Genomic Med. (2007) 1:129–138
DOI 10.1007/s11568-008-9016-y

RESEARCH ARTICLE

The geography of genetics: an analysis of referral patterns to a cancer genetics service

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Received: 22 October 2007 / Accepted: 31 December 2007 / Published online: 23 January 2008

Abstract This study uses a geographical information system (GIS) and statistical analysis to look for patterns in referrals to a British cancer genetics service. In this case, familial cancers are taken to be those that can develop when an individual inherits DNA mutations that cause an increased risk of cancer. Between 1998 and 2006 the Cancer Genetics Service for Wales received nearly 11,000 referrals for patients resident in Wales and it is the service database recording those referrals which is the subject of this secondary analysis. Using postcodes to match referred patients to areas, deprivation scores were assigned. Referral rates per 10,000 head of population across the 8-year study period by unitary authority are presented, as is information on referrals from primary and secondary care sources by year. Each patient referred has their family history of cancer recorded and is assigned to a risk category; high, medium or average. There are correlations between number of GPs (General Practitioners) in a practice, number of patients referred from a practice, and deprivation as measured by the overall Welsh Index of Multiple Deprivation 2005, such that the two former factors increase as deprivation decreases. Over time there were changes in referral sources, with referrals from primary care overtaking those from secondary care in percentage and absolute terms. There were also changes in the types of cancer referred, risk categories seen and to which centre referrals were made. Referral patterns reveal an inverse relationship between deprivation and health service availability and use.

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Keywords Geographical information system (GIS) · Cancer · Referrals · Wales

Abbreviations

CGSW	Cancer Genetics Service for Wales
DNA	Deoxyribonucleic acid
GIS	Geographical information system
GP	General practitioner
HNPCC	Hereditary non-polyposis colorectal cancer
ISCO	Information System for Clinical Organisation
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
UK	United Kingdom
WIMD	Welsh Index of Multiple Deprivation 2005

Introduction

The geographical and temporal spread of referrals to a cancer genetics service is not a topic that has been widely researched. This article presents an analysis of 8 years of referrals made to the Cancer Genetics Service for Wales (CGSW), using statistical techniques and a geographical information system (GIS) to investigate referral patterns. This study is innovative because it is the first time to our knowledge that a referrals database for a cancer genetics service has been subject to analysis using GIS. Although secondary analysis of service data is a common practice in health services research, the service data collected by CGSW since 1998 have not been subject to substantial research analysis before.

The rising demand for cancer genetics services was first highlighted at the start of the decade (Gray et al. 2000;

Lucassen et al. 2001; Wonderling et al. 2001). As Fry et al. (1999, p. 468) suggest the "*increasing demand for cancer genetics services has necessitated an urgent review of how these services are organised*". This, coupled with the availability of relatively new software tools based around GIS, presented a novel opportunity to research cancer genetics referrals in terms of spatial and temporal variations.

The CGSW follows the Calman–Hine model (Calman and Hine 1995) with distributed clinics in Cardiff, Swansea and Rhyl, and began receiving referrals from primary and secondary care sources in July 1998. Some inherited mutations are attributed to an increased risk of developing cancer and are responsible for the cancers that run in some families. The CGSW seeks to identify those people at greater than population risk of developing cancer and help them to manage their health accordingly. The study area for this research is Wales, as shown in Fig. 1. This composite map shows the road and railway system, together with a selection of towns and the three CGSW centres located in Glan Clwyd Hospital, Rhyl; Singleton Hospital, Swansea and University Hospital of Wales, Cardiff. These centres correspond with coverage, or catchment, areas of north Wales, mid and south west Wales and south east Wales, respectively.

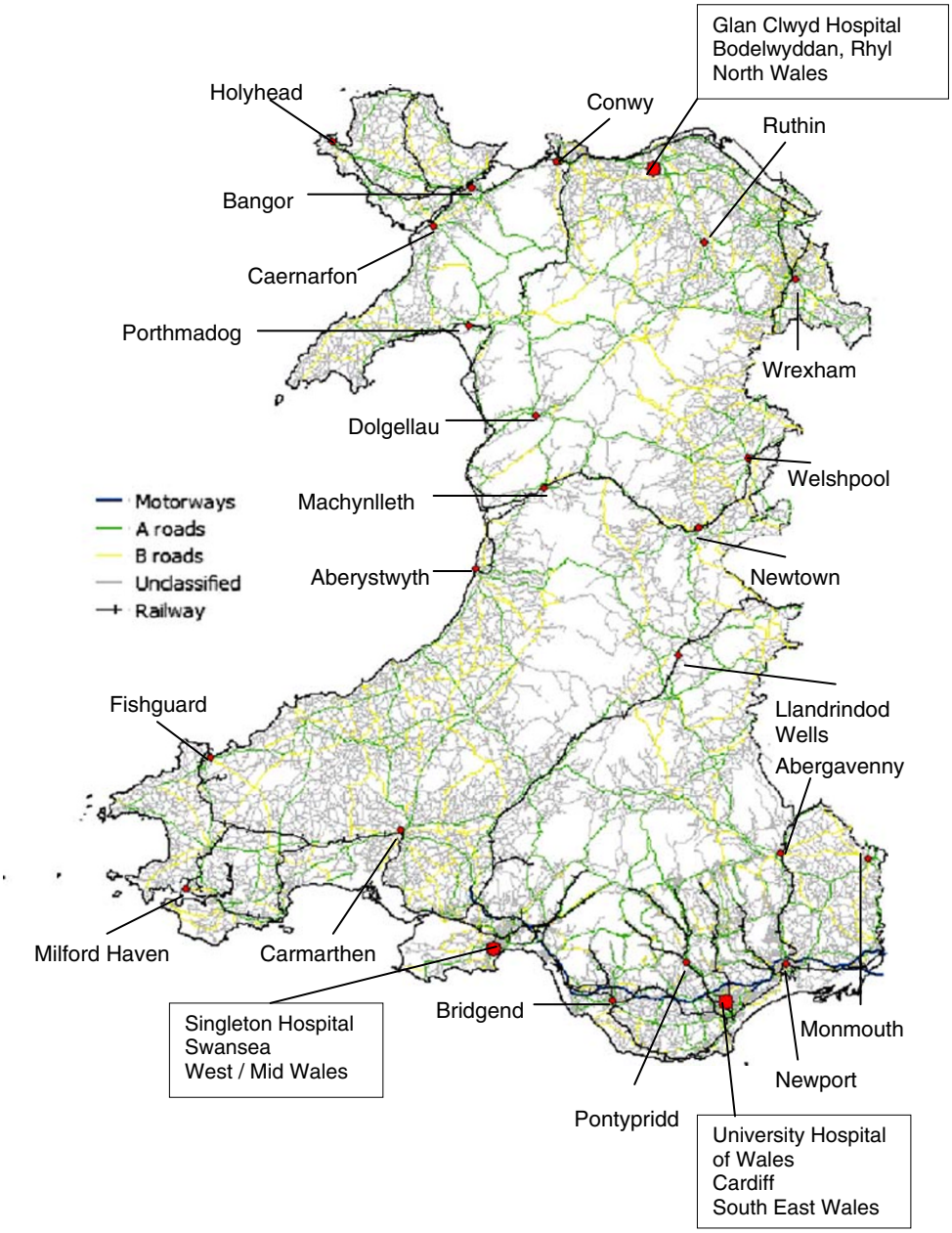

Fig. 1 Wales showing road and railway links, towns and CGSW centres

Referred patients are classified as either average, moderate or high risk. Referrals that do not meet the referral criteria are recorded as 'failed risk criteria'. For those that do meet the criteria, average risk means that a patient is at the same level as any other individual of the same age in the general population, therefore extra surveillance is unnecessary. Such patients are advised to continue health monitoring as they would normally and their care is passed to their GP. Moderate risk patients require ongoing primary care surveillance and management and appropriate specialist intervention, for example Breast Test Wales. Those patients in the high risk category are typically offered a genetic clinic appointment in addition to specialist surveillance, and genetic testing might be offered when relevant.

Wales is divided into 22 unitary authorities, which were created in 1996, each of which has a coterminous local health board, which were established in 2003. The unitary authorities are responsible for all the activities of a local authority except health, which is handled by the local health boards. Figure 2 shows the boundaries of these authorities and boards. The layer of government above the unitary authorities is the Welsh Assembly Government.

Referral patterns in general have been studied before. Coulter (1998) notes that the current NHS referral system is generally successful in terms of keeping health care costs down while ensuring patients are directed to the most appropriate secondary care when it is required. Fernandez et al. (2001) used a questionnaire approach to examine the referral patterns associated with a breast cancer support programme in relation to characteristics of the referring physicians. Trends were investigated in relation to the knowledge, beliefs and behaviour of the physicians; the characteristics of the patients they referred, and practice characteristics. The study presented in this paper is the first attempt at a large scale quantitative analysis of patterns in referrals from all sources to a cancer genetics service.

Methods

This study consists of secondary analysis of existing service data for more than 14,000 recorded referrals over an 8-year period. A patient is referred to the CGSW because either they have been diagnosed with an inherited cancer or they, or a health professional, are concerned that the patient might be at risk of developing an inherited cancer. The CGSW database is held by Information System to Clinical Organisation (ISCO), who provided an anonymised version. On first receipt there were 14,039 patients who had been referred to the CGSW between 1st July 1998 and 30th June 2006. As this study is only concerned with first referrals for patients domiciled in Wales, some deletions had to be made. Deleting follow-on familial referrals left 11,767 entries. After deleting duplicate entries and subsequent re-referrals for the same person, there were 10,976 entries remaining. A further 98 addresses from England were deleted, leaving 10,878 first referrals for Welsh resident patients. The rationale for choosing only first referrals was to avoid any bias that might arise from several familial referrals occurring after a first referral. These follow-on referrals could produce clusters that might not otherwise occur. The rationale for choosing only referrals living in Wales was to keep to the overall catchment area of the CGSW, namely Wales. This reduction in numbers was the first stage in data cleaning. The second stage was to attempt to fill any gaps that the researchers identified in the data, which was done by CGSW staff checking and updating patient records.

For each patient, the ISCO database contains inter alia an identification number used by the CGSW to track referrals, title, gender, name, address and telephone number. The GP for each referral is recorded, including a unique GP code. Referral details include the reason for referral given on the referral letter, who made the referral, the date it was made and the date it was received. Once a referral has been registered, the family history of cancer, type of referral (either primary, secondary or self-referred) and types of screening to be implemented, if applicable, are recorded. Risk assessment data are based on a questionnaire, which allows risk assessment classification and date of assessment to be recorded too.

The dataset obtained from ISCO did not include individual level socio-economic data beyond date of birth and gender, therefore it was necessary to assign characteristics to patients based on their residence postcode. This leaves this study open to the charge of ecological fallacy, that is using group characteristics to describe individuals, but given the lack of suitable point data, there was no practicable alternative. See Curtis (2004) and Phillips et al. (2000) for further discussions on ecological fallacy.

Data were drawn from other sources to complement the ISCO database. These sources included mapping data from Ordnance Survey, deprivation data from the Welsh Assembly Government (2007) and health data from the Department of Health (2007). Datasets were combined using common fields, for example two datasets might contain different data on the same unitary authority, so they could be merged using that common field. The combined datasets were analysed using GIS and standard statistical techniques. A GIS allows data to be mapped, visualised and analysed in spatial context.

To test if deprivation is related to health care provision, deprivation must be defined. There have been many attempts to measure deprivation such as the Townsend Material Deprivation Index (Townsend et al. 1988), the

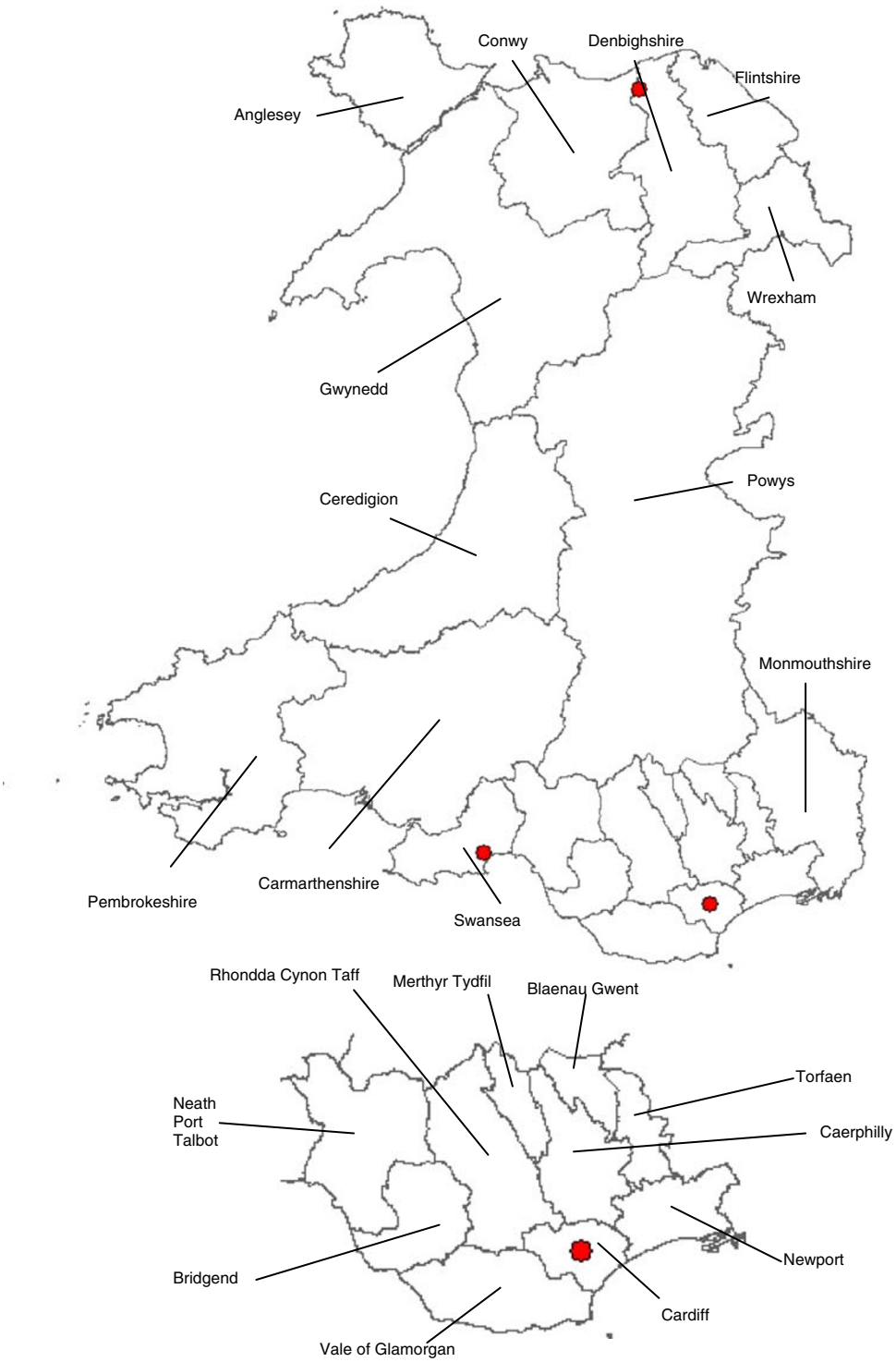

Fig. 2 Unitary authorities and local health boards

Carstairs Deprivation Index (Carstairs and Morris 1989, 1991) and the Index of Multiple Deprivation (National Assembly of Wales 2000). In 2005, the Index of Multiple Deprivation was updated to become the Welsh Index of Multiple Deprivation (WIMD) 2005 (Welsh Assembly Government 2005). All three indexes uses data from the UK-wide Census, the last of which took place 29th April 2001.

The WIMD gives an overall value for each of the 1896 lower super output areas, and comprises seven domains. Lower super output areas are the next level above Census enumeration districts (see Vickers and Rees (2007) for

more on the creation of 2001 Census output areas). The domains that make up the WIMD are: access to services; education, skills and training; employment; health; housing; income, and physical environment. For this study, the WIMD was chosen because it is the index used by the Welsh Assembly Government, and it has a domain which focuses on health, which is most relevant here.

Standard statistical tests used included partial correlation, as this allows for controlling factors, hence is more meaningful than total correlation. Cohen (1988) interpreted correlations within three bands: small (±0.10 to ±0.29), medium (±0.30 to ±0.49) and large (±0.50 to ±1.00). These values are acceptable within the multi-factorial social sciences, so are appropriate for this study. Using Cohen's bands, a correlation between 0 and ±0.09 is too trivial to be considered a correlation. As the direction of correlation was unknown, two tailed tests were used. Given the large number of statistical tests that are necessary when exploring a database of this size, a very strict definition of statistical significance is necessary. For this study, P is less than or equal to 0.001 before statistical significance is claimed.

Partial correlation is used to investigate the effects of primary care practice factors, deprivation and location. The controlling factors are age of referred patient at referral, gender of referred patient and referrer type. The factors investigated are presented in Table 1.

Results

Each referral was assigned to a CGSW centre, with 4,992 (46%) referrals going to Cardiff, 3,212 (29%) referrals going to Swansea and 2,548 (23%) referrals going to Rhyl. A further 126 (1%) referrals had insufficient information on the database to determine to which centre they were assigned. Over 91% (9,942/10,878) referred patients were female. Family histories of particular cancer types could be determined for 88% of referrals, as shown in Table 2.

From 10,878 referrals, around a quarter did not return the CGSW family history questionnaire requesting further information, so while they remained on file, no further action could be taken, see Table 3. Around 1% actively withdrew from the process, and a slightly higher percentage had a risk status that could not be determined from the information provided. A further 10% of referred patients either had no data to enter, or did not have any data entered onto the database concerning their risk assessment. Altogether, 43% of all referred patients had a high or moderate risk level, thus requiring active management.

As the residence of all but eight referred patients could be matched to a unitary authority, it was possible to show referral rates per 10,000 head of population over the 8-year study period for each unitary authority. Figure 3 maps these ranked referral rates for the whole study period. Of the 10,870 referred patients for whom data were available,

Table 1 Factors included in partial correlations

CGSW centre
12-month band during which referral was made
Unitary authority
Family history
Risk category
Number of GPs in a practice
Number of female GPs in a practice
Number of male GPs in a practice
Practice list size
Number of patients referred from the practice
WIMD 2005 overall score
WIMD health domain score.

Table 2 Family histories

Number	Percent	Cancer type
5,992	55.1	Breast cancer
1,468	13.5	Colorectal cancer
791	7.3	Breast and ovarian cancer
663	6.1	Ovarian cancer
589	5.4	Other cancer
46	0.4	Hereditary non-polyposis colorectal cancer (HNPCC)
24	0.2	Gastric cancer
13	0.1	Familial adenomatous polyposis coli
13	0.1	Renal cancer
12	0.1	Prostate cancer
9	0.1	von Hippel Lindau syndrome
1,248	11.5	No data
10	0.1	Not known, insufficient information in referral letter

Table 3 Risk assessment

Number	Percent	Risk category
1,719	15.8	High risk
2,946	27.1	Moderate risk
1,661	15.3	Average risk
477	4.4	Failed risk criteria
7	0.1	Living affected relative
173	1.6	Risk status uncertain
2,670	24.5	Non-returner
953	8.8	No data
160	1.5	Not entered
112	1.0	Withdrawn

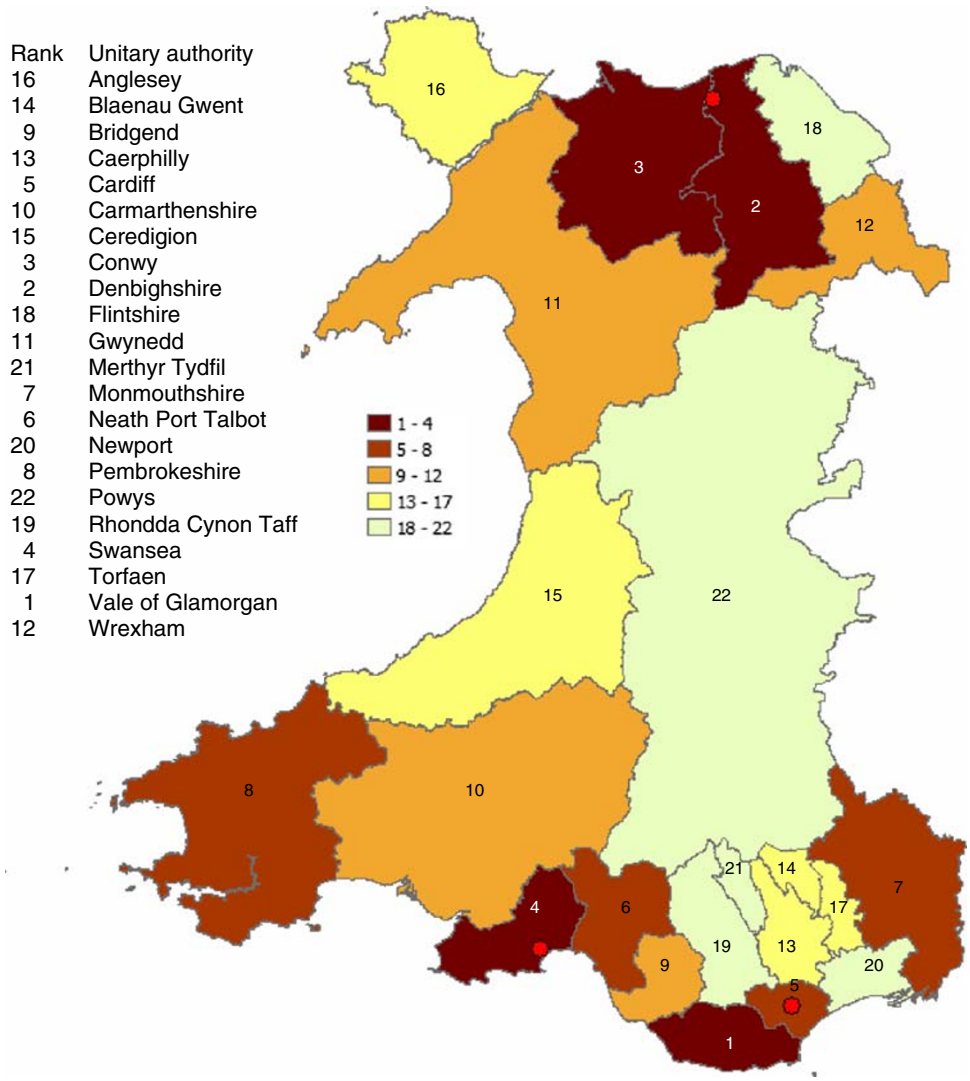

Fig. 3 Ranked referral rates per 10,000 head of population, by unitary authority

the highest referral rate was from the Vale of Glamorgan, with 52.5 referrals per 10,000 head of population, while the lowest rate came from Powys with just over 19 referrals per 10,000 head of population. The average for Wales as a whole was 36.75.

The CGSW receives referrals from primary (e.g. GP) and secondary care (e.g. gynaecologist) sources, therefore is both a secondary and tertiary service. There was also a minority of self-referrals (45/10,878. 0.04%). In the first 3 years, secondary care referrals outnumbered primary care ones, but that has reversed in recent years, and primary care referrals now make up 51% (5,642/10,878) of all referrals. In 1998/1999 primary care referrals accounted for 36% of all referrals, by 2005/2006 this had risen to nearly 57%. In absolute numbers, referrals from secondary care rose from 192 to 748 over the same 8-year period, but in percentage terms fell to less than 43% of all referrals in 2005/2006. Plotting risk category against referral source shows that high risk referrals are more likely to come from secondary care sources and moderate risk referrals are more likely to come from primary care ($\chi^2 = 121.431$, $P \leq 0.001$).

Adopting the stringent criteria for statistical significance and correlation strength noted above, there are some significant correlations which are unlikely to be the result of chance alone. The CGSW centre to which a referral is made is associated with unitary authority (0.174, $P \leq 0.001$), so that the centre to which a referral is made can be predicted from the unitary authority of residence. Further investigation reveals that Cardiff receives a higher proportion of referrals from primary care, while Swansea receives a higher proportion from secondary care. Rhyl receives the most self-referrals. The year in which a referral is made is correlated with the family history of cancer type of the referred patient (0.122, $P \leq 0.01$), and also with their risk assessment category (0.175, $P \leq 0.01$). Further investigations show that the correlation between

year in which a referral is made and family history of cancer type of the referred patient was due to an increase in the number of less frequently referred cancers and a decrease in the ovarian cancer referrals year on year. It also revealed that declining average and high risk assessments year on year were responsible for the correlation between risk category and year a referral is made. The preceding correlations are all significant but small (Cohen 1988).

All five primary care practice factors (total number of GPs, number of male GPs, number of female GPs, practice list size and number of patients referred from a practice) are correlated with each other (0.202–0.832, $P \leq 0.01$). The number of GPs within a practice is correlated weakly with the WIMD overall (0.120, $P \leq 0.01$) and WIMD health (0.112, $P \leq 0.01$). This shows that as levels of deprivation decrease, the number of GPs in a practice increase. The number of patients referred from a practice is correlated with the WIMD overall (0.169, $P \leq 0.01$), such that as deprivation decreases, so the number of patients referred from a practice increases.

There were changes in referral patterns to the CGSW centres over time. The percentage of referrals going to Rhyl fell and the percentage going to Swansea rose. For years 1999–2000 to 2002–2003, Rhyl was consistently receiving 26% of all referrals annually, but then from 2003–2004 to 2005–2006 this dropped to around 21%. Over the same time periods, referrals to Swansea rose from around a quarter to around a third of all referrals annually.

Discussion

Of 10,878 referrals considered, 25% were withdrawn or did not return the family history questionnaire, so did not continue with the referral. Only 43% had a risk level assessed and categorised as moderate or high risk, the remainder were at no greater than population risk, or their risk status was undetermined. One possible reason for a quarter of referrals not being pursued is that the patient did not request the referral, but was referred by a hospital consultant or their GP without their knowledge. Another is that the family history questionnaire is long and complicated, so some patients are put off by the amount of time it takes to complete, or perhaps lack the necessary language or comprehension skills. This might also, in part, explain the differences found in service access and use between most and least deprived areas.

Protheroe et al. (2006) found that CGSW guidelines placed some women referred for a family history of breast cancer into a higher risk category than the National Institute for Health and Clinical Excellence (NICE) guidelines. From their sample of 75 referred women, 23% would have been placed into a lower risk category if NICE guidelines had been adopted, which would have reduced the percentage of referred patients at moderate or high risk in this study even further.

Referred patients classed as high risk were more likely to come from secondary care than primary care sources, while moderate risk referrals are more likely to come from primary care. It is possible that further assessments undertaken in secondary care lead to a patient being considered at higher risk than was previously the case e.g. if a woman is in for a mammogram after having discovered a breast lump. In secondary care there are more resources immediately available than in primary care, with fewer patients to be seen per health care professional, and therefore more time to spend on assessing each patient. This greater level of resources, especially time, means that in secondary care it is possible that an appropriate high risk conclusion is reached before referral, and that someone at moderate risk, who can be managed in the community or hospital, is not referred on. It is also possible that specialists in secondary care have a greater knowledge of cancer genetics risk factors than generalists in primary care simply by virtue of seeing more such cases. Watson et al. (2001) reported that GPs were likely to raise the issue of family history with patients, even if those patients did not meet the referral guidelines from the regional genetics service, which might explain the higher level of moderate referrals from primary care.

Over 91% of referred patients were female. There are a number of factors that could account for this preponderance of female referrals. It is known that for breast cancer 99% of cases are in women (Cancer Research UK 2007), which is borne out by these data, with only 0.7% of breast cancer referrals being male. An additional explanation could be the reluctance of men to take care of their health (Conrad and White 2007). Those men that are referred are less likely to be at high or moderate risk than women. The fact that men are more likely to have an unknown or uncertain risk assessment could be due to the types of cancer that affect men. Breast and ovarian cancers combined account for 68.5% of all the CGSW referrals, and the screening tools for breast cancer are well validated and accurate, at least for older women.

Ranks of referral rates per 10,000 head of population by unitary authority showed that distance to a CGSW centre is not a predicting factor. While Powys, which is the furthest unitary authority from any CGSW centre in terms of distance has the lowest referral rate, Newport, which is adjacent to Cardiff, home of the largest CGSW centre, has the third lowest referral rate. The Vale of Glamorgan, which is also adjacent to Cardiff, has the highest referral rate. This is supported by previous work on referral patterns which show that distance is not necessarily the most influential factor (Martin and Williams 1992; Field and

Briggs 2001). Powys shares a long border with England, and Jones (2002) noted referrals being made to England. For this study, some of the genetics services on the English side of the border were contacted. One service in the North West received between five and ten cancer genetic referrals per year from Wales, all of which were returned with advice to make a referral to the CGSW. Another service in the West Midlands accepted about 25 referrals per year. As noted above, there were 98 referrals from England on the ISCO database that were removed during data cleaning. Therefore the number of patients crossing the border for cancer genetics services is small in comparison with the total number of referrals. McDonald et al. (2004) reported a correlation between distance of unitary authority from a CGSW centre and referral rates on a database of just over 4,000 referrals from 1998 to 2002. However, that pattern no longer holds true for the 10,878 referrals received between 1998 and 2006. This might be due to the rapid rise of primary care referrals as opposed to the more gradual increase of secondary care referrals.

At least two previous studies (Quinn et al. 2004; Murugan et al. 2005) have shown that referrals from secondary care outnumber those from primary care. This was the case with the CGSW initially, but that situation has now reversed. More referrals from primary care mean that patients are entering the CGSW system at an earlier stage, so if they are moderate or high risk, will come into contact with the surveillance services earlier that would otherwise have been the case if they had come via secondary care. One reason for patients referred from secondary care being at higher risk might be because they have already developed symptoms which could indicate an inherited cancer. For those patients who would benefit from screening, being referred from primary care means that they will have access to that screening sooner, which is beneficial.

The juxtaposition of high and low deprivation areas is clearly identified in cities, but rural areas appear to be more homogenous on maps. While it is possible that rural areas are indeed homogenous, it is also likely that the analysis failed to display any pockets of deprivation in deep rural areas. It is possible that, as suggested by Jordan et al. (2004) any small pockets of deprivation are in fact being "*diluted*", or masked by larger, less deprived parts of the same geographical areal unit.

Jones (2002) investigated potential reasons for variations in referral decisions using a semi-structured questionnaire approach to investigate referral behaviour of GPs in eight practices in Powys, a predominantly rural area of Wales. As well as gauging the level of awareness of cancer genetics services in general, Jones' study also investigated the extent to which GPs and practice nurses were aware of referral guidelines issued by the CGSW. During the course of the study, it became evident that several of the GPs had referred patients to centres across the border in England. Findings from the interviews with doctors and nurses suggested that patients in this rural area were just as likely to want to be referred to such tertiary services and that the distance patients would need to travel to access a cancer genetics centre was not an influence on their decision to refer but it might have any effect on where to make the referral. Thus, due to the topography and road and rail networks, patients in this locality were more likely to be referred to Birmingham (75 miles by road) than Swansea (105 miles). However, findings from the study suggest that "*rurality is not an issue when referral is important for nurses or doctors.*" (Jones 2002, p. 27).

Reasons for variations in the centres to which referrals are made are speculative but could include referrals to Rhyl reaching a plateau, or a saturation point where the number of referrals likely to be received each year will remain more or less constant in the future. Conjecturally, reasons for this might be that all families with inherited cancers have been identified in the north Wales catchment area, or all relevant health care professionals in that area are now fully aware of the CGSW. There might alternatively be evidence of an increasing affluence within the Swansea catchment area of mid and south west Wales, as more affluent people are more likely to be referred. A further reason could be changes in staffing levels across the centres due to natural wastage and new recruitment.

The correlation between the CGSW centre and the unitary authority in which a referred patient is resident is to be expected given CGSW's informal area-based referral policy. Where there are variations, these might be due to personal circumstances of the referred patient, or the preferences of the person making the referral. The catchment areas were set up for management purposes, so do not necessarily reflect the situation on the ground. For example, patients resident in north Powys live closest to the CGSW centre in Rhyl, those resident in south east Powys live closest to the centre in Cardiff, yet all Powys residents should be referred to Swansea.

Referral rates increase as deprivation decreases. This might be because less deprived people include those who better understand how to utilise the services available to them and are more vocal when they believe they are not receiving the care they deserve. This is a likely hypothesis given that Pell et al. (2000) demonstrated that affluent patients are more likely to have their cases classed as urgent. Affluent patients are less likely statistically to become seriously ill, therefore it can be concluded that, rather than simply having more urgent illnesses, they are better able to communicate a sense of urgency when being assessed by their doctors. More affluent people might be more aware and informed about the risks of familial cancer, therefore are more likely to seek a medical opinion.

Also, since only 43% of referrals to CGSW in this study were in fact found to have a higher than population risk, it can be argued that the referral system is susceptible to influence by those who are more able to argue their case, that perhaps some patients overstate the urgency or have a higher perceived sense of risk.

Research conducted in north Derbyshire by Maheswaran et al. (2006) studied the effects of deprivation and travel distance on breast cancer screening uptake. They found that attendance for screening was inversely proportional to socioeconomic deprivation and that increasing distance from a screening unit was associated with decreasing attendance levels, concluding that socioeconomic inequality in breast screening uptake continued to exist and that there was a small distance decay effect. In contrast, other studies have found that the relationship with distance is not uniformly linear. Field and Briggs (2001) for example, in a study of patients accessing services in Northamptonshire, found that utilisation did not decline linearly with distance but that instead the relationship tended to be 'U shaped', suggesting a more complex relationship. In this paper, there is no discernable linear distance decay effect, which also suggests a more complex relationship.

Conclusions

This study has revealed an inverse correlation between the WIMD and the number of patients referred from a practice, showing that more referrals come from practices in less deprived areas.

Building on the base established here, further research can follow. Areas of interest include finding explanations for why so many referrals are for patients at less then moderate or high risk. Further work with just high risk referrals would add to the understanding of inequalities and inequities in referral patterns.

The fact that inequalities in service use to a secondary/tertiary level service have been identified should be of interest to the government and those in charge of health care and health care policy-making in and for local authorities. Tackling inequalities in health is one of the top six NHS priorities, and GIS analyses can help to pinpoint exactly which areas are most in need of additional health care resources in order to meet the Health Inequalities Public Health Service Agreement (PSA) target of reducing inequalities by 2010 (Health Inequalities PSA Target 2006/2007).

More specifically, the findings of this research will be of direct use in informing service provision for the cardiac genetics service planned for Wales by 2010. The fact that referral patterns to the CGSW vary inversely with deprivation in lower super output areas should be of concern in the planning of a new tertiary genetics service for Wales, access from deprived areas should be a prominent factor guiding location decisions, and measures should be taken to ensure that GPs working in all practices are fully informed of referral guidelines.

Acknowledgements Dr. Paul Norman, University of Leeds, for kind permission to use his Townsend index data set. All maps used in this study are created from data provided by Ordnance Survey via EDINA Digimap, and used with kind permission. Tenovus the cancer charity for grant funding research at CGSW. Dr. Jonathon Gray for setting in place the facilities to allow this research to be conducted. Dr. Alex Murray for commenting on a draft of this paper.

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