

Pharmacogenomics and personalized health care

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Issue/Problem

There are large inter-individual differences in drug efficacy, or susceptibility to adverse effects. Adverse drug reaction (ADR)-related morbidity account for 3–9% of preventable hospital admissions.

Description of the project

There is evidence that ADR and inter-individual differences in drug efficacy are under strong genetic influence. Yet, a recent systematic review of pharmacogenetic studies found that the median sample size was smaller than 100, so that many published results are likely false positives. In this project, we will (i) summarize what is known on the role of currently identified pharmacogenomics genes in explaining ADR and drug efficacy, (ii) illustrate the potential use of pharmacogenomics with one practical example (genetic test for CYP2C9 activity and warfarin use), (iii) discuss the challenge of having adequate study design to address pharmacogenomics issues.

Lessons learned

Currently, there are about 30 very important genes in pharmacogenomics (VIP). So far, the approach has been mainly candidate gene driven, but genome-wide approaches should lead to a more unbiased way to tackle this issue. The potential for pharmacogenomics to help decreasing the burden of ADR is expected to be large, yet the clinical utility is unclear so far. The issue of inter-individual differences in drug efficacy according to the individual genomic background has been little explored so far.

Conclusions

Larger scale studies are needed to better explore the potential for pharmacogenomics to reduce the burden of ADR and further decipher the role of genes individual differences in drug efficacy. Innovative strategies are needed to explore how public health genomics may accelerate the translation of research genomic findings into clinical practice.

The Personal Genome Project

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Issue/Problem

The Personal Genome Project (PGP) is an ambitious research study directed by faculty members in the Department of Genetics at Harvard Medical School that aims to recruit as many as 100 000 informed participants to contribute genomic sequence data, tissues and extensive environmental, trait and other information to a publicly accessible and identifiable research database.

Description of the project

The Personal Genome Project is a new form of public genomics research. The main scientific goal of this study is to find ways to connect human genetic information (i.e. human DNA sequence) with human trait information (i.e. medical information, tissue samples and physical traits) in a public way so that such data may be used for research and other scientific, patient care and commercial purposes worldwide. Additional goals include (i) exploring the risks of public genomics research such as the PGP; (ii) developing a public dataset of information from willing participants to aid in the development of analytical tools for scientists, clinicians and individuals; and (iii) educating participants and the general public about the potential benefits, risks, and uncertainties posed by the widespread availability of genetic and related information. The PGP also seeks to develop a model system for experts on health care, molecular biology, genetic counselling, public health, law, education, and research to come together and collaborate.

Lessons learned

The approach taken by the PGP on matters of openness, in particular on open consent and interactive researcher-participant communication has meanwhile left its imprint on other research projects with more traditional protocols. Overall, the PGP has received a very positive societal uptake, as more than 5000 individuals have expressed their interest and are awaiting enrolment.

Conclusions

We hope that the PGP's proposed datasets will help to extend the discussions on the possible future impact of the availability of comprehensive genome-based information.

3.5. Workshop: Research on sick leave and return to work after breast cancer surgery

Chair: Peter Donceel, Belgium

Organizer: EUPHA Section on Social Security and Health

Breast cancer is the most prevalent cancer among women and on average breast cancer is diagnosed at a younger age than most other malignancies. The treatment of breast cancer is increasingly efficient and usually includes surgery followed by radiotherapy, chemotherapy and/or hormone therapy. Women who are professionally active usually have to interrupt their work activities during treatment. After successful treatment they are confronted with the problem of professional reintegration. Medical, psychological, and social problems may interfere with the process of return to work. Nevertheless, return to work is very important both from a personal as from a social point of view as prolonged sick leave often generate loss of income, social exclusion and loss of self esteem. For cancer survivors, return to work therefore not only confirms the medical recovery but also increases confidence, restores social relations and increases participation in general.

In this workshop knowledge about and methods for researching sick leave and return to work after breast cancer surgery

and factors that affect this will be in focus. First, a systematic review provides an overview of rates, duration and factors of importance for sick leave and return to work after breast cancer surgery. Second, the design and some results from an ongoing prospective cohort study in Sweden will be presented. The third abstract gives an overview of a register-based study in The Netherlands about sickness absence and return to work of employed women within 1 year after breast cancer. The final contribution discusses the methodology and results of a qualitative study exploring the experience of sick leave by breast cancer patients.

Return to work after breast cancer—an exploratory systematic literature review

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Breast cancer is the most common malignancy in women of working ages and the absolute majority of the women survive. An aspect of psychosocial long-term effects emphasized in cancer survivors are problems related to work capacity, sickness absence (SA) and return to work (RTW) with possible consequences for health and health-related quality of life. Previous reviews on this topic have mostly been conducted on cancer survivors in general with no distinction between specific diagnoses. However, the trajectories, treatments, symptoms and prognoses diverge much between different cancer diagnoses, why diagnoses specific knowledge is warranted.

The aim was to gain knowledge on time to and factors of importance for RTW and SA among women with breast cancer, through a systematic review of the literature.

Systematic searches of studies were conducted in MEDLINE, Psyc-INFO, AMED, CINAHL and SSCI. Inclusion criteria were; scientific studies published in peer reviewed journals in English or Scandinavian languages with empirical data of SA or RTW and breast cancer. Identified studies were assessed for relevance and data was systematically extracted from them. A total of 75 relevant studies were identified, mostly from North America followed by Scandinavia, The Netherlands, and UK. Of them 80% were published after year 2000 with an increasing number over time. Results will be presented in five areas; proportion of patients working before diagnose, proportions of patients who RTW, SA time, factors associated with RTW and influence on work capacity.

Return to work and sickness absence after breast cancer surgery—a prospective cohort study

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Breast cancer is the most common type of malignancy in women and many women are of working ages. The 5-year relative survival rate varies somewhat throughout Europe, in Sweden it is now 88%. Despite this, knowledge is still lacking about important areas of the future life for these women, such as impact on work capacity, and sickness absence, and return to work. To obtain such knowledge, prospective cohort studies are needed.

To sick list patients is a very common measure in cancer care. In the area of sickness-absence research, the perspective of the sick-listed persons is seldom used but needed to get a comprehensive understanding of processes. Most studies have taken the perspective of employers, society, or health care. In this presentation such a cohort study of 758 consecutively included women who had had breast cancer surgery for the first time were included. They were aged 23–63 years and are followed for 2 years prospectively. Also 2-year retrospective data from registers will be included.

A wide spectrum of data is collected via repeated comprehensive questionnaires (six measurements in total), focus group interviews, registers, and medical records. Inclusion started in 2007 and continued through 2009. Follow-up data will be collected until 2012.

The presentation will focus on study design and descriptive data from the first measurements.

Sickness absence and return to work after breast cancer: a descriptive sickness absence register study

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Background

Many breast cancer patients are of working age and improvements in diagnosis and treatment have increased their survival.

Therefore, it is likely that return to work after breast cancer is also increasing. The aim of this study was to investigate return to work of employed women with breast cancer over the years.

Methods

Data were obtained from the ArboNed occupational health register, containing sickness absence data of approximately one million employees representative for the Dutch workforce. Sickness absence episodes starting in 2002, 2005 or 2008 and medically certified with the ICD-10 code C50 were selected from the register. RTW ≥ 50 was defined as the proportion of return to work in $\geq 50\%$ of earnings before sickness absence, and was assessed at 12 months after diagnosis.

Results

The sickness absence register counted 698 women of working age with breast cancer in 2002, 962 in 2005 and 963 in 2008. In 2008, the median duration of sickness absence due to breast cancer was 349 days. RTW ≥ 50 in women aged 20–40 years was 48% compared with 51% in those aged 40–50 years and 55% in women aged 55–65 years. RTW ≥ 50 in 2008 was 52% and lower than in 2002 (59%) and in 2005 (56%). The time to RTW ≥ 50 among women aged 20–40 years diagnosed with breast cancer in 2008 was longer (HR = 0.68; 95% CI = 0.49–0.95) compared with women aged 20–40 years diagnosed in 2002.

Conclusions

Women aged <40 years had lower RTW ≥ 50 than older women with breast cancer, possibly due to poorer survival of young breast cancer patients. In contrast to increasing survival rates, RTW ≥ 50 among women aged <40 years has decreased and the time to RTW ≥ 50 has increased. This may be due to the broadened indication for chemotherapy in young breast cancer patients since 2004.

Breast cancer treatment and work disability: patient perspectives

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Background

Most female breast-cancer patients are forced to interrupt their professional activities during and some time after treatment. They have to make short- and long-term decisions about treatment, sickness absence and returning to work. We investigated women's experiences of being work-disabled because of breast cancer.

Methods

In-depth interviews were performed among twenty two breast cancer survivors from the Flanders Province of Limburg in Belgium) who had undergone a surgery in 2006. Age ranged from 43 to 58 years. A qualitative design was applied to analyse and understand women's experiences of being work-disabled and to gain more insight in their perspectives on living and working with and after breast cancer. All interviews were recorded and transcribed verbatim. Narrative summaries were discussed by all authors. Relevant themes were identified and detailed coding was performed with help from the Nvivo8 programme. The selection of themes and codes was repeatedly verified by interactive team discussions until consensus was reached. Final adjustments were made after discussion of the preliminary results with external experts.

Results

Patient's experiences differ considerably and women go through a process of finding equilibrium. We investigated

three main dynamical experiences of being work-disabled: (i) the feeling of irreparable loss and despair; (ii) an inconvenient period, after which life continues as before; (iii) a period of great importance during which new priorities are set.

Conclusions

Being aware of the different patient experiences might be of value for medical as well as insurance practitioners, company

doctors and employers. Different experiences require different types of support, especially concerning communication regarding treatment, sickness absence and returning to work. Our findings highlight the need for an individual approach of the patient in assessing and guiding disability after breast cancer surgery.

3.6. Health Inequalities

National wealth and familial socio-economic position explain variations in parental ratings of their children's health: a multilevel analysis in the EU27 countries

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Background

Sizeable variations in subjective health according to socio-economic status and national wealth have been observed. However, previous studies in adolescents have mainly employed ordinal-scaled health indicators with questionable cross-cultural comparability. This study assesses parents' reports on their children's health and well-being between and within the 27 EU member states. Covariations with socio-economic aspects were examined both individually and cross-culturally.

Methods

The Flash Eurobarometer 'Parents' views on the mental health of their child' was conducted for the European Commission. Overall, 12 783 telephone interviews were conducted in parents of children 6–17 years old in the EU27 States. Parents reported the subjective health of one eligible child on the Rasch-scaled KIDSCREEN-10 Index as well as their current occupational status and education level. Within a random intercept and slopes multilevel analysis, the KIDSCREEN was regressed on child's age and gender, parental occupational status and education level. Random intercepts and slopes were regressed on the national wealth indicators of gross domestic product per capita (GDP) and UN Gini Index. Analyses were repeated for the dichotomized KIDSCREEN score (normal versus noticeably low).

Results

Notably, low subjective health and well-being was reported in 11.6% of cases. Cross-national variation accounted for 13% of the total variance in the KIDSCREEN-10 Index. Higher national wealth and lower income inequality were associated with better population health and explained 13.5% of the country differences. Older age of the child [odds ratio (OR) = 2.2 (1.8–2.7) boys; 2.0 (1.5–2.6) girls] and a medium (OR = 1.2, 1.1–1.5) or low (1.4, 1.2–1.8) occupational status of the parent were associated with a higher risk for noticeably low subjective health outcomes. Low educational status also increased the risk for low health outcomes of the children [OR = 1.3 (1.1–1.5)].

Conclusions

Large variations in subjective health and well-being were found across countries with a sizeable proportion attributable to national wealth and income inequality. A consistent impact of

the parental occupational and educational status was also found within the countries.

Interrelationships between education, occupational class and income as determinants of disability retirement

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Background

Preventing early exit from the labour market due to disability is an important goal of ageing societies. The connection between low socio-economic status and disability retirement has been established in previous literature, but less is known about interrelationships between different socio-economic indicators. We examined the direct and indirect effects of education, occupational class and household disposable income on disability retirement.

Methods

Using nationally representative register data, over 266 000 people of the Finnish population aged 30–63 at the end of 1995 were followed up for disability retirement in 1996–2004. Cox regression analysis was used to calculate hazard ratios (HR) and relative index of inequality (RII) according to different socio-economic indicators.

Results

All socio-economic indicators had a linear negative association with disability retirement with very little gender variation. The effect of education was largely mediated through occupational class, but not much further through income. The effect of occupational class was to a great extent explained by education but not strongly mediated through income. The effect of income was largely explained by education and even further by occupational class. The independent impacts of education, occupational class and income measured by RII and its 95% confidence interval were 1.74 (1.60–1.90), 1.95 (1.78–2.15) and 1.35 (1.25–1.47) for men and 1.76 (1.61–1.92), 2.14 (1.95–2.34) and 1.14 (1.05–1.24) for women, respectively.

Conclusions

Socio-economic indicators reflect own, but also interrelated dimensions of socio-economic status. The association between socio-economic circumstances and disability retirement may not be fully captured if the pathways between various socio-economic determinants are not taken into consideration. The results imply that efforts to prevent or delay disability retirement should focus on both more distal life-style or cognitive factors associated with education and more proximate factors associated with occupational class such as power and working conditions.

Health inequalities in The Netherlands: the role of Type D personality

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