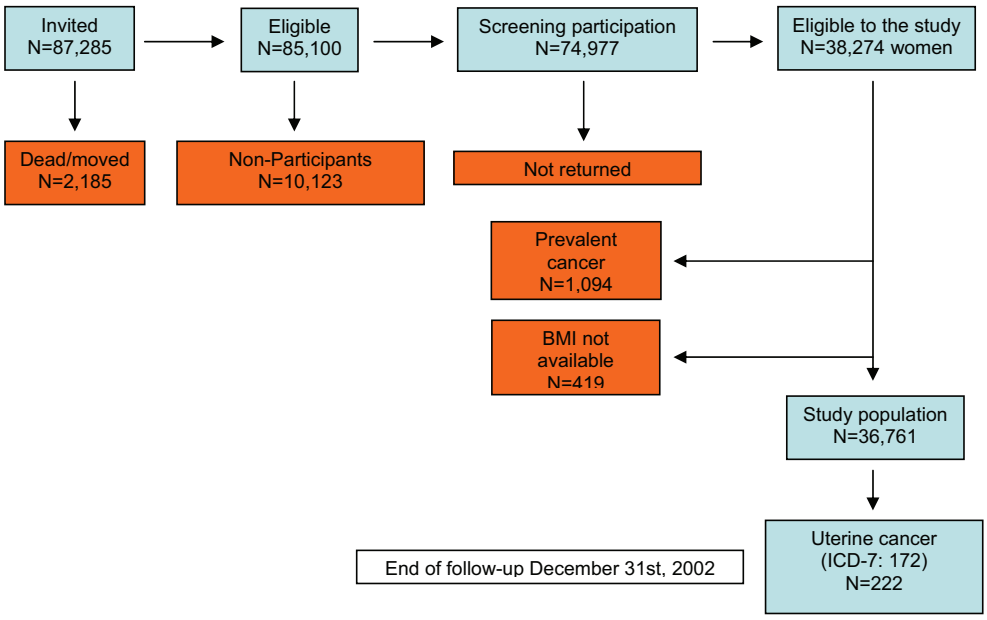


Figure V: Study population paper I (HUNT 1)

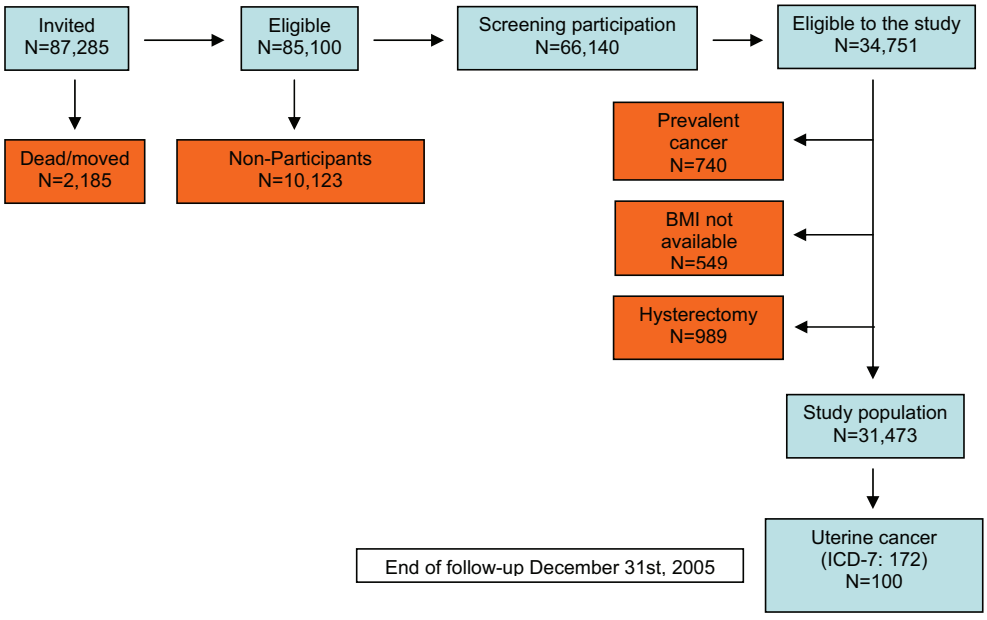


Figure VI: Study population paper II (HUNT 2)

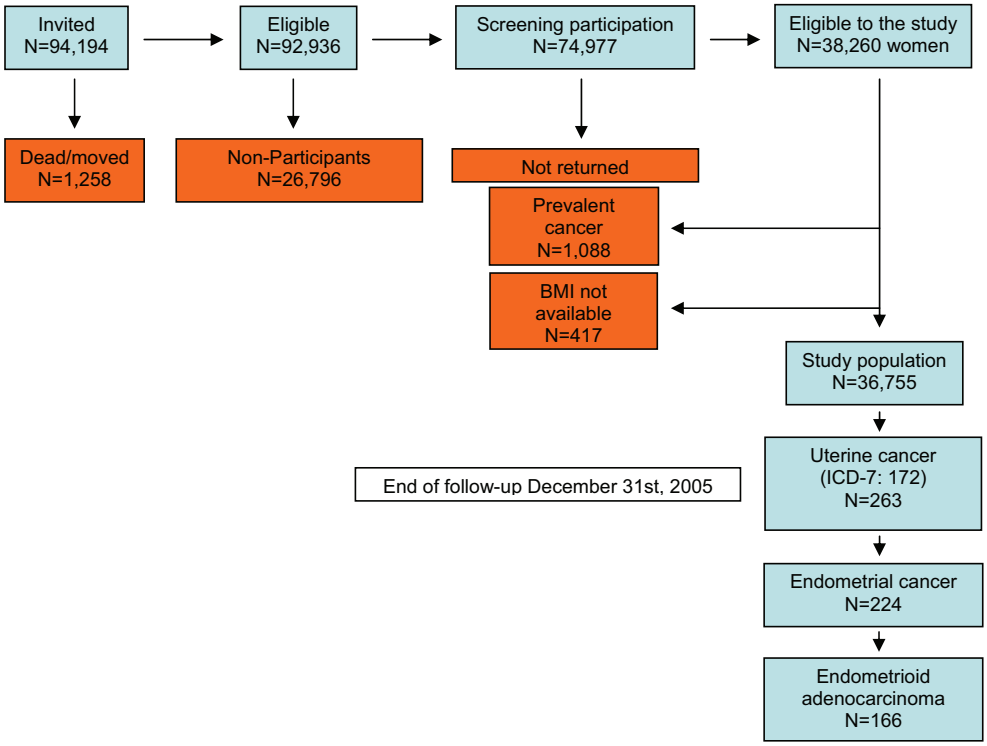


Figure VII: Study population paper III (HUNT 1)

Paper IV: The Cancer Registry of Norway

The Cancer Registry of Norway, Institute of Population-based Cancer Research, was established in 1951. It is one of the oldest national cancer registries in the world. All medical practitioners in the country are instructed by law to notify new cancer cases to this registry. Additionally, all pathological laboratories send copies of their reports to the Cancer Registry. To further achieve a high degree of completeness and data quality, the material is matched against the Register of Deaths at Statistics Norway. The cancer registration system is in concordance with international standards, with completeness estimated at around 98% overall and over 99% for cancers of the corpus uteri for the years 2001-2005 [98]. Such a high figure is considered the result of the efficient multiple source reporting and routine trace-back conducted by the registrars of the Cancer Registry.

In 1970 all topography codes were converted to ICD-7 (International Classification of Diseases, 7th revision) and to ICD-10 in 1993. The morphology of

cancers diagnosed before 1993 were classified according to the Manual of Tumour Nomenclature and Coding (MOTNAC), a 4-digit system. After 1993 tumours were classified according to ICD-O-2, a 6-digit code for morphology and grade of differentiation.

3.2 Data access and ethics

The study was approved by the Regional Committee for Medical Research Ethics, the Norwegian Directorate of Health and by the Norwegian Data Inspectorate.

3.3 Follow-up

Follow-up of women in the HUNT study with regard to development of endometrial cancer was performed by linkage to the Cancer Registry of Norway. The unique 11-digit identity number of Norwegian citizens enabled individual linkage of study participants to information on uterine cancer recorded at the Cancer Registry. All women diagnosed with uterine cancer in the study population (International Classification of Diseases, 7th revision, ICD-7, code 172) were identified, based on mandatory reporting from all pathological laboratories in Norway to the Cancer Registry. Time of follow-up was calculated from date of clinical examination until the date of uterine cancer or any other cancer (except basal cell carcinoma), emigration, death or to the end of follow-up (censoring), whichever occurred first.

3.4 Study factors

Dependent variables

Time from study inclusion to diagnosis of uterine cancer was used as dependent variable in our analyses. In the following, we give a detailed description of the dependent variables in the presented papers.

Paper I: Time from date of study inclusion (clinical examination in HUNT 1) until the date of uterine cancer, censoring or to the end of follow-up at December 31st, 2002, was the dependent variable. In separate analyses among women less than 55 years of age, time from date of clinical examination until uterine cancer before the age of 55 or until censoring at the age of 55 was used as dependent variable. Only women less than 55 years old at study inclusion were included in this analysis.

Paper II: In this study, time from date of clinical examination (in HUNT 1) until the date of uterine cancer, censoring or to the end of follow-up at December 31st, 2005, was the dependent variable.

Paper III: In this study, time from date of clinical examination (in HUNT 1) until the date of uterine cancer, censoring or to the end of follow-up at December 31st, 2005, was the dependent variable. In separate analyses we used time to i) endometrial cancer (ICD-O-2 codes 8380/3, 8570/3, 8262/3, 8382/3, 8383/3, 8480/3, 8441/3, 8310/3, 8323/3, 8070/3, 8120/3, 8041/3, 8020/3 and MOTNAC codes 8017, 8143, 8144, 8145, 8147, 8447, 8563, 8565, 8567, 8573, 9113) and ii) endometrioid adenocarcinoma (ICD-O-2 codes 8380/3, 8570/3, 8262/3, 8382/3, 8383/3 and MOTNAC codes 8143, 8144, 8145) as dependent variable.

Independent variables

Exposure data was collected from two sources: Clinical data were obtained at the physical examination at study inclusion. In addition, self-administered questionnaires provided information on lifestyle and demographic characteristics.

Age: Age was defined at age at syntax date, which was the date for control of punched data, performed 7 to 21 days after the date of clinical examination. Since age is a strong determinant of endometrial cancer, it is important to control for age in analyses of potential risk factors. We included age in the Cox regression model using 10-year categories. In paper III, we adjusted for age by using age as the time axis in the Cox model.

Body mass index (BMI): BMI was calculated as weight divided by height squared (kg/m^2). Height and weight were measured when the participants were wearing light clothes without shoes. Height was recorded to the nearest 1.0 cm and weight to the nearest 0.5 kg. BMI was categorized as <20, 20-24, 25-29, 30-34, 35-39, and ≥40 kg/m^2 in paper I and III and categorized as <25, 25-29, 30-39, or ≥40 kg/m^2 in paper II.

Blood lipids: Blood sampling in HUNT 2 was done whenever subjects attended, i.e. non- fasting or “random” state. At baseline, 7.5 ml of whole blood was drawn from each participant, and serum was separated by centrifuging at the screening site.

Serum lipids were measured at the Central Laboratory of Levanger Hospital in Nord Trøndelag County, on the same day or within two to three days of serum sampling. Total serum cholesterol, HDL cholesterol and triglycerides were measured enzymatically, using an autoanalyser (Hitachi 911, Hitachi, Mito, Japan) and reagents from Boehringer Mannheim (Mannheim, Germany). HDL cholesterol was measured after precipitation with phosportungsten and magnesium ions. The day-to-day coefficients of variation were 1.3-1.9% for cholesterol, 2.4% for HDL cholesterol and 0.7-1.3% for triglycerides. Non-HDL cholesterol was calculated as HDL cholesterol subtracted from total cholesterol, and LDL cholesterol was calculated using the Friedewald equation [99]. In the statistical analyses, we used quartiles of each serum lipid, based on the distribution in the cohort as a whole. In a separate analysis of triglycerides we also used the following categories: < 1.0, 1.1-1.5, 1.6-2.0, 2.1-3.0, 3.1-4.0, >4.0 mmol/l and treated them as a continuous variable in the data analysis.

Diabetes: Information on diabetes mellitus was assessed from the self-administered questionnaire at baseline (yes/no).

Smoking: Smoking status was coded as never, former, current or missing.

Other possibly confounding variables

Marital status: Marital status was classified as married, unmarried, widow or divorced/separated.

Educational level: Level of education was classified as <10 years, 10-12 years, >12 years or missing.

Waist and hip circumference: Waist and hip circumference were measured only in HUNT 2 with a steel band to the nearest 1.0 cm with the participant standing and with the arms hanging relaxed. The waist circumference was measured horizontally at the height of the umbilicus, and the hip circumference was measured likewise at the thickest part of the hip. We used quartiles of both these measurements and the waist-hip ratio in paper II.

Blood pressure: Blood pressure was measured by specifically trained nurses using a Dinamap 845XT (Critikon) based on oscillometry. Cuff size was adjusted to the arm

circumference. Blood pressure was measured three times, and the mean of the second and third systolic and diastolic blood pressures were used in this study. Blood pressure ≥140/90 mmHg was classified as hypertension.

Alcohol: Alcohol drinking was categorized as 0, 1-4, ≥5 times during the last two weeks, total abstainer or missing.

Physical activity: Information on physical activity (i.e. walking, skiing, swimming or other sports) was obtained by questions on frequency (0, <1, 2-3 and > 4 times per week), average duration (<15, 15-30, 30-60 and >60 min) and intensity (light, moderate and vigorous). We utilized this information to calculate a summary score of physical activity. Based on this score the participants were divided into five categories (no activity, low, moderate, high activity and missing).

3.5 Statistical analysis

We used the Cox proportional hazards model to examine the association between relevant exposure variables and endometrial cancer risk. This statistical regression procedure is a popular and robust mathematical model, often used to analyse data where survival time is available and where follow-up is censored. However, use of the Cox model requires that the hazard ratio is constant over time. We used analyses of Schoenfeld residuals in order to test the proportional hazard assumption. We estimated the age-adjusted relative risks (RR) of the relevant exposure variables with 95% confidence intervals. Since the risk of endometrial cancer strongly depends on age, we included age and the relevant exposure variables as independent variables in the regression model and individual number of person-years as the dependent variable. Multivariable analyses were conducted to assess potential confounding by other factors for which we had information. Statistical analyses were performed using the SPSS statistical package in paper I (version 14.0) and paper III (version 16.0). We used STATA statistical package, version 10.0, in paper II.

The statistical analyses in paper IV were performed by Freddie Bray, MSc, PhD at the Cancer Registry of Norway. The model analysis was performed using the APC functions available in the library *Epi* in R. STATA was used for data management and plotting of the observed trends.

4. SYNOPSIS OF THE PRESENTED STUDIES

Paper I:

Body mass, diabetes and smoking and endometrial cancer risk: a follow-up study

The incidence of endometrial cancer is increasing and obesity has been identified as a major risk factor. It is uncertain if there is a linear positive association of BMI (body mass index) with endometrial cancer risk.

We prospectively examined the association of body mass, diabetes and smoking with the risk of endometrial cancer in a cohort of 36,761 Norwegian women during 15.7 years of follow-up. 222 incident cases of endometrial cancer were identified by linkage to the Norwegian Cancer Registry. In multivariable analyses there was a strong and consistent increase in endometrial cancer risk with increasing BMI (p-trend <0.001). Compared to the reference (BMI 20-24), the adjusted relative risk (RR) was 0.53 (95% CI: 0.19-1.47) for BMI <20, 4.28 (95% CI: 2.58-7.09) for BMI of 35-39, and 6.36 (95% CI: 3.08-13.16) associated with BMI ≥40. Women with known diabetes at baseline were at three-fold higher risk (RR 3.13, 95% CI: 1.92-5.11), compared to women without diabetes, and women who reported current smoking at baseline were at reduced risk compared to never smokers (RR 0.55, 95% CI: 0.35-0.86).

We found a strong linear positive association of BMI with endometrial cancer risk, and a strongly increased risk among women with diabetes. The results suggest that any increase in body mass in the female population will increase endometrial cancer incidence.

Paper II:

Serum lipids and endometrial cancer risk: Results from the HUNT-II study

Obesity is a major risk factor for endometrial cancer. Still, the association of obesity-related metabolic factors, such as serum lipids and lipoprotein levels, is unclear.

We prospectively examined the association of serum levels of triglycerides, total cholesterol, LDL cholesterol, non-HDL and HDL cholesterol with endometrial cancer risk among 31,473 women. During nine years of follow-up, 100 cases of endometrial cancer were identified by linkage to the Cancer Registry of Norway. There was a positive association of serum triglyceride levels with endometrial cancer

risk. Comparing the highest to the lowest quartile of triglycerides, the age-adjusted hazard ratio was 2.34 (95% CI: 1.04-5.28), and further adjustment for body mass index (BMI) attenuated the association (hazard ratio 1.79, 95% CI: 0.79-4.05). For total serum cholesterol, LDL cholesterol and HDL cholesterol there were no associations with endometrial cancer risk, either without or after adjustment for BMI.

Serum triglyceride levels were positively associated with the risk of endometrial cancer, and some of the association appears to be attributable to obesity. Apart from higher estrogen levels produced in adipose tissue, mechanisms more specifically related to triglycerides may also be involved in endometrial cancer. Further prospective studies on this subject are needed to better understand the association of blood lipids with endometrial cancer risk.

Paper III:

The impact of BMI on subgroups of uterine cancer

Obesity increases uterine cancer risk, but the impact may be limited to endometrioid adenocarcinomas. We followed 36,755 women for 17.8 years and found that BMI was positively associated with uterine cancers as a whole, with a particularly strong association for endometrioid adenocarcinomas. Compared to the reference (BMI 20-24), the age-adjusted relative risk for BMI ≥40 was 6.7 (95% CI: 3.4-13.4) for all uterine cancers and 8.3 (95% CI: 4.1-16.7) for endometrial cancer. The corresponding estimate for endometrioid adenocarcinomas was 11.1 (95% CI: 5.2-23.8).

Paper IV:

Endometrial cancer incidence trends in Norway during 1953-2007 and predictions for 2008-2027

Endometrial cancer is the most common cancer of the female genital tract in Western countries. Monitoring the incidence is important for health care planning and the identification of risk factors.

We present an age-period-cohort analysis of incidence trends of endometrial cancer in Norway from 1953 to 2007 and compare the incidence trends with those in three other Nordic countries. Based on the observed trends we have predicted endometrial cancer rates in Norway in 2015 and 2025.

In women at postmenopausal age (≥55 years), the annual incidence increase was 2.1% (95% CI: 0.9%, 3.4%) from 1988 to 1997 and 1.7% (95% CI: 0.6%, 2.8%) from 1998 to 2007. In younger women, there was an annual reduction of 0.6% (95% CI: -2.3%, 2.2%) from 1988 to 1997, followed by an annual increase of 1.7% (95% CI: -0.4%, 3.9%) from 1998 to 2007. The secular changes are likely to reflect both cohort and period effects. Our prediction estimates by 2025 suggest an incidence increase in the range of 50% to 100%, relative to the observed incidence in 2005.

There has been a strong and consistent incidence increase in endometrial cancer in the Nordic countries over the last 50 years. The increase has been most pronounced in postmenopausal women, but in the last decade, rates have increased also in women younger than 55 years. The prediction for the next 20 years suggests that endometrial cancer rates will dramatically increase unless effective preventive strategies are implemented.

5. DISCUSSION

The discussion of the results will address two different aspects of this work

1.) Methodological considerations

2.) Obesity and endometrial cancer - Proposed mechanisms

5.1 Methodological considerations

An epidemiological study can reflect the true effect of an exposure on development of disease, but the findings may also have alternative explanations. The estimated effect may be attributed to chance or to systematic errors that also influence the association between exposure and disease. There are three types of errors that have to be considered. These include bias in the selection of study subjects to inclusion or follow-up, information bias and confounding.

5.1.1 The role of selection bias

Selection bias results from skewed selection to participation or follow-up. Selection bias occurs when the relationship between the exposure and the disease is different from those in the study than for those not in the study [100].

Participation in HUNT: Even if the participation rate in HUNT was fairly high compared to most other studies in Norway and abroad [101], there is still potential selection bias. The participation was highest among middle-aged women, among women who were married and among those living in small municipalities. However, a non-participation study in the HUNT 1 study could not find evidence of selection to participation with regard to health measures in younger age groups [102]. Elderly non-participants had, however, increased mortality and morbidity compared to the participants. Endometrial cancer is strongly associated with age. The higher rate of non-participation among older women may have caused an underestimation of the true incidence in this age group and thereby an underestimation of the effect of age on endometrial cancer risk. However, the impact of age was not a major objective of our study. If obese women, in particular among the elderly women, are underrepresented in our study, the impact of BMI may be underestimated.

Selection to inclusion in our study sample: Women with prevalent cancer of any site, except basal cell carcinoma, were excluded from our study sample, since the association of the exposure variables (BMI, blood lipids) with endometrial cancer in

women with prevalent cancer may differ from the general population of women. Women with a previous cancer may also have a higher risk of endometrial cancer later in life, in particular women with colon cancer caused by the hereditary nonpolyposis colorectal carcinoma syndrome (HNPCC). Hence, exclusion of women with prevalent cancer may have underestimated the true incidence of endometrial cancer. It remains unclear whether exclusion of women with prevalent cancers has caused biased estimates of the association of BMI with endometrial cancer.

A relatively high proportion of the women in HUNT 1 did not respond to the questionnaire including information on smoking, alcohol use and physical activity. Response was about 20% lower than to the first questionnaire. In order to reduce the possibility of selection bias and to maintain statistical power, we decided to include women with missing information on smoking (n=6,255), alcohol use (n=6,746) and physical activity (n=7,593) in our study sample. These variables were coded "missing".

Another possible selection bias may have been introduced by not having excluded women who had undergone hysterectomy at study baseline or during follow-up. Information on hysterectomy was lacking in HUNT 1. Even if the rate of hysterectomies used to be low in Norway [103], the number of women with intact uterus and thereby at risk of uterine cancer is lower than the denominator of our estimations. It has been suggested that incidence rates of endometrial cancer in women at risk, corrected for hysterectomy status, may yield rates up to 29% higher than in the total population of women [104]. Consequently, the endometrial cancer incidence in women at true risk may be underestimated in our studies. There is, however, no evidence of a difference in hysterectomy rates dependent on BMI. In HUNT 2 information on previous hysterectomy was available, but the estimates of BMI as a risk factor remained unchanged after having corrected for hysterectomy status (paper II). Hence, we have no reason to believe that lack of exclusion of women having undergone hysterectomy has biased our estimates of the association of BMI with endometrial cancer risk. However, our predicted future rates of endometrial cancer as presented in paper IV may be overestimates since increasing hysterectomy rates in Norway have reduced the number of women at risk for uterine cancer.

Selection in follow-up in our study sample: The HUNT databases were linked to the Cancer Registry of Norway and to the Cause of Death Registry at Statistics Norway. Hence, study participants could be followed until the date of uterine cancer diagnosis,

emigration, death or to the end of follow-up. Women with incident cancer other than basal cell carcinoma were also censored at date of diagnosis.

In order to avoid biased estimates, the association between exposure and the disease in censored individuals should not differ from the population that could be studied until the end of follow-up. Obesity, however, is a risk factor for several other cancers, such as colon-, kidney-, gallbladder- and postmenopausal breast cancer. Therefore, censoring of women with cancer of other organs than the uterus, may have led to an underestimation of the impact of BMI on endometrial cancer risk. Any cancer treatment during follow-up or prior to inclusion could have had an impact on the risk of endometrial carcinoma. However, the direction of the possible bias cased by such non differential selection is not easily determined.

5.1.2 The role of information bias

Information bias result from systematic differences in the way data are obtained and may affect both independent and dependent variables. Both systematic differences in registration of exposure according to the outcome or in registration of outcome according to exposure may result in information bias.

The independent variables: A form of information bias called recall bias occurs, when cases may be likely to remember their exposure differently than controls. The prospective design of the studies presented here will generally prevent recall bias, since information on exposure information was ascertained before the occurrence of cancer.

An inherent assumption of this type of study is that exposure stays constant over the observation period. However, body weight and smoking habits may have changed during follow-up. Longitudinal data from HUNT 1 and 2 indicate that most women (66%) have gained weight between the two surveys [105]. There was no association of weight change with initial BMI. Thus, we have no reason to assume changes in weight during follow-up differ systematically by weight at study induction. There is therefore little chance that changes in weight during follow-up have introduced systematic errors. Still, the impact of BMI in our study may be overestimated if weight gain during follow-up explains part of the association. There are to date no prospective studies with successive BMI measurements during follow-up which could elucidate the relationship between duration of obesity and

endometrial cancer risk. Endometrial cancer may also be initiated several years prior to the clinically detectable stage. Thus, the importance of constant exposure during the follow-up may not be as important as during the period prior to study induction.

Age at menopause or menopausal status could not be directly obtained from the HUNT 1 study. We have therefore chosen the age of 55 years as a proxy for age at menopause. Follow-up time was calculated from date of clinical examination until endometrial cancer before the age of 55 or until censoring at the age of 55. We cannot exclude that some postmenopausal women may have been misclassified as pre-/perimenopausal. Unless there is a differential misclassification of age at menopause according to BMI, there is little reason to assume that the effect of BMI in premenopausal women is biased. To my knowledge, BMI is not established as determinant of age at menopause.

The dependent variables: The completeness and validity of the cancer diagnoses (topographic codes) in the Cancer Registry is well documented [98]. Hence, endpoints were ascertained with limited error. It is possible that improved reporting of cancer and improved diagnostic efforts have contributed to the increase in endometrial cancer incidence over time. An easily performed endometrial sampling method introduced in the 1990s may have led to detection of more cases of cancer and also to earlier detection of endometrial cancer with a shift towards increased incidence among younger women. It is possible that the increased incidence in pre- and perimenopausal women could be explained by such a drift and may have influenced recent incidence rates (paper IV).

Women with high BMI tend to suffer from a range of comorbidities (diabetes mellitus, hypertension) that require medical treatment. This may increase the likelihood of being diagnosed with endometrial cancer since these women are more likely to have regular contact with doctors. If this is true, the impact of BMI on endometrial cancer may have been overestimated in our studies. It can also be argued that obese women die of other diseases before they would have been diagnosed with endometrial cancer. Then, the impact of BMI on endometrial cancer risk may have been underestimated.

In our studies we used the International Classification of Diseases, 7th revision, ICD-7, code 172 to identify women diagnosed with uterine cancer. Approximately 10% of the cancers registered by this code may, however, not

originate from the endometrium (Table I). Assuming that BMI is a risk factor for endometrial cancer only and not for other cancers localized in the uterus, the impact of BMI on cancer truly originating from the endometrium may be underestimated in our study.

The Cancer Registry also provided information on the histological subtype of endometrial cancer. However, in 1993 the Cancer Registry changed the classification system of tumour morphology from MOTNAC to ICD-O-2, also due to the growing awareness of type I and type II cancers. As the MOTNAC classification does not differentiate type I and type II tumours, we included unspecified adenocarcinoma, villoglandular adenocarcinoma, adenocarcinoma with squamous differentiation and endometrioid adenocarcinoma (MOTNAC codes 8143, 8144, 8145) in the analyses of endometrioid carcinomas in paper III. The remaining 111 (64%) of the endometrioid adenocarcinomas in this analysis were diagnosed after 1993, when the classification distinctly differentiated between type I, type II and other tumours of the endometrium. In total, 74% (n=166) of all endometrial cancers were classified as endometrioid adenocarcinomas (type I), which is in concordance with the distribution of histological subtypes in the literature [106]. Assuming that type II tumours falsely may have been classified as type I, the impact of BMI on endometrioid adenocarcinomas is underestimated in our study (paper III). However, there is no reason to assume a differential misclassification of tumour histology according to BMI, and biased estimates are therefore unlikely. A higher accuracy of the histological diagnoses and thereby increased validity of our dependant variable could have been achieved by pathological review of all uterine cancers included in our studies. This would also have enabled us to study type I and type II tumours separately. However, paraffin-embedded tissue of the women diagnosed with uterine cancer in the HUNT study was not available to us.

5.1.3 The role of confounding

Confounding is the systematic error generated when another factor that is associated with the disease under study, also is related to the exposure variable. Adequate adjustment for potential confounders depends on two conditions that must be satisfied: (i) the association with the disease is known and (ii) the identified or suspected confounders can be measured with adequate validity and accuracy.

Early menarche, nulliparity and hormone replacement therapy (HRT) are positively associated with the risk of endometrial cancer, whereas use of combined oral contraceptives (COCs) reduces the risk. Information on reproductive factors, the use of COCs and HRT could not be obtained from HUNT 1 and was missing in a high proportion of women in HUNT 2. High BMI is associated with infertility due to chronic anovulation, and a higher proportion of nulliparous women may therefore be observed in higher BMI categories. As nulliparity also is a risk factor for endometrial cancer, lack of controlling for this confounder may have led to an overestimation of the impact of BMI. One may also argue that BMI increases with parity which is negatively associated with risk. If this is true, our estimates may be an underestimation of the true association with BMI. However, information on parity was included in paper II but did not alter the reported associations between BMI or blood lipids and endometrial cancer risk.

Use of HRT was generally uncommon among Norwegian women. In the late 1980s less than 6% of postmenopausal women used HRT [107], but the use increased rapidly in the 1990s, reaching a peak of about 35% towards the end of the decade [108] with predominantly combined estrogen-progesterone preparations. A minor increase in risk compared to unopposed estrogen therapy has also been reported for the combined treatment [19;20]. There is no evidence that the use of HRT differs across BMI categories, and it is difficult to determine how inclusion of this confounder may have influenced our results.

The observed results may also be attributable to other, unmeasured variables not yet known to be related to the risk of endometrial cancer. The observed trends of endometrial cancer incidence over the last five decades presented in paper IV are complex and may not exclusively be explained by changes in key risk factors such as reproductive behaviour, use of HRT or combined oral contraception and the increased prevalence of obesity.

5.1.4 Statistical power

Another source of error can arise from failing to reject the null hypothesis given that the alternative hypothesis is actually true (type II error). A type II error is frequently due to sample sizes being too small. In our thesis we had limited statistical power to study different subgroups of i) exposure and ii) endometrial cancer.

Paper I: We conducted separate analyses for women at risk of endometrial cancer before and after the age of 55. Only 52 women developed cancer before 55 years of age, and of those very few (n=9) were obese (BMI ≥30). Thus, estimates of the impact of BMI in younger women were calculated with wide confidence intervals and limited precision in higher categories of BMI.

Paper III: The majority of endometrial carcinomas are classified as endometrioid adenocarcinomas (type I), and we were not able to conduct separate analyses in women with type II tumours with sufficient statistical power. We therefore chose to study the following subgroups: All uterine cancers, all endometrial cancers and all endometrioid adenocarcinomas. We also assessed the association of BMI and the risk of uterine cancers other than endometrioid adenocarcinomas. The results show an increased risk associated with BMI of 35 or higher but no associations for the other BMI categories. Both analyses suggest a stronger association with endometrioid adenocarcinoma than for uterine cancers as a whole.

Paper IV: We studied incidence trends of endometrial cancer in pre-/peri- and postmenopausal women separately. We suggest that the increasing BMI in Norwegian women since the mid-1980s may in part explain the increase in rates in postmenopausal women in recent years and the shift towards increased incidence in younger women. However, the underlying random variation due to small numbers limits the statistical power of our estimates in the younger age group.

5.2 Obesity and endometrial cancer – Proposed mechanisms

We found a strong positive and linear association of BMI with the risk of endometrial cancer. This association may be particularly strong in endometrioid adenocarcinomas. We also report a positive association of serum triglycerides with endometrial cancer risk. Adjustment for BMI partly attenuated the association, suggesting that some of the effect may be mediated through obesity. The strongest support for a link between obesity and endometrial cancer risk involves the metabolic and endocrine activity of adipose tissue, and the alterations that they induce in the production of peptide and steroid hormones.

An underlying assumption of our study is that body mass is an adequate measurement of adiposity. There are two types of adipose tissue, subcutaneous and visceral. Subcutaneous tissue is largely defined as fat tissue between skin and muscle, whereas visceral adipose tissue is found within the main cavities of the body,

primarily in the abdominal cavity. Abdominal visceral adipocytes are metabolically more active than abdominal subcutaneous adipocytes, as they have high lipolytic activity and release large amounts of free fatty acids [109]. Consequently, the ideal measurement of adiposity would consider both the amount and the site of deposition of the adipose tissue. Many methods of estimating total body fat mass have been developed, but they are generally too costly and complex to be used to estimate adiposity in general populations or large epidemiological studies. Thus, estimations of overweight and obesity have historically been based on anthropometric measures such as BMI. A recent study evaluated if DEXA (dual-energy X-ray absorptiometry) is a more precise measure of adiposity than BMI and if those two measurements can predict sex hormone levels in postmenopausal women [110]. They showed that measurement of adiposity just by using BMI was sufficient to accurately characterize sex hormone levels.

A number of biomarkers associated with both obesity and endometrial cancer may play a role in the neoplastic transformation of endometrial cells, and the main endocrine pathways are elucidated in the following.

Endogenous sex steroids: The predominant theory describing the relationship between endogenous steroid hormones and endometrial cancer risk is known as the unopposed estrogen hypothesis. This theory originated from two important observations: (i) Endometrial proliferation rates are increased during the follicular phase, when progestin levels are low, whereas E_2 levels are at normal premenopausal concentrations [111]. (ii) Continuous exposure to exogenous estrogen without progestin resulted in increased endometrial cancer risk [112]. Adiposity influences the synthesis and bioavailability of endogenous sex steroids through at least three mechanisms (Figure VIII). First, adipose tissue is an important source of endogenous estrogen due to the conversion of androstendione to estrone and the aromatization of androgen to estradiol [113]. Second, the mitogenic effect of estrogen in obese women is assumed not to be counterbalanced by progesterone due to chronic anovulation and thereby strongly reduced progesterone synthesis. Progesterone diminishes estrogenic action in the endometrium by stimulating the local synthesis of 17β-hydroxysteroid dehydrogenase and estrogen sulfo-transferase [114]. These enzymes favour the conversion of E_2 into the less potent E_1, and into estrogen sulfate. Both are rapidly excreted from the cells and from the body. Furthermore,

progesterone provides the key stimulus for endometrial gene expression and synthesis of IGFBP-1 (insulin-like growth factor binding protein 1), which inhibits IGF-1 (insulin-like growth factor 1) action in endometrial tissue [115;116]. IGF-1 is a peptide hormone that has a molecular structure very similar to that of insulin and regulates cellular proliferation in response to available energy and nutrients from diet and body reserves. It has been argued that low progesterone, rather than increased estrogen is the predominant determinant of endometrial cancer in premenopausal women and that the increased risk is only related to estrogen when estrogen concentrations are comparatively low, as found in postmenopausal women. In postmenopausal women, estrogen derived from peripheral adipose tissue is the primary source of endogenous E_2, and the rate of production is related to the size of the adipose depots [117]. It can be argued that only in those women, with comparably low estrogen concentration, endometrial cancer risk is directly related to circulating estrogen. Finally, adipose cells increase circulating levels of insulin and increase IGF-1 bioactivity. This results in reduced hepatic synthesis and blood levels of SHBG (sex-hormone binding globulin), a plasmatic binding protein with specific affinity for estradiol and testosterone. Adiposity-related decreases in SHBG levels generally increase the fraction of bioavailable estradiol. Our results may support the hypothesis of different mechanisms in the development of endometrial cancer in different age groups leading to a threshold effect of BMI in younger, premenopausal women. Still, there are only few cases (n=52) in this age group, and data from this study population are insufficient to draw a definite conclusion.

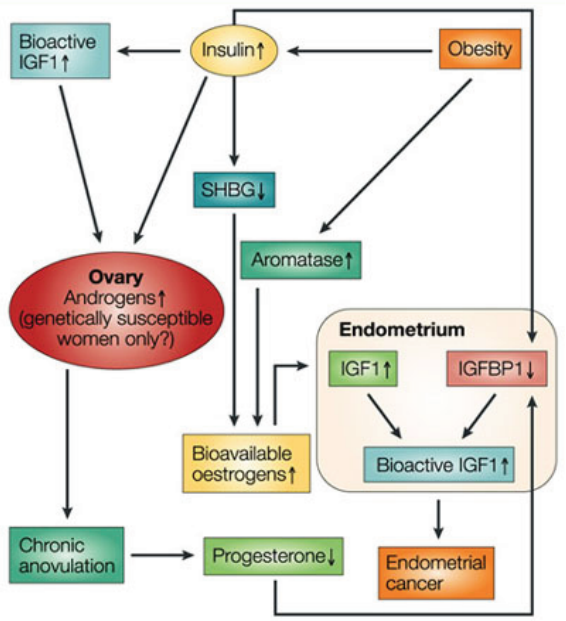


Figure VIII: Obesity, hormones and endometrial cancer [117]

Insulin, glucose, IGF-1 and SHGB: We found a positive association of diabetes with endometrial cancer risk after adjustment for potentially confounding factors. We also report a positive association of serum triglycerides with endometrial cancer risk. Adjustment for BMI partly attenuated the association, suggesting that some of the effect may be mediated through obesity. Excess weight, increased plasma triglyceride levels and low levels of physical activity can additionally raise circulating insulin levels. A number of mechanisms are thought to play a role in linking elevated insulin to endometrial cancer development, including growth enhancing properties of insulin, increased levels of IGF-1 receptors in endometrial cancer tissue [118;119] and suppressed gene expression of endometrial IGFBP-1 leading to increased biological activity of IGF-1 [120;121] (Figure IX). *In vitro* studies have clearly established that both insulin and IGF-1 act as growth factors that can promote cell proliferation and inhibit apoptosis [122]. Insulin also reduces hepatic synthesis and plasma levels of SHBG increasing bioavailable E_2 unbound to SHBG. *In vitro* studies have demonstrated that insulin also up-regulates the secretion and mRNA expression of VEGF, a potent angiogenic factor, that may contribute to endometrial carcinogenesis [123;124].

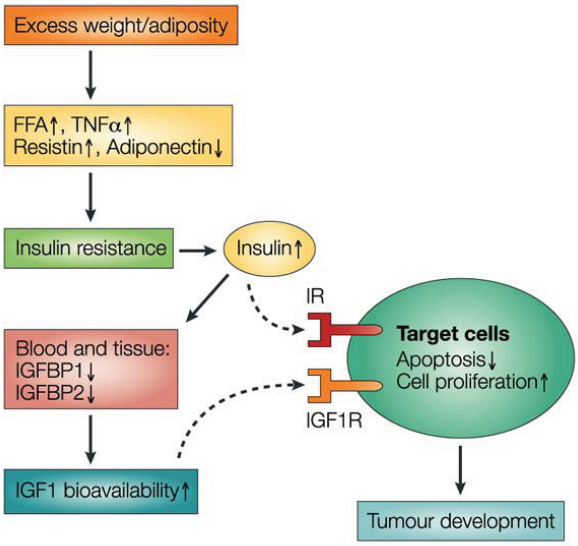


Figure IX: Effect of obesity on insulin and growth factor production [27]

Adiponectin: Adiponectin is a peptide hormone secreted in large amounts by adipocytes with reduced circulating levels in conditions related to insulin resistance, such as visceral obesity and type 2 diabetes [125]. Three relatively small case-control studies [126-128] and one larger prospective case-control study within the EPIC (European Prospective Investigation into Cancer and Nutrition) cohort study [129] showed adiponectin levels to be negatively associated with the risk of endometrial cancer, largely independent of other obesity related factors like IGF-1, IGF-2, IGFBP, leptin and BMI. Plasma adiponectin concentrations have been shown to be more closely related to insulin resistance than to the degree of obesity [130]. One major metabolic pathway through which adiponectin could influence endometrial cancer risk is by decreasing blood insulin and glucose levels as it increases fatty acid oxidation in the muscle, decreases hepatic glucose production and increases insulin sensitivity of peripheral tissue. Adiponectin may have strong anti-inflammatory activity and could thereby potentially counteract the proinflammatory and neoplastic effects of TNF-α (tumour necrosis factor alpha), IL-6 (interleukin 6) and C-reactive protein. These cytokines have an impact on endometrial carcinogenesis by increasing nuclear factor-κB, prostaglandin E_2 levels and cyclooxygenase-2 expression. TNF-α can also stimulate estrogen biosynthesis and angiogenesis [131].

Leptin: Leptin is another protein secreted by white adipose tissue. This hormone is strongly associated with obesity but there is to date only one small case-control study on the association of plasma leptin levels and the risk of endometrial cancer [132]. Leptin was unrelated to the risk of endometrial cancer when adjusted for BMI. *In vitro* studies, however, suggest that leptin may promote a proliferative response and invasiveness in human endometrial cancer cells. A recent study on six endometrial cancer cell lines identified several pathways (JAK2/STAT3, MAPK/ERK, PI3K/AKT and COX-2 signalling) that seemed to be implicated in the cell proliferative effect of leptin [133].

Peroxisome proliferator-activated receptors (PPARs): Besides a strong increase in risk of endometrial cancer in women with high body mass, we report a positive association of triglycerides with endometrial cancer risk. This association persisted after adjustment for the other serum lipids but was partly attenuated after adjustment for BMI. This suggests that some, but not all of the effect related to triglycerides may be mediated by body mass. The challenge is to understand how obesity and triglycerides influence the risk of endometrial cancer, either through their combined relation or as independent factors. Certain nuclear receptors can modulate both cellular lipid metabolism and tumorigenesis [134]. For instance, peroxisome proliferator-activated receptors (PPAR) can mediate lipid homeostasis and adipogenesis [135], as well as cancer cell growth [136;137]. Three subtypes, PPARα, β/δ and γ, have been identified. Activation of PPARα by fibrates leads to lower triglyceride levels and appears to be an effective treatment of dyslipidemia [138;139]. In endometrial cancer, PPARα seems to be up-regulated, and it has been shown that fenofibrate exhibits antiproliferative effects on endometrial cancer cells *in vitro* via inhibition of G1/S phase progression [140]. Cyclin D1 is known to be upregulated in endometrial cancer [141;142], and administration of PPARα agonists led to downregulation of cyclin D1 and upregulation of p21. In conclusion, there is growing evidence of direct action of this lipid-lowering agent on pathways known to be relevant to endometrial carcinogenesis.

A number of investigators have shown PPARγ expression in a variety of tumour cells, and Ota et al. [143] reported lower PPARγ expression in endometrial cancer tissue than in normal tissue. PPARγ expression was negatively correlated with BMI suggesting that genetic or environmental factors causing obesity might

interact with the PPAR gene. In addition, the PPARγ agonist 15d-PGJ_2 inhibited endometrial cell proliferation and raised plasma adiponectin levels making synthetic PPARγ ligands potential drug candidates for both prevention and endocrine treatment of endometrial carcinoma [72;140].

6. PUBLIC HEALTH IMPLICATIONS

Our studies imply that even a slight increase in BMI in the population will lead to an increase in endometrial cancer incidence. The incidence increase among premenopausal women during the last 15 years may be a direct effect of the marked increase in BMI in young women. We present two scenarios in this thesis of the future burden of endometrial cancer. The conservative scenario assumes decreasing exposure to underlying risk factors over time. The less optimistic scenario with an estimated 95% increase in the number of new cases by 2025 (1257 new cases) implies unchanged trends in exposure to underlying risk factors and that cumulative exposure to risk factors like high BMI causes a linear increase in risk.

Our findings may have important public health implications. There are to date no reliable predictions of the development of BMI in Norway, but an increasing and substantial proportion of adolescents are overweight or obese [144]. The proportion of endometrial cancers due to obesity has been estimated to about 40-60% [27;145], and by preventing obesity, a considerable proportion of endometrial cancer cases may be avoided.

Increased physical activity, healthy food choices and weight maintenance may contribute to prevent obesity and thereby endometrial cancer, even if an independent protective effect on endometrial cancer have yet not been observed [94]. Observational cohort studies have shown that bariatric surgery results in profound weight loss and reduced cancer risk [146].

One of the barriers to endometrial cancer prevention, however, is the lack of public awareness of the association between endometrial cancer and obesity. A survey study of 1,545 women in the Houston community in the US explored if women in the general population were aware of the relationship between excess weight and cancer risk [147]. 24% of the women were overweight and 45% were obese. 58% of all study participants were not aware that obesity increased the risk for endometrial cancer. There was no difference in knowledge associated with any of the demographic characteristics studied (age, racial/ethnic group, level of education, household income and access to insurance). In a similar study in Germany, 96% of participants felt they would benefit from more information regarding risk factors for endometrial cancer [148]. The development of public educational programs and interventional strategies, both at an individual and community level, are likely to be needed to maximize preventive

efforts. Those may be similar to the tobacco cessation efforts where benefits for lung and heart conditions were observed much earlier than a decrease in cancer rates [149;150]. The tobacco control efforts also taught us that policy and environmental changes are crucial to achieving changes in individual behaviour. Efforts to address the obesity epidemic will require the action of the government, industries, communities, schools, primary health care providers, specialists and the individual. Efforts should aim at increasing the awareness of the problem and its association with chronic illnesses and cancer, at changing attitudes regarding healthy nutrition and increased physical activity, helping individuals change their behaviour and introducing environment supports for behaviour change.

7. FUTURE PERSPECTIVES

Our studies encourage more detailed research on the association between body mass and endometrial cancer. Further epidemiological studies with sufficient power are needed to elucidate the impact of BMI in premenopausal women.

Knowledge on how the impact of risk factors differs by histology is still scarce. Future studies based on cases with accurate histological diagnoses may assess how obesity is related to different subtypes of uterine cancer. Incidence trends of uterine cancer according to histological subtype may also increase our knowledge of the nature of the endometrial cancer epidemic and elucidate if risk factors are differentially associated with histological subtypes. Analyses in countries with a similar BMI development like Norway would add to our suggestion that the increase in endometrial cancer incidence may be due to the marked increase in BMI in the population. They may also help to elucidate the role of improved diagnostic in the development of endometrial cancer incidence. Studies with successive BMI measurements during follow-up may help to understand the impact of cumulative exposure to overweight/obesity and their effect according to age.

It also remains to be determined whether serum triglycerides play an independent role in relation to endometrial cancer risk. Other prospective studies are needed to better understand the association of blood lipids and endometrial cancer.

Future research to understand the biological role of obesity in cancer development is needed. At present, the biological mechanisms that link overweight and obesity to endometrial cancer are insufficiently understood. Obesity-associated dysregulation of adipokines is likely to contribute not only to tumorigenesis and tumour progression, but also to the metastatic potential. Adipokines may cause changes in hormone metabolism and also interfere with the regulation of the inflammatory and immune response. It has also been hypothesized that adipokines influence vascular and stromal interactions and angiogenesis. Additional studies of these factors will add to our understanding of adipose tissue as an endocrine and regulatory organ.

Among postmenopausal women only, risk of endometrial cancer was directly related to levels of estrone and bioavailable estradiol [151]. Little is known about the impact of obesity-related increase in endogenous sex-steroid levels and endometrial cancer risk among premenopausal women. Studies should also examine the

relationship between blood levels of factors related to insulin resistance such as C-peptide, IGF-binding proteins and IGF-1 and endometrial cancer risk.

Knowledge on the molecular pathways linking obesity, insulin resistance, diabetes mellitus and endometrial cancer may allow for the development of targeted endocrine therapy. The administration of metformin, an antidiabetic drug, has been shown to decrease cancer risk in type-2 diabetes in one large observational study [152], but no effect was detected in another population-based cohort study [153]. Clinical studies are needed to evaluate the utility of metformin in the treatment of cancer patients. Synthetic PPARγ ligands (thiazolidinediones, including troglitazone and rosiglitazone) may be another treatment option. Various *in vitro* studies have demonstrated their antiproliferative activity for a wide variety of neoplastic cells [154]. Still, little is known about PPARγ expression in endometrial carcinoma, and the effects of PPARγ agonists in these patients are largely unknown.

There are to date few clinical studies that have assessed the prognostic impact of BMI. Two large cohort studies showed that women with high body mass index had a significant higher risk of death from any cancer [34;155]. The highest relative risk was observed for death from uterine cancer (relative risk 6.25, 95% CI: 3.75-10.42 for women with BMI ≥40). These results may be due to obesity-related differences in the diagnosis or treatment of cancer, as well as true biological effects of obesity on survival. A report of the Gynecologic Oncology Group found BMI not to be related to the risk of endometrial cancer recurrence but to a decreased overall survival. This may be explained as death caused by comorbidities related to obesity and not cancer progression [156]. Another report found obesity related to favourable histology, lower grade and earlier stage disease. Obesity was also associated with increased time-to-recurrence rates and survival [157;158]. In order to evaluate the prognostic impact of BMI it may be instructive to study the association of BMI with other pathologic and molecular features. Recently, inactivation of PTEN/$p27^{kip1}$ was observed to be a specific feature of endometrial cancer in obese women, suggesting that BMI may be related to a certain phenotype of endometrial cancer [159].

8. CONCLUSIONS

I. In this study there was a linear and strong positive association of BMI with the risk of endometrial cancer. The linear association between BMI and endometrial cancer implies that even a slight increase in population body mass will lead to an increase in endometrial cancer incidence.

II. Women with diabetes had three-fold higher risk of endometrial cancer.

III. This study suggests an inverse association of endometrial cancer with smoking.

IV. The results of this study suggest a positive association of serum triglycerides with endometrial cancer risk. Adjustment for BMI partly attenuated the association, suggesting that some of the effect may be mediated through obesity. There were no associations (positive or negative) between total serum cholesterol, HDL cholesterol, non-HDL cholesterol and LDL cholesterol and the risk of endometrial cancer.

V. Our results suggest a positive association of BMI with all subtypes of uterine cancer, but the association may be strongest for endometrioid adenocarcinomas.

VI. This study provides evidence of a consistent increase in the incidence of endometrial cancer during the last 50 years. The increase has been more pronounced in postmenopausal women, but in the last decade the same trend has been observed in pre- and perimenopausal women. Our long-term predictions imply that the burden of endometrial cancer will continue to increase in the forthcoming decades.

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APPENDIX

I

II

III

IV

Endometrial cancer incidence trends in Norway during 1953-2007 and predictions for 2008-2027

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Running title: Endometrial cancer incidence trends in Norway and predictions
Key words: Endometrial cancer, incidence trends, prediction, obesity
Abbreviations: CI- confidence interval, BMI- body mass index, HRT- hormone replacement therapy, COC- combined oral contraceptives, APC model- Age-period-cohort model

This study provides evidence of a consistent increase in the incidence of endometrial cancer during the last 50 years. We suggest that the obesity epidemic may in part explain the increasing rates in postmenopausal women, but in recent years, also in younger women. Based on the future predictions endometrial cancer rates will dramatically increase unless effective preventive strategies are implemented.

ABSTRACT

Endometrial cancer is the most common cancer of the female genital tract in Western countries. Monitoring the incidence is important for health care planning and the identification of risk factors.

We present an age-period-cohort analysis of incidence trends of endometrial cancer in Norway from 1953 to 2007 and compare the incidence trends with those in three other Nordic countries. Based on the observed trends we have predicted endometrial cancer rates in Norway in 2015 and 2025.

In women at postmenopausal age (≥55 years), the annual incidence increase was 2.1% (95% CI: 0.9%, 3.4%) from 1988 to 1997 and 1.7% (95% CI: 0.6%, 2.8%) from 1998 to 2007. In younger women, there was an annual reduction of 0.6% (95% CI: -2.3%, 2.2%) from 1988 to 1997, followed by an annual increase of 1.7% (95% CI: -0.4%, 3.9%) from 1998 to 2007. The secular changes are likely to reflect both cohort and period effects. Our prediction estimates by 2025 suggest an incidence increase in the range of 50% to 100%, relative to the observed incidence in 2005.

There has been a strong and consistent incidence increase in endometrial cancer in the Nordic countries over the last 50 years. The increase has been most pronounced in postmenopausal women, but in the last decade, rates have increased also in women younger than 55 years. The prediction for the next 20 years suggests that endometrial cancer rates will dramatically increase unless effective preventive strategies are implemented.

INTRODUCTION

Endometrial cancer is the most common cancer of the female genital tract in many Western countries and some of the highest incidence rates are observed in European populations (1). Temporal incidence trends appear to differ by menopausal status, and in Norway, as in other Nordic countries, the increasing incidence of postmenopausal endometrial cancer contrasts with the declining rates observed in premenopausal women (2).

Monitoring the incidence is important for health care planning purposes and for the identification of risk factors. The planning of health services is an integral component of cancer control programmes (3), and prediction of future rates is therefore of great interest to society.

The etiology of endometrial cancer is unknown, but the main hypothesis has emphasized exposure to high levels of circulating estrogens in conjunction with inadequate levels of progesterone (4). The use of unopposed estrogen replacement therapy in postmenopausal women is associated with increased risk (5), whereas use of combined oral contraceptives (COCs) confers a degree of protection (6). Other risk increasing factors include nulliparity (7-10), obesity and diabetes (11-16), while cigarette smoking (17) and delayed childbearing (18) may be inversely associated with endometrial cancer risk.

In this study we present an age-period-cohort analysis of the observed incidence trends of endometrial cancer in Norway from 1953 to 2007, comparing these trends with those in three other Nordic countries (Sweden, Denmark and Finland). Based on the Norwegian trends, we provide two model-based scenarios of the future burden of endometrial cancer in Norway, predicting the number of new cases and incidence rates in 2015 and 2025.

MATERIAL AND METHODS

Incidence data. Incident cases of corpus uterine cancer (ICD-10 C54) were extracted from the Cancer Registry of Norway for the years 1953-2007, with corresponding person-years at risk within age groups obtained from the population data available at Statistics Norway (http://www.ssb.no). The Norwegian cancer registration system is in accordance with international standards and has an estimated completeness of around 98% overall, and above 99% for cancers of the *corpus uteri* for the years 2001-2005 (19). A high level of ascertainment is considered the result of mandatory

reporting from all hospitals, laboratories and general practitioners in Norway, in combination with the routine trace-back systems in place (19).

The vast majority of cancers of the uterine corpus are endometrial adenocarcinomas, and hereafter we refer to the disease as endometrial cancer.

Statistical analysis. To assess the time trends, the age distribution of the world standard population (20;21) was used to calculate age- standardized incidence rates per 100 000 by five-year time periods (1953-57, 1958-62,..., 2003-07). Truncated age-standardized rates and cumulative risk for the age groups 0-54 and 55-79 years were also calculated, with lifetime risk estimated for all ages up until 80, on assuming an absence of competing causes of death. A comparison of five-year moving averages of the age-standardized rates in Denmark, Finland and Sweden were extracted from the NORDCAN website (22) to serve as a comparison.

Restricting the age range to 35 to 79 years, 10-year synthetic cohorts were defined for women born in 1874-83, 1879-98,..., 1964-73 on subtracting the midpoints of five-year age groups from the corresponding midpoints of five-year aggregates of calendar time. The observed trends were presented as rates versus birth cohort by age, and rates versus calendar period by age, with quasi-parallelism of the age-specific curves on either time scale, an indication of their respective influence on the temporal pattern.

Cohort effects are established if changes in rates are seen in successive birth cohorts. They commonly arise through a changing prevalence and distribution of one or more key risk factors for the disease under study. Period effects are characterized by an immediate or fixed-delayed change in the incidence for all age groups, and may therefore act as surrogate measures of exposures that quickly change rates across all age groups. They may include changes in classification criteria, the availability of new diagnostic tests, or specific interventions that affect rates in all studied age groups.

To formally assess the importance of the non-linear effects of period and cohort and the goodness of fit of sub-models, a standard analysis of deviance of nested age-period-cohort (APC) models was performed, treating age, period and cohort as factors (23;24).

The APC model cannot estimate the individual linear components of the age, period, and cohort effects due to their linear dependence (25).Thus, we present two

unique sets of estimates from the full APC model, one with an allocation of the net drift (the identifiable sum of the period and cohort slopes) to birth cohort, and another assigned to calendar period. By setting the linear component of the period (cohort) effects to zero, we present the cohort (period) effects, hypothesizing that they predominate the underlying trends. The method still enables presentation of the non-linear period (cohort) effects in each set of estimates. The model analysis was performed using the APC functions available in the library *Epi* (version 1.0.8) in R (26), and specifically the *apc.fit* command. Both period and cohort effects are presented as rate ratios, with the age-specific rates relative to the corresponding median cohort or period. Stata 10 was used for data management and the plotting of the observed trends (27).

Future predictions for 2015 and 2025

In order to predict incidence trends for four five-year periods (2008-2027), APC models were fitted that allowed two different scenarios of the disease burden by extrapolating the four most recently observed five-year periods (1988-2007): Scenario A involved use of (i) a power function to level off the growth, thus avoiding the overestimation of cases associated with the method based on the multiplicative model, and (ii) projection of the recent linear trend based on the last 10 years (1998-2007) of observed data, attenuated by 25%, 50% and 75% in the second (2013-17), third (2018-22) and fourth (2023-27) prediction period, respectively. In a previous comparison of 15 different prediction methods, it was shown that the underlying model provided among the best estimates of future cancer burden (28). The predicted rates and numbers based on scenario A represent a conservative future pattern. An alternative scenario B used the same specifications as in (i) above, but assumed no attenuation of the linear trend (a constant drift) in future periods. For both scenarios we present the numbers of new cases and incidence rates for the midpoints of the second and fourth period, in 2015 and 2025, respectively.

The numbers of new cases were predicted by multiplying the projected incidence rates by official national population forecasts for future years obtained from Statistics Norway for 2015 and 2025 by the 5-year age group, based on the ”medium variant” and assumptions on future fertility, life expectancy, internal mobility and net immigration. Differences predicted numbers of new cases, relative to those observed

around 2005 are presented on partitioning the changes into those due to demographics (population aging and growth) and those due to changing risk (rates).

RESULTS

Trends by calendar period in Norway and the Nordic countries

Endometrial cancer rates in women younger than 55 years tend to be higher in Norway than in other Nordic countries, but at older ages, rates in Norway, Sweden and Finland have converged during the last two decades (Figure 1). The cumulative risk (prior to 80 years) has increased over time and is estimated to approximately 2.5% for women diagnosed between 2003 and 2007. This estimate suggests that one in 40 women will be diagnosed with endometrial cancer during their lifetime.

Between 1988 and 2007, the annual incidence increase in endometrial cancer was 1.7 % among Norwegian women under 80 years of age (Table 1), however, the temporal increase differed by age group. In women 55-79 years, the annual increase was roughly the same during the two decades; 2.1% (95% CI: 0.9%, 3.4%) from 1988 to 1997 and 1.7% (95% CI: 0.6%, 2.8%) from 1998 to 2007. In women younger than 55 years, there was an annual reduction of 0.6% (95% CI: -2.3%, 2.2%) from 1988 to 1997, followed by an annual increase of 1.7% (95% CI: -0.4%, 3.9%) from 1998 to 2007. Estimated as cumulative incidence, about one in 250 women was diagnosed with endometrial cancer in Norway before the age of 55 years during 2003-7.

A similar decline among women at premenopausal age has taken place in the other Nordic countries, beginning in the early 1980s (Figure 1). In Sweden, the decline started before the three other countries, and has also been stronger. In Finland, there was first a decreasing incidence followed by increasing rates in women younger than 55 years. Denmark represents an exception to the uniform patterns of increased postmenopausal incidence since around 1985. The rates in women 55 years or older declined during the 1980s and early 1990s, however, there has been an increase in incidence in Denmark from the late 1990s.

Age-period-cohort analyses of the incidence 1953-2007 in Norway

Age-specific rates by birth cohort and period of diagnosis are complex and difficult to interpret (Figure 2). However, it is instructive to partition the rates into pre- and postmenopausal age groups. There was a decline in incidence in Norwegian women younger than 55 years both by calendar period and by cohort until 1998, followed by

an incidence increase. In women 55 years and older, the rates have consistently increased among successive birth cohorts from the late 19th century and thereafter, and in consecutive periods of diagnoses from the early 1960s.

The full APC model was required in order to yield an adequate fit to the data (deviance = 26.6 on 27 degrees of freedom) (Table 2). All effects in the tabulated models were significant with the exception of non-linear period effects over and above the drift, and on grounds of parsimony, the APC model can be considered the best-fitting model. Figure 3 presents the modeled trends by age, period and birth cohort based on the APC model and two parameterizations (see Methods). Whether we fix the linear trend for either period or cohort to zero, increasing rate ratios are observed by birth cohort in generations born from around 1880 through to 1925. In generations born from 1925 to 1945 the rates are reasonably stable, while for post-war cohorts, either parameterization indicates a decline in endometrial cancer rates among successive generations born after 1945. Assuming that the underlying linear trend is due to calendar period, the analysis of the period effects suggests that rates are uniformly increasing throughout the study period, with the observation of a possible acceleration in rates since around 1998.

Predicted incidence in 2015 and 2025

We present observed (1988-2007) and predicted (2008-2027) trends in age-adjusted rates in Figure 4. Rates in Norway are estimated to peak around 2020, and subsequently decline, assuming a future attenuation in trends (scenario A). With the constant drift (scenario B), rates would continue to increase almost linearly up to the mid-2020s. Table 3 shows the mean number of cases predicted in 2015 and 2025 by age on the basis of the two scenarios compared with the mean number observed in 2005. The differences are partitioned according to changing risk (rates) and demographic changes (population ageing and growth). On the basis of the more conservative scenario A, we predict around 873 new cases in 2015, which corresponds to an additional 200 diagnoses on top of the 650 cases observed in 2005, representing a 35% increase in endometrial cancer incidence. Changes in underlying risk (18 %) and population aging (17%) contribute almost equally. According to scenario A, there will be around 1016 new cases annually circa 2025; or 57% more cases than in 2005, with about one-third of the increase due to the ageing

of the population. By 2025 there will be a larger proportion (22%) of women diagnosed with the disease at the age of 80 or older.

Applying scenario B, assuming the recent linear increases in the past will continue in the future, we predict a doubling of the number of new cases by 2025, corresponding to 1257 new cases. The proportion of cases diagnosed at 80 years or older in 2025 is estimated to 21% (compared to 18% in 2005). The shift towards more cases at older ages is not only related to the ageing of the population, but also to a relatively higher mean annual increase in incidence (of about 4% per annum) is observed from 1998 to 2007 in women 80 years and older (data nor shown).

DISCUSSION

The age-specific incidence trends of endometrial cancer in Norway from 1953 through 2007 reveal interesting patterns that may be useful in generating hypotheses that are relevant for primary prevention. In women at postmenopausal age (55 years or older), there was a general increase in incidence over the entire period, but in younger women, patterns were not consistent. In women younger than 55 years, there was a general incidence increase until around 1980 that was followed by a decline until 1998, after which the rates again have increased until 2007.

Despite the high validity of the information recorded by the Norwegian Cancer Registry and the well defined Norwegian population, it is possible that increased reporting and improved diagnostic efforts have contributed to the increase in endometrial cancer incidence over time. An easily performed endometrial sampling method introduced in the 1990s may have led to earlier detection of endometrial cancer and thereby to a shift towards increased incidence among younger women. It is possible that the increased incidence in pre- and perimenopausal women could be explained by such a drift. However, it may also be explained by the underlying random variation due to small numbers that limit the statistical power of our estimates in this age group.

The lack of adjustment for the rate of hysterectomies in the population is a weakness of this study. Since all women are included in the denominator of our estimations – as opposed to including only women with the uterus in place – the true risk of endometrial cancer incidence may be underestimated in this population. While the rate of hysterectomies has been historically low in Norway, there was a rapid increase in the 1990s. Recent estimates suggest that about 12% of Norwegian women

will have a hysterectomy performed during their lifetime (29). It has been estimated that the incidence of endometrial cancer, adjusted for the prevalence of hysterectomy, may yield 30% higher rates than the crude rates without adjustment (30). However, the predicted future rates could be an overestimate given that increasing hysterectomy rates will reduce the number of women at risk of developing endometrial cancer.

Another limitation may be the calculation of synthetic birth cohorts based on period and age. This creates a linear dependency between the time components and a non-identifiability of the linear slopes for age, period and cohort. We were, however, able to report the estimates of drift, the sum of the period and cohort slopes, and we provide solutions based on an allocation of drift to either period or cohort. This dual presentation was considered necessary given the complexity of the trends and the inability to estimate the extent to which changes in key risk factors, including reproductive patterns, the use of hormone replacement therapy (HRT), use of oral contraceptives, and obesity, could have resulted in cohort or period-related linear changes. A change in use of oral contraceptives and HRT may affect highly specific age groups and time periods, whereas obesity may affect rates in women across all age groups over a fixed recent period.

The consistent increase in incidence observed in the youngest cohorts is most likely due to changes in reproductive factors, including earlier age at menarche and lower parity, that are associated with increased risk for endometrial cancer (7-9;18;31). Thus, the lowest risk in Norway was observed in the 1890-94 birth cohort. It has previously been estimated that about 27% of the increase in cumulative age-adjusted incidence from 1955 to 1984 may be attributed to changes in childbearing patterns (32). Birth rates have stabilized at around 1.8 during the last 30 years (http://www.ssb.no), and maternal age at first birth has gradually increased during the last 40 years. However, studies of the impact of age at first or last birth on endometrial cancer risk have shown conflicting results (7;9;10;18) and therefore, we do not know whether delayed childbearing has contributed to the increase in incidence.

Menopausal treatment using estrogens unopposed by progesterone increases the risk of endometrial cancer in a dose-risk manner (5), and combined regimens of estrogen and progesterone were introduced to prevent this side effect. Nevertheless, small increases in risk have been reported also for the combined treatment (33;34) and this may account for the increasing rates observed in postmenopausal women born after 1940. In the late 1980s less than 6% of postmenopausal Norwegian women

used HRT (35), but the use increased rapidly in the 1990s, and reached a peak of about 35% towards the end of the decade (36). At that time, the sale was dominated by combined estrogen-progesterone preparations. Since then, sales of HRT have decreased by more than 50% (37). It seems plausible that the recent decline could have attenuated the incidence increase and it is possible that the modest incidence reduction in the age group 55-59 years could reflect such an attenuation. Increased prevalence of other risk factors, including obesity and diabetes type 2, may have contributed to the persisting incidence increase in postmenopausal women.

It is well established that the use of combined oral contraceptives (COCs) protects against endometrial cancer later in life. In the late 1980s approximately 21% of Norwegian women in the age group 20-44 years were regular users of combined oral contraceptives (38), and the proportion of users has subsequently increased (37).In Norway, the Wholesaler-based Drug Statistics report total COC consumption from the late 1960s, and the sales have increased from 84,790 DDD/day (defined daily dose) during 1970-79 to 159,256 DDD/day in the period 1990-99. The declining endometrial cancer rates at premenopausal age starting from the early 1980s may therefore, in part, be ascribed to COC exposure.

The increasing incidence of endometrial cancer in the last decade across all birth cohorts born after 1950 seems to be in conflict with the increased use of hormonal contraception. Therefore one may speculate whether other risk factors, such as increasing body mass may have contributed to the increase in rates. Body mass index is linearly associated with the risk of endometrial cancer (11). Overweight doubles the risk, and the risk may be up to 6-fold higher among very obese women (BMI $\geq$40). In Norway, population-based health surveys have documented increases in BMI during the 1980s and the 1990s (39;40). Mean body weight has increased in all age groups younger than 70 years, and the largest increase (7.3 kg) has been observed in women 20-29 years old. The consistent increase in body mass has been observed since 1985, and the proportion of obese (BMI $\geq$30) women in the age group 20-29 years had tripled between the two surveys (3.7% vs. 11.9%). The most recent data (2000-03) from five Norwegian counties suggest that body mass continues to increase (41).

The recent increase in endometrial cancer incidence among women at premenopausal age coincides the strong increase in BMI in young women. The increased use of COCs may have contributed to an attenuation of an underlying

endometrial cancer epidemic caused by an increasing BMI in the population. A similar incidence increase has been observed in Finland, but not in Sweden. Also in Finland, mean BMI has increased in women younger than 30 years over the last 20 years (42), whereas in Sweden, an increase in mean BMI has not been observed (43;44).

The impact of BMI may be strongest for endometrioid adenocarcinoma (45), but few, if any studies have assessed the association of risk factors with different histological subtypes of endometrial cancer. We studied endometrial cancer as a single entity, and could not address the possibility that relevant risk factors may have different impact on different histological subtypes.

Previous predictions of endometrial cancer incidence in Norway were based on observations until 1997, and the results predicted a stabilization of rates thereafter (46). For the Nordic countries combined, a decline by 15% from 1993-1997 to 2018-2022 has been predicted. Our analyses suggest that previous predictions were too conservative, and based on attenuated future trends (scenario A) we predict a continuing increase of 57% until 2025 compared to the observed rate in 2005. This scenario implies a decreased exposure to underlying risk factors over time. There are to date no studies that have evaluated if the risk increase due to BMI depends on age or duration of exposure. If the BMI effect depends on duration, the full BMI effect is yet to be seen. The less optimistic scenario B in this study that predicts higher rates of endometrial cancer incidence implies unchanged trends in exposure to underlying risk factors in the years beyond the observation period. It is in accordance with our previous finding that even a modest increase in population body mass will lead to an increase in endometrial cancer incidence (11). We therefore believe this scenario may provide a more realistic prediction of future endometrial cancer incidence should recent trends hold into the future. There are to date no reliable predictions of the development of BMI in Norway, but an increasing and substantial proportion of adolescents are overweight or obese (47). The proportion of endometrial cancers due to obesity in Europe has been estimated to about 40% (48), and by preventing obesity, a considerable proportion of endometrial cancer cases could be avoided.

In conclusion, this study provides evidence of a consistent increase in the incidence of endometrial cancer during the last 50 years. The increase has been more pronounced in postmenopausal women, but in the last decade the same trend has been observed in pre-and perimenopausal women. Our long-term predictions imply that the burden of endometrial cancer will continue to increase in the forthcoming

decades. Further research that provides a better appreciation of the underlying risk factors and their prevention will therefore remain a major objective in coming years.

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Table 1: Endometrial cancer incidence in Norway: numbers of new cases, person-years and cumulative risk 1988-92 and 2003-7, and estimated annual percentage change 1988-1997 and 1998-2007 for ages 0-79, 0-54 and 55-79.

	1988-92			2003-07			1988-1997	1998-2007
Age Group	**Cases**	**Person-Years[+]**	**CR[*]**	**Cases**	**Person-years[+]**	**CR[*]**	**EAPC[**]**	**EAPC[**]**
0-79	370	2.02	1.85	518	2.17	2.49	1.7 (0.5, 2.8)	1.7 (0.7, 2.7)
0-54	87	1.54	0.39	113	1.67	0.37	-0.6 (-2.3, 2.2)	1.7 (-0.4, 3.9)
55-79	283	0.48	1.46	404	0.50	2.12	2.1 (0.9, 3.4)	1.7 (0.6, 2.8)

+ per million

* CR: cumulative risk

** EAPC: estimated annual percentage change based on a log-linear model with year and age. Due to small numbers in the youngest age groups, EAPC in 0-79 and 0-54 are based on data for ages 25-79 and 25-54, respectively.

Table 2: Analysis of deviance for nested APC models, Norway 1953-2007

Model	df*	Residual deviance	Effect tested	df*	Deviance	P(>|Chi|)
Age	50	1428.7				
			Drift	1	1273.5	<0.01
Age-Drift	49	155.2				
			Non-linear Cohort	13	83.7	<0.01
Age-Cohort	36	71.5				
			Non-linear Period	9	44.9	<0.01
Age-Period-Cohort**	27	26.6				
			Non-linear Cohort	-13	-120.6	<0.01
Age-Period	40	147.2				
			Non-linear Period	-9	-8.1	0.53
Age-Drift	49	155.2				

* degrees of freedom
** Best-fitting APC model on the grounds of parsimony

Table 3: Predicted mean annual numbers of endometrial incidence cases 2015 and 2025 by age group compared with the mean annual numbers observed in 2005, and for all-ages incidence, relative changes due to changing risk and changing demographics (population aging and growth). Predictions 2008-27 were obtained based on two scenarios A and B (see Material and Methods) on fitting APC models to the observed time trends 1988-2007.

Age group	observed 2005* (% of total)	predicted 2015** (% of total)	predicted 2025+ (% of total)
Scenario A			
All ages	647	873	1016
Difference from 2005 (% change)		+226 (35%)	+369 (57%)
(% change in risk / demographics)		(18% / 17%)	(22% / 35%)
Ages 0-54 (% of total)	113 (17%)	147 (17%)	182 (18%)
Ages 55-79 (% of total)	419 (65%)	577 (66%)	614 (60%)
Ages 80+ (% of total)	115 (18%)	150 (17%)	220 (22%)
Scenario B			
All ages	647	905	1257
Difference from 2005 (% change)		+258 (40%)	+609 (95%)
(% change in risk / demographics)		(23% / 17%)	(60% / 35%)
Ages 0-54 (% of total)	113 (17%)	153 (17%)	234 (19%)
Ages 55-79 (% of total)	419 (65%)	597 (66%)	757 (60%)
Ages 80+ (% of total)	115 (18%)	155 (18%)	266 (21%)

* mean annual observed cases 2003-7
** mean annual predicted cases 2013-17
+ mean annual predicted cases 2023-25

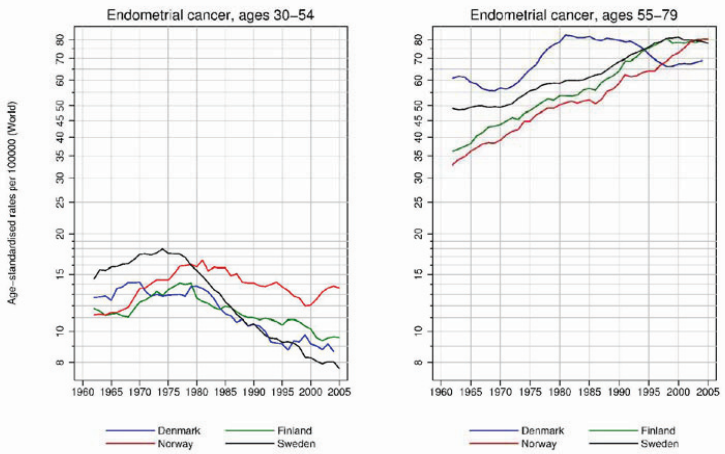
Legend to Figures

Figure 1: Trends in age-standardized (World) incidence rates of endometrial cancer versus calendar period in four Nordic countries by sex and menopausal status (aged 0-54 and 55-79). Rates are presented as five-year moving averages. Source: NORDCAN (22)

Figure 2: Observed trends in the incidence of endometrial cancer in Norway 1953-2007. Rates are presented as rates versus birth cohort by age (5-year age groups indicated) and calendar period cohort by age.

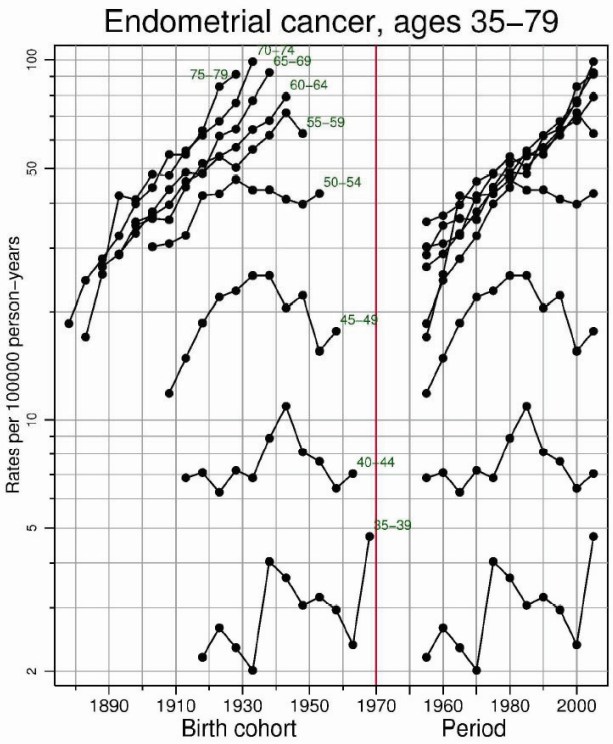
Figure 3: Age, period and cohort effects, based on Holford's approach for endometrial cancer, Norway 1953-2007, ages 35-79. Two sets of estimates are based on the full APC model assuming either a linear slope of zero for calendar period (red line), or for birth cohort (blue line).

Figure 4: Observed (1953-2007) and predicted (2008-2027) age-standardized (World) ratesbased on an APC model fitted to the period 1988-2007 on the basis of two scenarios regarding the future linear trend. Rates are based on five-year aggregates for all ages.



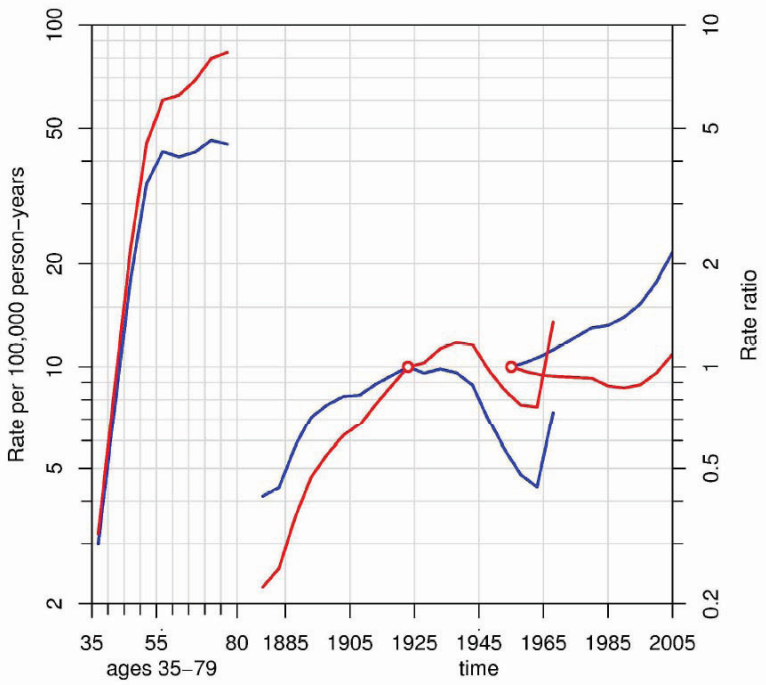
Trends in age-standardized (World) incidence rates of endometrial cancer versus calendar period in four Nordic countries by sex and menopausal status (aged 0-54 and 55-79). Rates are presented as five-year moving averages. Source: NORDCAN (22)
297x209mm (600 x 600 DPI)

Figure 1



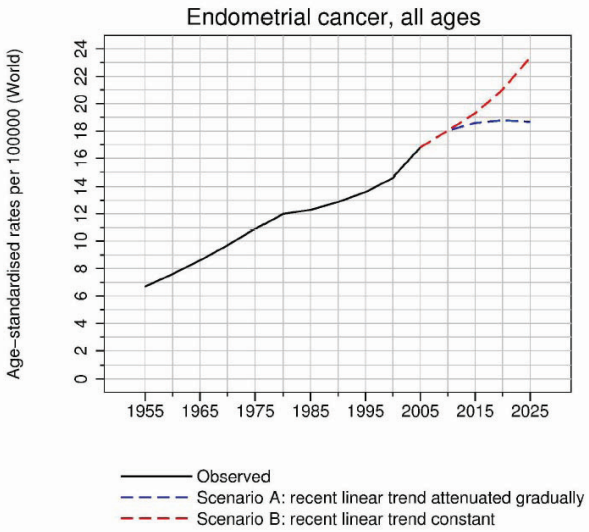
Observed trends in the incidence of endometrial cancer in Norway 1953-2007. Rates are presented as rates versus birth cohort by age (5-year age groups indicated) and calendar period cohort by age.
209x297mm (600 x 600 DPI)

Figure 2



Age, period and cohort effects, based on Holford's approach for endometrial cancer, Norway 1953-2007, ages 35-79. Two sets of estimates are based on the full APC model assuming either a linear slope of zero for calendar period (red line), or for birth cohort (blue line).
167x167mm (600 x 600 DPI)

Figure 3



Observed (1953-2007) and predicted (2008-2027) age-standardized (World) ratesbased on an APC model fitted to the period 1988-2007 on the basis of two scenarios regarding the future linear trend. Rates are based on five-year aggregates for all ages.
209x297mm (600 x 600 DPI)

Figure 4

Questionnaires HUNT 1 and 2

MELDING OM SKJERMBILDEFOTOGRAFERING OG UNDERSØKELSE AV BLODTRYKK OG BLODSUKKER

Skjermbildefotograferingen kommer nå til ditt distrikt. Denne gangen inngår fotograferingen i en større helseundersøkelse, og vi viser til orienteringen som er gitt i den vedlagte brosjyre.

Tid og sted for frammøte vil du finne nedenfor.

Vennligst fyll ut spørreskjemaet på baksiden og ta det med til undersøkelsen. Ta også med skjermbildebevis, tuberkulinkort eller helsebok om du har.

Det er viktig at du møter fram selv om du nylig har fått kontrollert blodtrykk eller blodsukker, og selv om du er under behandling for høyt blodtrykk eller for sukkersyke.

Med vennlig hilsen

Statens skjermbildefotografering

Postboks 8155 Dep, Oslo 1

Fylkeslegen ● Helserådet ● Statens Institutt For Folkehelse

Født dato | Personnr. | Kommune | Kretsnr.

Møtested | Kjønn | Første bokstav etternavn | Dag og dato | Klokkeslett

H. 14 | V. 18 | SBT_1 21 | DBT_1 24 | PULS 27 | SBT_2 30 | DBT_2 33 | SYKEPL 35

TID 38 | GLUC 39 | GLUC 42 | GLUC 45 | HG 46 | BT 47 | P 48 | Ø.M. 49

A. Hvordan er helsa di for tida?
(Sett kryss i bare *en* rute.)

Dårlig	50	1
Ikke helt god		2
God		3
Svært god		4

B. Har du i løpet av de siste 12 måneder vært hos?

	JA	NEI
Almenpraktiserende lege (distriktslege, privatpraktiserende lege,turnuskandidat) 51		
Bedriftslege 52		
Militærlege 53		
Lege ved sykehus (uten at du var innlagt) 54		
Annen lege 55		

C. Har du vært innlagt i sykehus de siste 5 åra? 56 | JA | NEI |

D. Bruker du, eller har du brukt, medisin for høyt blodtrykk? 57 | JA | NEI |

E. Har du eller har du hatt noen av disse sykdommene?

	JA	NEI
Sukkersyke 58		
Hjerteinfarkt 59		
Angina pectoris (hjertekrampe) 60		
Hjerneslag eller hjerneblødning 61		

F. Har du noen langvarig sykdom, skade eller lidelse av fysisk eller psykisk art som nedsetter dine funksjoner i ditt daglige liv? (Med langvarig menes at det har vart, eller vil vare i minst ett år.) 62 | JA | NEI |

Hvis «JA», vil du si at dine funksjoner er litt, middels eller mye nedsatt?

	LITT	MIDDELS	MYE
Er bevegelseshemmet 63			
Har nedsatt syn 64			
Har nedsatt hørsel 65			
Hemmet pga. kroppslig sykdom 66			
Hemmet pga. psykiske plager 67			

G. Har du noen søsken? (Nålevende eller døde) 68 | JA | NEI |

Hvis «JA», har en eller flere av dem hatt noen av disse sykdommene?

	JA	NEI	VET IKKE
Sukkersyke 69			
Hjerteinfarkt/hjertekrampe 70			
Forhøyet blodtrykk 71			

H. Når du tenker på hvordan du har det for tida, er du stort sett fornøyd med tilværelsen, eller er du stort sett misfornøyd?
(Sett kryss i bare *en* rute.)

Svært fornøyd 72		1
Meget fornøyd		2
Ganske fornøyd		3
Både/og		4
Nokså misfornøyd		5
Meget misfornøyd		6
Svært misfornøyd		7

SE BILDET AV BLODTRYKKSMÅLINGEN I DEN VEDLAGTE BROSJYREN

	JA	NEI	VET IKKE
I. Er blodtrykket ditt målt noen gang før? Hvis «NEI», gå videre til spørsmål M 73			

J. Hvilket år ble blodtrykket målt siste gang?
19 ☐☐ vet ikke 74
Skriv årstallet her (ca.)

K. Hvor ble blodtrykket målt siste gang?
(Sett kryss i bare *en* rute.)

Hos almenpraktiserende lege (distriktslege, privatpraktiserende lege, turnuskandidat 76		1
Hos bedriftslege		2
Hos militærlege		3
På sykehus		4
Hos annen lege		5
Vet ikke		6

L. Hva ble resultatet av målingen?
(Sett kryss i bare *en* rute.)

Jeg skulle begynne med eller fortsette med medisin for høyt blodtrykk 77		1
Jeg skulle komme til kontroll, men skulle *ikke* ta medisin		2
Jeg skulle *ikke* ta medisin og *ikke* komme til kontroll		3

M. Dersom denne helseundersøkelsen viser at du bør undersøkes nærmere: Hvilken almenpraktiserende lege ønsker du da å bli henvist til?
Skriv navnet på legen her

IKKE SKRIV HER

Ingen spesiell lege 78

OM ARBEIDET DITT

N. Er du i arbeid for tida?
(Sett kryss i bare *en* rute.)

Ja, heltidsarbeid (utenom husarbeid) 81		1
Ja, deltidsarbeid (utenom husarbeid)		2
Ja, heltids husarbeid		3
Nei, ikke i arbeid		4

O. Hvis du ikke er i heltids arbeid, er det på grunn av:
(Sett kryss i bare *en* rute.)

Arbeidsløshet, permittering 82		1
Pensjon eller trygd		2
Utdanning eller militærtjeneste		3
Annet		4

HVIS DU ER I ARBEID, VENNLIGST SVAR PÅ DE NESTE TO SPØRSMÅLENE:

P. Er det mye stress og mas på arbeidet ditt?
(Sett kryss i bare *en* rute.)

Nei, ikke i det hele tatt 83		1
Sjelden		2
Ja, en god del		3
Ja, nesten hele tida		4

Q. Kan du sjøl bestemme hvordan arbeidet ditt skal legges opp? (Sett kryss i bare *en* rute)

Nei, ikke i det hele tatt 84		1
I liten grad		2
Ja, stort sett		3
Ja, det bestemmer jeg sjøl		4

Vi takker for frammøtet til undersøkelsen.

Vi vil også be deg være vennlig å fylle ut dette spørreskjemaet. Opplysninger vil bli brukt i et større forskningsarbeid om forhold som har betydning for helsen.

Svar etter beste skjønn. Kryss av for bare en av svar-mulighetene (dersom det ikke står nevnt noe annet). Det utfylte skjema returneres i vedlagte svarkonvolutt. Porto er betalt.

Alle opplysningene er underlagt streng taushetsplikt.

Med hilsen

Statens skjermbildefotografering
Fylkeslegen ● Helserådet ● Statens Institutt For Folkehelse
Institutt for anvendt sosialvitenskapelig forskning/
Institutt for samfunnsforskning

Til etikett

Navn: _____

Adr. : _____

_____

_____

Postnr. Postkontor

F.nr. : _____

MOSJON

Med mosjon mener vi at du f.eks. går tur, går på ski, svømmer eller driver trening/idrett.

Hvor ofte driver du mosjon?
(Ta et gjennomsnitt)

Aldri	12	1
Sjeldnere enn en gang i uka		2
En gang i uka		3
2–3 ganger i uka		4
Omtrent hver dag		5

Dersom du driver slik mosjon så ofte som en eller flere ganger i uka:
Hvor hardt mosjonerer du?
(Ta et gjennomsnitt)

Tar det rolig uten å bli andpusten eller svett	13	1
Tar det så hardt at jeg blir andpusten og svett		2
Tar meg nesten helt ut		3

Hvor lenge holder du på hver gang?
(Ta et gjennomsnitt)

Mindre enn 15 minutter	14	1
16–30 minutter		2
30 minutter–1 time		3
Mer enn 1 time		4

SALT

Hvor ofte bruker du salt kjøtt eller salt fisk/sild til middag?

Aldri, eller sjeldnere enn en gang i måneden	15	1
1–2 ganger i måneden		2
Opptil en gang i uka		3
Opptil to ganger i uka		4
Mer enn to ganger i uka		5

Hvor ofte pleier du å strø ekstra salt på middagsmaten?

Sjelden eller aldri	16	1
Av og til		2
Ofte		3
Alltid eller nesten alltid		4

RØYKEVANER

		JA	NEI
Røyker du daglig for tiden?	17		
Hvis du svarte «JA», røyker du DAGLIG for tiden:		JA	NEI
Sigaretter?	18		
Pipe?	19		
Sigarer (eller serutter/sigarillos)?	20		
Hvis du IKKE røyker SIGARETTER daglig for tiden: Har du røykt SIGARETTER daglig tidligere?	21	JA	NEI

Hvis du svarte «JA», hvor lenge er det siden du sluttet å røyke sigaretter daglig?

Mindre enn 3 måneder	22	1
3 måneder– 1 år		2
1–5 år		3
Mer enn 5 år		4

Hvis du røyker SIGARETTER daglig nå, eller har gjort det tidligere:

Hvor mange sigaretter røyker eller røykte du pr. dag? (Oppgi antall pr. dag medregnet håndrullede) ..... 23 Antall

Besvares av dem som røyker daglig nå eller har røykt daglig tidligere:
(Gjelder både sigarett-, pipe- og sigar-røykere)

Hvor gammel var du da du begynte å røyke daglig?	25	år
Hvor mange år tilsammen har du røykt daglig?	27	år

ALKOHOLBRUK

Hvor ofte har du drukket alkohol (øl, vin eller brennevin) de SISTE 14 DAGENE?

Jeg har ikke drukket alkohol, men er ikke totalavholdende	29	1
Jeg har drukket 1–4 ganger		2
Jeg har drukket 5–10 ganger		3
Jeg har drukket mer enn 10 ganger		4
Jeg er totalavholdende, drikker aldri alkohol		5

		JA	NEI
Dersom du har drukket alkohol de siste 14 dagene, har det ført til at du noen gang har følt deg beruset?	30		

Har det vært perioder i livet ditt da du har drukket for mye, eller i hvert fall i meste laget?

Nei	31	1
I tvil, kanskje		2
Ja		3

BOSITUASJONEN

Bor du alene eller sammen med andre?
Kryss av for de du bor sammen med. (Her kan du sette flere kryss.)

- Bor alene 32
- Ektefelle eller samboer 33
- Foreldre eller svigerforeldre 34
- Andre voksne personer 35
- Barn under 5 år 36
- Barn 6–15 år 37
- Barn over 15 år 38

Bor du fast i institusjon?
(sykehjem, aldershjem eller liknende) 39

JA | NEI

UTDANNINGEN

Hvilken utdanning har du fullført?
Oppgi bare høyest fullførte utdanning.

- 7-årig folkeskole eller kortere ..... 40 — 1
- Framhalds- eller fortsettelsesskole 2
- 9-årig grunnskole 3
- Real- eller middelskole, grunnskolens 10. år 4
- Ett- eller to-årig videregående skole 5
- Artium, økonomisk gymnas eller almenfaglig retning i videregående skoler 6
- Høyskole eller universitet, mindre enn 4 år 7
- Høyskole eller universitet, 4 år eller mer 8

Har du fullført annen heldags utdanning, og i tilfelle i hvor mange år?

Skriv antall år her .... 41 — år

ARBEID

Hvis du er eller har vært i inntektsgivende arbeid, kan du angi hvilken av disse yrkesgruppene ditt yrke faller innenfor? (Hvis du ikke er i arbeid nå, svarer du ut fra det yrket du hadde sist.)

Hvis du har en ektefelle (eller samboer) som er i inntektsgivende arbeid nå, eller har vært det tidligere, angi tilsvarende hvilken yrkesgruppe han/hun tilhører. (Evt. angi om han/hun *ikke* har hatt inntektsgivende arbeid.)

	Deg selv	Ektefellen
Spesialarbeider, ufaglært arbeider 43, 44		1
Fagarbeider, håndverker, formann		2
Underordnet funksjonær (butikk, kontor, offentlige tjenester)		3
Fagfunksjonær (f.eks. sykepleier, tekniker, lærer)		4
Overordnet stilling i offentlig eller privat virksomhet		5
Gårdbruker eller skogeier		6
Fisker		7
Selvstendig i akademisk erverv (f.eks. tannlege, advokat)		8
Selvstendig næringsdrivende (Industi, transport, handel)		9
Har *ikke* hatt inntektsgivende arbeid (f.eks. pga. heltids husarbeid, studier, trygd)		0

Hvis du er i arbeid (gjelder også heltids husarbeid), **ber vi deg fylle ut de neste spørsmålene:**

Er arbeidet ditt så fysisk anstrengende at du ofte er sliten i kroppen etter en arbeidsdag?

- Ja, nesten alltid ..... 45 — 1
- Ganske ofte 2
- Ganske sjelden 3
- Aldri, eller nesten aldri 4

Krever arbeidet ditt så mye konsentrasjon og oppmerksomhet at du ofte føler deg utslitt etter en arbeidsdag?

- Ja, nesten alltid ..... 46 — 1
- Ganske ofte 2
- Ganske sjelden 3
- Aldri, eller nesten aldri 4

Hvordan trives du alt i alt med arbeidet ditt?

- Veldig godt ..... 47 — 1
- Ganske godt 2
- Godt 3
- Ikke særlig godt 4
- Dårlig 5

Hvis du er gårdbruker eller annen selvstendig næringsdrivende, har du noen ansatte som arbeider fast for deg?

- Ingen fast ansatte ..... 48 — 1
- 1–2 fast ansatte 2
- 3–10 fast ansatte 3
- Mer enn 10 fast ansatte 4

HVORDAN HAR DU DET?

Når du tenker på hvordan du har det for tida, er du stort sett fornøyd med tilværelsen, eller er du stort sett misfornøyd?

- Svært fornøyd ..... 49 — 1
- Meget fornøyd 2
- Nokså fornøyd 3
- Både - og 4
- Nokså misfornøyd 5
- Meget misfornøyd 6
- Svært misfornøyd 7

Føler du deg stort sett sterk og opplagt, eller trett og sliten?

- Meget sterk og opplagt ..... 50 — 1
- Sterk og opplagt 2
- Ganske sterk og opplagt 3
- Både - og 4
- Ganske trett og sliten 5
- Trett og sliten 6
- Svært trett og sliten 7

MEDISIN/PLAGER

Har du vanligvis:

		JA	NEI
Hoste om morgenen?	51	☐	☐
Oppspytt fra brystet om morgenen?	52	☐	☐

Hvor ofte har du brukt smertestillende medisin den siste måneden?

Daglig	53	1
Hver uke, men ikke hver dag		2
Sjeldnere enn hver uke		3
Aldri		4

Hvor ofte har du brukt avslappende/beroligende medisin eller sovemedisin den siste måneden?

Daglig	54	1
Hver uke, men ikke hver dag		2
Sjeldnere enn hver uke		3
Aldri		4

Har du i løpet av siste måned vært plaget av nervøsitet (irritabel, urolig, anspent eller rastløs)**?**

Nesten hele tida	55	1
Ofte		2
Av og til		3
Aldri		4

Har du i løpet av siste måned hatt innsoving- eller søvnproblemer?

Nesten hver natt	56	1
Ofte		2
Av og til		3
Aldri		4

Har du i det store og hele en rolig og god følelse inne i deg?

Nesten hele tida	57	1
Ofte		2
Av og til		3
Aldri		4

VENNER/HJELP

Dersom du ble syk og måtte holde senga i lengre tid, hvor sannsynlig tror du det er at du kunne få nødvendig hjelp og støtte av familie, venner eller naboer?

Svært sannsynlig	58	1
Nokså sannsynlig		2
Usikkert		3
Usannsynlig		4
Helt usannsynlig		5

Hender det ofte at du føler deg ensom?

Meget ofte	59	1
Ofte		2
Av og til		3
Meget sjelden		4
Aldri		5

HVORDAN ER DU?

Har du tendens til å ta dine oppgaver mer alvorlig enn folk flest?

Ja, nettopp slik er jeg	60	1
Ja, stort sett		2
Både - og		3
Nei, stort sett ikke		4
Nei, tvert imot		5

		JA	NEI	VET IKKE
Har du i løpet av det siste året ofte følt at du har presset deg, eller stadig drevet deg selv framover?	61	☐	☐	☐

Føler du deg alltid under tidspress, også når det gjelder daglige gjøremål?

Alltid, eller nesten alltid	62	1
Noen ganger		2
Aldri		3

Er du vanligvis glad eller nedstemt?

Svært nedstemt	63	1
Nedstemt		2
Nokså nedstemt		3
Både - og		4
Nokså glad		5
Glad		6
Svært glad		7

HVA ER VIKTIG?

Synes du det er viktig at man prøver å være fornøyd med det man har?

Dette er særlig viktig	64	1
Dette er viktig		2
Både - og		3
Dette er mindre viktig		4
Dette er overhodet ikke viktig		5

Synes du det er viktig at man kan slå av på kravene?

Dette er særlig viktig	65	1
Dette er viktig		2
Både - og		3
Dette er mindre viktig		4
Dette er overhodet ikke viktig		5

Synes du det er viktig at man alltid er i godt humør?

Dette er særlig viktig	66	1
Dette er viktig		2
Både - og		3
Dette er mindre viktig		4
Dette er overhodet ikke viktig		5

Tusen takk for den hjelp du har gitt oss ved å fylle ut dette skjema.

TILLEGGS-SKJEMA OM BLODTRYKK

På skjemaet du leverte ved helseundersøkelsen, svarte du at du har, eller har brukt, medisin for høyt blodtrykk.

I Nord-Trøndelag har det siden 1980 pågått en undersøkelse om blodtrykksbehandling. Formålet ved undersøkelsen er å gjøre behandlingen bedre. En viktig del av undersøkelsen er å få opplysninger om hvordan du og alle andre med høyt blodtrykk har det, og hvilke erfaringer dere har gjort.

Det er derfor meget viktig at du fyller ut dette skjemaet så nøye som mulig.

Enkelte spørsmål kan være vanskelig å svare på. Prøv likevel å svare etter beste skjønn, og legg vekt på det som er vanlig eller gjennomsnittlig for deg.

Alle opplysninger blir behandlet av oss med streng taushetsplikt.

På forhånd takk!

Når ble det påvist at du hadde høyt blodtrykk første gang? (Skriv årstallet i ruta)

19 ____

Vet ikke ... 67

Hvor ble det påvist?
(Sett kryss i bare *en* av rutene)

Hos almenpraktiserende lege (distriktslege, privatpraktiserende lege, turnuskandidat)	69	1
Hos militærlege		2
På sykehus		3
Vet ikke		4

JA NEI

Bruker du medisin for blodtrykk nå? ... 70
Hvis «NEI»: Gå til de to siste spm. nederst til venstre.

Hvis «JA»: Når begynte du med medisiner for blodtrykket? (Skriv årstallet i ruta)

19 ____

Vet ikke ... 71

JA NEI

Bruker du doserings-eske for tabletter? ... 220

Har du medisinkort som viser hva slags medisin du skal ta? ... 221

Hender det at du glemmer å ta medisinene?
(Sett kryss i bare *en* av rutene)

Aldri	73	1
Sjelden (ca. en gang i mnd.)		2
Oftere		3

Hvor viktig mener du at det er for deg at du tar blodtrykksmedisinen(e) akkurat som foreskrevet?
(Sett kryss i bare *en* av rutene)

Ikke så viktig	74	1
Viktig		2
Meget viktig		3

Vet du hva blodtrykket ditt var ved siste kontroll?
(Sett kryss i bare *en* rute)

Nei	75	1
Ja		2
Usikker		3

Hvis «JA» eller «USIKKER», skriv hvor mye du tror det var: 76

Ikke skriv her

Skriv her 79

Hvis du har brukt medisin for blodtrykket før, men ikke nå: Når slutta du med medisiner?
(Skriv årstallet i ruta)

19 ____

Vet ikke ... 82

Hvorfor slutta du med medisinene?
(Sett ett eller flere kryss)

Legen bestemte det	84
Jeg fikk plager av medisinene	85
Jeg mente det ikke var nødvendig med medisiner	86
Jeg var redd medisinene var skadelige	87
Annen årsak (skriv hvilken nedenfor)	88

Ikke skriv her

Skriv hvilken årsak det evt. var 89

Har legen gitt deg andre råd i forbindelse med at du har for høyt blodtrykk?
(Sett kryss i bare *en* av rutene)

Nei	91	1
Ja		2
Husker ikke		3

Hvis «JA»; Hvilke råd?

92 ____

Ikke skriv her

94 ____

Hvordan opplever du behandlingen for blodtrykket? Gir det deg:
(Sett ett eller flere kryss)

Lettelse, ro, trygghet	96
Anspenthet, engstelse, redsel, uro	97
Dårlig humør, depresjon	98
Ingen spesielle følelser	99

Synes du at det er noen ulemper ved det at du må ha behandling for høyt blodtrykk?

Nei, ingen ulemper	100
Ja	

Hvis «JA»: Hva synes du er mest plagsomt?
(Sett ett eller flere kryss)

At du må bruke medisiner hver dag	101
At du må gå til legekontroll	102
At du må følge de råd som legen har gitt	103
At du har ubehag av medisinene	104
At du er engstelig for at det er noe alvorlig som feiler deg	105
At du synes det er leit å bli betraktet som «pasient»	106
Annet	107

TILLEGGS-SKJEMA FOR SUKKERSYKE

Du har opplyst at du har sukkersyke. Et viktig mål for helseundersøkelsen er å finne ut hvordan sukkersyke best kan behandles for å gi minst mulig plager.

Alle som har eller har hatt sukkersyke, bes derfor om å svare så godt som mulig på disse spørsmålene om sukkersyke.

Noen har svart på et lignende skjema høsten 1982. Det er likevel av stor betydning at disse fyller ut dette skjemaet.

Alle opplysninger blir behandlet av oss med streng taushetsplikt.

På forhånd takk!

Når ble sukkersyken din oppdaget? ... 19 108
(Skriv årstallet i ruta)

Hvordan ble sukkersyken din oppdaget?

Jeg søkte lege på grunn av symptomer 110 1
Ble oppdaget uten at jeg hadde symptomer (ved legeattest, bedriftskontroll, undersøkelse for annen sykdom i eller utenfor sykehus) 2

Hva slags plager hadde du i tilfelle da sukkersyken ble oppdaget? (kryss evt. i flere ruter).

Ingen plager 111
Unormal tørste 112
Stor vannlating 113
Slapphet 114
Vekttap 115
Underlivskløe 116
Andre plager 117

Hvis «ANDRE PLAGER», skriv hvilke:

_____ 118 Ikke skriv her
_____ 120

Har noen av dine foreldre, søsken eller barn hatt sukkersyke? ..... 122 JA NEI
Hvis «JA», bruker eller brukte noen av disse insulinsprøyter? 123

BEHANDLING

Bruker du insulinsprøyter mot sukkersyken? ..... 124 JA NEI

Hvis «JA», bruker du sprøyter daglig?

Sprøyte en gang daglig 125 1
Sprøyte to eller flere ganger daglig 2

Om du bruker sprøyter, hvor mye insulin tar du tilsammen hver dag?
(Skriv antall ml i ruta – 1 «strek» svarer til 0,1 ml) ..... 126 , ml

Om du bruker sprøyter, hva heter den insulinen du bruker?
(Skriv navnet som står på glasset, begge dersom du bruker to sorter).

_____ 128 Ikke skriv her
_____ 130

Bruker du tabletter mot sukkersyken? ..... 132 JA NEI

Om du bruker tabletter mot sukkersyken, skriv nedenfor hva de heter, antall mg. som står på glasset/pakningen og hvor mange slike tabletter du tar hver dag:
(Skriv om begge sorter dersom du bruker mer enn en type tabletter mot sukkersyke)

_____ 133 , 138 139 Ikke skriv her
Skriv navn på tabletten her — mg. pr. tabl. — antall pr. dag

_____ 140 , 145 146 Ikke skriv her
Skriv navn på tabletten her — mg. pr. tabl. — antall pr. dag

Hvor mange måltider spiser du hver dag? ..... 147 Antall

Føler du at du vet nok om hva slags mat du kan spise? ..... 148 JA NEI

Hvis du skal svare på hva du virkelig spiser, og ikke hva legen din har sagt du bør spise, vil du da si at du: (Kryss av bare i den ruta som kommer nærmest det du virkelig gjør)

Spiser stort sett det samme som de som ikke har sukkersyke 149 1
Spiser hva jeg vil unntatt sukker og søtsaker 2
Bruker på øyemål bestemt mengde brød, potet, melk og frukt 3
Veier/måler bestemt mengde brød, potet, melk og evt. frukt en eller flere dager i uka 4

Kontrollerer du hjemme hvor mye sukker du har i urinen? (Kryss av også om noen hjelper deg eller gjør det for deg) ..... 150 JA NEI

Hva heter den metoden du i tilfelle bruker til å måle sukker i urinen?

_____ 151 Ikke skriv her
Skriv navnet som står på pakningen her

Kontrollerer du noen gang hjemme hvor mye sukker du har i blod (blodsukker)? 152 JA NEI
(Kryss av også om noen hjelper deg eller gjør det for deg)

Hva heter den metoden du i tilfelle bruker til å måle blodsukker?

_____ 153 Ikke skriv her
Skriv navnet på pakningen og navn på evt. apparat du måler med.

Hvis du selv kontrollerer sukker i urin eller blod, hvor ofte gjør du det?
(Kryss av også om noen hjelper deg eller gjør det for deg)

Hver dag 154 1
2-3 dager i uka 2
En dag i uka 3
En dag hver 14. dag 4
En dag i måneden 5
Sjeldnere enn en dag i måneden 6

VENDI

Hvis du selv kontrollerer sukker i urin eller blod: måler du flere ganger om dagen de dagene du gjør det? 155

JA | NEI

Dersom du tar urin- eller blodprøve selv, tar du resultatene med til legen ved kontroll?
(kryss av i den ruta som passer best)

- Aldri ..... 156 — 1
- Av og til ..... — 2
- Oftest ..... — 3
- Alltid ..... — 4

JA | NEI

Går du til regelmessig kontroll hos lege for sukkersyken din? 157

Hvis «JA», hvor lenge var det mellom de to siste gangene du var hos legen din til kontroll for sukkersyken?

Antall måneder (skriv i ruta) .... 158 mndr.

Hva slags lege går du til kontroll hos for sukkersyken?
(Sett kryss i bare *en* rute)

- Vanlig lege (distriktslege, almenpraktiserende lege, bedriftslege osv.) ..... 160 — 1
- Sykehuslege (poliklinikk på sykehus) ..... — 2
- Er innlagt i sykehjem eller annen institusjon og får kontroll der ..... — 3
- Andre ..... — 4

Hvis «andre», skriv hva slags lege på linja over 161

Ikke skriv her

ANNEN SYKDOM

JA | NEI

Bruker du regelmessig medisin for annet enn sukkersyken? 162

Dersom «JA», skriv hva disse medisinene heter
(Skriv det navnet som står på glasset eller pakningen. Ta med alle sortene du bruker regelmessig. Skriv x bak navnet om du brukte dette også *før* du fikk sukkersyke).

163 166 169 172 175 178 181

Ikke skriv her

JA | NEI

Tror du man er mer utsatt for å få enkelte andre sykdommer dersom man har dårlig kontrollert sukkersyke? 184

Hvis «JA», nevn navnet på 3 slike sykdommer:
(Du behøver ikke å ha hatt disse sykdommene selv).

185 187 189

Ikke skriv her

Har du selv hatt noen vedvarende (kroniske) plager etter at du fikk sukkersyke?
(Skriv hva slags sykdom/plager på linjene under).

191 193 195 197 199 201

Ikke skriv her

UNDERVISNING - STØTTE

JA | NEI

Er du medlem av Norges Landsforbund for Sukkersyke? 203

Har du noen gang deltatt på kurs eller møte om sukkersyke? 204

Får du grunnstønad gjennom trygdekontoret for sukkersyken? 205

Har du søkt om og fått særfradrag i skattelikninga fordi du har sukkersyke? 206

HVORDAN HAR DU DET?

Synes du det er vanskelig å ha sukkersyke?
(kryss av i den ruta som passer best).

- Ja, jeg føler det er som en plage hver dag ..... 207 — 1
- Ja, jeg tenker ofte på det ..... — 2
- Ja, av og til ..... — 3
- Nei, sjelden ..... — 4
- Nei, jeg tenker nesten aldri på det ..... — 5
- Føler meg akkurat som alle som ikke har sukkersyke .. — 6

Dersom du synes det er vanskelig å ha sukkersyke, hva synes du er verst?
(Skriv det du mener på linja nedenfor).

Skriv her

Ikke skriv her

Forteller du til andre at du har sukkersyke?
(kryss av i den ruta som passer best).

- Ja, alltid når jeg mener de bør vite det ..... 210 — 1
- Ja, men bare om de spør ..... — 2
- Nei, helst ikke ..... — 3
- Jeg er redd for at andre skal få greie på det ..... — 4

JA | NEI

Har du noen gang hatt for lavt blodsukker?
(«føling», «insulinsjokk») 211

Hvis «JA», hvor mange ganger har du hatt det den siste uka? (Skriv antall ganger i ruta)..... 212

Hvor mange ganger har du vært innlagt i sykehus de siste 5 årene? (Skriv antall ganger i ruta)..... 213

Dersom du har ligget i sykehus de siste 5 årene, hva har du ligget der for?
(Skriv på linjene nedenfor)

214 216 218

Ikke skriv her

HELSEUNDERSØKELSEN
I NORD-TRØNDELAG

Personlig innbydelse

Spørreskjemaet er en viktig del av Helseundersøkelsen. Her finner du spørsmål om tidligere sykdom og om andre forhold som har betydning for helsa. Vennligst fyll ut skjemaet på forhånd og ta det med til Helseundersøkelsen. Dersom enkelte spørsmål er uklare, lar du dem bare stå ubesvarte til du møter fram, og drøfter dem med personalet som gjennomfører undersøkelsen. Alle svar vil bli behandlet strengt fortrolig.

Flere steder i skjemaet ber vi deg oppgi din alder da eventuell sykdom inntrådte. Hvis du ikke husker nøyaktig hvor gammel du var, skriver du et tall som er nærmest det du antar er korrekt.

Når resultatene fra undersøkelsen foreligger, vil det være enkelte som trenger ny undersøkelse hos egen lege. Dette vil du få beskjed om i det brevet som vi sender deg om dine resultater. Samtidig sender vi melding om resultatene dine til legen din. Det er derfor om å gjøre at du i rubrikken helt til slutt i skjemaet oppgir navnet på den allmennpraktiserende lege, kommunelege eller det helsesenter som du ønsker skal ta hånd om eventuell etterundersøkelse, og som vi skal sende resultatene til.

Med vennlig hilsen

Helsetjenesten i Nord-Trøndelag • Statens helseundersøkelser • Statens Institutt for Folkehelse

DET HANDLER OM HELSA DI

Hvordan er helsa di nå?

Bare ett kryss

Dårlig	12	☐ 1
Ikke helt god		☐ 2
God		☐ 3
Svært god		☐ 4

LUFTVEGSPLAGER

	JA	NEI
Hoster du daglig i perioder av året?		
Hvis JA:		
Er hosten vanligvis ledsaget av oppspytt? 14		
Har du hatt hoste med oppspytt i minst 3 mnd. sammenhengende i hvert av de to siste åra?		
Har du hatt noe anfall med pipende eller tung pust de siste 12 måneder? 16		

	JA	NEI	Alder første gang
Har du eller har du hatt astma? 17			år

	JA	NEI
Har du brukt eller bruker du astmamedisiner? 20		

HJERTE-KARSYKDOMMER, DIABETES

Har du, eller har du hatt:	JA	NEI	Alder første gang
Hjerteinfarkt 21			år
Angina pectoris (hjertekrampe) 24			år
Hjerneslag/hjerneblødning 27			år
Diabetes (sukkersyke) 30			år

Hva ble resultatet siste gang du målte blodtrykket ditt?

Bare ett kryss

Begynne med/fortsette med blodtrykksmedisin	33	☐ 1
Komme til kontroll, men ikke ta blodtrykksmedisin		☐ 2
Ingen kontroll og ingen medisin nødvendig		☐ 3
Har aldri fått målt blodtrykket		☐ 4

Bruker du medisin mot høyt blodtrykk?

Bare ett kryss

Nå	34	☐ 1
Før, men ikke nå		☐ 2
Aldri brukt		☐ 3

	JA	NEI	VET IKKE
Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)?			

STOFFSKIFTE

Har du noen gang fått påvist:	JA	NEI	Alder første gang
for høyt stoffskifte 36			år
for lavt stoffskifte 39			år
struma 42			år
annen sykdom i skjoldbruskkjertelen			år
Bruker du eller har du brukt noen av disse medisinene:			
Thyroxin 48			år
Neo-Mercazole 51			år
Er du operert i skjoldbruskkjertelen			år
Har du fått radiojodbehandling 57			år

MUSKEL/SKJELETT-PLAGER

	JA	NEI
Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende? 60		

Hvis NEI, gå videre til neste side øverst.
Hvis JA, svar på følgende:

Hvor har du hatt disse plagene?	JA	NEI
Nakke 61		
Skuldre (aksler)		
Albuer		
Håndledd, hender		
Bryst/mage 65		
Øvre del av ryggen		
Korsryggen		
Hofter		
Knær		
Ankler, føtter 70		

Hvis du har hatt plager i flere områder i minst 3 mnd. det siste året, setter du ring rundt det ja-krysset hvor plagene har vart lengst

Hvor lenge har plagene vart sammenhengende?

Svar for det området hvor plagene har vart lengst

	Antall mnd.	Antall år
Hvis under 1 år, oppgi antall mnd. 71		
Hvis 1 år eller mer, oppgi antall år. 73		

Har plagene redusert din arbeidsevne det siste året?

Gjelder også hjemmearbeidende. Bare ett kryss

Nei/ubetydelig	I noen grad	I betydelig grad	Vet ikke
☐	☐	☐	☐

	JA	NEI	IKKE I ARBEID
Har du vært sykmeldt pga. disse plagene det siste året? 76			

	JA	NEI
Har plagene ført til redusert aktivitet i fritida?		

Har lege noen gang sagt at du har/har hatt noen av disse sykdommene:

	JA	NEI
Beinskjørhet (osteoporose) 78		
Fibromyalgi (fibrositt/kronisk smertesyndrom)		
Leddgikt (reumatoid artritt)		
Slitasjegikt (artrose)		
Bechterews sykdom 82		
Andre langvarige skjelett- eller muskelsykdommer		

Har du noen gang hatt:

	JA	NEI	Alder *siste* gang
Lårhalsbrudd 84			år
Brudd i håndledd/underarm 87			år
Nakkesleng (whiplash) 90			år
Skade som førte til sykehusinnleggelse			år

ANDRE PLAGER

I hvilken grad har du hatt disse plagene i de siste 12 månedene?

	Ikke plaget	Litt plaget	Mye plaget
Kvalme 96	☐	☐	☐
Brystbrann/sure oppstøt	☐	☐	☐
Diaré	☐	☐	☐
Treg mage	☐	☐	☐
Hjertebank	☐	☐	☐
Åndenød 101	☐	☐	☐

ANDRE SYKDOMMER

Har du eller har du noen gang hatt:

	JA	NEI	Alder første gang
Epilepsi 102			år
Psykiske plager hvor du har søkt hjelp			år
Kreftsykdom 108			år
Annen langvarig sykdom 111			

DAGLIGE FUNKSJONER

Har du noen langvarig sykdom, skade eller lidelse av fysisk eller psykisk art som nedsetter dine funksjoner i ditt daglige liv? ... 112

JA	NEI

Langvarig: minst ett år

Hvis JA:

Hvor mye vil du si at dine funksjoner er nedsatt?

	Litt nedsatt	Middels nedsatt	Mye nedsatt
Er bevegelseshemmet 113	☐	☐	☐
Har nedsatt syn	☐	☐	☐
Har nedsatt hørsel	☐	☐	☐
Hemmet pga. kroppslig sykdom.	☐	☐	☐
Hemmet pga. psykiske plager... 117	☐	☐	☐

MENN fortsetter øverst neste spalte

BESVARES BARE AV KVINNER

Hvor mange barn har du født?..... 118
Sett 0 hvis du ikke har født barn

Antall barn

Hvis du har født barn, besvar:

Hvor gammel var du da du fødte ditt første barn? 120

Hvor gammel var du da du fødte ditt siste barn? 122
Besvares ikke hvis du har født bare ett barn

Alder

år

Hvor gammel var du da du fikk menstruasjon? 124
Sett 0 hvis du ikke noen gang har hatt menstruasjon

år

Fortsett neste spalte øverst

RØYKING

Røykte noen av de voksne hjemme da du vokste opp? 126

JA	NEI

Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år? 127

JA	NEI

Hvor lenge er du vanlig vis daglig til stede i røykfylt rom? 128
Sett 0 hvis du ikke oppholder deg i røykfylt rom

Antall timer

Røyker du selv?

	JA	NEI
Sigaretter daglig? 130		
Sigarer/sigarillos daglig?		
Pipe daglig? 132		

Aldri røykt daglig ..... *(Sett kryss)* ☐

Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet? 134

Antall år

Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? 136

Antall sigaretter

Hvor gammel var du da du begynte å røyke daglig? 140

Alder år

Hvor mange år tilsammen har du røykt daglig? 142

Antall år

KAFFE/TE/ALKOHOL

Hvor mange kopper kaffe/te drikker du daglig?
Sett 0 hvis du ikke drikker kaffe/te daglig

	Antall kopper
Kokekaffe 144	
Annen kaffe 146	
Te 148	

Alkohol:
Er du total avholdsmann/-kvinne? 150

JA	NEI

Hvor mange ganger i måneden drikker du vanligvis alkohol? 151
Regn ikke med lettøl. Sett 0 hvis mindre enn 1 gang i mnd.

Antall ganger

Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av to uker?

Regn ikke med lettøl.
Sett 0 hvis du ikke drikker alkohol 153

Øl	Vin	Brennevin
glass	glass	glass

FYSISK AKTIVITET

I FRITIDA

Hvordan har din fysiske aktivitet i fritida vært det siste året? *Tenk deg et ukentlig gjennomsnitt for året.*

Arbeidsveg regnes som fritid

	Timer pr. uke: Ingen	Under 1	1-2	3 og mer
Lett aktivitet *(ikke svett/andpusten)* 159	☐	☐	☐	☐
Hard fysisk aktivitet *(svett/andpusten)* 160	☐ 1	☐ 2	☐ 3	☐ 4

UNDER ARBEID

Hvis du er i lønnet eller ulønnet arbeid:

Hvorledes vil du beskrive arbeidet ditt?
Bare ett kryss

For det meste stillesittende arbeid
(f.eks. skrivebordsarbeid, montering) ..... 161 ☐ 1

Arbeid som krever at du går mye
(f.eks. ekspeditørarb., lett industriarb., undervisning) ..... ☐ 2

Arbeid hvor du går og løfter mye
(f.eks. postbud, pleier, bygningsarbeid) ..... ☐ 3

Tungt kroppsarbeid
(f.eks. skogsarbeid, tungt jordbruksarb.,tungt bygningsarb.) ☐ 4

Bla om!

HVORLEDES FØLER DU DEG?

Har du de siste to ukene følt deg:

	Nei	Litt	En god del	Svært mye
Trygg og rolig? 162	☐	☐	☐	☐
Glad og optimistisk?	☐	☐	☐	☐
Har du følt deg:				
Nervøs og urolig?	☐	☐	☐	☐
Plaget av angst? 165	☐	☐	☐	☐
Irritabel?	☐	☐	☐	☐
Nedfor/deprimert?	☐	☐	☐	☐
Ensom? 168	☐	☐	☐	☐
	1	2	3	4

Her kommer noen flere spørsmål om hvorledes du føler deg. For hvert spørsmål setter du kryss for ett av de fire svarene som best beskriver dine følelser ***den siste uka.*** *Ikke tenk for lenge på svaret - de spontane svarene er best*

Jeg gleder meg fortsatt over ting slik jeg pleide før 169
Avgjort like mye ..... ☐ 1 Bare lite grann ..... ☐ 3
Ikke fullt så mye ..... ☐ 2 Ikke i det hele tatt ..... ☐ 4

Jeg har en urofølelse som om noe forferdelig vil skje 170
Ja, og noe svært ille .... ☐ 1 Litt, bekymrer meg lite . ☐ 3
Ja, ikke så veldig ille ... ☐ 2 Ikke i det hele tatt ..... ☐ 4

Jeg kan le og se det morsomme i situasjoner 171
Like mye nå som før .... ☐ 1 Avgjort ikke som før .... ☐ 3
Ikke like mye nå som før ☐ 2 Ikke i det hele tatt ..... ☐ 4

Jeg har hodet fullt av bekymringer 172
Veldig ofte ..... ☐ 1 Av og til ..... ☐ 3
Ganske ofte ..... ☐ 2 En gang i blant ..... ☐ 4

Jeg er i godt humør 173
Aldri ..... ☐ 1 Ganske ofte ..... ☐ 3
Noen ganger ..... ☐ 2 For det meste ..... ☐ 4

Jeg kan sitte i fred og ro og kjenne meg avslappet 174
Ja, helt klart ..... ☐ 1 Ikke så ofte ..... ☐ 3
Vanligvis ..... ☐ 2 Ikke i det hele tatt ..... ☐ 4

Jeg føler meg som om alt går langsommere 175
Nesten hele tiden ..... ☐ 1 Fra tid til annen ..... ☐ 3
Svært ofte ..... ☐ 2 Ikke i det hele tatt ..... ☐ 4

Jeg føler meg urolig som om jeg har sommerfugler i magen 176
Ikke i det hele tatt ..... ☐ 1 Ganske ofte ..... ☐ 3
Fra tid til annen ..... ☐ 2 Svært ofte ..... ☐ 4

Jeg bryr meg ikke lenger om hvordan jeg ser ut 177
Ja, har sluttet å bry meg ☐ 1 Kan hende ikke nok .... ☐ 3
Ikke som jeg burde ..... ☐ 2 Bryr meg som før ..... ☐ 4

Jeg er rastløs som om jeg stadig må være aktiv 178
Uten tvil svært mye ..... ☐ 1 Ikke så veldig mye ..... ☐ 3
Ganske mye..... ☐ 2 Ikke i det hele tatt ..... ☐ 4

Jeg ser med glede frem til hendelser og ting 179
Like mye som før ..... ☐ 1 Avgjort mindre enn før . ☐ 3
Heller mindre enn før ... ☐ 2 Nesten ikke i det hele tatt ☐ 4

Jeg kan plutselig få en følelse av panikk 180
Uten tvil svært ofte ..... ☐ 1 Ikke så veldig ofte ..... ☐ 3
Ganske ofte ..... ☐ 2 Ikke i det hele tatt ..... ☐ 4

Jeg kan glede meg over gode bøker, radio og TV 181
Ofte ..... ☐ 1 Ikke så ofte ..... ☐ 3
Fra tid til annen ..... ☐ 2 Svært sjelden ..... ☐ 4

UTDANNING

Hvilken utdanning er den høyeste du har fullført?

Grunnskole 7-10 år, framhaldsskole, folkehøgskole ..... 182 ☐ 1
Realskole, middelskole, yrkesskole, 1-2 årig videregående skole..... ☐ 2
Artium, øk.gymnas, allmennfaglig retning i videregående skole ..... ☐ 3
Høgskole/universitet, mindre enn 4 år ..... ☐ 4
Høgskole/universitet, 4 år eller mer ..... ☐ 5

ARBEID

Hva slags arbeidssituasjon har du nå?
Ett eller flere kryss

Lønnet arbeid ..... 183 ☐
Selvstendig næringsdrivende..... ☐
Heltids husarbeid ..... ☐
Utdanning, militærtjeneste ..... ☐
Arbeidsledig, permittert..... ☐
Pensjonist/trygdet..... 188 ☐

Hvor mange timer lønnet arbeid har du i uka? ..... 189 Antall timer

Har du skiftarbeid, nattarbeid eller går vakt? JA ☐ NEI ☐

ALT I ALT

Når du tenker på hvordan du har det for tida, er du stort sett fornøyd med tilværelsen eller er du stort sett misfornøyd?
Bare ett kryss

Svært fornøyd ..... 192 ☐ 1
Meget fornøyd ..... ☐ 2
Ganske fornøyd..... ☐ 3
Både/og..... ☐ 4
Nokså misfornøyd ..... ☐ 5
Meget misfornøyd..... ☐ 6
Svært misfornøyd..... ☐ 7

DIN LEGE

Hvis denne helseundersøkelsen viser at du bør undersøkes nærmere, hvilken allmennpraktiserende lege/kommunelege ønsker du skal foreta undersøkelsen?

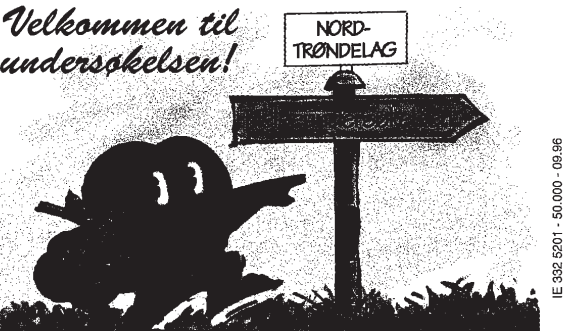
Skriv navnet på legen her: 193

Ikke skriv her

Takk for utfyllingen!

Nok en gang:

Velkommen til undersøkelsen!



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Helseundersøkelsen i Nord-Trøndelag

SKJEMA FOR KVINNER 20–69 ÅR

Takk for frammøtet til undersøkelsen!

Vi vil også be deg fylle ut dette spørreskjemaet. Opplysningene vil bli brukt i større forskningsarbeider om forebyggende helsearbeid. Noen av spørsmålene likner på spørsmål du har svart på i det skjemaet du fylte ut heime og leverte ved frammøte til helseundersøkelsen. Det er likevel viktig at du svarer på alle spørsmålene også i dette skjemaet. Det utfylte skjemaet returneres i vedlagte svarkonvolutt. Porto er betalt.

Alle opplysningene er underlagt streng taushetsplikt.

Vennlig hilsen

Helsetjenesten i Nord-Trøndelag

Statens Institutt for Folkehelse Statens helseundersøkelser

Hvis du ikke ønsker å besvare spørreskjemaet, sett kryss her og returner skjemaet. Da slipper du purring.

Jeg ønsker ikke å besvare skjemaet ○

UTFYLLING

Dato for utfylling av skjema: / 19 19

OPPVEKST

I hvilken kommune bodde du da du fylte 1 år?

*Hvis du ikke bodde i Norge, oppgi **land** i stedet for kommune.*

24

ARBEID

Nåværende eller tidligere arbeid:

Hva slags inntektsgivende arbeid har du og event. din ektefelle/samboer? *Hvis du/dere ikke har inntektsgivende arbeid nå: Oppgi det siste yrket.*

		Deg selv	Ektefelle/ samboer	
Spesialarbeider eller ufaglært arbeider	25	☐	☐	36
Fagarbeider, handverker, formann		☐	☐	
Underordnet funksjonær (f.eks. butikk, kontor, off. tjenester)		☐	☐	
Fagfunksjonær (f.eks. sykepleier, tekniker, lærer)		☐	☐	
Overordnet stilling i off. eller privat virksomhet		☐	☐	
Sjåfør	30	☐	☐	41
Gårdbruker eller skogeier		☐	☐	
Fisker		☐	☐	
Selvstendig i akademisk erverv (f.eks. tannlege, advokat)		☐	☐	
Annen selvstendig næringsvirksomhet		☐	☐	
Har ikke vært i inntektsgivende arbeid	35	☐	☐	46

Hvis du NÅ ikke har inntektsgivende arbeid eller du ikke har heltids husarbeid: Gå til BOLIG.

Har du i løpet av de siste 12 månedene hatt sykefravær:

		Ja	Nei
med egenmelding	47	☐	☐
med sykmelding fra lege	48	☐	☐

Hvis «Ja»: **Hvor lenge *tilsammen*?** *Bare ett kryss*

2 uker eller mindre	49	☐ 1
2-8 uker		☐ 2
Mer enn 8 uker		☐ 3

Har du i løpet av de siste 12 månedene vurdert å skifte yrke eller arbeidsplass? 50 Ja ☐ Nei ☐

Er arbeidet ditt så fysisk anstrengende at du ofte er sliten i kroppen etter en arbeidsdag? *Bare ett kryss* 51

Ja, nesten alltid ☐ 1 Ganske sjelden ☐ 3
Ganske ofte ☐ 2 Aldri, eller nesten aldri ☐ 4

Krever arbeidet ditt så mye konsentrasjon og oppmerksomhet at du ofte føler deg utslitt etter en arbeidsdag? 52

Ja, nesten alltid ☐ 1 Ganske sjelden ☐ 3
Ganske ofte ☐ 2 Aldri, eller nesten aldri ☐ 4

Hvordan trives du alt i alt med arbeidet ditt? 53

Veldig godt ☐ 1 Ikke særlig godt ☐ 3
Godt ☐ 2 Dårlig ☐ 4

BOLIG

Hvem bor du sammen med?

Ett kryss for hver linje og angi antall

		Ja	Nei	
Ektefelle/samboer	54	☐	☐	Antall
Andre personer over 18 år	55	☐	☐	
Personer under 18 år	58	☐	☐	Antall

Hvor mange av barna har plass i barnehage? 61

Hvilken type bolig bor du i? *Bare ett kryss*

Enebolig/villa	63	☐ 1
Gårdsbruk		☐ 2
Blokk/terrasseleilighet		☐ 3
Rekkehus/2-4 mannsbolig		☐ 4
Annen bolig		☐ 5

Hvor stor er din boenhet? 64 kvm

		Ja	Nei
Er det heldekkende tepper i stua?	67	☐	☐
Er det heldekkende tepper på ditt soverom?		☐	☐
Er det katt i boligen?	69	☐	☐
Er det hund i boligen?		☐	☐
Er det andre pelskledde dyr eller fugler i boligen?		☐	☐

ØKONOMI

Mottar du noen av følgende *offentlige* ytelser?

		Ja	Nei
Sykepenger/sykelønn/rehabiliteringspenger	72	☐	☐
Ytelser under yrkesrettet attføring		☐	☐
Uførepensjon	74	☐	☐
Alderspensjon		☐	☐
Sosialstøtte		☐	☐
Arbeidsløshetstrygd		☐	☐
Overgangsstønad		☐	☐
Etterlattepensjon	79	☐	☐
Andre ytelser		☐	☐

Har det i løpet av det siste året hendt at husholdningen har hatt vansker med å klare de løpende utgifter til mat, transport, bolig og liknende? *Bare ett kryss* 81

Ja, ofte ☐ 1 Ja, en sjelden gang ☐ 3
Ja, av og til ☐ 2 Nei, aldri ☐ 4

VENNER

Hvor mange gode venner har du?

Regn med de du kan snakke fortrolig med og som kan gi deg god hjelp når du trenger det 82

Antall

Tell ikke med de du bor sammen med, men regn med andre slektninger

		Ja	Nei
Føler du at du har mange nok gode venner?	84	☐	☐

Hvor ofte tar du vanligvis del i foreningsvirksomhet som f.eks. syklubb, idrettslag, politiske lag, religiøse eller andre foreninger? 85

Aldri, eller noen få ganger i året ☐ 1 Omtrent en gang i uka ☐ 1
1-2 ganger i måneden ☐ 2 Mer enn en gang i uka ☐ 2

DER DU BOR

Svar ut fra nærmiljøet, dvs. nabolaget/grenda:
Ett kryss for hvert spørsmål

Jeg føler et sterkt fellesskap med de som bor her 86
Helt enig ☐ 1 Delvis enig ☐ 2 Usikker ☐ 3 Delvis uenig ☐ 4 Helt uenig ☐ 5

Selv om noen tar initiativ, er det ingen som blir med på det som settes i gang her 87
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Hvis jeg flytter herfra, vil jeg lengte tilbake 88
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Man kan ikke stole på hverandre her 89
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Når noe skal gjøres her, er det lett å få folk med 90
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Det er vanskelig å få kontakt med folk her 91
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Det er godt samhold her 92
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Ingen orker å ta initiativ til noe lenger her 93
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Folk trives godt her 94
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Folk her kan ha store problemer uten at naboen vet noe 95
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Det er alltid noen som tar initiativ til å løse nødvendige oppgaver her 96
Helt enig ☐ Delvis enig ☐ Usikker ☐ Delvis uenig ☐ Helt uenig ☐

Folk snakker lite med hverandre her 97
Helt enig ☐ 1 Delvis enig ☐ 2 Usikker ☐ 3 Delvis uenig ☐ 4 Helt uenig ☐ 5

SYKDOM I FAMILIEN

Kryss av for de slektningene som har eller har hatt noen av sykdommene. Kryss av for "ingen" hvis ingen av slektningene har hatt denne sykdommen: *Evt. flere kryss på hver linje*

	Mor	Far	Bror	Søster	Barn	Ingen
Hjerneslag eller hjerneblødning 98	☐	☐	☐	☐	☐	☐
Hjerteinfarkt før 60 års alder 104	☐	☐	☐	☐	☐	☐
Astma 110	☐	☐	☐	☐	☐	☐
Allergi 116	☐	☐	☐	☐	☐	☐
Kreftsykdom 122	☐	☐	☐	☐	☐	☐
Høyt blodtrykk 128	☐	☐	☐	☐	☐	☐
Psykiske plager 134	☐	☐	☐	☐	☐	☐
Osteoporose (benskjørhet) 140	☐	☐	☐	☐	☐	☐
Diabetes (sukkersyke) 146	☐	☐	☐	☐	☐	☐
Alder da de fikk diabetes 152	år	år	år	år	år	

Har du *selv* høysnue eller neseallergi? ..... 162 Ja ☐ Nei ☐

BRUK AV HELSETJENESTER

Har du i løpet av de siste 12 månedene vært hos:
Ett kryss på hver linje

	Ja	Nei
allmennpraktiserende lege (kommunelege, privatpraktiserende lege, turnuskandidat) 163	☐	☐
bedriftslege	☐	☐
lege ved sykehus (uten at du var innlagt)	☐	☐
annen lege	☐	☐
fysioterapeut	☐	☐
kiropraktor	☐	☐
homøopat 169	☐	☐
annen behandler (naturmedisiner, fotsoneterapeut, håndspålegger, "healer", "synsk", e.l.)	☐	☐

Har du vært innlagt i sykehus de siste 5 åra? ..... 171 Ja ☐ Nei ☐

ALKOHOL

Hvis du er totalavholdskvinne: Gå til KOSTHOLD.

Ett kryss for hver spørsmål

Har du noen gang følt at du burde redusere alkoholforbruket ditt? ..... 172 Ja ☐ Nei ☐

Har andre noen gang kritisert alkoholbruken din? ..... 173 Ja ☐ Nei ☐

Har du noen gang følt ubehag eller skyldfølelse pga. alkoholbruken din? ..... 174 Ja ☐ Nei ☐

Har det å ta en drink noen gang vært det første du har gjort om morgenen for å roe nervene, kurere bakrus eller som en oppkvikker? ..... 175 Ja ☐ Nei ☐

KOSTHOLD

Hvor mange måltider spiser du vanligvis daglig (middag og brødmåltid)? ..... 176 Antall

Hvor mange dager i uka spiser du varm middag?

Hva slags type brød (kjøpt eller hjemmebakt) spiser du vanligvis? *Inntil to kryss*

Brødtypen ligner mest på 178	Loff	Fint brød	Kneipp-brød	Grov-brød	Knekke-brød
	☐	☐	☐	☐	☐

Hva slags *fett* blir vanligvis brukt i din husholdning?
Ett kryss for matlaging og ett kryss for brød

	Til matlaging 183	På brød 184
Bruker *ikke* smør eller margarin	☐ 1	☐ 1
Meierismør	☐ 2	☐ 2
Hard margarin	☐ 3	☐ 3
Bløt (soft) margarin	☐ 4	☐ 4
Smør/margarin blanding	☐ 5	☐ 5
Lettmargarin	☐ 6	☐ 6
Oljer	☐ 7	

MEDISINBRUK

Har du i deler av de siste 12 måneder brukt noen medisiner daglig eller nesten daglig? ..... 185 Ja ☐ Nei ☐

Hvis «Ja»:
Angi hvor mange måneder du brukte følgende medisiner: *Sett 0 hvis du ikke har brukt medisinene*

	Antall mndr.		Antall mndr.
smertestillende 186		hjertemedisin (ikke blodtrykksmedisin)	
sovemedisin 188		annen medisin	
beroligende medisin		*Kosttilskudd:*	
medisin mot depresjon		jerntabletter 202	
allergimedisin 194		vitamintilskudd	
astmamedisin 196		tran/fiskeoljer 206	

Hvor ofte har du brukt avslappende/beroligende medisin eller sovemedisin den siste måneden? 208

Daglig ..... ☐ 1 Sjeldnere enn hver uke ☐ 3
Hver uke, men ikke hver dag . ☐ 2 Aldri ..... ☐ 4

HODEPINE

Har du vært plaget av hodepine i løpet av de siste 12 måneder? 209
Ja, anfallsvis (migrene)..... ☐ 1
Ja, annen slags hodepine.... ☐ 2
Nei ..... ☐ 3

Antall anfall siste 12 mndr. 210 ☐☐☐

Hvis «Nei»: Gå til MUSKEL-/SKJELETTPLAGER

Omtrent hvor mange dager i pr. måned har du hodepine?
Mindre enn 7 dager ☐ 1 7 til 14 dager ☐ 2 Mer enn 14 d. ☐ 3

Hvor lenge varer hodepinen vanligvis hver gang? 213
Mindre enn 4 timer ☐ 1 4 timer–3 døgn ☐ 2 Mer enn 3 døgn ☐ 3

Hvor ofte er hodepinen preget av eller ledsaget av:

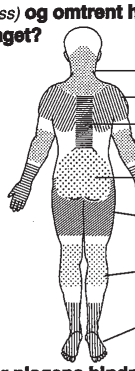
Ett kryss på hver linje	*Sjelden eller aldri*	*Av og til*	*Ofte*
bankende/dunkende smerte 214	☐	☐	☐
pressende smerte	☐	☐	☐
halvsidighet, alltid samme side	☐	☐	☐
halvsidighet, vekselvis h. og v. side	☐	☐	☐
smerter i «hele hodet»	☐	☐	☐
kvalme 219	☐	☐	☐
lys- og/eller lydskyhet	☐	☐	☐
forverring ved fysisk aktivitet.....	☐	☐	☐
synsforstyrrelser *før* hodepine 222	☐	☐	☐

Hvor mange tabletter/stikkpiller har du eventuelt brukt av disse medisinene *alt i alt i løpet av den siste måneden*?
Skriv 0 hvis du ikke har brukt medisinen.
Cafergot 223 ☐☐ Anervan 225 ☐☐ Imigran 227 ☐☐

MUSKEL-/SKJELETTPLAGER

Har du hatt plager (smerter, verk, ubehag) i muskler og/eller ledd i *den siste måneden*? 229 Ja ☐ Nei ☐

Hvis «Ja»: **Hvor har du hatt disse plagene** *(ett eller flere kryss)* **og omtrent hvor mange dager tilsammen var du plaget?**



Plager (Sett kryss)	Antall dager
Nakke 230	☐☐
Skuldre/aksler.....233	☐☐
Øvre del av ryggen	☐☐
Albuer 239	☐☐
Korsryggen 242	☐☐
Handledd/hender 245	☐☐
Hofter.....248	☐☐
Knær.....251	☐☐
Ankler/føtter 254	☐☐

*Dersom flere kryss: Sett **ring** rundt krysset **der plagen var verst***

Har plagene hindret deg i å utføre daglige aktiviteter den siste måneden?

	Ja	Nei
I arbeidet.....257	☐	☐
I fritida 258	☐	☐

SMERTER I BEINA

	Ja	Nei
Har du sår på tå, fot eller ankel som ikke vil gro? 259	☐	☐
Har du smerter i det ene eller i begge beina når du går? 260	☐	☐
Har du oppsøkt lege p.g.a. smerter i beina? 261	☐	☐

Hvis «NEI» på disse spørsmålene: Gå til MENSTRUASJON

	Ja	Nei
Kan du gå lenger enn 50 meter? 262	☐	☐
Forsvinner smerten når du står stille en stund? 263	☐	☐
Må du sette deg for at smerten skal gå over? 264	☐	☐

Hvor gjør det mest vondt? *Ett kryss* 265
Fot ☐ Legg ☐ Lår ☐ Hofte ☐

	Ja	Nei
Har du smerter i beina når du er i ro? 266	☐	☐
Er smertene verst når du ligger i senga? 267	☐	☐
Blir søvnen forstyrret av smertene? 268	☐	☐
Får du mindre vondt når beinet ligger høyt? 269	☐	☐
Får du mindre vondt når beinet ligger lavt, f.eks. om beinet henger utfor sengekanten? 270	☐	☐
Bedres smertene når du står opp og går litt? 271	☐	☐

MENSTRUASJON

Har du menstruasjon fremdeles?..... 272 Ja ☐ Nei ☐

Hvis «Nei»: **Hvor gammel var du da den sluttet?** 273 ☐☐ år

Er du gravid nå? ..... 275 Ja ☐ Nei ☐ Vet ikke ☐

Har du innsatt spiral nå? ..... 276 Ja ☐ Nei ☐

Når hadde du siste menstruasjon? ..... 277 Dag ☐☐ Måned ☐☐ År ☐☐☐☐
Husker du ikke dag, bare angi måned og år, husker du bare år, angi år.

Menstruasjonen din de siste 12 måneder:

Har du det siste året hatt regelmessige menstruasjoner?
At menstruasjonen har vart omtrent like lenge hver gang med omtrent like lange mellomrom ..... 283 Ja ☐ Nei ☐ Usikker ☐

Hvor mange dager hadde du blødning siste gang du hadde menstruasjon? ..... 284 Antall dager ☐☐

Hvor mange dager var du uten blødning mellom nest siste og siste menstruasjon? ... 286 Antall dager ☐☐

Har menstruasjonen din det siste året uteblitt i mer enn 3 måneder uten at du var gravid? 289 Ja ☐ Nei ☐

Hvis «Ja»: **Hvor mange måneder i trekk har du vært uten menstruasjonsblødninger?** ..... 290 Antall mndr. ☐☐

Hvis «Ja»: **Oppsøkte du lege?** ..... 292 Ja ☐ Nei ☐

Menstruasjonen tidligere (dvs. før de siste 12 månedene):

Har menstruasjonen din tidligere uteblitt uten at du var gravid? ..... 293 Ja ☐ Nei ☐

Hvis «Ja»: **Hvor lenge og hvor ofte var den borte sammenhengende?** *Sett kryss eventuelt flere steder*

	1 gang	*2 ganger*	*Oftere*
3–6 måneder..... 294	☐	☐	☐
6–12 måneder.....	☐	☐	☐
Over ett år..... 296	☐	☐	☐

OPERASJONER I UNDERLIVET

	Ja	Nei	Vet ikke
Har du noen gang blitt operert i underlivet? 297	☐	☐	☐

Hvis «Ja»: **Kryss av for hver operasjon:**

	Ja	Nei	Vet ikke
Fjernet deler av eller bare én eggstokk 298	☐	☐	☐
Fjernet begge eggstokkene (totalt) 299	☐	☐	☐

Hvis du har fjernet begge eggstokkene, hvor gammel var du da? 300 ___ år

	Ja	Nei	Vet ikke
Operert for endometriose 302	☐	☐	☐
Sterilisert	☐	☐	☐
Utskraping fra livmor (sykehus)	☐	☐	☐
Fjernet hele livmoren 305	☐	☐	☐

Hvis du har fjernet hele livmoren, hvor gammel var du da? 306 ___ år

P-PILLER

	Ja	Nei
Har du noen gang brukt p-piller, minipiller inkludert? 308	☐	☐

Hvis «Ja»: **Hvor gammel var du første gang du brukte p-piller?** 309 ___ år

Hvor lenge har du brukt p-piller i alt? 311 ___ år

Hvis under ett år, antall måneder 313 ___ mndr.

	Ja	Nei
Bruker du p-piller nå?	☐	☐

Hvilket merke bruker du? 316 ___

HORMONBEHANDLING

Utenom p-piller

Har du noen gang brukt medisiner som inneholder østrogen? Vanlige navn på slike medisiner er: Cyclabil, Estraderm, Kilogest, Ovesterin, Progynova, Trisekvens.

	Nå	Før	Aldri
Tabletter eller plaster 318	☐	☐	☐
Krem eller stikkpiller 319	☐	☐	☐

Hvis «Ja»: **Hvor gammel var du første gang du fikk østrogenmedisin, og omtrent hvor mange år brukte du slik medisin?**

	Din alder	Antall år
Tabletter eller plaster 320		
Krem eller stikkpiller 324		

Hvis du bruker østrogenmedisin nå, hvilket merke bruker du? 328 ___

PROBLEMER MED Å BLI GRAVID

	Ja	Nei
Har du noen gang prøvd i mer enn ett år å bli gravid? 329	☐	☐

Hvis «Ja»: **Hvor gammel var du første gang du hadde problemer med å bli gravid?** 330 ___ år

	Ja	Nei
Har du noen gang oppsøkt lege fordi du hadde problemer med å bli gravid? 332	☐	☐

GRAVIDITETER, FØDSLER OG AMMING

Hvor mange ganger har du vært gravid totalt?
*Regn med **alle** svangerskap, spontane eller selvbestemte aborter, så vel som fødsler (også dødfødsler)* 333 ___ ganger

Hvor mange barn har du født? 335 ___ barn

Fyll ut for hvert barn (de første 7) opplysninger om fødselsår og omtrent antall måneder du ammet hvert barn og antall måneder menstruasjonen din var borte etter fødselen (fylles ut også for dødfødte eller for barn som er døde senere i livet).

Barn	Fødselsår	Antall måneder med amming	Antall blødningsfrie måneder
1	336 19		
2	342 19		
3	348 19		
4	354 19		
5	360 19		
6	366 19		
7	372 19		

URINLEKKASJE

	Ja	Nei
Har du ufrivillig urinlekkasje? 378	☐	☐

Hvis «Nei»: Gå til KALK I KOSTEN ...

Hvor ofte har du urinlekkasje? 379
- sjeldnere enn en gang pr. måned ☐
- en eller flere ganger pr. måned ☐
- en eller flere ganger pr. uke ☐
- hver dag og/eller natt ☐

Hvor mye urin lekker du vanligvis hver gang? 380
dråper eller lite ☐ små skvetter ☐ større mengder ☐

	Ja	Nei
Har du lekkasje av urin i forbindelse med hosting, nysing, latter, tunge løft 381	☐	☐
Har du lekkasje av urin i forbindelse med plutselig og sterk vannlatingstrang? 382	☐	☐

Hvor lenge har du hatt urinlekkasje? 383
0-5 år ☐ 5-10 år ☐ Over 10 år ☐

	Ja	Nei
Har du søkt lege på grunn av urinlekkasje? 384	☐	☐

Hvordan opplever du lekkasjeplagene dine? 385 *Ett kryss*
- ikke noe problem ☐
- en liten plage ☐
- en del plaget ☐
- mye plaget ☐
- svært stort problem ☐

KALK I KOSTEN OG KOSTTILSKUDD

Hvor mange glass melk (alle sorter, også drikkeyoghurt) drikker du vanligvis daglig? *Bare ett kryss* 386
- Ingen ☐ 1
- Mindre enn ett ... ☐ 2
- 1–2 glass ... ☐ 3
- 3 eller mer ... ☐ 4

Hvor mange brødskiver med kvitost spiser du vanligvis daglig? *Bare ett kryss*
- Ingen ☐ 1
- Mindre enn en ... ☐ 2
- 1–2 skiver ... ☐ 3
- 3 eller mer ... ☐ 4

Bruker du vanligvis noen av disse kosttilskuddene?

	Ja	Nei
vitamin D-tilskudd 388	☐	☐
kalktabletter eller benmel	☐	☐

HUMØR OG TRIVSEL

Ett kryss på hver linje

Angi hvordan du har følt deg den siste måneden:

	Aldri	*Noen ganger*	*Ganske ofte*	*For det meste*
i godt humør 390	☐	☐	☐	☐
i dårlig humør 391	☐	☐	☐	☐

Er du rask til å oppfatte et humoristisk poeng? 392

Svært treg	*Ganske treg*	*Ganske rask*	*Svært rask*
☐	☐	☐	☐

Er du enig i at det er noe ansvarsløst over folk som stadig prøver å være morsomme? 393

Nei, slett ikke ..... ☐1 Ganske enig ..... ☐3
I noen grad ..... ☐2 Ja, absolutt ..... ☐4

Er du en munter person? 394

Nei, slett ikke ..... ☐1 Ganske munter ..... ☐3
I noen grad ..... ☐2 Ja, absolutt ..... ☐4

SINNE

Sett kryss på det svaret som best beskriver deg i forhold til de to påstandene nedenfor:

Jeg gir uttrykk for mitt sinne, og andre mennesker vet at jeg er sint 395

Nesten aldri ..... ☐1 Ganske ofte ..... ☐3
Noen ganger ..... ☐2 Nesten alltid ..... ☐4

Jeg koker av sinne, men jeg viser det ikke til andre 396

Nesten aldri ..... ☐1 Ganske ofte ..... ☐3
Noen ganger ..... ☐2 Nesten alltid ..... ☐4

HVILE OG AVSLAPPING

Hvor mange timer tilbringer du *vanligvis* i *liggende* stilling i løpet av et døgn?
(nattesøvn, middagshvil) .....397 Antall timer ☐☐

Hvor mange timer tilbringer du *vanligvis* i *sittende* stilling i løpet av et døgn?
(arbeid, måltider, TV, bil etc.) .....399 Antall timer ☐☐

Hvor ofte er du plaget av søvnløshet? 401

Aldri, eller noen få ganger i året ..... ☐1
1–2 ganger i måneden ..... ☐2
Omtrent 1 gang i uka ..... ☐3
Mer enn en gang i uka ..... ☐4

Har du siste år vært plaget av søvnløshet slik at det har gått ut over arbeidsevnen? .....402 *Ja* ☐ *Nei* ☐

Har du i løpet av siste måned hatt innsovningsproblemer? *Bare ett kryss* 403

Nesten hver natt ..... ☐1 Av og til ..... ☐3
Ofte ..... ☐2 Aldri ..... ☐4

Har du i løpet av siste måned våknet for tidlig og ikke fått sove igjen? *Bare ett kryss* 404

Nesten hver natt ..... ☐1 Av og til ..... ☐3
Ofte ..... ☐2 Aldri ..... ☐4

Har du i løpet av siste måned vært plaget av nervøsitet (irritabel, urolig, anspent eller rastløs)? 405

Nesten hele tida ..... ☐1
Ofte ..... ☐2
Av og til ..... ☐3
Aldri ..... ☐4

HVORDAN DU HAR HATT DET

Har det noen gang i løpet av ditt liv vært *sammenhengende perioder på 2 uker eller mer* da du:

	Ja	*Nei*
følte deg deprimert, trist og nedfor 406	☐	☐
hadde problemer med matlysten eller spiste alt for lite	☐	☐
var plaget av kraftløshet eller mangel på overskudd	☐	☐
virkelig bebreidet deg selv og følte deg verdiløs ...	☐	☐
hadde problemer med å konsentrere deg eller vanskelig for å ta beslutninger	☐	☐
hadde minst tre av de problemene som er nevnt ovenfor samtidig 411	☐	☐

HVORDAN DU SER PÅ DEG SELV

Folk ser på seg selv på ulike måter. Kryss av for hvert utsagn hvor enig eller uenig du er. *Ett kryss på hver linje*

	Svært enig	*Enig*	*Uenig*	*Svært uenig*
Jeg har en positiv holdning til meg selv 412	☐	☐	☐	☐
Jeg føler meg virkelig ubrukelig til tider 413	☐	☐	☐	☐
Jeg føler at jeg ikke har mye å være stolt av 414	☐	☐	☐	☐
Jeg føler at jeg er en verdifull person, i allefall på lik linje med andre 415	☐	☐	☐	☐

	Ja	*Nei*
Synes du at du har funnet et virkelig betydningsfullt innhold i livet ditt? 416	☐	☐
Føler du at du lever fullt ut? 417	☐	☐

HVORDAN DU FØLER DEG NÅ

*Sett kryss i den ruta utenfor det svaret som best beskriver dine følelser **den siste uka.** Bare ett kryss*

Er du vanligvis glad eller nedstemt? 418

Svært nedstemt ..... ☐1
Nedstemt ..... ☐2
Nokså nedstemt ..... ☐3
Både – og ..... ☐4
Nokså glad ..... ☐5
Glad ..... ☐6
Svært glad ..... ☐7

Har du i det store og hele en rolig og god følelse inne i deg? 419

Nesten hele tida ..... ☐1
Ofte ..... ☐2
Av og til ..... ☐3
Aldri ..... ☐4

Føler du deg stort sett sterk og opplagt, eller trøtt og sliten? 420

Meget sterk og opplagt ..... ☐1
Sterk og opplagt ..... ☐2
Ganske sterk og opplagt ..... ☐3
Både – og ..... ☐4
Ganske trøtt og sliten ..... ☐5
Trøtt og sliten ..... ☐6
Svært trøtt og sliten ..... ☐7

Legg det utfylte spørreskjemaet i den vedlagte svarkonvolutten og postlegg den så snart som mulig!
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hunt

Helseundersøkelsen i Nord-Trøndelag

SKJEMA FOR KVINNER 70 ÅR OG ELDRE

Takk for frammøtet til undersøkelsen!
Vi vil også be deg fylle ut dette spørreskjemaet. Opplysningene vil bli brukt i større forskningsarbeider om forebyggende helsearbeid. Noen av spørsmålene likner på spørsmål du har svart på i det skjemaet du fylte ut heime og leverte ved frammøte til helseundersøkelsen. Det er likevel viktig at du svarer på alle spørsmålene også i dette skjemaet. Det utfylte skjemaet returneres i vedlagte svarkonvolutt. Porto er betalt.
Alle opplysningene er underlagt streng taushetsplikt.

Vennlig hilsen
Helsetjenesten i Nord-Trøndelag
Statens Institutt for Folkehelse Statens helseundersøkelser

Hvis du ikke ønsker å besvare spørreskjemaet, sett kryss her og returner skjemaet. Da slipper du purring
Jeg ønsker ikke å besvare skjemaet ○

UTFYLLING

Dato for utfylling av skjema: / 19 19

OPPVEKST

I hvilken kommune bodde du da du fylte 1 år?
*Hvis du ikke bodde i Norge, oppgi **land** i stedet for kommune*

24

BOLIG

Hvilken type bolig bor du i? *Bare ett kryss*

Enebolig/villa	25	1
Gårdsbruk		2
Blokk/terrasseleilighet		3
Rekkehus/2-4 mannsbolig		4
Trygdebolig/aldersbolig/servicebolig		5
Sykeheim/aldersheim		6
Annen bolig		7

Hvor stor er din boenhet? 26 kvm

		Ja	Nei
Er det heldekkende tepper i stua?	29		
Er det heldekkende tepper på ditt soverom?			
Er det katt i boligen?	31		
Er det hund i boligen?			
Er det andre pelskledde dyr eller fugler i boligen?			

Hvem bor du sammen med? *Ett eller flere kryss*

Ektefelle/samboer	34	Søster/bror	37
Barn/svigerbarn		Annen familie/slekt	
Bor alene	36	Andre	39

SYKDOM I FAMILIEN

Kryss av for de slektningene som har eller har hatt noen av sykdommene. Kryss av for "ingen" hvis ingen av slektningene har hatt denne sykdommen. *Evt. flere kryss på hver linje*

		Mor	Far	Bror	Søster	Barn	Ingen
Hjerneslag eller hjerneblødning	40						
Hjerteinfarkt før 60 års alder	46						
Astma	52						
Allergi	58						
Kreftsykdom	64						
Høyt blodtrykk	70						
Psykiske plager	76						
Osteoporose (benskjørhet)	82						
Diabetes (sukkersyke)	88						
Alder da de fikk diabetes	94	år	år	år	år	år	

		Ja	Nei
Har du *selv* høysnue eller neseallergi?	104		

SIVILSTAND

Hva er din sivilstand? 105

Gift	1	Enke	3
Skilt/separert	2	Har aldri vært gift	4

BRUK AV HELSETJENESTER

Har du i løpet av de siste 12 månedene vært hos:
Ett kryss på hver linje

		Ja	Nei
allmennpraktiserende lege (kommunelege, privatpraktiserende lege, turnuskandidat)	106		
lege ved sykehus (uten at du var innlagt)			
annen lege			
fysioterapeut			
kiropraktor			
homøopat	111		
annen behandler (naturmedisiner, fotsoneterapeut, håndspålegger, "healer", "synsk", e.l.)			

SYKEHUS

		Ja	Nei
Har du vært innlagt i sykehus de siste 5 åra?	113		

Hvis «Ja»: Svar ut fra siste gang du var innlagt

Synes du at du ble utskrevet for tidlig, i passe tid eller for seint? 114

For tidlig	
I passe tid	
For seint	

Hvor ble du utskrevet til? 115

Heim	
Kuropphold	
Sykeheim	

		Ja	Nei
Fikk du tilstrekkelig hjelp og oppfølging etter utskrivingen?	116		

HEIMEHJELP

		Ja	Nei
Har du heimehjelp?			
Privat	117		
Kommunal	118		

Dersom du har KOMMUNAL heimehjelp: **Har du nok kommunal heimehjelp, eller trenger du mer?** 119

Ja, jeg har nok	
Nei, jeg trenger mer	

		Ja	Nei
I tilfelle du IKKE har kommunal heimehjelp: **Trenger du kommunal heimehjelp?**	120		

HEIMESYKEPLEIE

Har du heimesykepleie? ..... 121 — Ja ☐ Nei ☐

Hvis «Ja»:

Har du nok heimesykepleie, eller trenger du mer?

- Ja, jeg har nok ..... ☐
- Nei, jeg trenger mer ..... ☐

SYKEHEIM

Har du vært innlagt på sykeheim i løpet av de siste 12 månedene? 123

- Nei ..... ☐
- Ja, jeg har vært der en periode ..... ☐
- Ja, jeg bor der fast ..... ☐

Hvis «Nei», kan du hoppe over de neste to spørsmålene

Hvis «Ja»:

Hvor var du FØR du ble innlagt på sykeheimen siste gang? 124

- Bodde i egen heim ..... ☐
- Var innlagt i sykehus ..... ☐
- Var annet sted ..... ☐

Hvis du har vært på sykeheimen EN PERIODE i løpet av de siste 12 mndr.:

Bodde du på sykeheimen passe lenge? 125

- Det var for kort tid ..... ☐
- Passe tid ..... ☐
- Det var for lang tid ..... ☐

KOMMUNAL HJELP ALT I ALT

Hvordan er du alt i alt fornøyd med hjelpa du får fra kommunen? 126

- Meget fornøyd ..... ☐ 1
- Nokså fornøyd ..... ☐ 2
- Nokså misfornøyd .. ☐ 3
- Meget misfornøyd .. ☐ 4

Jeg får ingen hjelp, men burde ha hatt det ..... ☐ 5

Jeg får ingen hjelp, og trenger det ikke ..... ☐ 6

KOSTHOLD

Hvor mange måltider spiser du vanligvis daglig (middag og brødmåltid)? ..... 127 — Antall

Hvor mange dager i uka spiser du varm middag?

Hva slags type brød (kjøpt eller hjemmebakt) spiser du vanligvis? *Inntil to kryss*

Brødtypen ligner mest på 129	*Loff*	*Fint brød*	*Kneipp-brød*	*Grov-brød*	*Knekke-brød*
	☐	☐	☐	☐	☐

Hva slags *fett* blir vanligvis brukt i din husholdning?

Ett kryss for matlaging og ett kryss for brød	*Til matlaging*	*På brød*
Bruker *ikke* smør eller margarin	134 ☐ 1	135 ☐ 1
Meierismør	☐ 2	☐ 2
Hard margarin	☐ 3	☐ 3
Bløt (soft) margarin	☐ 4	☐ 4
Smør/margarin blanding	☐ 5	☐ 5
Lettmargarin	☐ 6	☐ 6
Oljer	☐ 7	

Hvor mange glass melk (alle sorter, også drikkeyoghurt) drikker du vanligvis daglig? *Bare ett kryss* 136

- Ingen ..... ☐ 1
- Mindre enn ett ..... ☐ 2
- 1–2 glass ..... ☐ 3
- 3 eller mer ..... ☐ 4

Hvor mange brødskiver med kvitost spiser du vanligvis daglig? *Bare ett kryss* 137

- Ingen ..... ☐ 1
- Mindre enn en ..... ☐ 2
- 1–2 skiver ..... ☐ 3
- 3 eller mer ..... ☐ 4

HVILE OG AVSLAPPING

Hvor mange timer tilbringer du *vanligvis* i *liggende* stilling i løpet av et døgn? (nattesøvn, middagshvil) ..... 138 — Antall timer

Hvor mange timer tilbringer du *vanligvis* i *sittende* stilling i løpet av et døgn? (arbeid, måltider, TV, bil etc.) ..... 140 — Antall timer

Har du i løpet av siste måned hatt innsovningsproblemer? *Bare ett kryss* 142

- Nesten hver natt ..... ☐ 1
- Ofte ..... ☐ 2
- Av og til ..... ☐ 3
- Aldri ..... ☐ 4

Har du i løpet av siste måned våknet for tidlig og ikke fått sove igjen? *Bare ett kryss* 143

- Nesten hver natt ..... ☐ 1
- Ofte ..... ☐ 2
- Av og til ..... ☐ 3
- Aldri ..... ☐ 4

MEDISINBRUK

Har du i deler av de siste 12 måneder brukt noen medisiner daglig eller nesten daglig? ..... 144 — Ja ☐ Nei ☐

Hvis "Ja":

Angi hvor mange måneder du brukte følgende medisiner: *Sett 0 hvis du ikke har brukt medisinene*

	Antall mndr.		Antall mndr.
smertestillende 145		hjertemedisin (ikke blodtrykksmedisin)	
sovemedisin 147		annen medisin	
beroligende medisin		*Kosttilskudd:*	
medisin mot depresjon		jerntabletter 161	
allergimedisin 153		vitamin D-tilskudd	
astmamedisin 155		andre vitamintilskudd	
		tran/fiskeoljer 167	

Hvor ofte har du brukt avslappende/beroligende medisin eller sovemedisin den siste måneden? 169

- Daglig ..... ☐ 1
- Hver uke, men ikke hver dag ☐ 2
- Sjeldnere enn hver uke ☐ 3
- Aldri ..... ☐ 4

VENNER

Hvor mange gode venner har du?

Regn med de du kan snakke fortrolig med og som kan gi deg god hjelp når du trenger det ..... 170 — Antall

Tell ikke med de du bor sammen med, men regn med andre slektninger

Føler du at du har mange nok gode venner? .... 172 — Ja ☐ Nei ☐

Hvor ofte tar du vanligvis del i foreningsvirksomhet som f.eks. syklubb, eldresenter, pensjonistforening, politiske lag, religiøse eller andre foreninger? *Bare ett kryss* 173

Aldri, eller noen
få ganger i året ..... ☐1 Omtrent en gang i uka ... ☐3
1–2 ganger i måneden ... ☐2 Mer enn en gang i uka ... ☐4

HUMØR OG TRIVSEL

Ett kryss på hver linje

Angi hvordan du har følt deg den siste måneden:	*Aldri*	*Noen ganger*	*Ganske ofte*	*For det meste*
i godt humør 174	☐	☐	☐	☐
i dårlig humør 175	☐	☐	☐	☐

	Svært treg	*Ganske treg*	*Ganske rask*	*Svært rask*
Er du rask til å oppfatte et humoristisk poeng? 176	☐	☐	☐	☐

Er du enig i at det er noe ansvarsløst over folk som stadig prøver å være morsomme? 177

Nei, slett ikke ..... ☐1 Ganske enig ..... ☐3
I noen grad ..... ☐2 Ja, absolutt ..... ☐4

Er du en munter person? 178

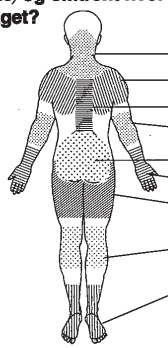
Nei, slett ikke ..... ☐1 Ganske munter ..... ☐3
I noen grad ..... ☐2 Ja, absolutt ..... ☐4

MUSKEL-/SKJELETTPLAGER

Har du hatt plager (smerter, verk, ubehag) i muskler og/eller ledd i *den siste måneden*? ..... 179 *Ja* ☐ *Nei* ☐

Hvis «Nei»: Gå til HODEPINE

Hvis «Ja»: Hvor har du hatt disse plagene *(ett eller flere kryss)* **og omtrent hvor mange dager tilsammen var du plaget?**



Plager (Sett kryss)	Antall dager
Nakke 180	
Skuldre/aksler.....183	
Øvre del av ryggen	
Albuer 189	
Korsryggen 192	
Handledd/hender	
Hofter.....198	
Knær.....201	
Ankler/føtter 204	

*Dersom flere kryss: Sett **ring** rundt krysset **der plagen var verst***

Har plagene hindret deg i å utføre daglige aktiviteter den siste måneden? ..... 207 *Ja* ☐ *Nei* ☐

HODEPINE

Har du vært plaget av hodepine i løpet av de siste 12 måneder? 208

Ja, anfallsvis (migrene)..... 1☐
Ja, annen slags hodepine.. 2☐
Nei ..... 3☐

Antall anfall siste 12 mndr. 209 ☐

Hvis «Nei»: Gå til URINLEKKASJE

Omtrent hvor mange dager pr. måned har du hodepine?
Mindre enn 7 dager ☐1 7 til 14 dager ☐2 Mer enn 14 d. ☐3

Hvor lenge varer hodepinen vanligvis hver gang? 212
Mindre enn 4 timer ☐1 4 timer–3 døgn ☐2 Mer enn 3 døgn ☐3

Hvor ofte er hodepinen preget av eller ledsaget av:
Ett kryss på hver linje

	Sjelden eller aldri	*Av og til*	*Ofte*
bankende/dunkende smerte 213	☐	☐	☐
pressende smerte	☐	☐	☐
halvsidighet, alltid samme side	☐	☐	☐
halvsidighet, vekselvis h. og v. side	☐	☐	☐
smerter i «hele hodet»	☐	☐	☐
kvalme 218	☐	☐	☐
lys- og/eller lydskyhet	☐	☐	☐
forverring ved fysisk aktivitet.....	☐	☐	☐
synsforstyrrelser *før* hodepine 221	☐	☐	☐

Hvor mange tabletter/stikkpiller har du eventuelt brukt av disse medisinene *alt i alt i løpet av den siste måneden*?
Skriv 0 hvis du ikke har brukt medisinen.

Cafergot 222 ☐ Anervan 224 ☐ Imigran 226 ☐

URINLEKKASJE

Har du lekkasje av urin (uansett mengde) minst to ganger per måned? ..... 228 *Ja* ☐ *Nei* ☐

Hvis «Nei»: Gå til MENSTRUASJON OG OVERGANG...

Hvor ofte har du urinlekkasje? 229

noen få ganger per måned ..... ☐
en eller flere ganger per uke ..... ☐
hver dag og/eller natt ..... ☐

Hvor mye urin lekker du vanligvis hver gang? 230

dråper eller lite ..... ☐
små skvetter eller mer ..... ☐

Har du lekkasje av urin i forbindelse med	*Ja*	*Nei*
hosting, nysing eller latter 231	☐	☐
løft	☐	☐

Hender det at du har lekkasje av urin i forbindelse med plutselig og sterk vannlatingstrang? 233 *Ja* ☐ *Nei* ☐

Hvordan opplever du lekkasjeplagene dine? *Bare ett kryss*

ikke noe problem ..... ☐
en liten plage ..... ☐
en del plaget ..... ☐
mye plaget ..... ☐
svært stort problem ..... ☐

Har du søkt lege pga. urinlekkasje? ..... 235 *Ja* ☐ *Nei* ☐

MENSTRUASJON OG OVERGANGSALDER

Hvor gammel var du da menstruasjonen sluttet? ☐ år

HORMONBEHANDLING

Utenom p-piller

Har du noen gang brukt medisiner som inneholder østrogen? Vanlige navn på slike medisiner er: Cyclabil, Estraderm, Kilogest, Ovesterin, Progynova, Trisekvens.

	Nå	*Før*	*Aldri*
Tabletter eller plaster 238	☐	☐	☐
Krem eller stikkpiller 239	☐	☐	☐

Hvis «Ja»: Hvor gammel var du første gang du fikk østrogenmedisin, og omtrent hvor mange år brukte du slik medisin?

	Din alder	*Antall år*
Tabletter eller plaster 240		
Krem eller stikkpiller 244		

Hvis du bruker østrogenmedisin nå, hvilket merke bruker du? 248 ☐

OPERASJONER I UNDERLIVET

	Ja	Nei	Vet ikke
Har du fått fjernet begge eggstokkene (totalt)? 249	☐	☐	☐

Hvis du har fjernet begge eggstokkene, hvor gammel var du da? 250 ☐ år

	Ja	Nei	Vet ikke
Har du fått fjernet hele livmoren? 252	☐	☐	☐

Hvis du har fjernet hele livmoren, hvor gammel var du da? 253 ☐ år

GRAVIDITETER, FØDSLER OG AMMING

Hvor mange ganger har du vært gravid totalt?
*Regn med **alle** svangerskap, spontane eller selvbestemte aborter, så vel som fødsler (også dødfødsler).* 255 ☐ ganger

Hvor mange barn har du født? 257 ☐ barn

Fyll ut for hvert barn (de første 6) opplysninger om fødselsår og omtrent antall måneder du ammet hvert barn og antall måneder menstruasjonen din var borte etter fødselen (fylles ut også for dødfødte eller for barn som er døde senere i livet).

Barn	Fødselsår	Antall måneder med amming	Antall blødningsfrie måneder
1	258 19		
2	264 19		
3	270 19		
4	276 19		
5	282 19		
6	288 19		

HVORDAN DU SER PÅ DEG SELV

Folk ser på seg selv på ulike måter. Kryss av for hvert utsagn hvor enig eller uenig du er. *Ett kryss på hver linje*

	Svært enig	Enig	Uenig	Svært uenig
Jeg har en positiv holdning til meg selv 294	☐	☐	☐	☐
Jeg føler meg virkelig ubrukelig til tider 295	☐	☐	☐	☐
Jeg føler at jeg ikke har mye å være stolt av 296	☐	☐	☐	☐
Jeg føler at jeg er en verdifull person, i allefall på lik linje med andre 297	☐	☐	☐	☐

	Ja	Nei
Synes du at du har funnet et virkelig betydningsfullt innhold i livet ditt? 298	☐	☐
Føler du at du lever fullt ut? 299	☐	☐

HVORDAN DU FØLER DEG NÅ

*Sett kryss i den ruta utenfor det svaret som best beskriver dine følelser **den siste uka.** Bare ett kryss*

Føler du deg stort sett sterk og opplagt, eller trøtt og sliten? 300

- ☐ 1 Meget sterk og opplagt
- ☐ 2 Sterk og opplagt
- ☐ 3 Ganske sterk og opplagt
- ☐ 4 Både – og
- ☐ 5 Ganske trøtt og sliten
- ☐ 6 Trøtt og sliten
- ☐ 7 Svært trøtt og sliten

Har du i det store og hele en rolig og god følelse inne i deg? 301

- ☐ 1 Nesten hele tida
- ☐ 2 Ofte
- ☐ 3 Av og til
- ☐ 4 Aldri

Er du vanligvis glad eller nedstemt? 302

- ☐ 1 Svært nedstemt
- ☐ 2 Nedstemt
- ☐ 3 Nokså nedstemt
- ☐ 4 Både – og
- ☐ 5 Nokså glad
- ☐ 6 Glad
- ☐ 7 Svært glad

LEGEMLIGE FUNKSJONER

Klarer du selv, uten hjelp av andre, i det daglige å:
Ett kryss på hver linje

	Ja	Med noe hjelp	Nei
Gå innendørs i samme etasje 303	☐	☐	☐
Gå på toalettet	☐	☐	☐
Vaske deg på kroppen 305	☐	☐	☐
Bade eller dusje	☐	☐	☐
Kle på og av deg 307	☐	☐	☐
Legge deg og stå opp	☐	☐	☐
Spise selv 309	☐	☐	☐

Hvis du har hatt hjelp til noe av dette, omtrent hvor lenge har du hatt hjelp? *Bare ett kryss* 310

- ☐ 1 Under 3 måneder
- ☐ 2 3 – 6 måneder
- ☐ 3 1/2 – 1 år
- ☐ 4 1 – 5 år
- ☐ 5 Mer enn 5 år

Hvis du trenger hjelp til ett eller flere av disse gjøremålene, hvem er det som for det meste hjelper deg?
Bare ett kryss

- ☐ 1 Ektefelle/samboer
- ☐ 2 Barn/svigerbarn
- ☐ 3 Søster/bror
- ☐ 4 Annen familie/slekt
- ☐ 5 Andre

DAGLIGE OPPGAVER

Klarer du selv disse gjøremålene i det daglige uten hjelp fra andre? *Ett kryss på hver linje*

	Ja	Med noe hjelp	Nei
Lage varm mat 312	☐	☐	☐
Gjøre lett husarbeid (f.eks. oppvask)	☐	☐	☐
Gjøre tyngre husarbeid (f.eks. gulvvask) 314	☐	☐	☐
Vaske klær	☐	☐	☐
Betale regninger 316	☐	☐	☐
Ta medisinene	☐	☐	☐
Komme deg ut 318	☐	☐	☐
Gjøre innkjøp	☐	☐	☐
Ta bussen 320	☐	☐	☐

Hvis du trenger hjelp til ett eller flere av disse gjøremålene, omtrent hvor lenge har du hatt hjelp?
Bare ett kryss 321

- ☐ 1 Under 3 måneder
- ☐ 2 3 – 6 måneder
- ☐ 3 1/2 – 1 år
- ☐ 4 1 – 5 år
- ☐ 5 Mer enn 5 år

Hvis du trenger hjelp til ett eller flere av disse gjøremålene, hvem er det som for det meste hjelper deg?
Bare ett kryss 322

- ☐ 1 Ektefelle/samboer
- ☐ 2 Barn/svigerbarn
- ☐ 3 Søster/bror
- ☐ 4 Annen familie/slekt
- ☐ 5 Andre

Legg det utfylte spørreskjemaet i den vedlagte svarkonvolutten og postlegg den så snart som mulig!
Porto er betalt.

Hjertelig takk for hjelpa!

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