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REVIEW

The use of genealogy databases for risk assessment in genetic health service: a systematic review

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Abstract The use of electronic genealogical databases facilitates the construction of accurate and extensive pedigrees for potential use in genetic services. Genealogy databases can be linked to specific disease databases, such as cancer registries, in order to increase the accuracy of pedigrees used, and inform the genetic risk assessment. To review the published literature on the use of genealogy databases to construct pedigrees for risk assessment in genetic health service, a systematic literature search was undertaken using 12 combined search terms to identify all relevant published articles. Data sources**:** EbscoHost, PubMed, Web of Science, Ovid and the "grey literature", as well as the reference lists of identified studies. Of 1,035 titles identified, two papers described a study on the use of genealogy databases in cancer risk assessment and two were discussion papers. While authors of the four papers described the potential use of genealogy databases in clinical genetic services, such use has not been adequately investigated and further research is required.

Keywords Genealogy databases · Genetic service · Cancer registry · Risk assessment · Systematic review · Genealogy · Databases · Health services

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Introduction

Genealogical records, both private and public, exist in many forms and have often been kept for a long time. Examples of old genealogy records are from the Royal Family of Japan, the genealogy descriptions in the Holy Bible and in an Irish textbook written in 1649 describing the Irish settlement (Wikipedia 2011; Firbishigh 1649–1653?). Recently, genealogy data have been stored in an electronic format and are sometimes available online (General Register Office for Scotland 2007). As an example "The Scotland's People" database, holding approximately 50 million records, which is accessible to those paying a small fee (General Register Office for Scotland 2007). The Mormon Church in Utah maintains a large public genealogy database, "FamilySearch" (New FamilySearch 2007) and has supported genealogical research for decades. This database is widely accessible and includes information on living or deceased individuals. Members of the church are encouraged to supply information

about their family history, relationships, and other data (New FamilySearch 2007; Cannon Albright 2008). The Utah Population Database (UPDB; Cannon Albright 2008) is another large database holding genetic, demographic, epidemiological, and medical information on approximately 6.4 million people, mostly Utah Mormon pioneers and their descendants. This database was created for research only and has restricted access. In some cases, databases have been formed to enable genealogical studies to identify specific disease genes. One example is the Anabaptist Genealogy Database of Old Order Amish of Lancaster County (Agarwala et al. 1999).

The Scandinavian countries and some other countries have National Population Registries that are updated regularly (Population Registry Centre 2006; Ekbom 2011; CPR-kontoret (http://www.skra.is/pages/1003); Hagstofan 2007; Folkeregisteret 2007). The information documented is demographic, i.e. names, dates of birth and death, addresses, identification numbers and citizenship. Other databases containing personal information on a large number of people are disease registries and of those, the cancer registries are the most common. Available in most Western countries, population-based cancer registries provide a source of information on the occurrence and outcome of cancer in defined population groups (Ringborg et al. 2008). Another example of specific disease registries are the rare bleeding disorder registries (Peyvandi and Spreafico 2008).

Iceland has a number of population-based genealogy databases, due to a longstanding general interest in genealogy. The first census to cover a whole nation was conducted in Iceland in 1703 (Tulinius 2011). As the Icelandic population has been historically stable and detailed genealogy records have been kept for centuries, genealogical records in Iceland are highly reliable and comprehensive, making ancestral tracing relatively straightforward (Stefansson and Taylor 2006; Tulinius 2011). One large electronic database is the genealogy database of the Genetical Committee of the University of Iceland (GCU) available for research and clinical use (unpublished data/personal communication, 15). The GCU database was launched in the 1960s and is now run jointly by Landspitali–National University Hospital and the University of Iceland. This database was constructed using the records from the national census from 1910 onwards and has, since 1953, been updated with data from the National Registry. Information from old parish records on births, deaths and marriages were added to the database as well as available information on migration. The database holds accurate information on almost all Icelanders born after 1840 and a number of individuals born before that time. To link individuals, a "mother's record" has been created for each woman who has given birth, including her name and identification as well as the name and identification code for each of her children and the father of each child (Tulinius 2011). A large number of studies that have been based on the database have been published; among them, most of the Icelandic cancer family studies. Islendingabok, another recent and large Icelandic genealogy database, is run by deCODE Genetics (OoSPa 2004). It is privately owned and accessible with restrictions to all Icelanders with a unique Icelandic personal identification number (kennitala). Individuals are able to use the database for themselves; to find out how they are linked to other Icelanders and to trace their ancestry. Islendingabok is not used in clinics and has been used in research by deCode Genetics. The database has been used in numerous research projects such as in mapping of loci-affecting disease phenotypes and other genetic traits (Gulcher et al. 2001).

The Icelandic National Registry (Þjóðskrá 2007) was established in 1953. It holds extensive information on all Icelanders (Íslands) and is accessible to all Icelanders in a restricted way. The population-based Cancer Registry is operated by the Icelandic Cancer Society (2010). In Iceland, cancer diagnosis recording is mandatory, making the registry comprehensive and accurate for its use in surveillance and research. Information regarding the accuracy and completeness of the Cancer Registry has not been published, but these parameters are thought to be up to 99 % (personal communication).

The pedigree is an essential tool for identifying individuals at risk of genetic diseases, to determine needs for genetic testing and for genetic counselling (Bennett et al. 1995). Genealogy databases have the potential to facilitate the construction of pedigrees. For instance, the clinical genetics service at Landspitali, the Cancer Registry and the GCU has collaborated in generating cancer pedigrees for genetic counselling since 2006 (personal communication). The accuracy of databases may however differ depending on how the data was collected and this may limit their clinical application. We were interested in identification and analysis of existing work on the use of genealogical databases in genetics healthcare. We did this by performing a systematic literature review (22) of the published literature in English. In this paper, we describe our results and discuss the possible reasons for the apparently very limited use of such databases.

Materials and methods

Data sources and searches

We conducted a systematic review following the method described by the Centre for Reviews and Dissemination (Dissemination CfRa 2009). We carried out a systematic search in October 2011 for papers in English on the use of genealogy databases in genetic health care. Four electronic

databases, PubMed, Web of Science, OVID and CINAHL EbscoHost were searched for papers published in peer-reviewed journals, theses, reference lists of relevant papers and articles in the "grey literature". The "grey literature", is "the term used for documents and ephemeral material issued in limited amounts outside the formal channels of publication and distribution" (Library HS Grey Literature 2011). The search was conducted using the following combined search terms:

- Genealogy database* AND genetic risk AND family history
- Genealogy database* AND clinical genetics
- Genealogy Database* AND medical AND family history
- Cancer registry AND genetic service
- Cancer registration AND clinical genetics AND genealogy
- Database* AND family history AND genetic risk assessment
- Genealogy database* AND cancer registry
- Database* AND genealogy AND genetics
- Genealogy AND database
- Genetic counsel* and clinical genetics AND genealogy
- Cancer genetic counsel* and genealogy.

The inclusion and exclusion criteria are described in Table 1.

Abstracts of the identified papers were reviewed for relevance by the authors VS and HS using the inclusion and exclusion criteria. In total, 1,035 titles were retrieved (Fig. 1). Of those, 260 were double publication, 598 were excluded on the basis of title alone. Of the remaining 125 papers, 121 were excluded after further examination, leaving four articles for inclusion in the review (Table 2).

Table 1 Inclusion and exclusion criteria

Parameter	Inclusion criteria	Exclusion criteria
Location	Any country	
Population	Human genealogy databases	Epidemiological studies
Language	English	Non-English
Time frame	January 1970–October 2010	
Type of paper	Research articles, conference papers, discussion papers, thesis	Magazine and newspaper articles, internet news
Main theme	Focused on the use of genealogy databases in genetic health services	Focused solely on use of genealogy databases for the purposes of genetic research rather than clinical service (e.g., mapping a gene)

Quality appraisal

The authors VS and HS used the quality appraisal tool for cohort studies designed by the Critical Appraisal Skills Program (Health SfP Critical Appraisal Skills Programme 2010) to evaluate the research-based paper (Brewster et al. 2004). The score was set at 93 %. The quality of the discussion-based papers was not formally appraised.

Data analysis

We constructed a table of the papers to record the salient features of each (Table 2). The papers were then thematically analysed (Clark 2003) for key codes, categories and themes within and across papers. As a meta-analysis was not possible, we present the findings in textual form under themes.

Findings

Description of selected papers

The search resulted in identification of two discussion papers from the USA (Cannon Albright 2006; Tu and Mason 2004) and two research papers, one from Scotland (Brewster et al. 2004) and the other one Icelandic (Thorsson et al. 2003). The Scottish research paper, described the use of a cancer registry-based service health care (Brewster et al. 2004). The Icelandic paper described how using a genealogy database in finding relatives for screening for familial hypercholesterolemia (FH) identified more patients than the conventional method. Overall, we found very little written evidence in the literature of the use of genealogy databases in genetic health service. However, none of the selected articles argued against such use. On the contrary, the main concept of the four articles was the recognised need for electronic genealogy databases and their possible linking to medical records or disease databases. The key outcomes of each paper are presented in Table 2. We present the findings under the themes (1) perceived value of electronic databases, (2) privacy issues and (3) future use of genealogy databases.

Perceived value of electronic databases

The perceived use of databases differed in the selected papers. While both the Scottish one and the Icelandic one (Brewster et al. 2004; Thorsson et al. 2003), described the use of a genealogy database in clinical service, Cannon Albright (2006) discussed the enormous possibilities of using such databases in both clinical service and research.

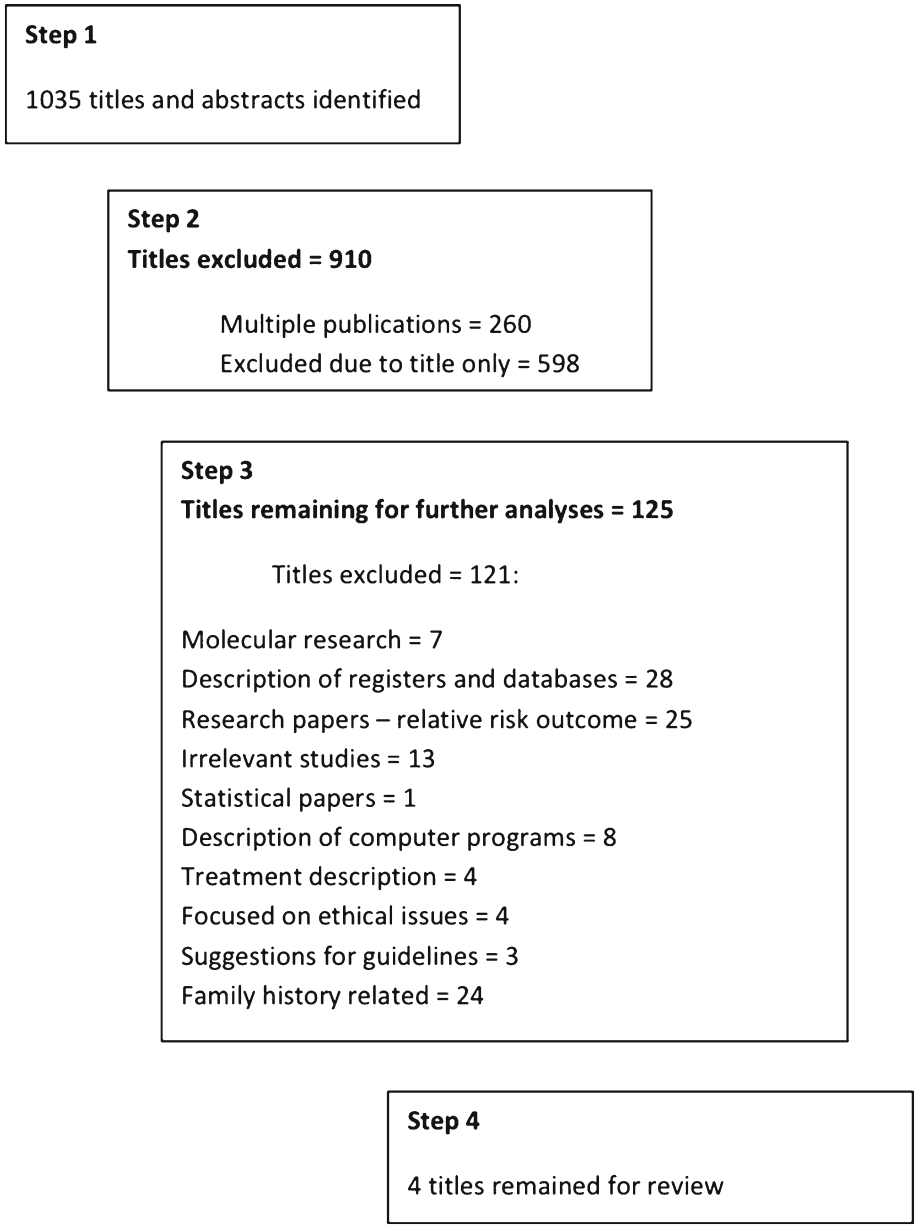

Fig. 1 Retrieval and selection of papers

Tu and Mason (2004) focused on the value of linking different databases to facilitate better surveillance in clinical care. Genealogy databases, linked to medical history or disease databases, could be used to guide medical decision making (Cannon Albright 2006), to identify individuals at risk (Thorsson et al. 2003), to make accurate risk assessment, for evaluation of cancer screening and treatment services (Brewster et al. 2004) and to follow up and coordinate service for individuals and whole families even if the family structure changes (Tu and Mason 2004; Thorsson et al. 2003). It was also described how the cancer registry-based genealogy service using the online public records of the General Register Office of Scotland (birth, death and marriage records) led to changes in the family history and enabled different risk categorisation and management for a number of counselees over a 12-month period (Brewster et al. 2004). Their article did not report on differences in accuracy when using the database as opposed to proband-generated pedigrees.

The tracing of FH probands to common ancestors, using a genealogy database, added considerably to the conventional method of FH cascade screening, where first-degree relatives are tested (Thorsson et al. 2003). The possibility of linking data from different databases, some already existing, by either of two methods was described (Tu and Mason 2004). The first method was a first-order linkage where information on a single individual could be linked together in different databases.

Table 2 Main outcome of selected papers

Authors	Title	Type of paper	Description	Results	Conclusion
Tu and Mason (2004)	Organising population data into complex family pedigrees: application of a second-order data linkage to State Birth Defects Registries	This paper is a discussion paper and includes no primary data	Discusses the possibility of using previously collected data in clinical health care. Also describes the best way of organising and collecting such data	Description of available data in diverse national and regional databases and how the data can be used	The power of data collected routinely into regional and national databases is underused in clinical health care
Cannon Albright (2006)	Computerized genealogies linked to medical histories for research and clinical care—a national view	Symposium proceedings. This is a discussion paper with no primary data collection or results	Discussion of the possibilities of combining genealogy data with medical histories	The use of linked genealogy databases and medical histories can enhance the power of research and make clinical care better	Genealogy data can contribute widely to the understanding of familial and genetic factors in human health and disease
Brewster 2004	Impact of a cancer registry-based genealogy service to support clinical genetics services	Short research paper describing a survey	The paper describes the effect of database-generated pedigrees on cancer genetic risk assessment in four major centres in Scotland	The pedigrees provided by the Scottish Cancer Registry were accurate and extensive and often changed risk category (41 %) and management (23 %)	Linking of pedigrees to a cancer registry results in more comprehensive family history and can change cancer genetic counselling
Thorsson . 2003	Systematic family screening for familial hypercholesterolemia in Iceland	Research paper comparing two methods of screening	The paper describes a novel approach in screening for familial hypercholesterolemia and compares it with conventional method	The systematic family screening identified 19 % more individuals than the conventional one	The new method adds considerable to the conventional method of FH screening

This is a similar method to the one many cancer registries use, with limited personal identification. The second method they called a second-order linkage. With this method, individuals can be organised into large family pedigrees within available databases if the appropriate fields are used. One way would be to create an individual ID for each person and include mothers and fathers identifier fields in the databases in question. This is a similar method to the one used in the Nordic countries for the National Population Registries and in the widely used Genealogical Data Communication data standard. Although the article focuses on birth defect registries, the formation and design of a family pedigree database is described. Similar is the possibility of linking genealogical resources such as the Veterans Administration data and the Social Security Death Index to the already available UPDB database, expanding their use (Cannon Albright 2006).

Authors agreed on the great impact that genealogy databases linked to disease registries, can have on research. Cannon Albright has described the UPDB and the Icelandic genealogy database as examples of such use (Cannon Albright 2006; Tu and Mason 2004).

Privacy issues

Cannon Albright (2006) discussed how the use of genealogy databases in clinical service required dealing with many issues, among them privacy and security issues concerning the data, as well as the liability implied in their use. Similarly, Tu and Mason recognised the potential concerns regarding privacy and confidentiality as it is possible that some could view such data linkage as intrusive (Tu and Mason 2004). They all stressed the importance of defining clear rules and procedures for the use of linking data. Brewster et al. mentioned the fundamental principles of the UK Data Protection Act 1988 (Brewster et al. 2004; Archives 1998).

Future use of genealogy databases

As for the future, Cannon Albright envisioned in her paper that a US genealogy database could be made by using already available data, such as the Veterans Administration Database and Social Security Death Index (Cannon Albright 2006). Tu and Mason pointed out the benefits that linked databases could have for applied public health service, using their suggested second-order linkage (Tu and Mason 2004). That method would probably be better than first-order linkage as name changing is frequent in the USA due to marriages. Also, families may move between states, making surveillance and paper follow-up difficult. Lastly, Brewster et al. claimed that the interaction between cancer registries and genetics clinics would likely increase in the future

(Brewster et al. 2004). They also stressed the benefit of such linking while Thorsson et al. discussed the limitation of using genealogy databases in clinical service caused by the lack of a comprehensive and accurate genealogy information in large multi-ethnic populations (Thorsson et al. 2003). Authors agreed on that suggestions for future genealogy databases used in clinical service will need to comply with strict requirements for privacy.

Discussion

This systematic review reports the results of a comprehensive search for papers describing the use genealogy databases in health care. Only four papers were identified, of which two described the actual existing use a genealogy database. The other two were discussion papers describing potential use. Presently, we are only aware of the use of genealogy databases in health care in Iceland and cancer genetics service in Scotland (Brewster et al. 2004; Thorsson et al. 2003). Thus the use of genealogy databases in health care appears very limited. However, it is possible that there is an ongoing use of databases that we are not aware of since reports may not have been published. Such use is unlikely to be common without us being aware of it from experience or through literature search. As an example of non-published use, except in a conference abstract form (Jonsson 2009) in Iceland, the GCU genealogy database is used by the cancer genetic counselling service. Files from the Icelandic Cancer Registry and the GCU database are linked to generate cancer pedigrees allowing for the construction of three to five generation pedigrees with cancer diagnosis. Similarly to the suggestion made by Tu and Mason, the linking used in the GCU database is made with a specific ID number issued to all Icelanders (Tu and Mason 2004). With this method, it is possible to make large family trees and to link almost all Icelanders. The GCU database is also used to generate pedigrees for other clinical use and to trace relationships between individuals. The FH familial screening method described by Thorsson et al. is a good example of such use (Thorsson et al. 2003).

Although we searched with many combinations of keywords and in comprehensive databases, the search may not have identified all papers. For example, the article by Thorsson et al. was not found by the search and only identified through a personal communication (Thorsson et al. 2003).

Genealogy databases of the size and quality suitable for clinical use are rare. However, this is likely to change. Family-based genealogy databases are becoming more common reflecting a growing interest in family history and user friendly computer programs. Such databases can now be generated with a modest effort by knowledgeable individuals. Large genealogy databases can be created with a reasonable effort, as the examples from Iceland and Utah show. Data from various existing demographic and family-based genealogy databases can be used to facilitate the creation of larger databases. There are existing databases that could potentially be used for health care with some modification and added information where needed. One is the Swedish Multi-generation Register (Ekbom 2011) and another one is the large UPDB in Utah which includes several million individuals coming from different countries (Cannon Albright et al. 2005). Some other large public genealogy databases exist and could potentially be linked with clinical information, given that the accuracy and reliability is acceptable. As for disease databases, cancer registries are well suited for such linking due to their size, formation and amount of information collected.

Our findings of limited publication may reflect legal or regulative restrictions based on perceived autonomy or information risk as well as worry about perceived risk for invasion of privacy. This is interesting as census microdata (Minnesota 2011) as well as large genealogy databases are freely available on the internet, making genealogy information public. Cannon Albright has suggested that the use of resources to assess an individual's risk of a disease requires different methods than for scientific research (Cannon Albright 2006). The quality of the available genealogical data must be very good and a medical history with diagnosis must be accessible and available for linking. Care must be taken to ensure privacy and to restrict the information to those who need it for the benefit of the family in question. It is debatable to what degree privacy is more endangered when linked databases are used by genetic professionals to form familial genetic risk assessment, as contrasted by the usual way by using the information received from the counselee. Of interest in this regard is the accepted practice of sharing genetic family trees between health services, apparently without risking privacy or needing specific consent of all family members. Genetic professionals are using family histories in their work, most often received only from counselees. The family information supplied by the counselee is often not fully accurate potentially causing risk misclassification (Janssens et al. 2012; Bensen et al. 1999). In some cases, there is information available about both affected and unaffected members of the family, either from previous communication or from Cancer Registry files. Cancer registries are generally accurate and comprehensive. In contrast, the disease information reported by health professionals on relatives is often incomplete. Linking information from cancer registries to genealogy databases should improve the efficiency of cancer genetics clinics (unpublished data; Reis et al. 2006; Gregory et al. 2007).

Genealogy databases have great potential for risk assessment in genetic health care but their use apparently very limited. Further studies are needed to address the benefits and drawbacks including requirements for data accuracy.

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