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REVIEW

# From Expanded Carrier Screening to Dynamic and Personalised Preconceptional Genomics

Belén Lledo[1,2] | Ruth Morales[1] | Jose A. Ortiz[1] | Amelia Rodríguez-Aranda[3] | Andrea Bernabeu[2,4]

[1]Instituto Bernabeu Biotech, Alicante, Spain | [2]Cátedra de Medicina Comunitaria y Salud Reproductiva, Miguel Hernández University, Alicante, Spain | [3]Eugin Group, Barcelona, Spain | [4]Reproductive Medicine, Instituto Bernabeu of Fertility and Gynaecology, Alicante, Spain

**Correspondence:** Belén Lledo (blledo@institutobernabeu.com)

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## ABSTRACT

Expanded carrier screening (ECS) has substantially broadened the scope of preconception genetic screening, but the expansion of fixed gene panels has also highlighted important limitations related to population diversity, genomic coverage, variant interpretation, residual risk and the clinical value of increasingly large panels. Recent advances in population genomics, sequencing technologies, longitudinal variant reassessment, quantitative risk assessment and artificial intelligence (AI) provide opportunities to move beyond static screening models. This review examines current challenges in ECS and explores the transition towards a more dynamic and individualised framework for preconceptional genomics. Rather than continually expanding fixed panels, genomic information could be selectively interpreted within the reproductive context and reassessed as knowledge, variant classifications and individual circumstances evolve. Emerging technologies, including exome- and long-read sequencing and AI-assisted variant interpretation, may facilitate this transition, although limitations related to validation, population diversity, penetrance and clinical interpretation remain. Genetic counselling and professional oversight will therefore remain essential to ensure that increasingly complex genomic information is translated into meaningful reproductive risk assessment and informed reproductive decision-making.

## 1 | Introduction: From Carrier Screening to Preconceptional Genomics

Carrier screening was originally designed around a limited number of severe recessive disorders enriched in defined ancestral or ethnic groups. Next-generation sequencing (NGS) made broad screening feasible without relying on self-reported ancestry, and professional recommendations progressively shifted towards pan-ancestry approaches [1–4]. Today, in reproductive medicine, ECS can identify couples at increased risk for autosomal recessive or X-linked disease before conception, expanding their reproductive options, including natural conception with or without prenatal diagnosis, use of donor gametes, adoption, or in vitro fertilisation with pre-implantation genetic testing for monogenic disease (PGT-M).

The clinical value of ECS lies not in analytical sensitivity alone, but in generating valid, interpretable and meaningful information for reproductive decision-making. As panels expand, they include genes with lower carrier frequencies, less certain genotype–phenotype relationships, variable penetrance, later onset or heterogeneous severity, while increasing curation demands and amplifying inequities arising from uneven ancestral representation in reference databases [3–8]. The question is shifting from how many genes can be screened to which genomic information should be generated, interpreted, retained and communicated.

Exome-based screening can identify at-risk couples missed by restricted panels, although modelling shows diminishing

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**Highlights**

- What's already known about this topic?
  - Expanded carrier screening enables broad, pan-ancestral assessment of reproductive genetic risk.
  - Increasing the number of genes screened introduces challenges related to clinical utility, variant interpretation, population diversity and residual risk.
  - Advances in sequencing technologies and genomic databases are expanding the scope of reproductive genetic screening.
- What does this review add?
  - Preconception genetic screening may evolve from fixed panels towards dynamic genomic assessment with selective, evidence-based reporting.
  - Population genomics, longitudinal variant reinterpretation, emerging sequencing technologies and AI may support more individualised reproductive risk assessment.
  - Genetic counselling and professional oversight remain essential for translating increasingly complex genomic information into reproductive decisions.

incremental yield as panels become very large [3, 9–11], and updated gnomAD data have altered carrier-frequency estimates [4, 12]. A fixed panel is thus a snapshot of current knowledge rather than a permanent representation of reproductive risk. Conventional ECS also incompletely addresses parental germline mosaicism, structural and repeat variants, evolving variant classifications and variable penetrance [13–19]. These limitations support a broader concept of preconceptional genomics: a longitudinal, evidence-updated framework in which genomic information is interpreted in the couple's context and their reproductive goals, and revisited as knowledge or circumstances change.

Artificial intelligence (AI) may support this transition through variant prioritisation, evidence integration and quantitative risk estimation [20–24], provided it undergoes rigorous validation and expert oversight. This review examines the main limitations of current ECS and explores how population genomics, emerging sequencing technologies, longitudinal variant reinterpretation, quantitative risk assessment, genetic counselling and AI could contribute to a more dynamic individualised model of preconception genetic screening.

## 2 | Ancestry and Equity in Expanded Carrier Screening

Ancestry-based carrier screening has been effective for founder populations but may perform unequally in diverse and multi-ancestry populations since self-reported ethnicity does not always reflect genetic ancestry, particularly in admixed populations. Pan-ancestry ECS therefore advanced equity by removing predefined ancestry as a criterion for offering screening [1, 2].

Offering the same panel to everyone does not however, guarantee equitable performance. Population databases contain substantially more data from individuals of European ancestry, affecting allele-frequency estimates and variant classification. Variant of uncertain significance (VUS) burden is generally higher among individuals from underrepresented ancestry groups [7] and similar concerns rise in reproductive and newborn-screening datasets [8]. Studies using gnomAD v4 and population-specific data show that carrier frequencies vary markedly between ancestries and that relevant genes may be absent from established lists [4, 5, 12]; genomic data from 9051 Chinese, Indian and Malay individuals in Singapore identified severe paediatric-onset recessive conditions absent from existing panels5. Equity should therefore be assessed at several levels: equal access to screening; comparable analytical performance and interpretive certainty; appropriate representation of disease-associated variation; and equitable access to counselling and reproductive options.

## 3 | Balancing Panel Size and Clinical Utility in Expanded Carrier Screening

Falling sequencing costs have enabled progressively larger panels although broader screening does not necessarily mean greater clinical utility. Because carrier screening is performed in healthy populations, gene inclusion should reflect disease validity, severity, penetrance, age of onset, inheritance, and the reproductive decision-making [1, 2, 9].

The ACMG tiered approach recommends pan-ancestry screening with gene-selection criteria integrating carrier frequency with disease severity [1]. Mackenzie's Mission, the Australian Reproductive Genetic Carrier Screening Project, provides a complementary example of these principles in a population-based programme. Conditions were selected through a structured process emphasising disease severity, gene–disease validity and other condition-specific considerations [2]. This illustrates that the panel value depends not only on its breadth but also on its clinical relevance.

The optimal scope of ECS nevertheless remains unsettled. Modelling using updated gnomAD and ClinVar data shows progressively smaller gains as panel size increases [3]. In the 2025 Goldilocks analysis, panels of 152, 248, 531 and 725 genes captured approximately 90%, 95%, 99% and 99.7% of modelled positive couple yields, respectively [3]. Similarly, an analysis of 89 panels from 30 providers found substantial variation in panel composition and no consistent association between the gene number and clinical utility [25].

In a real-world PGT-M cohort, five representative ECS panels covered 71.8%–91.5% of cases but only 20.9%–79.1% of the 110 distinct genes involved; most genes absent from all panels were rare indications observed in a single case [26], illustrating the difficulty of capturing the long tail of rare disorders in predefined lists. These limitations have provided a rationale for broader genomic approaches. Exome- and genome-based screening has identified at risk couples missed by guideline-limited panels [9, 10]. Capalbo et al. demonstrated an exome-based approach retaining explicit criteria for severity, penetrance, inheritance and age of onset [9], while Belnap et al. found that only a minority of at-risk couples identified by exome/genome analysis would have been detected by the

current ACMG panel [10]. Cai et al. subsequently demonstrated the feasibility of clinical exome-based carrier screening in a large ART and sperm-donation cohort [27]. This highlights the distinction between breadth of data generation and breadth of clinical reporting. Exome- or genome-scale data could be generated while applying a curated, updateable reporting layer based on current evidence and reproductive context, reducing the reporting of poorly validated findings and allowing the reportable gene set to evolve.

## 4 | Challenges in the Interpretation of Expanded Carrier Screening

### 4.1 | Variants of Uncertain Significance

NGS has shifted the limiting step in many genetic workflows from variant detection to interpretation. A VUS reflects insufficient evidence to classify a variant as disease-causing or benign, which matters particularly when findings may influence reproductive decisions. Professional recommendations generally discourage the use of VUS for clinical decision-making, although disclosure practices vary according to testing context and professional guidance [1, 6].

Virtual-mating approaches can generate large numbers of hypothetical at-risk couples involving VUS [6] and among 1.69 million individuals undergoing hereditary disease genetic testing, 41.0% received at least one VUS, with marked variation across ancestries [7]. This supports a high evidentiary threshold for actionable findings in reproductive medicine.

### 4.2 | Variant Reinterpretation as Genomic Evidence Evolves

Variant classification is dynamic: a VUS may later be reclassified as pathogenic or likely pathogenic, while other variants may be downgraded [7]. Between 2019 and 2022, VUS increased by 103% and variants with conflicting classification (VUS/pathogenic or VUS/likely pathogenic) by 235% [28].

This creates particular challenges in preconception screening, where several years may separate testing from a subsequent reproductive decision. Reanalysis may therefore alter the clinical relevance of previously generated genomic data. However, longitudinal reinterpretation also raises questions regarding responsibility for reassessment, duration of follow-up, patient recontact and management of updated findings [29–33]. A dynamic model would therefore require defined policies for when reassessment and recontact are clinically appropriate.

### 4.3 | Penetrance and Variable Expressivity in Reproductive Risk Assessment

Pathogenicity does not necessarily predict the probability or severity of phenotypic expression as penetrance and expressivity vary according to age, sex, ancestry, genetic background and environmental or clinical context [16].

Population-scale genomic and electronic health record data are beginning to support more quantitative approaches. Forrest et al. developed an ML-based framework to estimate variant penetrance [17]. Such models are not yet a basis for routine reproductive decisions but suggest that interpretation could be complemented by context-specific estimates of phenotypic risk.

### 4.4 | Residual Risk and Interpretation of Negative Results

A negative result does not eliminate reproductive risk as residual risk reflects undetected or unrecognised pathogenic variants, genes excluded from reporting, technical limitations, and biological mechanisms outside the tested model. Residual-risk estimation is challenging when ancestry-specific carrier frequencies and detection rates are uncertain [34].

As panels expand, patients may perceive a large negative panel as absence of risk; counselling should distinguish analytical coverage from genetic risk, particularly with exome or genome sequencing, where broad data generation can imply comprehensiveness despite persistent blind spots.

## 5 | Expanding the Genomic Scope of Reproductive Screening

### 5.1 | Structural Variation and Complex Loci

Short-read NGS reliably detects many single-nucleotide variants and small insertions/deletions, but is less suited to repetitive regions, pseudogenes, complex rearrangements, repeat expansions and some copy-number or structural variants. This limits detection in conditions commonly included in carrier screening, such as spinal muscular atrophy, alpha-thalassemia, congenital adrenal hyperplasia and fragile X syndrome.

Targeted long-read carrier-screening studies have demonstrated simultaneous assessment of complex monogenic disorders with improved haplotype and structural characterisation [35, 36]. Genome-wide long-read methods also continue to improve in structural-variant detection and phasing [37]. Long-read sequencing may thus complement conventional approaches for poorly resolved loci.

### 5.2 | Germline Mosaicism and de Novo Recurrence

Carrier screening focuses on inherited autosomal recessive and X-linked conditions, whereas parental germline mosaicism is a distinct source of reproductive risk. In families with an apparently de novo pathogenic variant, low-level mosaicism may be undetectable in blood but present at a higher frequency in the germline. Consequently, recurrence risk may differ substantially from estimates assuming a truly de novo event [13–15].

Breuss et al. identified mosaic variants in sperm and showed transmission to human blastocysts at frequencies related to their abundance [14]. More recently, genome-wide phasing and deep sequencing of parental blood and sperm showed that sperm can be more informative than blood for detecting paternal germline mosaicism and estimating the recurrence risk of paternally phased de novo variants [15]. Such testing should remain indication-driven and carefully validated, but illustrates that preconception assessment involves not only more genes but also other variant types, genomic regions and biological sources of risk.

## 6 | Genetic Counselling in an Increasingly Complex Genomic Landscape

As screening becomes more comprehensive, genetic counselling is essential to translate genomic findings into reproductive information, interpreting results in relation to severity, penetrance, residual risk, reproductive options and the couple's values. These considerations become particularly relevant as screening moves from predefined panels towards broader genomic approaches.

Broader genomic testing may also identify findings relevant to the health of the individual's health, raising questions of consent, disclosure and management of secondary or incidental findings [38]. Pre-test counselling should therefore clarify the scope of analysis and the types of findings that may be returned.

Within a dynamic preconceptional genomics framework, informed consent would also need to address the future use and reinterpretation of genomic data: the distinction between information generated and findings reported, the possibility that new evidence alters interpretation, the circumstances for recontact, whether secondary findings will be sought, and whether individuals may decline categories of results. These considerations are particularly relevant when broader genomic approaches are used, as the information generated may extend beyond the original reproductive indication.

Gamete donation illustrates these challenges: genetic matching can reduce the risk of shared recessive conditions without excluding healthy carriers, although broader screening raises further questions regarding incidental findings, reclassification, recontact and the feasibility follow-up [39], reinforcing the need for clear testing, reporting and consent policies in third-party reproduction.

The increasing complexity of reproductive genomic information also raises questions of scalability. Providing individualised interpretation and counselling becomes more demanding than the number and diversity of finding increase, while access to genetics professionals remains uneven. Recent reviews have highlighted the importance of accessible, evidence-based educational resources and communication strategies to support informed decision-making in carrier screening [40]. This creates a need for models that preserve individualised counselling for complex or clinically consequential findings while enabling more scalable approaches to information delivery and follow-up.

Dynamic preconceptional genomics requires genetic counselling that addresses initial assessment and clinically relevant updates. Pre-test counselling should cover genomic scope and limitations, differences between data generation and clinical reporting, potential reinterpretation, and recontact conditions. Post-test counselling should address reproductive implications, residual risk, and available options, with reassessment when reinterpretation substantially changes risk estimates. To address workforce limitations, standardised educational resources and validated digital tools could support routine counselling, while genetics professionals manage complex findings, reproductive decisions, and significant updates. These models require evaluation to ensure scalability without compromising informed consent, equity, or counselling quality. Overall, the evolution of preconception screening depends not only on expanding genomic coverage but also on improving the interpretation, longitudinal management and clinical translation of complex genomic information (Table 1), with scalable tools supporting evidence integration and reassessment under expert oversight.

## 7 | The Emerging Role of Artificial Intelligence in Preconceptional Genomics

The growing volume of genomic data makes comprehensive manual review challenging. AI may support the integration of heterogeneous genomic, clinical and literature-derived evidence, variant interpretation, integration of emerging evidence, quantitative risk estimation, and patient communication.

Variant interpretation is one of the main areas in which AI may support genomic medicine. Computational approaches include machine-learning models trained on variant databases, models integrating ACMG/AMP evidence criteria with genomic annotations, and gene- or protein-specific models incorporating sequence and structural information [41–44]. These approaches may support evidence retrieval and synthesis, prediction of functional effects, variant prioritisation, and integration of genotype and phenotype information.

Generative-AI and natural-language interfaces may also facilitate access to complex genomic information for clinicians without specialised computational expertise. VarChat, for example, was developed to retrieve and summarise literature relevant to genomic variants [20]. Nevertheless, generative AI tools may produce inaccurate summaries, unsupported interpretations or misleading conclusions, particularly when dealing with incomplete or conflicting scientific evidence. Therefore, AI-generated information should be critically evaluated and verified against primary scientific sources and established variant interpretation criteria before being used in clinical decision-making. These limitations reinforce the role of AI as a decision-support tool rather than a substitute for expert genetic interpretation. Automated systems perform better for variants with well-established benign or pathogenic evidence and remain less reliable for VUS, where expert assessment and additional biological evidence are particularly important [22]. Recent reviews therefore support a human-in-the-loop model in which AI standardises evidence synthesis while clinical interpretation and responsibility remain with qualified professionals [22, 24].

AI may also provide quantitative estimates of phenotypic risk. The ML-penetrance framework developed by Forrest et al. illustrates how large-scale EHR and genomic data can be used to estimate penetrance for specific variants [17]. Analogous approaches could eventually integrate variant-level evidence with penetrance, inheritance, age of onset, disease severity, ancestry and family history to provide more clinically interpretable estimates of reproductive risk. However, performance and generalisability depend on the populations represented in genomic and clinical datasets. Underrepresentation of diverse

**TABLE 1** | Current challenges in reproductive genetic screening and emerging strategies towards dynamic preconceptional genomics.

| Current challenge | Clinical implication | Emerging strategy | Potential contribution of AI | Remaining limitation |
|---|---|---|---|---|
| VUS | Uncertain reproductive significance | Periodic reinterpretation; functional evidence | Evidence integration and variant prioritisation | Insufficient evidence cannot be replaced by prediction |
| Variable penetrance/ expressivity | Genotype does not directly predict phenotype | Quantitative penetrance estimation | Integration of genomic, phenotypic and population data | Calibration and external validation |
| Residual risk | Negative result may be misinterpreted as absence of risk | Quantitative residual-risk estimation | Integration of detection rates and population data | Incomplete population and assay-specific data |
| Underrepresented populations | Greater interpretive uncertainty | More diverse population databases | Ancestry-aware models | Bias in training datasets |
| Structural/ complex variants | False-negative or incomplete detection | Long-read sequencing/ complementary assays | Variant calling/ prioritisation | Cost and validation |
| Germline mosaicism | Recurrence risk may be underestimated from blood | Tissue-specific analysis, particularly sperm when appropriate | Mosaic variant detection/ risk modelling | Limited evidence and maternal germline accessibility |
| Reclassification | Clinical meaning changes over time | Longitudinal reinterpretation | Automated evidence monitoring | Responsibility for review/recontact |
| Increasing counselling demand | Limits scalability | Tiered/digital counselling | Education and triage | Human oversight remains essential |

Abbreviations: AI, artificial intelligence; VUS, variant of uncertain significance.

populations may therefore propagate disparities into AI-based models [45, 46]. AI-derived risk estimates require validation across diverse populations, uncertainty assessment and transparent reporting [47].

Computational tools may also facilitate longitudinal reassessment. iVar and Genome Alert! track changes in variant classifications and prioritise relevant updates for expert review [48, 49]. iVar additionally helps identify patients carrying a reclassified variant, supporting recontact when clinically appropriate [48]. Such approaches may be particularly relevant when several years separate initial testing from a subsequent reproductive decision. Importantly, new evidence does not itself determine reclassification or a recontact; these decisions require expert assessment [29–33].

AI-assisted tools may also support genetic counselling through standardised education, pre-test information, informed consent and selected aspects of result communication, while identifying cases requiring individualised specialist counselling. In 225 couples undergoing carrier screening, a Digital Genetic Assistant provided digital patient intake, pre-test education and automated communication of low-risk results while referring higher-risk cases for face-to-face counselling [50]. Only 4.2% of low-risk couples requested additional counselling, and genetic counsellor–participant face-to-face interactions were reduced by 69.3%, with high participant comprehension and satisfaction [50]. This supports a tiered model in which digital tools facilitate standardised communication while specialist counselling is prioritised for clinically significant, uncertain or complex findings.

## 8 | Towards a Dynamic Model of Preconceptional Genomics

The challenges discussed above not only highlight the limitations of current ECS strategies but also support their evolution. As summarised in Table 1, emerging genomic, analytical and clinical approaches, potentially supported by computational and AI-based tools, could improve reproductive risk assessment. Their integration into a coherent and adaptable framework provides the basis for dynamic and personalised preconceptional genomics.

We define dynamic and personalised preconceptional genomics as a framework that adapts reproductive genetic risk assessment to individual or couple-specific clinical and reproductive circumstances, incorporates evolving genomic technologies and evidence, and enables reassessment when clinically justified. This framework has two defining features.

Personalisation involves tailoring genomic approaches and reporting on ancestry, family history, consanguinity, reproductive route (natural conception, IVF or gamete donation), partner status and reproductive preferences rather than indiscriminately expanding screening panels. It also requires interpreting findings in terms of overall reproductive risk, including couple-level residual risk and the probability of affected offspring.

Dynamism involves incorporating advances in genomic technologies and variant interpretation and reassessing existing genomic information as evidence evolves. Rather than continuous reanalysis, reassessment should follow predefined clinical

criteria, such as variant reclassification, new gene–disease associations, improved detection of previously inaccessible variation (e.g., copy-number variants or repeat expansions), partner changes or a previously affected pregnancy. The developments discussed throughout this review suggest a transition from fixed carrier-screening panels towards a broader and more dynamic concept of preconceptional genomics (Figure 1). In contrast to conventional ECS approaches, which generally rely on predefined gene panels and single-time-point reporting, this framework would allow the scope of analysis, clinical reporting and timing of reassessment to be adapted to the reproductive context of each couple and to evolve with scientific evidence. Such a model could combine broader genomic data generation with selective clinical reporting, couple-centred interpretation, technologies adapted to different forms of genomic variation, and more quantitative assessment of reproductive risk.

Dynamism could operate through two complementary dimensions: genomic data generation and interpretation of reproductive significance. Broader approaches, such as exome or genome sequencing, could provide genomic information beyond initially reported genes, while technological advances may improve the detection of previously challenging variations. In parallel, interpretation could evolve through updated population databases, gene–disease associations, variant classifications and evidence on penetrance and reproductive risk. Existing data could be reinterpreted as knowledge advances, whereas improved variant detection may require additional testing. Thus, ECS could evolve from a fixed panel to an adaptable screening system guided by scientific evidence and reproductive context. Implementation would require clearly defined responsibilities: laboratories would maintain validated analytical pipelines and identify potentially relevant updates, while clinical teams would assess reproductive implications and determine the need for recontact. Automated computational and AI-based systems could support evidence monitoring and prioritise changes for expert review without implying automatic reinterpretation or recontact. Individual reassessment would follow predefined criteria, prioritising changes that could meaningfully affect reproductive decisions.

A potential clinical workflow would include: (i) pre-test counselling and informed consent addressing genomic scope, future reinterpretation and recontact conditions; (ii) genomic data generation and selective reporting based on reproductive context and predefined criteria; (iii) post-test counselling

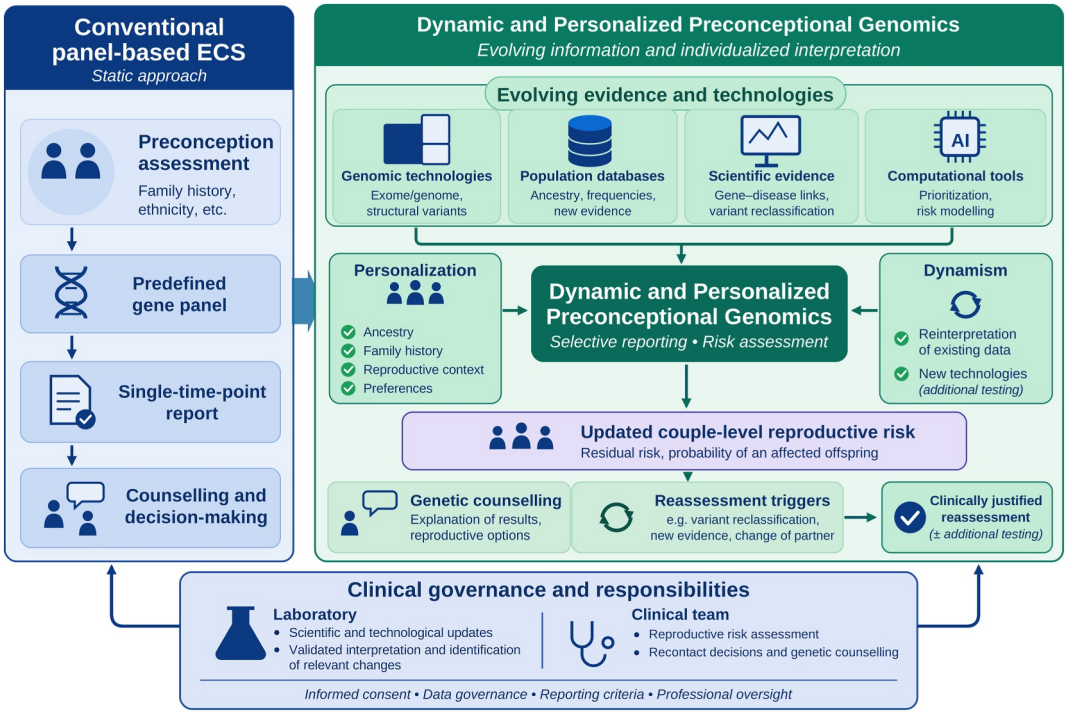



**FIGURE 1** | Conceptual framework for the transition from conventional expanded carrier screening (ECS) to dynamic and personalised preconceptional genomics. Left: conventional panel-based ECS based on a predefined gene panel and single-time-point reporting. Right: proposed adaptable framework in which advances in genomic technologies, population databases, scientific evidence and computational tools inform genomic analysis and individualised reproductive risk assessment. Personalisation refers to adapting the genomic approach and scope of reporting to individual and couple-level characteristics. Dynamism encompasses the periodic monitoring and integration of evolving genomic evidence, potentially supported by automated computational and AI-based tools, alongside clinically justified individual reassessment when predefined triggers arise (e.g., variant reclassification, new gene–disease evidence, change of partner or previously affected pregnancy). Such monitoring does not imply routine clinical reanalysis or recontact of all previously screened individuals. Reinterpretation of existing data may be possible without repeat testing, whereas new analytical capabilities may require additional genomic data generation. Genetic counselling remains central to reproductive risk communication and decision-making. Clinical governance, including informed consent, data governance, reporting criteria, professional oversight and the respective responsibilities of laboratories and clinical teams for reinterpretation and recontact, is integral to the framework. ECS, expanded carrier screening.

**TABLE 2** | Comparison between conventional expanded carrier screening and the proposed dynamic and personalised preconceptional genomics framework.

| Dimension | Conventional ECS | Proposed dynamic and personalised framework |
|---|---|---|
| Screening strategy | Predetermined gene panels, with broadly standardised screening approaches | Genomic strategy and reporting scope adapted to the individual or couple's reproductive context |
| Genomic information | Analysis generally restricted to selected genes and variants | Potentially broader genomic data generation with selective, clinically justified analysis and reporting |
| Reproductive risk assessment | Carrier status and couple-level risk assessment based on panel findings | More contextualised and potentially quantitative couple-level risk assessment, including residual risk |
| Adaptability to new evidence | Panel and interpretation updates may require new analyses or testing | Reinterpretation of existing data when clinically justified, with additional testing when new capabilities are required |
| Reassessment and recontact | Variable practices, depending on programme policies | Predefined criteria for reassessment and explicitly allocated responsibilities for recontact |
| Genetic counselling | Primarily focused on initial screening and results | Initial counselling with additional counselling when clinically relevant reassessment occurs |
| Implementation requirements | Established clinical workflows and laboratory infrastructure | Additional requirements for data governance, storage, analytical validation, professional oversight and economic evaluation |

addressing couple-level risk and reproductive options; and (iv) clinically justified reassessment through reinterpretation or additional testing when appropriate. Clinically significant changes would be evaluated by the clinical team to determine the need for recontact and further counselling (Figure 1).

Compared with conventional ECS, this framework could enable more personalised genomic approaches and reporting, improved couple-level reproductive risk assessment, incorporation of emerging evidence and clearer responsibilities for reinterpretation and recontact (Table 2). However, clinical benefits remain unproven. Implementation challenges include genomic data storage and infrastructure costs, ethical and legal considerations, uncertain findings, unequal access and increased demands on laboratories and counselling services. Prospective comparative studies evaluating clinical utility, cost-effectiveness and reproductive decision-making are therefore needed.

Computational and AI-based tools could facilitate evidence integration, identify relevant changes in variant classification or gene–disease associations, and support reproductive risk estimation and communication. However, clinical use requires validation, transparency, traceability and human oversight to mitigate errors, unsupported conclusions and biases. Expert interpretation and genetic counselling must remain central to clinically consequential decisions.

Implementation would also require policies governing genomic data storage, access and future use. Secure retention of broader sequencing data could enable reinterpretation without repeat testing, subject to regulatory requirements and informed consent. Clinical reporting should follow predefined criteria based on gene–disease validity, disease severity, variant classification and reproductive relevance. Broader data generation would not imply unrestricted analysis or disclosure, while secondary findings unrelated to reproductive risk would require separate policies and consent. Economic feasibility must also consider storage, computational infrastructure, reinterpretation, counselling and recontact costs. Whether these expenses could be offset by reduced repeat testing and improved reproductive decision-making requires comparative cost-effectiveness studies. The proposed framework should therefore be understood as a conceptual model with defined operational components rather than an established clinical protocol. Its translation into routine practice would require the development and validation of context-specific clinical pathways, together with further evaluation of analytical and clinical validity, population diversity, data governance, cost-effectiveness, genetic counselling capacity and the impact on reproductive decision-making. Rather than simply increasing the number of genes tested, the future challenge will be to determine how increasingly comprehensive genomic information can be translated into clinically meaningful, equitable and appropriately communicated reproductive risk.

## 9 | Conclusion

Expanded carrier screening has transformed reproductive genetic testing and continues to evolve alongside advances in genomic technologies and population-scale evidence. These developments, together with AI-assisted approaches, may support a transition towards more dynamic preconceptional genomics, in which genomic information is interpreted in the reproductive context and reassessed as evidence evolves. The challenge will be to translate increasingly comprehensive genomic information into valid, equitable and interpretable reproductive risk while preserving expert genetic counselling and informed reproductive decision-making.

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## Conflicts of Interest

The authors declare no conflicts of interest.

## Data Availability Statement

Data sharing is not applicable to this article, as no datasets were generated or analysed during the current study.

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