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Combining environmental and medical datasets to explore potential associations between environmental factors and health: Policy implications for human health risk assessments

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**ABSTRACT (SUMMARY)**

This review paper discusses the use of Tellus and Tellus Border soil and stream geochemistry data to investigate the relationship between medical data and naturally occurring background levels of potentially toxic elements (PTEs) such as heavy metals in soils and water. The research hypothesis is that long-term low level oral exposure of PTEs via soil and water may result in cumulative exposures that may act as risk factors for progressive diseases including cancer and chronic kidney disease. A number of public policy implications for regional human health risk assessments, public health policy and education are also explored alongside the argument for better integration of multiple data sets to enhance ongoing medical and social research. This work presents a partnership between the School of Geography, Archaeology and Palaeoecology, Northern Ireland Cancer Registry, Queen’s University Belfast, and the nephrology (kidney medicine) research group.

**RATIONALE**

Several factors combine to make Northern Ireland an important exemplar for the UK and Ireland for advancing collaborative approaches to investigate potential associations between environmental factors and health. These are: a complex geology that represents a microcosm of the UK and Ireland; the availability of comprehensive geological, environmental and medical datasets; and a pioneering collaborative research culture between health professionals, practitioners, and geoscientists. The acquisition, quality assurance and maintenance of data are crucial to ensure an ethical and robust collaborative partnership. Key datasets within the Northern Irish context include detailed information on bedrock and superficial geology (Geological Survey Northern Ireland, GSNI), the comprehensive GSNI Tellus (2004-7) soil and stream geochemistry data surveys. In addition, the Northern Ireland Cancer Registry (NICR), the UK Renal Registry (UKRR) and the Northern Ireland Neighbourhood Information Service (NINIS) provide additional sources of anonymised population data. Combining geological, soil and medical data together with demographic information offers the unique potential to examine the impact of specific environment factors on public health. The accuracy and potential complementarity of the datasets creates the opportunity for a multidimensional spatial investigation of a range of variables. These include: the influence of geographical distribution; total concentration and level of oral bioaccessibility of harmful trace elements in soil on human epidemiology and renal disease. Northern Ireland, as an area with traditionally little movement of people provides greater potential for prolonged exposure at one location or area. Any indications of spatial correlations and inferred links between harmful elements in soil and health have wider implications beyond Northern Ireland for human health risk assessments, and strategic health and education policy development.
Related to such potential risks. The findings from the Tellus Survey and anonymised, population based medical data (cancer and renal) offer the possibility for comparative studies in the Republic of Ireland (related to the recently completed EU funded Tellus Border survey (Geological Survey Ireland, GSI and GSNI) and across the UK.

EXPANDING THE NARRATIVE- COMBINING MULTIPLE DATASETS

Cancer
Cancer remains the second most common cause of death in Ireland, after diseases of the circulatory system (CSO, 2014) with overall cancer incidence expected to increase by 20% between 2010 and 2020, and by 30% between 2010 and 2030 (NCR, 2011) mainly due to population ageing. On average there were 11,861 cases of cancer (including non-melanoma skin cancer) diagnosed in Northern Ireland each year between 2008 and 2012 (NCR, 2014). Complete and reliable incidence information provided by cancer registries is key for use in comparability and disease clustering studies (Zanetti et al. in press). In Northern Ireland, between 1993 and 2003, 8,640 new cancer cases were diagnosed every year. The registry receives and collects electronic data information on all neoplasms diagnosed in Northern Ireland including non melanoma (NM) skin cancers and has an extensive programme of quality assurance of the registry data (NCR, 2008). It allocates area of residence based on postcode. All information is held securely and anonymised before analysis, environmental agents such as radon and asbestos have been causally linked with cancer. The information contained in the NICR database is a uniquely valuable resource and makes Northern Ireland a prime location in which to undertake a multi-layered spatial analysis of the potential links between potentially toxic elements (PTEs) in soil and different cancer diseases.

Renal Disease
An increasing prevalence of Chronic Kidney Disease (CKD) is resulting in a significant strain on health budgets. In the UK, the prevalence of CKD stages three to five is 8.5% with an average cost of renal replacement therapy, including dialysis and kidney transplants, of between £20,000 to £30,000 per patient per year comprising 1-2% of the annual health budget (NHS, 2010; Lewis, 2012). CKD is increasing annually in prevalence within Northern Ireland with an average prevalence of 3% in 2007 rising to 4.8% in 2014 (NISRA, 2014). The UKRR reports on all patients, starting on renal/kidney replacement therapy (RRT, needing dialysis or a kidney transplant) using a detailed dataset electronically downloaded every quarter from all 72 UK renal units (Gilg et al., 2012). Regional and centre level variations in prevalence rates are observed in the UKRR that are not explained by the known factors of age, ethnicity or preceding diseases such as hypertension and diabetes. The unknown aetiology (or causes) in renal disease patients in Northern Ireland was 17.2% of the total incidence rates in 2010 (Gilg, et al., 2012). Arsenic, cadmium, lead and mercury have been identified as nephrotoxins on the human body through the dermal, inhalation and oral ingestion exposure pathways (Ekong et al., 2006; Brewster, 2007; Soderland et al., 2010; Jackson et al., in review). Exploring the spatial distribution of naturally occurring nephrotoxins in soils offers the potential for fresh insights into the observed geographic variation of long-term chronic disease.

Potentially Harmful Elements in Soils
A key focus of research since the completion of the Tellus Survey has been to investigate the potential risk to human health associated with elevated total concentrations of PTEs in soils. Using Tellus Survey shallow soil geochemical data in conjunction with supplementary bioaccessibility testing of selected soil samples following the Unified BARGE Method (UBM), Barsby et al., (2012) found that for some soil parent materials
hosting elevated PTE concentrations, the measured oral bioaccessible fraction was relatively low. For other soil parent materials with relatively moderate total PTE concentrations, the measured oral bioaccessible fraction was relatively high. The discrepancy between high recorded total concentrations with lower oral bioaccessibility for certain areas has been related to elemental speciation and solubility both in the soil environment and during UBM extraction (Palmer et al., 2014; Cox et al., 2013). Palmer et al. (2015) found similarities in total and partial lead concentrations suggesting a large proportion of lead in Northern Ireland may be highly soluble and therefore potentially bioaccessible.

AN INTEGRATED SPATIAL METHODOLOGY

Medical data
Ethical approval is required to use medical data. An interdisciplinary study by McKinley et al. (2013) investigated the incidence of twelve different cancer types (lung, stomach, leukaemia, oesophagus, colorectal, bladder, kidney, breast, mesothelioma, melanoma and non-melanoma basal and squamous skin cancers), over a 12 year period (1993 to 2006). Ethics approval for this study was given by the NHS National Research Ethics Committee. Anonymised cancer datasets were provided by the NICR in the form of postcode, gender age group and disease code. In any study of medical data, population density and age distribution variations across the area of investigation need to be take into account. Age standardisation takes the frequency of disease by age (and gender) group in each administrative unit and the standard population (Bland, 1996; Donnelly & Gavin, 2007) to provide the Age Standardised Incidence Rate (ASIR). Several wards in county Armagh showed high ASIRs for stomach cancer for the period 1993–2006. Mapped ASIRs demonstrated highest incidences rates for NM squamous skin cancer for both sexes located in the Southeast of Northern Ireland (Fig. 1a). High measured oral bioaccessibility shown for arsenic and lead align with the south Armagh region (Palmer et al., this volume). A local cluster technique Moran’s I was used by McKinley et al. (2013) to identify statistically significant spatial outliers in the cancer disease datasets (Fig. 1b).

Geochemical data
Several tens of elemental components, obtained from different sample materials and with different analytical techniques, are generated by geochemical surveys such as the Tellus and Tellus Border surveys (Young & Donald, 2013). The data are used to produce elemental concentration maps and to explore associations between elements. Fundamental in the use of geochemical data within a multidimensional spatial approach is an awareness that geochemical maps do not actually represent absolute abundances. At every sampled or interpolated point on an elemental map, a concentration value provides information only on the relative weight of one particular element to the total (Tolosana-Delgado & van den Boogaart, 2013). The challenge is how to respect this relative nature of geochemical data in the integration of multiple data sets. A log-ratio approach (Aitchison, 1986; Pawlowsky-Glahn & Buccianti, 2011) was undertaken by Jackson et al. (in review) to analyse interactions between elements. The aim was to shed light on the interactions between elements: the role of essential elements as protecting mechanisms against toxic elements, while others increase the uptake of toxic elements as a result of similar absorption mechanisms. A deficiency of calcium can enhance the uptake of Pb (Loghman-Adham, 1997). Several areas (Fig. 1c; for example the Mourne mountain areas) show a deficiency of Ca relative to Pb and therefore may indicate a higher uptake of Pb.

Exploring spatial relationships between disease data and explanatory factors
Care needs to be taken in comparing medical data aggregated to a certain spatial level to explanatory factors measured at regional or other levels of aggregation. This can lead to misconceptions of relations that are more related to the change of aggregation level than the data. McKinley et al. (2013) used Geographically Weighted Regression (GWR) to provide a local model of the relation between disease data and PTEs. Although the strongest relationship observed in this study was for stomach cancer with arsenic for wards in South Armagh, the results are complex (Fig. 1d). A link may be suggested with high levels of bioaccessible arsenic associated with the metasediments of the Gala Group of the Southern Uplands-Down Longford Terrain (Barsby et al., 2012). However, it is important to note that GWR does not establish a causal relationship and further multivariate data analysis is required within a multidimensional spatial framework.
IMPPLICATIONS FOR POLICY: THE NEED FOR GREATER DIALOGUE BETWEEN SCIENTISTS AND POLICY MAKERS

The aim of interdisciplinary collaboration is to ensure that research findings are made available and any implications discussed between health professionals, practitioners, and geoscientists. This ongoing partnership between geoscientists, NICR and the nephrology (kidney medicine) research group has raised a number of public policy implications for regional human health risk assessments and education. In addition this innovative interdisciplinary research strengthens the argument for better integration of multiple data sets to enhance ongoing medical and social research. In turn this underlines the need for greater dialogue between scientists and politicians.

Impact on the strategic public health agenda

The implications from the existing research are that the complex geological history of Northern Ireland has resulted in geographic variation in elevated total concentrations and levels of bioaccessibility of environmental toxins. Combined with observed and potentially linked geographic variation of long-term CKD and cancer this advocates the need for a more nuanced health policy that reflects this degree of variation across Northern Ireland. One implication from the findings is that screening priorities may need to change to adopt a targeted approach by all health care professionals (GPs, community and school nurses etc.). For example increased screening for certain types of cancer such as stomach cancer specifically in geographic areas with elevated bioaccessible levels of arsenic. This has consequences for resource allocation to support early screening and detection and poses the question whether the current system have sufficient capacity to respond to this at present.

Avoiding a siloed approach to policy development

Information to increase awareness for all health care professionals is key if the implications are to be understood and implemented. The scientific message that cumulative environmental exposures pose risk factors for progressive diseases including cancer and chronic kidney disease needs to be communicated in an understandable way. This also raises the issue of how to educate the next generation about the potential risks of PTEs and certain types of cancers or renal disease.

Enhance opportunities for data linkage

This research has demonstrated the benefits of an integrated multi-layered approach to multivariate data analysis facilitated by a cooperative partnership. However it is clear that more work needs to be done investigating environmental and health variables within a multidimensional spatial investigation. Opportunities include co-harvesting with other cross-discipline data sets, supporting integrative future planning of large spatial environmental surveys and longitudinal health studies. The main roadblocks to integrating multiple data sources as part of mainstream research (such as cost and disparate methods of data capture) need to be identified. Enhanced opportunities for data linkage need to be encouraged and expedited to allow a multicomponent data analysis approach that will help generate even better insights to elucidate the relationship between our environment and health.

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Northern Ireland Cancer Registry (NICR), 2008. [http://www.qub.ac.uk/researchcentres/nicr/AboutUs/, 2008](http://www.qub.ac.uk/researchcentres/nicr/AboutUs/).


