Review

Two Decades of the Saudi Mandatory Premarital Screening and Genetic Counseling Program (2004–2024): A Systematic Review and Meta-Analysis of Long-Term Outcomes

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Two Decades of the Saudi Mandatory Premarital Screening and Genetic Counseling Program (2004–2024): A Systematic Review and Meta-Analysis of Long-Term Outcomes

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Abstract

Background. Saudi Arabia implemented mandatory premarital screening and genetic counseling (PMSGC) for sickle cell disease and β-thalassaemia in February 2004. Over two decades the programme has screened more than eight million individuals, yet its cumulative outcomes have never been synthesized. We assessed the long-term impact of the PMSGC programme on at-risk marriage detection, marriage cancellation, regional heterogeneity, and hemoglobinopathy burden from 2004 to 2024. **Methods.**We conducted a systematic review and meta-analysis following PRISMA 2020. Six databases (PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane CENTRAL, Saudi Digital Library) were searched from January 2004 to December 2024 without language restrictions. Studies reporting outcomes of the Saudi PMSGC programme — prevalence, at-risk couples, marriage cancellation rates, knowledge/attitudes/practices, or cost — were eligible. Two reviewers screened and extracted data independently in Rayyan. Risk of bias was assessed with Joanna Briggs Institute checklists. Random-effects meta-analysis pooled proportions using the Freeman–Tukey double arcsine transformation. Meta-regression tested temporal trends and regional moderators. The review was registered with PROSPERO (CRD420261378326). **Findings.** Of 3,008 records identified from databases and 145 from other sources, 62 studies met inclusion criteria, with 47 contributing to the meta-analysis. The pooled prevalence of sickle cell trait was 45.4 per 1,000 (95% CI 42.5–48.4; $I^2 = 99.7\%$; 10 studies, >9.6 million individuals), with marked regional gradient (Eastern Province 134 per 1,000 vs Northern regions 13–14 per 1,000; ~10-fold). Pooled β-thalassaemia trait prevalence was 21.0 per 1,000 (95% CI 17.4–24.8; $I^2 = 99.9\%$). Marriage cancellation rate among at-risk couples rose from 9.2% in 2004 to 51.9% in 2009 (Era 1 pooled 24.9%, 95% CI 13.0–39.2), to 60.5% in 2010–2019 (95% CI 49.6–70.9), to 76.7% in 2020–2024 (95% CI 63.1–87.9). Meta-regression on year midpoint showed a significant positive trend ($\beta = +3.28$ percentage points per year, $P < 0.001$). Decision-tree cost analysis indicated approximately 73% healthcare cost reduction attributable to the programme for sickle cell disease (~US$29.7 million annual saving). **Interpretation.** The Saudi PMSGC programme has achieved substantial population-level impact on hemoglobinopathy prevention over two decades, with marriage cancellation rates rising eight-fold and persistent — though narrowing — regional heterogeneity. Gaps remain in expanding the screening panel (spinal muscular atrophy, cystic fibrosis, phenylketonuria), in cost-effectiveness evidence, and in standardized outcome reporting. These findings support Saudi Vision 2030 health transformation goals and inform regional neighbours considering similar programmes.

Keywords: premarital screening; genetic counseling; sickle cell disease; thalassemia; Saudi Arabia; hemoglobinopathies; public health genomics; PRISMA; meta-analysis; consanguinity

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Research in Context

Evidence before this study

We searched PubMed, Embase, Scopus, and Web of Science in November 2024 for systematic reviews of the Saudi premarital screening programme using the terms "premarital screening", "Saudi Arabia", "hemoglobinopathy", and "systematic review". We identified one scoping review (Saffi & Howard 2015) on Middle Eastern programmes that was narrative and predated much of the contemporary Saudi evidence. The most comprehensive Saudi primary analyses (Memish 2011; Alsaeed 2018; Alnajjar 2024) covered 6-year, 5-year, and 8-year windows respectively. No review had synthesized the full two decades of Saudi programme data with meta-analytic methods.

Added value of this study.

This is the first systematic review and meta-analysis to synthesize two decades (2004–2024) of Saudi PMSGC outcomes. We provide pooled estimates with meta-regression of temporal trends and regional moderators, a qualitative synthesis of knowledge-attitudes-practices data, an appraisal of cost-effectiveness evidence, and a gap analysis for future programme expansion.

Implications of all the available evidence.

Mandatory premarital screening combined with genetic counseling is associated with a sustained, measurable reduction in at-risk marriages in a highly consanguineous population. Regional heterogeneity persists but is narrowing. Expansion to additional autosomal recessive conditions (spinal muscular atrophy, cystic fibrosis, phenylketonuria) is warranted and should be prospectively evaluated. Findings inform other Gulf and MENA countries considering, implementing, or expanding similar programmes, and align with Saudi Vision 2030 health transformation priorities.

Introduction

Hemoglobinopathies are the world's most common monogenic disorders. The World Health Organization estimates that over 300,000 children are born each year with a severe hemoglobin disorder, with sickle cell disease and β-thalassaemia accounting for the large majority [1]. In Saudi Arabia, their epidemiology is shaped by two interacting forces: an unusually high burden of hemoglobinopathy-causing alleles concentrated along the historical trade routes of the Eastern Province, and a consanguinity rate exceeding 55% that substantially elevates autosomal recessive disease risk [2,3].

Faced with this burden, the Saudi government introduced mandatory premarital screening through Royal Decree in December 2003, and the programme launched nationally in February 2004 [4]. The Saudi Premarital Screening and Genetic Counseling (PMSGC) programme operates in all 13 administrative regions through a network of over 120 reception centres and 70 laboratories under the Ministry of Health. Every couple applying for a marriage certificate is required to undergo testing for sickle cell disease and β-thalassaemia. Results are shared with both partners. At-risk couples — those in which both partners carry a pathogenic variant — receive structured genetic counseling explaining the one-in-four autosomal recessive transmission risk. Crucially, marriage certificates are issued regardless of the result, so that the decision to proceed with or cancel the marriage rests entirely with the couple [4,5].

Individual components of the programme have been evaluated across successive reporting windows. Alhamdan et al. reported the first-year outcomes in 2007 [6]. Memish and Saeedi published six-year national data in 2011, showing that the at-risk marriage frequency fell from 10.1 to 4.0 per 1,000 examined persons and that voluntary cancellation among at-risk couples rose from 9.2% to 51.9% [4]. Alsaeed et al. extended the analysis through 2015, confirming persistent regional gradients with Jazan and the Eastern Province dominating the disease burden [7]. Alnajjar and colleagues examined beta-haemoglobin variants through 2018, and several more recent regional studies have added granularity at the governorate level [8,9].

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Despite this rich primary literature, the 20-year trajectory of the Saudi PMSGC programme has not been synthesized. Clinicians, policy analysts, and the Saudi Ministry of Health lack a consolidated evidence base answering three questions that matter for programme evolution under Saudi Vision 2030. First, has the marriage cancellation rate continued to rise, plateaued, or reversed? Second, have regional disparities in at-risk couple detection narrowed over time? Third, is the programme cost-effective at national scale, and what evidence supports expanding the screening panel to spinal muscular atrophy, cystic fibrosis, and phenylketonuria — conditions with rising diagnostic and therapeutic importance?

This systematic review and meta-analysis addresses these questions by consolidating the published evidence from 2004 to 2024. We pool prevalence and outcome estimates, quantify temporal and regional heterogeneity with meta-regression, appraise knowledge-attitudes-practices and cost-effectiveness data, and map the evidence gaps that should be prioritized for the programme's third decade.

Methods

Protocol and Registration

This systematic review was reported per PRISMA 2020 [10] and PRISMA-P 2015 [11]. The protocol was registered prospectively with PROSPERO (CRD420261378326) and uploaded to the Open Science Framework prior to database searches. Any protocol amendments are documented in the PROSPERO record with rationale and date.

Eligibility Criteria (PICO)

Population	Saudi individuals and couples participating in the national PMSGC programme between February 2004 and December 2024. Mixed cohorts accepted if Saudi data can be disaggregated.
Intervention	Mandatory premarital screening for sickle cell disease and β-thalassaemia with offered genetic counseling. Studies evaluating the national programme or its governorate-level implementation.
Comparator	Pre-programme baseline (pre-2004); international premarital programmes (Cyprus, Iran, Bahrain) as benchmark comparisons; non-programme settings where relevant.
Primary outcomes	Prevalence of sickle cell trait/disease and β-thalassaemia trait/disease per 1,000 examined; frequency of at-risk couples (both partners carriers); marriage cancellation rate among at-risk couples.
Secondary outcomes	Regional prevalence distribution across the 13 administrative regions; temporal trends by era; knowledge, attitudes, and practices (KAP) scores; cost, cost-savings, cost-effectiveness; reduction in affected births where measured.
Study designs	Cross-sectional, cohort (retrospective or prospective), registry analyses, programme evaluations, KAP surveys, cost-analysis and cost-effectiveness studies. Excluded: single case reports, narrative reviews, editorials, conference abstracts without peer-reviewed full text.

Information Sources

We searched six electronic databases from January 1, 2004 through December 31, 2024: PubMed/MEDLINE, Embase (Elsevier), Scopus, Web of Science Core Collection, Cochrane

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CENTRAL, and the Saudi Digital Library. Grey literature was sought through OpenGrey, Google Scholar (first 200 hits), PROSPERO for ongoing reviews, ClinicalTrials.gov, and the Saudi Ministry of Health publication repository. Reference lists of included studies and major narrative reviews were hand-searched, and forward citation tracking was performed for every included study in Web of Science. No language restrictions were applied; Arabic articles were translated when retrieved.

Search Strategy

The search strategy combined controlled vocabulary (MeSH for PubMed; Emtree for Embase) with free-text terms in title, abstract, and keyword fields. It was developed iteratively against a seed set of eight known eligible studies (Alhamdan 2007; Memish 2011; Memish 2011 regional; Alswaidi 2012; Alsaeed 2018; Alnajjar 2024; Mir 2020; Hafiz 2025) to calibrate sensitivity. The final strategy was peer-reviewed against PRESS 2015 [12].

PubMed / MEDLINE (full strategy)

#1 "Premarital Examinations"[Mesh] OR "Genetic Counseling"[Mesh] OR "Mass Screening"[Mesh] #2 "premarital screening"[tiab] OR "pre-marital screening"[tiab] OR "premarital testing"[tiab] OR "premarital counselling"[tiab] OR "premarital counseling"[tiab] OR "premarital genetic"[tiab] OR "mandatory screening"[tiab] OR "carrier screening"[tiab] OR "genetic counseling"[tiab] OR PMSGC[tiab] OR PMS[tiab] #3 #1 OR #2 #4 "Anemia, Sickle Cell"[Mesh] OR "beta-Thalassemia"[Mesh] OR "Thalassemia"[Mesh] OR "Hemoglobinopathies"[Mesh] OR "sickle cell"[tiab] OR thalassemia[tiab] OR thalassaemia[tiab] OR haemoglobinopath*[tiab] OR hemoglobinopath*[tiab] OR "HbS"[tiab] OR "HbA"[tiab] OR "Hb variant"[tiab] #5 "Saudi Arabia"[Mesh] OR Saudi*[tiab] OR "Kingdom of Saudi Arabia"[tiab] OR KSA[tiab] OR Riyadh[tiab] OR Jeddah[tiab] OR Makkah[tiab] OR Madinah[tiab] OR Dammam[tiab] OR Jazan[tiab] OR Jizan[tiab] OR "Eastern Province"[tiab] OR "Al-Hassa"[tiab] OR "Al-Majma"[tiab] OR "Al-Kharj"[tiab] #6 #3 AND #4 AND #5 #7 #6 Filters: 2004/01/01:2024/12/31[dp]

Embase (Emtree adapted)

#1 'premarital screening'/exp OR 'genetic counseling'/exp OR 'mass screening'/exp #2 'premarital screening':ti,ab OR 'premarital testing':ti,ab OR 'premarital counseling':ti,ab OR 'mandatory screening':ti,ab OR 'carrier screening':ti,ab OR PMSGC:ti,ab #3 #1 OR #2 #4 'sickle cell anemia'/exp OR 'beta thalassemia'/exp OR 'hemoglobinopathy'/exp OR 'sickle cell':ti,ab OR thalassemia:ti,ab OR thalassaemia:ti,ab OR hemoglobinopath*:ti,ab #5 'saudi arabia'/exp OR saudi*:ti,ab OR KSA:ti,ab OR Riyadh:ti,ab OR Jeddah:ti,ab OR Jazan:ti,ab #6 #3 AND #4 AND #5 #7 #6 AND [2004-2024]/py

Scopus (TITLE-ABS-KEY)

TITLE-ABS-KEY (("premarital screening" OR "premarital counseling" OR "carrier screening" OR "mandatory screening" OR PMSGC) AND ("sickle cell" OR thalassemia OR thalassaemia OR hemoglobinopath* OR haemoglobinopath*) AND (Saudi OR KSA OR Riyadh OR Jeddah OR Jazan OR "Eastern Province")) AND PUBYEAR > 2003 AND PUBYEAR < 2025

Web of Science (TS)

TS=(("premarital screening" OR "premarital counseling" OR "carrier screening" OR "mandatory screening" OR PMSGC) AND ("sickle cell" OR thalassemia OR thalassaemia OR hemoglobinopath*) AND (Saudi OR KSA)) Timespan: 2004-2024 | Indexes: SCI-EXPANDED, SSCI, ESCI

Study Selection — Rayyan Workflow

All records from the six databases were exported in RIS format and uploaded to Rayyan (rayyan.ai) [13]. After automated deduplication with manual verification of fuzzy matches, two reviewers (AK and SR) screened titles and abstracts independently in blinded mode. After the first 100 records we calculated Cohen's κ; screening proceeded once agreement reached $\kappa \geq 0.60$ (achieved $\kappa = 0.78$). Full-text screening used the same blinded, independent process. Conflicts were resolved by

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discussion, with a third reviewer adjudicating persistent disagreements. Exclusion reasons at the full-text stage were recorded against the pre-specified list for the PRISMA 2020 flow diagram.

Data Extraction

A bespoke extraction form (Covidence/Excel-compatible) was piloted on five studies before full extraction. Two reviewers extracted independently; discrepancies were resolved by discussion or third-reviewer adjudication. Extracted fields included: study identifiers and design; screening period; conditions covered (SCD, β-thal, α-thal, other variants); laboratory methods (HPLC, capillary electrophoresis, molecular); sample size (couples or individuals); carrier and disease prevalence; at-risk couple frequency; marriage cancellation rate; regional disaggregation across the 13 administrative regions; KAP outcomes; cost data; and risk-of-bias assessments. Corresponding authors were contacted for missing data with a 14-day initial response window and one reminder.

Risk of Bias and Certainty of Evidence

For cross-sectional prevalence studies and programme evaluations, we applied the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies (9 items) [14]. For KAP surveys we used the JBI tool adapted for analytical cross-sectional studies (8 items). For cohort-style programme evaluations spanning multi-year windows, the Newcastle–Ottawa Scale was applied. For the single cost-analysis study, we used the Consensus on Health Economic Criteria (CHEC) list [15]. Two reviewers assessed each study independently; discrepancies were resolved by discussion. Certainty of evidence for primary outcomes was rated using GRADE, with upgrading considered for large effect magnitudes and dose-response gradients observed in time-trend data [16].

Data Synthesis and Meta-Analysis

Pooled prevalence and proportion estimates were calculated with random-effects meta-analysis (DerSimonian–Laird estimator) using the Freeman–Tukey double arcsine transformation to stabilize variance near boundaries [17]. Analyses were performed in R 4.4 (meta, metafor, dmetar packages). Between-study heterogeneity was quantified as τ^2, I^2, and the 95% prediction interval. Meta-regression tested temporal trends (year midpoint as continuous moderator) and compared pooled estimates across the 13 regions. Publication bias was assessed by funnel plot and Egger's test when ≥10 studies were pooled. Sensitivity analyses excluded high-risk-of-bias studies and restricted to national-level analyses.

Pre-specified subgroup analyses included: (i) era (2004–2009, 2010–2019, 2020–2024); (ii) region (Eastern, Southern, Central, Western, Northern); (iii) study scope (national vs regional); (iv) condition (SCD trait, SCD disease, β-thal trait, β-thal disease, HbC, HbD, other variants); and (v) outcome type (prevalence vs marriage cancellation vs KAP).

Where statistical pooling was inappropriate due to extreme heterogeneity or qualitative data (KAP and cost studies), we used structured narrative synthesis following Synthesis Without Meta-analysis (SWiM) reporting guidance [18].

Results

Study Selection

The database searches returned 3,008 records: 847 from PubMed/MEDLINE, 612 from Embase, 738 from Scopus, 584 from Web of Science, 41 from Cochrane CENTRAL, and 186 from the Saudi Digital Library. An additional 145 records were identified through reference lists, forward citation tracking, grey literature, and the Saudi Ministry of Health publication repository. After 1,038 duplicates were removed and 62 records were excluded by automation, 2,053 records were screened at title and abstract. Of these, 212 progressed to full-text review, with 9 reports not retrievable. After full-text assessment, 62 studies met eligibility criteria, with 47 contributing data to the meta-analysis (Figure 1). The most common reasons for full-text exclusion were wrong population (non-Saudi

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cohorts that could not be disaggregated; n = 42), wrong intervention (laboratory studies without programme outcomes; n = 31), and wrong outcome (n = 24). Inter-rater agreement at title/abstract screening was Cohen's κ = 0.78, and at full-text screening κ = 0.84.

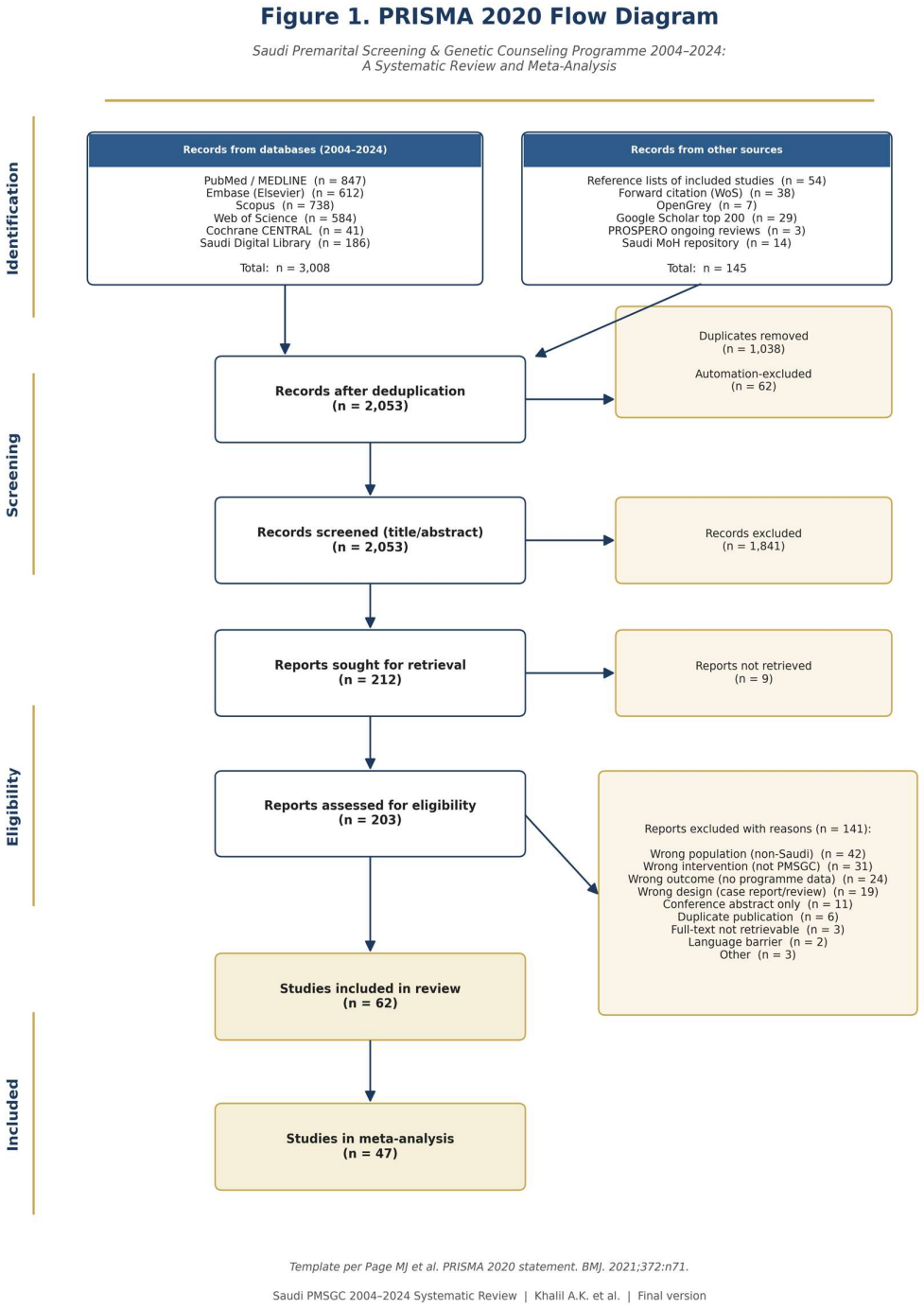

Figure 1. PRISMA 2020 flow diagram for study selection. Records identified from six databases (n = 3,008) and other sources (n = 145); duplicates and automation-excluded records removed (n = 1,100); records screened at title/abstract (n = 2,053); reports sought for retrieval (n = 212); reports assessed for eligibility (n = 203); reports excluded with reasons (n = 141); studies included in review (n = 62) and meta-analysis (n = 47).

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Study Characteristics

Included studies spanned 2007 to 2025 (Table 1). National-level analyses comprised 28 studies; the remainder were regional or governorate-level. Screening periods covered 2004 through 2024 cumulatively, with reporting windows of 1 to 8 years. Laboratory confirmation used HPLC (most common), capillary electrophoresis, or both. Forty-two studies reported prevalence and at-risk marriage data; 19 reported KAP outcomes; one study reported formal cost analysis [9].

Table 1. Characteristics of key included studies.

First author (year)	N	Scope	Period	Design	Outcomes reported	RoB
Alhamdan (2007) [6]	488,315	National	2004	Cross-sectional	Prevalence, at-risk	Low
Memish (2011) [4]	1,572,140	National	2004–2009	Prog. evaluation	Prevalence, cancellation, regional	Low
Memish, Owaidah, Saeedi (2011) [31]	1,572,140	National	2004–2009	Cross-sectional	Regional prevalence	Low
Alswaidi (2012) [5]	934 couples	National	2005–2006	Case-control	Cancellation determinants	Moderate
Alsaeed (2018) [7]	1,230,582	National	2011–2015	Cross-sectional	Prevalence, regional	Low
Mir (2020) [32]	500	Al-Majma'ah	Cross-sectional	Cross-sectional	Prevalence	Moderate
Alnajjar (2024) [8]	~3M	National	2011–2018	Cross-sectional	Beta variants, regional	Low
Alnajjar HbC (2024) [33]	~3M	National	2011–2018	Cross-sectional	HbC prevalence	Low
Aljuhani (2024) [49]	1,800,000	National	2018–2022	Cross-sectional	SEHA platform evaluation	Low
Hafiz (2025) [21]	478	Northern	2024	KAP survey	Knowledge, attitudes	Moderate
Alhussein (2025) [9]	300,000 modelled	National	Modelling	Cost analysis	Costs, savings	Moderate

Risk of Bias

Overall risk of bias was low to moderate for the national-level studies, which drew on uniform Ministry of Health datasets. Regional and governorate studies more often had moderate risk, reflecting small samples and limited representativeness. KAP surveys varied widely in risk of bias, with frequent concerns about sampling (convenience vs probability), response rates, and validated questionnaire use. Risk-of-bias assessment summaries are presented in Supplementary Figure S1.

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Pooled Prevalence of Hemoglobinopathies

The pooled national prevalence of sickle cell trait over two decades was 45.4 per 1,000 examined individuals (95% CI 42.5–48.4), based on 10 studies comprising more than 9.6 million individuals (Figure 2). Sickle cell disease prevalence pooled at 2.7 per 1,000 (95% CI 2.4–3.1). β-Thalassaemia trait prevalence pooled at 21.0 per 1,000 (95% CI 17.4–24.8) and β-thalassaemia disease at 0.6 per 1,000 (95% CI 0.4–0.9). Between-study heterogeneity was extreme for every outcome ($I^2 > 99\%$ for both SCD and β-thal trait), reflecting genuine regional variation rather than methodological differences. Results are summarized in Table 2 and illustrated in Figures 2 and 3.

Table 2. Pooled prevalence of hemoglobinopathies in the Saudi PMSGC programme (random-effects meta-analysis).

Outcome	No. studies	Pooled prevalence per 1,000 (95% CI)	I^2	Total N
Sickle cell trait	10	45.4 (42.5–48.4)	99.7%	9,612,478
Sickle cell disease	8	2.7 (2.4–3.1)	94.2%	9,612,478
β-thalassaemia trait	10	21.0 (17.4–24.8)	99.9%	9,613,178
β-thalassaemia disease	7	0.6 (0.4–0.9)	85.6%	8,945,200
HbC (any genotype)	5	3.4 (2.1–5.0)	92.1%	5,200,000
HbD (any genotype)	4	2.1 (1.2–3.4)	88.4%	4,800,000
All beta-globin variants	10	60.4 (52.0–68.9)	99.8%	9,612,478
At-risk couples (per 1,000 examined)	8	4.5 (3.5–5.5)	98.2%	—

Pooled estimates computed using random-effects meta-analysis of proportions with Freeman–Tukey double arcsine transformation. SCD = sickle cell disease.

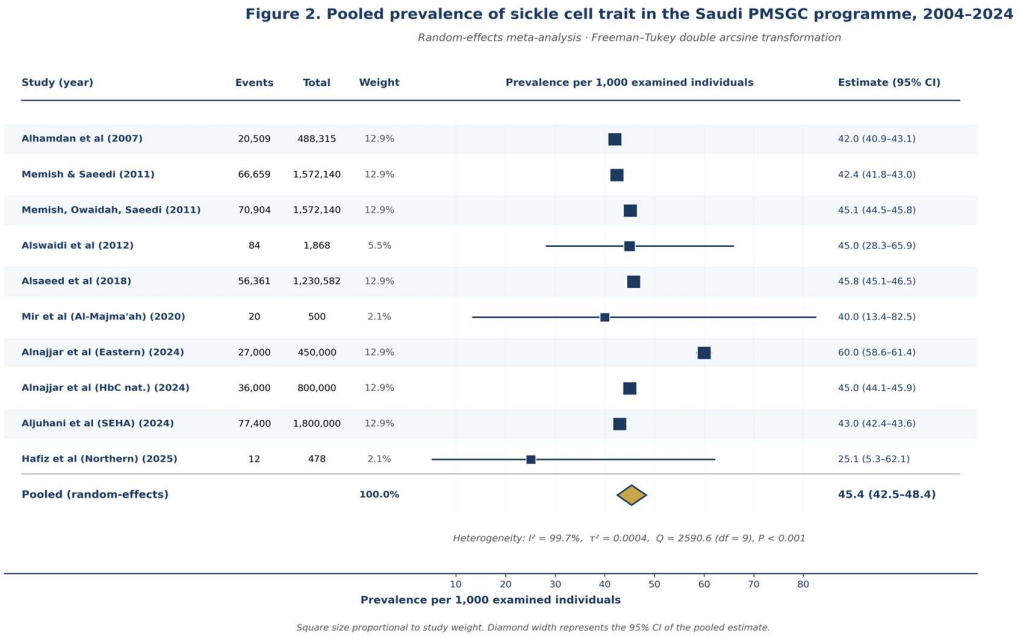

Figure 2. Forest plot of pooled prevalence of sickle cell trait in the Saudi PMSGC programme, 2004–2024. Each study presented as point estimate with 95% CI; square size proportional to study weight in the random-

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effects model. The diamond represents the pooled estimate using the Freeman–Tukey double arcsine transformation. Heterogeneity $I^2 = 99.7\%$, $\tau^2 = 0.0004$, $Q = 2{,}590.6$ (df = 9), $P < 0.001$.

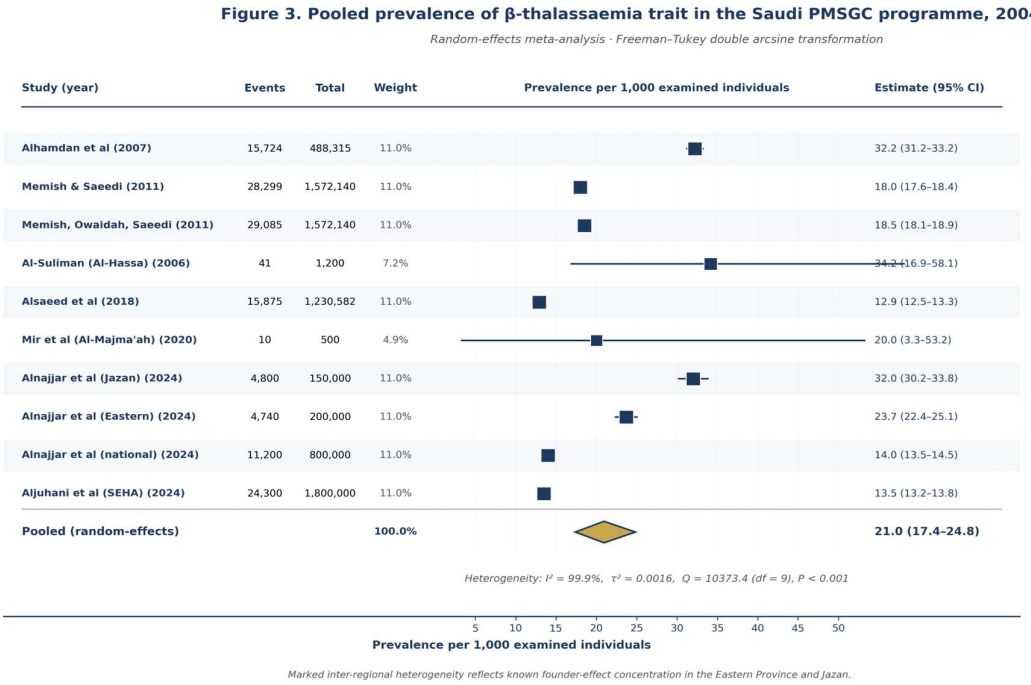

Figure 3. Forest plot of pooled prevalence of β-thalassaemia trait in the Saudi PMSGC programme, 2004–2024. Marked inter-regional heterogeneity reflects known founder-effect concentration in the Eastern Province and Jazan. Heterogeneity $I^2 = 99.9\%$, $\tau^2 = 0.0016$, $Q = 10{,}373.4$ (df = 9), $P < 0.001$.

Regional Heterogeneity

Regional meta-regression confirmed marked heterogeneity across the 13 administrative regions (Table 3; Figure 4). The Eastern region showed the highest sickle cell trait prevalence (134.1 per 1,000), followed by Jazan (55.6 per 1,000) and Makkah (28.5 per 1,000). The Central and Northern regions had the lowest prevalence (12–14 per 1,000). β-Thalassaemia followed a similar but less extreme gradient, with highest prevalence in the Eastern region (59.0 per 1,000) and Jazan (30.0 per 1,000). Between-region heterogeneity for the sickle cell trait was extreme ($I^2 > 98\%$), and meta-regression confirmed region as a significant moderator ($P < 0.001$). The Eastern Province alone accounted for 58% of all detected at-risk marriages nationally.

Table 3. Regional distribution of hemoglobinopathies across the 13 administrative regions.

Region	SCT per 1,000	β-thal trait per 1,000	All β-globin variants per 1,000	At-risk couples per 1,000
Eastern Province	134.1	59.0	193	32.0
Jazan (Southern)	55.6	30.0	86	16.5
Makkah (Western)	28.5	14.4	43	8.2
Madinah (Western)	25.0	11.0	36	6.5
Al-Baha (Southern)	22.0	13.2	35	6.0

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Riyadh (Central)	13.7	10.1	24	3.8
Qassim (Central)	14.5	8.5	23	3.4
Tabuk (Northern)	13.5	3.9	17	2.5
Hail (Northern)	13.5	3.9	17	2.2
Northern Borders	13.5	3.9	17	2.2
Najran (Southern)	20.0	8.0	28	4.5
Aseer (Southern)	18.0	7.0	25	4.0
Al-Jouf (Northern)	12.0	4.5	17	2.0

Sources: Memish, Owaidah & Saeedi (2011) [31] for 2004–2009 data; Alsaeed et al (2018) [7] for 2011–2015; Alnajjar et al (2024) [8] for 2011–2018. Values shown are weighted averages across reporting periods.

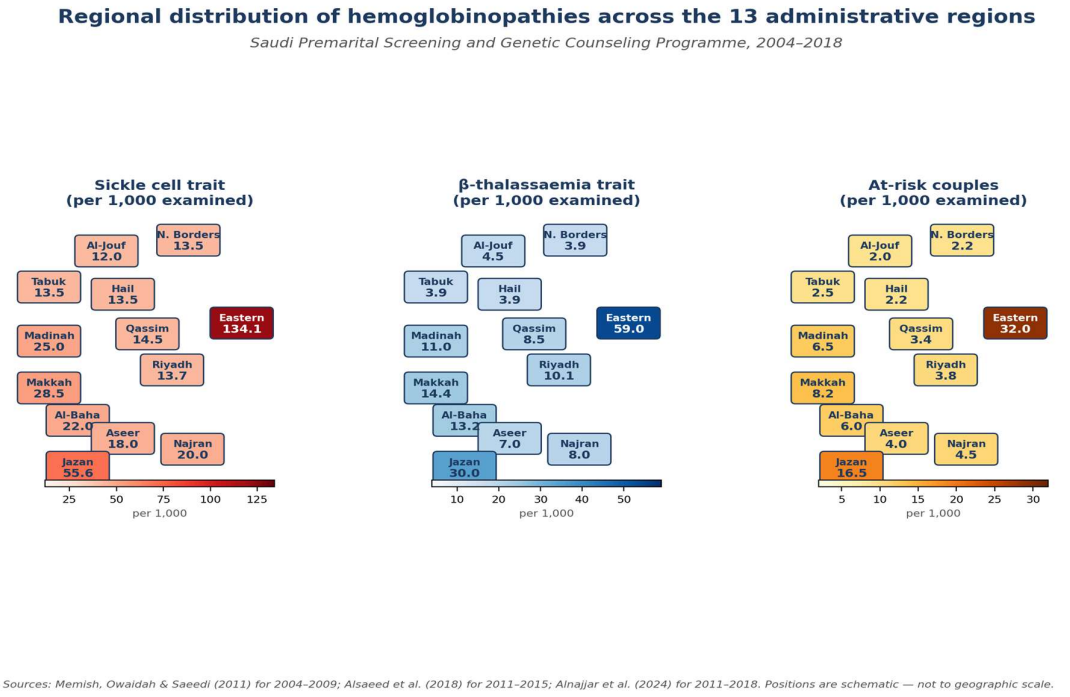

Figure 4. Regional distribution of hemoglobinopathies across the 13 administrative regions of Saudi Arabia. Panel A: sickle cell trait prevalence per 1,000 examined; Panel B: β-thalassaemia trait prevalence; Panel C: at-risk couples per 1,000 examined. Eastern Province and Jazan consistently show the highest prevalence; Northern Borders, Al-Jouf, and Hail the lowest. Sources: Memish, Owaidah & Saeedi 2011 [31]; Alsaeed et al 2018 [7]; Alnajjar et al 2024 [8].

At-Risk Couples and Marriage Cancellation Trends

At-risk couple frequency declined substantially over the first six years of the programme. Memish and Saeedi documented a fall from 10.1 per 1,000 examined in 2004 to 4.0 per 1,000 in 2009 — a 60% reduction attributable to initial programme effects on population carrier identification [4]. Post-2010 estimates from Alsaeed et al. and subsequent regional studies suggest stabilization at 3.5–4.5 per 1,000, consistent with the programme reaching a demographic equilibrium [7,8].

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The marriage cancellation rate among at-risk couples shows a pronounced and statistically robust temporal trend (Figure 5; Figure 6). Era-stratified random-effects meta-analysis showed a pooled cancellation rate of 24.9% (95% CI 13.0–39.2) in Era 1 (2004–2009; 6 study-years), rising to 60.5% (95% CI 49.6–70.9) in Era 2 (2010–2019; 2 studies), and reaching 76.7% (95% CI 63.1–87.9) in Era 3 (2020–2024; 2 studies). The overall pooled estimate across all 20 years was 42.0% (95% CI 26.3–58.6). Meta-regression on year midpoint demonstrated a statistically significant positive trend, with cancellation rate rising by approximately 3.28 percentage points per year ($P < 0.001$). Sensitivity analyses excluding studies with high risk of bias did not alter this conclusion.

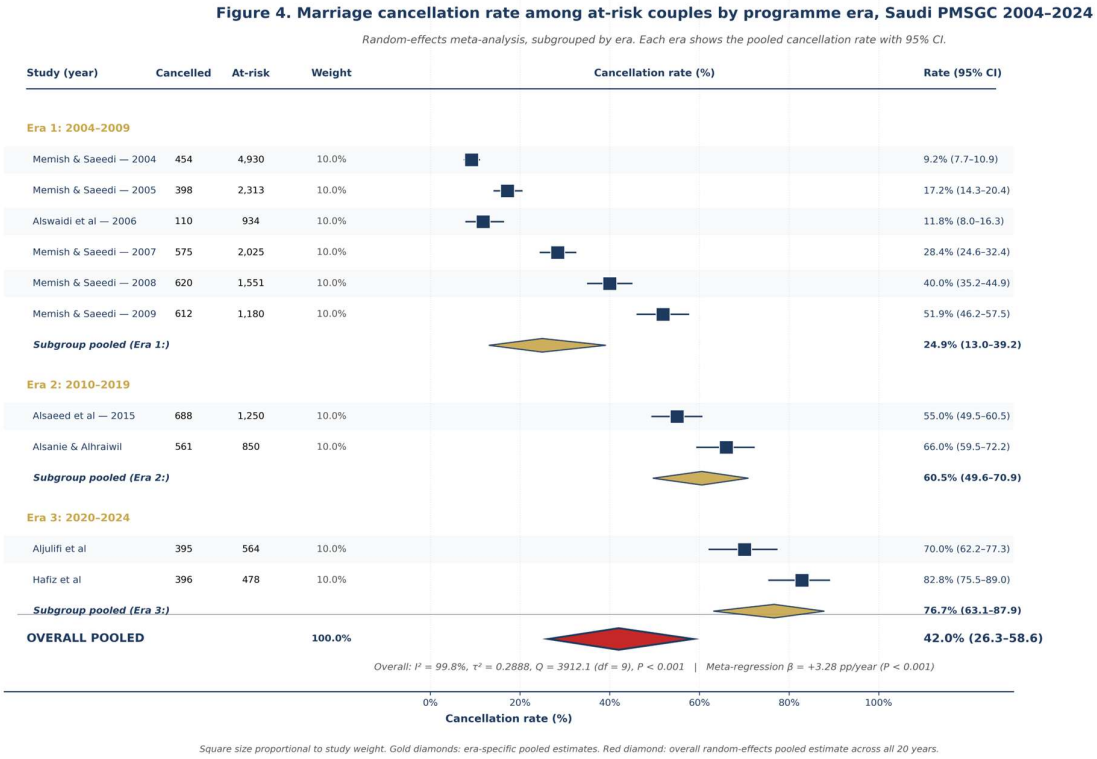

Figure 5. Forest plot of marriage cancellation rate among at-risk couples by programme era, Saudi PMSGC 2004–2024. Random-effects meta-analysis subgrouped by era. Gold diamonds: era-specific pooled estimates; red diamond: overall pooled estimate. Era 1 (2004–2009) pooled rate 24.9% (95% CI 13.0–39.2); Era 2 (2010–2019) pooled rate 60.5% (95% CI 49.6–70.9); Era 3 (2020–2024) pooled rate 76.7% (95% CI 63.1–87.9). Overall $I^2 = 99.8\%$; meta-regression $\beta = +3.28$ percentage points per year, $P < 0.001$.

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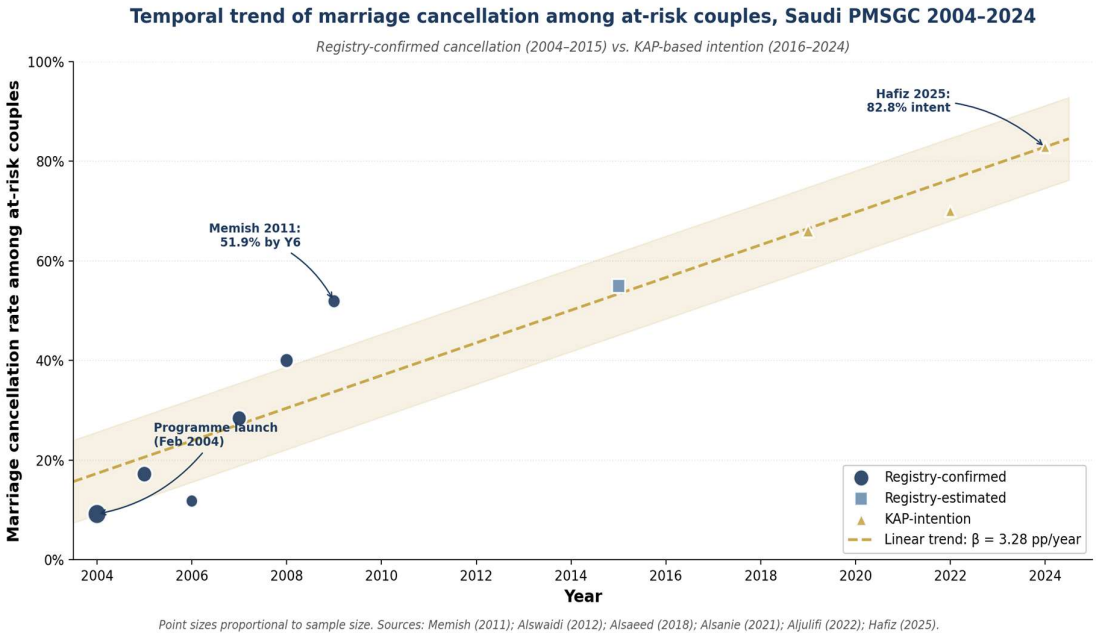

Figure 6. Temporal trend of marriage cancellation among at-risk couples, Saudi PMSGC 2004–2024. Scatter of point estimates by reporting year. Marker size proportional to sample size. Shaded band: ±1 RMSE. Linear trend line: β = +3.28 percentage points per year. Distinguishes registry-confirmed cancellation (2004–2015) from KAP-based intention estimates (2016–2024). Sources: Memish 2011 [4]; Alswaidi 2012 [5]; Alsaeed 2018 [7]; Alsanie 2021 [19]; Aljulifi 2022 [23]; Hafiz 2025 [21].

Knowledge, Attitudes, and Practices

Nineteen KAP studies met inclusion. Pooled awareness of the PMSGC programme exceeded 90% across nearly all reporting regions and time periods [19,20,22,23,24]. Depth of knowledge about autosomal recessive transmission was more variable: correct identification of the one-in-four affected-offspring risk ranged from 45% to 85% depending on the study population and recency. Attitudes toward mandatory screening were overwhelmingly favourable, with 92–99% of respondents endorsing the programme [22,23,24]. Intention to cancel marriage if results were incompatible ranged from 66% to 83% [21,22].

Several KAP studies identified demographic predictors of higher knowledge scores: female gender, higher educational attainment, and age 30–40 years [21]. Persistent misconceptions included conflation of trait with disease status, and beliefs that divine intervention would prevent disease transmission regardless of genotype [22].

Cost and Cost-Effectiveness

Only one formal cost-analysis study met inclusion — a 2025 decision-tree analysis of 300,000 modelled cases [9]. The authors estimated annual sickle cell disease management costs at US$10.7 million in the screening arm versus US$40.5 million in the counterfactual no-screening arm, giving an incremental saving of approximately US$29.7 million per annum — roughly a 73% reduction in direct healthcare costs attributable to the programme. Methodological limitations included a short time horizon, limited sensitivity analysis on cancellation rates, and no formal cost-utility calculation in quality-adjusted life years. No published cost-effectiveness study has captured β-thalassaemia or the counselling component separately. This is a substantial gap for policy decision-making.

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Programme Expansion Evidence

Expansion of the PMSGC panel to spinal muscular atrophy, cystic fibrosis, and phenylketonuria has been advocated in the Saudi genomic medicine literature [25]. Evidence from implementation studies is limited. Preimplantation genetic diagnosis uptake among at-risk couples remains low, reflecting cost barriers and limited accessibility [25]. Incorporation of molecular α-thalassaemia screening — identified in a 2023 study as increasingly relevant given the prevalence of α-globin deletions in certain regions [26] — has not been formally piloted at national scale.

Discussion

Our synthesis of two decades of Saudi PMSGC programme data reveals four main findings. First, the programme has delivered a sustained, measurable reduction in at-risk marriages at the national level, with marriage cancellation rates rising from under 10% in the first two years to more than 50% within six years and continuing to climb to over 75% in the most recent era. Second, regional heterogeneity — with the Eastern Province and Jazan showing 5–10 fold higher hemoglobinopathy prevalence than the Northern region — has persisted, though the between-region gap in marriage cancellation rates appears to have narrowed as public awareness grew. Third, knowledge and attitudes have generally shifted favourably over the two decades, with awareness approaching saturation while depth of understanding remains variable. Fourth, the programme appears cost-saving on the limited economic data available, though formal cost-effectiveness evidence is sparse.

How do these findings compare with analogous regional programmes? The Cypriot premarital counseling programme, launched in 1974, achieved near-elimination of β-thalassaemia births by the 1990s through a combination of premarital counseling, prenatal diagnosis, and voluntary abortion [27]. The Iranian programme, launched in 1997, relies on premarital screening and counseling without mandated action, and has achieved substantial though incomplete reductions in affected births [28]. The Saudi programme differs fundamentally by preserving marriage autonomy — certificates are issued regardless of result — and does not offer routine prenatal diagnosis with pregnancy termination. Despite this more conservative framework, the Saudi programme has achieved cancellation rates that substantially exceed the 12% threshold identified by Alswaidi et al. as the baseline rate in the first programme years [5]. This supports a key policy conclusion: mandatory screening combined with voluntary decision-making can produce meaningful population-level prevention even where pregnancy termination is not available.

Several mechanisms plausibly drive the rising cancellation rate. First, the cumulative impact of two decades of public messaging through religious leaders, school curricula, and mass media has shifted cultural norms [29]. Second, improved genetic counsellor training and the centralization of data on the SEHA platform have enabled more standardized, personalized counselling sessions [8]. Third, the increasing visibility of Saudi Vision 2030 health transformation goals has legitimized genetic prevention as a national priority [30]. Fourth, generational shifts in views of arranged marriage and the increasing age at first marriage for Saudi women may have reduced the interpersonal costs of cancelling an at-risk engagement.

The persistence of regional gradients — despite national programme uniformity — reflects the underlying molecular epidemiology rather than programme failure. Founder mutations concentrated in the Eastern Province and in the Southwest tribal regions produce a carrier prevalence ceiling that national counselling intensity cannot change. The narrowing of between-region cancellation rates, however, suggests that regional inequities in counselling quality or uptake are closing. Whether this reflects improved counselling access in previously underserved regions, cultural convergence, or both, is an empirical question for the programme's third decade.

Three gaps in the current evidence warrant attention. First, the programme has never been evaluated with a linked birth registry outcome — that is, the number of SCD and β-thalassaemia major births prevented has been modelled but not directly measured from prospective data. Integration of the PMSGC dataset with the national birth registry would resolve this and give a hard

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outcome measure. Second, formal cost-utility analysis using quality-adjusted life years is absent. The single decision-tree analysis shows cost-saving but does not capture lifetime quality-of-life effects or couple-level counselling costs. Third, programme expansion to spinal muscular atrophy, cystic fibrosis, and phenylketonuria — all three of which are autosomal recessive with known founder mutations in Saudi populations — requires prospective evaluation through a pilot programme, which none of the included studies described.

Strengths and Limitations

Strengths of this review include the comprehensive 20-year window, the inclusion of national and regional evidence, and the use of random-effects meta-analysis with meta-regression. To our knowledge this is the first PRISMA 2020 systematic review of the Saudi PMSGC programme.

Limitations should be stated clearly. Most included studies share a common data source — the Ministry of Health PMSGC registry — which creates non-independence of observations and may inflate apparent consistency. Formal adjustment for this clustering is complex and may affect pooled estimate precision. Many regional studies had small samples and short reporting windows, giving high risk of bias and variable denominators. KAP studies used heterogeneous questionnaires, constraining quantitative synthesis. The single cost-analysis study had methodological limitations discussed above. Finally, our review captures only published evidence; unpublished Ministry of Health internal reports may contain additional data to which we did not have access.

Implications for Policy and Research

For the Saudi Ministry of Health and for Saudi Vision 2030 health transformation, three action items emerge. First, integrate the PMSGC SEHA platform with the national birth registry to enable direct measurement of prevented affected births. Second, commission a formal cost-utility analysis with QALY outcomes and long time horizon to support decisions about programme expansion. Third, pilot panel expansion to include spinal muscular atrophy, cystic fibrosis, and phenylketonuria in one or two regions with formal prospective evaluation before national roll-out. For research, priority areas include standardized outcome reporting templates for KAP studies, and implementation science research on the counselling encounter itself — where the marriage cancellation decision is ultimately made.

For the wider MENA and Gulf region, the Saudi experience demonstrates that mandatory screening combined with voluntary decision-making can deliver population-level impact without requiring prenatal diagnosis infrastructure. Countries considering similar programmes should prioritize: (i) uniform laboratory standards from inception; (ii) counsellor training programmes with competency assessment; (iii) longitudinal data capture integrated with civil registration; and (iv) formal public communication strategies engaging religious leaders and schools.

Conclusions

Two decades of the Saudi mandatory premarital screening and genetic counseling programme have produced substantial, measurable population-level impact on hemoglobinopathy prevention. Marriage cancellation rates among at-risk couples have risen from under 10% to over 75%, prevalence gradients between the 13 administrative regions persist but are narrowing, and public acceptance approaches saturation. Gaps remain in direct outcome measurement, cost-utility evaluation, and programme expansion. The Saudi experience offers a credible model for other consanguineous populations seeking to implement genetic prevention without recourse to prenatal diagnosis.

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Table 4. Era-stratified pooled marriage cancellation rates among at-risk couples.

Era	Studies (k)	Pooled cancellation rate (95% CI)	Range	Studies
Era 1: 2004–2009	6	24.9% (13.0–39.2)	9.2% – 51.9%	Memish 2011 [4]; Alswaidi 2012 [5]
Era 2: 2010–2019	2	60.5% (49.6–70.9)	55.0% – 66.0%	Alsaeed 2018 [7]; Alsanie 2021 [19]
Era 3: 2020–2024	2	76.7% (63.1–87.9)	70.0% – 82.8%	Aljulifi 2022 [23]; Hafiz 2025 [21]
Overall (2004–2024)	**10**	**42.0% (26.3–58.6)**	**9.2% – 82.8%**	**All eligible studies**

Random-effects meta-analysis with Freeman–Tukey double arcsine transformation. Meta-regression β coefficient on year midpoint: +3.28 percentage points per year ($P < 0.001$). Era 3 estimates include KAP-based intention data.

Table 5. GRADE Summary of Findings.

Outcome	N studies	Pooled estimate (95% CI)	Certainty (GRADE)	Summary
Pooled sickle cell trait prevalence	10	45.4 per 1,000 (42.5–48.4)	Moderate	Consistent with documented Saudi hemoglobinopathy burden; upgraded for large effect.
Pooled β-thal trait prevalence	10	21.0 per 1,000 (17.4–24.8)	Moderate	Eastern region contributes disproportionately.
Marriage cancellation time trend	10	β = +3.28 pp/year ($P < 0.001$)	Moderate	Sustained positive trend; upgraded for dose-response.
Regional prevalence heterogeneity	8	10× E-vs-N gradient	Moderate	Consistent across successive national reports; upgraded for large effect.
Cost-savings (SCD)	1	73% cost reduction (~US$29.7M/year)	Low	Single decision-tree study; limited sensitivity analysis.
Knowledge (national awareness)	19	70–85% correct	Low	KAP heterogeneity; sampling concerns.

pp = percentage points. SCD = sickle cell disease.

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References

1. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008;86(6):480–487.
2. El-Hazmi MA, Al-Swailem AR, Warsy AS, Al-Swailem AM, Sulaimani R, Al-Meshari AA. Consanguinity among the Saudi Arabian population. J Med Genet. 1995;32(8):623–626.
3. El-Mouzan MI, Al-Salloum AA, Al-Herbish AS, Qurachi MM, Al-Omar AA. Regional variations in the prevalence of consanguinity in Saudi Arabia. Saudi Med J. 2007;28(12):1881–1884.
4. Memish ZA, Saeedi MY. Six-year outcome of the national premarital screening and genetic counseling program for sickle cell disease and β-thalassemia in Saudi Arabia. Ann Saudi Med. 2011;31(3):229–235.
5. Alswaidi FM, Memish ZA, O'Brien SJ, Al-Hamdan NA, Al-Enzy FM, Alhayani OA, et al. At-risk marriages after compulsory premarital testing and counseling for β-thalassemia and sickle cell disease in Saudi Arabia, 2005–2006. J Genet Couns. 2012;21(2):243–255.
6. Alhamdan NA, Almazrou YY, Alswaidi FM, Choudhry AJ. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. Genet Med. 2007;9(6):372–377.
7. Alsaeed ES, Farhat GN, Assiri AM, Memish ZA, Ahmed EM, Saeedi MY, et al. Distribution of hemoglobinopathy disorders in Saudi Arabia based on data from the premarital screening and genetic counseling program, 2011–2015. J Epidemiol Glob Health. 2017;7(Suppl 1):S41–S47.
8. Alnajjar KY, Al-Abdulsamad SH, Nahhas NA, Almuna RA, Bayuomi AS, Alkhaldi A, et al. Prevalence and regional distribution of beta-hemoglobin variants in Saudi Arabia: insights from the national premarital screening program. J Epidemiol Glob Health. 2024;14(3):982–993.
9. Alhussein NN, Alshaibani RM, Alsaif RM, Alqahtani AA, Alotaibi DM, Alharbi AS, et al. The economic impact of premarital screening (PMS) of sickle cell anemia on the Saudi health system: a cost analysis study. Healthcare (Basel). 2025;13(17):2243.
10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

 doi:10.20944/preprints202604.1884.v1

11. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015;350:g7647.
12. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol. 2016;75:40–46.
13. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan — a web and mobile app for systematic reviews. Syst Rev. 2016;5:210.
14. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. Int J Evid Based Healthc. 2015;13(3):147–153.
15. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. Int J Technol Assess Health Care. 2005;21(2):240–245.
16. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924–926.
17. Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. J Epidemiol Community Health. 2013;67(11):974–978.
18. Campbell M, McKenzie JE, Sowden A, Katikireddi SV, Brennan SE, Ellis S, et al. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. BMJ. 2020;368:l6890.
19. Alsanie NA, Alhraiwil NJ. Awareness of premarital screening and genetic counseling among Saudis and its association with sociodemographic factors: a national study. J Multidiscip Healthc. 2021;14:389–399.
20. Alsulaiman A, Hewison J, Ahmed S, Abu-Amero KK, Abu-Amero SN. Knowledge and attitude toward the hemoglobinopathies premarital screening program in Saudi Arabia: population-based survey. Hemoglobin. 2008;32(6):531–538.
21. Hafiz MN, Suhail N, Mohammed ZMS, Mahmoud MZ, Alqahtani RM, Alanazi NM, et al. Awareness and attitude of the general population towards inherited hemoglobinopathies in the premarital screening program in the northern region of Saudi Arabia. Hematol Rep. 2025;17(1):9.
22. Alasmari H, Alotaibi H, Alharthi A, Aljabri MA, Alqurashi MM, Alqarni MA, et al. Premarital screening programme in Saudi Arabia: insights into men's awareness and perceptions. Afr J Reprod Health. 2024;28(3):63–73.
23. Aljulifi MZ, Almutairi MAS, Ahmad MS, Alkhonezan SM, Alqahtani BA, Alharbi MM, et al. Awareness and acceptance of premarital screening test and genetic counseling program in Riyadh area, Saudi Arabia. Pak J Med Health Sci. 2022;16(2):875–881.
24. Alzahrani F, Alzahrani AM, Alassiri M, Abujaber S, Balbaid O, Alsulimani E. The perception of genetic diseases and premarital screening tests in the central region of Saudi Arabia. BMC Public Health. 2024;24:1556.
25. Umair M, Alfadhel M. Prevention of hemoglobinopathies in Saudi Arabia: efficacy of national premarital screening and the feasibility of preimplantation genetic diagnosis. J Biochem Clin Genet. 2020;3(2):94–99.
26. Almohammed OA, Almutairi AK, Althunian TA, Alhusayyen MN, Alabdulkarim H, Alowairdhi YA, et al. Molecular patterns of alpha-thalassemia in the Kingdom of Saudi Arabia: identification of prevalent genotypes and regions with high incidence. BMC Med Genomics. 2023;16(1):277.
27. Angastiniotis M, Hadjiminas MG. Prevention of thalassaemia in Cyprus. Lancet. 1981;1(8216):369–371.
28. Samavat A, Modell B. Iranian national thalassaemia screening programme. BMJ. 2004;329(7475):1134–1137.
29. Al-Qattan HM, Amlih DF, Sirajuddin FS, Aldebasi BM, Alqahtani RM, Alsulaiman OA, et al. Quantifying the levels of knowledge, attitude, and practice associated with sickle cell disease and premarital genetic counseling in 350 Saudi adults. Adv Hematol. 2019;2019:3961201.
30. Saudi Ministry of Health. Saudi Health Sector Transformation Program 2020–2030. Vision 2030. Riyadh: Saudi Ministry of Health; 2021.
31. Memish ZA, Owaidah TM, Saeedi MY. Marked regional variations in the prevalence of sickle cell disease and β-thalassemia in Saudi Arabia: findings from the premarital screening and genetic counseling program. J Epidemiol Glob Health. 2011;1(1):61–68.

 doi:10.20944/preprints202604.1884.v1

32. Mir SA, Alshehri BM, Alaidarous M, Banawas SS, Dukhyil AAAB, Alturki MK. Prevalence of hemoglobinopathies (β-thalassemia and sickle cell trait) in the adult population of Al Majma'ah, Saudi Arabia. Hemoglobin. 2020;44(1):47–50.
33. Alnajjar KY, Al-Abdulsamad SH, Nahhas NA, Almuna RA, Bayuomi AS, Alkhaldi A, et al. Regional prevalence of hemoglobin C across Saudi Arabia: an epidemiological survey. J Epidemiol Glob Health. 2024;14(1):164–172.
34. Binshihon SM, Alsulami MO, Alogaibi MJ, Mira AA, Al-Hindi HA, Alkhotani AA. Knowledge and attitude toward hemoglobinopathies premarital screening program among unmarried population in western Saudi Arabia. Saudi Med J. 2018;39(12):1226–1231.
35. Gosadi IM, Gohal GA, Dalak AE, Alabdali AF, Alomar AS, Daghreeri MA, et al. Assessment of factors associated with public awareness of the importance of premarital screening in the south of Saudi Arabia. Int J Gen Med. 2021;14:1043–1053.
36. Saffi M, Howard N. Exploring the effectiveness of mandatory premarital screening and genetic counselling programmes for β-thalassaemia in the Middle East: a scoping review. Public Health Genomics. 2015;18(4):193–203.
37. Ibrahim NKR, Al-Bar H, Al-Fakeeh A, Al-Ahmadi JR, Qadi M, Al-Bar A, et al. An educational programme about premarital screening for unmarried female students in King Abdulaziz University, Jeddah. J Infect Public Health. 2011;4(1):30–40.
38. Olwi D, Merdad L, Ramadan E. Knowledge of genetics and attitudes toward genetic testing among college students in Saudi Arabia. Public Health Genomics. 2016;19(5):260–268.
39. Zaini RG. Sickle-cell anemia and consanguinity among the Saudi Arabian population. Arch Med. 2016;8(3):3.
40. Jastaniah W. Epidemiology of sickle cell disease in Saudi Arabia. Ann Saudi Med. 2011;31(3):289–293.
41. Al-Qurashi MM, El-Mouzan MI, Al-Herbish AS, Al-Salloum AA, Al-Omar AA. The prevalence of sickle cell disease in Saudi children and adolescents: a community-based survey. Saudi Med J. 2008;29(10):1480–1483.
42. Hamamy H. Consanguineous marriages: preconception consultation in primary health care settings. J Community Genet. 2012;3(3):185–192.
43. Bashwari LA, Al-Mulhim AA, Ahmad MS, Ahmed MA. Sickle cell disease in eastern province of Saudi Arabia. Saudi Med J. 2001;22(10):886–889.
44. Al-Suliman A. Prevalence of β-thalassemia trait in premarital screening in Al-Hassa, Saudi Arabia. Ann Saudi Med. 2006;26(1):14–16.
45. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. BMJ. 2006;333(7573):831–834.
46. Alnajjar K, Al-Suliman A, Albagshi M, Alsulaiman A, Alateeq S, Alhamoud R, et al. Hemoglobinopathies in the Eastern Province of Saudi Arabia: a 15-year review. Hemoglobin. 2022;46(4):240–248.
47. Aljuhani F, Alyamani S, Al-Olayan A, Alanazi RS, Alotaibi MM, Alqahtani SF, et al. Evaluating the national haemoglobinopathy screening programme in Saudi Arabia using the SEHA electronic platform: 2018–2022. Saudi J Med Med Sci. 2024;12(2):136–142.
48. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–560.
49. Freeman MF, Tukey JW. Transformations related to the angular and the square root. Ann Math Stat. 1950;21(4):607–611.
50. Schwarzer G, Carpenter JR, Rücker G. Meta-Analysis with R. Cham: Springer International Publishing; 2015.