

An Overview of Computer-Aided Medical Pedigree Drawing Systems

Voon Fui Wong¹, Meow Keong Thong^{2*} and Siew Hock Ow³

^{1,3}*Faculty of Computer Science & Information Technology, Department of Software Engineering, University of Malaya, 50603 Kuala Lumpur, Malaysia*

²*Department of Paediatrics, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia*

* Corresponding author. E-mail: thongmk@um.edu.my

ABSTRACT

The family history or pedigree is the main clinical diagnostic tool when the medical practitioner suspects an inherited or genetic component in a medical condition. Information and communication technology (ICT) has begun to play a significant role in transforming medical pedigree drawing from a 'paper and pen' into a computer-aided system approach. The system would replace the laborious and time-consuming manual creation of the pedigree or family tree charting. The system employs modules that are capable of assigning the appropriate genetic symbols, family relationships and disease status, using standardised nomenclature that is internationally accepted and used in genetic counselling. This paper discusses the background of pedigree creation in medical practice. A comparative review of various computer-aided pedigree drawing systems was performed with emphasis on the system features, editing capabilities, creation of databases, system security, ease of use and compatibility with needs of the medical profession.

Key words: Pedigree drawing system, Genetic symbols, Genetic counselling, Family history

INTRODUCTION

Genetic and inherited diseases are major medical problems in the world. As infectious diseases and malnutrition are being reduced, chronic medical disorders have emerged as the main cause of mortality and morbidity. These disorders include mental disorders, birth defects and blood diseases that are passed on from one generation to another. Many common medical conditions such as diabetes mellitus, cancers and hypercholesterolaemia have familial predisposition. According to a study in the United Kingdom, 40.3% of patients who attended clinics for examination and consultation had one or more diseases with genetic component in their family history (Rose et al., 1999). The diseases with genetic components could have an effect on the patients' health and potentially their offspring.

Family history contains important information about each family member. It can be used as a diagnostic tool and help guide decisions on genetic counselling. The social aspect of a family history has shifted to the evaluation of genetic or inherited conditions running in a family. Many medical doctors often inquire about family diseases as part of their medical evaluation process. This information is recorded in a narrative form and may be difficult to analyse or interpret.

For example, Sarina's grandmother died of breast cancer while two of her five aunts were diagnosed to have breast cancer. This statement does not indicate how her aunts are related to Sarina's mother or father. Do the aunts have a biological relation with Sarina's grandmother who had cancer? The exact relationship of her aunt to Sarina, together with other details, will make a difference in the interpretation of the family history during genetic counselling. In view of this, the Center for Disease Control and Prevention (CDC) in the United States of America has advocated Family History Public Health Initiative (2002). This was undertaken as a positive family history was found to be a risk factor for many common (multifactorial) diseases and underutilised in preventive medicine. Many members of the public are familiar with the charting of their own family tree due to the relative widespread use of pedigrees in public domain. This approach will complement existing current public health strategies such as advice on diet, exercise and avoidance of smoking.

Therefore, by drawing a family tree or "pedigree", a graphic record of the family's health history can be obtained. The medical practitioner may be able to provide further medical information regarding the condition and the actual genetic risk to the client and other family members. The client may be reassured if the risk is small. If there is significant recurrence risk or presence of elements of uncertainty existing, the doctor may refer the client to a medical geneticist for counselling. The process of preparing a pedigree may be laborious or time-consuming and it may be difficult to perform in a busy medical practice. In addition, the doctor is expected to prepare the pedigree that can be viewed at a glance, is easy to update and interpret during genetic counselling.

A pedigree or family tree chart is informative with regards to the relationship of a person with his family members and his/her ancestors, as well as the documentation of the phenotype and genotype, if available. It is standard practice for genetic professionals to construct a genetic pedigree during encounters with patients seeking genetic services (Benkendorf et al., 2000). The pedigree may be used to analyse Mendelian inheritance of certain traits. This is particularly useful in paediatric practice where the family may seek genetic counselling following the birth of a child with birth defects or severe learning disabilities. Other situations that may require a detailed pedigree include a positive family history of single-gene disorders, members of a high-risk ethnic group, consanguineous marriages, prenatal diagnosis, inherited metabolic disorders and adult onset genetic disorders such as Huntington's disease and familial cancers (Bankhead et al., 2001).

The pedigree may assist in alerting physicians to the possibility that there are genetic factors running through the family and may be used to establish the type of

inheritance. It is also used to estimate the risk to other family members and to summarise individual genetic data (Rose and Lucassen, 1999). The pedigree data serve an important role in facilitating communication between clinical geneticists. The collection of extended pedigrees represents a powerful sampling design for quantitative genetic and linkage studies of both normal and disease-related quantitative traits (Williams-Blangero and Blangero, 2006).

In constructing a pedigree, some information related to the reason for seeking genetic counselling is required. According to the National Society of Genetic Counselors (NSGC), family history together with medical and health information should be collected (National Society of Genetic Counselors (NSGC), 2006). The general information for family members may include their age or year of birth; year of death or age of death (for family members who are dead); cause of death and the year or age diagnosed (for family members who are dead); relevant diseases with year and age of diagnosis and genetic testing results for those who are gene-carrier/affected individuals. The Pedigree Standardization Task Force (PSTF) was established through the Professional Issues Committee of the NSGC to make recommendations for standardized human pedigree nomenclature (Bennett et al., 1995). There are some common recognised symbols used for constructing the pedigree chart.

Figure 1 shows the common symbols for an individual, the affected individual, multiple individuals with known number of family members and unknown number of family members, diseased individuals, stillbirth, pregnancy, proband and consultant and from five generations (Roman numerals I to V).

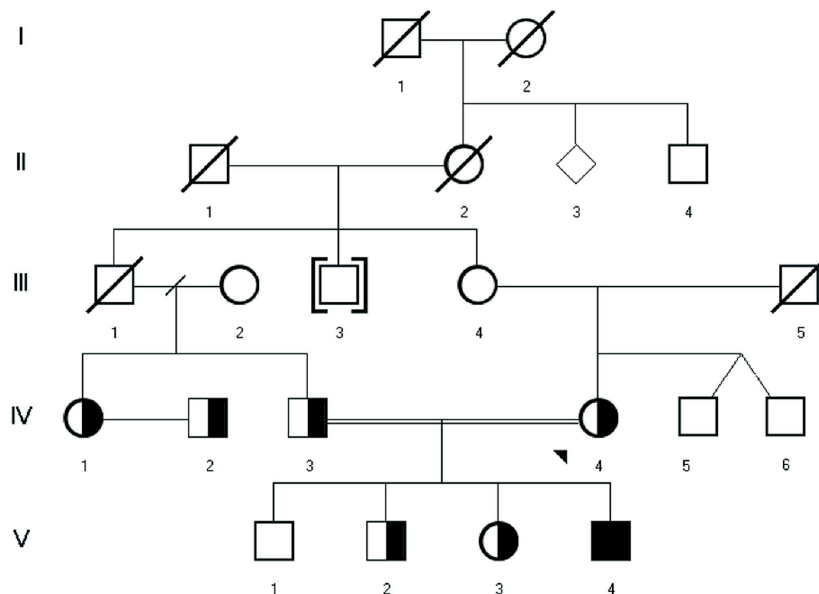


Figure 1. Pedigree Chart for Family with Five Generations.

It is important to keep the generation lines clearly defined. Individual IV-4 (arrowed bottom left) is the consultand. She and her husband (IV-3) are first cousins (double lines). The client, her partner and two of their offspring are carriers for an autosomal recessive condition. One of their offspring (V-4) is affected with the disorder. Both the maternal and paternal grandfathers are deceased. Individuals of the same generation are placed on the same line, even though they have a big age difference. The generation lines should be numbered from top (oldest generation) to bottom (youngest generation) with Roman numerals I, II, III, and so on. The individuals on each generation line should be numbered 1, 2, 3, and so on, moving from left to right (Johnson and Christianson, 2006).

On the basis of the information represented in a pedigree, doctors may stratify risk to identify those who can be reassured and to refer those with an elevated risk for further testing to a genetic centre clinic (Knottnerus, 2003). A screening pedigree, when no particular diagnosis is suspected, will be scrutinized for a common diagnosis or common theme running through. A pedigree with a positive finding may lead to further enquiries regarding risk factors that may point to a possible genetic cause or a particular mode of inheritance. Common Mendelian modes of inheritance such as autosomal dominant, autosomal recessive, X-linked dominant or recessive, chromosomal or mitochondrial inheritance may be inferred from a comprehensive pedigree. This may lead to estimation of the recurrence risk and what testing or preventive measures that may be required.

A brief description followed by comparative analysis of the existing pedigree software packages available in the market is performed. These software packages normally come in the form of CDs and some are accessible from the Internet. Screenshots of the evaluation programs are provided.

1. Family Tree Maker 2005

This package was developed by MyFamily.com. Inc. It is a system for creating a family tree. This system allows the user to enter the family members' names and their detailed information (FamilyTree Maker 2005, 2006) (Figure 2a and Figure 2b). This software is simple to use and the input method is user-friendly. FamilyTree Maker has a number of functions such as pedigree view, individual data maintenance, family members photo insert, scrapbook and internet online link. Stand-alone help file and online help are provided. The software does not utilize standard human pedigree symbols for the family relationships or medical symbols to denote genetic information.

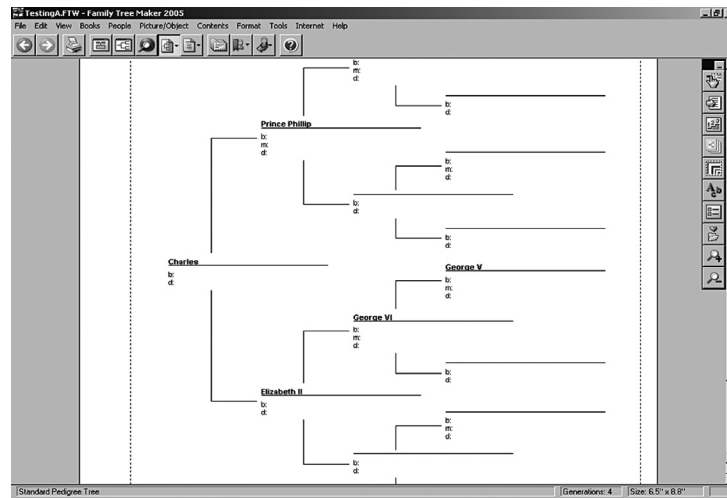


Figure 2a. Standard Pedigree Tree at Family Tree Maker 2005.

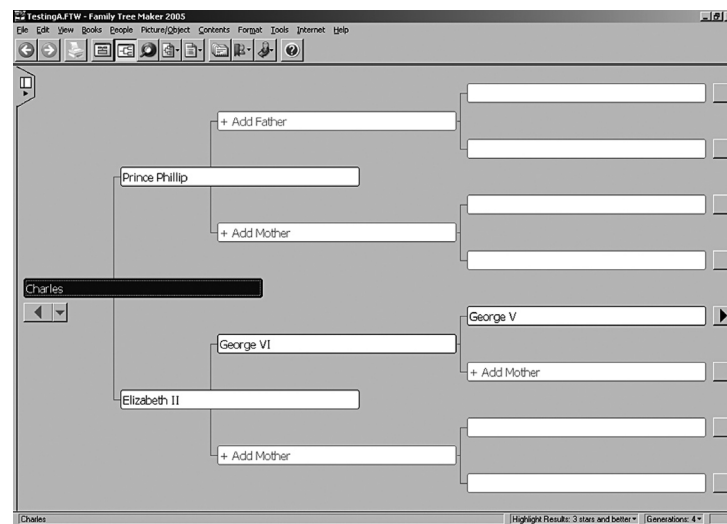


Figure 2b. Pedigree View at Family Tree Maker 2005.

2. Cyrillic 2.02

This package was developed by C. J. Chapman and published by Cherwell Scientific Publishing Ltd (Chapman, 1996). This system was developed specifically for the drawing of the pedigree chart (Figure 3). Cyrillic has a number of functions such as adding individual data, spouse, siblings, parents, relative information as well as annotation and haplotypes with the arrangement performed sequentially. Printing of the pedigree is permitted. It has many useful functions, including ability to document multiple pregnancies and twin status as well as a help file with the explanation of each function provided by the system. However, this software

package is accessible on a local machine without user authentication. Any person may gain access to the pedigree chart information after logging into the local workstation. Each pedigree chart is stored in a single file with the risk of missing important data if any damage occurs on the local machine or if the file is accidentally deleted.

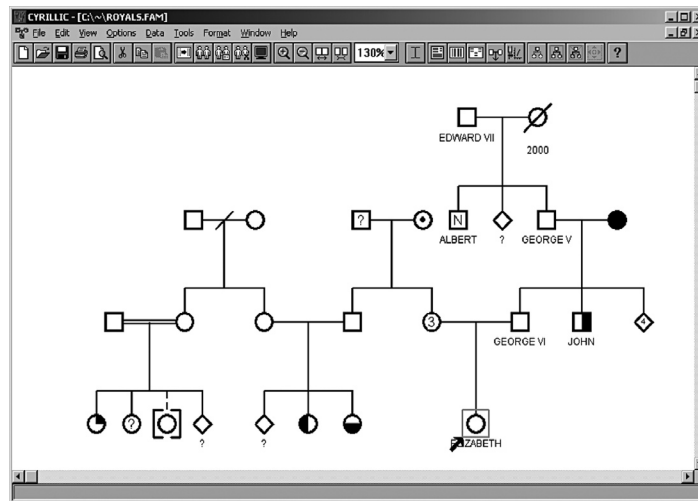


Figure 3. Pedigree Chart Drawing at Cyrillic 2.02.

3. GenoPro version 1.91b

This package was developed by Monica McGoldrick and Randy Gerson (GenoPro, 2002) specifically for the recording of medical history and to show genetic traits. It includes various mental health symbols to allow psychological medicine professionals and therapists to identify and understand social patterns in the family history (Figure 4). It has functions such as adding new individuals, parents, offspring and the actual photograph of the person and a family table layout. It allows the user to preview the family tree before sending the print job to the printer. The family 'wizard' is included in the family members' data. A help file with a simple tutorial is provided to guide the user as well as to explain the functionality and tools provided. However, this software package does not produce standard pedigree chart and some of the genetic symbols used are not identical with standard pedigree genetic symbols. This software package lacks security features and the chart is stored in a single file like Cyrillic2.02.

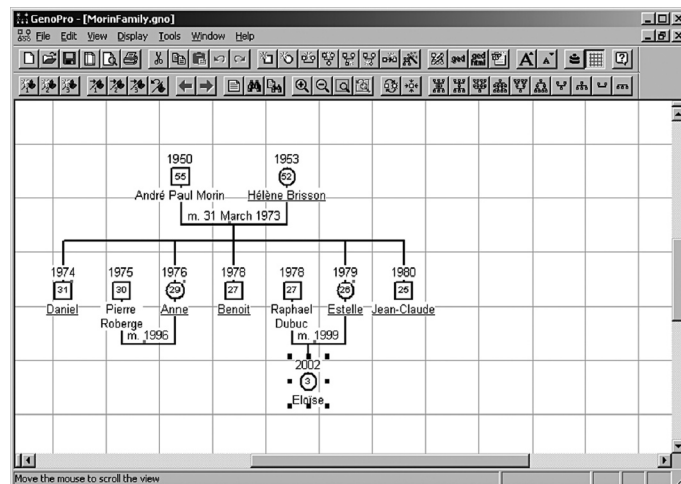


Figure 4. Pedigree Chart Drawing at GenePro Version 1.91b.

4. GenealogyJ 2.3.2

The system was developed under the terms of the GNU General Public Licence as published by the Free Software Foundation (GenealogyJ, 2005). GenealogyJ is a viewer and editor for genealogic data and allows nested information to be edited in its hierarchical form. All defined properties are treated in a way that offers specific input for editing. Hence, there is no need to look at the text-file. GenealogyJ has a number of functions such as adding child, parents, spouse, sibling with a tree view, timeline view and print preview (Figure 5). A help file is provided. However, GenealogyJ does not produce a standard pedigree chart and some of the genetic symbols are not identical with standard pedigree genetic symbols and it lacks system security features and can be accessible without authentication.

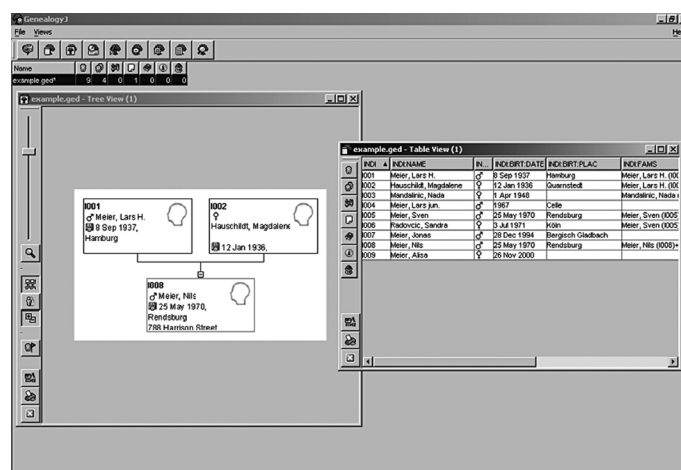


Figure 5. Pedigree View at GenealogyJ.

5. PED 5 Pedigree Drawing Software

PED 5 was first introduced at the European Society of Human Genetics (ESHG) Conference in 1997. PED 5 can fetch family information from a data file, using CSV (comma separated values) format where each line describes an individual by the pedigree ID, the individual's ID, the IDs of his/her father and mother, the gender, the phenotype or affection status and any other data related to the individual (PED 5, 2006). At PED 5, only menu bar and button at the toolbar were used to create a pedigree chart (Figure 6). PED 5 complies with the "Recommendations for Standardized Human Pedigree Nomenclature" and it has the usual functions such as adding son, daughter, ancestors function, annotation, edit pedigree comment as well as import and export family information into a CSV file. However, auto-drawing input window at PED 5 does not indicate generation by Roman numerals and each individual is not designated a specific number. Although the drawing input module at PED 5 provides most of the pedigree symbols, it is difficult to construct a pedigree tree showing the relationship between individuals because the drawing module does not provide auto-relationship checking during construction of pedigree tree. This will take a longer time to construct a pedigree tree. Although PED 5 can produce standard pedigree chart but it lacks of system security features where it can be accessible without authentication.

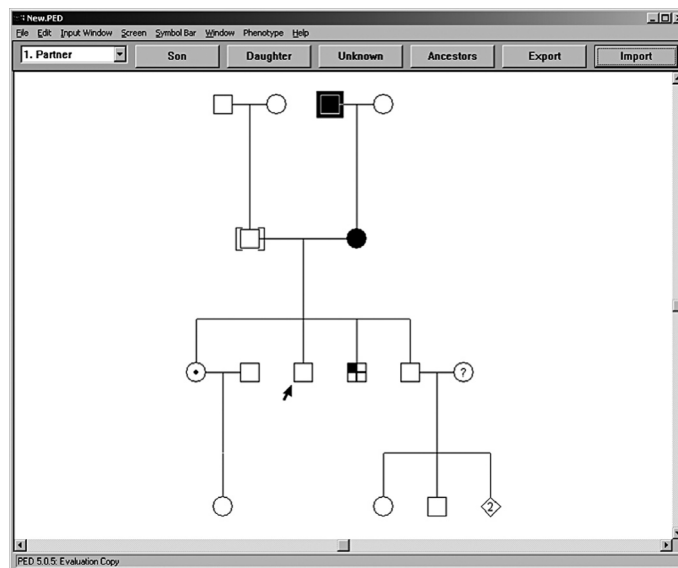


Figure 6. Pedigree Chart Drawing at PED 5.

6. Pedigree Assistant

Pedigree Assistant was developed by C. J. Chapman, author of Cyrillic (Pedigree Assistant Pedigree Drawing Software, 2006), for drawing the pedigree chart (Figure 7). It uses the human pedigree symbols similar to Cyrillic. Pedigree Assistant uses Microsoft Access as its databases. Pedigree Assistant has a number of functions such

as adding individual data, add parents and siblings function, pedigree chart printing, picture export, import family function from Cyrillic, interface with patient databases and questionnaire database entry. It has symbols for multiple pregnancy and twin status. It has a security feature that secures pedigree data from unauthorized access. However, Pedigree Assistant does not indicate the generation number by using Roman numerals. In addition, while each individual is assigned a specific number, it does not follow the recommended numbering system of moving from left to right.

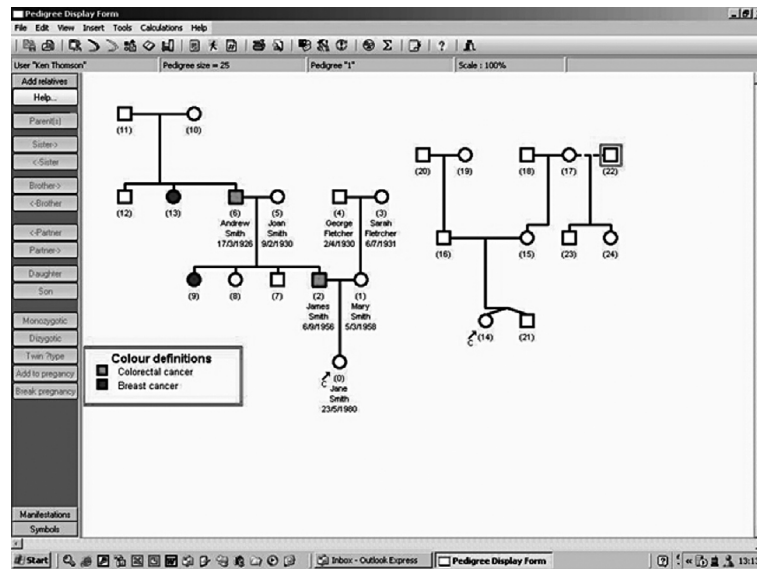


Figure 7. Pedigree Chart Created using Pedigree Assistant.

7. Progeny

Progeny is a pedigree drawing component developed by Progeny Software, LLC (Progeny Software, LLC, 2006) specifically for the recording of genetic data. It assigns the human pedigree symbols into the pedigree chart one by one (Figure 8). Progeny uses Sybase SQL Anywhere database. Progeny can be executing at Microsoft NT or Novell Network Server via local area network. It has two types of software packages, Enterprise edition and Desktop edition. Enterprise edition supports multiple users accessing the same pedigree data. It also provides user securities management and row assignment module to enhance the system securities. Desktop edition is a stand-alone single user pedigree drawing system. Progeny has a number of functions such as adding individual data, parents and siblings function, pedigree chart printing, export of pedigree chart as an image function with properties of each individual and individual palette. However, the pedigree chart does not indicate the generation number and each individual is not assigned specific numbers moving from left to right. Although it provides many icons and tabs at user interfaces, the interface requires the user to undergo training in order to construct and maintain the pedigree. The program involves many steps in order to update each individual genetic symbol and its data.

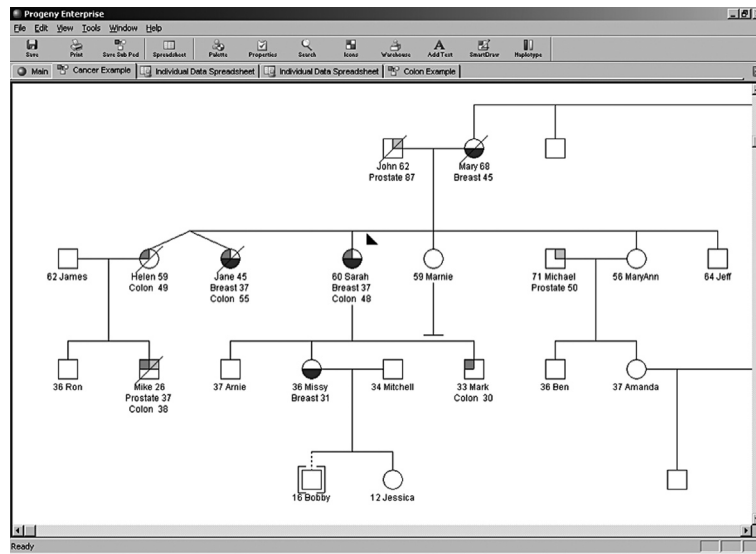


Figure 8. Pedigree Chart Created using Progeny.

The comparative analysis on existing pedigree drawing software packages was performed, based on system features, pedigree analysis functions and the use of pedigree symbols.

Comparisons of the pedigree symbols, system features and pedigree analysis functions are tabulated in Tables 1–3, respectively.

Table 1. Comparison of the Pedigree Symbols used.

Pedigree software packages	Family Tree Maker	Cyrillic 2.02	GenoPro ver 1.91b	Genealogy J 2.3.2	PED 5	Pedigree Assistant	Progeny
Male / Female	No	Yes	Yes	No	Yes	Yes	Yes
Unknown Gender	No	Yes	Yes *	No	Yes	Yes	Yes
Affected status	No	Yes	Yes *	No	Yes	Yes	Yes
Affected with different sectors (q1, q2, q3, q4)	No	Yes	No	No	Yes	Yes	Yes
Obligate carrier	No	Yes	No	No	Yes	Yes	Yes
Possibly affected	No	Yes	No	No	Yes	Yes	Yes
Unaffected	No	Yes	No	No	Yes	Yes	Yes
Spontaneous abortion (SAB) and its status	No	Yes	No	No	Yes *	Yes	Yes
Termination of pregnancy (TOP) and its status	No	Yes	No	No	Yes *	Yes	Yes
Individual death	No	Yes	Yes *	No	Yes	Yes	Yes
Multiple individuals with number known.	No	Yes	No	No	Yes	Yes	Yes

Table 1. Comparison of the Pedigree Symbols used. (Continue)

Pedigree software packages	Family Tree Maker	Cyrillic 2.02	GenoPro ver 1.91b	GenealogyJ 2.3.2	PED 5	Pedigree Assistant	Progeny
Adoption	No	Yes	No	No	Yes	Yes	Yes
Proband	No	Yes	No	No	Yes	Yes	Yes
Identical twins	No	Yes	Yes	No	No	Yes	Yes
Marriage	No	Yes	Yes	No	Yes	Yes	Yes
Consanguineous marriage	No	Yes	Yes	No	No	Yes	Yes
Extramarital Marriage	No	Yes	Yes	No	No	Yes	Yes
Divorced	No	Yes	Yes	No	No	Yes	Yes
Generation numbered with Roman numerals I, II, III, etc.	No	Yes	No	No	No	No	No
Individual numbered 1,2,3,etc.	No	Yes	No	No	No	No	No

* Different symbols used from the common pedigree symbols recommended.

Table 2. Comparison of Pedigree Software Packages on System Features.

Pedigree software packages	Family Tree Maker 2005	Cyrillic 2.02	GenoPro version 1.91b	GenealogyJ	PED5	Pedigree Assistant	Progeny
Platforms	MS Windows	MS Windows	MS Windows	MS Windows	MS Windows	MS Windows	MS Windows for Clients. MS Windows. NT/2000/XP, Linux or Novell Net Ware for Server
Architecture	Standalone	Standalone	Standalone	Standalone	Standalone	Standalone	Standalone and Client Server
Database	Store in a file	Store in a file	Store in a file	Store in a file	Store in a file	Microsoft Access	RDBMS (Paradox)
Security	No	No	No	No	No	Yes	Yes
Import/Export	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Print	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Patient Record	No	No	No	No	No	Yes	Yes

Table 3. Comparison of Pedigree Software Packages on Pedigree Analysis Function.

Pedigree software packages	Family Tree Maker	Cyrillic 2.02	GenoPro ver 1.91b	GenealogyJ 2.3.2	PED 5	Pedigree Assistant	Progeny
Standard Pedigree Symbols	No	Yes	Yes	No	Yes	Yes	Yes
Marital Status	Yes	Yes	Yes	No	Yes	Yes	Yes
Pregnancy with Twins	No	Yes	Yes	No	No	Yes	Yes
Pregnancy Multiples	No	Yes	Yes	No	No	Yes	Yes
Adoption	No	Yes	Yes	No	Yes	Yes	Yes
Multiple Marriages (Polygamous)	Yes*	Yes	Yes	No	No	Yes	Yes
Able to join family branches	No	Yes	Yes	No	No	Yes	Yes
Pedigree analysis to determine mode of inheritance	No	Yes	Yes	No	Yes	Yes	Yes

* Unable to show the multiple marriages at pedigree tree.

CONCLUSION

A computer-aided pedigree drawing system is essential to allow doctors to document the family history efficiently and in the quickest manner. A comprehensive pedigree drawing system using standardized human pedigree symbols will facilitate analysis of genetic risk, namely, by establishing the mode of inheritance, determining recurrence risk to the client and other family members and with the ability to summarise individual genetic data. This will save precious consultation time and enhance communications between members of the medical profession and geneticists, thus improving the quality of health care for families with inherited conditions.

Majority of the systems in use are of standalone architecture and do not use any database. All systems should preferably be able to provide clients server architecture with database. This will allow different physicians to exchange pedigree information and to use the updated family data. The system should adopt common pedigree symbols in the pedigree chart. The system must be able to print the data and permit import and export of the information. Most importantly, an ideal pedigree drawing system should employ security features on its application to protect the private medical and confidential family data.

As the manual traditional drawing of the family tree is laborious and time-consuming, a high-quality pedigree drawing system should provide intuitive, fast and user-friendly plotting of the pedigree with minimal training. The system must allow a quick review of genetic disease transmission over the past few generations and be able to assist the doctor in quickly determining whether a client can be reassured or a referral is required for further management. Most important, it must be cost-effective and able to save time, so that the doctor will have more time for the

patient and the family to discuss their medical problems. As genetic and inherited disorders are becoming the main cause of ill health in the world, the computer-aided pedigree drawing system will be here to stay.

ACKNOWLEDGEMENTS

The first author would like to acknowledge the financial support from the University of Malaya through the Vote F grant (Project No.: F0213/2005A).

REFERENCES

- Bankhead, C., J. Emery, N. Qureshi, H. Campbell, J. Austoker, and E. Watson. 2001. New developments in genetics—knowledge, attitudes and information needs of practice nurses. *Family Practice* 18 (5): 475–486.
- Benkendorf, J. L., B. N. Peshkin, and C. Lerman. 2000. Impact of genetic information and genetic counseling on public health. *Genetics and Public Health in the 21st Century: Using Genetic Information to Improve Health and Prevent Disease*, Part IV. 19: 361–383.
- Bennett, R. L., K. A. Steinhaus, S. B. Uhrich, C. K. O’Sullivan, R. G. Resta, D. Lochner-Doyle, D. S. Markel, V. Vincent, and J. Hamanishi. 1995. Recommendations for Standardized Human Pedigree Nomenclature. *Journal of Genetic Counseling* 4 (4): 267–279.
- Chapman, C. K. 1996. Cyrillic version 2.02. Oxford Science Park. Cherwell Scientific Publishing Ltd.
- FamilyTree Maker 2005. 2006. Do you need help with Family Tree Maker? Let us guide you in the right direction [Online]. Available: <http://www.familytreemaker.com/help/tutorials/tour/> [25 January 2006].
- Genealogy J. 2005. GenealogyJ [Online]. Available: <http://genj.sourceforge.net> [25 January 2006]. Last Update: February 3rd 2005.
- GenoPro v1.91. 2002. GenoPro Inc.
- Johnson, V. P., and C. Christianson. 2006. Clinical genetics, a self-study guide for health care providers, Lesson 2 Assessment Strategies: How to identify families - Taking a family history [Online]. Available: <http://www.usd.edu/med/som/genetics/curriculum/2BHIST2.htm>. [25 September 2006]. Last update: 08 October 2006.
- Knottnerus, J. A. 2003. Community genetics and community medicine. *Family Practice* 20(5): 601-606.
- National Society of Genetic Counselors (NSGC). 2006. Your family history ñ Your future. [Online]. Available: <http://www.nsgc.org/consumer/familytree/index.cfm> [16 September 2006].
- PED 5. 2006. Hansjoerg Plendl. Abstract - PED 5 Pedigree Drawing Software [Online]. Available: <http://www.medgen.de/ped5/index.html> [21 September 2006]. Last Update: December 4, 2005.

- Pedigree Assistant Pedigree Drawing Software, 2006. Pedigree Assistant Pedigree Drawing Software [Online]. Available: <http://www.pedigreeassistant.com/> [25 September 2006].
- Progeny Software, LLC. 2006. Genetic Data Management Software That Evolves With You [Online]. Available: <http://www.progeny2000.com> [25 January 2006].
- Rose, P., E. Humm, K. Hey, L. Jones, and S. M. Huson. 1999. Family history taking and genetic counselling in primary care. *Family Practice* 16(1): 78-83.
- Rose, P., and A. Lucassen. 1999. *Practical genetics for primary care*. New York, Oxford University Press.
- Williams-Blangero, S., and J. Blangero. 2006. Collection of pedigree data for genetic analysis in isolate populations. *Human Biology* 78(1): 89-100.