**Exploring the effectiveness of mandatory premarital screening and genetic counselling programmes for beta thalassemia in the Middle East: a scoping review**

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**ABSTRACT**

**Background**

Beta thalassemia is a common genetic blood disorder in the Middle Eastern region. Mandatory premarital screening and genetic counselling (PMSGC) programmes are implemented in eight Middle East countries to reduce at-risk marriages and thus disease prevalence. A scoping review was conducted to explore effectiveness of these programmes.

**Methods**

Arksey and O’Malley’s six-stage scoping framework was used. Reported outcomes were analysed per country with success defined as achieving a 65% reduction in at-risk marriages and/or thalassemia-affected births. Emergent enablers and barriers were analysed thematically.

**Results**

Twenty-one sources were included from 1,348 identified, discussing seven country programmes with 95% (20/21) published during 2003-2013. Five publications each were included for Iran and Saudi Arabia, three for Turkey, two each for Bahrain and Iraq (Kurdistan), one for UAE, plus two multi-country evaluations. No programmes achieved 65% at-risk marriage cancellation rates. Though data were minimal on thalassemia-affected birth reductions, programmes in Iran, Turkey, and Iraq reported at least 65% reductions. Thematic analysis found screening timing, access to prenatal detection and abortion, socio-religious issues, awareness, and counselling affected decisions.

**Conclusion**

This review found PMSGC programmes were unsuccessful at discouraging at-risk marriages, but successful in reducing prevalence of affected births in countries providing prenatal detection and therapeutic abortion. A life-cycle approach to prevention, incorporating school screening, awareness campaigns, reconsideration of therapeutic abortion, and screening and counselling of couples married prior to programme inception, is likely to improve effectiveness of such programmes in the Middle Eastern region.

**INTRODUCTION**

Beta thalassemia (β-thalassemia) is a single-gene inherited haemoglobinopathy, characterised by a decreased production of globin chains, resulting in chronic anaemia and skeletal and organ deformities. The World Health Organization (WHO) estimates that β-thalassemia affects 2.9% of the world’s population, creating a major public health problem that burdens healthcare systems and significantly effects the quality of life for affected patients [[1](#_ENREF_1)]. Survival of individuals with β-thalassemia major is reliant on monthly blood transfusions and iron chelation therapy [[2](#_ENREF_2)]. Without blood transfusions, death usually occurs within the first few years of life. Average life expectancy for those with β-thalassemia major is 32 years, much less if untreated [[3](#_ENREF_3)]. Additionally, regular blood transfusions may cause iron overload, leading to progressive cardiac damage and death [[4](#_ENREF_4)]. Many β-thalassemia patients in the Middle East progress to advanced stages within a few years of diagnosis, due to inadequate supportive infrastructure [[5](#_ENREF_5)]. The only treatment for β-thalassemia is bone-marrow transplantation, which is expensive, risky, difficult to identify a suitable donor, and the required infrastructure is unavailable in most Middle Eastern countries. The cost of blood transfusions for β-thalassemia major patients in the Middle East has been estimated at US$3,200 annually per patient, with lifetime costs of approximately US$284,145 [[6](#_ENREF_6), [7](#_ENREF_7)]. β-thalassemia is inherited and couples where both partners are carriers (i.e. at-risk couples) have a one in four chance of having a child with β-thalassemia major.

β-thalassemia prevalence is high in the Middle East, where 1-15% of the population carries the trait [[5](#_ENREF_5), [8](#_ENREF_8)]. A major contributor to high β-thalassemia prevalence in the Middle East is the high 25-60% prevalence of consanguineous marriages, particularly among first cousins [[9](#_ENREF_9)]. Consanguineous or common-ancestry marriages increase the chances of offspring inheriting disease traits, with closer consanguineous relationships at increased risk [[10](#_ENREF_10)]. Consanguineous marriages are socially favoured in many Arab-majority countries [[9](#_ENREF_9)]. Sociological studies indicate they increase the couple’s stability due to compatibility between husband, wife, and in-laws, strengthen family ties and solidarity, support transmission of shared values, and ease premarital negotiations particularly by allowing wealth and property to remain within the family [[11](#_ENREF_11)]. A study in Egypt found that men with educational and occupational status were considered ‘valuable assets’ and pressured to marry within the family [[3](#_ENREF_3)]. Consanguinity predates Islam and the Qur’an does not encourage the practice [[11](#_ENREF_11)].

Due the high burden β-thalassemia places on patients, families, and healthcare systems in the Middle East, WHO advocates prevention and reduction of the burden of β-thalassemia through voluntary genetic screening [[12](#_ENREF_12)]. In Iran, total costs of preventing one case of β-thalassemia were estimated at US$100, less than the cost for a single year of optimum support for a case of β-thalassemia [[13](#_ENREF_13)]. Similar findings in Cyprus and Greece indicated the cost of prevention was equal to that of treating one affected newborn for one year, while the annual cost of the screening programme was equivalent to treating the thalassemia-affected population for one week [[3](#_ENREF_3)]. Prevention thus appears significantly more cost-effective while reducing psychosocial implications of this chronic disease [[7](#_ENREF_7)].

Premarital screening and genetic counselling (PMSGC), popular in the Middle East as it is religiously and socially unacceptable to bear children outside marriage, aims to identify β-thalassemia carriers among couples planning to marry [[2](#_ENREF_2)]. Genetic counselling is provided to at-risk couples to ensure they understand reproductive risks and available options [[4](#_ENREF_4)]. PMSGC programmes aim to reduce β-thalassemia births through: (i) prevention of at-risk marriages by discouragement during counselling, and where legal (ii) termination of affected foetuses through prenatal diagnosis (PND) and therapeutic abortion. Alswaidi and O’Brian suggest that screening can reduce β-thalassemia burden by reducing at-risk marriages and preventing up to 95% of affected births [[10](#_ENREF_10)].

Several countries in the Mediterranean and Middle Eastern regions have implemented mandatory PMSGC programmes to reduce prevalence of genetic disorders [[4](#_ENREF_4)]. Mandatory PMSGC programmes began in the 1970s to eradicate β-thalassemia in the Mediterranean region (Table 1). Cyprus was first in 1973 and very successful, decreasing the number of affected births from 51 to 8 annually between 1974 and 1979 and to zero since 2002 [[12](#_ENREF_12)]. Similar programmes were implemented in Italy and Greece, also achieving 100% β-thalassemia birth reductions [[12](#_ENREF_12), [14](#_ENREF_14)]. As less than 5% of reductions was attributed to separation of engaged couples, success was linked to provision of free PND and availability of abortion, effective education, and counselling [[3](#_ENREF_3), [15](#_ENREF_15)].

Mediterranean successes created an approach for the Middle East that foundered with the illegality of therapeutic abortion in several countries (Table 2). Abortion is restricted by nearly all major world religions, including Islam. Scholars from the four Sunni and the Shi’ite schools, agree that abortion may be performed to save the mother’s life, but disagree over the status of the foetus before four months gestation. While Muslim scholars have differing opinions on abortion, all agreed the human ‘spirit’ enters the body at four months gestation (120 days), at which point the foetus is ‘‘another creation’’ according to Islamic metaphysics (Quran 23:14) and abortion is forbidden unless the life of the mother is threatened [[16](#_ENREF_16)]. In 1990, the Islamic Jurisprudence Council of the World Islamic League in Mecca issued a *fatwa* (Islamic legal ruling) allowing for select termination of pregnancies if a committee of physicians determined that the foetus is severely malformed and its birth would have seriously negative effects on itself and its family [[3](#_ENREF_3)]. The Organization of Islamic Conference - an organisation of countries with Muslim majorities or pluralities - has 57 members, of which 12 allow unrestricted access to abortion. With the exception of Turkey and Tunisia, these are mainly former Soviet Bloc states. Bahrain, a politically and socially conservative Muslim state, is the twelfth to permit unrestricted abortion. Among socially conservative Muslim countries, seven permit abortion in the first four months for foetal deformities, four of these in sub-Saharan Africa (i.e. Benin, Burkina Faso, Chad, Guinea) and three in the Middle East (i.e. Iran, Kuwait, Qatar) [[16](#_ENREF_16)]. In countries where abortion for foetal impairment is illegal (i.e. Jordan, Saudi Arabia, UAE), mandatory PMSGC programmes aim to reduce the prevalence of β-thalassemia through genetic counselling to discourage at-risk marriages. Countries offering PND and abortion aim to reduce β-thalassemia prevalence through discouraging at-risk marriages and terminating affected pregnancies.

**Aim and objectives**

The review aimed to explore outcomes of mandatory PMSGC programmes for β-thalassemia in the Middle East region. Objectives were to: (i) summarise the nature of the literature; (ii) discuss programme effectiveness in reducing at-risk marriages and β-thalassemia births; (iii) identify barriers and enablers to programme effectiveness in the Middle East.

**METHODS**

A scoping review was conducted using Arksey and O’Malley’s six-stage methodological framework adapting Levac et al’s revisions [[17](#_ENREF_17), [18](#_ENREF_18)].

**Identifying the research question**

Authors selected the research question ‘Are PMSGC programmes in the Middle East associated with successful reductions in at-risk marriages or β-thalassemia births?’ For this review, programme success was defined as at least a 65% at-risk marriage cancellation rate, or 65% reduction in β-thalassemia birth incidence, after programme implementation. These levels were selected after consultation with regional experts as being high enough to have a significant impact on β-thalassemia responses while still low enough to be achievable by most programmes if the PMSGC model was effective.

**Identifying relevant work**

Multiple literature sources were searched to increase comprehensiveness [[17](#_ENREF_17)]. First, electronic databases PubMed, MEDLINE, ScienceDirect and Embase were searched systematically using key terms ‘genetic, premarital, haemoglobinopath\*, thalassemia, β-thalassemi\*, genetic abnormalit\*, genetic disorder\*, haemoglobinopath\*’ AND screen\* OR ‘counsel\*’ OR ‘evaluat\*, effect\*, outcome\*, accept\*, decision\*, prevent\*, marr\*.’ Second, the database OpenGray was searched systematically, using the same keywords, for unpublished literature and a *Google Scholar* search of ‘premarital screening and β-thalassemia’ was conducted. Third, key genetics journals *European Journal of Human Genetics, Public Health Genomics, Journal of Medical Genetics,* and *Genetic Epidemiology* were purposively hand-searched*.* Finally, websites of UN and civil-society organisations *UNICEF*, *WHO, Thalassemia International Federation, UAE Genetic Disease Association, and Emirates Thalassemia Society* were purposively searched for studies, reports and conference proceedings*.* Relevant citations were snowballed to identify further relevant sources.

**Source selection**

To ensure relevance, inclusion criteria were primary or secondary research on outcomes of PMSGC programmes for genetic diseases implemented in countries within the Middle Eastern region, published in English from 2000 onwards. The first author screened title, abstract, then full text against criteria. After removal of duplicates, remaining sources were checked against exclusion criteria (i.e. no English abstract, no full-text available, not implemented in a Middle East country, not specific to β-thalassemia, not a mandatory programme, no discussion of programme outcomes) and removed if they met at least one. Remaining sources were charted.

**Data charting**

Data for each source was charted using the following headings: source authors, publication year, source title, type of search (e.g. database, hand-search), country, study design, study participants, programme description, availability of PND, legal status of abortion, main findings and conclusions. The first author was primarily responsible for data extraction with support from the second author.

**Collating, summarising, and reporting**

The nature and distribution of studies were summarised in accordance with the research question. Potential contributors to programme success that emerged from thematic analysis were reported.

**Stakeholder consultation**

A stakeholder group was organised to provide feedback on preliminary results. Seven experts were contacted via telephone and six agreed to participate. Stakeholders reviewed a draft of the results section and provided feedback on potential additional sources, any obvious gaps or unexpected findings, how best to display findings, and policy or practice recommendations that could inform the discussion section.

**Ethics**

Ethics approval, though not required for a review, was provided by the Research Ethics Committee of the London School of Hygiene & Tropical Medicine (approval number 8272).

**RESULTS**

**Extent, distribution, and nature of the literature**

Figure 1 provides a flow diagram of the 21 sources included of 1,358 identified. Most sources (6/21; 29%) were published in 2013. Two sources included several country programmes [[10](#_ENREF_10), [12](#_ENREF_12)]. Iran and Saudi Arabia were best represented with 5 (24%) sources each, followed by Turkey with 3 (14%), Bahrain and Iraq with 2 (10%) each, Jordan and the UAE with 1 (5%) each, and none for the Palestinian Territories. Approximately half (11/21) were retrospective reviews, 4 were cohort studies, and 3 each were case-control and cross-sectional studies.

**Programme effectiveness**

Literature from six countries (i.e. Bahrain, Iran, Iraqi Kurdistan, Jordan, Saudi Arabia, Turkey) included indicators of programme effectiveness, shown in Table 3 [[1](#_ENREF_1), [4](#_ENREF_4), [10](#_ENREF_10), [12-14](#_ENREF_12), [19-27](#_ENREF_19)]. One source reviewing the UAE programme included satisfaction surveys and recommendations, but provided no statistics [[8](#_ENREF_8)].

*Bahrain*

The PMSGC programme was mandated in 2004 and PND and therapeutic abortion are legal. A cross-sectional study of 1,070 PMSGC attendees reported a 43.3% at-risk marriage cancellation rate [[23](#_ENREF_23)]. No analysis of changes in β-thalassemia incidence rates in Bahrain was found in the literature.

*Iran*

In 1997, PMSGC became mandatory in the Islamic Republic of Iran and included premarital screening and genetic counselling for carrier couples found at risk of having β-thalassemia affected children [[13](#_ENREF_13)]. Iran is the only Islamic Republic whose legal system is founded solely on Shi’ite *shari’a* (Islamic law), and the first contemporary Islamic country attempting to combine principles of theocracy and religious law with representative, parliamentary democracy. Iran serves as a model politically, socially, and religiously through its seminaries, for other Shi’ite countries (e.g. Iraq) and Shi’ite minorities in Sunni-majority countries (e.g. Bahrain, Kuwait, Lebanon). In 2003, the addition of prenatal detection (PND) initiated reforms in abortion-related laws. While abortion for any reason other than saving the mother’s life was illegal in Iran, Islamic clergies declared a *fatwa* permitting abortion of homozygote β-thalassemia foetuses up to 16 weeks of gestational age [[13](#_ENREF_13)]. Prior to adding PND, genetic counselling aimed to convince at-risk couples not to marry [[19](#_ENREF_19)].

Evaluation in West-Azerbaijan province found 53% of marriages among at-risk couples during 2002-2006 were cancelled after screening [[13](#_ENREF_13)]. Similarly, Cousens *et al* noted that prior to provision of PND and pregnancy termination in Iran, about half of at-risk couples identified by premarital screening proceeded to marriage [[12](#_ENREF_12)]. Lower cancellation rates, averaging 19.4%, were found in central Iran in 1995-2010 [[19](#_ENREF_19)]. Ahmadnazhad *et al* reported an increase in West-Azerbaijan from 38% in 2003 to 69% in 2006 [[13](#_ENREF_13)]. Zeinalian *et al* found decreased marriage cancellations in central Iran from 50.4% in 1997 to 9.4% in 2010 and significantly increased PND uptake from 7 couples in 2003 when it was legalized to 560 in 2010 [[19](#_ENREF_19)]. In southern Iran, 292 couples underwent PND between 2002 and 2004, resulting in detection and termination of 69 thalassemia-affected foetuses [[14](#_ENREF_14)]. In West-Azerbaijan, 92 thalassemia-affected foetuses were terminated in 2005-2010, thus 70% of β-thalassemia births over 10 years occurred within the first five years of the programme before availability of PND and legal abortion. Uptake of PND among at-risk couples increased from 2.8% in 2003 to 85% in 2010, leading to an estimated 1,000 fewer β-thalassemia births annually [[19](#_ENREF_19)].

β-thalassemia birth prevalence in southern Iran decreased by 81.1% from 2.53/1,000 births in 1995 to 0.82/1,000 births in 2004 [[14](#_ENREF_14)]. β-thalassemia incidence decreased by 96.5% over 10 years in central Iran, from 43.7/100,000 in 1997 to 1.5/100,000 in 2010 [[19](#_ENREF_19)]. Iran’s successful β-thalassemia reduction placed the Iranian PMSGC programme as a benchmark for other national programmes.

*Iraqi Kurdistan*

The PMSGC programme was mandated in 2008 in Kurdistan, northern Iraq, with PND and therapeutic abortion available. In the first three years (2008–2010), 91% of at-risk couples proceeded with marriage. PND was sought by 38% of those deciding to marry and all affected pregnancies were terminated [[24](#_ENREF_24)]. A five-year evaluation found 98% of at-risk couples proceeded with marriage, with PND sought by 76% and 10 of the 11 affected pregnancies terminated. Thirty couples, married prior to 2008 with at least one thalassemia-affected child, were offered PND and all three affected foetuses identified were aborted [[4](#_ENREF_4)]. The number of thalassemia-affected births in Kurdistan decreased from 20 to 7 over five years, a reduction of 65% [[4](#_ENREF_4)].

*Jordan*

The PMSGC programme was mandated in Jordan in 2004. PND is legal, upon request on a self-pay basis, but therapeutic abortion is illegal. Oseroff found that PMSGC discouraged 40% of at-risk marriages, while PND demand was low due to cost and unavailability of abortion [[3](#_ENREF_3)]. Hamamy and Al-Allawi found that of 48 at-risk couples identified in 2006, only three (6%) cancelled marriage plans [[24](#_ENREF_24)]. There were no findings in the literature regarding changes in β-thalassemia incidence rates in Jordan.

*Saudi Arabia*

The national PMSGC programme, mandated in 2004, offers screening to all couples registered to marry. Couples found at-risk receive counselling, as PND and therapeutic abortion are illegal [[1](#_ENREF_1)]. Alhamdan reported a 10.4% at-risk marriage cancellation rate in 2004-2005 [[20](#_ENREF_20)]. Alswaidi *et al* reported 11.8% for 2005-2006 [[10](#_ENREF_10)], Al Sulaiman *et al* reported 2% [[21](#_ENREF_21)], while Memish & Saeedi found 26.5% in 2004-2009 [[1](#_ENREF_1)]. An increasing at-risk marriage cancellation trend of 9.2% in 2004 to 51.9% in 2009 was found [[1](#_ENREF_1)]. Alswaidi *et al* reported that carriers with prior knowledge of their status were more likely to cancel marriage with another carrier than those without prior knowledge (11.8% versus 28.8% cancellation rates respectively) [[10](#_ENREF_10)]. While Cousens *et al* reported that β-thalassemia incidence has changed little in Saudi Arabia, statistics were not found in the literature reviewed [[12](#_ENREF_12)].

*Turkey*

PMSGC was mandated in Turkey in the 1990s, Denizli from 1995 and Mersin from 1998. PND and therapeutic abortion are legal. A four-year evaluation in Denizli found a 13.3% marriage cancellation rate among at-risk couples, while 40% sought PND with one foetus diagnosed with β-thalassemia and terminated [[22](#_ENREF_22)]. Of 135 at-risk pregnancies in 1999-2004, 80 received PND and only two receiving PND delivered an affected baby, one due to late referral (Tosun et al, 2006). A national review indicated Turkey’s PMSGC programme achieved a 90% reduction in β-thalassemia births annually, reducing from 272 births in 2002 to 25 in 2010 [[25](#_ENREF_25)]. No analysis of changes in β-thalassemia incidence rates in Turkey was found.

**Barriers and enablers**

Literature on six countries (i.e. Bahrain, Iran, Iraqi Kurdistan, Jordan, Saudi Arabia, Turkey) discussed barriers and enablers of programme success [[1](#_ENREF_1), [4](#_ENREF_4), [10](#_ENREF_10), [12-14](#_ENREF_12), [19-27](#_ENREF_19)]. Analysis identified seven emergent themes (Table 4). Influences included culture and stigma (11 sources), religion (11), thalassemia awareness (10), timing of screening (7), availability of PND and abortion (7) PND costs (7), and counsellor skills (4).

*Bahrain*

A study of at-risk couples who decided to marry, attributed their decisions to: (i) low perceived risk, (ii) low perceived seriousness of thalassemia, as people can live a long time with the disease, (iii) fatalism, and (iv) being informed of the availability of PND and therapeutic abortion during counselling rather than being discouraged to marry [[23](#_ENREF_23)].

*Iran*

The Iranian PMSGC programme was associated with significantly reduced β-thalassemia births, but rates remained above zero as at-risk couples continued to marry and have children [[10](#_ENREF_10)]. Major barriers described were marriage before programme initiation (51.4%), cultural issues (15%), and genetic counselling inadequacy (9%) [[19](#_ENREF_19)]. Karimi *et al* reported similar findings in southern Iran, including marriages before programme implementation, culture and religion, and declined PND and abortion [[14](#_ENREF_14)]. Ahmadnazhad *et al* attributed low PND uptake in West-Azerbaijan to inaccessibility (e.g. if PND was not offered locally and couples needed to travel to the capital) and costs not covered by insurance [[13](#_ENREF_13)].

*Iraqi Kurdistan*

The main barriers in northern Iraq were identified as: (i) limited awareness of β-thalassemia inheritance allowing high consanguineous marriage rates (24-27%), (ii) distrust of test results (2%), (iii) high user costs for PND, (iv) short time between testing and marriage dates limiting cancellations, and (v) social and cultural discomfort with marriage cancellation on short notice [[24](#_ENREF_24)]. Religion apparently had limited effect on selective termination decisions for affected pregnancies [[24](#_ENREF_24)].

*Jordan*

Major barriers to success of the Jordanian programme included: (i) unregulated private laboratories (e.g. families could fabricate negative test results through personal connections, if private laboratories accepted reports without testing to increase revenues), and (ii) exploitation of abortion rules (e.g. women with affected pregnancies could find two physicians, usually private-sector, to sign that the pregnancy posed a threat to her life) [[3](#_ENREF_3)]. Abortion is thus essentially semi-legal, displaying the inadequacies of a programme that provides PND without providing legally-sanctioned responses.

Reasons for fabricating results included stigma of carrier status, particularly for bride and family who were ‘tainted’ by a positive result, with potentially long-term effects on the marriageability of other women in the family. In nearly half of cases where the woman alone was a carrier, the husband left despite the non-existent risk of an affected child [[3](#_ENREF_3)]. This indicates both gender disparities and lack of accurate β-thalassemia knowledge. Alswaidi *et al* noted many Jordanians considered results of their union as fate, with one Jordan Times interviewee stating: “*All my ten children are disabled; they will get their reward in Heaven*” [[3](#_ENREF_3), [10](#_ENREF_10)]. Counselling was provided by general practitioners, with minimal or no training in genetic counselling, leading to inadequate counselling provision and violation of WHO PMSGC guidelines [[3](#_ENREF_3)].

*Saudi Arabia*

Alswaidi *et al* concluded the main barriers to the Saudi PMSGC programme’s success were: (i) completed non-cancellable wedding plans (43%), (ii) fear of social stigma (21%), (iii) familial commitment/pressures (17%), and (iv) religious considerations (14%) [[10](#_ENREF_10)]. Almost all couples were screened just before the wedding ceremony, and 52% who proceeded to marry attributed their decision to wedding arrangements already being made with cancellation not a viable option (e.g. after providing a new house and expensive bride dowry). Alhamdan agreed that late timing of screening was the major barrier to programme success given non-cancellable wedding plans [[20](#_ENREF_20)]. Premarital screening often comes too late for couples, who are already committed to their relationship. Two studies concluded that socio-cultural pressures were among the main reasons at-risk Saudi couples proceeded with marriage [[1](#_ENREF_1), [21](#_ENREF_21)]. Stigma associated with carrier status, fear of publically declaring incompatibility, and lack of education or awareness of hereditary diseases, were additional barriers [[20](#_ENREF_20)]. Religion was a barrier in some circumstances, as Islam teaches acceptance of fate and some interpreted this as accepting the risk of a sick child. However, Islamic teaching promotes healthy marriage and families, allowing scope for many interpretations favouring the role of counselling [[10](#_ENREF_10)]. Counsellors’ inability to provide adequate information to at-risk couples was identified as a barrier [[20](#_ENREF_20)]. However, Cousens *et al* concluded that failure of the Saudi programme was primarily due to termination of affected pregnancies being illegal [[12](#_ENREF_12)].

*Turkey*

Availability of PND and therapeutic abortion were identified as crucial enablers to programme success in Turkey, as prevention based solely on screening and counselling produced no consistent effect on β-thalassemia birth rates [[25](#_ENREF_25)]. A study of barriers to PND usage found: (i) lack of social security financing, (ii) insufficient knowledge of hereditary diseases (e.g. 15-20 minute counselling sessions could not provide adequate information), and (iii) culture [[28](#_ENREF_28)].

**DISCUSSION**

**Extent and distribution of the literature**

A scoping design was selected due to the minimal relevant literature expected. Gaps in extent and distribution include minimal literature comparing β-thalassemia birth rates following mandatory PMSGC programme implementation, especially for Saudi Arabia, Bahrain and Jordan, and none for the Palestinian Territories. Thus, it was not possible to fully ascertain programme impact.

**Effectiveness**

The success criteria used in this review were 65% reductions in at-risk marriages or β-thalassemia births (Table 3). None of the programmes reviewed achieved 65% reductions in at-risk marriages. Findings suggest programmes in Saudi Arabia and Jordan have only achieved 10% and 40% reductions in at-risk marriage rates respectively. Without legal therapeutic abortion, programmes will only succeed by separating carrier couples. Given low marriage cancellation rates and abortion remaining illegal in these countries, it is unlikely a large decrease in β-thalassemia births could have occurred. Data on reduction of β-thalassemia births was unavailable for programmes in Bahrain, Jordan, and Saudi Arabia, but programmes in Turkey, Iran, and Iraqi Kurdistan achieved reductions in β-thalassemia births of approximately 90%, 80%, and 65% respectively (Table 3).

The sole impact of premarital genetic testing in reducing β-thalassemia incidence appeared minimal, as programmes lacking therapeutic abortion did not successfully reduce numbers of β-thalassemia births. Success was most evident in programmes including free PND and legal accessible therapeutic abortion [[3](#_ENREF_3), [4](#_ENREF_4), [13](#_ENREF_13), [24](#_ENREF_24), [28](#_ENREF_28)]. As a comparison, less than 5% of the 100% success rates of programmes implemented in the Mediterranean region in the 1970s (Table 3) was attributed to separation of engaged at-risk couples [[15](#_ENREF_15)].

**Barriers and enablers**

Success of PMSGC programmes in Iran, Turkey and Iraqi Kurdistan was attributed to availability of PND and therapeutic abortion. Main barriers to at-risk marriage cancellation were similar to those for seeking PND and therapeutic abortion (e.g. social unacceptability, lack of knowledge, access, costs). Thus, increasing at-risk marriage cancellation rates noted in West-Azerbaijan and Saudi Arabia may be due to increased understanding of β-thalassemia, while decreasing cancellations in central Iran and Iraqi Kurdistan may relate to increased PND uptake and increased acceptability of PND and therapeutic termination.

**Life-cycle approaches**

Life-cycle or life-course approaches provide a holistic framework for identifying health challenges and critical periods for intervention throughout the life-cycle from preconception to death [[29](#_ENREF_29), [30](#_ENREF_30)]. Findings indicated adopting a life-cycle approach to β-thalassemia prevention, and intervening at critical periods during youth, premarital/preconception, prenatal, and neonatal life-stages, could be more successful than premarital screening alone [[31](#_ENREF_31)]. Life-cycle approaches provide a more holistic public health response, which can address barriers to programme success in the Middle East found in the literature (i.e. limited knowledge and awareness, non-timeliness of screening directly before marriage, lack of therapeutic abortion).

*Population*

Media campaigns could increase knowledge and awareness of risks and prevention of genetic diseases and consanguineous marriages. Two major barriers identified, fear of stigma associated with carrier status and familial pressures for consanguineous marriages, could be reduced through increased general understanding of the disorder [[8](#_ENREF_8)]. Support from religious authorities, essential to encouraging programme acceptance, was found to be a major enabler in the Mediterranean region [[1](#_ENREF_1), [10](#_ENREF_10), [28](#_ENREF_28)].

*Youth*

β-thalassemia screening programmes should initially target people before marital and child-bearing ages, to allow more time for avoiding or planning around high-risk marriages and births. Screening could be incorporated into school health packages (e.g. as in parts of India and Canada [[12](#_ENREF_12), [15](#_ENREF_15)]), or required for university entry, along with health education on hereditary diseases and consanguineous marriages. While results from India indicated school screening was insufficient alone, school health programmes appeared a feasible entry point for screening [[15](#_ENREF_15)]. Conducting initial screening as part of a life-cycle approach, well in advance of marital arrangements, would avoid barriers related to social commitments. Sources indicated those with prior knowledge of their status were less likely to proceed with at-risk marriages [[4](#_ENREF_4), [32](#_ENREF_32), [33](#_ENREF_33)].

*Premarital/Preconception*

Provision of genetic screening and counselling in government-regulated facilities for all couples wishing to marry remains essential. To be effective, counselling should be provided by trained professionals who can provide accurate advice regarding risks and childbearing options.

*Prenatal*

PND and therapeutic abortion were described as particularly important in the available literature. The traditional stance on therapeutic abortion should be reviewed in light of legal precedents in Bahrain, Iran, Iraqi Kurdistan, and Turkey allowing therapeutic abortion before 16 weeks gestation for thalassemia-affected foetuses. If therapeutic abortion is legalised, it is important that national policies ensure PND is: (i) conducted as early in pregnancy as possible to enable completion of diagnostic testing before 16 weeks gestation and (ii) subsidised by government or insurance schemes to be affordable and accessible for all population groups.

*Neonatal*

Appropriate support for those affected remains an important aspect of life-cycle approaches. Thalassemia-affected infants require considerable care. Couples married prior to PMSGC programme inception and still of childbearing age require screening. This could be done in a relatively non-disruptive way at antenatal services presentation if the father is present and adequate counselling for at-risk couples provided. Couples with a thalassemia-affected child require both support and counselling regarding options for future pregnancies.

**Limitations**

A limitation of reviews is not capturing all relevant sources. Reviewing literature in English may have excluded important publications in Arabic. However, screening of translated abstracts should have captured most such publications. Scoping reviews do not evaluate the quality of sources and discussion of programme effectiveness should be interpreted accordingly. However, they are most appropriate for topics such as this with little published literature available.

**CONCLUSIONS**

PMSGC programmes were unsuccessful at discouraging at-risk marriages, primarily due to poor timing of premarital screening, lack of knowledge regarding inherited diseases, and sociocultural and religious concerns. Programmes that significantly reduced β-thalassemia births (e.g. Iran, Iraqi Kurdistan, Turkey) did so through accessible PND and therapeutic abortion. Lack of 100% reductions appeared due to cultural and awareness barriers. Comprehensive β-thalassemia prevention (e.g. life-cycle approaches) would likely be more effective than PMSGC alone in reducing β-thalassemia prevalence in the Middle Eastern region.

**Conflicts of interest**

None declared.

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**TABLES**

**Table 1** Countries in the Mediterranean and Middle East regions with mandatory PMSGC programmes, by implementation date

|  |  |
| --- | --- |
| **Countries - Mediterranean** | **Implementation year** |
| Cyprus | 1973 |
| Italy | 1975 |
| Greece | 1975 |
| **Countries - Middle East** |  |
| Turkey  | 1995 |
| Iran | 1997 |
| Palestinian Territories | 2000 |
| Jordan | 2004 |
| Saudi Arabia | 2004 |
| Bahrain | 2005 |
| Iraqi Kurdistan | 2008 |
| United Arab Emirates | 2011 |

Source: Adapted from [[10](#_ENREF_10), [12](#_ENREF_12)].

**Table 2** Grounds for legal abortion in Middle Eastern countries with mandatory PMSGC programmes

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **To save woman’s life** | **To preserve woman’s physical health** | **To preserve woman’s mental health** | **Rape or incest cases** | **Foetal impairment** | **Economic or social cases** | **On request** |
|
| Bahrain | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Iran | ✓ | - | - | - | ✓ | - | - |
| Iraq | ✓ | - | - | - | ✓ | - | - |
| Jordan | ✓ | ✓ | ✓ | - | - | - | - |
| Palestine  | ✓ | ✓ | ✓ | ✓ | ✓ | - | - |
| Saudi Arabia | ✓ | ✓ | ✓ | - | - | - | - |
| Turkey | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| UAE | ✓ | ✓ | ✓ | - | - | - | - |

NB: Source: [[34](#_ENREF_34)]; ‘✓’ indicates the reason listed in column heading is used as grounds for legal abortion in the countries listed in rows; ‘-’ indicates no data available.

**Table 3** Programme effectiveness

|  |
| --- |
| **Countries - Mediterranean** |
| **Country** | **Implementation year** | **Availability of additional services** | **Effectiveness** |
|  |  | PND | Abortion | At-risk marriage cancellation  | At-risk births reduction |
| Cyprus | 1973 | ✓ | ✓ | <5% | 100% |
| Italy | 1975 | ✓ | ✓ | <5% | 100% |
| Greece | 1975 | ✓ | ✓ | <5% | 100% |
| **Countries - Middle East** |
| Turkey | 1995/1998 | ✓ | ✓ | 13% | 90% |
| Iran | 1997 | ✓ | ✓ | 53% | 80% |
| Palestinian Territories | 2000 | X | X | - | - |
| Jordan | 2004 | ✓ | X | 40% | -  |
| Saudi Arabia | 2004 | X | X | 10% | -  |
| Bahrain | 2005 | ✓ | ✓ | 58% | -  |
| Iraqi Kurdistan | 2008 | ✓ | ✓ | 2% | 65% |
| United Arab Emirates | 2011 | X | X | - | - |

NB: ‘✓’ indicates service availability; ‘X’ indicates service not available/accessible; ‘-’ indicates no data.

**Table 4** Emergent themes per source, ordered by country and lead author

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Design** | **Study population** | **PND/ Abortion access** | **Culture/ Stigma** | **Religion** | **Awareness** | **Screening timing** | **Counsellor Skill** |
| Bahrain |  |  |  |  |  |  |  |  |
| Al-Arrayed (2005) | Review  | N/A |  |  |  |  |  | x |
| Almutawa & Alqamish (2009) | Cross-sectional | 1,070  |  | x | x | x |  | x |
| Iran  |  |  |  |  |  |  |  |  |
| Ahmadnazhad et al (2012) | Review/ Cost analysis  | N/A | x |  |  |  |  |  |
| Hashemzadeh-Chaleshtori (2013) | Cohort | 661 | x | x | x |  |  | x |
| Karimi et al(2007) | Case study | 5,182 couples  | x | x | x |  |  |  |
| Samavat et al (2004)  | Cohort | 10,298 couples |  | x | x | x |  |  |
| Zeinali (2013) | Review | N/A | x |  | x | x |  |  |
| Iraq (Kurdistan) |  |  |  |  |  |  |  |  |
| Al-Allawi et al (2013) | Cross-sectional | 130 couples  |  |  |  | x | x |  |
| Hamamy & Al-Allawi (2013) | Review  | N/A | x | x | x | x | x |  |
| Jordan  |  |  |  |  |  |  |  |  |
| Oseroff (2011) | Review  | N/A | x |  | x |  | x |  |
| Saudi Arabia |  |  |  |  |  |  |  |  |
| Al-Enzy et al (2012) | Case-control | 934 |  | x | x | x | x |  |
| Al-Hamdan et al (2007) | Cross-sectional  | 2,375 |  | x |  |  | x |  |
| Al-Sulaiman Et al (2010)  | Cohort | 129 |  | x |  |  |  |  |
| El-Hazmi (2004) | Review | N/A | x |  |  | x | x |  |
| Memish et al (2011) | Review  | 5,370 |  | x | x | x | x |  |
| Turkey  |  |  |  |  |  |  |  |  |
| Canatan (2013) | Review | N/A | x |  |  |  |  |  |
| Keskin et al(2000) | Case-control | 15 couples  | x |  |  |  |  |  |
| Tosun et al (2006)-Mersin | Cohort | 134 couples | x | x | x |  |  |  |
| UAE |  |  |  |  |  |  |  |  |
| Belhoul et al (2013) | Review  |  | x |  |  | x |  |  |
| Global  |  |  |  |  |  |  |  |  |
| Cousens et al (2010) | Review | N/A | x |  |  |  |  |  |
| Alswaidi & O'Brien (2009) | Review  | N/A | x | x | x | x | x | x |
| **Total N=21** |  |  | **N=13** | **N=11** | **N=11** | **N=10** | **N=7** | **N=4** |

NB: ‘x’ indicates data on this theme is included in the source.

**FIGURES**

**Figure 1** Flow diagram of selection of records included in scoping review

