INHERITANCE RISK CALCULATION STRATEGIC AND FORMULATION FOR GENETIC DISEASES: A SCOPING REVIEW

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ABSTRACT

Genetic disorders are diseases caused by changes (mutations) in certain genes. This condition can be passed from parents to children, or occur randomly due to exposure to certain factors. Genetic diseases are caused by a number of factors, including defects in the mother's or father's genes, excessive abortion, a lack of blood cells, and a low white blood cell count. For premature or adolescent life development, early detection of genetic diseases is essential. Although it is difficult to predict genetic disorders in advance, these predictions are very important because the progress of a person's life depends on it. This scoping review focused on articles published in English from 1984 to 2022. The review included interventions related to calculating the inheritance patterns of genetic diseases and outcomes associated with these patterns. Encompassing randomized controlled trials, quasi-experimental studies, and cross-sectional research, the inclusion criteria excluded literature reviews, systematic reviews, and other scoping reviews. The review was conducted across four databases included PubMed, Scopus, ProQuest, and ScienceDirect, with critical appraisal conducted using the Joanna Briggs Institute's Critical Appraisal Checklist. Upon meeting the inclusion criteria, seven cross-sectional studies and quasi-experiments were identified. The review of intervention methods for calculating genetic diseases revealed outcomes associated with the inheritance patterns of genetic diseases. The intervention method for calculating genetic diseases has demonstrated its effectiveness in determining the inheritance patterns passed from parents to their children. This information is crucial for devising appropriate treatment plans for individuals affected by genetic diseases.

Keywords: Genetic Counseling, Genetic Risk, Inheritance Pattern, Risk Calculation

INTRODUCTION

Diseases with genetic implications serve as primary contributors to morbidity and mortality rates, significantly impacting societal health concerns (Zhou *et al.*, 2019). Chromosomal abnormalities often lead to miscarriages and physical disabilities, as chromosomes are essential structures where DNA and genetic material reside in human beings (Yahaya *et al.*, 2021).

Chromosomes are thread-like structures of genetic material (DNA) present in every cell of living organisms. Typically, each normal

cell contains 46 chromosomes, consisting of 22 pairs of autosomes and one pair of sex chromosomes (X and Y chromosomes) that determine gender (Biesecker, 2020). Manifestations of chromosomal abnormalities may include stunted growth, delayed cognitive development, and a variety of physical abnormalities such as heart valve defects, cleft lip, and intellectual disabilities (Taylor *et al*., 2023).

In addition to chromosomal irregularities, genetic disorders can arise from mutations in dominant or recessive genes located on autosomes or sex chromosomes, leading to conditions like epilepsy, Down syndrome, diabetes mellitus, cancer, and thalassemia (Laksono *et al*,. 2011).

The prevalence of genetically inherited diseases varies among different ethnic groups, geographic locations, and genders. Globally, there are 6172 distinct rare diseases, of which 71.9% are attributed to genetic factors. The prevalence of genetic diseases is reported to be 58 cases per 1000 births, while in Indonesia, 5-15% of the population is affected by genetic disorders (Wakap *et al*., 2020). Individuals with genetic conditions often present with physical disabilities, heart abnormalities, mental health issues, and blood disorders, leading to psychological challenges such as anxiety and depression, ultimately impacting their quality of life (El-Baky *et al*,. 2020).

The integration of information technology into the realm of biology has revolutionized research processes, including studies in human genetics, enabling scientists to streamline their investigative endeavors (Lefranc *et al*., 2015). In biological terms, a child inherits genes from both parents, with these genes encoding various traits, observable characteristics, and hidden genetic predispositions (Ruehle, 2017).

The foundational principles of genetics and the modern understanding of trait inheritance were established by Gregor Mendel. Through his studies on seven inherited traits in pea plants, Mendel introduced the theory of gene independent assortment (Cheng, 2022). According to this theory, a child's genetic makeup results from the combination of genes inherited from both parents. Genes are segments along DNA molecules, with the majority containing instructions for protein synthesis (Berry & Browne, 2022).

Human cells typically consist of 46 chromosomes, including two sex chromosomes and 22 pairs of autosomes. In males, the chromosome composition is denoted as "46, XY," while in females, it is "46, XX." Chromosomes comprise protein and long DNA strands (Kido & Lau, 2015). Predicting the likelihood of inheriting specific genes can be accomplished through genetic algorithms. To investigate human gene inheritance, it is essential to model marriage possibilities and gene transmission within families. Information technology, utilizing branch and bound algorithms, can be employed to simulate human gene inheritance systems (Tamannaei & Irandoost, 2019). This model aims to determine the probability or percentage of gene transmission resulting from the genetic combination of both parents (Ezugwu *et al*., 2019).

Couples who check their health before getting married are still relatively few, this is important in order to know each other's health condition in order to avoid various diseases that arise and help take necessary preventive measures or treatment (Kiecolt-Glaser, 2017). In society, there are quite a few children who have deviant

characteristics from their father and mother, this situation is closely related to human genetics, these genes are carriers of certain characteristics, either physically, or visible through their characteristics (Kolk & Andersson, 2020).

Heredity is the transfer of genetics from parents to offspring, even though this event is not that easy. Because children basically do not inherit physical features such as height, skin color or hair. A child does not inherit musical talent or criminal tendencies, what a child inherits from their father and mother is the genotype of their parents (Lacal & Ventura, 2018). Some symptoms of mental decline are passed on by parents to their children. One of the mental disorders caused by genetic factors is a person's inability to form the enzyme phenylalanine hydroxylase which converts phenylalanine into tyrosine. Decision Support System is an interaction system that can provide solutions to problems in structured or unstructured conditions in the form of information, predictions, and better guidance to its users (Klaassen *et al.*, 2021).

Several previous researchers have conducted research to examine heredity using computerized methods using discrete probability theory methods such as those carried out by (Akbar, R. T et al., 2015; Alianto & Huda, 2015; Gulo, 2018) to predict the decline in genetic diseases. The application of discrete probability using Mendel's law of crossing in Android-based single gene inheritance is still relatively small. Based on statistical data conducted by apjii.or.id, internet use is mostly accessed per day using smartphones at 93.9% compared to computers and tablets at 9.6% and 5.2%.

The most widely used operating system is Android with a percentage of 37.66% compared to the use of Windows and iOS, namely 35.94% and 15.28%. Based on these data, Android smartphones are widely used by the public, so it can be an opportunity to review the heredity communication system using Mendel crosses to digital systems by utilizing Android smartphone technology. (Bioethics, 2015).

Meanwhile, techniques used manually are no longer effective for diagnosis, so it is the right decision to review research using computerized methods for diagnosis.

LITERATURE REVIEW

All diseases have a genetic component. However, the extent to which genes contribute to disease varies and much remains to be learned. Advances in understanding the genetic mechanisms behind these diseases enable the development of early diagnostic tests, new treatments, or interventions to prevent disease onset or minimize disease severity.

This chapter provides information about the importance of clinical signs such as family history that may be suggestive of a genetic disease, the different uses of genetic testing, and the different types of genetic diseases. All diseases have a genetic component. Mutations may be inherited or developed in response to environmental stresses such as viruses or toxins. The ultimate goal is to use this information to treat, cure, or if possible, prevent the development of disease (Claussnizzer, 2020).

History and Physical Examination

The diagnosis of a genetic disease requires a comprehensive clinical examination composed of three major elements:

a. physical examination
b. detailed medical family history
c. clinical and laboratory testing if available.

While primary care providers may not always be able to make a definitive diagnosis of a genetic disease, their role is critical in collecting a detailed family history, considering the possibility of a genetic disease in the differential diagnosis, ordering testing as indicated and when available, appropriately referring patients to genetic specialists.

Red Flags for Genetic Disease

There are several factors that raise the possibility of a genetic disease in a differential diagnosis. One major factor is the occurrence of a condition among family members that is disclosed when the family history is obtained (see Chapter 3 on Pedigree and Family History Taking). The occurrence of the same condition in more than one family member (particularly first-degree relatives), multiple miscarriages, stillbirths, and childhood deaths are all suggestive of a genetic disease. Additionally, family history of common adult conditions (heart disease, cancer, dementia) that occur in two or more relatives at relatively young ages may also suggest a genetic predisposition.

Other clinical symptoms that are suggestive of a genetic disease include developmental delay/mental retardation and congenital abnormalities. Dysmorphologies, often involving the heart and face, as well as growth problems are suggestive of a genetic disorder caused by an inherited mutation, a spontaneous mutation, a teratogen exposure, or unknown factors.

While these clinical features may be caused by a number of factors, genetic conditions should also be considered as part of the differential diagnosis, particularly if the patient expresses several clinical features together that might be indicative of a syndrome (for example, mental retardation, distinct facies, and heart defect). Some physical features may appear unique or slightly different than the average such as wide-set or droopy eyes, flat face, short fingers, and tall stature. While these rare and seemingly mild features may not immediately be suggestive of a genetic disease to a primary care provider, an evaluation by a genetics specialist may be helpful in ruling in/out a genetic disease (Allience, 2010).

RESEARCH METHODOLOGY

This research uses a scoping review with a methodology developed by Arksey and O'Malley. The following five steps identify a clear and objective research question; Identify relevant articles; article selection, data extraction; and data graphing, organizing, summarizing, analyzing, and reporting data. This scoping review aims to explore and synthesize scientific literature on strategies and formulations for calculating the inheritance of genetic disease risk.

Articles included in this review had to be published in an open access English version and full text in their original form from 1976 to 2023. The participants or population (P) of this study were patients with genetic problems who received intervention (I) method of calculating genetic disease. Outcome (O) is the inheritance of genetic disease. The research design (S) is a Randomized Controlled Trial, quasi-experimental research. Exclusion criteria Patients with psychiatric problems, literature review articles, systematic reviews, and umbrella reviews. Several journal databases, including PubMed, Scopus, ScienceDirect, Proquest, use search techniques using advanced search engine keywords:

Table 1. Keywords In Advanced Search Engines

Sources	Search strategy	Results
Scopus	"patients with genetic problems" AND "method for calculating genetic diseases" AND "inheritance of genetic diseases" AND "randomized controlled trial"	542
PubMed	((((("method for calculating genetic diseases"[Mesh]) AND "patients with genetic problems"[Mesh]) AND "inheritance of genetic diseases"[Mesh]) AND "Randomized Controlled Trial"	319
ProQuest	(patients with genetic problems) AND (method for calculating genetic diseases) AND (inheritance of genetic diseases) AND (randomized controlled trial)	37
Science Direct	"patients with genetic problems" AND " method for calculating genetic diseases" AND " inheritance of genetic diseases" AND "Randomized controlled trial"	63

Selection of Relevant Studies

To determine specific criteria for research eligibility, the PIOS framework was used. The population consists of people who have diseases with genetic problems. In this study, the intervention was compared with usual care, defined as a face-to-face consultation with a doctor or nurse. Intervention is a method of calculating the inheritance of genetic diseases carried out by experts, which is defined as the inheritance of traits inherited from the parent or parent to the child or offspring which is coordinated and delivered by a counselor.

After searching for previous articles in the EndNote X9 bibliographic software entries and eliminating duplicates, two reviewers independently selected the titles and abstracts of the articles. Further analysis was carried out on the abstracts of selected articles. If there was any doubt about whether a research article should be included in the second round of selection, the authors reviewed the article in its entirety. if necessary, resolved by talking to another appraiser.

Critical Assessment

Using the Joanna Briggs Institute (JBI) critical appraisal for data effectiveness report, the methodological quality of eligible studies was assessed independently through two reviews. For each study, reviewers assigned a score of "yes," "no," "unclear," or "not applicable" for each critical criterion of the assessment tool. Based on Heratanti et al. (2021), we categorize quality. The total score is calculated as the percentage of "yes" answers to the critical assessment results using the JBI tool. The checklist for randomized controlled trials that will be included in the data extraction table is assigned a minimum score of 9 (70% of the total score of 13). During the research quality assessment process, errors can be resolved by talking to other reviewers if necessary.

RESULTS RESEARCH

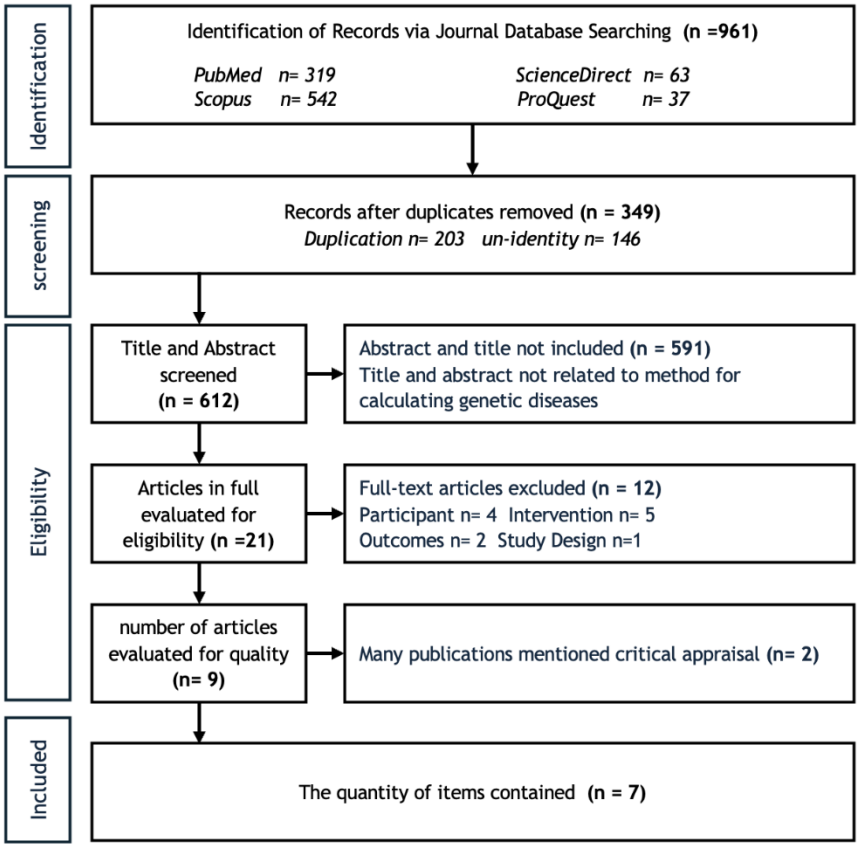

Figure 1. Prisma Flowchart

Table 2. Data extraction

Author (year) country	Design	Disease types	Purpose	Participant	Outcome
(Farbrother *et al.*, 2004) United Kingdom	Cohort study	Miopi	In a UK population, the purpose of this study was to calculate the risk of sibling recurrence (KS) and the sibling recurrence risk ratio (S) for extreme myopia.	Patient data was collected between January 2000 and December 2001, with just the most current data providing information. 1,846 participants satisfied the predetermined requirements for high myopia, which included	Only a tiny fraction of high myopia cases are thought to be accounted for by the high penetrance autosomal dominant loci for high myopia that have

		having a minimum minus meridian of each eyeglass refraction of 6.00 D. Since these values correlate to unbiased estimates of the prevalence of high myopia in white people in the United States, they were used to calculate the sibling recurrence risk ratio (S) in the lack of data of the prevalence of high myopia in the Americas or elsewhere in Europe. The mail is the main means of communicatio n. However, 16 surveys were also given over the phone to a sample of high myopes in an attempt to assess potential response bias from patients with a favorable family history. A total of 361 high myopes received postal questionnaires .	been found to date, according to the sibling recurrence risk ratio (S 4.9) presented here. Moreover, most occurrence s of extreme myopia cannot be explained by high penetranc e autosomal dominant heredity or even high penetranc e recessive inheritanc e. Conversely , it could be crucial to see excessive myopia as a "complex disease" brought on by environme ntal variables, penetranc e-decreasing alleles (also known as "susceptibi lity genes"), or both.

(Fotouhi *et al.*, 2007) iran	cross sectional study	Miopi	The purpose of this study is to ascertain if hereditary variables may have an impact on Tehran's myopia prevalence.	Urban dwellers of all ages who were residing in Tehran in 2002 made up the study's population; only those who were older than 15 were considered for the report's analysis. A Topcon automated refractometer (Topcon KR 8000, Topcon Corporation, Tokyo, Japan) was used to test each participant's refraction. Complete subjective and true refraction begin with the outcomes of autorefraction. In situations where autorefraction is not feasible, particularly in the presence of medium opacity, manual and subjective manifest refraction is carried out. When the ophthalmologist determines there are no contraindications, a cycloplegic refraction is carried out. In	Regardless of age, gender, height, or educational attainment, these results point to a comparatively high degree of family aggregation of myopia in the Tehran population. There are two possible causes of this residual aggregation: broad, unmeasured environmental influences or inherited variables.

				this instance, thirty and twenty-five minutes before to the refraction, one drop of cyclopentolate (1%) was administered. The symptoms associated with cyclopentolate usage were disclosed to the subjects. Statistical techniques A sphere equal to 20.5 diopters (D) or less was considered myopia. Using two more myopia thresholds (21 D and 22 D), we then looked at family aggregation at higher myopia levels.	
(Daetwyler *et al.*, 2008) inggris	cross sectional study	Genetic disease	The purpose of this work is to evaluate a straightforward deterministic method for estimating the precision of genetic risk estimates.	The accuracy of genetic risk projections from population or case-control studies may be predicted using a straightforward deterministic formula that we developed utilizing a genomic	Understanding the relative benefits of case control and disease population research is improved by this work. These forecasts show the maximum

		approach and the assumption of dichotomous disease phenotypes with underlying continuous liability. We demonstrate that the more general issue of forecasting the precision of genetic value estimations from continuous phenotypes is a special example of prediction equations. Our prediction formulas are independent of effect distributions and allele frequencies, and they respond to all factors affecting accuracy. When validated through simulation, deterministic prediction errors are typically negligible. All accuracy expressions have one thing in common: the number of phenotypic	level of accuracy that might be attained with improved techniques for effect estimation. Researchers will be able to estimate genetic risk with a higher degree of precision by using the generated formula to calculate the appropriate sample size.

				records multiplied by the number of detected risk and heredity loci may be used to best characterize each expression.	
(Lannoy & Hermans, 2020) Belgia	A practical review	haemophilia	The goal of this study is to understand the many forms of mosaicism, as well as the processes that lead to the illness and the likelihood that harmful variations will be passed down to future generations.	When high-grade mosaicism is present at 70% or above, it is typically not identified and is not tested in clinical settings. In contrast, because of difficulties in detecting them during standard molecular diagnostic procedures, low- and intermediate-grade mosaicism may be an underreported source of genetic diseases. Due to their requirement for the detection of a minimum of 10%–20% of mutated cells, traditional molecular screening methods like single-strand	About 80 percent of instances of sporadic hemophilia are in moms who are not carriers. The patient's mother's oocytes at the time of fertilization or in the early stages of embryonic development most likely include de novo pathogenic mutations that are the source of this status. It has been demonstrated that moms who do not appear to be virus carriers have a high percentage

				conformational polymorphism analysis, heteroduplex analysis, denaturing high-performance liquid chromatography, and Sanger sequencing are unable to identify low levels of somatic mosaicism. 3, 36, 37 Genetic testing has become less expensive and time-consuming thanks to new molecular technologies including droplet digital polymerase chain reaction (ddPCR), synthesis-based extension tests, next generation sequencing (NGS), and quantitative polymerase chain reaction (qPCR).	of mosaicism, necessitating substantial work to create sensitive tools for variant identification in addition to analyzing the DNA of specific organs.
(Phung & Nordmann, 1984) France	A Bayesian Approach	Porfirian	We examined the distribution of PBG-deaminase activity among 2,17 unrelated	In the Louis Mourier Hospital's Department of Biochemistry, 108 individuals with AIP were examined. The activity of	We have demonstrated that there is a substantial difference in the distribution of PBG-

			normal persons in order to calculate the proportion of potential misclassification.	PBG-deaminase was examined in 78 patients' relatives (a total of 655 individuals including patients). Only responses for those who were at least 1.5 years old were taken into consideration, as youngsters reported lower levels of activity than adults. Assay for PBG-Deaminase Activity PBG-deaminase activity was measured in erythrocytes by Grandchamp's spectrophotometric technique. Because reticulocytosis is linked to elevated PBG-deaminase, patients with high activity levels and reticulocytosis levels of at least 2% were not included.	deaminase activity among control persons and a Gaussian distribution. Three mixed normal distributions proved to be the best match for the data. These findings are not consistent with those of Wetterberg, who discovered a sex impact not present in our data. Additionally, they saw a p power transformation that differed significantly from our estimations, and there was no proof that more than one distribution was possible.
(Trunca, Mendell, & Schilit, 2022) US	experimental study	genetic disease	seeks to develop a viable model that would enable	Because balanced translocation carriers produce	The findings indicate that carriers of

		genetics experts to instantly determine the danger of their patients.	chromosomally imbalanced gametes, they are more likely to encounter reproductive problems, such as miscarriage and abnormalities in their offspring. When making reproductive decisions, people need to know how likely it is that they will have an imbalanced pregnancy, but estimating the risk can be challenging because most balanced translocations are unique. Drs. Trunca and Mendell developed a model based on logistic regression analysis of a data set comprising over 6000 people from over 1000 family translocations in order to enhance reproductive risk estimations. Although risk assessment using this model has	translocations with breaks close to the terminal terminus are more likely to have live-born offspring with imbalanced translocations, and that terminal spacing is another significant factor in predicting reproductive risk. There is an increased risk of miscarriage or stillbirth in translocation carriers whose tears are more medially located.

				been given as a free service for many years, this procedure. This protocol provides instructions on how to collect clinical data, utilize a Java software to create model-based risks, and analyze the results of the program.	
(Dunlop *et al.*, 1997) Inggris	experimental study	Cancer	Because the families investigated so far have been specifically chosen, it is uncertain how far mutations can penetrate to overcome conventional HNPCC families.	MMR gene examination Using in vitro synthesized protein scission (IVSP) tests in conjunction with single-strand conformational polymorphism analysis (SSCP PCR), RNA and DNA isolated from lymphoblastoid cell lines or from peripheral blood lymphocytes from patients with RER tumors were tested for MMR gene mutations. As previously mentioned (3, 18), IVSP analysis was carried out on PCR products	The findings of this investigation enable evaluation of the cancer risk in people with mutations in the mismatch repair gene. Because ascertainment bias invariably occurs when studying cancer risk prior to identifying HNPCC families, their risk estimates are less vulnerable to it.

			generated from cDNA templates reverse transcribed from peripheral blood lymphocyte or cell line RNA. While missense mutations are not detected by IVSP, truncating or splicing mutations are reliably detected (3,18, 26–28).

The journal database yielded 961 articles. After removing duplicates, checking the title and abstract, and checking the full text, 9 articles were released. Researchers then conducted a quality assessment of 9 articles; 2 articles with a score below 70% were excluded, and 7 articles that met the inclusion criteria were included in the systematic review (Fig. 1).

DISCUSSION

This review examines methods for calculating the inheritance of genetic diseases in humans. Analysis and synthesis was carried out on seven studies to look at the effect of interventions, on research Farbrother *et al.*, (2004) The method for calculating the heritability of genetic diseases in the cited articles involves estimating the sibling recurrence risk (KS) and the sibling recurrence risk ratio (λS) for high myopia. These estimates are based on studies of familial aggregation of high myopia in siblings with high probability of myopia and evaluating the influence of parental myopia on the sibling's risk of recurrence. The study suggests that high myopia is influenced by genetic and environmental factors, with the potential contribution of recessive genes. These findings suggest that high myopia may be a complex disease influenced by genetic factors, environmental factors, or both, and that the genetic factors known to cause high myopia occur in only a small proportion of cases.

The study Fotouhi *et al.*, (2007) addressed the familial aggregation of myopia in a Tehran population, highlighting the complex and multifactorial genetics of myopia. This study used the GEE model to analyze the data and found that cycloplegic refraction yielded less biased odds ratio estimates. Education level is associated with the prevalence of myopia, but it is not known for certain whether this is an independent risk factor or a

substitute for other factors. These findings suggest a high rate of aggregation of myopia within families, with siblings and parent-child pairs having a higher risk, indicating the potential influence of genetic factors on the prevalence of myopia. This study emphasizes the importance of genetic and environmental factors in the development of myopia, demonstrating that myopia exists on a spectrum influenced by complex genetic factors.

The study conducted by Daetwyler *et al.*, (2008) presented an equation to predict the accuracy of genetic risk prediction for complex diseases using a genomic approach. These equations are derived for continuous and dichotomous phenotypes and take into account factors such as heritability, number of loci, and sample size. The accuracy in predicting genetic disease risk in population and case-control studies was investigated, taking into account disease prevalence, heritability, known loci, and model selection approaches. The formula for the accuracy of genetic risk prediction on continuous and dichotomous phenotypes is the same, as long as the heritability is on the observed scale, and simulations confirm the accuracy of the formula on a wide range of parameters. Additionally, this equation is robust to changes in the distribution of allele effects and can be applied to case-control studies with adjustments for case and control selection.

Research Trunca, Mendell, & Schilit, (2022) discusses scenarios for calculating risk estimates in genetic counseling, focusing on factors such as translocations, miscarriage, and age-related risks. It emphasizes the importance of appropriate ascertainment categories and provides step-by-step calculations for determining risk estimates in complex situations. This study also presents a logistic regression model to estimate reproductive risk for balanced translocation carriers, taking into account variables such as carrier gender, familial ascertainment, and the chromosomes involved. This model provides an estimate of the probability of miscarriage or having a child with an unbalanced translocation, with the c value indicating the predictive power of the model. Analysis of data from translocation carriers revealed that structural characteristics of the translocation, sex of carrier, method of ascertainment, and chromosomal involvement all influence reproductive risk. Structural factors impact the type of segregation, female carriers have a higher risk of unbalanced translocations, and certain chromosomes and breakpoint locations increase risk, with terminal distance being an important factor in reproductive risk.

The article Lannoy & Hermans, (2020) discusses genetic mosaicism in hemophilia and provides practical information for evaluating the risk of disease transmission. This highlights the importance of detecting mosaicism for genetic counseling and risk estimation in hemophilia. The use of molecular techniques such as qPCR, NGS, single base extension assays, and ddPCR has improved the detection of low-grade mosaicism. It also advises against assuming non-carrier status in mothers who do not appear to be affected by the disease, and recommends prenatal diagnosis in subsequent pregnancies to assess the risk of transmission of the condition. New technology can help detect mosaicism and predict the pathological phenotype of the unborn baby, thereby reducing the need for invasive procedures.

The study Phung & Nordmann, (1984) used a Bayesian approach to estimate the risk of recurrence of Acute Intermittent Porphyria (AIP) based on analysis of Porphobilinogen

Deaminase activity. The researchers found an overlap between the values of the carrier and control groups, indicating a dual distribution. They proposed a Bayesian method to determine risk for individuals belonging to overlapping groups. By applying this approach, they were able to calculate the risk for specific families in the sample. Additionally, this study addresses the non-Gaussian distribution of PBG-deaminase activity among control individuals, indicating three interrelated normal distributions as the best fit. The study also explored interkin correlations in enzyme activity, strategies to reduce distributional overlap, and potential factors influencing disease progression. This study refers to various previous research articles on acute intermittent porphyria to support its findings and conclusions.

The study Dunlop *et al*., (1997) used a practical approach to identify carriers of MMR gene mutations and assess the risk of cancer in the family. This study assessed the risk of cancer associated with germline DNA mismatch repair gene mutations in individuals not from known HNPCC families. The study found that men with this mutation had a higher risk of colorectal cancer than women, while women had a higher risk of uterine cancer. This approach provides insight into the biological impact of defective DNA mismatch repair and may guide genetic counseling and clinical surveillance for individuals at high risk of cancer.

CONCLUSION

This article discusses various studies exploring the risk and recurrence of genetic diseases, including research on chromosomal translocations, genetic mosaicism in hemophilia, the risk of recurrence of Acute Intermittent Porphyria, DNA mismatch repair gene mutations, and risk factors for genetic diseases such as high myopia, hemophilia, and cancer. These studies highlight the importance of genetic factors in the development of these diseases, as well as their complexity and the importance of accurate risk prediction for genetic counseling. The intervention method for calculating genetic diseases has been proven to be able to determine the inheritance patterns passed down from parents to their children, so that this can follow up on further treatment that should be given to genetic disease sufferers.

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Conflict of interest

There is no conflict of interest.

Ethical approval

This research was approved by Health Research Ethics Committee, STIKes Muhammadiyah Ciamis in March 25, 2024 with the number 022/KEPK-STIKESMUCIS/III/2024.

Authors contributions

Each author contributed equally in all the parts of the research. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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