

# mGWAS-Explorer 2.0 Tutorial

-- Browse mPheWAS



# Introduction

- Welcome to the tutorial on the pre-computed Phenome-Wide MR Analysis module of mGWAS-Explorer 2.0.
- This feature allows for the systematic exploration of potential causal relationships between **825 metabolites** and **236 phenotypes**.
- This tutorial will guide you through how to use this module effectively.

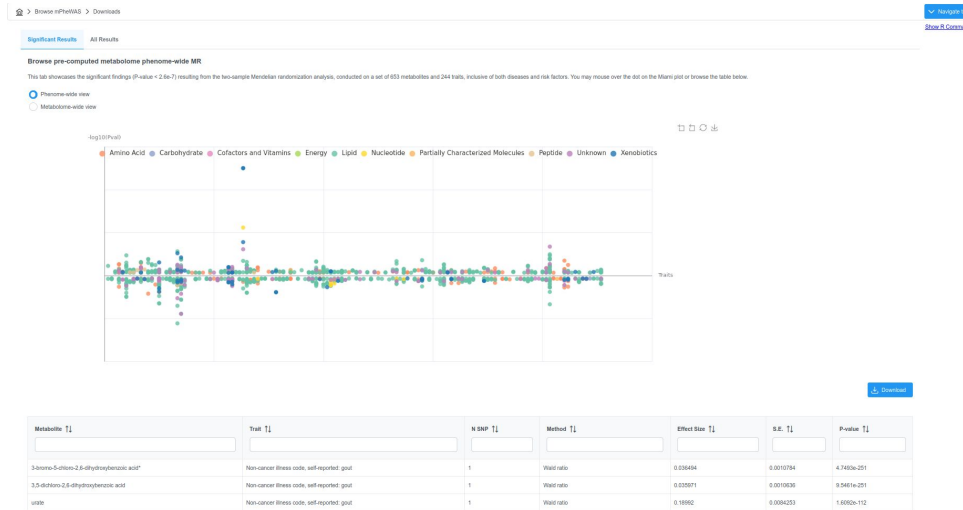
The screenshot displays the mGWAS-Explorer 2.0 interface. At the top is a dark blue navigation bar with the logo on the left and links for Home, Tutorial, Forum, mGWASR, and Updates on the right. Below the navigation bar is a grid of eight feature cards arranged in two rows and four columns:

<b>Start with Metabolites</b> Connect metabolites to SNPs, genes or diseases	<b>Start with SNPs</b> Connect SNPs to genes, metabolites or diseases	<b>Start with Genes</b> Connect genes to SNPs, metabolites or diseases	<b>Integrated Search</b> Joint search of individual SNP and/or metabolite
<b>MR Analysis</b> Perform Mendelian randomization analysis	<b>Browse mPheWAS</b> Browse phenome-wide MR of metabolome	<b>Browse mGWAS</b> Browse 65 manually curated mGWAS studies	<b>mGWASR Package</b> Use R package for batch processing or extension

A red arrow points to the 'Browse mPheWAS' card. Below the grid, a note states: 'Please use [OmicsForum](#) for support & troubleshooting request'. At the bottom center, the text 'Main Features' is displayed.

# The scope of pre-computed MR analysis

- Our Phenome-Wide MR analysis is based on five recent mGWAS, where we identified 1825 SNPs associated with 1016 metabolites.
- Post-selection criteria, we retain 1544 SNPs and 825 metabolites to perform a two-sample Mendelian Randomization (2SMR) analysis on 236 phenotypes.



# Unpacking MR results

- In the user interface, you'll notice that the results are neatly organized under two separate tabs for easy navigation.
- The first tab is labeled "Significant Results," where you'll find only those associations that meet our significance threshold (table + plot).
- The second tab, labeled "All Results," provides a comprehensive view of all the associations analyzed, regardless of their significance level (table only).



# Significant results

- The cutoff for a significant P value in our MR results is  $2.57 \times 10^{-7}$ .
- This stringent threshold is established by applying Bonferroni correction to adjust for multiple testing.

Enter your metabolite of interest into the search box.

Metabolite $\uparrow\downarrow$	Trait $\uparrow\downarrow$	N SNP $\uparrow\downarrow$	Method $\uparrow\downarrow$	Effect Size $\uparrow\downarrow$	S.E. $\uparrow\downarrow$	P-value $\uparrow\downarrow$
3-bromo-5-chloro-2,6-dihydroxybenzoic acid*	Non-cancer illness code, self-reported: gout	1	Wald ratio	0.036494	0.0010784	4.7493e-251
3,5-dichloro-2,6-dihydroxybenzoic acid	Non-cancer illness code, self-reported: gout	1	Wald ratio	0.035971	0.0010636	9.5461e-251
urate	Non-cancer illness code, self-reported: gout	1	Wald ratio	0.18992	0.0084253	1.6092e-112
nervonylcarntine (c24:1)*	Crohn's disease	3	Inverse variance weighted	-1.235	0.054936	6.3268e-112
x-11351	Inflammatory bowel disease	3	Inverse variance weighted	-0.82511	0.041097	1.1679e-89
nervonylcarntine (c24:1)*	Inflammatory bowel disease	3	Inverse variance weighted	-0.90932	0.042291	1.1679e-89
levulinoylcarntine	Non-cancer illness code, self-reported: gout	5	Inverse variance weighted	0.017739	0.00094414	9.4124e-79
margaroylcarntine (c17)*	Crohn's disease	2	Inverse variance weighted	-1.4977	0.084053	5.738e-71
x-11351	Non-cancer illness code, self-reported: asthma	3	Inverse variance weighted	0.047816	0.0027428	4.6252e-68
pc ae c36:3	Non-cancer illness code, self-reported: asthma	8	Inverse variance weighted	-0.021023	0.0012098	1.2411e-67
margaroylcarntine (c17)*	Height	2	Inverse variance weighted	-0.34545	0.020239	2.5643e-65
linoleoylcarntine (c18:2)*	Height	2	Inverse variance weighted	-0.28003	0.016406	2.5643e-65
x-24241	Non-cancer illness code, self-reported: gout	6	Inverse variance weighted	0.005736	0.00034507	4.7689e-62
pc ae c34:2	Crohn's disease	5	Inverse variance weighted	0.60583	0.038069	5.0594e-57
margaroylcarntine (c17)*	Inflammatory bowel disease	2	Inverse variance weighted	-1.0991	0.06922	8.9079e-57

Download

Click here to download the table.

# Interpreting the Miami plot

Switch between phenome-wide or metabolome-wide view.

Phenome-wide view  
 Metabolome-wide view



- The Miami plot provides a clear visual summary of the phenome-wide Mendelian randomization results.
- Traits are sorted according to biologically meaningful categories on the x-axis.
- The y-axis represents the  $-\log_{10} P$  value of the MR results.
- Positive and negative effect MR results are depicted on the top and bottom half of the plot respectively.
- The color coding indicates different metabolite super pathways.
- Hover your mouse over any point to display more detailed information.

# Browse all results

- To start exploring all the results, simply click on the tab labeled "All Results." Once there, you will see a search box. This is where you can enter the name of a metabolite or trait that you're interested in. For example, you could type in 'glycine' or 'coronary heart disease.'
- Below the search box, you'll see options to select between "MR results," "Sensitivity tests," or "Single SNP analysis." Choose the one that is most relevant to your research needs. Once you've made your selection, click on the "Browse" button to start viewing the data.

Significant Results **All Results**

**Browse pre-computed metabolome phenome-wide MR**

This tab currently contains the results of the two-sample Mendelian randomization and sensitivity analyses performed on 653 metabolites and 244 traits, including both diseases and risk factors. To initiate the utilization of this tool, please enter a metabolite or trait in the designated "Browse" field. For instance, you may input terms such as 'glycine' or 'coronary heart disease'.

1

e.g., glycine

2 MR results

3

Metabolite ↓↑	Trait ↓↑	N SNP ↓↑	Method ↓↑	Effect Size ↓↑	S.E. ↓↑	P-value ↓↑
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
glycine	e.g., glycine	20	Inverse variance weighted	-0.4136	0.079042	1.6704e-07
glycine		17	Inverse variance weighted	0.0025755	0.00059544	1.523e-05
glycine		17	Inverse variance weighted	0.0026912	0.00063188	2.0533e-05
glycine		20	Inverse variance weighted	-0.40442	0.096492	2.7748e-05
glycine		20	Inverse variance weighted	-0.015261	0.0038772	8.2787e-05
glycine		17	Inverse variance weighted	-0.0033961	0.0009295	0.0002585
glycine	Diagnoses - main ICD10: D22.3 Melanocytic naevi of other and unspecified parts of face	17	Inverse variance weighted	-0.0019779	0.00055865	0.00039946

# Conclusion - utilizing pre-computed phenome-wide MR

- Phenome-Wide MR analysis is a powerful tool that allows for the systematic investigation of potential causal relationships between metabolites and phenotypes.
- We invite you to use mGWAS-Explorer 2.0 to explore these pre-computed results and apply these insights to your research.
- Your feedback and questions are invaluable to us. If you encounter any issues, have suggestions for improvements, or simply want to share your success stories with mGWAS-Explorer 2.0, please do not hesitate to post on our OmicsForum: <https://omicsforum.ca/c/mgwas-explorer/12>