039 REGIONAL DISPARITIES IN CANCER SURVIVAL FOLLOWING THE NHS NATIONAL CANCER PLAN FOR ENGLAND: AN ANALYSIS BY CANCER NETWORK

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Objective Reducing geographic inequalities in survival from cancer in England was a key aim of the Calman-Hine Report (1995) and the NHS Cancer Plan (2000). In this paper we assess whether regional differences have diminished following these policy developments by analysing the trend in one-year relative survival from six cancers in the 28 Cancer Networks of England.
Methods We estimated population-based relative survival at one year for 1.4 million patients who were diagnosed with cancer of the breast (women), cervix, stomach, oesophagus, lung or colon in England during 1991-2006 and followed up to 31 December 2007. Relative survival is the ratio of the observed survival of cancer patients relative to the expected mortality in the general population (background mortality) and it can be interpreted as the survival of cancer patients after other causes of death have been taken into account. Background mortality was estimated by age, sex, calendar year, deprivation category and Government Office Region. Age-standardised relative survival was estimated by Cancer Network in three calendar periods: 1991–1995, 1996–2000 and 2001–2006. Funnel plots were used to display spatial and temporal variation in survival. The number of Cancer Network, sex and age combinations that were outside of the 99.8% control limits of the England-wide estimate of relative survival was charted over time.
Results One-year relative survival improved over time for all patients except those diagnosed with cervical cancer. There were large regional differences in relative survival for each of the six cancers. Cancer Networks that were low-survival outliers across several cancers were clustered across Northern England and the Midlands. The north-south divide became less marked over time although the overall number of lower outliers compared to the national value remained stable.
Conclusion Policy changes over the past two decades coincided with improved relative survival, without seeing an increase in regional disparity. The north-south divide in the distribution of low-survival Cancer Networks became less pronounced over time but regional disparities persist. Further methodological development is needed to obtain more robust estimates of age-standardised relative survival for small populations, in order to monitor these regional trends.

040 EARLY AND MID-ADULTHOOD BMI IN RELATION TO LATER CANCER MORTALITY: OVER YEARS OF FOLLOW-UP IN THE HARVARD ALUMNI HEALTH STUDY

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Objective The association between adiposity in early adulthood and subsequent development of specific malignancies is still unclear. Additionally, the potential mediating role of adiposity in middle age has not been well examined. We investigated the association of body mass index (BMI; weight(kg)/height(m^2)) in early adulthood with later mortality from several cancers.
Design Cohort study of male Harvard University students who had a medical examination at university between 1914 and 1952 (mean age 18.4 years) when height and weight were measured. Data on smoking habits were recorded and physical activity details were ascertained from athletic records. Alumni were traced and mailed a health questionnaire in 1962 or 1966 (mean age 45.1 years) which included enquiries regarding height and weight. They were then followed for subsequent mortality experience – which is >99% complete—until the end of 1998 (mean age at follow-up 56.5 years). In Cox regression models, adjustment was made for university smoking and physical activity levels; joint models were used to explore mediation by BMI in middle age. Imputation was used to allow inclusion of 4040 men with missing data for at least one variable.
Setting US.
Participants 19 593 males in the Harvard Alumni Health Study cohort who had a medical examination at university and returned a mailed questionnaire in 1962 or 1966.
Main outcome measure Mortality from cancer.
Results There were 8445 deaths in total, 2395 of which were from cancer. A one SD increase in early adulthood BMI was associated with an increased risk of death from cancer from all sites combined (adjusted hazard ratio 1.11; 95% CI 1.05, 1.17), plus lung (1.24; 95% CI 1.10 to 1.40) and skin (1.29; 95% CI 0.96 to 1.75). Cancers of the pancreas, stomach, liver, brain, prostate, kidney, bladder, lymphatic and haematopoietic tissue were not associated with BMI in early adulthood. Results were equivalent when based on multiply imputed data and accounting for the role of middle age BMI.
Conclusion In this cohort, higher BMI in early adulthood appears to be a risk factor for some malignancies several decades later, and appeared to be neither confounded by lifestyle factors nor meditated via BMI in middle-age. These findings suggest that strategies to tackle obesity early in life may be important for the prevention of selected cancers.

Epidemiology

041 CHILDHOOD RESIDENTIAL STABILITY AND HEALTH STATUS IN EARLY ADULTHOOD AND MIDLIFE

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Background Previous studies have shown that making multiple residential moves in childhood leads to an increased risk of emotional and behavioural problems in early adulthood and to poorer self-reported health in midlife. Such studies tend to focus on one or two health variables, measured at one time point. This study examines health status in early adulthood and midlife across a wider range of measures.
Aim To compare subjects who were residentially stable in childhood with those who had moved more often in terms of a wide range of health measurements at 18 and 36.
Methods Analysis of the 1970s cohort of the West of Scotland Twenty-07 Study. In total, 850 respondents who participated in waves 1 (1987/88), 2 (1990/92) and 5 (2007/8) of the study, and whose childhood residential history was available, were included in regression analyses. Residential stability was derived from the number of addresses at which the respondent had lived between birth and age 15 and 18. We considered directly measured health variables (BMI, waist-hip ratio and lung function), self-reported health, psychological wellbeing (GHQ12) and self-reported health behaviours (smoking, drinking and trying drugs).
Results Twenty percent of respondents remained residentially stable during childhood, 59% had moved 1-2 times and 21% had moved at

least 3 times. Directly measured health variables were not associated with number of residential moves made at 18 or 36. Odds of scoring at least 3 on the GHQ12 questionnaire were significantly increased at age 18 for those moving 1-2 times (OR 2.01 (1.36–2.96)) and those moving 3 times or more (OR 2.04 (1.3, 3.22)) compared to those who remained stable. Similarly, odds of reporting a long-standing illness at 18 were increased for 1-2 moves (OR 1.88 (1.11, 3.18)) and at least 3 moves (OR=2.03 (1.11, 3.69)). Odds were elevated, but not significant, at 36 for these health variables. Odds of trying drugs and smoking at 18 were significantly increased but only for those moving at least 3 times. Although elevated, odds for these health behaviours were not significant at 36.

Conclusions Increased mobility during childhood is independently associated with adverse health status. At 18, the relationships between residential mobility and self-reported health outcomes, psychological wellbeing and some health behaviours were significant; however, by 36 findings were no longer significant. Directly measured health variables, at 18 and 36, do not appear to be associated with childhood mobility.

042 LIFECOURSE PREDICTORS OF ADULT PARENCHYMAL BREAST TISSUE DENSITY: RESULTS FROM THE NEWCASTLE THOUSAND FAMILIES STUDY

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Objective To investigate the relative influences of factors acting throughout life on breast tissue density at age 49-58 years.

Design Follow-up of the Newcastle Thousand Families birth cohort study.

Setting In 1947, all 1142 babies born in May and June to mothers resident in the city of Newcastle-upon- Tyne were recruited into the Newcastle Thousand Families birth cohort. This study details a sample of women from this cohort who returned for follow-up 49+ years later, and is therefore drawn from throughout the UK and beyond.

Participants At age 50, 574 study members returned a self-completion questionnaire. The 307 surviving women who returned questionnaires at age 50 were sent a questionnaire asking for details of mammographic screening and for details of their reproductive and contraceptive history. 199 women who gave access to their previous mammograms and had completed both questionnaires were included in this analysis.

Main outcome measures Breast tissue density patterns were coded into Wolfe categories (N1=lowest risk, P1=low risk, P2=high risk, PY=highest risk). This was analysed, by ordinal logistic regression, in relation to a range of variables at different stages of life, including birthweight, gestational age, duration breast fed, age at menarche, gravidity, age at first pregnancy, menopausal status, breast feeding history, hormonal contraceptive history, use of hormone replacement therapy, cigarette smoking history, alcohol consumption, height, body mass index, physical activity levels, age at scan, and socio-economic status both at birth and in adulthood.

Results Eleven % (n=22) of women were classified in the lowest Wolfe category of risk (N1), 20% (n=39) as low risk (P1), 48% (n=95) as high risk (P2), and 22% (n=43) as being in the highest category of risk (PY). Increased standardised birthweight (adjusted odds ratio, aOR 1.42 (95% CI 1.08 to 1.87), p=0.01) and not having entered the menopause (aOR, compared to perimenopausal women 3.99 (95% CI 1.78 to 8.97), p=0.001) were both significant independent predictors of being in a higher density group. In contrast, increasing body mass index was independently predictive of being in a lower density group (aOR 0.85 (0.80 to 0.91), p<0.001).

Conclusions After adjustment for factors acting throughout life, this study identified a significant association between increased birthweight, standardised for sex and gestational age, and increased breast tissue density in adulthood. This observation is consistent with previous research suggesting that heavier babies have an increased risk of breast cancer in later life.

043 ADJUSTING MISCLASSIFICATION OF OUTCOME IN CASE-CONTROL STUDIES

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Objective Misclassification of outcome may cause biased estimation for associations of potential risk factors with important diseases. For example, case-control studies of localised prostate cancer frequently measure blood levels of circulating prostate specific antigen (PSA) in healthy men and biopsy those with an elevated level. Inevitably, some men with prostate cancer will be misclassified as controls, either because they do not have an elevated PSA level or because cancer was not detected at biopsy. This misclassification may be differential if the risk factor itself influences PSA level.

Design We reviewed the literature for methods that correct for non-differential and differential misclassification of outcome in case-control studies. We apply these methods to estimating the association between two established risk factors and prostate cancer: family history and diabetes. We use published data on prostate cancer risk in men with low PSA levels to inform our estimates of the amount of misclassification in our data.

Results Potential approaches range from simple sensitivity analyses to probabilistic sensitivity modelling and Bayesian models, incorporating estimates of sensitivity and specificity. Simple sensitivity analyses recalculate cell frequencies accordingly to produce corrected odds ratios (OR). One accurate estimate of sensitivity and specificity can be used to produce a "corrected" effect-estimate, or a range of values can be used as a sensitivity analysis to assess the direction and magnitude of potential bias. Probabilistic and Bayesian methods incorporate uncertainty in the estimates of sensitivity and specificity as probability distributions so producing a frequency distribution of corrected results from which a median corrected estimate can be presented. Using varying estimates of sensitivity (fixing specificity 100%, feasible in the current example), the direction of the association between family history and prostate cancer (assuming non-differential misclassification) did not change, although the OR increased. The magnitude and direction of the association between diabetes and prostate cancer (assuming differential misclassification) becomes increasingly inverse when the sensitivity in the exposed group is greater than in the non-exposed group. When the sensitivity in the exposed group is smaller than in the non-exposed group, the OR increased, potentially even changing the direction of the association.

Conclusion Correction for misclassification of disease allows presentation of results that incorporate estimates of systematic error due to misclassification bias. That such misclassification may change both the magnitude and direction of an association is demonstrated in real data. Careful consideration is required as to the objective of applying these methods.