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Venous thromboembolic disease in cancer patients in Europe – an opportunity for improved prevention: the VITAE Thrombosis Study

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On behalf of the **V**TE **I**mpact **A**ssessment Group in **E**urope (VITAE)

Background: Venous thromboembolism (VTE) is a common and potentially fatal complication of cancer. However, the often silent nature of VTE, difficulty of diagnosis and follow up, and lack of routine post-mortems make its prevalence and associated morbidity and mortality difficult to assess. This may have led to marked underestimates of its true burden. We aimed to determine the prevalence and burden of VTE in cancer patients based on data from the first large-scale study performed at a European level – The VITAE Study.

Material and methods: A modified incidence-based epidemiological model was developed to estimate the numbers of VTE events and deaths taking into consideration recurrence and complications. Separate models were constructed for France, UK, Germany, Italy, Sweden and Spain; the total number VTE events were extrapolated for the EU. These comprehensive models were populated with published literature when available and expert observation when necessary. Both community-acquired and hospital-acquired events were derived. The former were based on a large European epidemiological study (EPI-GETBO) and the latter were derived using a hospital episode statistics database in conjunction with a "bottom-up" approach. Adjustment of the data based on published reports of the proportion of total VTE events and deaths that occur in cancer patients gave estimates of the prevalence of events in this patient group.

Results: The total annual burden of VTE in the EU exceeds 1.5 million events (see Table). In total, 28% of symptomatic deep-vein thromboses (DVT), 27% of non-fatal pulmonary embolism (PE) and 30% of VTE-related deaths were attributable to the cancer patient population. Of the latter, 10,335 deaths (7%) were patients diagnosed with VTE and treated, 48,915 (34%) had a sudden fatal PE and 84,300 (59%) followed undetected PE. These findings were tested using probabilistic sensitivity analyses.

Table: Annual burden of VTE and associated mortality in the EU

	Overall number of events	Number of events in cancer patients
DVT	641,275	181,449
Non-fatal PE	382,550	103,289
VTE-related deaths	478,500	143,550

Conclusions: Our data confirm that VTE is a major public health problem in the EU, and of particular importance in cancer patients. Many VTE events and associated deaths in cancer patients were sudden or followed asymptomatic VTE disease. The use of available effective thromboprophylaxis may have prevented many of these events and deaths. Further research to estimate the impact of increased thromboprophylaxis use in cancer patients is urgently needed.

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A systematic review of the natural history of high risk HPV among adult women

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Background: A systematic review of published literature on the natural history of high-risk cervical human papillomavirus (HR HPV) infections in adult women aged 25–55 years was conducted to increase our understanding of the potential role of HPV prophylactic vaccination in this population.

Materials and methods: We searched the PubMed database for studies on HR HPV incidence, persistence and clinical progression to high-grade cervical intraepithelial neoplasia (CIN). Criteria for study inclusion included: use of sensitive PCR or Hybrid Capture for HPV DNA detection, average participant age of between 25 and 55 years, normal baseline cytology, and presentation of results for high-risk HPV types only.

Results: A total of 29 studies were identified, from which we present preliminary results from 14. Based on studies from Brazil and Columbia (Munoz et al., 2004; Franco et al., 1999), the annual incidence of HR HPV was approximately 5–10% after the age of 35 years. Persistence of HR HPV one year after baseline was consistently <50% in 6 geographically diverse studies with varying study designs (weighted average of 44.9% persistence from studies which presented data at one year). The negative predictive value of an HR HPV test for subsequent CIN grade 3 (CIN3) was over 99.5% in four separate studies with duration up to 10 years. The corresponding positive predictive values from these studies was 3–10%. Two studies indicated that only recent sexual behaviour was a risk factor for incident HR HPV infection. HPV viral type (HPV16 and related types versus other high risk HPV types) and viral load were associated with increased risk of HPV persistence. There are limited data from two prospective studies indicating an association between cigarette smoking and increased risk of developing CIN3 or cervical cancer among HR HPV positive women at baseline. Overall, there is a general lack of data on HR HPV incidence and persistence among adult women as well as on HR HPV incidence in developed countries where the risk of cervical cancer is low.

Conclusions: The incidence of HR HPV appears to be relatively high (5–10%) among adult women, with approximately 45% of these infections persisting more than one year. The association of age and non-viral co-factors with HPV persistence and progression is currently unclear and therefore merits further investigation.

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Recreational physical activity, relative body weight and risk of bladder cancer in Canadian men and women: a case-control study

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Background: Bladder cancer is the second most frequently diagnosed neoplasm of the urinary tract. The effects of physical activity and body weight on risk of bladder cancer have not been well studied. Physical activity and/or body weight may exert their effects on bladder cancer risk through hormonal, immune, or other unknown causal pathways. This population-based case-control study investigated the association between recreational physical activity, body mass index (BMI), and risk of bladder cancer in men and women separately.

Material and methods: Bladder cancer cases and controls recruited between 1994 and 1997 in seven Canadian Provinces provided self-reported data on anthropometrical, socio-demographic, life-style, occupational history, and reproductive characteristics.

Results: The analyzed samples were 2,312 men (670 cases and 1,642 controls) and 1,824 women (359 cases and 1,465 controls). In men and women, the estimates of adjusted odds ratio (OR) (highest vs. lowest quartile) and 95% confidence intervals (95%CI) for physical activity were 1.24 (95%CI: 0.93–1.66) and 0.76 (95%CI: 0.52–1.21), respectively. The corresponding estimates of OR for BMI were 1.29 (95% CI: 0.96–1.72) and 1.07 (95%CI: 0.74–1.55), respectively. Parous women were at reduced risk of bladder cancer compared to nulliparous women (OR = 0.56, 95%CI: 0.39–0.80). Both in men and women, certain occupations and cigarette smoking were associated with increased risk of bladder cancer. In men, but not in women, coffee consumption was associated with a slightly increased risk of bladder cancer ($\geqslant$ 1 cup per day vs. < 1 cup per day or never: OR = 1.30, 95%CI: 1.00–1.68).

Conclusions: There was not enough evidence in this study to conclude that recreational physical activity and BMI were related to risk of bladder cancer.

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Acute and chronic leukemia incidence in Kyrgyzstan

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Background: To study age, sex, geographic, site specific and ethnic leukaemia incidence in Kyrgyzstan.

Material and methods: Calculated the incidence of acute and chronic leukaemia between 2000 and 2004 in all population. There were 135 males and 166 females (total 301) registered with new diagnoses of leukaemia. Male-female proportion = 0.81. In present study collected date from forms submitted along with cytological findings, and deaths certificates. Estimated population relative risk for main types of leukaemia's in urban and rural areas. Detailed population figures from census are available from Kyrgyz National Center of Statistics. Official estimates are available for intercensus years. There are based on the census and date on natural population change. The population figures and leukaemia incidence rates for this report were provided in for age groups (15–19, 20–24, ... 85 >), ethnic

groups, for each sex and calendar years of study period. Counted crude, age-standardised rates per 100,000. The classification scheme used by ICD-10.
Results: Age-standardised (ASR) annual total cancer incidence was in males 201.2 and females 137.9 (total 169.55 per 100,000). The most frequent diagnostic groups in males were tumours of the stomach (44.65), lung (41.0), skin (27.8); in females – skin (23.5), breast (19.1), stomach (16.2). There were 301 registered with leukaemia (84 – acute myeloid, 66 – chronic myeloid, 48 – non differentiated, 42 – chronic lymphoid, 23 – acute lymphoid, 10 – erythraemia, 15 – other myeloid leukaemia, and 13 with myeloid dysplastic syndrome. Both acute and chronic leukaemia ASR in the Kyrgyz republic was 1.22 per 100,000.
Leukaemia incidence was slightly higher in urban (1.62) than rural (1.18) regions. High incidence rate in leukaemia was registered in North area; Bishkek (2.99) and Chuy (2.22). Lower incidence was registered in South region (Osh, Batken, Djalal-Abad) with ASR from 0.2 to 0.3 per 100 000.
Leukaemia incidence was significantly higher in the Slavic ethnic groups (Russians, with an ASR of 3.21 cases per 100,000, Ukrainians 3.03) compared with 1.09 for Kyrgyzs, 0.54 for Kazakhs and 0.27 for Uzbeks people.
Conclusion: Leukaemia incidence in Kyrgyzstan is low and similar to those reported from some Asian developing countries. The data could be use for a wide range of epidemiological and other studies. These include analyses of geographical variations in incidence, trends in survival, health of long-term survivors.

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Ethnic disparities in cancer incidence, mortality, stage at diagnosis and survival, in Aotearoa/New Zealand

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Background: The recently established New Zealand Cancer Control Strategy aims to reduce inequalities throughout the cancer care continuum – yet little information is available on baseline ethnic disparities in cancer outcomes. This study examined disparities in cancer incidence, mortality, stage at diagnosis and survival between Maori, (the indigenous people of Aotearoa/New Zealand), and the colonial settler population.
Methods: New cancer registrations from the New Zealand Cancer Registry during 1996 to 2001were linked to national mortality data. For 25 cancers, age-standardised incidence and mortality rates and ratios were calculated. Poisson regression was used to calculate Maori: non-Maori odds ratios for stage at diagnosis, adjusted for age and sex at diagnosis. Cox's regression was used to estimate relative risks of cancer-specific death after diagnosis (hazard ratios), adjusted for sex, age and stage at diagnosis, and within each stage-group (localised, regional, distant, unknown). Survival curves were calculated using Kaplan-Meier estimates.
Results: Leading cancer types differed for Maori and non-Maori. Incidence was higher among Maori for lung, stomach, cervix, testis, liver, and higher among non-Maori for colorectal, melanoma, prostate, bladder, brain cancers.
Maori were 18% more likely to be diagnosed with cancer than non-Maori (RR 1.18; 95%CI: 1.15–1.21) but nearly twice as likely to die from cancer (RR 1.93; 95%CI: 1.87–1.99). Mortality/incidence ratios were higher among Mäori than non-Mäori for most cancers. Maori had lower survival than non-Maori for cancers of the breast, cervix, prostate, colorectum, lung, uterus, kidney, leukaemia, NHL.
Unknown stage at diagnosis was more common among Maori than non-Maori for most common cancers. Maori were more likely than non-Maori to be diagnosed at a later stage with cancers of the breast, lung, colon and rectum, cervix, prostate, testis, kidney, oral cancers, and melanoma. Stage at diagnosis accounted for only part of the survival disparity between Maori and non-Maori for lung (18%), breast (30%), cervix (20%), colorectal (49%), prostate (47%) cancers.
Conclusions: These findings indicate the existence of disparities between Maori and non-Maori in timely access to definitive diagnostic procedures, staging procedures, and optimal treatment or management of cancer. Ethnic disparities in pathways through care must be investigated and addressed.

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Diagnostic and therapeutic delay after mammography screening in the Hungarian nation wide organized breast cancer screening programme

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Background and Aim: After the evaluation of pilot projects, the Hungarian nation wide breast cancer programme was launched in January 2002. Women between the age of 45–65 are invited by a personal letter for mammography screening and a 2 years screening interval is applied. The aim of the study is to analyse diagnostic and therapeutic delay after mammography screening in the Hungarian organized breast cancer screening programme.
Methods: The data derive from the database of the National Health Insurance Fund Administration containing routinely collected financial data. The study includes all the patients having mammography screening in the year of 2002. The starting point (T_0) was defined as the time of the mammography screening. T_1 denotes the time of the first diagnostic procedure after the mammography screening. T_2 denotes the time of the first therapeutic procedure after mammography screening and diagnosis. We calculated the average delay between the time of mammography screening (time = T_0), further diagnostic (time = T_1) and therapeutic (time = T_2) procedures. For the calculation of the average period spent from the time of mammography screening we used the median value instead of arithmetic mean.
Results: Altogether N = 314.395 women were included into the study. The average diagnostic delay between T_0 and T_1 time was 20 days measured by the time of ultrasound examination in axilla and 26 days measured by the time of ultrasound examination in breast. The average therapeutic (surgical) delay between T_0 and T_2 time was 43–47 days, 50–53 days and 57 days measured by the time of subtotal mastectomy, total mastectomy or breast operations because of non-malignant causes respectively. The average chemo or radio therapeutic delay between T_0 and T_2 time was 83 days and 136 days measured by the time of chemotherapy or radiotherapy respectively. The average delay between the time of diagnosis (T_1) and the first therapeutic event (T_2) was 26 days with a 16 days shortest and 38 days longest delay in the different Hungarian counties.
Conclusion: The diagnostic and therapeutic delay in the Hungarian breast cancer screening programme is similar to the value reported by other national programmes. We realized significant regional differences, which result in large discrepancies in the equity. We can assume that these differences can be reduced by better organization and the more consistent application of professional guidelines.

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The network on rare tumours in Italy

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Background: Rare tumours (RT) pose huge difficulties in terms of quality of care, access to health resources and clinical research. The Network on Rare Tumors (Rete Tumori Rari – RTR) is a collaborative effort in Italy aimed at improving quality of care, making institutions share patients, define clinical practice guidelines on RT and rationalize access to health facilities. It promotes collaborative clinical research by encouraging patient accrual into trials.
Methods: RTR includes 70 institutions across Italy. Internet access is the only requirement to join. Clinical cases are shared and messages exchanged through a secure Web resource, and all data, images and transactions are stored in a data base. Patients may be i) "logically" shared, ie the case is dealt with following clinical practice guidelines previously agreed upon; ii) "virtually" shared, ie the case is discussed over the network; iii) "physically" shared, ie the patient moves from a center to another to receive appropriate care as needed. A network moderator "switches on" the institutions to involve in each case sharing, inasmuch