

CLINICAL DECISION SUPPORT SYSTEM  
FOR THE HEALTHY MARRIAGE PROGRAM

---

A Thesis

Presented to

The Faculty of the Graduate School  
At the University of Missouri-Columbia

---

In Partial Fulfillment

Of the Requirements for the Degree

Master of Science

---

By

AHMED ALSHARIT

Dr. Patricia Alafaireet, Thesis Supervisor

MAY 2015

The undersigned, appointed by the dean of the Graduate School, have examined the thesis entitled

CLINICAL DECISION SUPPORT SYSTEM

FOR THE HEALTHY MARRIAGE PROGRAM

Presented by Ahmed Alsharit, a candidate for the degree of Master in Science, and hereby certify that, in their opinion, it is worthy of acceptance.

---

Professor William Salzer

---

Professor Patricia Alafaireet

---

Professor Win Philips

## ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my mother Madinah Alburaih and my siblings for the continuous support to continue my education. After the death of my father, my mother and siblings guided me to the right path.

Dr. Patricia Alafaireet served as my advisor during the time that I was a student at the University of Missouri. I appreciate her patience, and motivation. Her guidance helped me in all the time of research and writing of this thesis. I don't think I could have had a better advisor and mentor for my MS study.

Besides my advisor, I would like to thank my friends Taylor Vohsen, Ayoub Darkhalil, Yagoob Alsarouj, Zach Kurth and Holly Simonsen for their encouragement, insightful comments, and positive attitudes.

My sincere thanks also goes to Vrena Flint for offering me my first internship opportunities in a health care setting at Intermountain Health Care. She introduced me her group and had me working on diverse exciting projects.

Last but not the least, I would like to thank my Fiancé: Taylor Bernstien "Future Ms. Alsharit" for supporting me spiritually throughout my master degree.

# TABLE OF CONTENTS

ACKNOWLEDGMENT.....	ii
Table of Figures .....	iv
Table of Tables.....	v
Definitions.....	1
1. Executive Summary .....	1
2. Background and Introduction.....	2
2.1 Environmental Scan .....	4
2.2 Cultural Factors .....	12
2.3 Clinical Factors .....	13
3. Literature Review .....	13
3.1 Clinical Factors .....	14
3.2 Cultural Factors .....	22
3.3 Technical Factors .....	23
3.4 Problem Statement and Specific Aims .....	24
4. Methodology .....	25
4.1 IRB .....	25
4.2 Data sources, data clean up etc.....	25
4.3 Design Elements.....	26
4.4 Description of complete design or product.....	44
4.4.1 User Interface (UI) .....	44
4.4.2 Process.....	46
4.4.3 Implementing and training .....	47
4.4.4 CDSS Maintenance .....	48
4.5 Evaluation and Usability of design and/or product .....	54
4.5.1 Usability .....	55
4.5.2 Evaluation.....	55
5. Results and Conclusions.....	58
Limitations .....	60
Conclusions and Recommendations.....	61
References .....	62

## TABLE OF FIGURES

Figure 1 Map of Genetic blood disorders in Saudi Arabia .....	4
Figure 2 sickle cell disease inheritance patte.....	32
Figure 3 Thalassemia inheritance patt .....	33
Figure 4 Haemophilia a inheritance pattern.....	34
Figure 5 Fanconi Anemia inheritance pattern .....	35
Figure 6 Hereditary hemochromatosis inheritance pattern.....	36
Figure 7 erythropoietic protoporphyria inheritance pattern .....	37
Figure 8 hemochromatosis inheritance patte .....	38
Figure 9 Porphyria RECESSIVE INHERTANCE pattern .....	39
Figure 10 Porphyria dominant inheritance pattern .....	40
Figure 11 STI and Hepatites in healthy marriage program .....	41
Figure 12 Genetic blood disorders in healthy marriage program .....	43
Figure 13 UI for marriage agencies.....	44
Figure 14 Positive results .....	44
Figure 15 Negative results.....	45
Figure 16 UI for counslors .....	45
Figure 17 UI Searching option .....	46
Figure 18 Organization data architacture .....	53

## TABLE OF TABLES

Table 1 evaluation measure .....	55
----------------------------------	----

## DEFINITIONS

Parents: a man and a woman who can potentially have kids

Couple: man and a woman who have the potential of getting married

Child: a boy or girl birthed from a biological parent

Risky Marriage/ at risk marriage: a marriage that could cause a spouse to get an STI or have a child with a genetic blood disorder

*Fatwaa*: Islamic rule made by an Islamic leader (Inhorn, 2005)

*Ayah*: Quranic verse (Ismail, Rahman, Bakar, & Sembok, 2007)

*Bedouins*: traditional Arabs who lived in the dessert (Musil, 1928)

## 1. EXECUTIVE SUMMARY

This paper discusses the replacement of the traditional laboratory premarital screening in Saudi Arabia and other countries that follow the Islamic laws “Healthy Marriage Program” with Clinical Decision Support Systems (CDSS). CDSS uses the couple’s electronic health records to determine if the match is harmonious. The traditional premarital screening consist of couples undergoing a screening process for Sexual Transmitted Infections (STI) and genetic blood disorders prior to becoming engaged or getting married. The traditional screening practice faces many challenges, such as being culturally unaccepted, time consuming, and unorganized. The CDSS would eliminate the challenges of the traditional process by giving marriage agencies, marriage licensors and traditional matchmakers access to insert the national identification number of new couples to see if their potential marriage would be healthy or not. Unhealthy marriages would be required to go through sex/genetic counseling sessions as an attempt to prevent the spread of the STI’s and genetic blood disorders.

The clinical aspects of the CDSS discusses additional diagnosis that can be added to the traditional program. Most premarital screening has a specific set of diagnosis that are screened for. After literature review, a greater number of STI and genetic blood disorder diagnosis have been added to the CDSS.

The cultural aspects section discusses the acceptability of premarital screening. The culture surrounding marriage is structured upon a society’s religions and traditions. Some cultures

reject religious marriages that involve STI patients. Additionally, several cultures force couples to share their results with their religious leaders.

The technical aspects of the CDSS are the different elements needed to make the CDSS work. Elements of CDSS include diagnostic codes, electronic health records, and data warehouses. The marriage agency would insert the couple's information into the CDSS portal, which would search for the couple's health records for tests and diagnosis in order to determine if the match is compatible. Some couples would require vaccination, treatment, or be cured before they are granted permission to marry. If STI's or genetic blood disorders are incurable, or if the marriage might result in affected children, a marriage counselling session would be required. The counselling session would consist of an explanation of consequences to the couple.

The design process tried to deal with all challenges facing the traditional healthy marriage program. The design was made to replace current legal and religious laws in place to prevent unhealthy marriages with increasing awareness and education. The design is made specifically for Saudi Arabia and can be used by countries that follow Islamic laws.

Since the CDSS has not yet been implemented, it was compared to the traditional premarital screening for evaluation. Although the traditional healthy marriage program is a success, it needs to undergo changes in order to improve the program and gain acceptability.

Saudi Arabia is moving from paper health records to electronic health records (EHR). CDSS would be used as a tool to help health care providers deliver higher quality service by using patients' records stored in EHR. CDSS could potentially minimize clinical visitation and provide treatments to couples before getting engaged.

## 2. BACKGROUND AND INTRODUCTION

Premarital screening is a practice that is used in numerous places. The practice's acceptability varies depending on the culture, religious, medical and political values of where it is implemented. Medicine may not always be the customary solution for all diseases and disorders. Educating people on the facts and how they can prevent the spread of various infections can also be effective. Some governments have made it a priority to educate people by teaching preventative healthcare by establishing new programs, such as sex education and premarital screening. It is the government's decision to determine if these programs are mandatory. Consequently, the mandatory programs typically exhibit better results; typically because these programs are better structured. Many people avoid premarital screening because they have sexual transmitted infections or genetic blood disorders; these people might feel unaccepted or discriminated against. Additionally, governments spend a lot of money in order to implement such programs to screen every couple.



Saudi Arabia is located in the Arabia Peninsula. Saudi Arabian's culture, laws, and politics built by the influence of Islamic and *Bedouin* values. The government is entitled to provide free health care. To provide the best health care, the government of Saudi Arabia choose to implement the most advanced health care practices despite the cost. The country has a mandatory Premarital Screening called Healthy Marriage for Sickle Cell Disease, Thalassemia, Human Immunodeficiency Virus (HIV)/ AIDS, Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) due to the increasing number of Saudi citizens with these diagnosis. In the map below, Sickle Cell Disease (A) and Thalassemia (B) are really high in some areas.

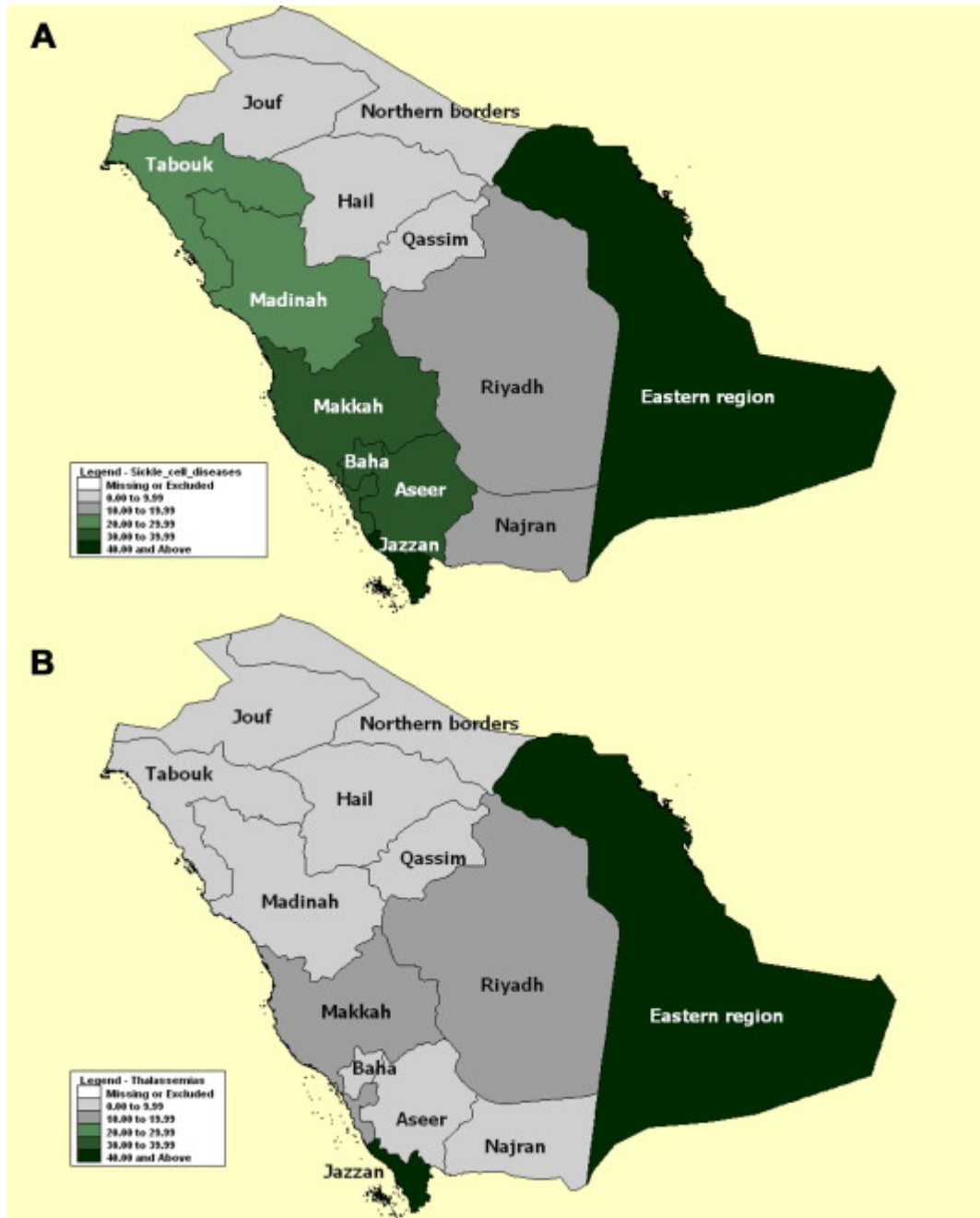


FIGURE 1 MAP OF GENETIC BLOOD DISORDERS IN SAUDI ARABIA

(ZIAD, TARIQ, & MOHAMAD, 2011)

A 2011 study Sickle Cell Disease and Thalassemia cases were 45.1 and c 18.5 respectively. (Ziad et al., 2011)

## 2.1 ENVIRONMENTAL SCAN

I searched PubMed and Medline Ovid for “Premarital Examinations/es” between 2000 and 2014.

### **Premarital Screening**

Researchers in many countries stress the importance of premarital screening and genetic counseling to reduce the number of newborns with STI from the mother or a genetic blood disorder(s) from both parents (Jain et al., 2012). Premarital screening also reduces the number of spouses who might get a Sexual Transmitted Infection after a sexual activity (De Cock, Mbori-Ngacha, & Marum, 2002; G. Marks, Crepaz, Senterfitt, & Janssen, 2005). The traditional premarital screening process takes blood and urine samples at the laboratory from partners to evaluate the outcomes for the marriage between a man and a wife (McIlhaney, 2000; Morabia & Zhang, 2004). While premarital screening already exists in numerous countries, such as Saudi Arabia, Bahrain, Italy, Greece, Cyprus, China, India, Iran, United Arab Emirates, Indonesia, Malaysia, the Maldives, Singapore and Thailand, prenatal diagnosis with abortion as the prevention strategy is used in UK, Northern Ireland and other northwest European countries (Sulaiman et al., 2012).

#### **Status of Premarital Screening- Saudi Arabia**

Saudi Arabia has a mandatory premarital screening program called Healthy Marriage where screening includes only haemoglobinopathies, Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV) (El-Menyar et al., 2009). Couples go to the lab to give blood and urine samples to be tested for haemoglobinopathies, HIV, HCV and HBV (Hamdan, Sibai, Srour, Sabra, & Deeb, 2007). The screening is required to be done by public hospitals to insure the accuracy of the results and they must have the proper policies and procedures established for all outcomes (El-Menyar et al., 2009; Sulaiman et al., 2012). The screening usually takes place before the prospective parents are given permission to get married (El-Menyar et al., 2009; Sulaiman et al., 2012). The results are revealed to the couple by genetic counselors. If the parents are going to produce one or more child with Sickle Cell Anemia or Thalassemia, the prospective union is not recommended without genetic counseling (El-Menyar et al., 2009; Sulaiman et al., 2012). If there is any chance that the marrying couple will have the risk of one of the partners transmitting an STI, the marriage is possible, but only after undergoing a counseling session countries (Sulaiman et al., 2012). Genetic counselors, mostly pediatricians due to limitation in trained genetic counselors, teach at risk parents ways to avoid a risky marriage (El-Menyar et al., 2009). In the case of HIV or HCV, parents are discouraged from getting married while HBV patients are advised to be vaccinated before any sexual contact (El-Menyar et al., 2009). A 2005-2006 study showed that 90% of parents that are going to have a child with sickle cell disease and/or beta-thalassemia still

end up getting married because of cultural or social aspects (Alswaidi et al., 2012). Alswaidi also mentioned the low effectiveness of the genetic counseling and the need for improvement. Religious beliefs, cultural norms, traditions, literacy, education, government policy and attitudes of the parents reduced the chance of the healthy marriage program to be successful (Alswaidi et al., 2012). Research in 2011 showed a reduction in the number of at risk marriages after initiating the healthy marriage program (Memish & Saeedi, 2011). The effectiveness of this premarital screening depends on the knowledge and attitude of the couples (Al-Aama JY., 2010). A survey of students at King Abdulaziz University between the ages 18-29 years old indicated that most females had a strong attitude that premarital screening should be mandatory. The timing of the premarital screening also has an effect on the unhealthy marriage and it should, therefore, be conducted before the prospective parents are engaged (Al-Aama, 2010; El-Menyar et al., 2009; Hamdan et al., 2007). The Saudi Arabian premarital screening is both ethical and cost effective (El-Menyar et al., 2009). Two surveys showed positive feedback from participants about the screening program followed by genetic counseling (Al Sulaiman, Suliman, Al Mishari, Al Sawadi, & Owaidah, 2008). According to Alswaidi, premarital screening for HIV, HBV, and HCV should be optional after four years of the initial screening program implementation in order to allow time for educational efforts to increase the population's knowledge (El-Menyar et al., 2009).

#### Status of Premarital Screening- China

Premarital screening is mandatory in China (Hesketh, 2003; Wu, Rou, Xu, Lou, & Detels, 2005) with screening for prenatal diagnosis in thalassemia (Zhou et al., 2012). The Chinese premarital screening includes physical and genetic testing, as well as appearance. This screening includes height, weight, a full blood count, liver function tests, testing for hepatitis B surface antigen, trichomonas, chlamydia, blood pressure, and hair color. Furthermore, the screening includes hereditary illnesses, learning disorders and psychiatric problems, as well as anything that might jeopardize one's parenting ability (Hesketh, 2003). After the screening, parents are introduced to the potential outcomes of their prospective children (Hesketh, 2003). In most cases, parents receive a certificate that allows them to get married unless there is a chance of unhealthy marriage caused by STI's, potentially ill child, or inability of parenting. In these cases, parental screening is followed by intensive genetic counseling with the possibility of permanent contraception (Hesketh, 2003). HIV screening as part of premarital screening is highly unaccepted between Chinese couples due to little or no knowledge about HIV (Wu et al., 2005). To improve Chinese population's knowledge and attitude surrounding HIV, the Chinese Ministry of Health must correct misconceptions, reduce stigmas, and introduce significant structural changes in current intervention programs (Wu et al., 2005).

## Status of Premarital Screening-Iran

Iran has a mandatory national thalassemia-screening program, which includes premarital health education (Fallah, Samavat, & Zeinali, 2009; Ghotbi & Tsukatani, 2005; Karimi et al., 2007; Samavat & Modell, 2004; Zlotogora, Carmi, Lev, & Shalev, 2009). The Iranian premarital screening is at its first stage, screening for only thalassemia (Samavat & Modell, 2004), and is not applicable to screen for rare atypical minor beta-thalassemia cases (Ranjbaran et al., 2013). The program also provides continuing education for hospital clinicians regarding any of the screened for disorders (Samavat & Modell, 2004). The program's acceptability is well established (Samavat & Modell, 2004). The educational program followed by the premarital screening showed successful results in decreasing at-risk marriages (Fallah et al., 2009; Haghpanah, Nasirabadi, Rahimi, Faramarzi, & Karimi, 2012; Ranjbaran et al., 2013). If both the man and woman are microcytic, the A<sub>2</sub> concentration is measured (Samavat & Modell, 2004). If the concentration measure is more than 3.5%, then the parents are sent to genetic counselors (Samavat & Modell, 2004). Couples can attend several genetic counseling sessions to receive education on diagnosis, both before and after having a child, until they feel that they fully comprehend the risk of having an ill child (Fallah et al., 2009; Ghotbi & Tsukatani, 2005; Haghpanah et al., 2012; Karimi et al., 2007; Samavat & Modell, 2004). According to the religious *Fatwaa* "if keeping and bringing up the child with malformation, mental retardation, and handicap has extreme difficulty and hardship for the parents, abortion the child before ensoulment is permitted" (Fallah et al., 2009). This means that abortion after 16-18 weeks of pregnancy is forbidden, even after prenatal diagnosis (Fallah et al., 2009; Samavat & Modell, 2004). Most parents refuse prenatal diagnosis resulting in abortion; however, acceptance has increased since 2005 (Haghpanah et al., 2012). Some parents accept diagnosis ending in early termination due to economic and cultural factors, while others oppose early termination because of strong religious beliefs, superstition, and faith in supernatural solutions (Haghpanah et al., 2012). The cost of the genetic counseling, as well as the cost of planning, educating, surveillance, is covered by the government while the parents pay the screening cost of five dollars (Samavat & Modell, 2004). Insurance companies are willing to pay for prenatal diagnosis to avoid escalating costs in the future (Samavat & Modell, 2004).

## Status of Premarital Screening-Nigeria

Nigeria has a mandatory HIV/AIDS premarital screening (Arulogun & Adefioye, 2010; Dibua, 2010; Umar & Oche, 2012). The religious leaders in Nigeria, Muslims and Christians in general, have a poor understanding of HIV/AIDS premarital screening, which has an ill effect on the followers of the their respective religions (Umar & Oche, 2012).

Since most marriages license are granted by the church, the religious leaders are in charge of insisting the parents undergo the premarital screening or not (Umar & Oche, 2012). Thus, education programs for religious leaders must be established to ensure better results in the program (Dibua, 2010; Umar & Oche, 2012). A survey between unmarried youth from the Ibadan Northwest Local Government Area has shown a positive attitude, especially among males, towards the mandatory premarital HIV screening (Arulogun & Adefioye, 2010). Additionally, with fifty percent of sickle cell patients residing in Nigeria, Nigeria needs to expand the premarital screening program to include sickle cell anemia. Attitude and knowledge of sickle cells anemia is positive among Nigerians despite a high mortality rate caused by poor availability of medical treatment (Moronkola & Fadairo, 2007).

#### Status of Premarital Screening-Democratic Republic of Congo

While The Democratic Republic of Congo has a high prevalence of HIV patients, it also has a premarital HIV screening program which was initially supported by local churches until being adopted by the government (Rennie & Mupenda, 2008). Both civil and religious marriages cannot be performed without a HIV premarital screening certificate (Rennie & Mupenda, 2008)(Rennie S., 2008). Churches insist on having the HIV test results; if either parent has HIV, the marriage is prohibited in the church (Rennie & Mupenda, 2008). Despite the test results, civil marriages at government institutions require only HIV premarital screening certificate (Rennie & Mupenda, 2008).

#### Status of Premarital Screening-Greece

Greece has a haemoglobinopathies,  $\beta$ -thalassemia major and sickle-cell disease premarital screening program that showed successful results within 30 years of implementation (Ladis, Karagiorga-Lagana, Tsatra, & Chouliaras, 2013; Theodoridou et al., 2008). However, there is a small decline in the current results due to parental choices, unawareness, and the significant number of immigrants in 1990's from African origins with sickle cell traits (Ladis et al., 2013). The offering genetic counseling is needed to improve the outcomes of the current premarital screening program (Ladis et al., 2013). Research in Greece showed that prenatal diagnosis ending with abortion is highly accepted (Theodoridou et al., 2008).

#### Status of Premarital Screening-United Arab Emirates

United Arab Emirates (UAE) also has a mandatory haemoglobinopathies premarital screening based on complete blood counts and hemoglobin (Belhouli, Bakir, &

Abdulrahman, 2013). Most parents refuse abortion, even if they are aware of the risk of having an ill child, after parental diagnosis or pre-implantation genetic screening (Belhoul et al., 2013). To improve the premarital screening program, UAE must increase the community awareness of the program and provide genetic counseling, prenatal diagnosis and pre-implantation genetic counseling (Belhoul et al., 2013). UAE also has a mandatory premarital screening for HIV along with testing for syphilis, hepatitis B, and genetic disorders (Barss et al., 2009). HIV patients are reported to the police in order to trace the source of transmission (Barss et al., 2009). Moreover, HIV patients are still legally permitted to get married, but religious and cultural traditions makes it complicated (Ganczak, 2010).

#### Status of Premarital Screening-India

India Sub-Continent including the Sri Lankan island does not have a mandatory premarital screening program, but studies showed that premarital screening and genetic counseling is very accepted (Balgir, 2010; Mudiyanse, 2006; Tamhankar et al., 2009). Likewise, premarital screening and parental diagnosis is well received by extended family members (Tamhankar et al., 2009). Studies have shown the need for a premarital screening program in the region (Jain et al., 2012; Mohanty & Mukherjee, 2002). Furthermore, genetic counseling is well received between the Indian tribes, although there is a need for permanent public education centers (Mohanty & Mukherjee, 2002). Research conducted on the Delhi Kharia tribal families of Orissa revealed the importance of birth control for parents who have a high probability of having an ill child in order to avoid the high costs of redundant hospital visits (Balgir, 2010). This research also revealed the importance of limiting the number children born from carrier families (Balgir, 2010). Numerous studies have shown the significance of premarital screening for haemoglobinopathy related diseases and HIV, as well as the Indian government's intention to implement such a program in order to increase the population's awareness ailments (Mohanty & Mukherjee, 2002).

#### Status of Premarital Screening-Malaysia

A premarital HIV screening program conducted in a public hospital at Johor, Malaysia has partially contributed to an increase HIV awareness (Khebir, Adam, Daud, & Shahrom, 2007).

#### Status of Premarital Screening-Bahrain

Bahrain has established a premarital screening for sickle cell glucose-6-phosphate dehydrogenase (G6PD) deficiency as a prevention program (S. Al Arrayed, Hafadh, Amin, Al Mukhareq, & Sanad, 2003; S. S. Al Arrayed & Al, 2005).

#### Status of Premarital Screening-Iraq

The Iraqi government has mandated the premarital screening for HIV, syphilis, and HBV but not for haemoglobinopathic related diseases (Al Allawi & Al Dousky, 2010). According to a study in Dohuk, Iraq, Iraq is in need for premarital screening of haemoglobinopathic related diseases due to the high number affected patients (Al Allawi & Al Dousky, 2010).

#### Status of Premarital Screening-The Jewish Community

Jewish communities commonly engage in premarital screening for Tay-sachs, and thalassemia (Zlotogora, 2009). In the United States, Tay-sachs screening has proved effective in educating the public and reducing new cases of Tay-sachs (Zlotogora, 2009). Since, the Jewish laws forbid the termination of pregnancy after the first 40 days, the Ultra-Orthodox Jews refused to participate since the program implemented had an early termination of at risk fetuses, thus causing the development of the Dor Yeshorim program (Prainsack & Firestine, 2006; Zlotogora, 2009). The Dor Yeshorim program was implemented with the understanding of the Jewish match making tradition by withdrawing blood from Ultra-Orthodox Jewish high school students and sending it for genetic screening at a laboratory (Prainsack & Firestine, 2006; Zlotogora, 2009). The results are stored in the Dor Yeshorim offices without informing the students the results. When it is time for the students to get married, the records from the blood testing are used in the match making process in order to avoid unhealthy marriages (Zlotogora, 2009). Dor Yeshorim is not mandatory, but the Ultra-Orthodox church will not allow a marriage in the church without certification showing that the couple has been genetically screened (Zlotogora, 2009). The Dor Yeshorim strategy between Jewish communities exists in the United States, Europe, and Israel and has proved to be advantageous in increasing awareness (Prainsack & Firestine, 2006; Zlotogora, 2009). The Israeli government voluntarily provides the Israelis with premarital screening for Tay-sachs, thalassemia, cystic fibrosis and 37 other genetic disorders carried among non-Jewish free of charge (Zlotogora, 2009).

#### Status of Premarital Screening-Italy



Italy has a premarital screening for thalassemia (Cao & Kan, 2013). In Sardina, an Italian island, there is a voluntary thalassemia premarital screening program (Cao, Rosatelli, Monni, & Galanello, 2002). The main concern of the program is the education of the public about the risk (Zlotogora, 2009). In Sardina, a majority of parents refused genetic counseling (Zlotogora, 2009). Further, some partners admitted that they would not have been in a relationship if they knew they were both carriers (Zlotogora, 2009). While there are not any negative effects of the screening, the program lacks of success (Zlotogora, 2009).

#### Status of Premarital Screening-Cyprus

Cyprus has a free of charge thalassemia premarital screening program (Bozkurt, 2007; Zlotogora, 2009). Three methods are used to decrease the number of affected newborns: education, laboratory screening, and prenatal diagnosis (Bozkurt, 2007). The Greek Orthodox Church supports the program, despite its opposition to abortion, by telling prospective parents they should choose not to get married in order to avoid abortion (Zlotogora, 2009). The Greek Orthodox Church requires screening and potential must present a certificate showing that they have done a premarital screening and genetic counseling (Zlotogora, 2009). The Cyprian premarital screening has shown successful results (Bozkurt, 2007).

#### Status of Premarital Screening-United Kingdom

The UK has a premarital screening for hemoglobin disorders and another for cystic fibrosis that is not been fully implemented (Locock & Kai, 2008). A survey showed that hemoglobin premarital screening is accepted by parents because it helps to make an informed decision (Locock & Kai, 2008). People from both Islamic and Christian faiths are more likely to refuse prenatal diagnosis, such as refusing treatment or reject the idea, since they believe that God gave them a sick child for a reason (Locock & Kai, 2008). However, people of other faiths or of no faith do not refuse the idea of prenatal diagnosis (Locock & Kai, 2008).

#### Status of Premarital Screening-Turkey

By 1998, there were three centers for hemoglobin premarital screening in Southern Turkey and at-risk marriages are referred to Çukurove University Hospital (Çürük et al., 2008). Since the implementation of premarital screening, the number of parents who accept prenatal diagnosis in Southern Turkey has increased (Çürük et al., 2008). The

implementation of the same program in Denizli, Turkey was also another success and parents are accepting of early pregnancy termination after prenatal diagnosis (Kahraman et al., 2000).

#### Status of Premarital Screening-Egypt

Egypt is in need for a premarital screening for hemoglobin related disorders, particularly thalassemia because it appears to be increasing in certain areas (El-Beshlawy & Youssry, 2009).

#### Status of Premarital Screening-United States

The first sickle cell premarital screening implemented in the United States faced many challenges, mainly due to the lack of clinicians and the population's limited awareness of the disorder (Zlotogora, 2009). Subsequently, a survey among African American women designed to comprehend their dissention of prevention and screening revealed that those women understand the risk of having a sick child, but do not believe it will happen to them personally. (Gustafson, Gettig, Watt-Morse, & Krishnamurti, 2007)

Care for an unplanned pregnancy or parents with no previous premarital screening gets preconception and prenatal screening, intended to reduce the maternal and fetal risk that is implemented in countries around the world (Zlotogora, 2009). Some countries have different prospective and laws of premarital pregnancy and dealt with differently (Al-Aama, 2010; Alswaidi et al., 2012; El-Menyar et al., 2009; Zlotogora, 2009).

## 2.2 CULTURAL FACTORS

I searched PubMed and Medline Ovid for "Premarital Examinations/es, px [Ethics, Psychology]" between 2000 and 2014.

Different human rights organizations have recommended that governments avoid HIV premarital screening because it violates the rights of an individual (Luginaah, Elkins, Maticka-Tyndale, Landry, & Mathui, 2005). Illinois' law of mandatory premarital HIV screening resulted in many residents leaving the state of Illinois in order to get married elsewhere (Luginaah et al., 2005). Most Western religious leaders see the importance of increasing awareness and education between the communities (Luginaah et al., 2005). Most Muslim and Christian religious leaders have accepted HIV premarital testing as shown above (Alswaidi et al., 2012; Ghotbi & Tsukatani, 2005; Umar & Oche, 2012). Some religious leaders require that they see the results before they allow religious marriages. Despite the mode of transmission, religious rules and traditions consider HIV patients as sinners, thus not accepted in the church. In some countries, such as the Congo, if either parent has HIV, they are allowed to have a civil marriage at government

institutions (Arulogun & Adefioye, 2010; Rennie & Mupenda, 2008). The religious and government support towards premarital screening can change a society's attitude towards the practice. (Al Sulaiman et al., 2008) Research conducted in Nigeria devised three recommendations for HIV premarital screening:

1. Promotion of HIV testing centers should be sustained and increased.
2. Utilization of health education strategies should be increased to promote public awareness, specifically targeting youth surrounding the risk of HIV/AIDS.
3. Intensification of advocacy strategies by religious institutions which require premarital HIV testing in order to address the ethical issues of test results, such as confidentiality, and dissention of status associated with the practice. (Arulogun & Adefioye, 2010)

## 2.3 CLINICAL FACTORS

Health care around the world differs immensely from hospital to hospital. Most departments or ministries of health, as well as some churches, require hospitals to report patients with positive STI and GBD. Most premarital screenings are exclusively conducted in the lab at public hospitals. Some of those hospitals do not have billing systems since the government pays for healthcare. Numerous paper based health records are to be changed to electronic health records, where data can be stored and reused for analyzing patients' data.

In Saudi Arabia, HBV parents are offered vaccinations in the event that one of the parents presents with the disease due to low occurrence (Al Sulaiman et al., 2008). However, in China, HBV is a massive problem and there are many attempts to reduce that percentage (Hesketh, 2003). In China, premarital screening is sensible since there are many impoverished people who cannot afford treatment of an ill child (Hesketh, 2003). Public healthcare in Saudi Arabia renders premarital screening to be a practical method of reducing the number of ill children, as public hospitals cannot handle the vast number of sickle cell anemia and thalassemia cases.

## 3. LITERATURE REVIEW

While a number of hospitals are converting from using paper based medical records to electronic health records (EHR), a clinical decision support system (CDSS) to evaluate the data from the data warehouse could potentially speed up this procedure. Furthermore, CDSS would allow people to make informed decisions towards marriage. A genetic counselor could use CDSS and lab results to better serve couples. Decisions supported by the CDSS would tell the marrying couple the statistical risk of bearing infected children.

In this case, the couple could sign the review, stating that they take the financial responsibility for their future children's health care if the percentage of risk is greater than 25%. This paper examines the techniques and methods that could be made to create a CDSS to be placed in the EHR's. This literature review is to help improve the Healthy Marriage program in Saudi Arabia. Are there any other diseases and disorders that should be included in the Healthy Marriage program to improve it? How is it possible to successfully implement a CDSS to help achieve the Health Marriage program goals?

I searched PubMed and Medline Ovid for ("Premarital Screening"), AND [{"Hemoglobinopathies"}] OR ("Sexually Transmitted Diseases") OR ("Hepatitis")] between 01/01/2000 until 06/15/2014 to see the different action that has been taken to prevent genetic blood disorders and Sexual Transmitted Infections.

I searched PubMed and Medline Ovid for ("Detection") AND [{"Information Systems"}] OR ("Decision Support Techniques") OR ("Diagnosis, Computer-Assisted") OR [{"Decision Support Systems, Clinical"}] AND [{"Hemoglobinopathies"}] OR ("Sexually Transmitted Diseases") OR ("Hepatitis"). The search was between 01/01/2000 until 06/15/2014 to look for a research that has been done to detect those diseases using a computer based clinical decision support system but the results came as 0. As of right now, the laboratory results are the best way to detect STI's and GBD's.

I searched ("Sexually Transmitted Diseases") and ("Saudi Arabia")

I searched ("Sexually Transmitted Diseases") and ("Curable")

I searched ("Sexually Transmitted Diseases") and ("Incurable")

I searched ("Genetic Blood Disorders")

I searched ("Blood Disorders") and ("inherited")

I searched ("Saudi Arabia") AND [{"Medical Health Records"}] OR ("Electronic Health Records")]

I searched [{"Decision Support Techniques"}] OR [{"Decision Support Systems, Clinical"}] AND ("Computer-Aided Design") AND [{"Medical Health Records"}] OR ("Electronic Health Records")]

### 3.1 CLINICAL FACTORS

#### **Sexual Transmitted Infections**

Sexual Transmitted Infections (STI) is defined as a collected group of diseases that can be transmitted by having sexual contact or through birth. Two articles discussed the most common STI's in Saudi Arabia (Al-Ghamdi & Kabbash, 2011; Madani, 2006). There are cases of trichomonas, gonorrhea, syphilis, HIV, genital herpes, and chancroid. (Al-Ghamdi & Kabbash, 2011; Madani, 2006) However, there is a variety of additional STI's spread around the world to be included in the study. Some of these STI's are curable while others are not. Education of STI's and their treatments is one effort to reduce incurable STI's such as HIV (Eaton et al., 2012; Hayes, Watson-Jones, Celum, van de Wijgert, & Wasserheit, 2010; Korenromp et al., 2005; Kurth, Celum, Baeten, Vermund, & Wasserheit, 2011; Steen, Wi, Kamali, & Ndowa, 2009; White et al., 2008).

### **Curable STI's**

Some of the STI's listed in the table can be cured, especially with an early diagnosis.

#### Trichomonas

Trichomonas is a curable STI that is caused by *Trichomonas Vaginalis*, a protozoan parasite infection (McGowin, Rohde, & Redwine, 2014; Workowski & Berman, 2006). *Trichomonas* causes irritation, discharge and burning in the genital areas. It can also increase a person's susceptibility to HIV (Coleman, Gaydos, & Witter, 2013; McGowin et al., 2014; Sutcliffe, Neace, Magnuson, Reeves, & Alderete, 2012; Workowski & Berman, 2006). It is acknowledged as non-gonococcal urethritis for men, but can differ in women between asymptomatic to acute inflammatory vaginitis (Muzny & Schwebke, 2013). Additionally, trichomonas can be transmitted to newborns by their mothers during birth (Coleman et al., 2013). Traditionally, trichomonas is diagnosed by direct microscopic examination of a wet mount of vaginal fluid or via culture (Bachmann et al., 2000; Muzny & Schwebke, 2013; Zarakolu, Alp, & Yağci, 2010). Recently, nucleic acid amplification tests have been used as a diagnostic tool (Coleman et al., 2013; Muzny & Schwebke, 2013). Physicians can cure trichomonas by means of antibiotic medication unless the patient has a nitro-imidazole allergy. In the event of such an allergy, intravaginal therapies can be used as a replacement, though this method has not proven as effective (Muzny & Schwebke, 2013).

#### Pelvic Inflammatory Disease (PID)

Pelvic Inflammatory Disease (PID) is an infection of a women's reproductive organs (Mitchell & Prabhu, 2013; Workowski & Berman, 2006). PID can be caused by having an STI, such as gonorrhea or chlamydia, which goes untreated (Mitchell & Prabhu, 2013; Workowski & Berman, 2006). While PID is an infection that only affects women, it can be transmitted by having sex with a man who carries the disease (McGowin et al., 2014; Mitchell & Prabhu, 2013; Workowski & Berman, 2006). Antibiotics which treat

anaerobic infections should be considered to treat severe PID (Mitchell & Prabhu, 2013). Cefotetan, Cefoxitin or Doxycycline cover anaerobic bacteria and can be used to cure PID (Workowski & Berman, 2006). If PID is not treated, it can cause serious health complications (Mitchell & Prabhu, 2013). There are a variety of diagnostic tools to help examine a patient for PID (Mitchell & Prabhu, 2013). Immediate hospitalization and treatment is required for pregnant women with PID in order to avoid complications (Workowski & Berman, 2006).

### Chlamydia

Chlamydia can be cured if diagnosed early, but it could affect women by causing trouble during pregnancy (Workowski & Berman, 2006). Chlamydia can cause throat, rectum, and genital infections. Symptoms may include a burning sensation while urinating, abnormal discharge in the penis or vagina, pain or swelling in one or both testicles, or a rectum infection that causes rectal pain, discharge or bleeding (Workowski & Berman, 2006). Chlamydia trachomatis is recognized in men as urethritis in males and endocervicitis in women (Malhotra, Sood, Mukherjee, Muralidhar, & Bala, 2013). Chlamydia trachomatis is typically diagnosed using culture but today some clinics use diagnostic techniques, particularly molecular methods, though these may not be as reliable as diagnostic cultures (Malhotra et al., 2013). Other diagnosis may be supported by performing optic immunoassay by using endocervical specimens.

Chlamydia can increase the chance of getting HIV and Pelvic Inflammatory Disease in women (Gottlieb, Xu, & Brunham, 2013; Malhotra et al., 2013). Pregnant women who give birth with chlamydia trachomatis can face many challenges such as low birth weight, neonatal death, decreased gestational periods, preterm delivery and premature rupture of membranes (Malhotra et al., 2013). On average, most cases of Chlamydia trachomatis can be treated by one gram of azithromycin orally in a single dose, 100 mg doxycycline orally twice a day (bid), 500 mg orally four times a day (qid) or ofloxacin 300 mg orally (bid) for seven days with avoidance of sexual contact (Malhotra et al., 2013). The risk of obtaining Chlamydia a second time after it is initially cured is exceptionally high (Malhotra et al., 2013) (Gottlieb et al., 2013).

### Syphilis

Syphilis can be cured; however, the cure will not fix the harm that has been caused by the disease (Goh, 2005; Workowski & Berman, 2006). Syphilis has three stages: primary, secondary and late. In the primary stage, there will be painless sores, either single or multiple (Goh, 2005; Workowski & Berman, 2006). After a going untreated or after unsuccessful treatment, the disease develops to the secondary stage (Goh, 2005; Workowski & Berman, 2006). Symptoms of this stage are a skin rash and/or sores in the vagina, anus or mouth (Goh, 2005; Workowski & Berman, 2006). The late stage follows

with paralysis, dementia, blindness, numbness, and difficulty managing muscle movements (Workowski & Berman, 2006). It can be examined by rapid plasma regain (RPR) or syphilis serologic testing (Bachmann et al., 2000; Goh, 2005; Zarakolu et al., 2010). Syphilis can be cured by penicillin G with a variation in the dose between early and late diagnosis (Workowski & Berman, 2006).

### Gonorrhea

Gonorrhea can be cured if diagnosed early, but it could affect women by causing trouble during pregnancy (Bai, Bao, Cheng, Yang, & Li, 2012; Workowski & Berman, 2006). Gonorrhea can cause throat, rectum, and genital infections. Symptoms such as a burning sensation while urinating, abnormal discharge in the penis or vagina, pain or swelling in one or both testicles, or a rectum infection that causes rectal pain, discharge or bleeding (Workowski & Berman, 2006). Nucleic acid amplification tests have been used for diagnosis (Coleman et al., 2013). Alternatively, microscopic examination of Gram stained endocervical smears for the existence of gram-negative intracellular diplococci can be used to formulate a diagnosis (Zarakolu et al., 2010).

### Chancroid

Chancroid is a HIV related disease and can be diagnosed by culture to identify *H. ducreyi* (Workowski & Berman, 2006). The chancroid cure options are Azithromycin, Ceftriaxone, Ciprofloxacin, or Erythromycin based (Workowski & Berman, 2006).

### Lymphogranuloma Venereum

This disease is associated with *Chlamydia trachomatis* (Workowski & Berman, 2006). Doxycycline or Erythromycin based medications can cure Lymphogranuloma Venereum (Workowski & Berman, 2006).

### Bacterial Vaginosis

This disease occurs mostly in women who have sex with multiple partners (Workowski & Berman, 2006). While there is no beneficial cure for bacterial vaginosis in men, it can be cured in women by Metronidazole, Metronidazole gel, Clindamycin cream, Clindamycin or Clindamycin (Workowski & Berman, 2006). Pregnant women with bacterial vaginosis require immediate treatment (Workowski & Berman, 2006).

### Epididymitis

Epididymitis is associated with gonorrhea and chlamydia. Symptomatically, it causes pain, swelling, and inflammation of the epididymis (Workowski & Berman, 2006). It can

be clinically diagnosed by culture, nucleic acid hybridization tests, or nucleic acid amplification tests (Workowski & Berman, 2006).

### **Incurable STI's**

There are two kinds of incurable STI's, treatable and untreatable.

#### Herpes simplex virus (HSV)-1/2

Both HSV-1 and HSV-2 can cause genital herpes (Workowski & Berman, 2006). HSV-1 is the first stage to cause genital herpes and HSV-2 is recognized as genital herpes (Workowski & Berman, 2006). Virologic and specific serologic tests can be used to diagnose HSV. Antiviral therapy treatments such as acyclovir, famciclovir, and valacyclovir are used for patients with their first clinical episode of genital herpes. (STIs: flushing out the "hidden epidemic". 2000) (Workowski & Berman, 2006). 2006) Pregnant mothers typically pass genital herpes to their infants during natural childbirth (Workowski & Berman, 2006).

#### Human Immunodeficiency Virus (HIV)/ AIDS

HIV is a virus that destroys the immune system and can cause neurological complications (Nath, 2002). HIV can be diagnosed clinically through blood tests for HIV antibodies after two to 6 weeks of being infected (Nath, 2002; Workowski & Berman, 2006). Any individuals diagnosed with HIV should be referred to a psychology clinic as a way to help cope with emotional distress and mental health issues that may arise from being diagnosed (Workowski & Berman, 2006). HIV cannot be cured but some medications can reduce the reproduction of HIV (Nath, 2002; Workowski & Berman, 2006). HIV can infect all ages and genders and can be spread to others (Nath, 2002; Workowski & Berman, 2006). Transmission typically occurs by:

- A mother to her child
- Sexual activities
- Blood transfusions
- Injection equipment

Women should be tested before planned pregnancies since an infected mother can transmit HIV to their infant(s) during pregnancy. If HIV is not clinically treated by antiretroviral medications or the use of other interventions, HIV infected individuals can develop AIDS after a period of ten years (Nath, 2002; Workowski & Berman, 2006).

#### Granuloma Inguinale (Donovanosis)



This ulcerative disease is a rare condition caused by the intracellular gram-negative bacterium (Workowski & Berman, 2006). The disease is painful and the symptoms are progressive ulcerative lesions without regional lymphadenopathy (Workowski & Berman, 2006). The infection's treatment is the use of doxycycline, azithromycin, ciprofloxacin, erythromycin base or trimethoprim-sulfamethoxazole (Workowski & Berman, 2006).

## **Hepatitis**

Not all cases of hepatitis are considered as STI; however, they are very contagious by blood and body fluids (Workowski & Berman, 2006).

### Hepatitis B Virus (HBV)

Hepatitis B is can exist in body fluids and blood (Workowski & Berman, 2006). It is transmitted by the exposure of an infected individual's blood, body fluid or through having unprotected sex with hepatitis b infected patient (Workowski & Berman, 2006). To prevent transmission to healthy individuals, proper vaccination routines should utilized, especially for people who live close to or in close contact with a hepatitis b infected patient (Workowski & Berman, 2006). Infants from infected mothers should receive routine prenatal vaccinations (Workowski & Berman, 2006). Monogamy can decrease the risk spreading the infection widely (Workowski & Berman, 2006). Serologic testing for HBsAG can diagnose hepatitis b (Workowski & Berman, 2006). In some cases, therapeutic agents can sustain the suppression of HBV replication and remission (Workowski & Berman, 2006).

### Hepatitis C Virus (HCV)

Hepatitis C is caused by HCV and is not always considered an STI (Workowski & Berman, 2006). The most common mode of transmission is via injected-drug use (Workowski & Berman, 2006). However, it is possible for a mother to pass HCV on to her infant during delivery (Workowski & Berman, 2006). HCV presents in the DNA after one to three weeks of exposure (Workowski & Berman, 2006). Some chronic HCV patients have shown active liver disease (Workowski & Berman, 2006). The most common treatment method is combination therapy with pegylated interferon and ribavirin (Workowski & Berman, 2006). Currently there is no vaccination available for HCV (Workowski & Berman, 2006).

## **Genetic Blood Disorders**

Genetic disorders are spread in different parts of the world, especially the Arab world because of high consanguinity rates, high prevalence of haemoglobinopathies, high rate of children with Down's syndrome, lack of public health measures directed at the prevention of congenital and genetic disorders, and services for the prevention and control of genetic disorders are restricted by certain cultural, legal, and religious limitations (Al-Gazali, Hamamy, & Al-Arrayad, 2006). In this intervention, the focus is on Genetic Blood Disorders (GBD). GBD's are usually inherited from parents and their treatment can be complicated, especially if the person is affected by more than one GBD.

### Sickle Cell Disease (SCD)

Sickle cell disease (SCD) is a deadly monogenic disorder. SCD is “a mutation in the hemoglobin beta resulting in a single amino acid substitution of the normal glutamic acid” (Norman & Miller, 2011; Paul, 2012; Prevention, 2014). SCD patients inherit two abnormal genes from each parent (Paul, 2012; Prevention, 2014). SCD can be diagnosed using hemoglobin electrophoresis testing method (Paul, 2012). Having one abnormal gene is considered an SCD trait, as these individuals can carry the gene to the next generation (Paul, 2012). Any person can be categorized with one of the following classifications as a relationship to SCD:

- HbAA, normal genotype
- HbAS, sickle cell trait
- HbSS, sickle cell disease

There are many ways to prevent new cases of SCD such as:

- Prenatal diagnosis and abortion (Paul, 2012),
- Avoid marrying two infected parents HbSS : HbSS,
- Avoid marrying infected parent with another who carry the genes HbSS : HbAS
- Avoid marrying two carrier parents HbAS : HbAS

There is no effective cure for SCD, but it can be treated by blood transfusion (Paul, 2012). SCD can present in many conditions such as leg ulcers, Splenectomy, Roentgenogram Cardiomegaly, Gallstones, Hemiplegia, Meningitis (all bacterial), Meningitis (pneumococcal), Priapism, Osteomyelitis, Femoral Head Necrosis, and Hand-foot syndrome, Hepatic "Crisis" (PERRINE, PEMBREY, John, Perrine, & SHOUP, 1978).

### Thalassemia

Thalassemia is a recessive disease (Jagannath, Fedorowicz, Al Hajeri, Hu, & Sharma, 2011) a number of missing genes/defects in the synthesis of alpha or beta hemoglobin chains determines the severity of one's thalassemia (Paul, 2012). Thalassemia can be diagnosed using the hemoglobin electrophoresis testing method (Paul, 2012). Every healthy human being has four genes that make alpha hemoglobin chains, two genes from each parent. Additionally, each healthy human being has two beta genes, one from each parent (Paul, 2012). A person with one missing or defective alpha genes is a silent carrier, two missing or defective alpha genes can cause sub-clinical anemia, three missing or defective alpha genes results in hemoglobin H disease, and four missing alpha genes results in infant death (Paul, 2012). Missing or defective beta genes can be varies between minor, asymptomatic, or major anemia, which is known as Cooley's anemia (Paul, 2012). Patients with major thalassemia show splenomegaly and bone malformations and they are more likely to die before the age of 20, but it can be treated with bone marrow transplantation (Paul, 2012). Severe thalassemia conditions might require blood transfusions (Abuljadayel et al., 2006; Paul, 2012). Moreover, it is possible for a child to have a combination of both thalassemia and SCD(Paul, 2012).

### Haemophilia A

Haemophilia occurs when the blood clotting process is damaged, resulting in severe internal and external bleeding (Knight, 2005). While there is no cure for this disorder, it can be treated with infusions of clotting factor VIII (FVIII) (Knight, 2005). Most bleeding is internally into the muscles or joints. (Knight C. 2005) Some patients develop inhibitor, neutralizing antibodies, to FVIII and require a different type of treatment (Knight, 2005).

### Fanconi anemia (FA)

FA is a rare and complex condition that is associated with 15 genes (Korthof et al., 2013). The most frequent mutations happen between three genes:

- FANCA (FA complementation group A)
- FANCC (FA complementation group C)
- FANCG (FA complementation group G)

### Porphyria

Porphyria has many different stages and metabolic clinical entities (Standerwick, Yen, & Pliska, 2013); however, they all have common features, such as accumulation of porphyrins or their precursors, red urine color (Paul, 2012). Porphyria Cutanea Tarda (PCT) is a common porphyria condition, which occurs later in life (Paul, 2012).

Porphyria is rare but it exists (Paul, 2012). Porphyria can be autosomal dominant and recessive depending in the type of porphyria in each couple (D. B. S. Marks, Todd;

Sandra I Kim; Marc Glucksman, 2007). Porphyria can be diagnosed by urine porphobilinogen (PBG) screening for fluorescence (Paul, 2012). Removing blood every two weeks to help the overload of the iron level (Paul, 2012).

### Erythropoietic Protoporphyria (EEP)

EEP is the defective development of the heme group of hemoglobin, “a deficiency of the enzyme ferrochelatase”, causing accumulation of protoporphyrin and painful photosensitivity of the skin and tissues (Standerwick et al., 2013). This disorder might be treated by therapies, but there are no positive results for therapy treatments resulting in a cure (Standerwick et al., 2013). EEP patients show one or more symptoms, after the exposure to the sun, such as stinging, itching, burning sensations and blistering (Standerwick et al., 2013).

### Hereditary Hemochromatosis (HH)

This is an iron overload disease (Paul, 2012). (Paul Starr S. 2012) HH is a recessive gene that can be inherited from the parents. The HH gene can also be carried and inherited from older generations (Paul, 2012). (Paul Starr S. 2012) Most HH patients can be treated with phlebotomy (Paul, 2012). (Paul Starr S. 2012)

### Hemochromatosis (Iron Storage Disease)

Hemochromatosis is a genetic blood disorder where the body obtains too much iron from food and other sources. Hemochromatosis is treated by removing blood via phlebotomy, but it is not curable. It can be diagnosed by conducting blood tests and measuring the iron levels. It can be inherited if both parents have it.

## 3.2 CULTURAL FACTORS

Most religions recommend that their communities have healthy families. One of the main goals of premarital screening is to protect newborn children from getting incurable disorders. Different countries have different laws and acceptance levels of premarital screenings. Cultural and governmental perspectives of premarital screening are reflected on to society, causing varied acceptance.

In Islam, Qur’anic laws state following:

الْحَبِيثَاتُ لِلْحَبِيثِينَ وَالْحَبِيثُونَ لِلْحَبِيثَاتِ وَالطَّيِّبَاتُ لِلطَّيِّبِينَ وَالطَّيِّبُونَ لِلطَّيِّبَاتِ ۗ أُولَٰئِكَ مُبَرَّءُونَ مِمَّا يَقُولُونَ ۗ لَهُمْ مَغْفِرَةٌ ۗ وَرِزْقٌ كَرِيمٌ

The previous *Ayah* from the Quran can be explained differently as a general law (Alro7) but one of the meanings could be translated as unhealthy women are for unhealthy men and healthy women are for healthy men. The passage from the Quran suggests that society should stop the spread of HIV and STI's. Generally speaking, unhealthy individuals should not marry healthy individuals in an effort to reduce the number of people with incurable diseases.

Some Islamic countries promote a program called Healthy Marriage (Mohammed Ali Albar, 1991). Healthy Marriage is a premarital screening program used in many countries such as Saudi Arabia, Qatar, United Arab Emirates, and others. The program is for use in marrying prospective couples. Marriage involves sex, which could be risky if one of the partners has an STI and is engaging in unprotected sex. If one or both parents carry any STI's or genetic blood disorders, a resulting child could potentially be adversely affected. Currently, the program is developed in parts of the world where GBD's and STI's are a problem for financial reasons. "Termination pregnancy of affected fetuses is not very popular in the region [17], although it may be starting to gain acceptability [19]" (Al-Aama, 2010). In some cultures, especially in the Middle Eastern area, individuals are encouraged to marry relatives, first and second cousins, in order to keep the next generations close to the family. In addition, Islamic laws do not prevent consanguinity. Even though relatives might carry the same harmful genes of a genetic blood disorder, the tradition continues (Mohammed A Albar, 2002). Consanguinity is one of the main reasons of increases in genetic blood disorders (Bittles & Black, 2010; Carter, 1977; El Mouzan, Salloum, Herbish, Qurachi, & Omar, 2008; Vogel, 1997).

Most religions, specifically Islam, Christianity, and Judaism, refuse abortion as a solution because of the belief it is God's plan. However, Islamic and Jewish leaders came up with a new religious law to allow abortion before ensoulment. The Jewish community allows abortions during the first 40 days of pregnancy while Muslims allow abortion during the first 120 days of pregnancy.

### 3.3 TECHNICAL FACTORS

Results from premarital screening tested by only one laboratory source might not be accurate. Despite the new developments and various ways to genetically test for GBD's, antenatal screening has been proving to be more effective than mass screening and genetic counseling to increase the number of newborns with GBD's (Lippman, 1991; Marteau, 1995). In the near future, antenatal screening might be replaced by DNA technology, ultrasound scanning and assaying maternal blood factors (Kuliev & Modell, 1990). HIV and Hepatitis screening is highly controversial in terms of cost and ethics; however, some countries can afford it (Al Sulaiman et al., 2008).

### **Electronic Health Records**

An Electronic Health Record (EHR) is a database that contains patient information from one or more sources. EHR's primary purposes are to support, maintain and improve health care respectfully (Hoerbst & Ammenwerth, 2010). EHR is used in different types of health care such as tertiary, secondary, primary and even home care. EHR's should be secure, reliable, portable, interoperable, and efficient (Hoerbst & Ammenwerth, 2010). Some EHRs allow patients to access their electronic records from home or on the cloud through Patient Portal or Personal Electronic Records (PHR). While data is being input from different resources, all of it is stored in one place where it can be used again and easily accessed. Historical data in EHR is a useful resource for clinicians in critical situations. One of the benefits of the data in EHR's database is the ability to use Clinical Decision Support Systems.

Despite the barriers of implementing EHR's in Saudi Arabia, many Saudi hospitals are in the process of implementing HER (Khalifa, 2013, 2014). As a part of moving towards EHR in Saudi Arabia, National Guard Health Affairs (NGHA) and that of the King Faisal Specialist Hospital and Research Center (KFSH & RC) in Riyadh (Altuwaijri, 2008) received recognition for their eHealth integration and applying the Health Level Seven (HL7) international standards (International, 2007-2015).

### **Clinical Decision Support Systems**

Clinical Decision Support Systems (CDSS) are decision-making tools that use data stored in EHR. CDSS are mostly used in communities where EHRs are implemented. CDSS and EHR work together to improve health care and reduce its cost (Hillestad et al., 2005; Kuperman et al., 2007; Musen, Middleton, & Greenes, 2014). Drug interaction CDSS is an example of a support system that prevents prescription mistakes. Data is stored where it can be used later to support a decision. "These systems provide several modes of decision support, including alerts of critical values, reminders of overdue preventive health tasks, advice for drug prescribing, critiques of existing health care orders, and suggestions for various active care issues" (Garg et al., 2005).

### **3.4 PROBLEM STATEMENT AND SPECIFIC AIMS**

While the Healthy Marriage Program is the current program used to prevent the growing number of newborns suffering from thalassemia, SCD, HIV infections, HBV and HCV; it is redundant, slow, incomplete and inaccurate. The current process is limited to only a few disorders and infections. The transformation from paper medical records to electronic health records presents the opportunity to screen for additional diseases and disorders.

Premarital Screening in Saudi Arabia, Qatar and United Arab Emirates is stopping people from having the freedom to choose to whom they want to marry instead of educating them of the sexual and genetic outcomes of getting married. The aim of this study is to increase

screening for as many diseases and disorders electronically. The design of this CDSS depends in the marriage culture of the demographic where CDSS is implemented like Dor Yeshorim premarital screening between the Jewish communities.

The premarital screening programs main goal is the prevention of disorders and increased awareness for them. That program cannot be successful without genetic/sex counselors to educate the public. Places like Saudi Arabia do not have enough trained counselors.

“The purpose of this Research is design a Clinical Decision Support System to replace the traditional Healthy Marriage in Saudi Arabia. The research is to help stretch the number of diagnosis screened in the program. The healthy marriage program will be redefined to fit the Saudi Arabia culture.”

## 4. METHODOLOGY

### 4.1 IRB

### 4.2 DATA SOURCES, DATA CLEAN UP ETC

#### Ministry Of Health (MOH)

MOH is in charge of keeping records of infected people. Those records are used to evaluate the health and medical outcomes of the health care system. It is also used to help patients in need financially by giving them a recommendation showing their disability to work. Those records are mostly documented on paper and are outdated. Their usefulness would not be as efficient in this project

#### Electronic Health Records (EHR)

Data in EHR's could be stored differently using various coding systems. Any information stored in EHR can be retrieved at any time and in any place simply by connecting different EHRs to the portal. Even though different hospitals might be using different EHR system from different providers, data from hospitals and clinics is accessible and comprehended by EHR as long as they use HL7 standards. EHRs use one or more different coding systems. (Coates, 2014) The coding systems are:

#### LOINC

Universal Lab Order Codes Value Set from LOINC ([www.loinc.org](http://www.loinc.org)). LOINC consists of a set of codes in multiple languages to fit with the HL7 standards. ([www.loinc.org](http://www.loinc.org)). (Coates, 2014)

## ICD

The World Health Organization (WHO) developed and monitors the International Classification of Disease (ICD). ICD consists of alphanumeric codes for diagnosis, symptoms, or cause of death. On October 1, 2014, ICD was upgraded from ICD-9 to ICD-10 version. (Coates, 2014)

## SNOWMED CT

SNOMED Clinical Terms (SNOMED CT) are more than 311000 active concepts that can be mapped to any coding systems. It is used to standardize terms between different providers and EHR's. (Coates, 2014)

## CPT

The American Medical Association (AMA) developed and monitors Current Procedural Terminology (CPT). Insurance companies use CPT for billing purposes and the coding in CPT standardizes medical communication across the board. (Coates, 2014)

## Ministry Of Foreign Affairs (MOFA)

Some Islamic countries such as Saudi Arabia do not allow premarital sex. That does not stop people from having premarital sex while traveling to other countries. Couples who have traveled should be tested before being able to get married in order to protect the healthy couple. The MOFA's database can provide the entry and exits of every resident. CDSS has to have access to custom's database to look up exit dates using the national ID number. The number will force the person to have to undergo STI testing, even if they have been previously tested, before allowing them to get married.

### 4.3 DESIGN ELEMENTS

The CDSS overall design consists of a variety of STI's, hepatitis, and genetic blood disorder decision trees. The transforming patterns of STI's or hepatitis are not as complicated as genetic blood disorders. Below, I creating the inheritance pattern of all genetic blood disorders used in the CDSS. The inheritance pattern helped recognize the risk factor in every single genetic blood disorder.

The design engine contains inputs, process and outputs:

#### Inputs

- Male national ID



- Female national ID

#### Process

- Retrieve country last exit time
  - If exit date is after STI and hepatitis testing
    - Red flag/Proceed after retesting
  - If either or both couple is outside the country
    - Red flag/Proceed after testing at one of the hospitals or clinics assigned by MOH
  - Else
    - Proceed
- Retrieve STI tests dates
  - If no test date
    - Red flag/Proceed after testing again
  - If test date is more than six months old
    - Red flag/Proceed after testing again
  - Else
    - Proceed with the most recent diagnoses
- Retrieve STI diagnoses
  - If one of the couples has a STI
    - If STI curable
      - Red flag/Proceed after curing STI then
    - If STI treatable
      - Red flag/Proceed after treating STI and informing the other couple
    - If STI Untreatable
      - Red flag/Proceed after informing the other couple on the risk
  - If both couples have the same type of STI
    - If STI curable
      - Red flag/Proceed after curing STI
    - If STI treatable
      - Red flag/Proceed after treating STI and informing the couple
    - If STI Untreatable
      - Red flag/Proceed after informing the other couple on the risk
  - Else
    - Proceed
- Retrieve Hepatitis tests dates
  - If no test date
    - Red flag/Proceed after testing again
  - If test date is more than six months

- Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for hepatitis B
  - If both have no Hepatitis B
    - Proceed
  - If both have hepatitis B
    - Red flag/Proceed after consultation
  - If either has Hepatitis B
    - If the other couple has the same type of Hepatitis B
      - Green flag with consultation recommendation
    - Else
      - Red flag until vaccination, counselling and education session
  - If either or both has Hepatitis C
    - If the other couple has the same type of Hepatitis C
      - Green flag with consultation recommendation
    - Else
      - Red flag until counselling and education session
- Retrieve Sickle Cell Disease tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for Sickle Cell Disease
  - If one parent is carrier and the other is infected
    - Red flag/Proceed after consultation
  - If both parents are infected
    - Red flag/Proceed after consultation
  - If both parents are carrier
    - Red flag/Proceed after consultation
  - If either parent is healthy
    - Green flag
  - If both parents are healthy
    - Green flag
- Retrieve Thalassemia tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed

- Retrieve tests and diagnosis for Thalassemia
  - If one parent is carrier and the other is infected
    - Red flag/Proceed after consultation
  - If both parents are infected
    - Red flag/Proceed after consultation
  - If both parents are carrier
    - Red flag/Proceed after consultation
  - If either parent is healthy
    - Green flag
  - If both parents are healthy
    - Green flag
- Retrieve Fanconi Anemia tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for Fanconi Anemia
  - If one parent is carrier and the other is infected
    - Red flag/Proceed after consultation
  - If both parents are infected
    - Red flag/Proceed after consultation
  - If both parents are carrier
    - Red flag/Proceed after consultation
  - If either parent is healthy
    - Green flag
  - If both parents are healthy
    - Green flag
- Retrieve Hereditary Hemochromatosis tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for Hereditary Hemochromatosis
  - If one parent is carrier and the other is infected
    - Red flag/Proceed after consultation
  - If both parents are infected
    - Red flag/Proceed after consultation
  - If both parents are carrier
    - Red flag/Proceed after consultation
  - If either parent is healthy

- Green flag
  - If both parents are healthy
    - Green flag
- Retrieve Hemochromatosis tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for Hemochromatosis
  - If one parent is carrier and the other is infected
    - Red flag/Proceed after consultation
  - If both parents are infected
    - Red flag/Proceed after consultation
  - If both parents are carrier
    - Red flag/Proceed after consultation
  - If either parent is healthy
    - Green flag
  - If both parents are healthy
    - Green flag
- Retrieve Haemophilia A tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for Haemophilia A
  - If one parent is carrier and the other is infected
    - Red flag/Proceed after consultation
  - If both parents are infected
    - Red flag/Proceed after consultation
  - If both parents are carrier
    - Red flag/Proceed after consultation
  - If both parents are healthy
    - Green flag
- Retrieve Erythropoietic Protoporphyrin tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for Erythropoietic Protoporphyrin
  - If one parent is carrier and the other is infected

- Red flag/Proceed after consultation
  - If both parents are infected
    - Red flag/Proceed after consultation
  - If both parents are carrier
    - Red flag/Proceed after consultation
  - If either parent is healthy
    - Green flag
  - If both parents are healthy
    - Green flag
- Retrieve Porphyria tests
  - If no test
    - Red flag/Proceed after testing again
  - Else
    - Proceed
- Retrieve tests and diagnosis for Porphyria
  - If the Porphyria type is congenital erythropoietin porphyria (CEP) and Doss porphyria/ALA dehydratase deficiency
    - If one parent is carrier and the other is infected
      - Red flag/Proceed after consultation
    - If both parents are infected
      - Red flag/Proceed after consultation
    - If both parents are carrier
      - Red flag/Proceed after consultation
    - If either parent is healthy
      - Red flag/Proceed after consultation
    - If both parents are healthy
      - Green flag
  - Else
    - If one parent is carrier and the other is infected
      - Red flag/Proceed after consultation
    - If both parents are infected
      - Red flag/Proceed after consultation
    - If both parents are carrier
      - Red flag/Proceed after consultation
    - If either parent is healthy
      - Green flag
    - If both parents are healthy
      - Green flag

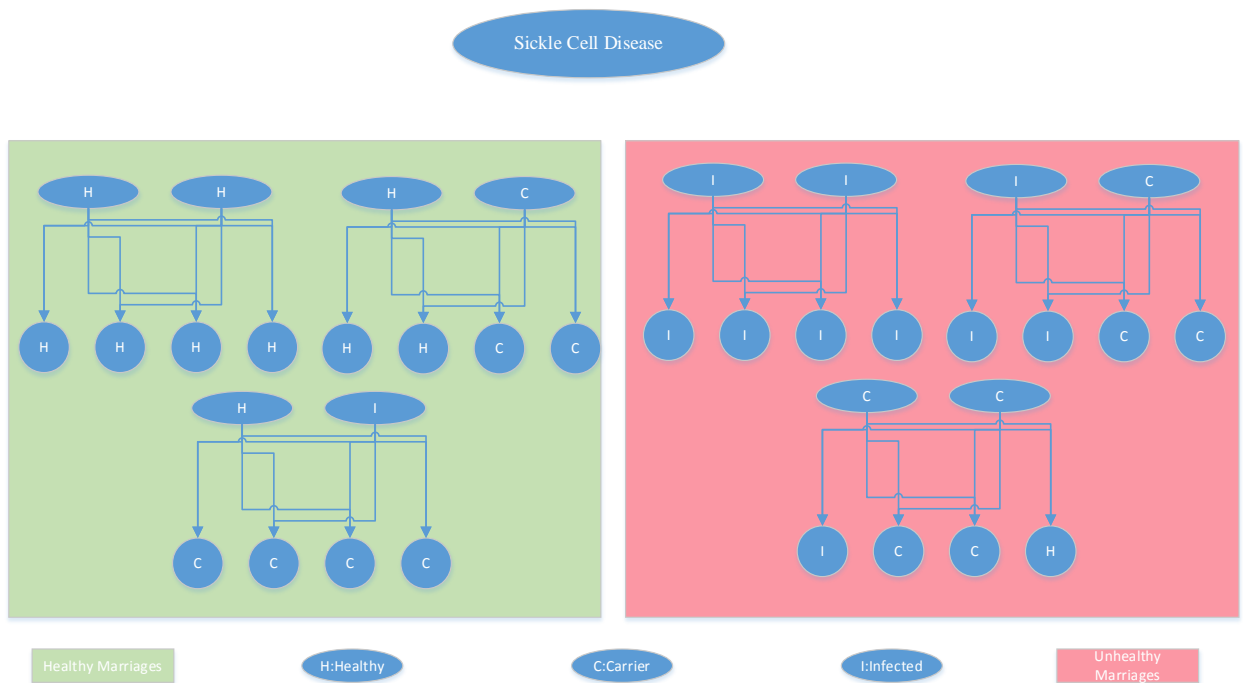
Outputs

- HMID that shows
  - o Red flag
    - The HMID will show to the counsellor but not the user
      - Reasons why it is red
  - o Green flag
    - The HMID will show to the counsellor and the user
      - Couple can get married

## Inheritance Pattern

### Sickle Cell Disease

It has an autosomal recessive inheritance pattern (Sciences, 2015). Healthy marriages are between two healthy parents. Healthy but not recommended marriages are the ones that have a chance of having carrier children. Unhealthy marriages are where one or more children might be sick.

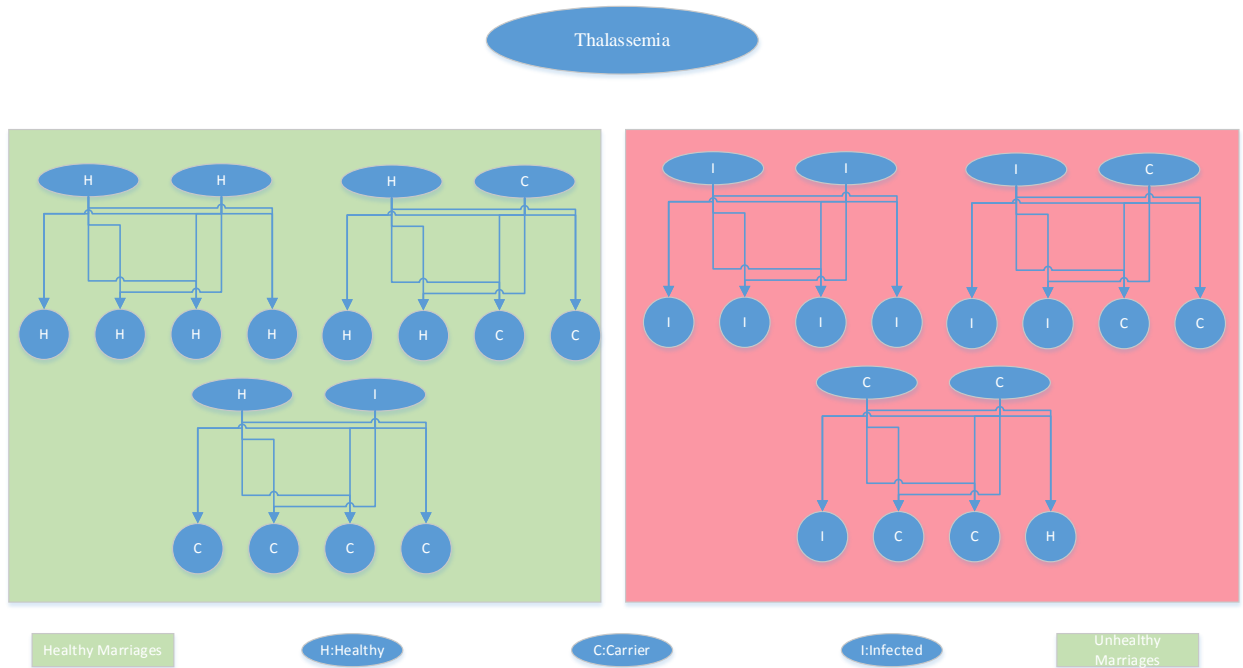


**FIGURE 2 SICKLE CELL DISEASE INHERTANCE PATTE**

### Thalassemia

Both Beta (Communications, 2009) and Alpha(Origa, Moi, Galanello, & Cao, 2013) Thalassemia have an autosomal recessive inheritance pattern. Healthy marriages are between two healthy parents. Healthy but not recommended marriages are the ones that

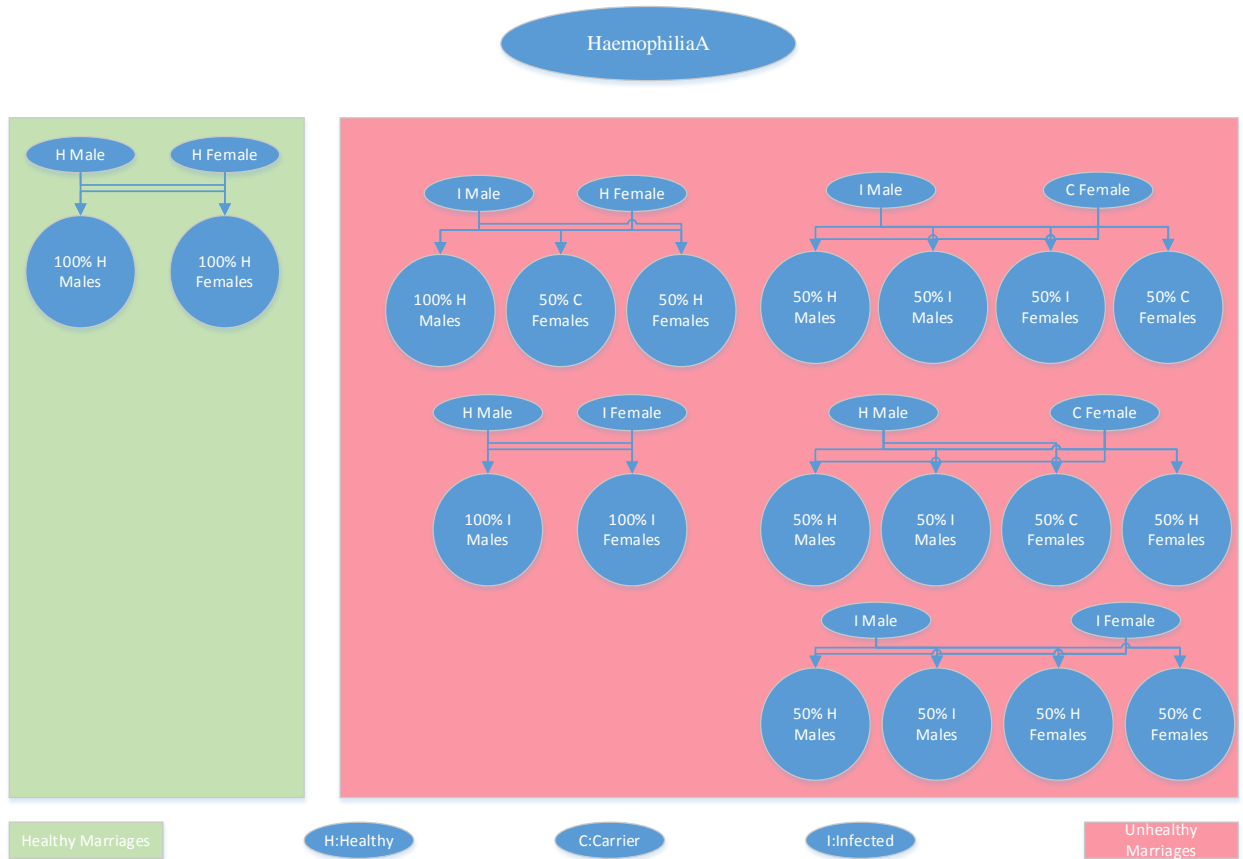
have a chance of having carrier children. Unhealthy marriage is where one or more children might be sick.



**FIGURE 3 THALASSEMIA INHERTANCE PATT**

### Haemophilia A

It has an X-linked recessive pattern (Communications, 2012c). Healthy parents are the only way to have healthy marriage; otherwise, all other choices are unhealthy.



**FIGURE 4 HAEMOPHILIA A INHERTANCE PATTERN**

### Fanconi Anemia

It has an autosomal recessive inheritance pattern (Communications, 2012a). Healthy marriages is between two healthy parents. Healthy but not recommended marriages are the ones that have a chance of having carrier children. Unhealthy marriage is where one or more children might be sick.



Fanconi Anemia

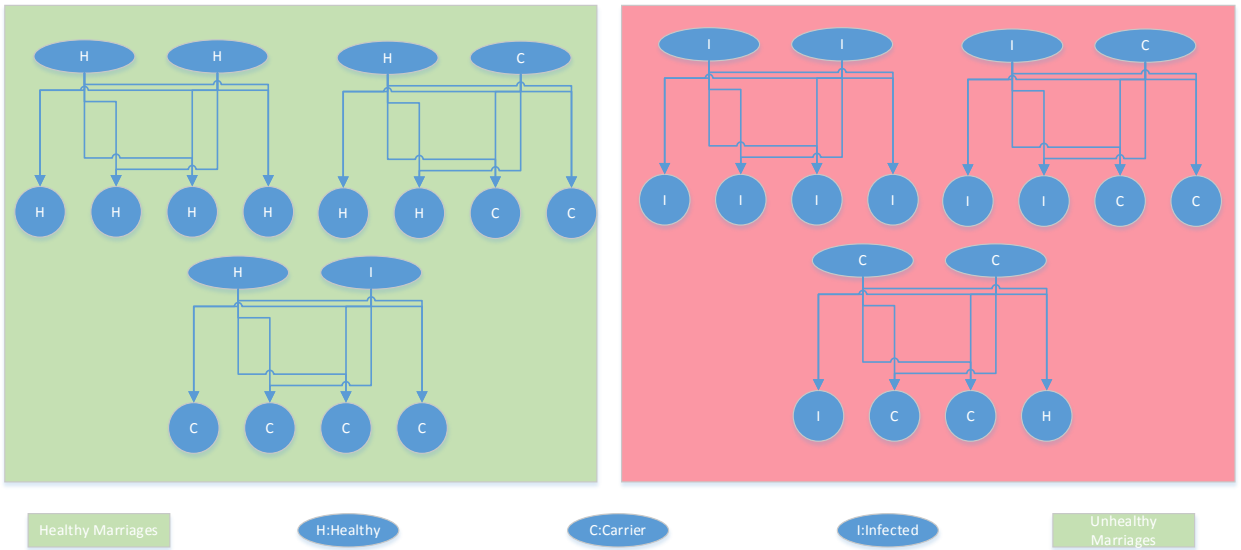
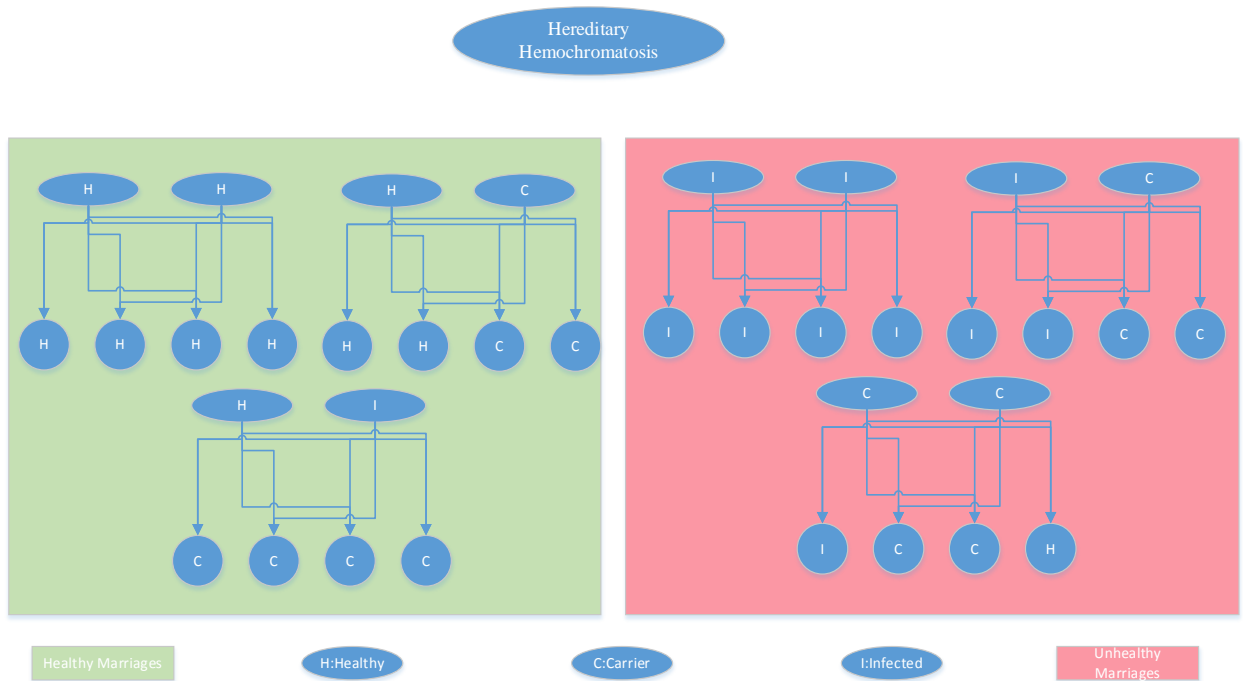


FIGURE 5 FANCONI ANEMIA INHERTANCE PATTERN

## Hereditary Hemochromatosis

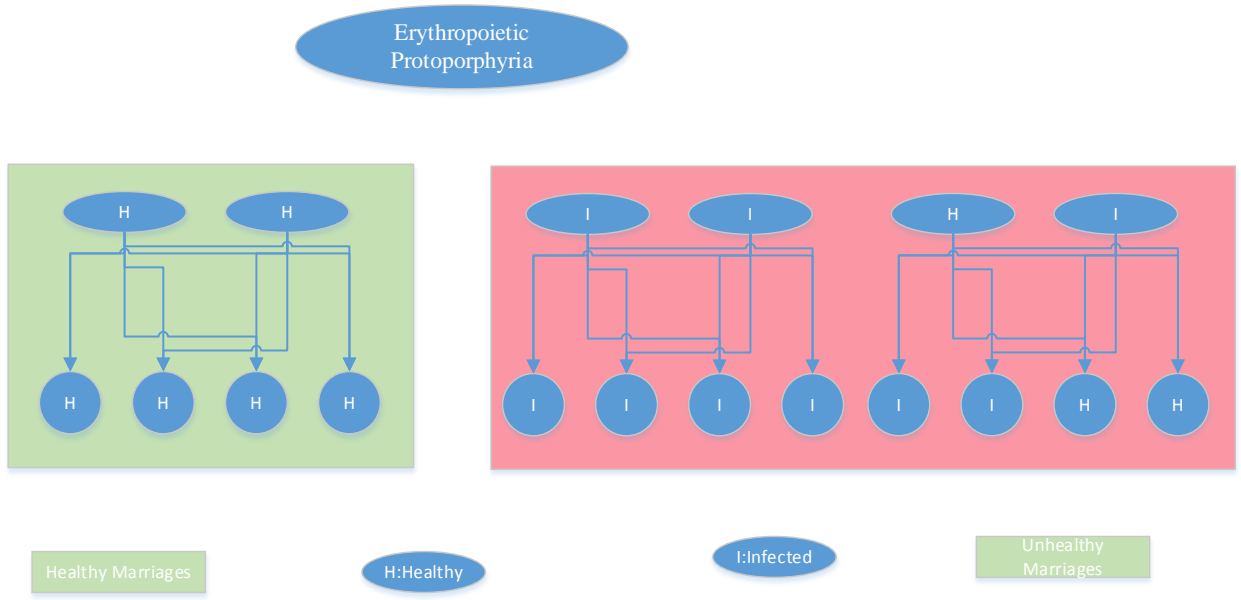
It has an autosomal recessive inheritance pattern (Charles Patrick Davis, 2014). Healthy marriages are between two healthy parents. Healthy but not recommended marriages are the ones that have a chance of having carrier children. Unhealthy marriage is where one or more children might be sick.



**FIGURE 6**HEREDITARY HEMOCHROMATOSIS INHERTANCE PATTERN

## Erythropoietic Protoporphyria

It has an autosomal dominant pattern (Gouya et al., 1999). To have healthy marriage, both parents have to be healthy. If either or both parents are infected, it is an unhealthy marriage.



**FIGURE 7 ERYTHROPOITIC PROTOPORPHYRIA INHERTANCE PATTERN**

### Hemochromatosis

It has an autosomal recessive inheritance pattern (Communications, 2006). Healthy marriages are between two healthy parents. Healthy but not recommended marriages are the ones that have a chance of having carrier children. Unhealthy marriage is where one or more children might be sick.

Hemochromatosis

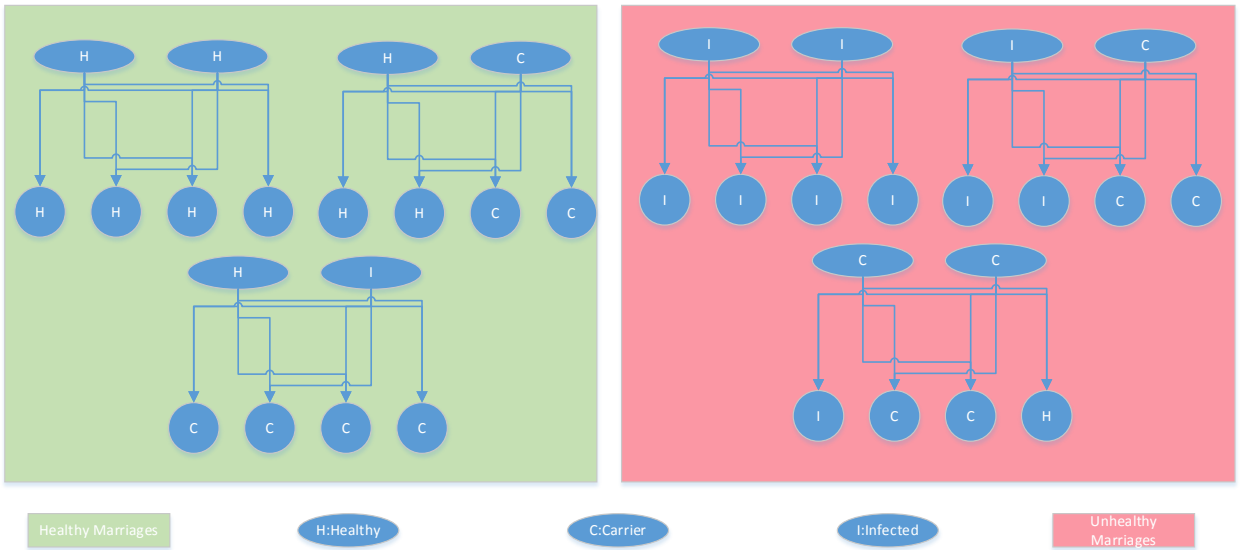
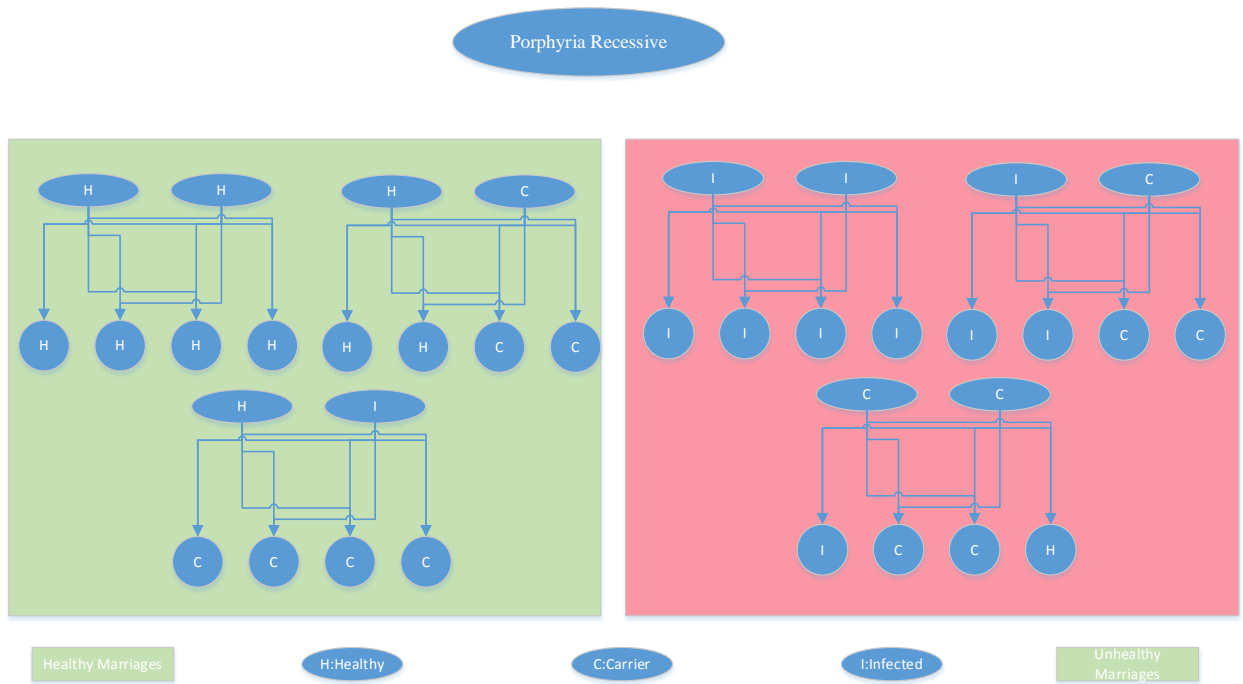


FIGURE 8 HEMOCHROMATOSIS INHERTANCE PATTE

## Porphyria

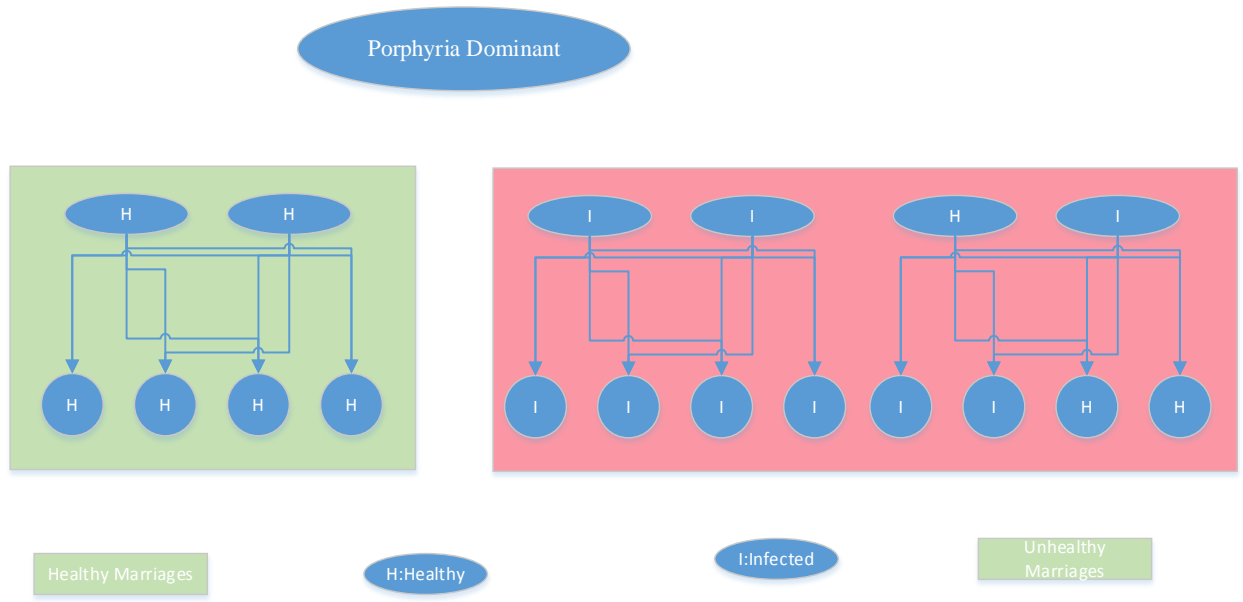
Porphyria has different inheritance patterns depending in the porphyria type (D. B. S. Marks, Todd; Sandra I Kim; Marc Glucksman, 2007). Most porphyria types have an autosomal dominant inheritance pattern except congenital erythropoietin porphyria (CEP) and Doss porphyria/ALA dehydratase deficiency have autosomal recessive patterns (D. B. S. Marks, Todd; Sandra I Kim; Marc Glucksman, 2007).

For the autosomal recessive porphyria, Healthy marriages are between two healthy parents. Healthy but not recommended marriages are the ones that have a chance of having carrier children. Unhealthy marriage is where one or more children might be sick.



**FIGURE 9 PORPHYRIA RECESSIVE INHERTANCE PATTERN**

For the autosomal dominant porphyria, to have healthy marriage, both parents have to be healthy. If either or both patients infected, it is unhealthy marriage.



**FIGURE 10PORPHYRIA DOMINANT INHERTANCE PATTERN**

### Workflows

The user may insert the national ID once and that will separately look for STI and Hepatitis, and genetic blood disorders.

### STI and Hepatitis

The system will search for tests and diagnosis. Tests are needed if there is not one within the last six months, or if the person left the country. If there are tests and there are no diagnosis, were done in the acceptable six month time frame, and if the individuals have not left the country, the marriage moves forward to being processed without counselling. After getting all diagnosis and tests, the couple should go through sex counselling to receive treatment, a cure, or/and vaccinations for any that apply. In genetic counselling, after agreeing to share information with each other, the couple can be matched. Sex counselors share the results of marrying with the couple and any potential consequences. The couple can make an informed decision after a counselling session, complete with proper education. The couple will then have to sign a paper stating that they understand any potential consequences.



FIGURE 11 STI AND HEPATITES IN HEALTHY MARRIAGE PROGRAM

### Genetic Blood Disorder

The system will search for tests and diagnosis. Tests are needed if there is not one within the last six months, or if the person left the country. If there are tests and there are no

diagnosis, were done in the acceptable six month time frame, and if the individuals have not left the country, the marriage moves forward to being processed without counselling. In genetic counselling, after agreeing to share information with each other, the couple can be matched. Genetic counselors share the results of marrying with the couple and any potential consequences. The couple can make an informed decision after a counselling



session, complete with proper education. The couple will then have to sign a paper stating that they understand any potential consequences..

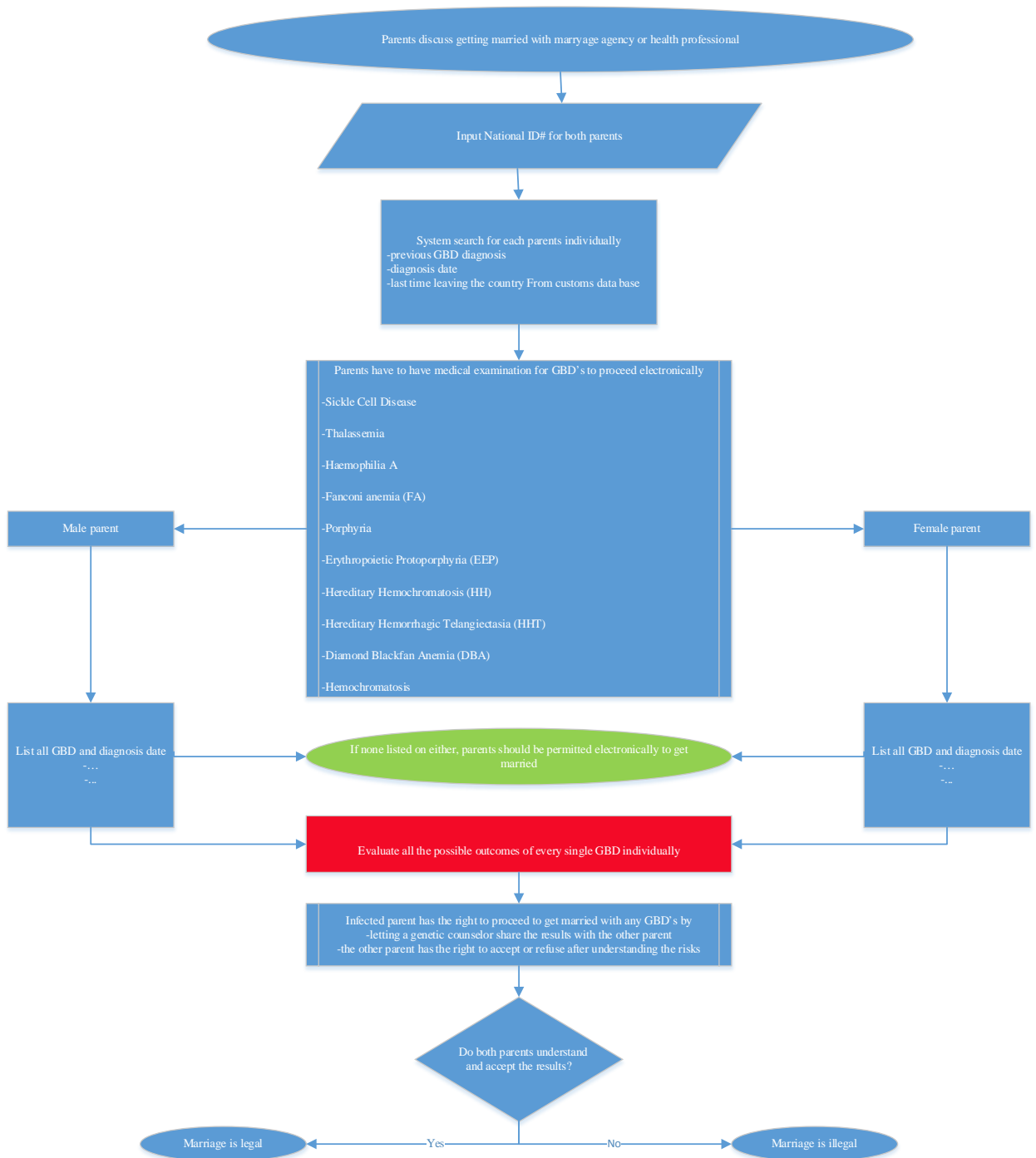


FIGURE 12 GENETIC BLOOD DISORDERS IN HEALTHY MARRIAGE PROGRAM

#### 4.4 DESCRIPTION OF COMPLETE DESIGN OR PRODUCT

##### 4.4.1 USER INTERFACE (UI)

The marriage agency/Licensors

The interface is designed for the marriage agency to be able to verify the healthy marriage. The marriage agency should not be able to see or access the couple's health records. However, the marriage agency can see the results of the CDSS. The portal is a software installed locally in the marriage agency.

The screenshot shows a window titled "Healthy Marriage Portal". Inside the window, there are two input fields side-by-side. The left field is labeled "Type the man national ID" and the right field is labeled "Type the woman national ID".

FIGURE 13 UI FOR MARRIAGE AGENCIES

The positive results show a green flag that contains the couple's national ID and names for verification. The confirmation number should contain three letters to help color blind individuals, who cannot see the green color, to understand the results (i.e. CAN000000001)

The screenshot shows a window titled "Healthy Marriage Portal". The main content area has a green background. On the left, it says "The couple with the following national ID's CAN get married". Below this, there are two columns: "ID#" and "Name". The first row shows "ID#" and "Name", and the second row shows "ID#" and "Name". On the right side of the green area, it says "Provide the couple with the confirmation number" and "Confirmation#".

FIGURE 14 POSITIVE RESULTS

Negative results show a red flag that contains the couple's national ID and names for verification. The confirmation number should also contain three letters to help colorblind individuals to understand the results (i.e. NOT000000001)

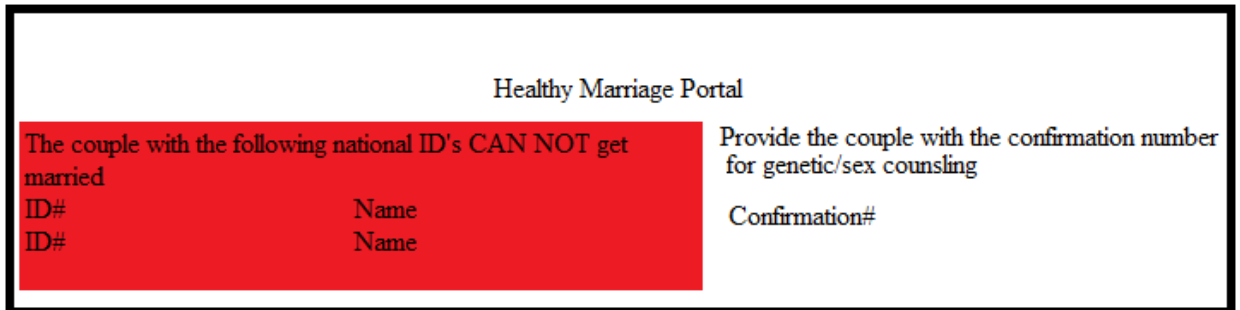


FIGURE 15 NEGATIVE RESULTS

The counselor

Genetic counselors have greater access than the marriage agency/licensor. They can start to check the results for couples, as well as review and edit them. Counselors see the following in addition to what the agencies and licensors can see:

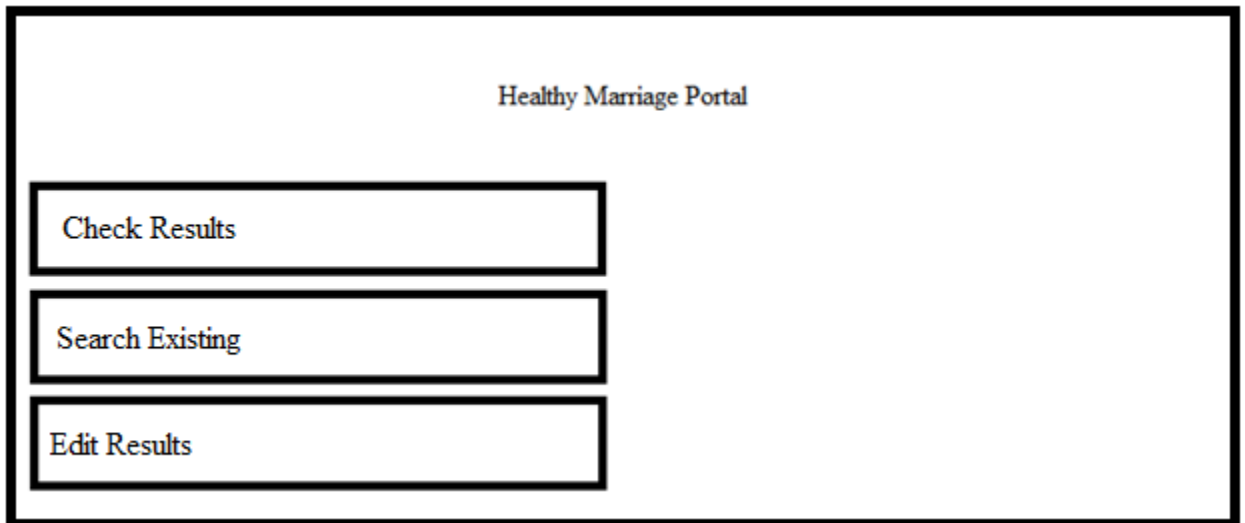


FIGURE 16UI FOR COUNSLORS

Check results is the same window that the agencies and licensors have access to. Searching the results is by searching by the HMID number or the national IDs for the couple.

Healthy Marriage Portal	
Return to the menu	Man National ID
View results	Woman National ID
Edit results	HMID

FIGURE 17 UI SEARCHING OPTION

The counselors can view or edit the results. If the counselors choose the view the results they will be able to see the HMID number along with the results. If the results are red flagged then it should show the reason behind it. The counselors can edit the results after providing the action recommended by the portal. Actions could be asking the couple to take or retake a test, providing consultation needed, or providing treatment.

#### 4.4.2 PROCESS

The back end process is made for Saudi in consideration of:

- Cultural values: premarital screening is acceptable by a majority of people especially between university students.
- Religious values: Islamic laws prohibit people with STI's to marry someone who is healthy from that STI. However, people should make the decision after being aware of the consequences.
- Political values: the Saudi Arabian government pays for the Saudi citizens' health care but most public hospitals cannot handle a large number of clinical visitation.
- Medical values: the purpose of the Healthy Marriage program is decrease the number of STI's and genetic blood disorder patients as well as to increase public awareness.

The design below demonstrates the process of screening couples using their electronic health records. Marriage agencies (AKA. matchmakers or marriage licensors) insert the couples national ID. The CDSS creates a healthy marriage ID (HMID) and looks up the couples' diagnosis and reviews them as a match to calculate the risk of unhealthy marriage. If either individuals or both have not been tested for a specific diagnosis, he/she has to visit

the lab for more screening. The couple will receive the HMID/Confirmation# to follow up at the lab.

STI's patients would be considered for healthy marriage only if both couples have the same STI. If one of the couple has any type of STI, the couple will be sent for sex counseling. If the STI is curable, then the patient will receive treatment after counselling. After counseling, the couples with the risk of incurable STI are allowed to get married after signing an informed consent to agree that they understand the risk and are willing to deal with the consequences.

Hepatitis cases vary based in the type of hepatitis. In this CDSS, the screening is for only B and C types. Individuals, who are marrying someone with hepatitis B, are supposed to be vaccinated for hepatitis B after counselling. Hepatitis C is treated the same as an incurable STI, where the couple has to agree to proceed with the marriage after sex counselling.

Genetic blood disorders are more complicated and have different situations depending on the genetic blood disorders' inheritance patterns. For example, in the case of having any risk of having a child with sickle cell disease, the couple can get married if they undergo genetic counselling and agree to take the risk and accept the consequences. Green is a healthy marriage, orange is not recommended, and red is an unhealthy marriage. Green means a high percentage of having healthy children with no carriers and no infected ones. If there is any chance of having carrier children, the orange light signifies that the marriage is not recommended and the couple has the option to get genetic counselling to make an informed decision. Red light means it is not a healthy marriage. Red alerts have to receive genetic counselling. During the counselling session, the couple should be familiarized with all options, including prenatal screening and birth control. For other genetic blood disorders, if one of the individuals has the diagnosis, there will still be a high risk regardless of the other person's health. In all cases of having unhealthy child, not including a carrier, the couple will have to go through genetic counselling.

The HMID is representative of any case between individuals in a couple. HMID carries all unhealthy reasons for a marriage to not be complete, such as getting laboratory tests or receiving counselling to increase awareness. It could be retrieved again to see if the status of the case has been changed after counselling. The counsellors are the only ones who can change the status of the marriage after providing evidence of increased awareness, such as signature from the couple. Counselors can order testes and attach them to the HMID. Successful completion of all recommendations by the CDSS allows the counselor the ability to change the status of the HMID.

#### 4.4.3 IMPLEMENTING AND TRAINING

## **Implementation Strategy**

Since Saudi Arabia is still in the first stage of implementing EHR, implementation will start in bigger hospitals that already have EHR. Other hospitals and clinics will be able to participate after implementing EHR.

No clinical changes should be effected during implementation. The main changes during implementation will affect the IT and medical departments. The IT department needs to troubleshoot their HL7 messages sent across to the CDSS's portal and fix the issues. The medical records department need to use national standards coding systems.

The old process consists of visiting a governmental hospital before the engagement process. Visiting the clinic might not be necessary if patient's test and records are up to date. CDSS will require a new workflow to replace the traditional screening. The new system will screen people only if tests are needed to get a finalized result. The traditional workflow is repetitive; every time someone plans to get married, the couple must go through the healthy marriage program by visiting the healthy marriage laboratories. The Saudi Arabian government will have to hire genetic and sex counselors whose primary job is to increase the public about having a healthy marriage.

Training will be needed for everyone who will use the CDSS, including but not limited to, users and genetic/sex counselors. Login credentials will be provided after training. Users need to be trained on how to insert national IDs, and explain the results to couples. The counselors will be trained on how to insert national IDs, explain results to couples, order missing tests, educating couples, and changing the status of the CDSS from red to green. Information Technology department (IT) at hospitals will be trained in understanding the process and monitoring the fields in EHRs to ensure that the CDSS is functioning correctly.

Different hospitals might use different EHRs and coding procedures, which requires the IT department at those hospitals to make sure coding procedure is the same. After implementation, the IT department from different hospitals can meet to make sure that HL7 messages get to be sent the right way. To maintain data integrity, regular testing scenarios should be implemented to ensure best quality of care in production.

### **4.4.4 CDSS MAINTENANCE**

In case of CDSS downtime, a recovery plan depends on the downtime period. The vendor should test the portal and the results in a regular basis. If the downtime is between one to three days, the recovery plan should be to wait until the CDSS is fixed. If the downtime is more than three days, the couple can visit sex/genetic counselors to manually search the EHR for the couples' records, match them together and request missing tests.

CDSS is to be supported and monitored by the developing and implementing vendor. Vendor will be providing the training to the user, installing the portals, providing support team to answer users' questions and issue, and making sure the data received and results are valid. The vendor of the CDSS is in charge of testing with records coming from different EHRs. Since different hospitals might be using different EHR and different coding strategy, it is important to test in regular basis. The CDSS's users and counsellors can report any errors of records not matching between records. Downtime for any system update should be between 12 am and 12 pm after informing the users of downtime.

### **Maintainability**

The time between inserting the national IDs and the results for the user should be less than 60 seconds. If results take more than five minutes for the user to see, the portal should report the issue. The IT department at the hospital, where test results come from, should get a detailed report of what slow down the data transferring from the hospital EHR. The IT department is to diagnose the issue looking at the HL7 messages sent from that hospital. If anything is wrong with HL7 messages, the EHR's vendor can usually fix that.

### **System Support**

The vendor is in charge of

- Communicating with EHR vendors and users to maintain the functionality and availability of the CDSS
- Understanding the goals of this CDSS such as decreasing the clinical visitation, thus creating a healthier community
- Testing the product and providing accountable results
- Maintaining and supporting the product
- Providing solutions and customer service for users in case of errors

The IT and medical records departments are in charge of

- Reporting errors to the vendor
- Diagnosing HL7 to ensure they are in accord to the national standards

Troubleshooting by testing the portal to make sure it is efficient and errorless. By troubleshooting, the vendor can find the error of it is internally or externally. Internal error are the ones related to the portal. Any coding mismatch or no inaccessibility to EHR's is an external error. The vendor has to alert, by email and in the portal, the user in case of Internal and external errors. The vendor has to communicate with other EHR vendors and hospitals about external errors.

In Saudi Arabia, EHR vendors are required by the Ministry of Health to use the HL7 standards, which should match between records coming from different hospitals. A patient

can do tests at different hospitals, yet still allowing the CDSS to pull records from the different EHRs used at those hospitals.

## **Security**

The CDSS portal will have a login to increase security and the privacy of patient information. Logins are created to marriage agencies after training in how to use the CDSS and its value. The marriage agencies have to provide the hardware, which has to have antivirus to protect the portal from any attackers. The marriage agencies have to sign a confidentiality agreement to protect patients' data and only use it for its purpose. In case of a security breach, the antivirus should protect the portal and provide an alert to the vendor. When there is a suspected breach, the user has to contact the vendor and enable it after investigating the breach. The vendor also has to sign a confidentiality agreement to protect patients' health records.

The user can access the portal using any internet network. If necessary, the vendor can increase the security of the portal by making users access the portal through an online portal such as Citrix. That will allow the user to access the portal from anywhere. The user does not have to be clinician or computer literate; however, the user should be able to read and write in Arabic.

The CDSS will have a database that tracks the efficiency of the product. Reports are created for the Ministry of Health such as:

- Reports of how many couples get green and red flags
- Reports of how many people decide to go to counselling after green and red flag
- Reports of how many people have to retake STI and hepatitis tests
- Reports of how many errors reported by users
- Reports of how many people missing tests
- Reports of how long from inserting the national IDs until getting a green flag
- Reports of how much database available and used

## **Data Storage**

HMID may be retrieved for a year since it was processed. HMIDs will require storage to carry the results of each process. Every HMID is going to have results between one to thirty Kilobytes (KB). Since the Saudi Arabian population is close to thirty million (Services, 2013) divided by two; there would be a minimum number of 15 million HMID. The minimum requirement for the CDSS is 429 Gigabytes (GB) The maximum number of HMID during a yearly period should four for every person as an average. The maximum needed is 3.35 Terabytes (TB).

## **Reliability**



To have a reliable CDSS, all parties, including users, IT, and counselors, must work together to have a good understanding of the CDSS's goals. Errors should be reported manually and automatically immediately. CDSS cannot work unless there is EHR connectivity is reliable. If an individual had a test(s) in one hospital that is having connectivity issue for any reason, the individual has to retake the test(s) by visiting a counselor. Data integrity depends in how coders code using national standards. HMID number is created, it can be searched to view and edit by the only counselors and hospital clinicians. Any confusion by the portal caused by technical difficulties in the data deliveries will be red flagged by the portal. Counselors can avoid any confusion by the portal and either reporting to IT or ask the couple to retake the test again to decrease the down time.

The HMID will be saved in accessible nationwide server with about two to three backup servers located in different places in the country. If the main server down then the backup servers should be able to deliver data needed to create a reliable result. The servers should be available at all time except for maintenance for one server at a time while the backup servers deliver the needed data.

Every EHR within the country should send the data requested by the portal as soon as requested by the portal. When the national IDs inserted into the portal, the portal will collect all diagnoses and their date. The portal will collect the last country exit and reentry.

Windows servers with VMware: that will allow virtual sessions to be created for users to use the portal. The virtual machines need to allow the user to use the locally installed printers in the users' workstation.

Citrix Receiver: It will allow users to access the portal of the CDSS from anywhere. The instillation process will be handled during the training session. The Citrix receiver license will be provided by MOH.

Windows .NET Framework: It will allow user to access the portal within a MOH trusted internet environment. It does not require as much security as Citrix Receiver.

Adobe Acrobat: This will allow users to create a soft copy to email or save for the couple.

Visual Basic and HTML Code: The Portal will be built in Visual Basic code. Visual Basic and HTML have enough features to create user friendly interfaces.

C# and C++: The CDSS will be built in both C# and C++ codes. C# and C++ have been used to build EHR's. Those two languages are currently famous languages that are used and familiar to most programmers.

HL7 International Standards: Patients data can be sent in HL7 messages across. Most EHR's already use HL7 messages to connect with different EHR's.

XML viewer or Microsoft Office Word: Those two software can be used to auto fill and create forms based on the results.

Microsoft Office Excel: This software can be used to show reports after they are created by the CDSS. Excel spreadsheets have features to let the user manipulate the data and create charts from the data create by the CDSS.

### **Availability**

The results should not take more than five minutes after the entry of both national IDs. If the portal is taking more than five minutes, a report should be automatically sent to IT to review the problem. The problem could be a slow data delivery from EHRs or customs logs. Besides creating the report, the portal will issue a red flagged. The downtime from a specific EHR or custom log is longer than two weeks long to provide the information needed, IT needs to contact the institution's IT department to investigate the issue and look into the replacing the software or hardware needed. The portal will use the latest data received to calculate the results. Using the latest data will always ensure the correct results based on the latest technology used in the country when the test was taking. To ensure the availability of data at all time the backup tasks should be scheduled every 15 minutes.

The portal should be built to be available in all cities in Saudi Arabia along with all hospitals. The average number of users at a time could be up to one thousand. The portal can be accessed remotely for marriage agencies and licensors while genetic counselors can have the portal as a part of the hospital or clinic application. Every hospital or clinic may have different security requirement for their application. The marriage counselors and licensors will have access in any computer with the login. The portal might require a citrix or vmware that makes it accessible anywhere. The ministry of health is required to buy the license for the software needed for the agencies and licensors. Data entry needs a mouse and a keyboard while used in a computer. However the portal will be accessible but portable devices with touch screens.

### **Architectural fit with organization**

The portal is accessible in both public and protected network. The portal will request the specific data needed to process the results. The processors will calculate the results based on the data returned from the custom's log and EHRs. The result will show which might be later edit or viewed to the user.

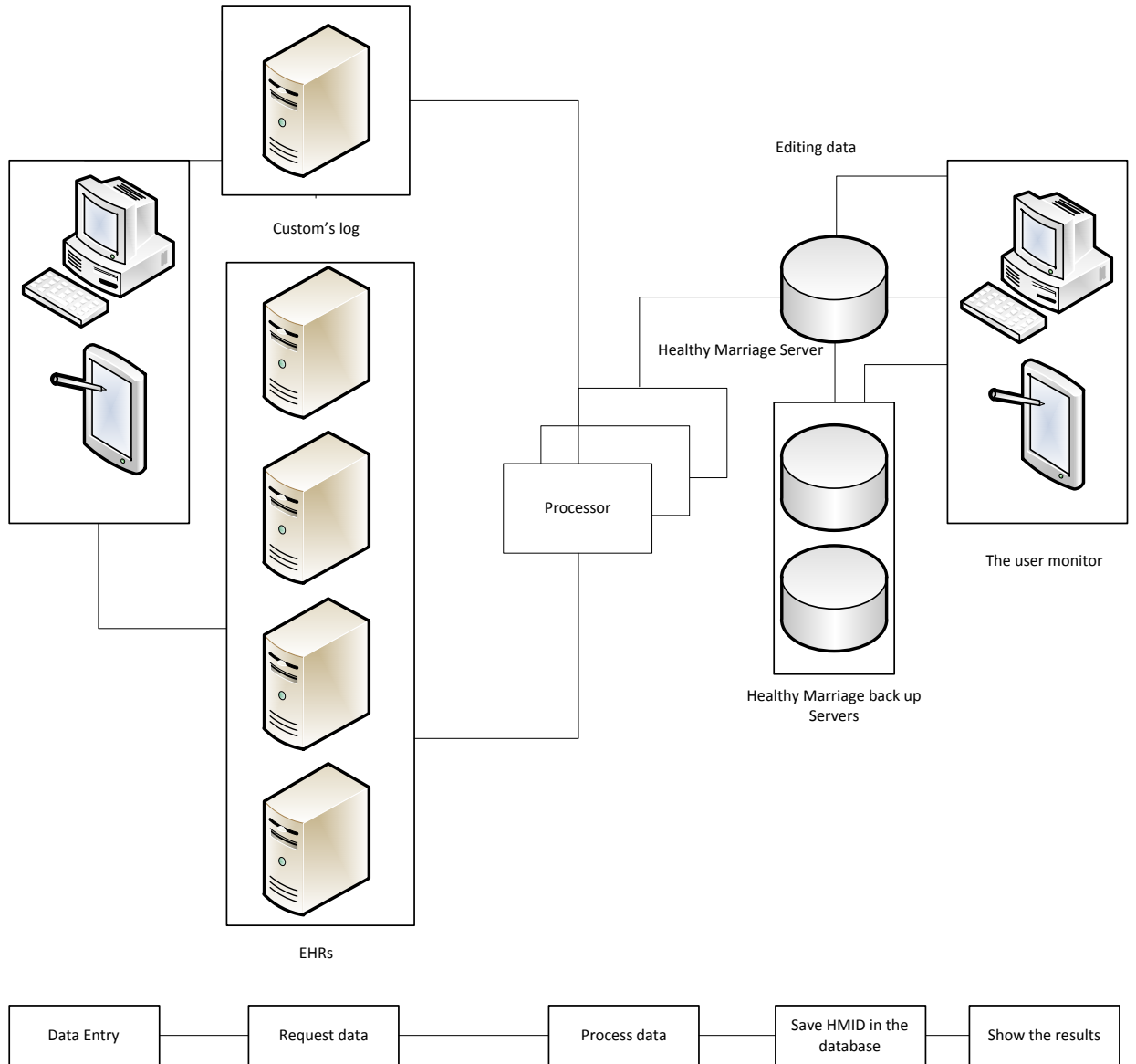


FIGURE 18 ORGANIZATION DATA ARCHITECTURE

### Data model including extensibility and agility

Data received from EHR is diagnoses and their dates. The portal will request diagnoses with the medical coding system used at the providers' EHR. The EHR will respond with the diagnoses results and the results date. Some EHR might be using different medical coding system at once. Using HL7 international standards is required for EHR's to support the portal. HL7 standards is capable of manipulating the data received from different medical coding systems. The CDSS will be able to identify the different entity types. The CDSS will have multiple interfaces such as:

**Sending Interface:** After the portal accept the entry in the portal. The interface will send the request of diagnosis, their dates and the last country exit.

**Receiving Interface:** In this interface, the data will be manipulated to translate codes from the different medical coding system. This interface will filter the data up to what is needed in the CDSS.

**Processing Interface:** After receiving the data and organizing it for a couple the data will calculate the results to measure how healthy this marriage is going to be.

**Publishing interface:** In this interface, the decision will be published to the marriage agencies and licensors. The result will be only red or green. No details can be shown in this stage. Also a HMID will be created based on the result. The HMID will be consisting of a three letter (CAN/NOT) to avoid confusions by color blind users.

**Editing Interface:** This is to allow counselors edit the publish results and change it from red to green. The counselors will have the full results with the explanation why the results were red. A counselor will be able to change the result after taking the necessary steps asked by CDSS. There might be more than one reason why the results are red.

### **Disaster avoidance**

This CDSS is a non-mission critical system.

### **Database design**

The CDSS is designed to comprehend the data from different EHR and custom logs. If there is an EHR that uses a foreign medical coding system than what is used in this CDSS, there should be a translation table created. Database will use SQL and to consist of tables, relations and fields. Users must be granted access to what they need. Different type of access must have different limitations in the system. Every user has 3 chances of logging in with the wrong password until the system lock. The lock can be opened by IT after confirming the same person. Most recent security measures should be used. Secondary authentication is an option if purchased by the user. That will help user avoid the chance of locking the account and waiting until IT unlock it.

### **Integration design**

The integration engine is the database server where it grants interoperability and connectivity between the portal, processor, EHRs and custom logs. Most data files should be less than 100 Kilobyte. Any communication between servers should be created in a secure connection using TCPIP through the internet.

## **4.5 EVALUATION AND USABILITY OF DESIGN AND/OR PRODUCT**

#### 4.5.1 USABILITY

The CDSS is created to be fit the Heuristic Evaluation Usability Techniques (Kushniruk, Monkman, Tuden, Bellwood, & Borycki, 2014).

It is should provide enough information to inform the users of what is going on by providing feedback in a practical time. The CDSS has a consistency when the user is working in the system. The users interface should have a basic portal where the user has only access to see the results of the healthy marriage program. The user should also be able to print the results to give a copy to the couple. In case of any errors, the user should be giving enough description of the error. The user should have a menu to move around the portal. The user should be informed of their limitation in the portal. In case of a delay of searching for records, the user should be informed of what is coming up next ad how to cancel the function the pressed on. The respond time should be less than ten seconds. The user should be aware of where he/she is at in the process. In Saudi Arabia, a homosexuality is illegal and there should be a clear error when that has processed in the CDSS.

The CDSS should match the real world by providing information that are understandable by a non-clinician. The results are to be colored as red for “not suggestive but possible after counselling” and red for “it is a healthy marriage based on the information stored in the EHR”. The results ID for following up is should be able to show what type of result it is. The user should be provided with the name of the person with the national ID inserted to verify the results. After inserting the national ID of the couple, the user can just click “Enter” to see the results.

The user should not be able to access, alter, delete, or modify records. The user should also be able to back up. The user can zoom in the results if needed.

#### 4.5.2 EVALUATION

The evaluation criteria are comparison between the traditional methodology and the one discussed in this paper. The satisfaction will be measured by all key players who use and manage the system. Users, IT and management can evaluate the system once every six months. Users who participate in the evaluation rate all aspects from 0-5, 5 being efficient. All over evaluation percentage is =total of users evaluations/number of evaluators.

TABLE 1 EVALUATION MEASURE

Evaluation	Users rating	Weight percentage	Product Satisfaction total
Time Effective	0-5	$=(100)*rate/(5*9)$	

Cost Effective	0-5	$=(100)*rate/(5*9)$	Total Weight percentages
Efficiency	0-5	$=(100)*rate/(5*9)$	
Provide decision without clinical visitation	0-5	$=(100)*rate/(5*9)$	
Reduce misdiagnosis	0-5	$=(100)*rate/(5*9)$	
Increase knowledge	0-5	$=(100)*rate/(5*9)$	
Protecting patient privacy	0-5	$=(100)*rate/(5*9)$	
Provide treatment to curable infections	0-5	$=(100)*rate/(5*9)$	

### Time Effective

The lab results for genetic blood disorders can never change after but the traditional system is repetitive but in the CDSS, the information can just be retrieved in seconds. Another advantage of that is patients do not need to take more of the laboratory time. Giving the marriage agencies the availability to look up how healthy a marriage is by either getting a green or red light. Laboratory results can take up to a week sometimes.

### Culturally Accepted

The CDSS is designed for Saudi Arabia where most people are Muslims, Islamic believers, where people with certain STI's can only marry others with the same STI's. There is no Islamic law that prohibits the prevention of infections. In addition, the CDSS show be more acceptable since the Islamic laws does not prohibit people legally to get married and just increase their awareness.

### Cost Effective

EHR and CDSS has been approved in too many researches to be cost effective (Hillestad et al., 2005). This particular CDSS can use information store in data warehouses instead of repetitive laboratory works. If someone were missing one or more tests for the CDSS to get a result, the couple would have to only have tests for those specific diagnoses. In addition, reducing the clinical visitation is another way to decreasing the cost of the healthy marriage program. In a long-term plan, people with a high risk of unhealthy marriage should be offered special health insurance plans to treat for STI's and genetic blood disorders. With the CDSS, the Saudi Arabian government will save money preventing instead of treating.

### Efficiency

While prohibiting couples is the main way in some premarital screening; in this CDSS, couples are making an informed decision after offering treatment to curable infections and education session. Since a person can get infected with STI and hepatitis viruses at any time, the traditional way is better because of the screening is repetitive; however, in the CDSS to eliminate that, a person can needs to have only the STI and hepatitis screening if the person left the country since the last screening or the screening has been done over six months. The main reason behind that is in the Saudi Arabian culture, prostitution and premarital sex is highly prohibited. The traditional program force couple to get results in the same clinic to match the results locally while the CDSS match diagnosis electronically from different EHR's and clinics. The CDSS can prevent what happened in the UAE where most couples do the premarital screening after making a decision, discussed in the literature, because marriage agencies can help couples make informed decisions.

### Provide decision without clinical visitation

The CDSS design reduces the clinical visitation to make an informed decision. CDSS looks up all couple's historical health records instead of new laboratory screening. In most cases, individuals will not need to have any clinical visitation unless there is a risky marriage or a test or more are missing. If couples have not left the country, have been screened for hepatitis and tested negative for Genetic blood disorders, no clinical visitation is required to get the results of the healthy marriage program.

### Reduce misdiagnosis

In case of any misdiagnoses in the laboratory screening, the CDSS uses the all couple's data to search for the history of the above diagnosis. The traditional program avoid any past diagnosis because it requires a new screening and ignore the previous screening results. In the case of two screenings contradicting, the traditional way is to take the new one and avoid the old screening. The CDSS will refer the couple to a counseling session.

### Increase knowledge

While the traditional way takes a legal effects on the, the main purpose of the CDSS counseling is to increase patient and community awareness. Telling people “Yes, you can get married” or “No, you can’t get married”, makes couples who want to really want to get married try to find other ways to get married illegally or civil instead of religious. The Healthy Marriage CDSS methodology is not about stopping people to get married but to offer them counselling sessions to increase their awareness of the risks and how to be protected.

### Protecting patient privacy

Now, when two decide on getting lab results, most people assume that they are getting married. However, when it does not happen, people also assume that there is something wrong with those two. That does not protect patient’s privacy. The CDSS process can avoid that because people will not be going to the laboratory. The marriage agencies will have to sign a confidentiality and privacy to not publish any results before they can have access to the portal.

### Provide treatment to curable infections

The CDSS suggests treating curable infections and vaccinating the other healthy couples in certain cases while the traditional way does not take any father decision to cure or vaccinate. If an individual has a curable STI, he/she will receive an immediate cure during a genetic counselling.

## 5. RESULTS AND CONCLUSIONS

Creating a CDSS to replace the traditional Healthy Marriage Program would be a great success if implemented. This paper discussed all issues that might run across creating and implementing the CDSS. After doing the literature review for the about the existing Healthy Marriage Program, the CDSS has proven to be more acceptable and successful (Frize, Weyand, & Bariciak, 2010).

Utilizing EHR's database for the use of better care of the community is the main goal of this CDSS. There are many advantage of using electronic health record over the traditional paper health record. This Healthy Marriage Program can benefit from EHR by reusing all the diagnoses in the database. HL7 standards that are used in Saudi Arabia make it possible for EHR's to integrate. In addition, using EHR can find any contradicting results for any specific diagnosis. The Couples’ will not need to be screened at the same clinic or be screened at the same time.



CDSS is capable of screening for more diagnosis and order missing tests in a short time. For premarital screening, timing is sensitive. In some cases, people make decision before screening. To prevent that CDSS is needed to help with making the decision faster. In addition, in the case of match making, the marriage agency can look up the couple in the CDSS before making a further step.

Different places in the world screen for a particular number of diagnosis because it is very expensive to screen for multiple diagnoses. Screening for more diagnosis can help prevent instead of treat. EHR is capable of retrieving health records with in seconds. Genetic blood disorders tests don't have to be screened. STI's can be transmitted at any point of a life time. Saudi Arabia does not allow any type of adultery or prostitution which means there is a small chance of STI's to exist. However, Saudi citizens can travel outside Saudi Arabia and bring back STI's. Likewise, patients with curable STI might be treated since the last test. For those reasons, STI's screenings have expiration date of six months or if the person traveled outside Saudi Arabia.

Saudi Arabia has two holy places of the Islamic faith; those places get visitors in regular basis since the beginning of Islam. Before Islam, Saudi Arabia used to desert with mainly *Bedouins*, people who travel around the Arabian Peninsula looking for food and water. Since Muslims from all over the world travel to Saudi Arabia, a lot of them started staying because they either can't make it back home or they would rather be closer to the holy places. That puts Saudi Arabia to be one of the most diverse places in the world. For that reason, diagnoses screened can't be only done for a specific race (Vassiliev, 2013).

The Saudi Arabian government committed to pay and support free public health which encourage people tom make unnecessary clinical visitation to out-patient and emergency room services (Al-Turki, 2006). One of this CDSS goals is to help decrease clinical visitation, which can be resolved by public awareness. The CDSS was created to decrease the number of clinical visitation unless there are complications or more testing needed. In addition, genetic/sex counselling should be able to increase the public awareness and help make informed decisions.

Islam, Saudi Arabian main religion, does not allow people with STI's to marry or practice sex with someone who is healthy from that STI (Mohammed Ali Albar, 1991). However, Islam has that rule to punish people who have sex practicing adultery or prostitution and get STI's (DeJong, Jawad, Mortagy, & Shepard, 2005). However, practicing adultery and prostitution are not the only reason to be infected with an STI. Since, it might be hard to identify the source of STI, not everyone should be punished (DeJong et al., 2005). Sex counselling is a way for people to marry the person they want after getting the proper treatment and increasing awareness. This should give people the freedom needed to marry who they want after knowing the risk taken.

One of the CDSS goals is to provide the care needed to make a healthy marriage. STI's can be divided into three types, curable, treatable, and untreatable. Curable STI's might disappear if diagnosed in the early stages. Treatable STI's can be treated for the rest of the patient's life but can't be cured completely. Untreatable STI's can't be cured not treated and mostly happen if they don't get diagnosed in early stages and also rare.

The Jewish community created Dor Yeshorim, premarital screening that is culture specific (Prainsack & Firestine, 2006). Due to the decreased number of people with Jewish heritage after the World War Two, where a large number of European Jewish people were killed by the German army. Dor Yeshorim was created help the Jewish community recover from all the loses during the war. Starting 1980's, Dor Yeshorim was implemented to genetically test teenagers for specific disorders to match make them when they decide to get married. Likewise, the CDSS was created to fit in the Saudi Arabia culture.

The Islamic Saudi Arabian culture refuse abortion after ensoulment, after 16-18 weeks of pregnancy. Muslim pregnant with risky marriage should receive prenatal screening to give families the option of abortion or prenatal treatment. Some families with strong Islamic believes might refuse any type of prenatal screening because it is against the destiny of God. If God wants them to have a sick child then that is just the family's destiny.

#### LIMITATIONS

The main limitation of this research is that it has not been implemented. This research is just theory to suggest the replacement of the traditional premarital screening implemented in Saudi Arabia. Implementing this CDSS will require communication from the Saudi Arabian Ministry of Health, Ministry of Foreign Affairs, and EHR vendors to implement this CDSS.

Some Muslims find it a sin to change marriage culture or discuss STI's. It is highly encouraging religious aspect of accepting the destiny of having sick children. Some people with strong Islamic believe refuse abortion, premarital and prenatal screening. Since discussing STI's is a taboo, that limits and decrease the opportunity of how dangerous STI's are.

EHR's are in the first stage of implementation, which means Saudi Arabia is not ready to implement the CDSS in all parts of Saudi Arabia. EHR vendors are foreign business companies that only sells EHR. There is a small number of medical research centers for CDSS development. Hospital workers are Arabic speakers while most EHR vendors use English as the main language of communication.

The Evaluation of this CDSS was only conducted by comparing it with the traditional. Since the CDSS has not been implemented, users and hospital administration could not do the evaluation.

#### CONCLUSIONS AND RECOMMENDATIONS

The healthy marriage program is a premarital screening method to help government create healthier and more educated public about the marriage culture. The current program is limited and inflexible with the cultural values of people in Saudi Arabia. The Saudi government works closely with the religious leaders to control the laws in Saudi Arabia. The Islamic religion is strongly influencing the Saudi Arabian culture. Islamic leaders are also very involved in changing the public attitude about every single aspect of Muslims' lives. The Saudi Arabian government should put pressure Islamic leaders to educate the public and encourage the public to learn about the danger of STI's.

Saudi Arabia is in the first stage of implementing EHR's with many opportunities for vendors to sell. It is time for Cerner, Epic and other EHR vendors selling EHR services in Saudi Arabia to invest in the development in making healthier communities. There is too many opportunities for EHR vendors in making a healthy community such as opening medical research centers.

The design contains all diagnosis found in the literature review. In addition, it is made to be flexible to add any additional diagnosis recommended by health providers working in Saudi Arabia. Regular yearly statistics of increasing diagnosis that caused by marriage and reproduction.

This CDSS should be implemented and evaluated by users and hospital administrators. The evaluation should measure the user interface, design, implementation process, integration process, and diagnosis.

## REFERENCES

- Abuljadayel, I. S., Ahsan, T., Quereshi, H., Rizvi, S., Ahmed, T., Khan, S. M., . . . Dhoot, G. (2006). Infusion of autologous retrodifferentiated stem cells into patients with beta-thalassemia. *The Scientific World Journal*, 6, 1278-1297.
- Al-Aama, J. Y. (2010). Attitudes towards mandatory national premarital screening for hereditary hemolytic disorders. *Health Policy*, 97(1), 32-37.
- Al-Gazali, L., Hamamy, H., & Al-Arrayad, S. (2006). Genetic disorders in the Arab world. *Bmj*, 333(7573), 831-834.
- Al-Ghamdi, A. S., & Kabbash, I. A. (2011). Awareness of healthcare workers regarding preventive measures of communicable diseases among Hajj pilgrims at the entry point in Western Saudi Arabia. *Saudi medical journal*, 32(11), 1161-1167.
- Al-Turki, Y. A. (2006). Smoking habits among medical students in Central Saudi Arabia. *Saudi medical journal*, 27(5), 700-703.
- Al Allawi, N., & Al Dousky, A. (2010). Frequency of haemoglobinopathies at premarital health screening in Dohuk, Iraq: implications for a regional prevention programme.
- Al Arrayed, S., Hafadh, N., Amin, S., Al Mukhareq, H., & Sanad, H. (2003). Student screening for inherited blood disorders in Bahrain.
- Al Arrayed, S. S., & Al, H. (2005). Premarital genetic counseling: a new law in the Kingdom of Bahrain. *Journal of Health, Social and Environmental Issues, Middle Sex University*, 6(2), 31-34.
- Al Sulaiman, A., Suliman, A., Al Mishari, M., Al Sawadi, A., & Owaidah, T. M. (2008). Knowledge and attitude toward the hemoglobinopathies premarital screening program in Saudi Arabia: population-based survey. *Hemoglobin*, 32(6), 531-538.
- Albar, M. A. (1991). Islamic view on organ transplantation *Organ Transplantation 1990* (pp. 573-578): Springer.
- Albar, M. A. (2002). Ethical considerations in the prevention and management of genetic disorders with special emphasis on religious considerations. *Saudi medical journal*, 23(6), 627-632.
- Alro7. Tafseer Quran. from <http://www.alro7.net/ayaq.php?langg=english&aya=26&sourid=24>
- Alswaidi, F. M., Memish, Z. A., O'Brien, S. J., Al-Hamdan, N. A., Al-Enzy, F. M., Alhayani, O. A., & Al-Wadey, A. M. (2012). At-risk marriages after compulsory premarital testing and counseling for  $\beta$ -thalassemia and sickle cell disease in Saudi Arabia, 2005–2006. *Journal of genetic counseling*, 21(2), 243-255.
- Altuwaijri, M. M. (2008). Electronic-health in Saudi Arabia. Just around the corner? *Saudi medical journal*, 29(2), 171-178.
- Arulogun, O. S., & Adefioye, O. A. (2010). Attitude towards mandatory pre-marital HIV testing among unmarried youths in Ibadan Northwest Local Government Area, Nigeria. *African journal of reproductive health*, 14(1).
- Bachmann, L. H., Lewis, I., Allen, R., Schwebke, J. R., Leviton, L. C., Siegal, H. A., & Hook 3rd, E. (2000). Risk and prevalence of treatable sexually transmitted diseases at a Birmingham substance abuse treatment facility. *American Journal of Public Health*, 90(10), 1615.

- Bai, Z., Bao, X., Cheng, W., Yang, K., & Li, Y. (2012). Efficacy and safety of ceftriaxone for uncomplicated gonorrhoea: a meta-analysis of randomized controlled trials. *International journal of STD & AIDS*, 23(2), 126-132.
- Balgir, R. (2010). Genetic diversity of hemoglobinopathies, G6PD deficiency, and ABO and Rhesus blood groups in two isolates of a primitive Kharia Tribe in Sundargarh District of Northwestern Orissa, India. *Journal of community genetics*, 1(3), 117-123.
- Barss, P., Grivna, M., Ganczak, M., Bernsen, R., Al-Maskari, F., El Agab, H., . . . Al-Dhahri, J. (2009). Effects of a rapid peer-based HIV/AIDS educational intervention on knowledge and attitudes of high school students in a high-income Arab country. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 52(1), 86-98.
- Belhoul, K. M., Bakir, M. L., & Abdulrahman, M. (2013). Misdiagnosis of Hb D-Punjab/ $\beta$ -thalassemia is a potential pitfall in hemoglobinopathy screening programs: a case report. *Hemoglobin*, 37(2), 119-123.
- Bittles, A., & Black, M. (2010). Consanguinity, human evolution, and complex diseases. *Proceedings of the National Academy of Sciences*, 107(suppl 1), 1779-1786.
- Bozkurt, G. (2007). Results From The North Cyprus Thalassemia Prevention Program\*. *Hemoglobin*, 31(2), 257-264.
- Cao, A., & Kan, Y. W. (2013). The prevention of thalassemia. *Cold Spring Harbor perspectives in medicine*, 3(2), a011775.
- Cao, A., Rosatelli, M. C., Monni, G., & Galanello, R. (2002). Screening for thalassemia: a model of success. *Obstetrics and gynecology clinics of North America*, 29(2), 305-328.
- Carter, C. (1977). Genetics of common disorders *Problems of Birth Defects* (pp. 152-157): Springer.
- Charles Patrick Davis, M. (2014). Iron Overload. from [http://www.medicinenet.com/iron\\_overload/page2.htm](http://www.medicinenet.com/iron_overload/page2.htm)
- Coates, S. (2014). What's the difference between ICD, CPT, LOINC, and SNOMED CT? , 2014, from <http://www.healthfusion.com/blog/2014/health-topics/medical-coding/whats-difference-icd-cpt-loinc-snomed-ct/>
- Coleman, J. S., Gaydos, C. A., & Witter, F. (2013). Trichomonas vaginalis vaginitis in obstetrics and gynecology practice: new concepts and controversies. *Obstetrical & gynecological survey*, 68(1), 43.
- Communications, L. H. N. C. f. B. (2006). hemochromatosis. from <http://ghr.nlm.nih.gov/condition/hemochromatosis>
- Communications, L. H. N. C. f. B. (2009). Beta thalassemia. from <http://ghr.nlm.nih.gov/condition/beta-thalassemia>
- Communications, L. H. N. C. f. B. (2012a). Fanconi anemia.
- Communications, L. H. N. C. f. B. (2012c). Hemophilia. from (<http://ghr.nlm.nih.gov/condition/hemophilia#inheritance>)
- Çürük, M. A., Zeren, F., Genç, A., Ozavci-Aygün, S., Kilinç, Y., & Aksoy, K. (2008). Prenatal diagnosis of sickle cell anemia and  $\beta$ -thalassemia in southern Turkey. *Hemoglobin*, 32(6), 525-530.

- De Cock, K. M., Mbori-Ngacha, D., & Marum, E. (2002). Shadow on the continent: public health and HIV/AIDS in Africa in the 21st century. *The Lancet*, 360(9326), 67-72.
- DeJong, J., Jawad, R., Mortagy, I., & Shepard, B. (2005). The sexual and reproductive health of young people in the Arab countries and Iran. *Reproductive health matters*, 13(25), 49-59.
- Dibua, U. (2010). Socio-economic and socio-cultural predisposing risk factors to HIV/Aids: case study of some locations in eastern Nigeria. *The Internet Journal of Tropical Medicine*, 6(2), 9.
- Eaton, J. W., Johnson, L. F., Salomon, J. A., Bärnighausen, T., Bendavid, E., Bershteyn, A., . . . Hontelez, J. A. (2012). HIV treatment as prevention: systematic comparison of mathematical models of the potential impact of antiretroviral therapy on HIV incidence in South Africa. *PLoS medicine*, 9(7), e1001245.
- El-Beshlawy, A., & Youssry, I. (2009). Prevention of hemoglobinopathies in Egypt. *Hemoglobin*, 33(S1), S14-S20.
- El-Menyar, A., Zubaid, M., Rashed, W., Almahmeed, W., Al-Lawati, J., Sulaiman, K., . . . Al Suwaidi, J. (2009). Comparison of men and women with acute coronary syndrome in six Middle Eastern countries. *The American journal of cardiology*, 104(8), 1018-1022.
- El Mouzan, M. I., Salloum, A., Herbish, A., Qurachi, M. M., & Omar, A. (2008). Consanguinity and major genetic disorders in Saudi children: a community-based cross-sectional study. *Annals of Saudi medicine*, 28(3), 169.
- Fallah, M. S., Samavat, A., & Zeinali, S. (2009). Iranian national program for the prevention of thalassemia and prenatal diagnosis: mandatory premarital screening and legal medical abortion. *Prenatal diagnosis*, 29(13), 1285-1286.
- Frize, M., Weyand, S., & Bariciak, E. (2010). *Suggested criteria for successful deployment of a Clinical Decision Support System (CDSS)*. Paper presented at the Medical Measurements and Applications Proceedings (MeMeA), 2010 IEEE International Workshop on.
- Ganczak, M. (2010). The impact of premarital HIV testing: a perspective from selected countries from the Arabian Peninsula. *AIDS care*, 22(11), 1428-1433.
- Garg, A. X., Adhikari, N. K., McDonald, H., Rosas-Arellano, M. P., Devereaux, P., Beyene, J., . . . Haynes, R. B. (2005). Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. *Jama*, 293(10), 1223-1238.
- Ghotbi, N., & Tsukatani, T. (2005). Evaluation of the national health policy of thalassaemia screening in the Islamic Republic of Iran.
- Goh, B. T. (2005). Syphilis in adults. *Sexually transmitted infections*, 81(6), 448-452.
- Gottlieb, S. L., Xu, F., & Brunham, R. C. (2013). Screening and treating Chlamydia trachomatis genital infection to prevent pelvic inflammatory disease: interpretation of findings from randomized controlled trials. *Sexually transmitted diseases*, 40(2), 97-102.
- Gouya, L., Puy, H., Lamoril, J., Da Silva, V., Grandchamp, B., Nordmann, Y., & Deybach, J.-C. (1999). Inheritance in erythropoietic protoporphyria: a common wild-type ferrochelatase allelic variant with low expression accounts for clinical manifestation. *Blood*, 93(6), 2105-2110.

- Gustafson, S. L., Gettig, E. A., Watt-Morse, M., & Krishnamurti, L. (2007). Health beliefs among African American women regarding genetic testing and counseling for sickle cell disease. *Genetics in Medicine*, 9(5), 303-310.
- Haghpanah, S., Nasirabadi, S., Rahimi, N., Faramarzi, H., & Karimi, M. (2012). Sociocultural challenges of beta-thalassaemia major birth in carriers of beta-thalassaemia in Iran. *Journal of medical screening*, 19(3), 109-111.
- Hamdan, A.-L., Sibai, A. M., Srour, Z. M., Sabra, O. A., & Deeb, R. A. (2007). Voice disorders in teachers. The role of family physicians. *Saudi medical journal*, 28(3), 422-428.
- Hayes, R., Watson-Jones, D., Celum, C., van de Wijgert, J., & Wasserheit, J. (2010). Treatment of sexually transmitted infections for HIV prevention: end of the road or new beginning? *AIDS (London, England)*, 24(0 4).
- Hesketh, T. (2003). Getting married in China: pass the medical first. *BMJ: British Medical Journal*, 326(7383), 277.
- Hillestad, R., Bigelow, J., Bower, A., Girosi, F., Meili, R., Scoville, R., & Taylor, R. (2005). Can electronic medical record systems transform health care? Potential health benefits, savings, and costs. *Health Affairs*, 24(5), 1103-1117.
- Hoerbst, A., & Ammenwerth, E. (2010). Electronic health records. *Methods Inf Med*, 49(4), 320-336.
- Inhorn, M. C. (2005). Fatwas and ARTs: IVF and gamete donation in Sunni v. Shi'a Islam. *J. Gender Race & Just.*, 9, 291.
- International, H. L. S. (2007-2015). Introduction to HL7 Standards. from <http://www.hl7.org/implement/standards/>
- Ismail, N. K., Rahman, N. A., Bakar, Z. A., & Sembok, T. T. (2007). *Terms visualization for Malay translated Quran documents*. Paper presented at the Proceedings of the International Conference on Electrical Engineering and Informatics Institut Teknologi Bandung, Indonesia June.
- Jagannath, V., Fedorowicz, Z., Al Hajeri, A., Hu, N., & Sharma, A. (2011). Transplantation of blood-forming stem cells for people with  $\beta$ -thalassaemia major. *Health*.
- Jain, B. B., Roy, R. N., Ghosh, S., Ghosh, T., Banerjee, U., & Bhattacharya, S. K. (2012). Screening for thalassaemia and other hemoglobinopathies in a tertiary care hospital of West Bengal: Implications for population screening. *Indian journal of public health*, 56(4), 297.
- Kahraman, S., Yakın, K., Dönmez, E., Şamlı, H., Bahce, M., Cengiz, G., . . . İmirzalıoğlu, N. (2000). Relationship between granular cytoplasm of oocytes and pregnancy outcome following intracytoplasmic sperm injection. *Human Reproduction*, 15(11), 2390-2393.
- Karimi, M., Jamalain, N., Yarmohammadi, H., Askarnejad, A., Afrasiabi, A., & Hashemi, A. (2007). Premarital screening for  $\beta$ -thalassaemia in Southern Iran: options for improving the programme. *Journal of Medical Screening*, 14(2), 62-66.
- Khalifa, M. (2013). Barriers to health information systems and electronic medical records implementation. A field study of Saudi Arabian hospitals. *Procedia Computer Science*, 21, 335-342.

- Khalifa, M. (2014). Technical and Human Challenges of Implementing Hospital Information Systems in Saudi Arabia. *Journal of Health Informatics in Developing Countries*, 8(1).
- Khebir, B., Adam, M., Daud, A., & Shahrom, C. (2007). Premarital HIV screening in Johor--(2002-2004). *The Medical journal of Malaysia*, 62(1), 19-22.
- Knight, C. (2005). Health economics of treating haemophilia A with inhibitors. *Haemophilia*, 11(s1), 11-17.
- Korenromp, E., White, R., Orroth, K., Bakker, R., Kamali, A., Serwadda, D., . . . Hayes, R. (2005). Determinants of the impact of sexually transmitted infection treatment on prevention of HIV infection: a synthesis of evidence from the Mwanza, Rakai, and Masaka intervention trials. *Journal of Infectious Diseases*, 191(Supplement 1), S168-S178.
- Korthof, E. T., Svahn, J., Latour, R. P., Terranova, P., Moins-Teisserenc, H., Socié, G., . . . Tol, M. (2013). Immunological profile of Fanconi anemia: a multicentric retrospective analysis of 61 patients. *American journal of hematology*, 88(6), 472-476.
- Kuliev, A., & Modell, B. (1990). Problems in the control of genetic disorders. *Biomedical science*, 1(1), 3-17.
- Kuperman, G. J., Bobb, A., Payne, T. H., Avery, A. J., Gandhi, T. K., Burns, G., . . . Bates, D. W. (2007). Medication-related clinical decision support in computerized provider order entry systems: a review. *Journal of the American Medical Informatics Association*, 14(1), 29-40.
- Kurth, A. E., Celum, C., Baeten, J. M., Vermund, S. H., & Wasserheit, J. N. (2011). Combination HIV prevention: significance, challenges, and opportunities. *Current HIV/AIDS Reports*, 8(1), 62-72.
- Kushniruk, A. W., Monkman, H., Tuden, D., Bellwood, P., & Borycki, E. M. (2014). Integrating heuristic evaluation with cognitive walkthrough: development of a hybrid usability inspection method. *Studies in health technology and informatics*, 208, 221-225.
- Ladis, V., Karagiorga-Lagana, M., Tsatra, I., & Chouliaras, G. (2013). Thirty-year experience in preventing haemoglobinopathies in Greece: achievements and potentials for optimisation. *European journal of haematology*, 90(4), 313-322.
- Lippman, A. (1991). Prenatal genetic testing and screening: constructing needs and reinforcing inequities. *Am. JL & Med.*, 17, 15.
- Locock, L., & Kai, J. (2008). Parents' experiences of universal screening for haemoglobin disorders: implications for practice in a new genetics era. *British Journal of General Practice*, 58(548), 161-168.
- Luginaah, I., Elkins, D., Maticka-Tyndale, E., Landry, T., & Mathui, M. (2005). Challenges of a pandemic: HIV/AIDS-related problems affecting Kenyan widows. *Social Science & Medicine*, 60(6), 1219-1228.
- Madani, T. A. (2006). Sexually transmitted infections in Saudi Arabia. *BMC infectious diseases*, 6(1), 3.
- Malhotra, M., Sood, S., Mukherjee, A., Muralidhar, S., & Bala, M. (2013). Genital Chlamydia trachomatis: an update. *The Indian journal of medical research*, 138(3), 303.



- Marks, D. B. S., Todd; Sandra I Kim; Marc Glucksman. (2007). If not otherwise specified, reference is. *Biochemistry and molecular biology*.
- Marks, G., Crepaz, N., Senterfitt, J. W., & Janssen, R. S. (2005). Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, 39(4), 446-453.
- Marteau, T. M. (1995). Towards informed decisions about prenatal testing: a review. *Prenatal diagnosis*, 15(13), 1215-1226.
- McGowin, C., Rohde, R., & Redwine, G. (2014). *Trichomonas vaginalis*: common, curable and in the diagnostic spotlight. *Clinical laboratory science: journal of the American Society for Medical Technology*, 27(1), 53.
- McIlhaney, J. S. (2000). Sexually transmitted infection and teenage sexuality. *American journal of obstetrics and gynecology*, 183(2), 334-339.
- Memish, Z. A., & Saeedi, M. Y. (2011). Six-year outcome of the national premarital screening and genetic counseling program for sickle cell disease and  $\beta$ -thalassemia in Saudi Arabia. *Annals of Saudi medicine*, 31(3), 229.
- Mitchell, C., & Prabhu, M. (2013). Pelvic inflammatory disease: current concepts in pathogenesis, diagnosis and treatment. *Infectious disease clinics of North America*, 27(4), 793-809.
- Mohanty, D., & Mukherjee, M. B. (2002). Sickle cell disease in India. *Current opinion in hematology*, 9(2), 117-122.
- Morabia, A., & Zhang, F. (2004). History of medical screening: from concepts to action. *Postgraduate medical journal*, 80(946), 463-469.
- Moronkola, O., & Fadairo, R. (2007). University students in Nigeria: knowledge, attitude toward sickle cell disease, and genetic counseling before marriage. *International quarterly of community health education*, 26(1), 85-93.
- Mudiyanse, R. M. (2006). Thalassaemia treatment and prevention in Uva province, Sri Lanka: a public opinion survey. *Hemoglobin*, 30(2), 275-289.
- Musen, M. A., Middleton, B., & Greenes, R. A. (2014). Clinical decision-support systems *Biomedical informatics* (pp. 643-674): Springer.
- Musil, A. (1928). *The manners and customs of the Rwala Bedouins* (Vol. 6): American Geographical Society.
- Muzny, C. A., & Schwebke, J. R. (2013). The clinical spectrum of *Trichomonas vaginalis* infection and challenges to management. *Sexually transmitted infections*, sextrans-2012-050893.
- Nath, A. (2002). Human immunodeficiency virus (HIV) proteins in neuropathogenesis of HIV dementia. *Journal of Infectious Diseases*, 186(Supplement 2), S193-S198.
- Norman, B. J., & Miller, S. D. (2011). Human genome project and sickle cell disease. *Social work in public health*, 26(4), 405-416.
- Origa, R., Moi, P., Galanello, R., & Cao, A. (2013). Alpha-thalassaemia.
- Paul, S. S. (2012). Genetic blood disorders: questions you need to ask. *The Journal of family practice*, 61(1), 30-37.
- PERRINE, R. P., PEMBREY, M. E., John, P., Perrine, S., & SHOUP, F. (1978). Natural history of sickle cell anemia in Saudi Arabs: a study of 270 subjects. *Annals of internal medicine*, 88(1), 1-6.

- Prainsack, B., & Firestone, O. (2006). 'Science for survival': biotechnology regulation in Israel. *Science and Public Policy*, 33(1), 33-46.
- Prevention, C. f. D. C. a. (2014, July 14, 2014). Sickle Cell Disease (SCD). from <http://www.cdc.gov/ncbddd/sicklecell/index.html>
- Ranjbaran, R., Okhovat, M. A., Mobarhanfard, A., Aboualizadeh, F., Abbasi, M., Moezzi, L., . . . Sharifzadeh, S. (2013). Analysis of  $\beta/\alpha$  Globin Ratio by Using Relative qRT-PCR for Diagnosis of Beta-Thalassemia Carriers. *Journal of clinical laboratory analysis*, 27(4), 267-271.
- Rennie, S., & Mupenda, B. (2008). Ethics of mandatory premarital HIV testing in Africa: the case of Goma, Democratic Republic of Congo. *Developing World Bioethics*, 8(2), 126-137.
- Samavat, A., & Modell, B. (2004). Iranian national thalassaemia screening programme. *Bmj*, 329(7475), 1134-1137.
- Sciences, U. o. U. H. (2015). Sickle Cell Disease. from <http://learn.genetics.utah.edu/content/disorders/singlegene/sicklecell/>
- Services, B. N. (2013). Saudi Arabia profile. from <http://www.bbc.com/news/world-middle-east-14703476>
- Standerwick, R. G., Yen, E. H., & Pliska, B. (2013). Orthodontic treatment considerations for a patient with erythropoietic protoporphyria. *American Journal of Orthodontics and Dentofacial Orthopedics*, 144(6), 899-908.
- Steen, R., Wi, T. E., Kamali, A., & Ndowa, F. (2009). Control of sexually transmitted infections and prevention of HIV transmission: mending a fractured paradigm. *Bulletin of the World Health Organization*, 87(11), 858-865.
- Sulaiman, K., Prashanth, P., Al-Zakwani, I., Al-Mahmeed, W., Al-Motarreb, A., Al Suwaidi, J., . . . Al Faleh, H. (2012). Impact of anemia on in-hospital, one-month and one-year mortality in patients with acute coronary syndrome from the Middle East. *Clinical medicine & research*, 10(2), 65-71.
- Sutcliffe, S., Neace, C., Magnuson, N. S., Reeves, R., & Alderete, J. (2012). Trichomonosis, a common curable STI, and prostate carcinogenesis—a proposed molecular mechanism. *PLoS pathogens*, 8(8), e1002801.
- Tamhankar, P. M., Agarwal, S., Arya, V., Kumar, R., Gupta, U., & Agarwal, S. (2009). Prevention of homozygous beta thalassemia by premarital screening and prenatal diagnosis in India. *Prenatal diagnosis*, 29(1), 83-88.
- Theodoridou, S., Alemayehou, M., Prappas, N., Karakasidou, O., Aletra, V., Plata, E., . . . Sinopoulou, K. (2008). Carrier screening and prenatal diagnosis of hemoglobinopathies. A study of indigenous and immigrant couples in northern Greece, over the last 5 years. *Hemoglobin*, 32(5), 434-439.
- Umar, S. A., & Oche, O. M. (2012). Knowledge of HIV/AIDS and use of mandatory premarital HIV testing as a prerequisite for marriages among religious leaders in Sokoto, North Western Nigeria. *Pan African Medical Journal*, 11(1).
- Vassiliev, A. (2013). *The History of Saudi Arabia*: Saqi.
- Vogel, F. (1997). *Vogel and Motulsky's Human Genetics: Problems and Approaches* (Vol. 878): Springer Science & Business Media.
- White, R. G., Glynn, J. R., Orroth, K. K., Freeman, E. E., Bakker, R., Weiss, H. A., . . . Hayes, R. J. (2008). Male circumcision for HIV prevention in sub-Saharan Africa: who, what and when? *Aids*, 22(14), 1841-1850.

- Workowski, K. A., & Berman, S. M. (2006). *Sexually transmitted diseases treatment guidelines, 2006*: US Department of Health and Human Services, Centers for Disease Control and Prevention.
- Wu, Z., Rou, K., Xu, C., Lou, W., & Detels, R. (2005). Acceptability of HIV/AIDS counseling and testing among premarital couples in China. *AIDS Education & Prevention, 17*(1), 12-21.
- Zarakolu, P., Alp, S., & Yağci, S. (2010). [Frequency of curable sexually transmitted infections among registered female sex-workers in Ankara City]. *Mikrobiyoloji bulteni, 44*(1), 117-121.
- Zhou, Y., Shang, X., Yin, B., Xiong, F., Xiao, Q., Zhou, W., Xu, X. (2012). [Large-scale population-based genetic screening and prenatal diagnosis for thalassemias in Zhuhai City of Guangdong Province]. *Zhonghua fu chan ke za zhi, 47*(2), 90-95.
- Ziad, A., Tariq, M., & Mohamad, Y. (2011). Marked regional variations in the prevalence of sickle cell disease and b-thalassemia in Saudi Arabia: findings from the premarital screening and genetic counseling program. *The Journal of Epidemiology and Global Health, 1*, 61-68.
- Zlotogora, J. (2009). Population programs for the detection of couples at risk for severe monogenic genetic diseases. *Human genetics, 126*(2), 247-253.
- Zlotogora, J., Carmi, R., Lev, B., & Shalev, S. A. (2009). A targeted population carrier screening program for severe and frequent genetic diseases in Israel. *European Journal of Human Genetics, 17*(5), 591-597.