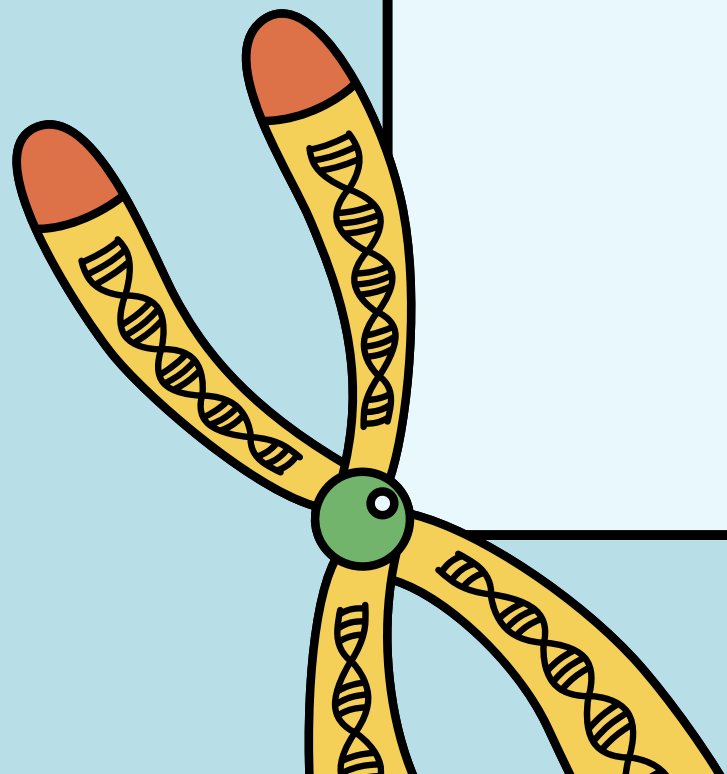
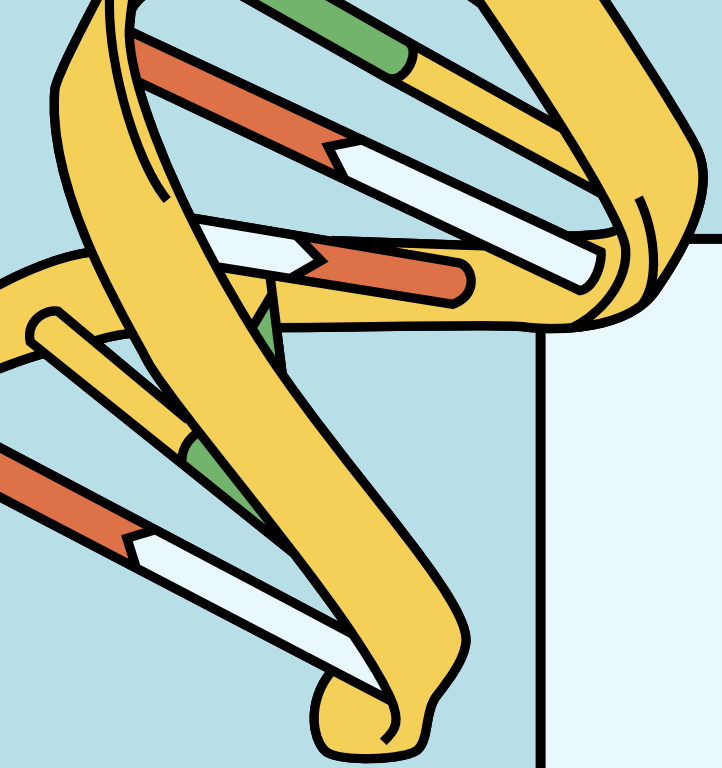


# Identifying the Biomarkers for Congenital Heart Disease



# Problem Statement

Identification of reliable and accurate biomarkers that can aid in the diagnosis and management of congenital heart disease

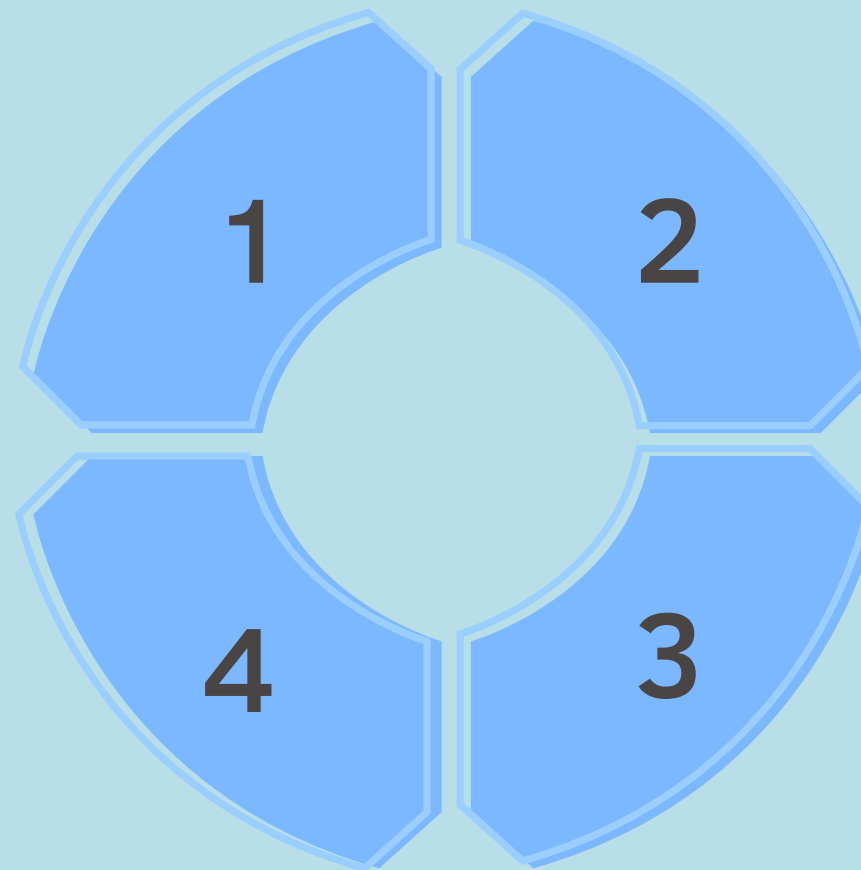
# Proposed Solution

Finding and filtering articles

Handling bias

Manual Review

Named Entity Recognition



1

# Finding and Filtering Articles

Performed by Nirmal, Vinayak Goel, Vinayak Arora and Ishan

# Pubmed Search Query

The screenshot displays the PubMed Advanced Search Builder interface. At the top, the NIH National Library of Medicine logo and a 'Log in' button are visible. The main heading is 'PubMed Advanced Search Builder'. Below this, a status bar indicates 'Filters applied: Free full text. Clear all'. The 'Add terms to the query box' section features a dropdown menu set to 'All Fields' and a text input field containing 'Enter a search term'. To the right of this input are buttons for 'AND' and 'Show Index'. The 'Query box' section contains a large text area with the following search query:   
(((biological markers OR biomarkers OR prognostic biomarkers) AND (heart defects, congenital OR congenital heart abnormalities OR congenital heart malformations)) NOT (adult OR elderly))  
[("Child"[Mesh]) AND "Biomarkers"[Mesh]) AND "Heart Defects, Congenital"[Mesh]  
To the right of the query box are buttons for 'Search' and a dropdown arrow.

Created a search query using PubMedAdvanced Search Builder using keywords from our problem statement like Biomarkers, Congenital heart disease, Target Age

# Pubmed Results

NIH National Library of Medicine  
National Center for Biotechnology Information

Log in

PubMed®

(((biological markers OR biomarkers OR prognostic biomarkers) AND (hear...))

Advanced Create alert Create RSS

Search  
Clear search input  
User Guide

Save Email Send to

Sorted by: Best match Display options

77 results

Filters applied: in the last 5 years. Clear all

MY NCBI FILTERS

RESULTS BY YEAR

Reset

2018 2023

TEXT AVAILABILITY

☐ Abstract

☐ Free full text

☐ Full text

☐ Pulmonary hypertension in children with Down syndrome.

1 Bush D, Galambos C, Dunbar Ivy D.

Cite Pediatr Pulmonol. 2021 Mar;56(3):621-629. doi: 10.1002/ppul.24687. Epub 2020 Feb 12.

PMID: 32049444 Review.

Share The presence of an additional copy of chromosome 21 (trisomy 21) increases the risk of developing PH in children with DS through many mechanisms, including increased hemodynamic stress in those with **congenital heart** disease, hypoxemia through impaired ventilation to ...

☐ Neutrophil-Lymphocyte Ratio in Congenital Heart Surgery: What Is Known and What Is New?

2 Manuel V, Miana LA, Jatene MB.

Cite

The search query fetched 77 results, with filters like papers from past 5 years and target age of under 23 months



# Rayyan - Literature Review

The screenshot displays the Rayyan Literature Review interface. On the left sidebar, there are sections for 'Auto Deduplicated' (3 exact matches, 77), 'Inclusion decisions' (Undecided: 77, Maybe: 0, Included: 0, Excluded: 0), 'Search methods' (Uploaded References: 77), 'Keywords for include' (Children: 51, Congenital Heart Disease: 35, CHD: 28, Biomarkers: 27, compared with: 9, Heart Failure: 7, Genes: 6, VSD: 6, control groups: 5, trial: 3), and 'Keywords for exclude' (cohort: 11, regression analysis: 7, observational: 6, cells: 5, cross-sectional: 4). The main panel shows a search for '2023-05-11: Meta-Analysis-Research' with 38 to 43 of 77 unique entries. A table lists search results with columns for Date, Title, Authors, and Rating. The selected entry is 'Comparative proteomic analysis of plasma of children with congenital heart disease' by Huang Q; Geng Z; Chen T; et al., dated 2019-07-01. Below the table, there are buttons for 'Include', 'Maybe', 'Exclude', 'Add Note', 'Highlights ON', and 'Upload PDF full-texts'. The article details section shows the title, abstract, authors, journal, publication types, locations, and topics. The abstract discusses the study of congenital heart disease (CHD) and its association with ventricular septal defect (VSD) in children, highlighting the use of tandem mass tags label-based quantitative proteomic analysis to compare plasma proteins.

**2023-05-11: Meta-Analysis-Research**

Showing 38 to 43 of 77 unique entries

Date	Title	Authors	Rating
2022-12-09	Role of serum cystatin C in the prediction of acute kidney injury following pediatric ca...	Zakaria M; Hassan T; Refaat...	
2019-07-01	Comparative proteomic analysis of plasma of children with congenital heart disease .	Huang Q; Geng Z; Chen T; ...	
2022-12-01	Acute Effects of Sodium Bicarbonate in Children with Congenital Heart Disease with ...	Loomba RS; Villarreal EG; D...	
2019-03-01	Procalcitonin and Other Common Biomarkers Do Not Reliably Identify Patients at Ris...	D'Souza S; Guhadasan R; Je...	
2022-04-01	Neuromarkers which can predict neurodevelopmental impairment among children wi...	Chineri LE; Tassew G; Tassew B...	

**Comparative proteomic analysis of plasma of children with congenital heart disease .**

**Abstract:** Congenital heart disease is one of the largest class of birth defects. Eight subjects with ventricular septal defect (VSD, a kind of congenital heart disease) and 11 healthy children were enrolled in tandem mass tags label-based quantitative proteomic analysis to compare plasma proteins differentially abundance. A total of 66 proteins were significantly upregulated or downregulated in VSD patients compared with healthy children. These proteins were involved in pathways linked to platelet activation, fructose and mannose metabolism, complement and coagulation cascades, glycolysis/gluconeogenesis, regulation of actin cytoskeleton, and carbon metabolism. The amount of ten proteins changed significantly ( $p < 0.05$ ) in newly recruited 30 VSD compared with 15 control children, which were validated by ELISA. The areas under the receiver operating characteristic curve values of fructose-bisphosphate aldolase B (ALDOB) and thymosin beta-4 (Tβ4) were higher than those of other candidate proteins. ALDOB and Tβ4 might be potential biomarkers applied for identifying VSD in the further works.

**Authors:** Huang Q; Geng Z; Chen T; Cheng X; Gu H; Li Q; Li D; Liu R;

**Journal:** Electrophoresis - Volume 40, Issue 14, pp. 1848-1854 - published 2019-07-01

**Publication Types:** Journal Article | Research Support, Non-U.S. Gov't

**Locations:** First Affiliated Hospital | Nanjing | Second Affiliated Hospital

**Topics:** Adolescent | Biomarkers | Blood Platelets/metabolism | Blood Proteins/\*analysis | Child | Child, Preschool | Female | Fructos...

Vinayak

Rayyan was used for screening the articles. The nbib files were uploaded to Rayyan.ai which used AI and NLP to filter out articles relevant to our research topic

2

# Handling Bias in Studies

Performed by Arbaaz, Arman and Ieshaan



# RoB2 for risk-of-bias

1

Randomization process

2

Deviations from intended interventions

3

Missing outcome data

4

Measurement of the outcome

5

Selection of the reported result

Intention-to-treat	Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall	
	11	11	-	-	biomarkers	1	+	!	+	+	!	!	+
	12	12	-	-	biomarkers	1	+	+	+	+	!	+	
	13	13	-	-	biomarkers	1	+	+	+	!	+	+	
	14	14	-	-	biomarkers	1	+	+	+	+	!	+	
	15	15	-	-	biomarkers	1	!	+	+	+	!	!	D1
	16	16	-	-	biomarkers	1	+	+	+	+	!	+	D2
	17	17	-	-	biomarkers	1	+	+	+	+	+	+	D3
	31	31	-	-	biomarkers	1	+	+	+	+	+	+	D4
	32	32	-	-	biomarkers	1	+	+	+	+	+	+	D5
	33	33	-	-	biomarkers	1	+	+	+	+	+	+	
	34	34	-	-	biomarkers	1	!	+	+	+	+	!	
	35	35	-	-	biomarkers	1	+	!	+	+	+	+	
	36	36	-	-	biomarkers	1	+	+	+	+	+	+	
	37	37	-	-	biomarkers	1	+	+	+	+	+	+	
	38	38	-	-	biomarkers	1	+	+	!	+	+	+	
	22	22	-	-	bimarkers	1	+	+	!	+	+	!	
	24	24	-	-	biomakers	1	+	+	+	+	+	+	
	23	23	-	-	biomarker	1	+	!	+	+	+	!	
	25	25	-	-	biomarkers	1	+	+	+	+	+	+	
	26	26	-	-	biomarkers	1	+	+	+	+	+	+	

+

Low risk

!

Some concerns

-

High risk

D1

Randomisation process

D2

Deviations from the intended interventions

D3

Missing outcome data

D4

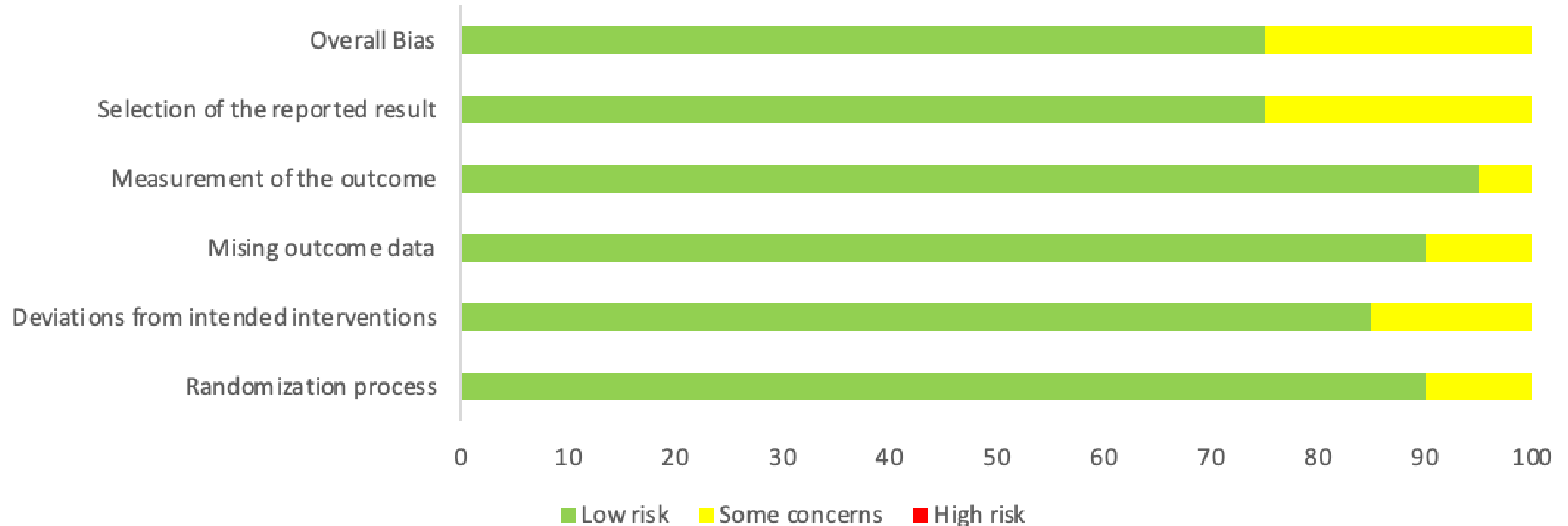
Measurement of the outcome

D5

Selection of the reported result

Used RoB2 tool, as mentioned by the cochrane guidelines, for finding risk of bias in all the selected studies

## As percentage (intention-to-treat)



No high risk studies were found. As a consequence, all selected studies were analyzed

3

# NER using ScispaCy

Performed by Harshil

# Named Entity Recognition on studies to identify potential biomarkers

abbreviated food-frequency questionnaire (17) was administered and information about the current use of multivi-tamins cigarettes alcohol ORGANISM and caffeine SIMPLE\_CHEMICAL intake was obtained

FIGURE 1 The interactive and interdependent pathways of folate SIMPLE\_CHEMICAL and methionine SIMPLE\_CHEMICAL metabolism as related to the synthesis of glutathione THF GENE\_OR\_GENE\_PRODUCT tetrahy- drofolate; MTHFR methylenetetrahydrofolate reductase; GENE\_OR\_GENE\_PRODUCT CBS ORGANISM\_SUBSTANCE cystathionine H9252-synthase; GCL glutamate-cysteine ligase GENE\_OR\_GENE\_PRODUCT ; GSH SIMPLE\_CHEMICAL reduced glutathione SIMPLE\_CHEMICAL ; GSSG SIMPLE\_CHEMICAL oxidized glutathione SIMPLE\_CHEMICAL ; GSTs GENE\_OR\_GENE\_PRODUCT glutathione-S transferases GENE\_OR\_GENE\_PRODUCT ; GR GENE\_OR\_GENE\_PRODUCT glutathione reductase GENE\_OR\_GENE\_PRODUCT ; BHMT GENE\_OR\_GENE\_PRODUCT betaine homocysteine SIMPLE\_CHEMICAL methyltransferase; GS glutathione synthase GENE\_OR\_GENE\_PRODUCT ; SAM CELLULAR\_COMPONENT S-adenosylmethionine SIMPLE\_CHEMICAL ; SAH S-adenosylhomocysteine ORGANISM ; CysGly GENE\_OR\_GENE\_PRODUCT cysteinylglycine SIMPLE\_CHEMICAL ; GluCys glutamylcysteine HEART GENE\_OR\_GENE\_PRODUCT

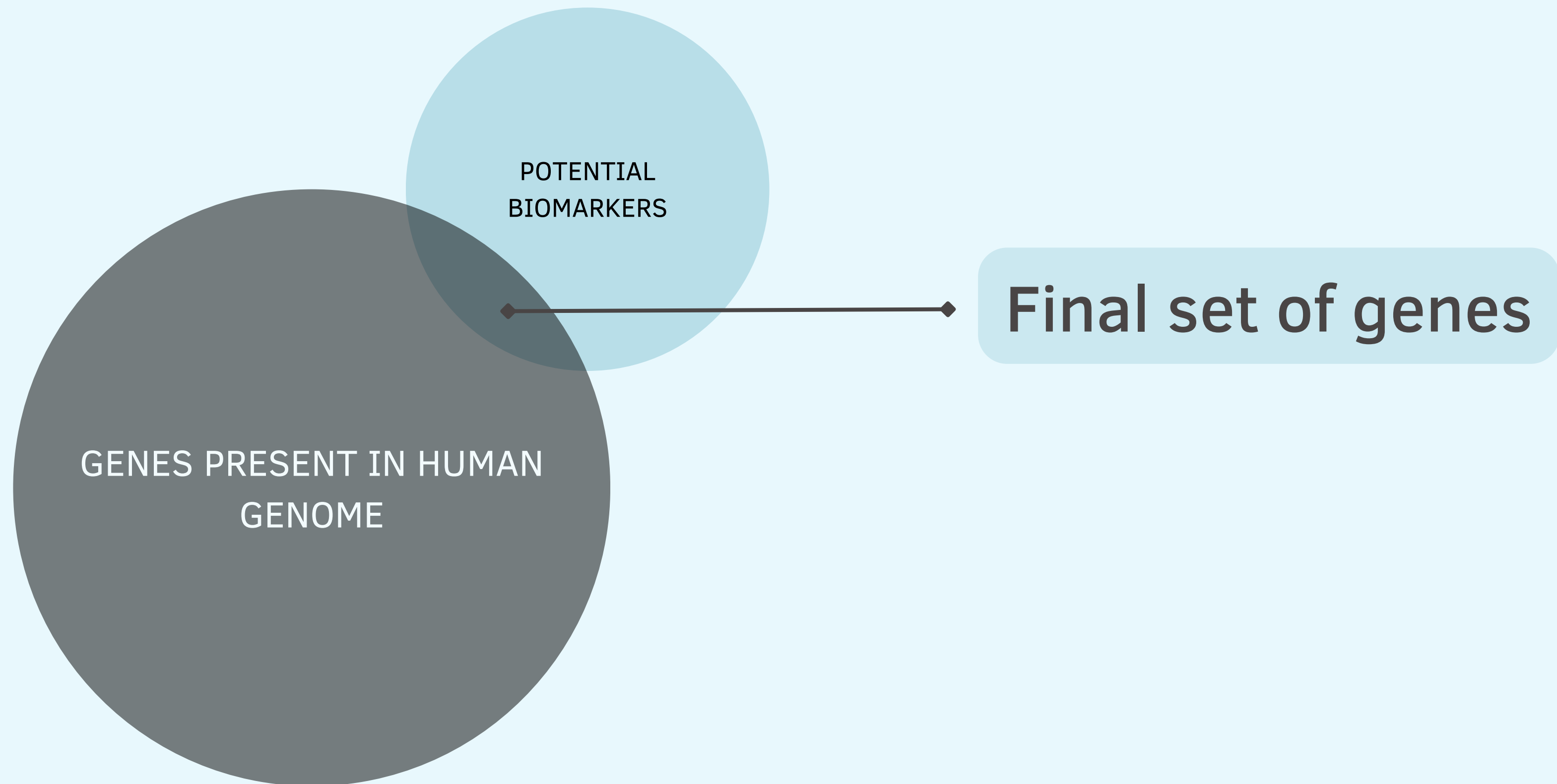
DEFECTS AND MATERNAL BIOMARKERS 599 Downloaded from https://academic.oup.com/ajcn/article/82/3/598/4862988 by guest on 11 May 2023

Sample preparation and biomarker measurement Blood samples CANCER were collected into evacuated tubes ( B-D GENE\_OR\_GENE\_PRODUCT Bio- sciences Dallas TX) containing EDTA SIMPLE\_CHEMICAL and immediately chilled on ice before being centrifuged at 4000 L1154g for 10 min at 4 ° C Plasma CELL aliquots were transferred into cryostat tubes TISSUE and stored at L115280 AMINO\_ACID °C until extraction and HPLC quantification To measure total homocysteine SIMPLE\_CHEMICAL cysteine and GSH SIMPLE\_CHEMICAL concentrations SIMPLE\_CHEMICAL 50 H9262L of a freshly prepared solution to reduce all sulf- hydryl bonds (1.43 mmol sodium borohydride SIMPLE\_CHEMICAL L 1.5 H9262mol EDTA L 66 SIMPLE\_CHEMICAL mmol NaOH L SIMPLE\_CHEMICAL and 10 H9262L isoamyl alcohol was added to 200 H9262L plasma ORGANISM\_SUBSTANCE

The samples CANCER were incubated at 40 °C in a shaker for 30 min To precipitate proteins 250 H9262L ice-cold 10% metaphosphoric acid was added and mixed well and samples CANCER were incubated for an additional 10 min on ice After centrifugation at 18 000 L1154g for 15 min at 4 ° C ORGANISM\_SUBSTANCE the supernatant fluid

NER Model : *'en\_ner\_bionlp13cg\_md'* trained on BIONLP13CG corpus

# Finding the final biomarkers with biomaRt



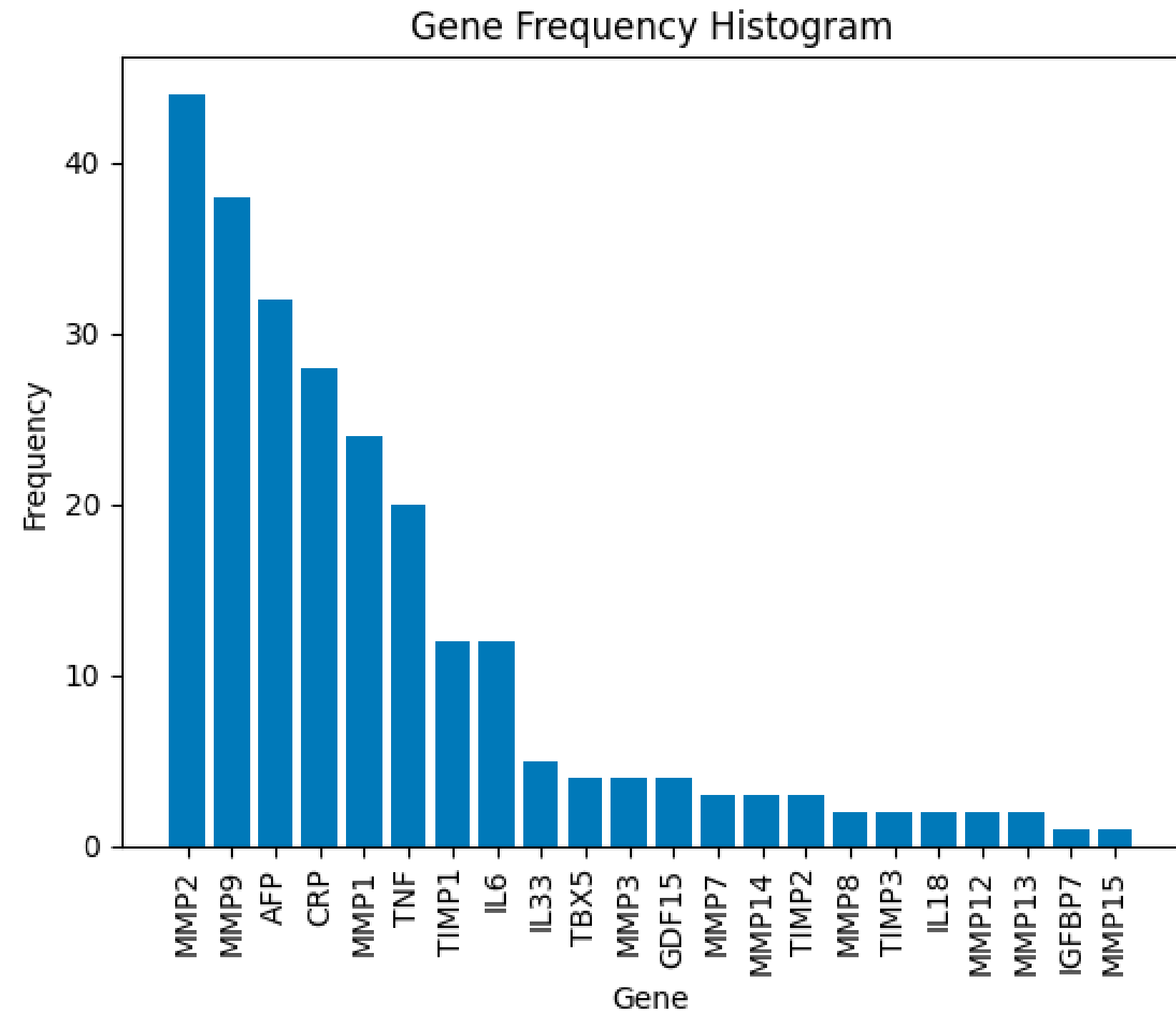


4

# Manual Review

Performed by Everyone

# Final Findings



# Future Perspective

Moving forward, further research could involve functional studies, validation experiments, and potentially exploring the clinical applications of the identified biomarkers in a real-world setting.

# Contributions & Acknowledgements

Arbaaz Choudhari (2021034) - Handling Bias in Studies

Arman Ganjoo (2021018) - Handling Bias in Studies

Harshil Mital (2021050)- NER using ScispaCy

Ishaan Awasthy (2021054)- Handling Bias in Studies

Ishan Saini (2021465)- Finding and Filtering Articles

Nirmal (2021074) - Finding and Filtering Articles

Vinayak Arora (2021112) - Finding and Filtering Articles

Vinayak Goel (2021113) - Finding and Filtering Articles

Special Thanks to **Mr. Alok Anand** for his help and guidance

# References for Project

## Articles

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<https://www.mdpi.com/1422-0067/23/9/4993>  
<https://sci-hub.se/https://www.futuremedicine.com/doi/full/10.2217/bmm.14.71>  
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## Documentation and Resources

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