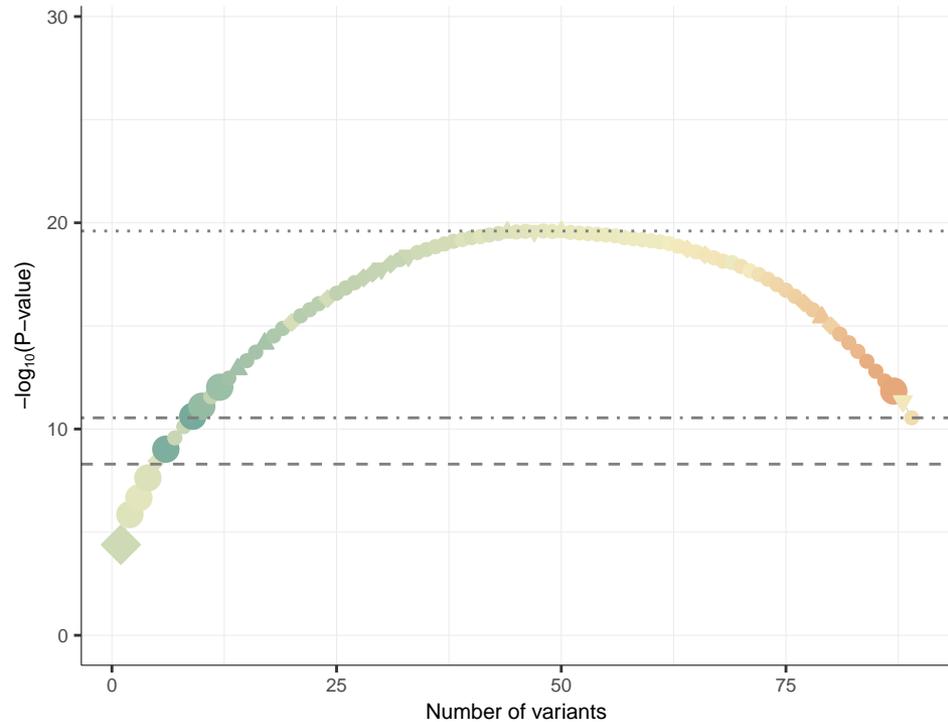


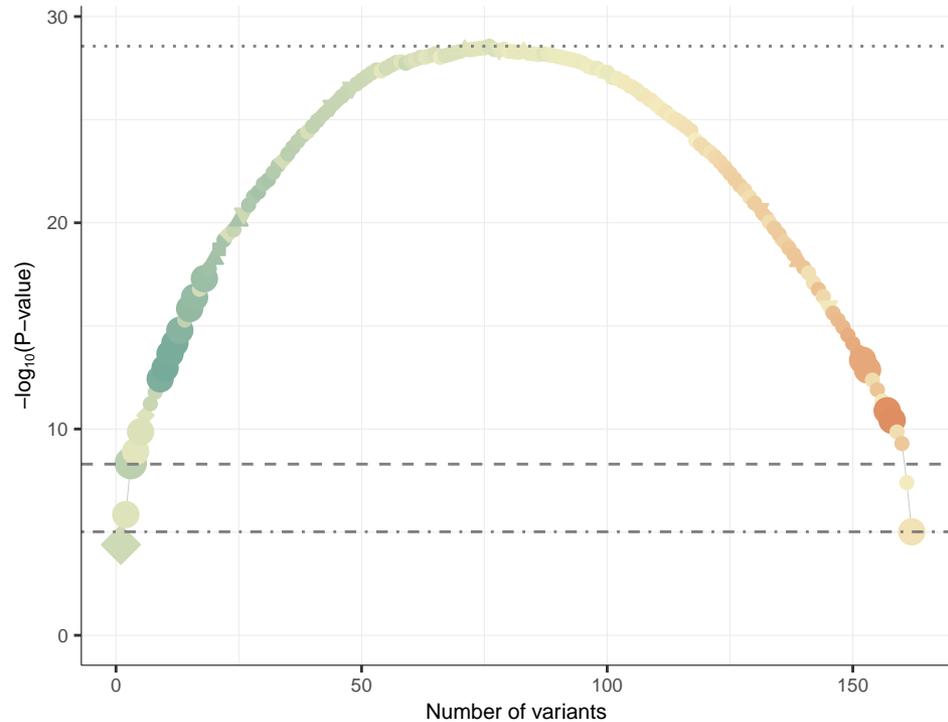
Supplementary Data 2: Contribution of individual QVs to their gene-based association signal with plasma and urine metabolite levels.

For each significant gene-metabolite pair in plasma and/or in urine (sorted by gene and metabolite's biochemical name), the symbols visualize the $-\log_{10}(\text{P-value})$ (y-axis) for the successive aggregation of the most influential QVs with respect to the forward selection procedure (Bomba et al. 2022, PMID: 35568032, Methods) based on burden tests for both masks (LoF_mis on the left, HI_mis on the right). The number of QVs aggregated for burden testing is given on the x-axis. Symbol shape indicates the variant's consequence. The symbol color and size reflect the effect size and the P-value of the variant based on its single-variant association test. The gray dashed lines represent the significance threshold ($-\log_{10}(5.04\text{e-}9)$ for plasma and $-\log_{10}(4.46\text{e-}9)$ for urine), the total $-\log_{10}(\text{P-value})$ of the aggregate variant test including all QVs in the respective gene and mask, and the $-\log_{10}(\text{lowest P-value})$ that can be reached by aggregating only the driver variants from the forward selection procedure. Hence, the variants sorted on the left, which provide the lowest P-value when aggregated, represent the driver variants (for further variant annotation see **Supplementary Tables 7a,b**).

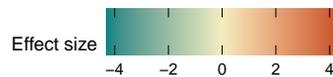
lactosyl-N-nervonoyl-sphingosine (d18:1/24:1)* in plasma at ABCA7 (LoF_mis)



lactosyl-N-nervonoyl-sphingosine (d18:1/24:1)* in plasma at ABCA7 (HI_mis)

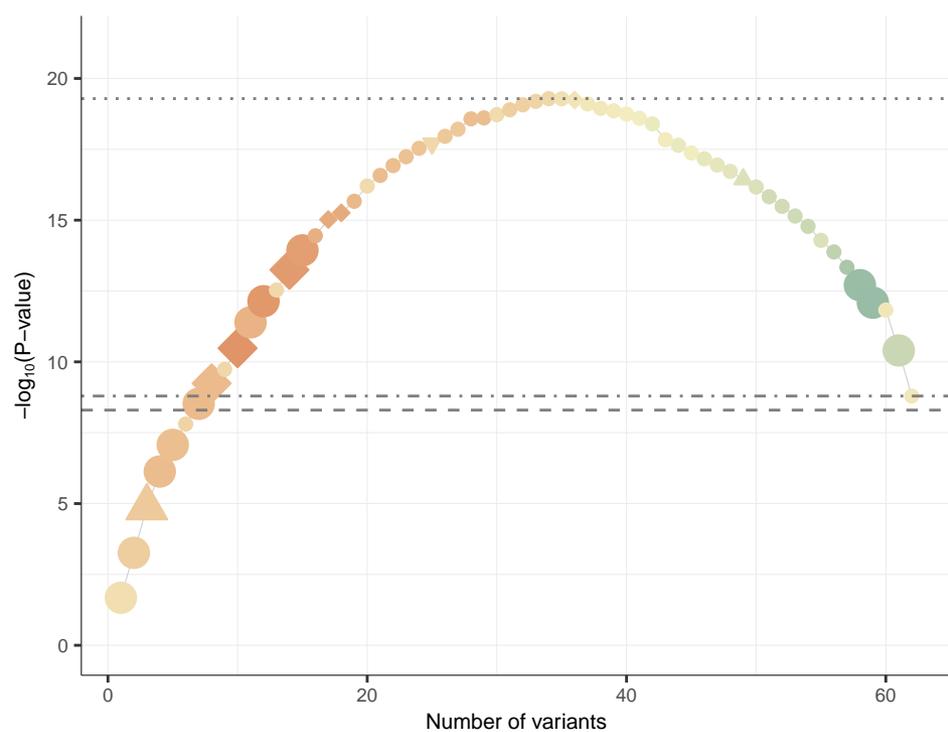
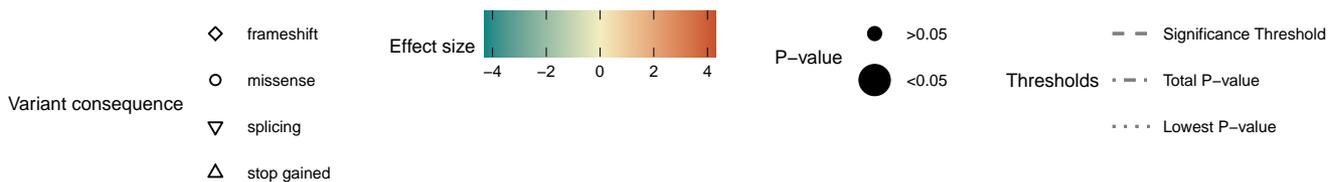
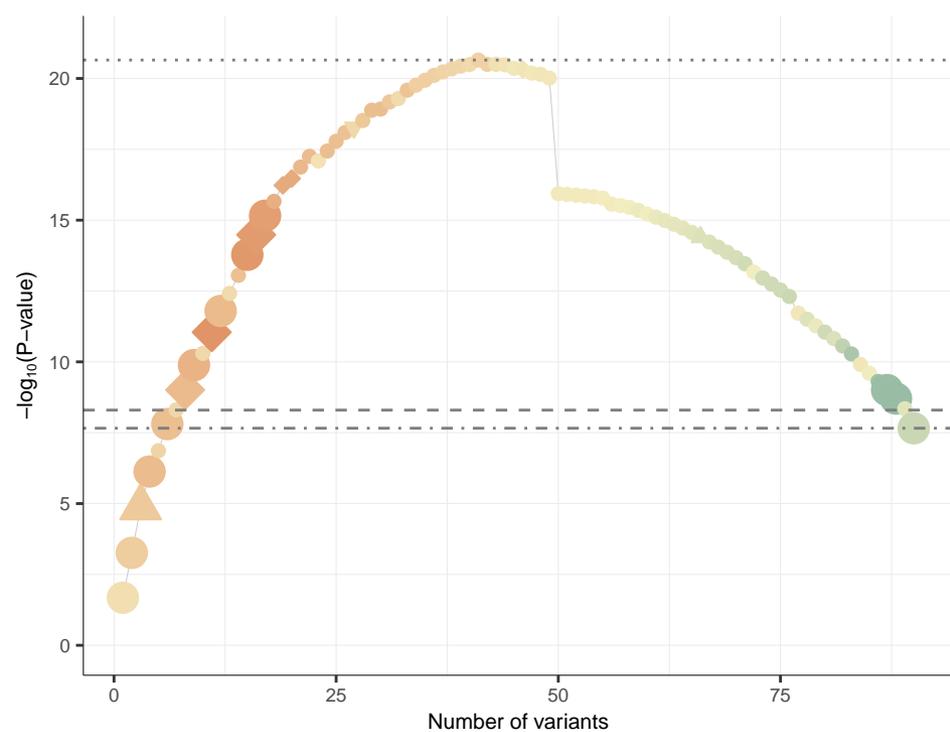


- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - start/stop lost
 - △ stop gained

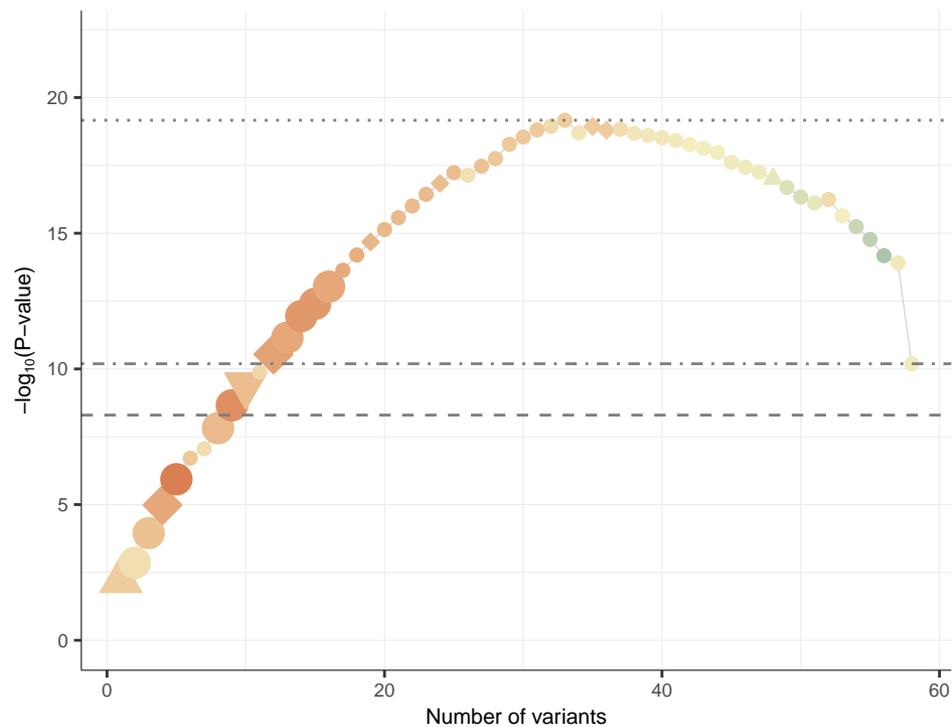


- P-value
- >0.05
 - <0.05
 - <1e-3

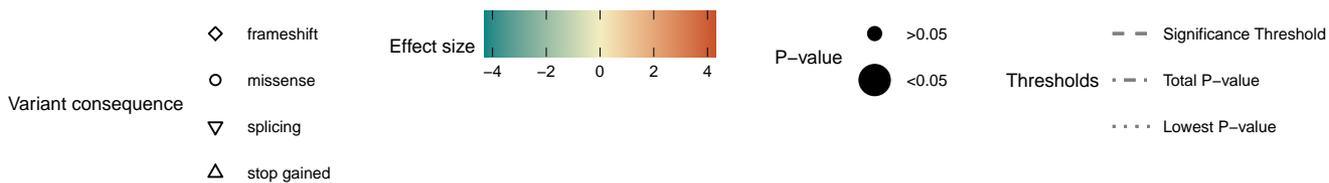
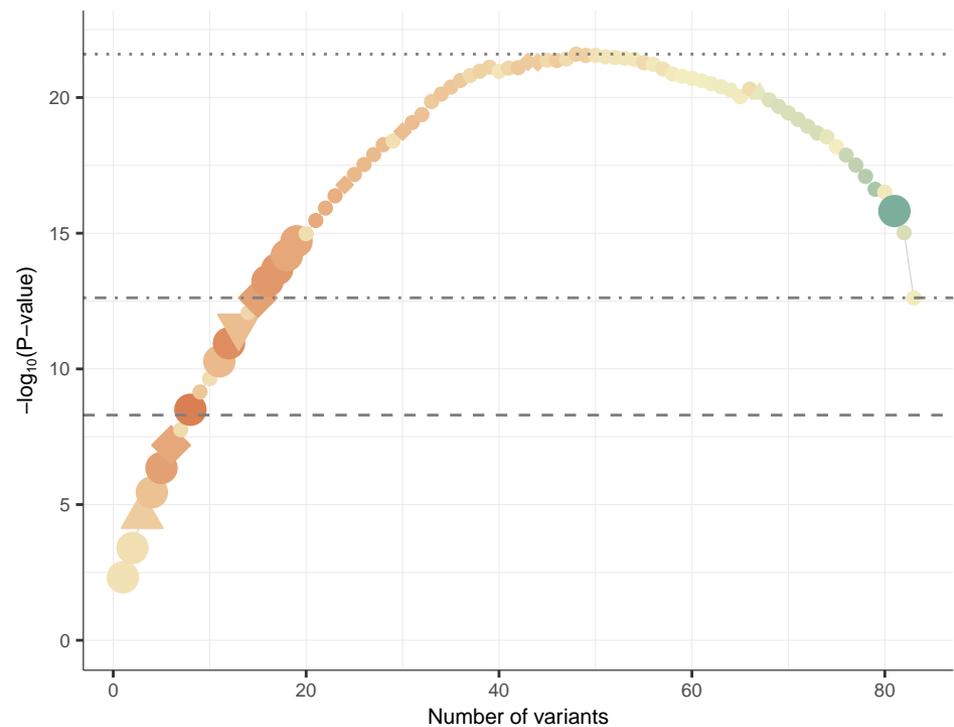
- Thresholds
- Significance Threshold
 - - - Total P-value
 - ⋯⋯ Lowest P-value

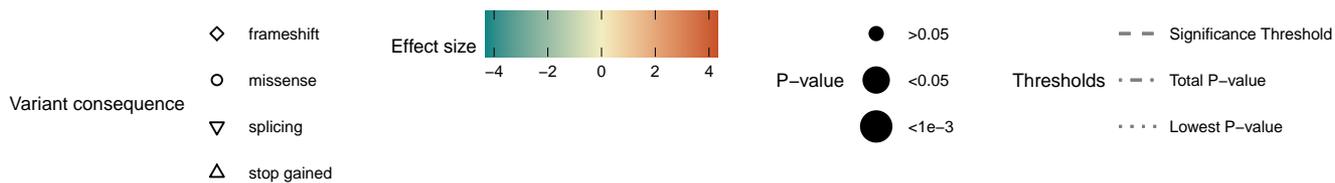
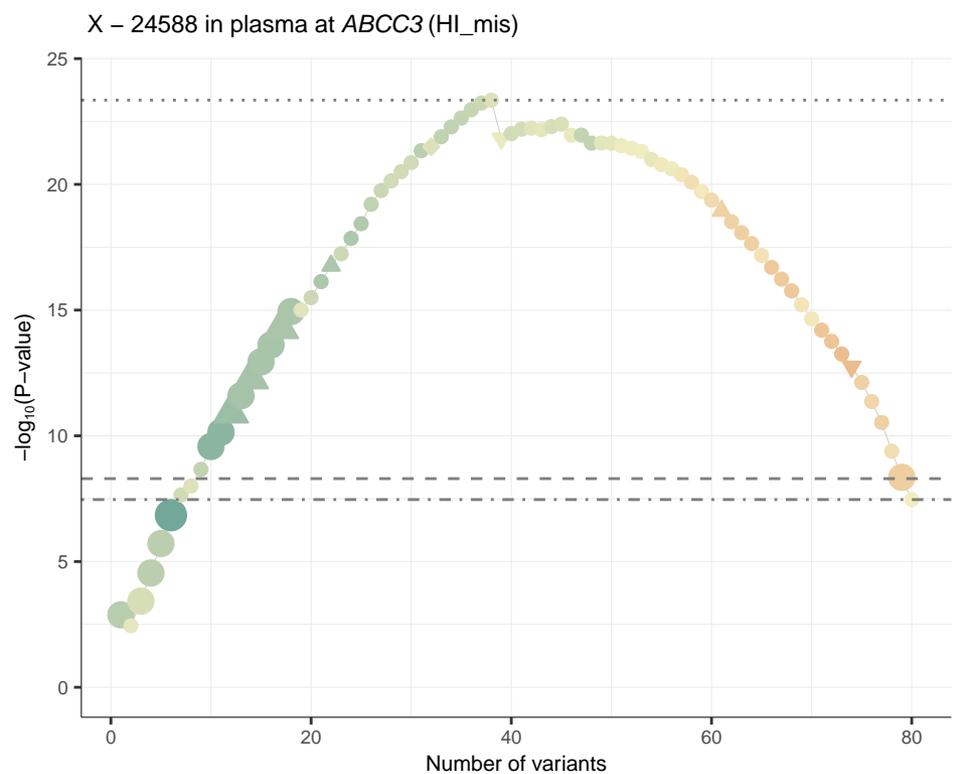
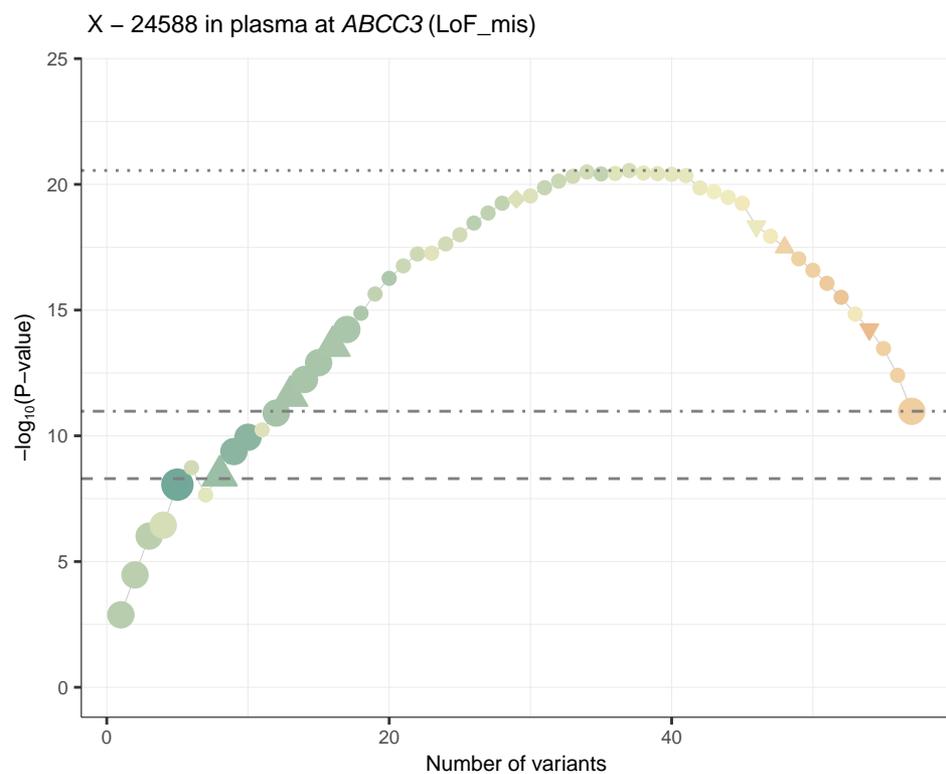
glycocholenate sulfate* in plasma at *ABCC2* (LoF_mis)glycocholenate sulfate* in plasma at *ABCC2* (HI_mis)

X - 21441 in plasma at *ABCC2* (LoF_mis)

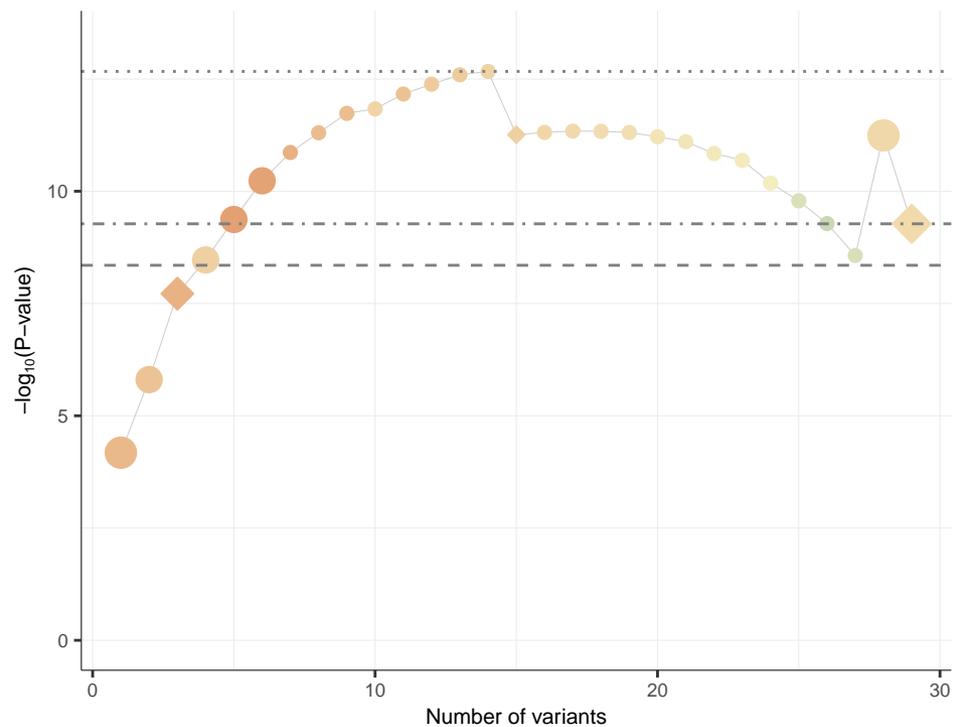


X - 21441 in plasma at *ABCC2* (HI_mis)

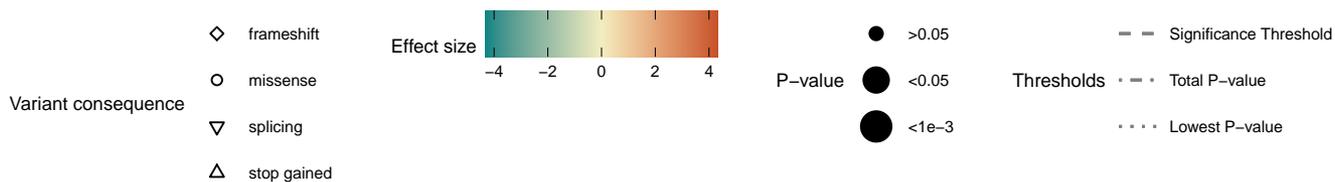
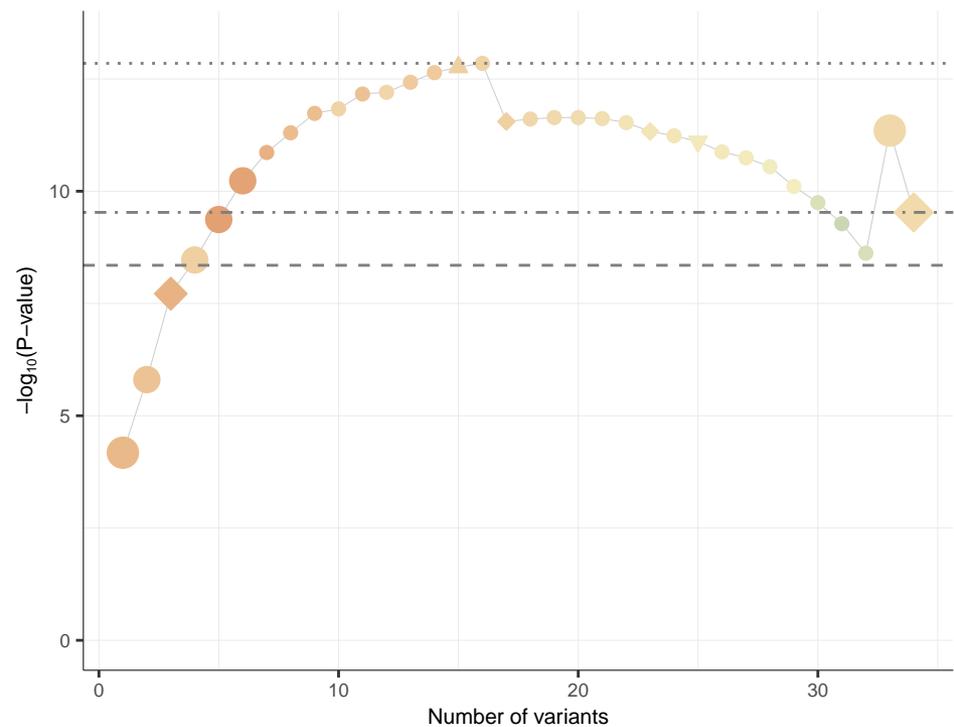




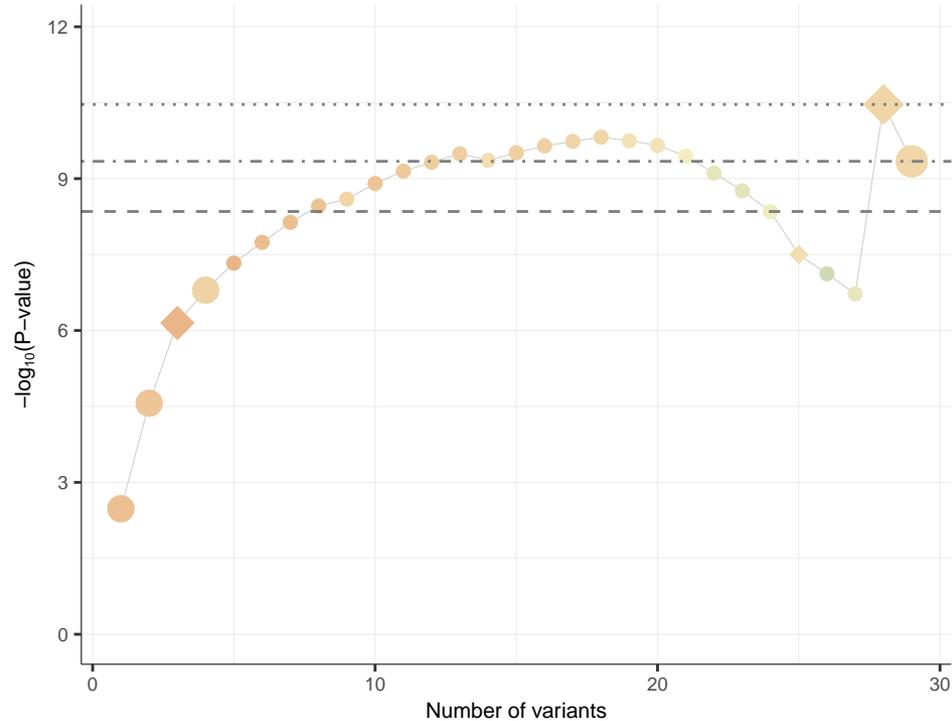
glycine conjugate of C9H16O2* in urine at ACADL (LoF_mis)



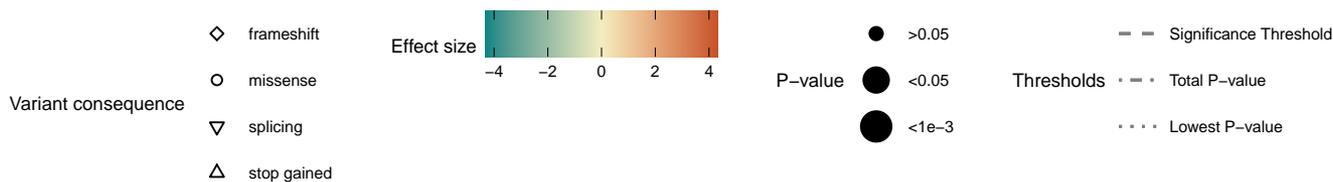
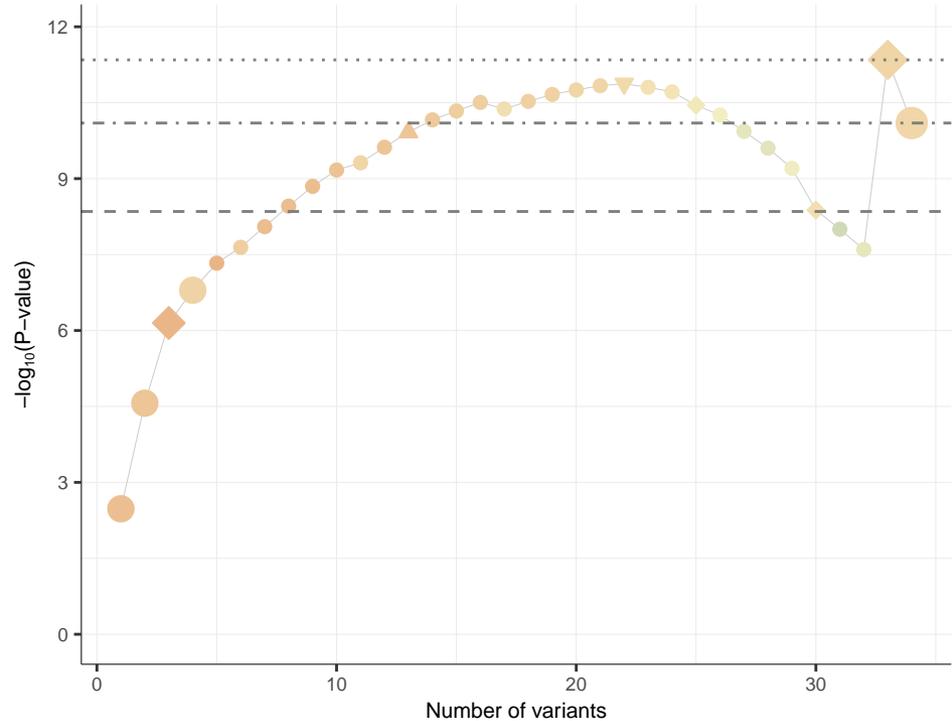
glycine conjugate of C9H16O2* in urine at ACADL (HI_mis)



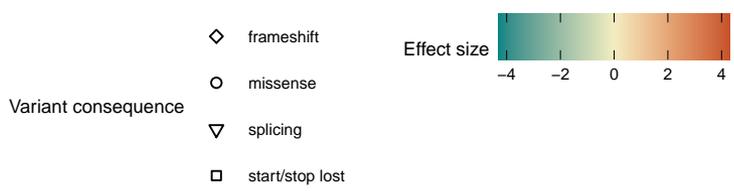
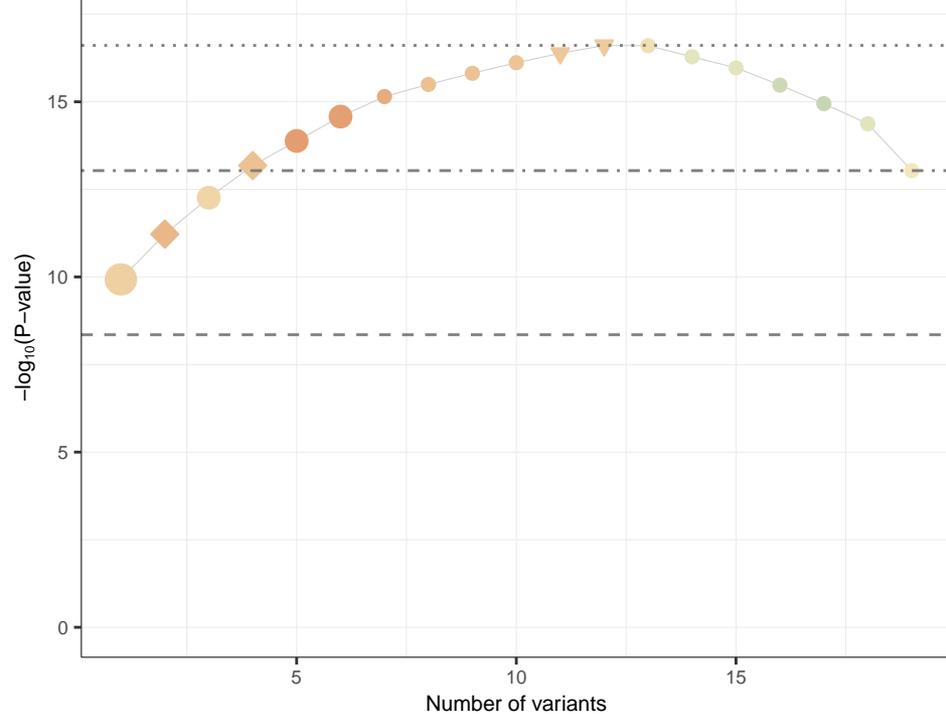
X - 24798 in urine at ACADL (LoF_mis)



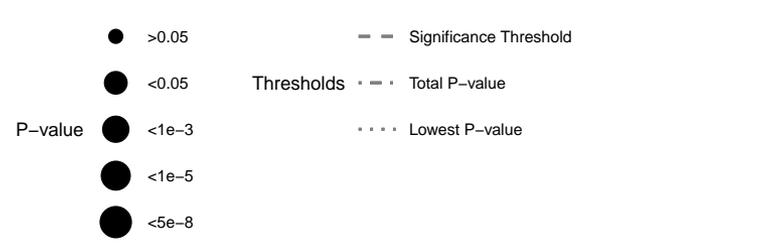
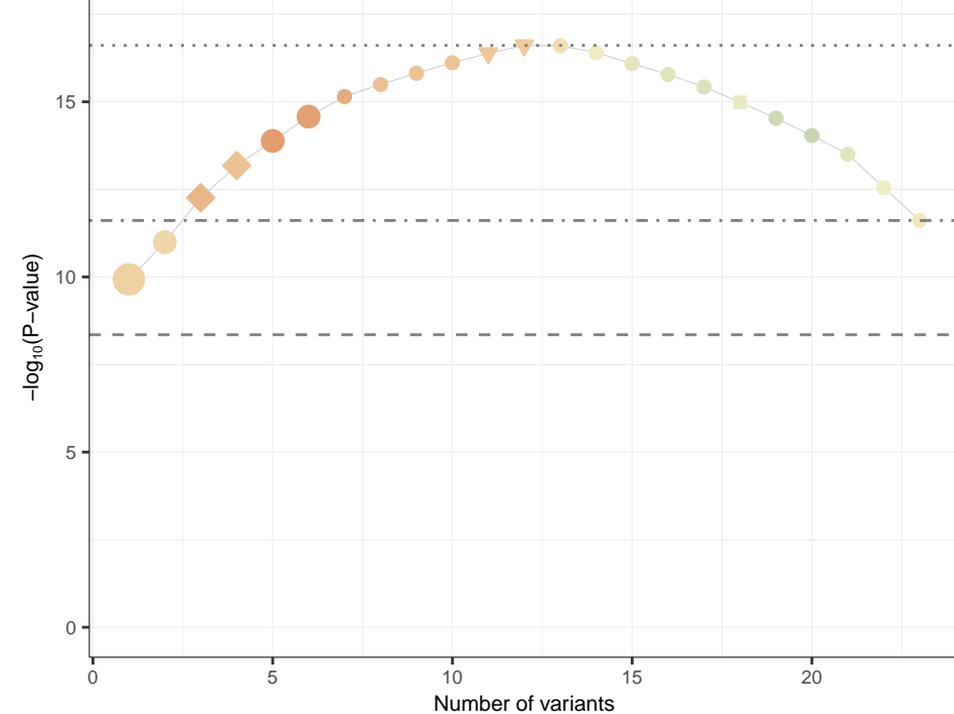
X - 24798 in urine at ACADL (HI_mis)



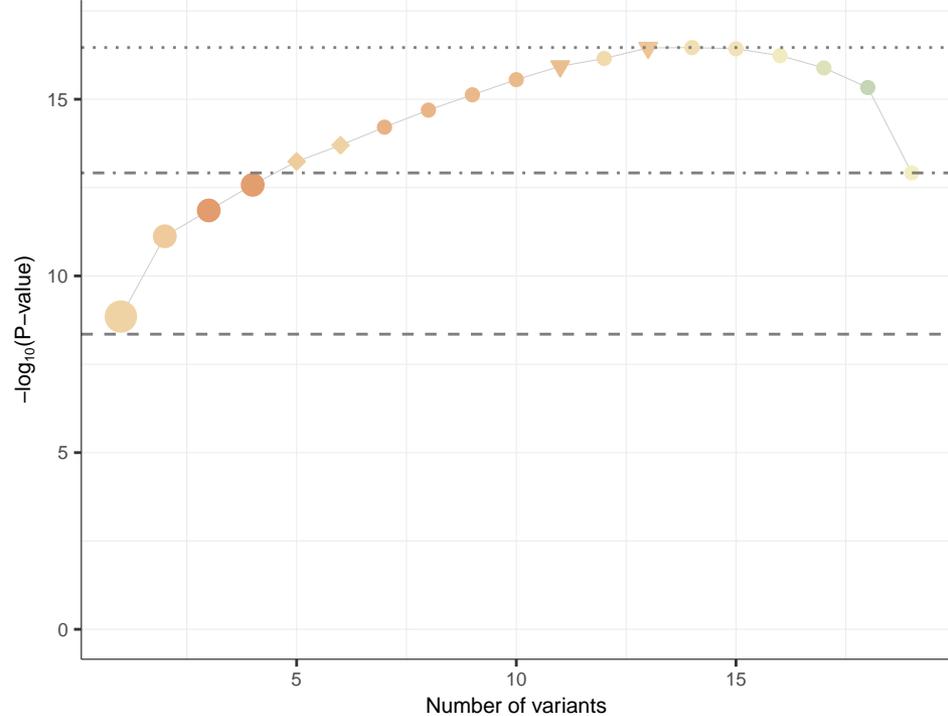
4-methylhexanoylglutamine in urine at ACADM (LoF_mis)



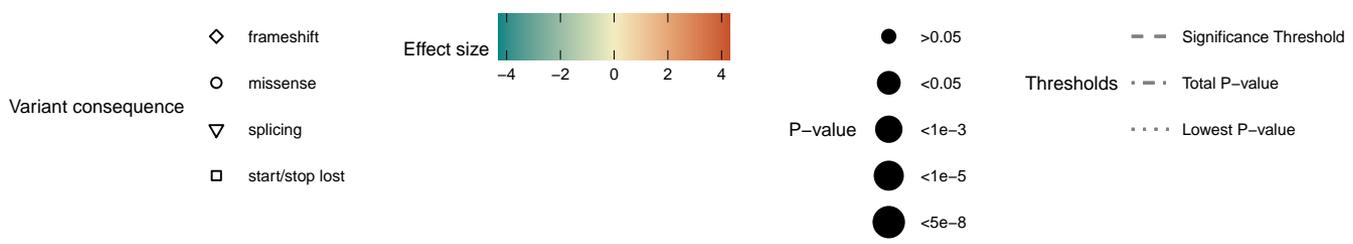
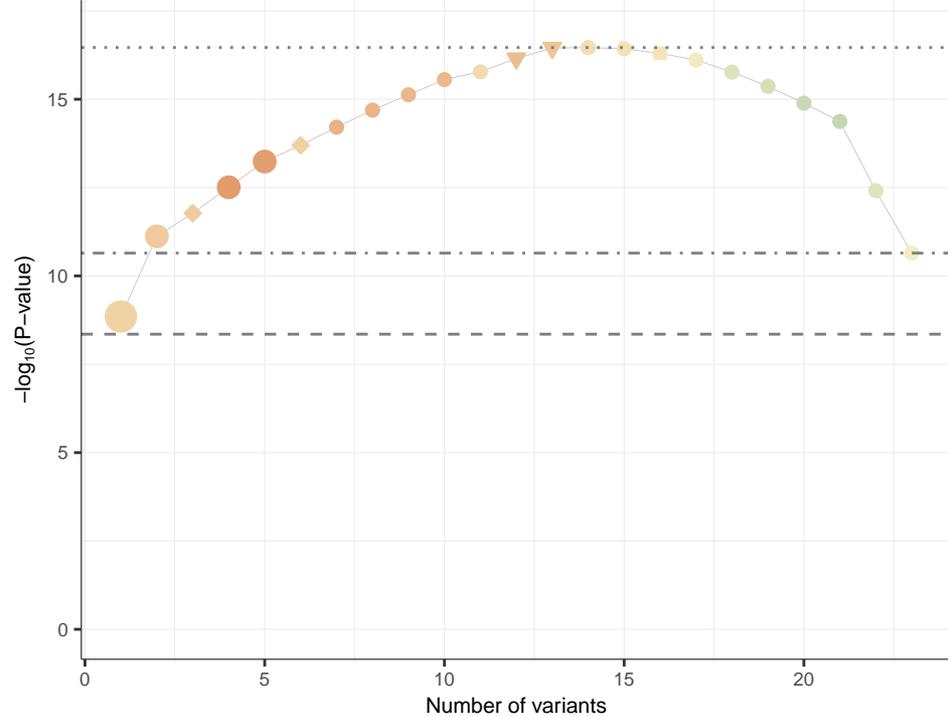
4-methylhexanoylglutamine in urine at ACADM (HI_mis)



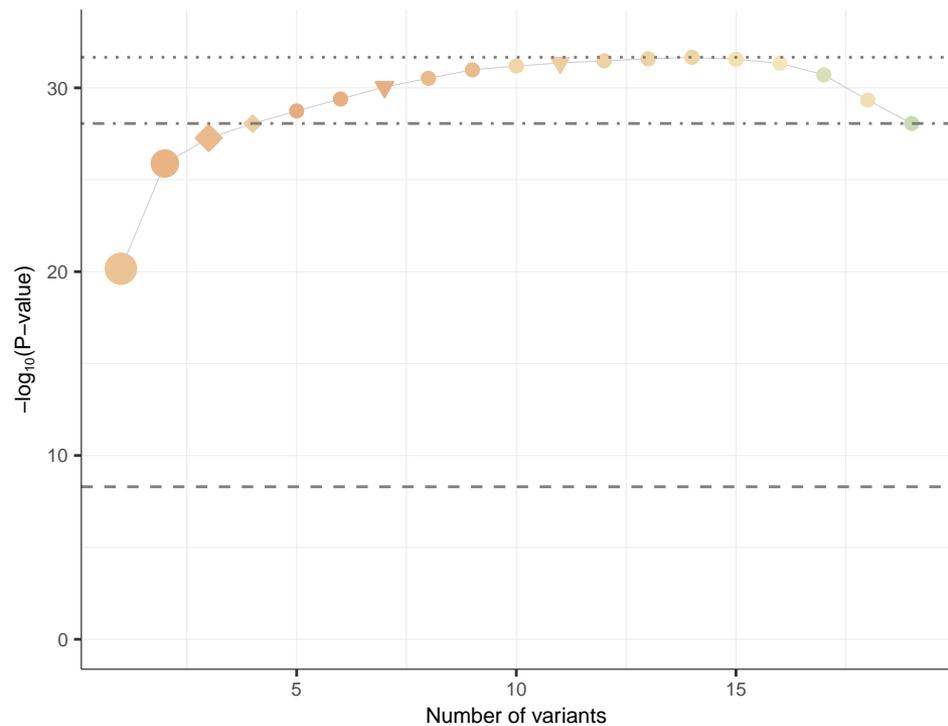
4-methylhexanoylglycine in urine at ACADM (LoF_mis)



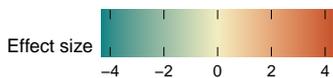
4-methylhexanoylglycine in urine at ACADM (HI_mis)



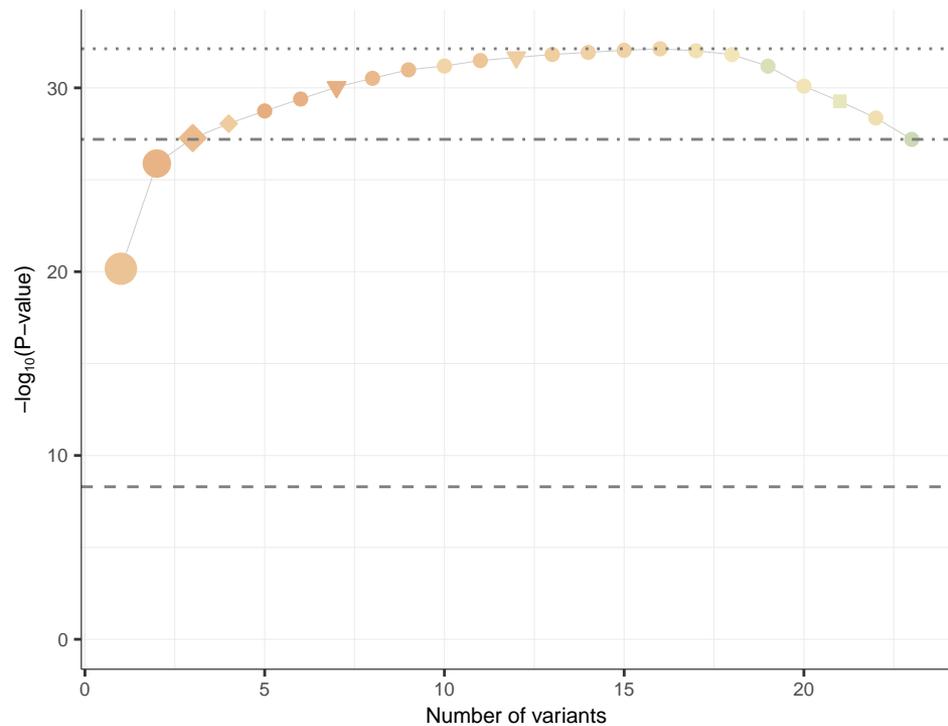
cis-4-decenoate (10:1n6)* in plasma at ACADM (LoF_mis)



- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - start/stop lost



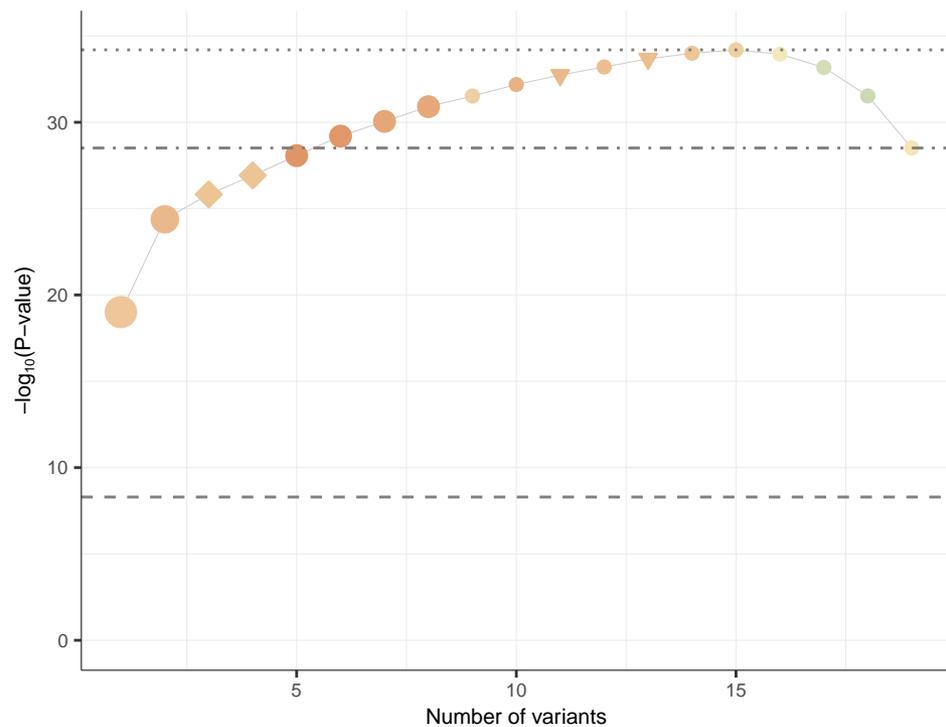
cis-4-decenoate (10:1n6)* in plasma at ACADM (HI_mis)



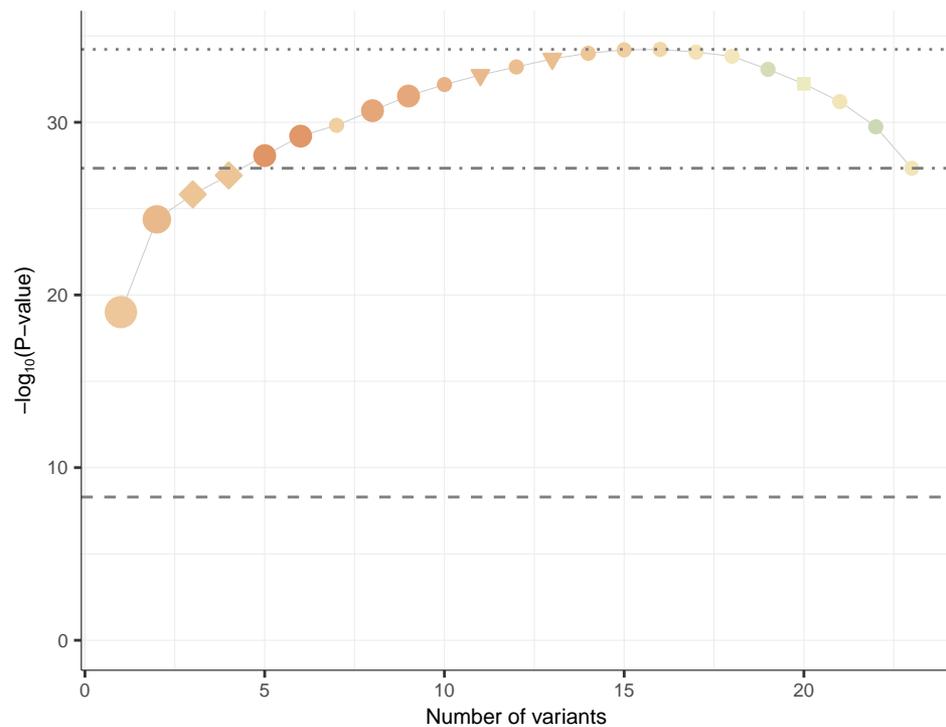
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

- Thresholds
- - - Significance Threshold
 - · - Total P-value
 - · · Lowest P-value

cis-4-decenoylcarnitine (C10:1) in plasma at ACADM (LoF_mis)

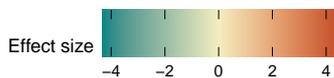


cis-4-decenoylcarnitine (C10:1) in plasma at ACADM (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- start/stop lost



P-value

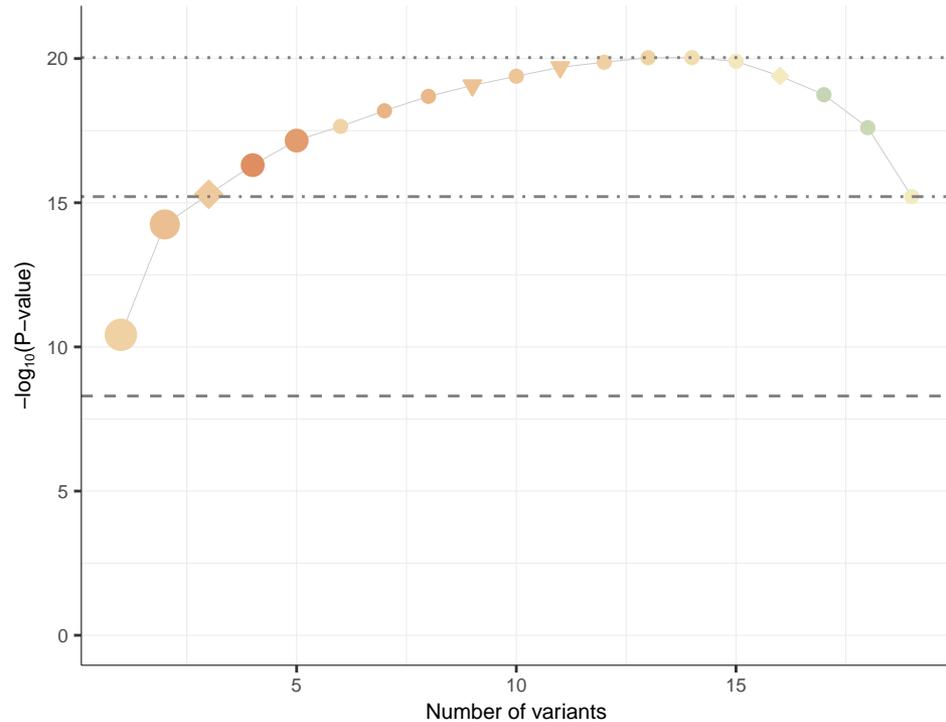
- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Significance Threshold

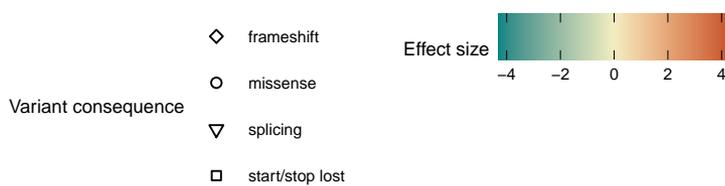
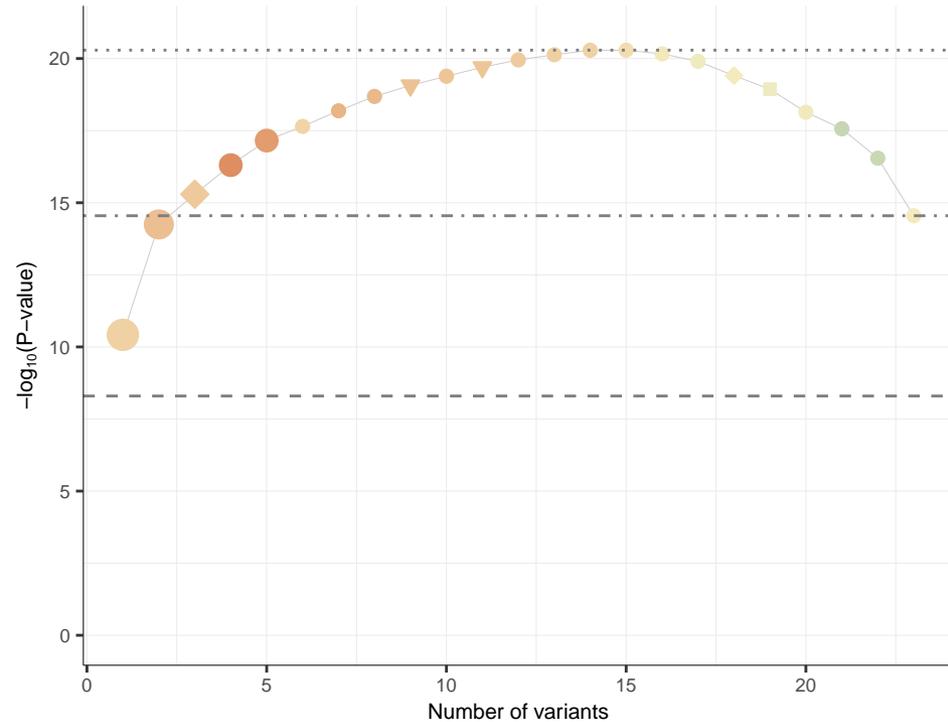
Total P-value

Lowest P-value

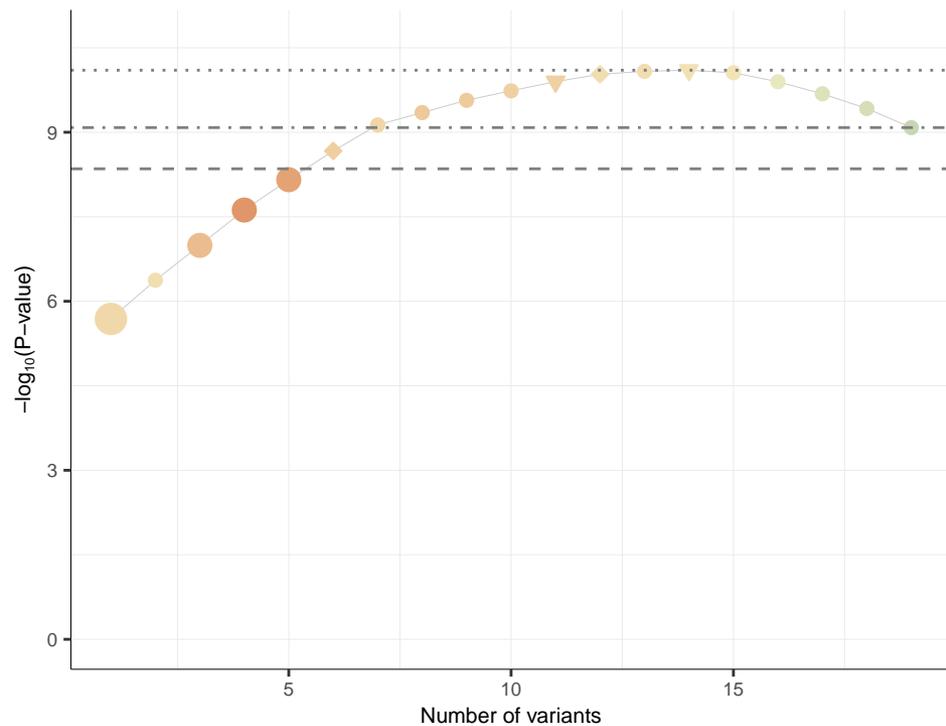
decanoylcarnitine (C10) in plasma at ACADM (LoF_mis)



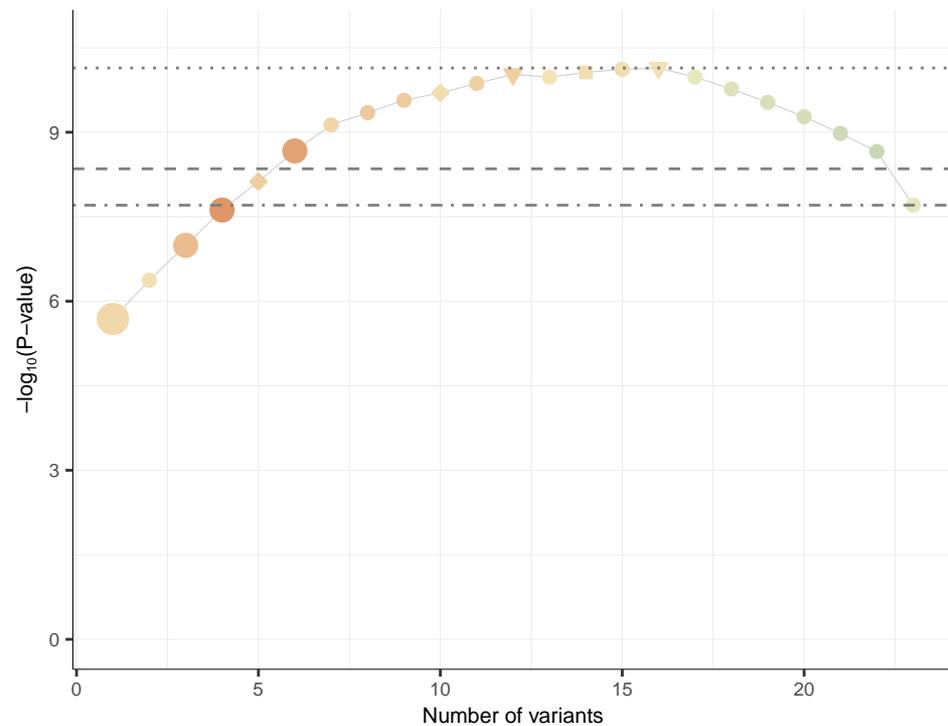
decanoylcarnitine (C10) in plasma at ACADM (HI_mis)



glycine conjugate of C6H10O2 (1)* in urine at ACADM (LoF_mis)

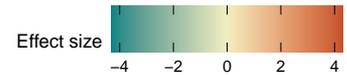


glycine conjugate of C6H10O2 (1)* in urine at ACADM (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- start/stop lost



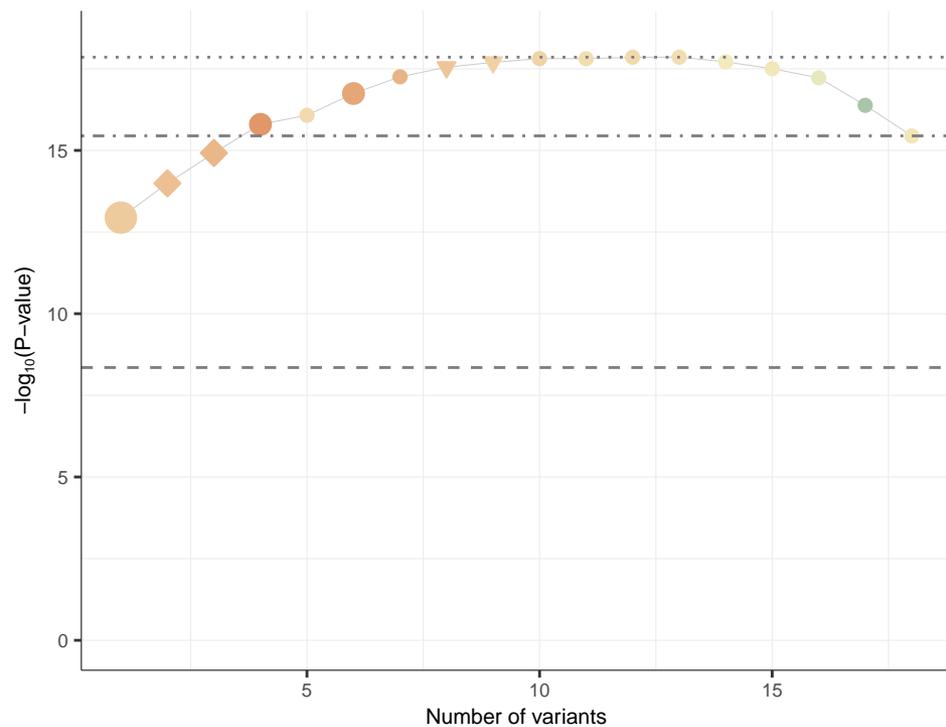
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

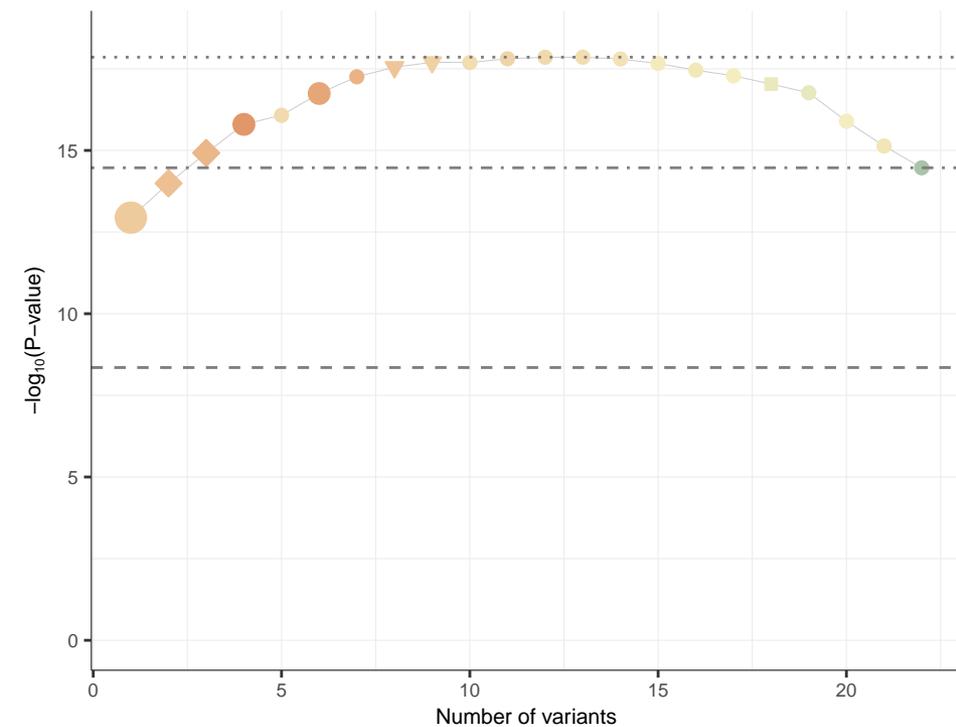
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯⋯ Lowest P-value

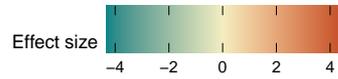
heptanoylglutamine in urine at ACADM (LoF_mis)



heptanoylglutamine in urine at ACADM (HI_mis)



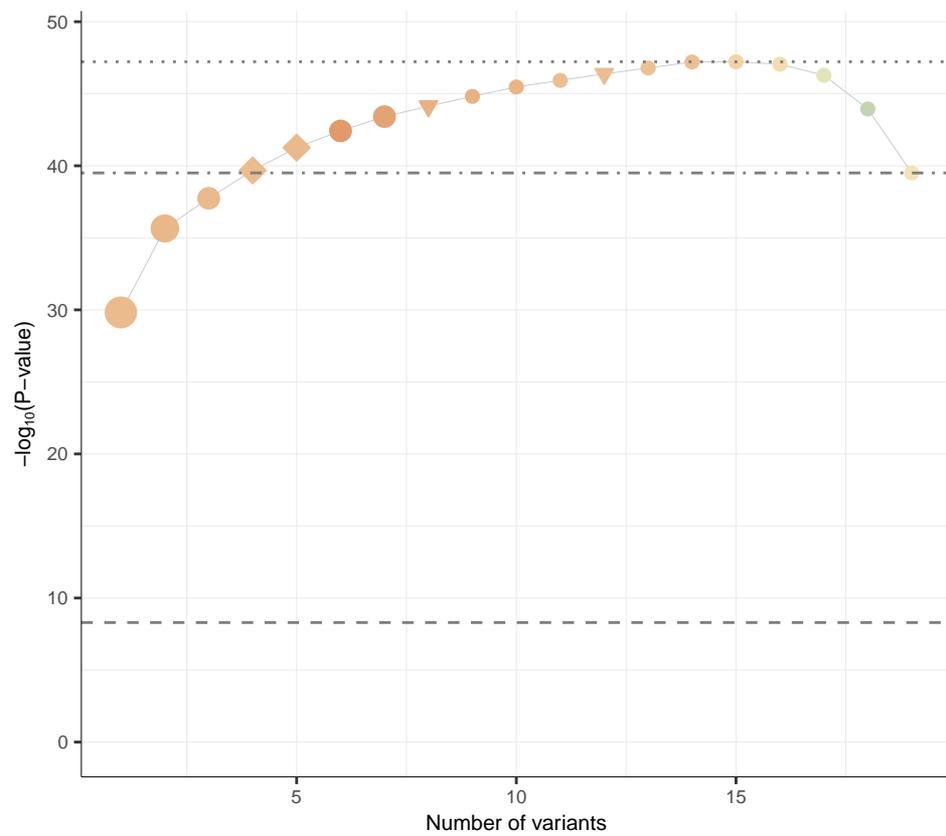
- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - start/stop lost



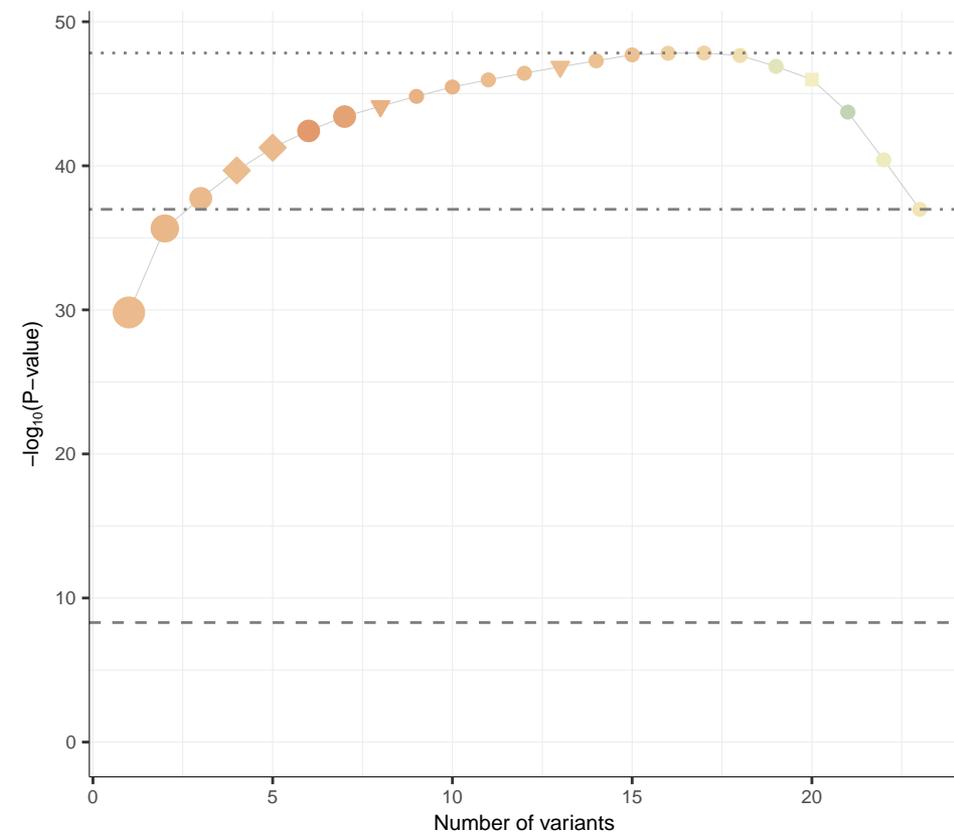
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

- Thresholds
- Significance Threshold
 - - - Total P-value
 - ... Lowest P-value

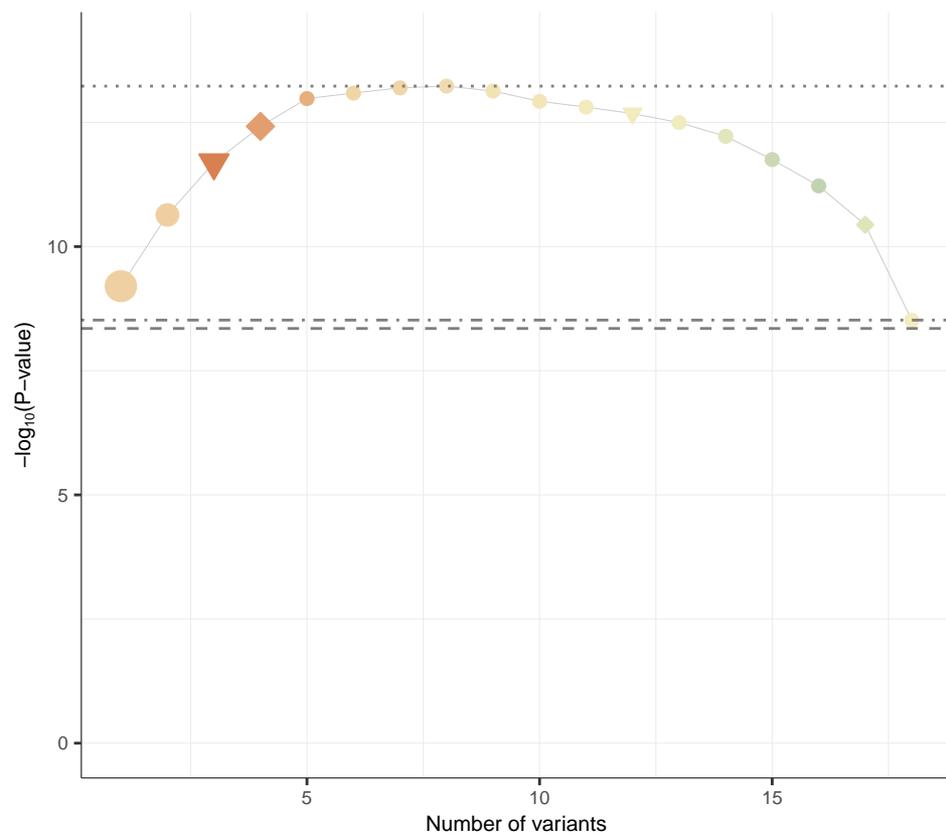
hexanoylcarnitine (C6) in plasma at ACADM (LoF_mis)



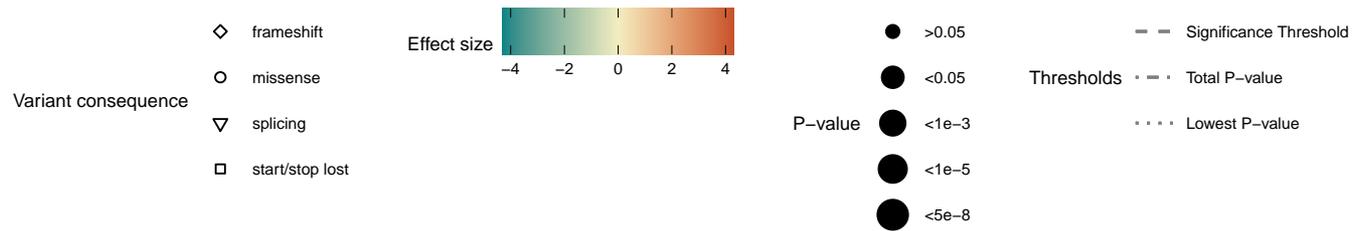
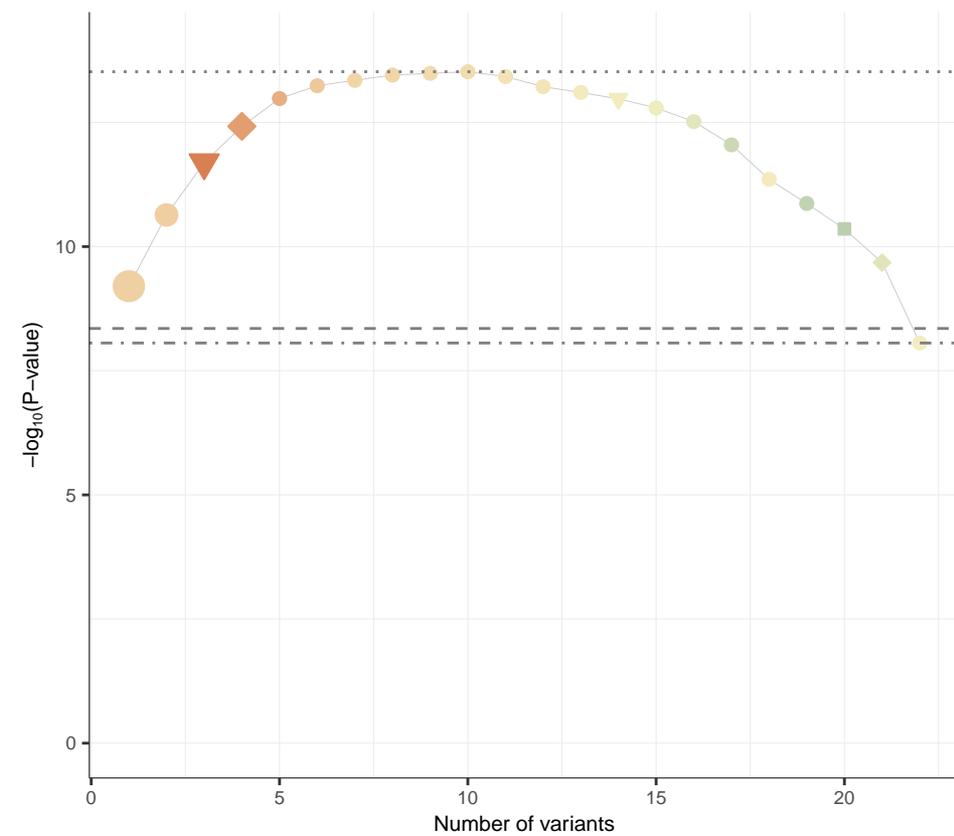
hexanoylcarnitine (C6) in plasma at ACADM (HI_mis)



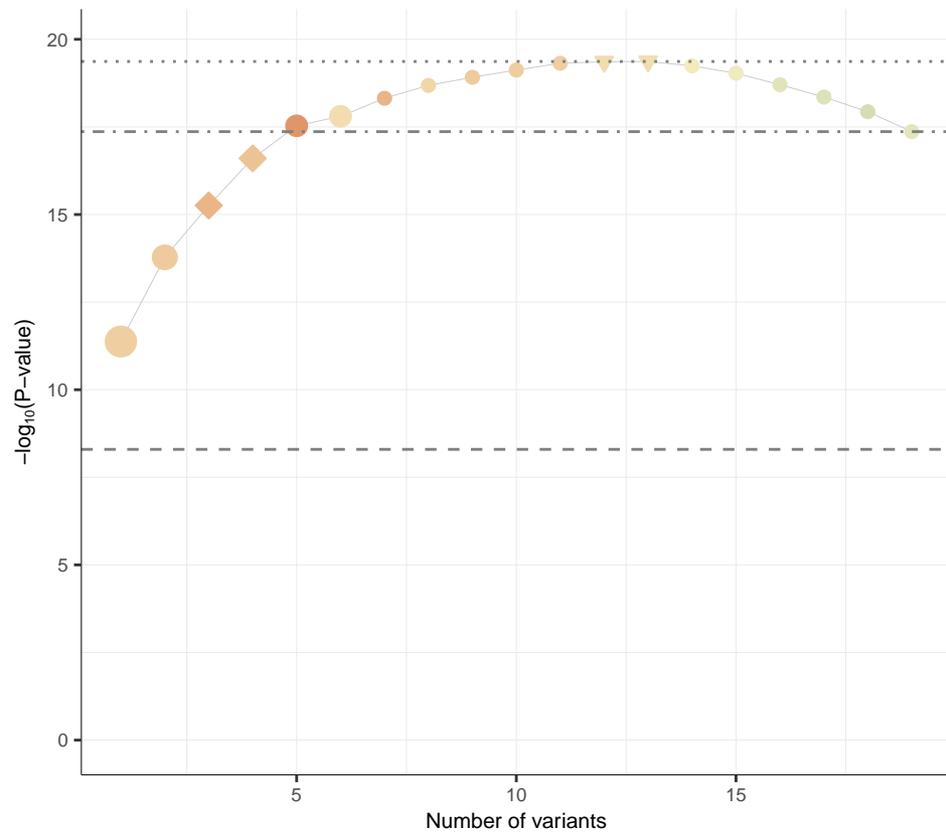
hexanoylcarnitine (C6) in urine at ACADM (LoF_mis)



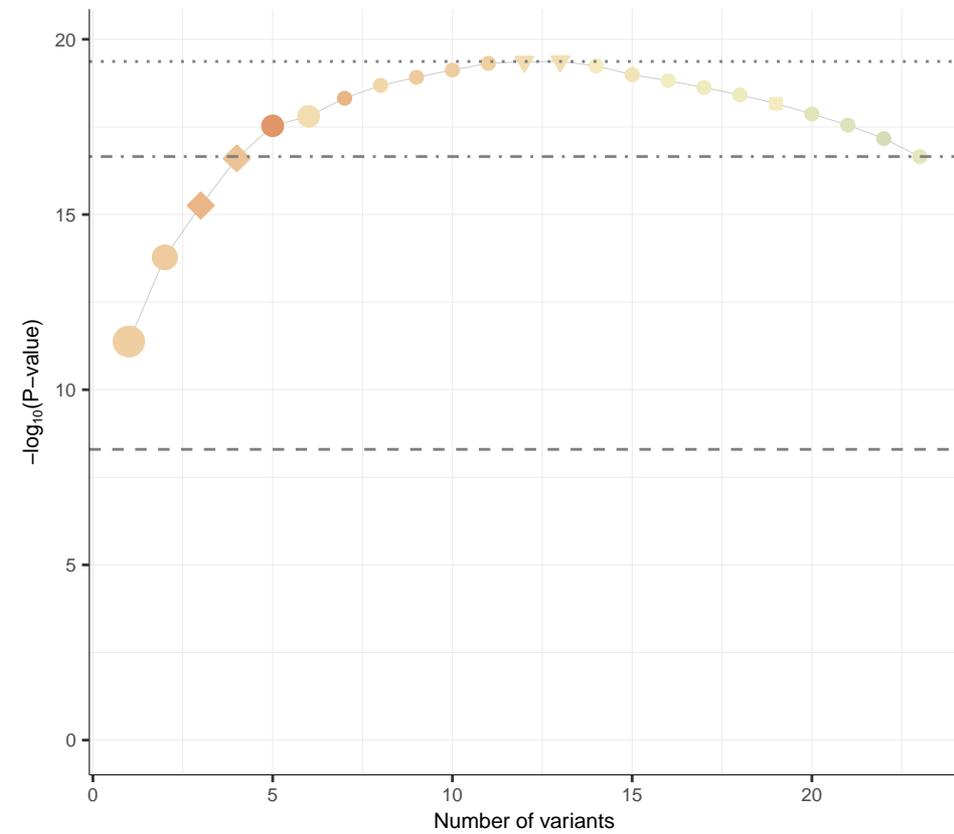
hexanoylcarnitine (C6) in urine at ACADM (HI_mis)



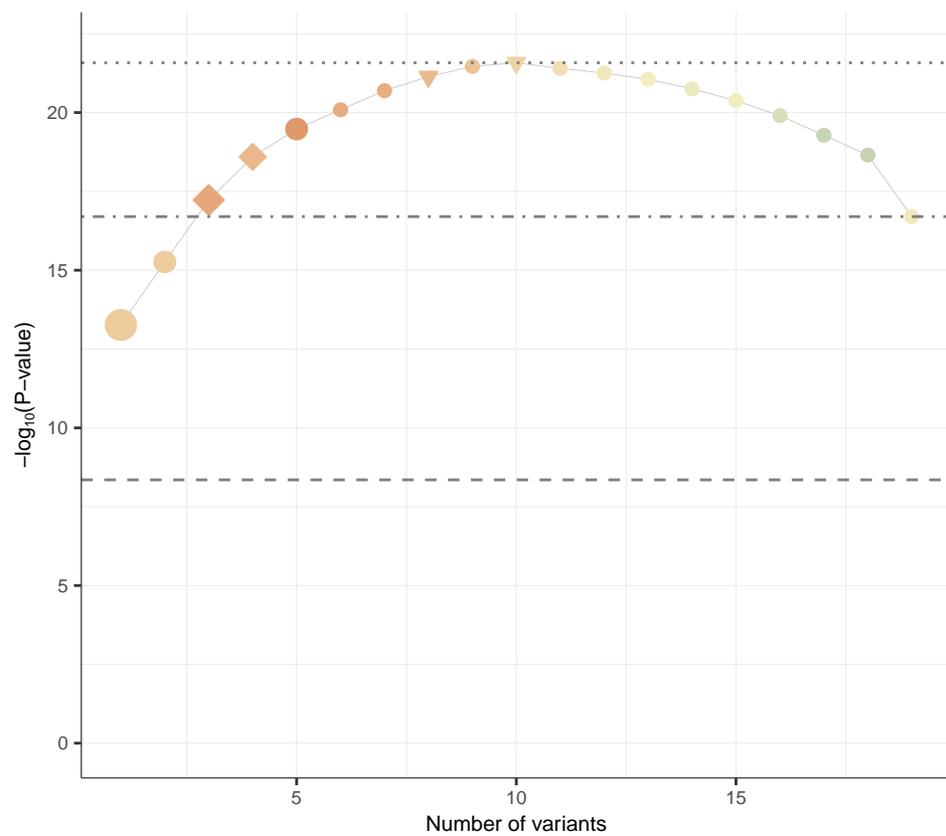
hexanoylglutamine in plasma at ACADM (LoF_mis)



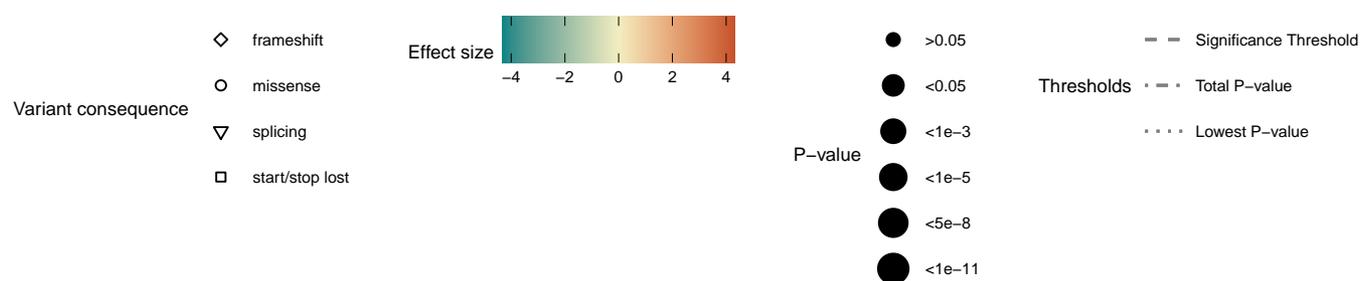
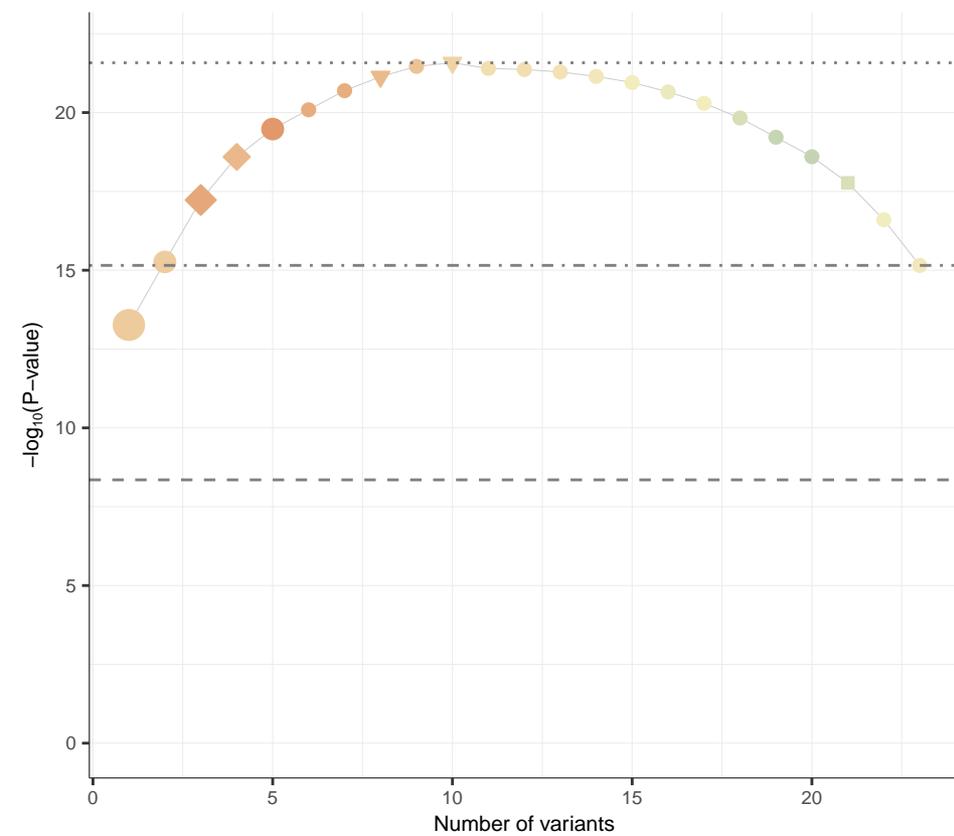
hexanoylglutamine in plasma at ACADM (HI_mis)



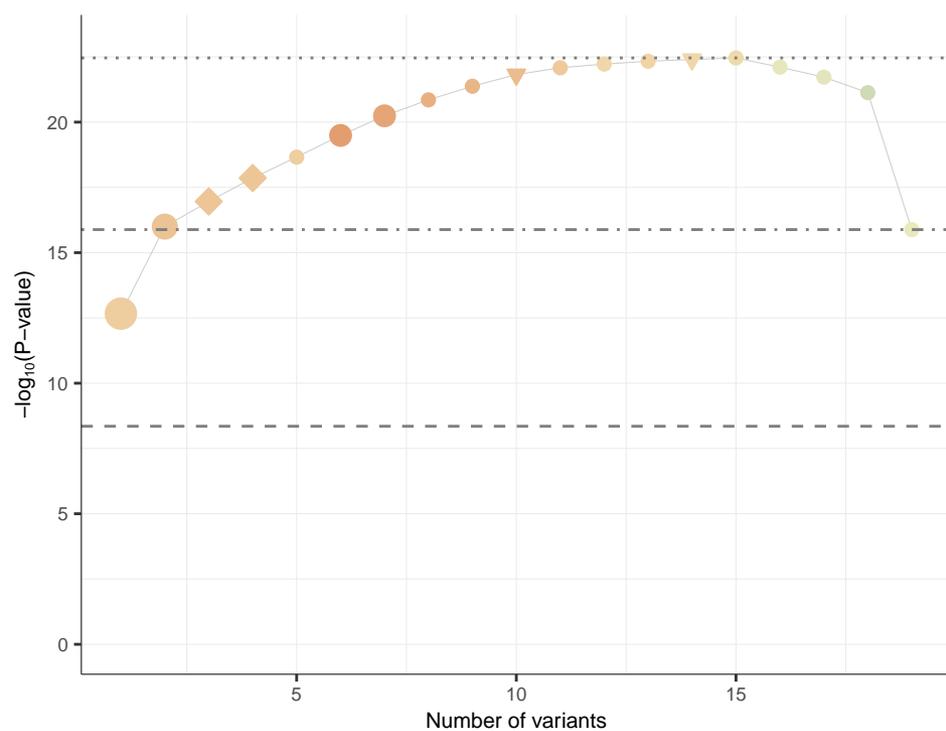
hexanoylglutamine in urine at ACADM (LoF_mis)



hexanoylglutamine in urine at ACADM (HI_mis)

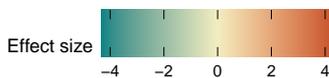


hexanoylglycine in urine at ACADM (LoF_mis)

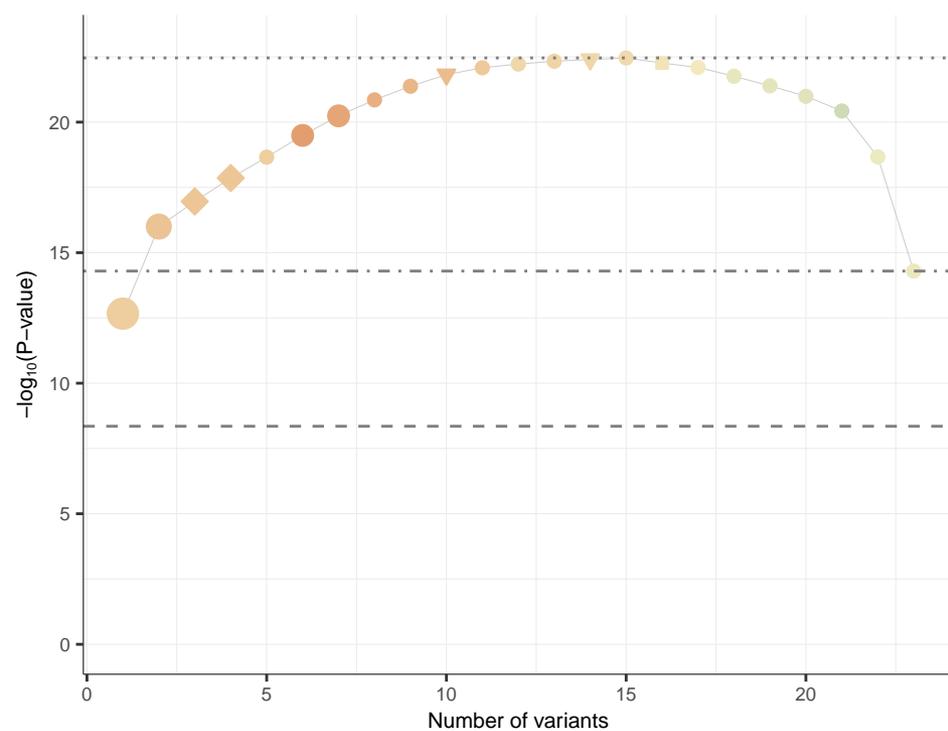


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- start/stop lost



hexanoylglycine in urine at ACADM (HI_mis)



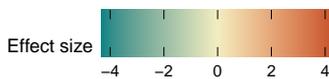
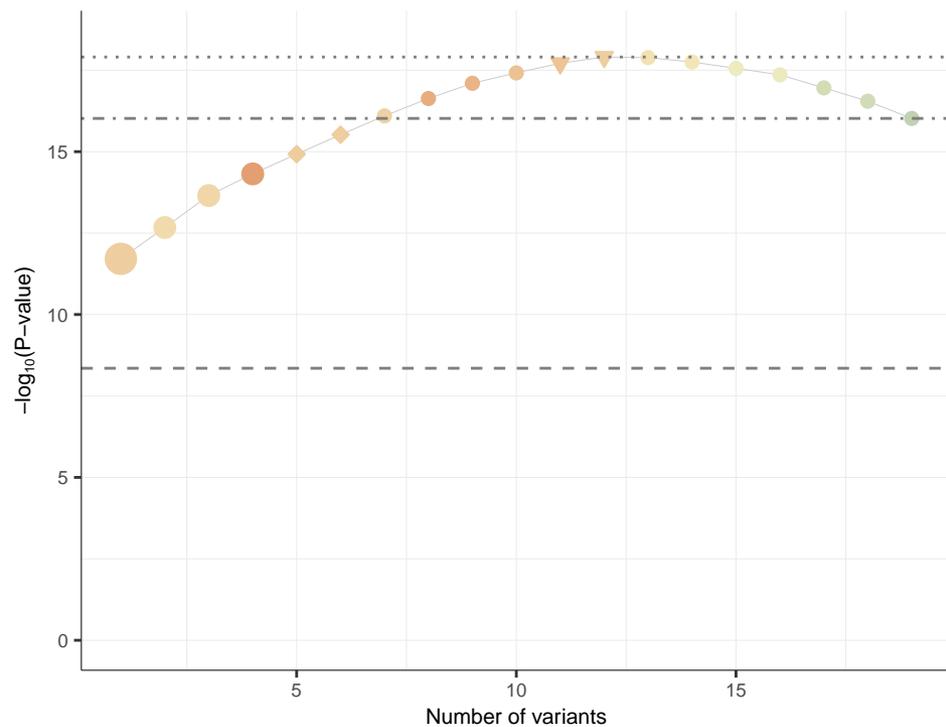
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

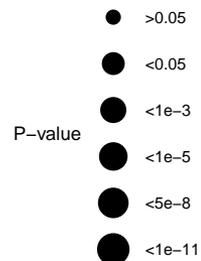
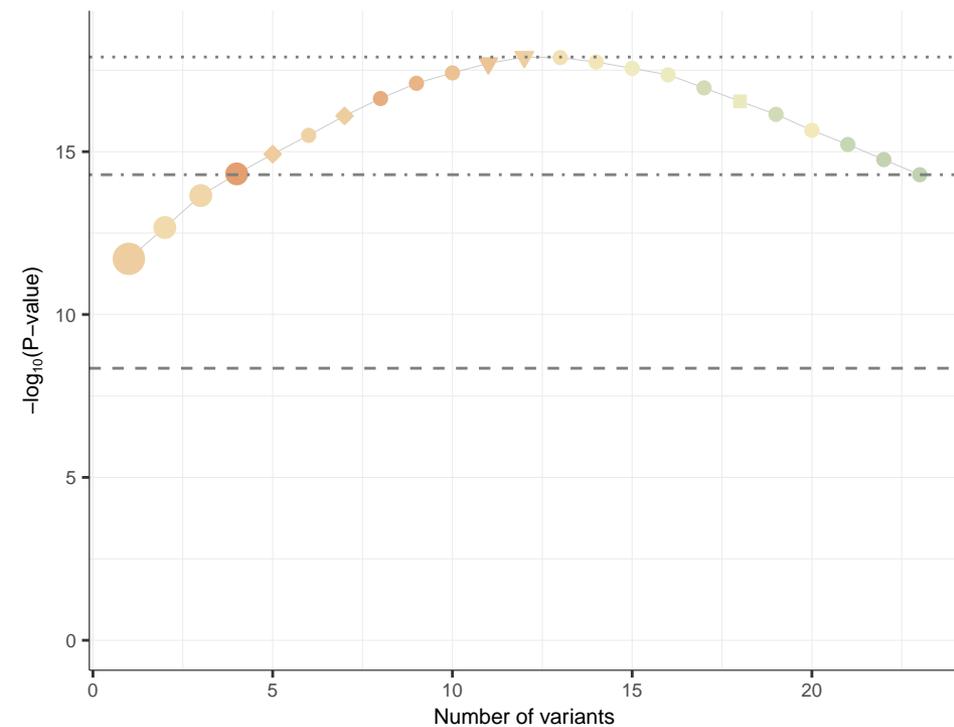
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

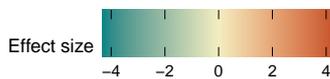
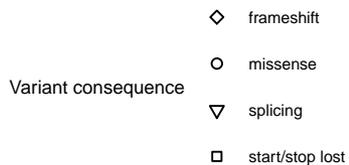
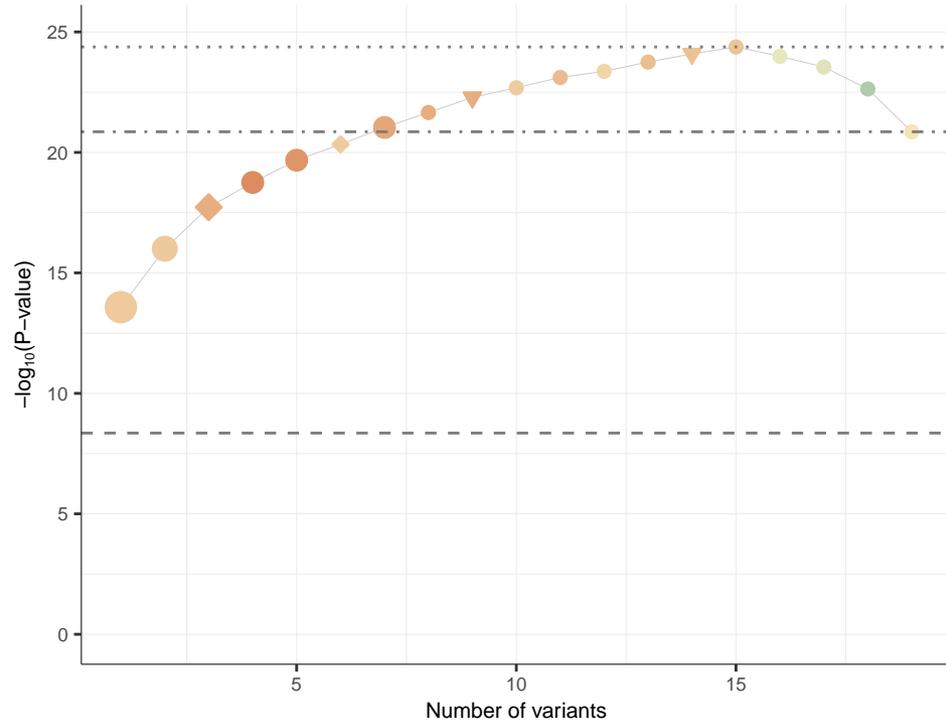
hexanoyltaurine in urine at ACADM (LoF_mis)



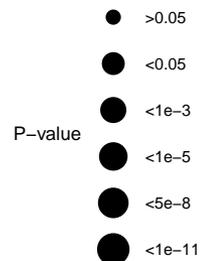
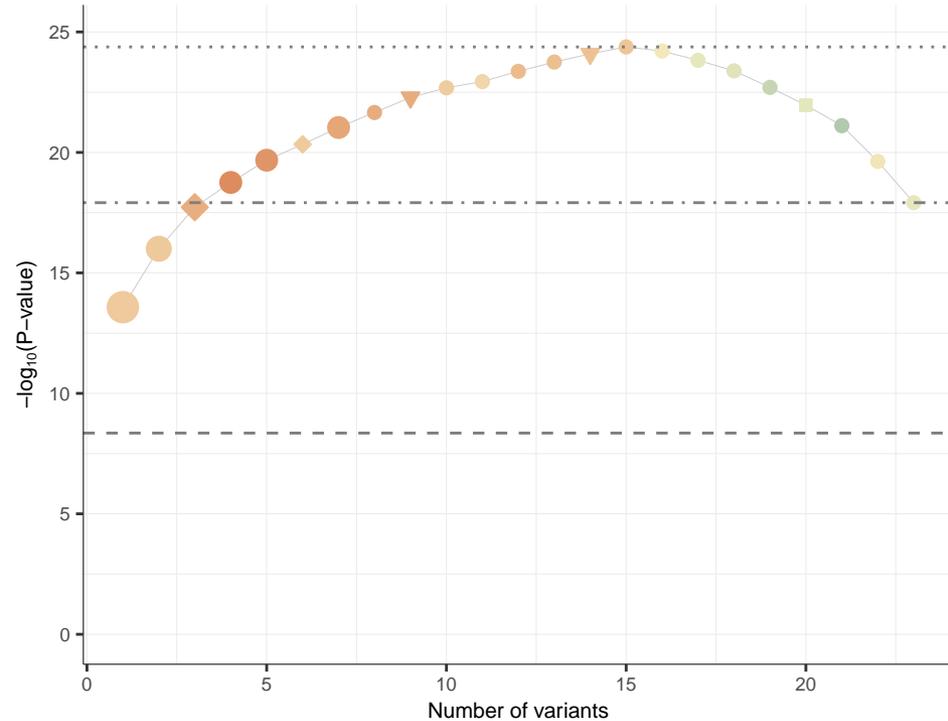
hexanoyltaurine in urine at ACADM (HI_mis)



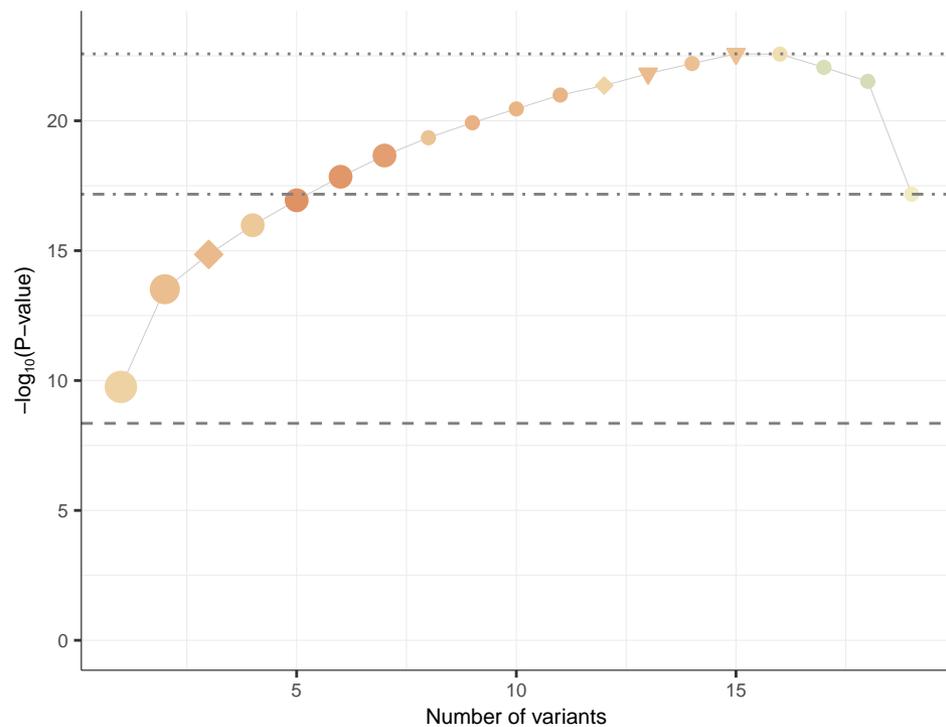
isocaproylglutamine in urine at ACADM (LoF_mis)



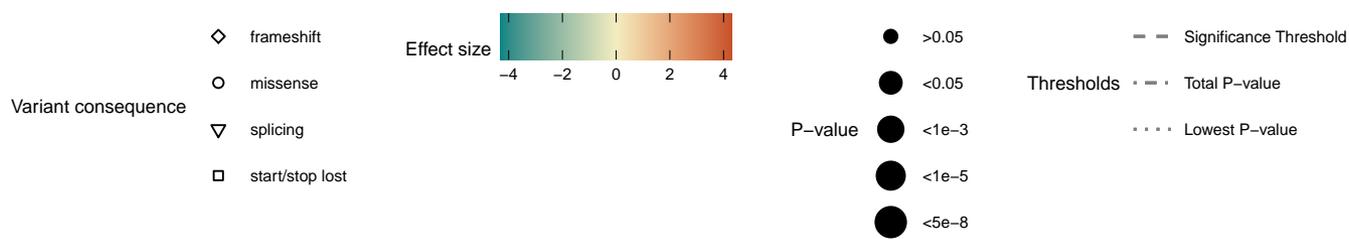
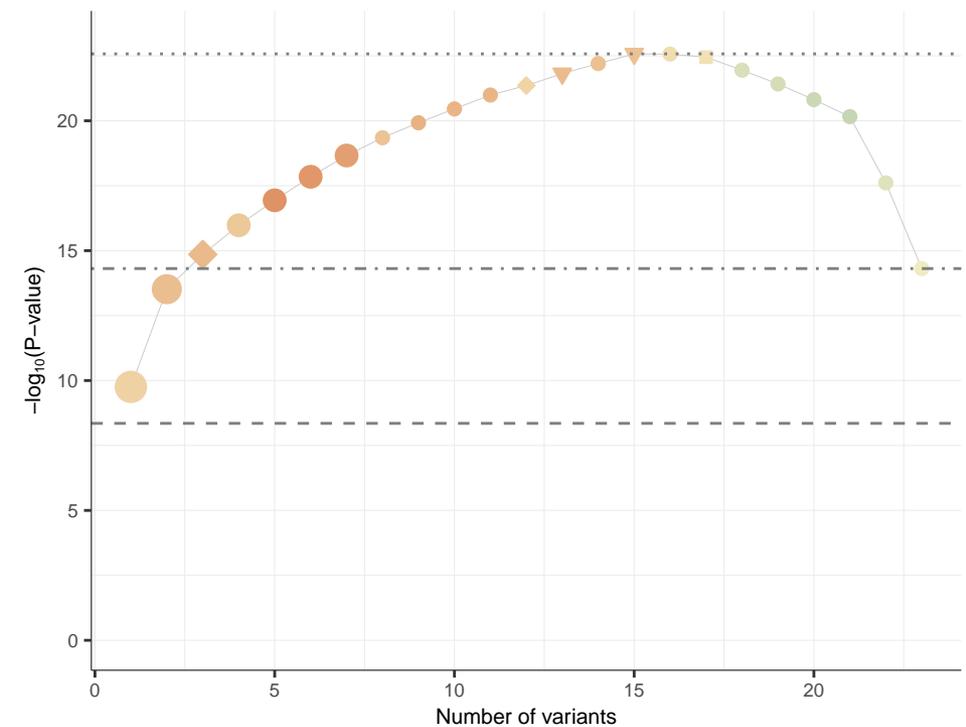
isocaproylglutamine in urine at ACADM (HI_mis)



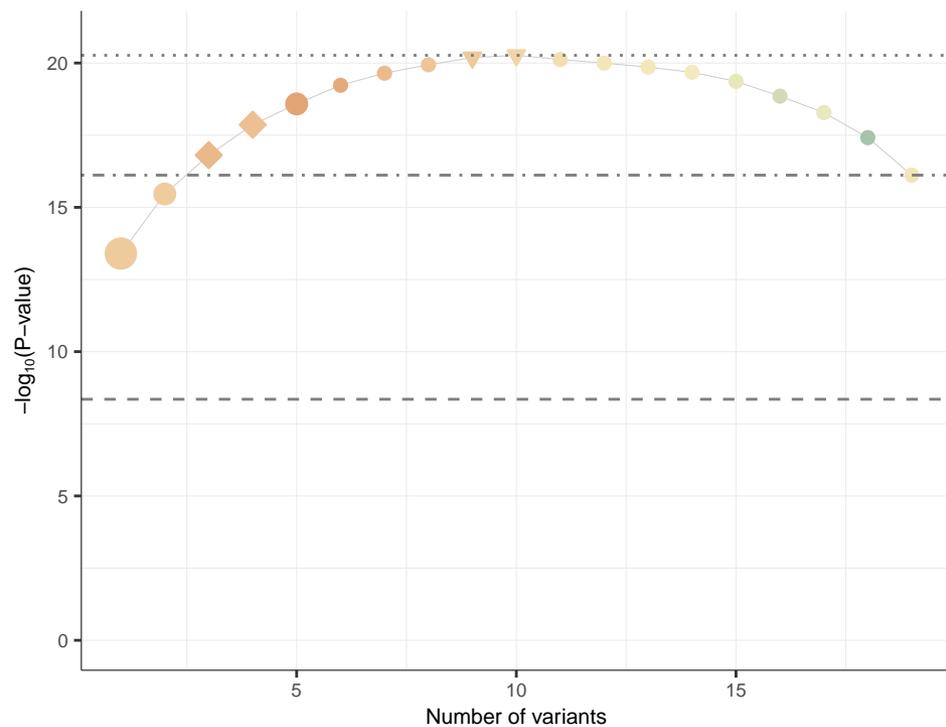
isocaproylglycine in urine at ACADM (LoF_mis)



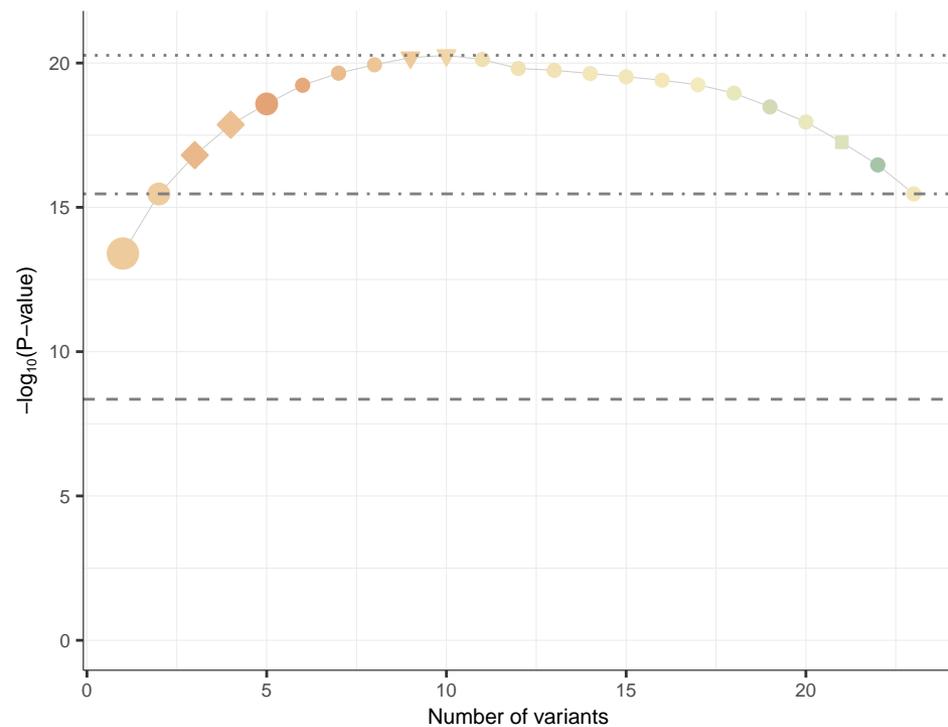
isocaproylglycine in urine at ACADM (HI_mis)



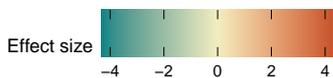
N-octanoylglutamine in urine at *ACADM* (LoF_mis)



N-octanoylglutamine in urine at *ACADM* (HI_mis)



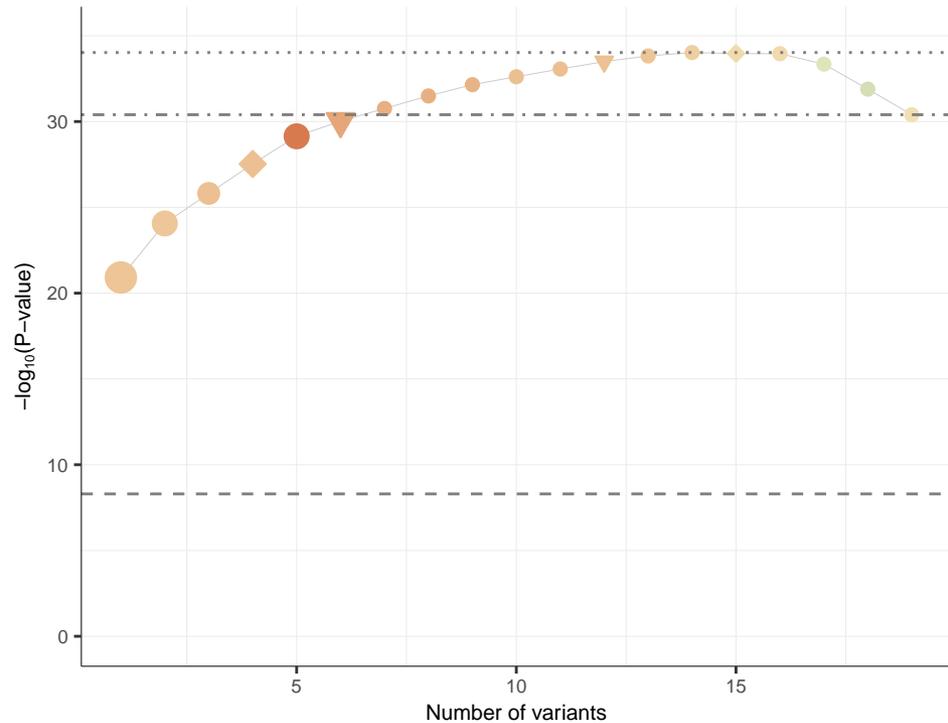
- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - start/stop lost



- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

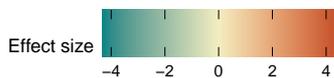
- Thresholds
- - - Significance Threshold
 - · - · Total P-value
 - · · · · Lowest P-value

nonanoylcarnitine (C9) in plasma at ACADM (LoF_mis)

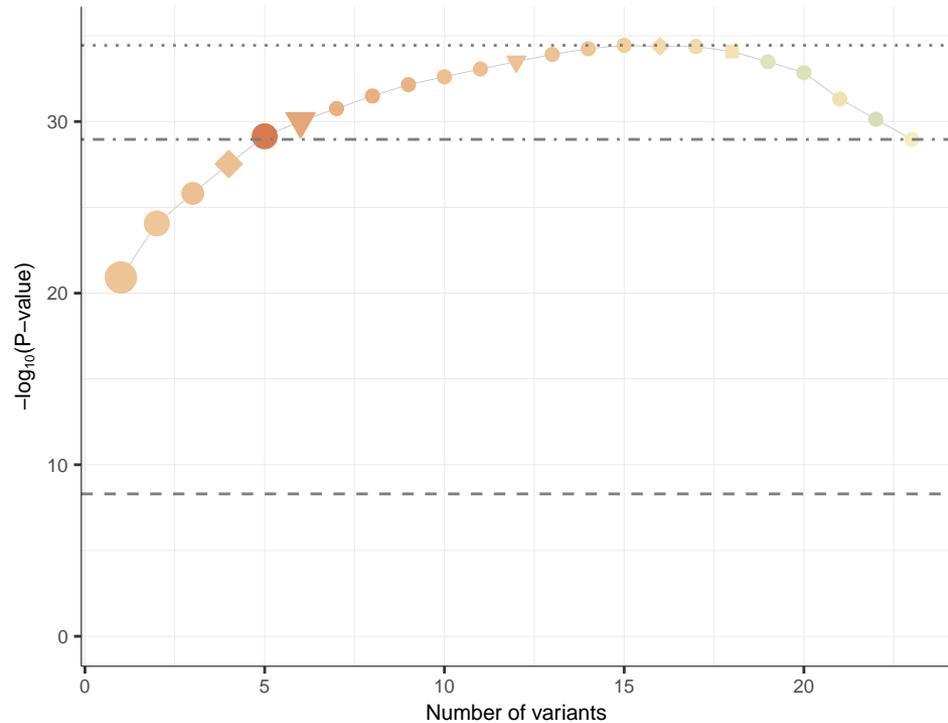


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- start/stop lost



nonanoylcarnitine (C9) in plasma at ACADM (HI_mis)



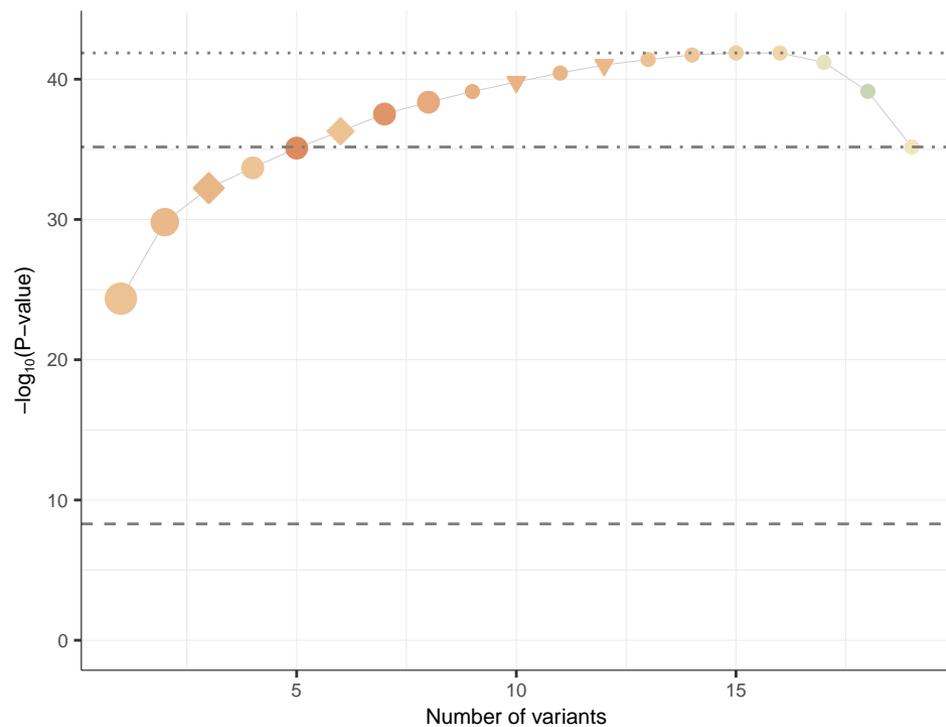
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

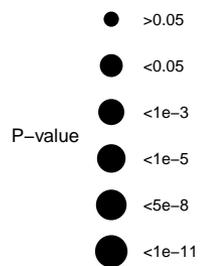
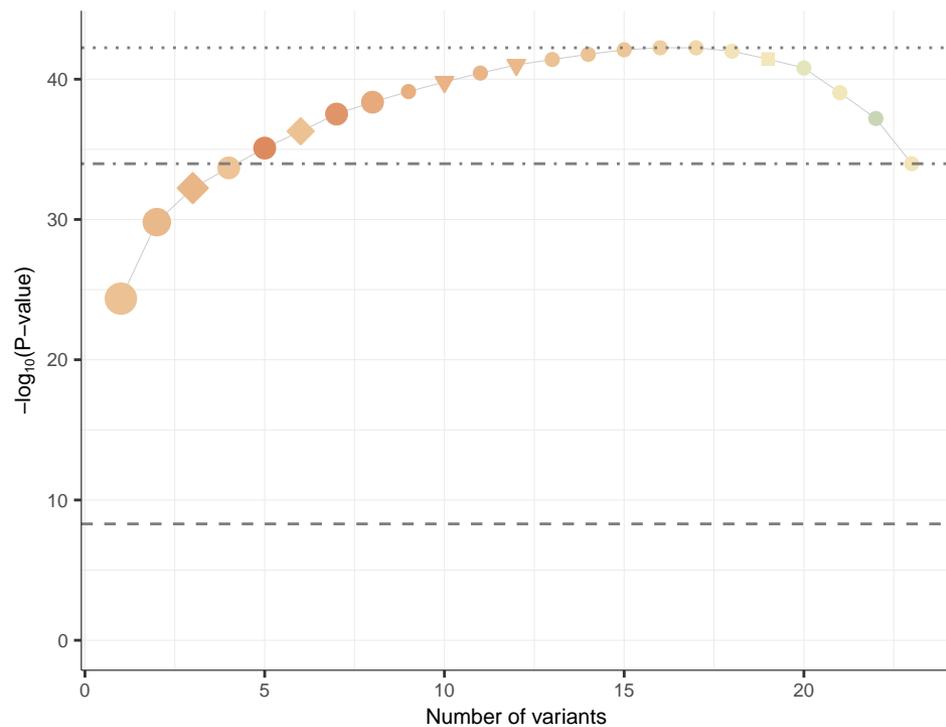
Thresholds

- Significance Threshold
- · - Total P-value
- Lowest P-value

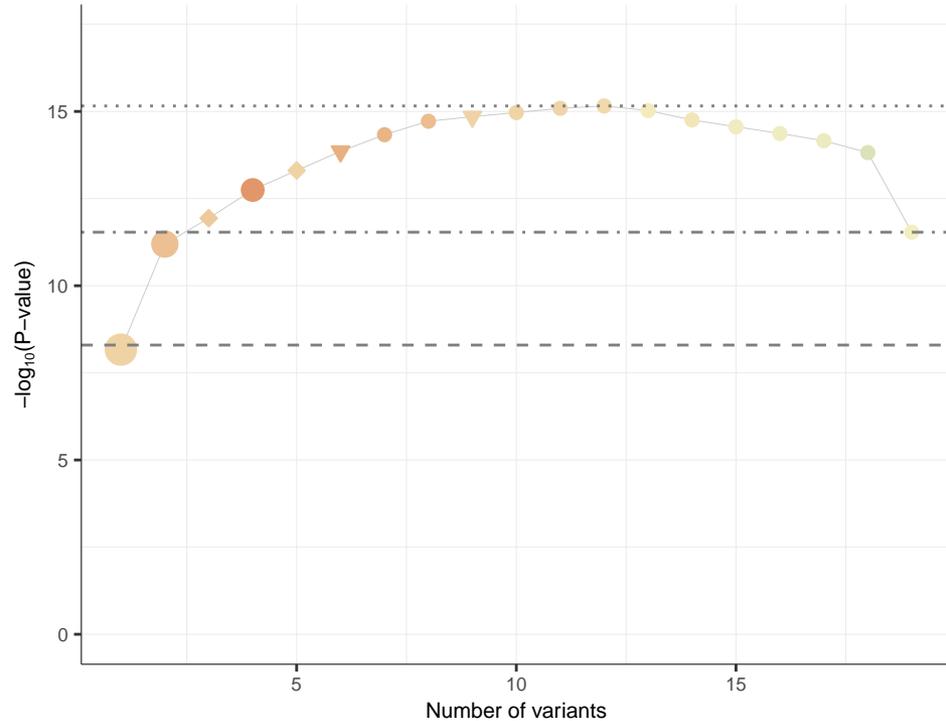
octanoylcarnitine (C8) in plasma at ACADM (LoF_mis)



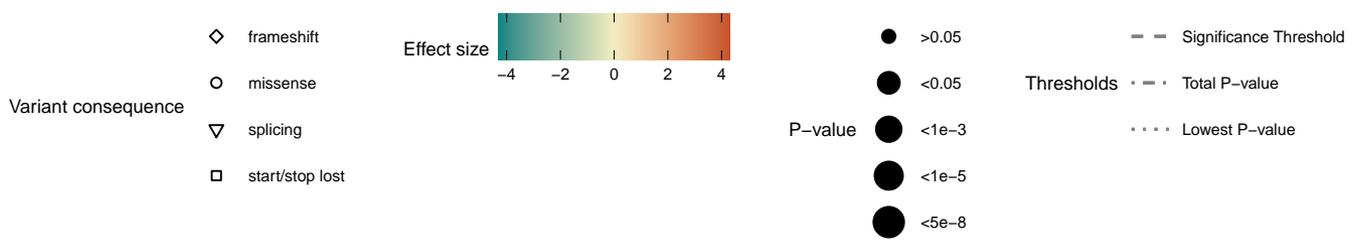
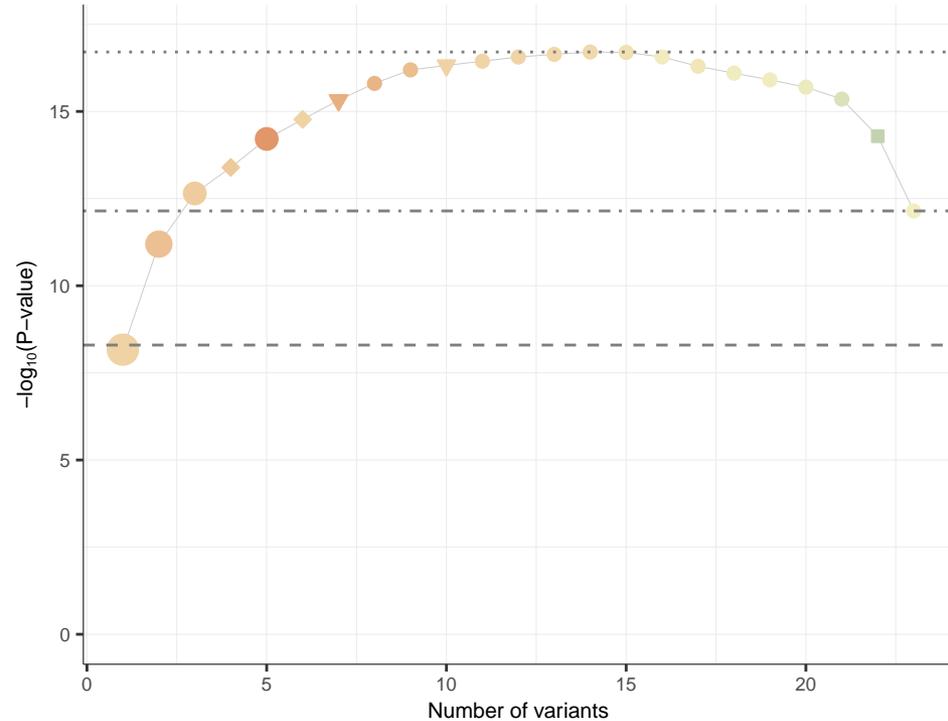
octanoylcarnitine (C8) in plasma at ACADM (HI_mis)



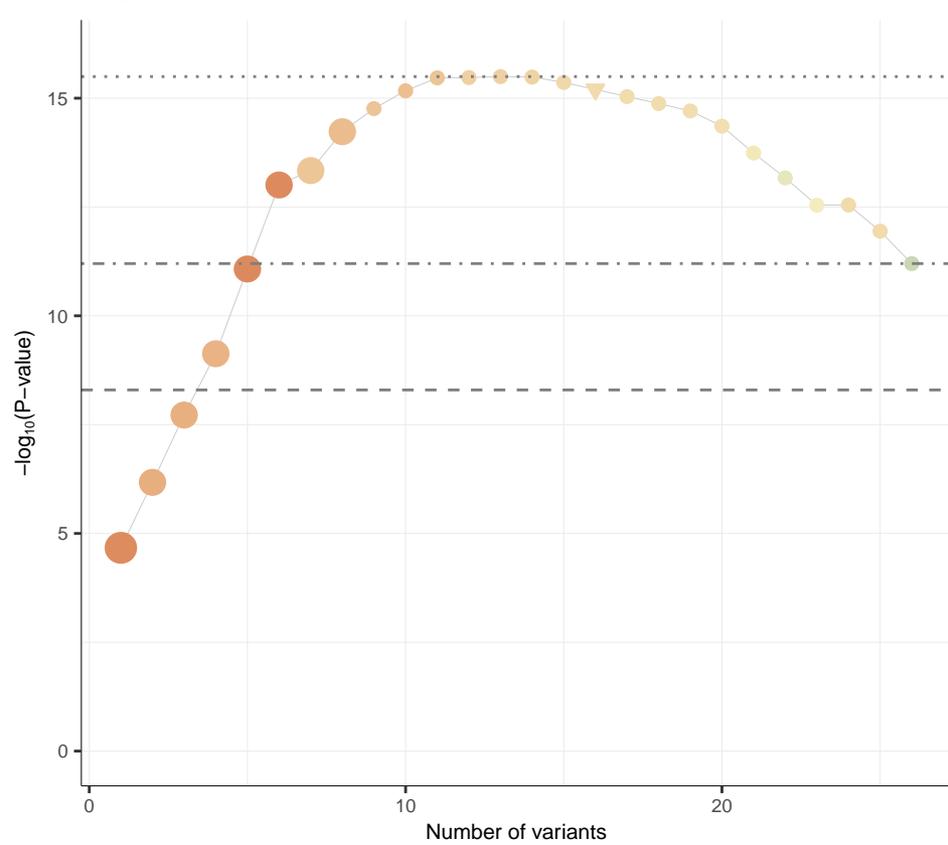
X - 21607 in plasma at ACADM (LoF_mis)



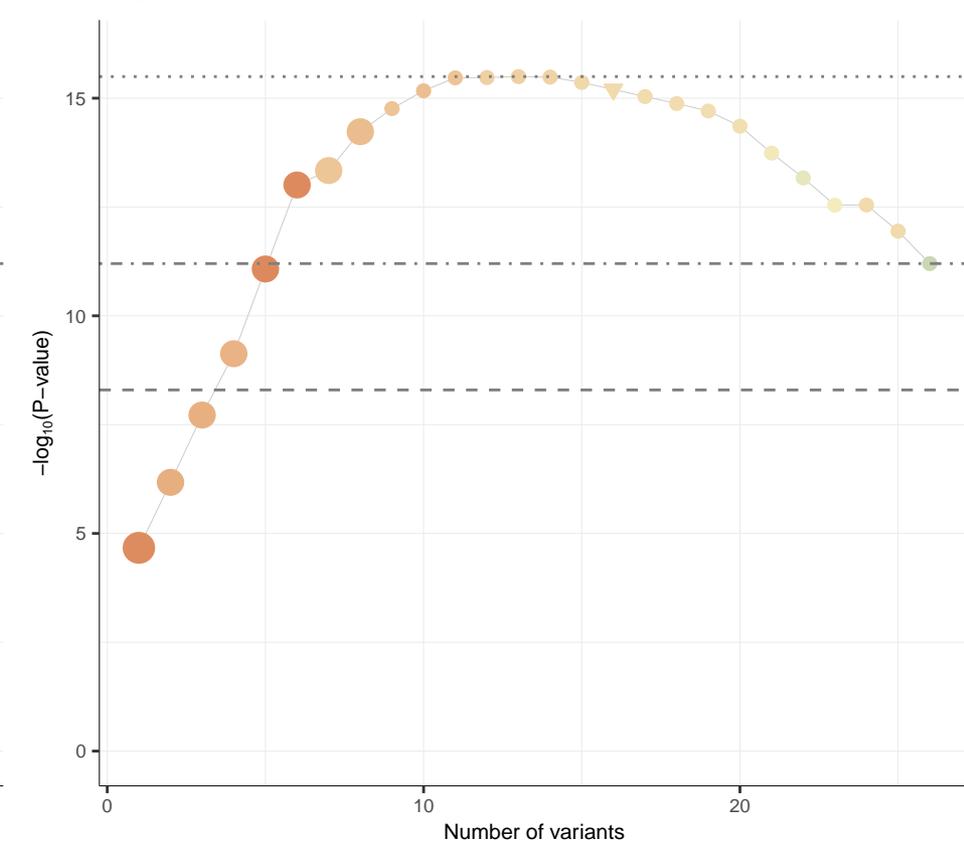
X - 21607 in plasma at ACADM (HI_mis)



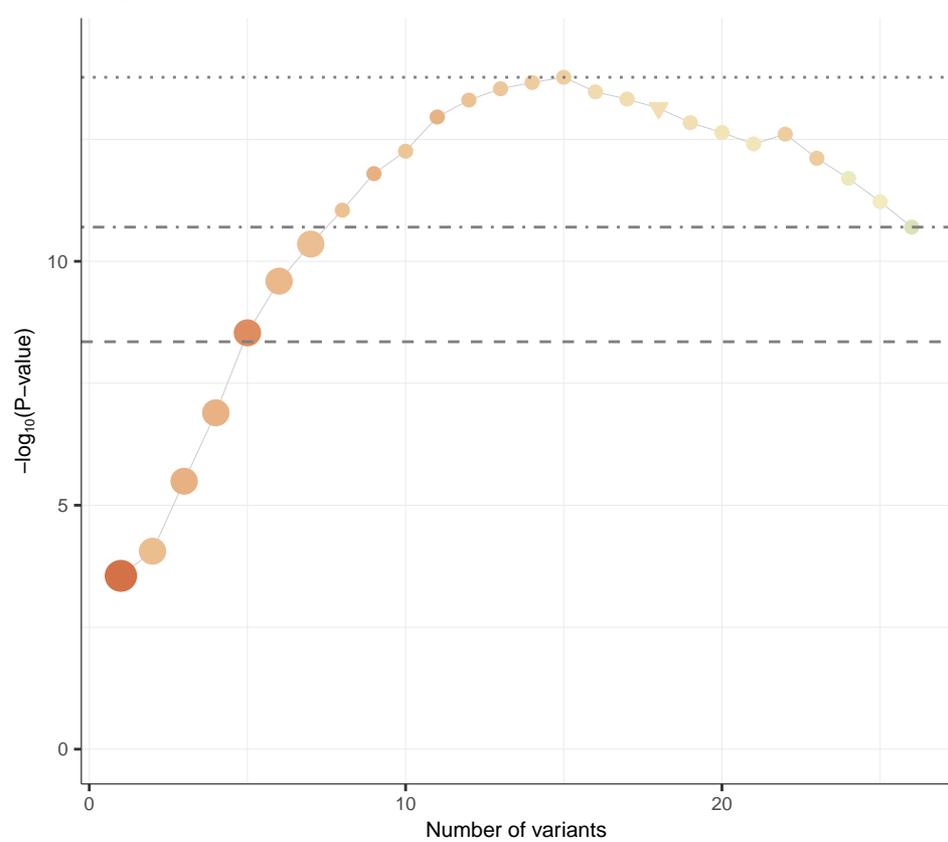
ethylmalonate in plasma at ACADS (LoF_mis)



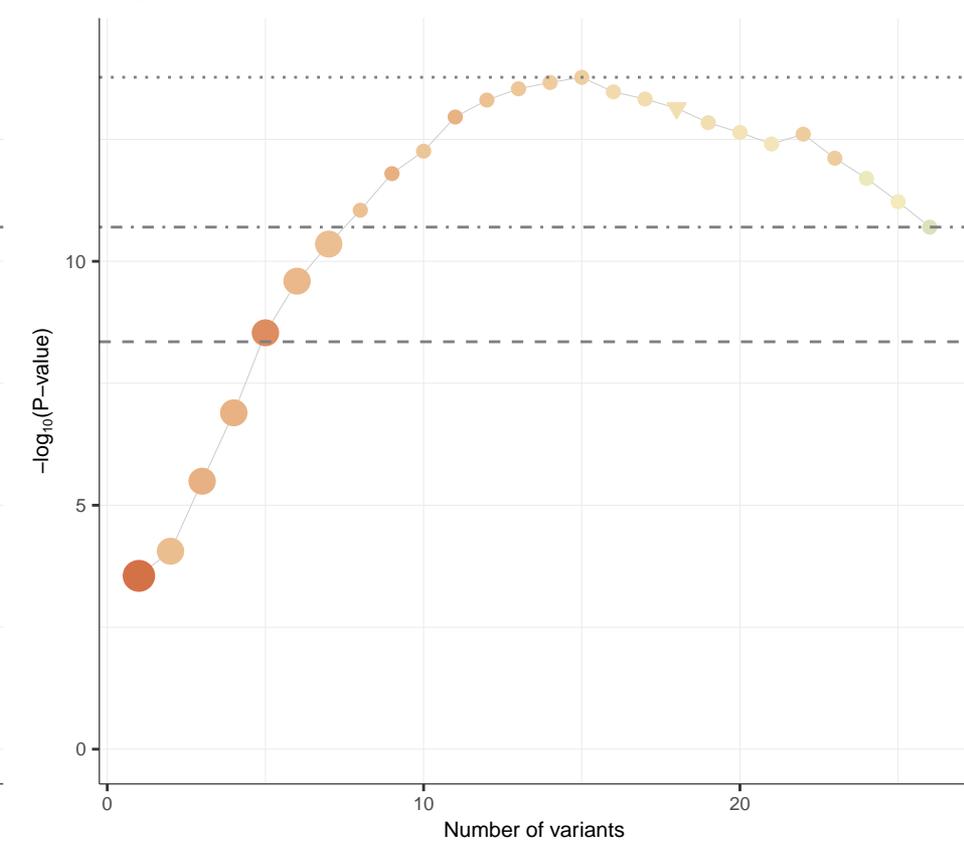
ethylmalonate in plasma at ACADS (HI_mis)



ethylmalonate in urine at ACADS (LoF_mis)



ethylmalonate in urine at ACADS (HI_mis)



Variant consequence

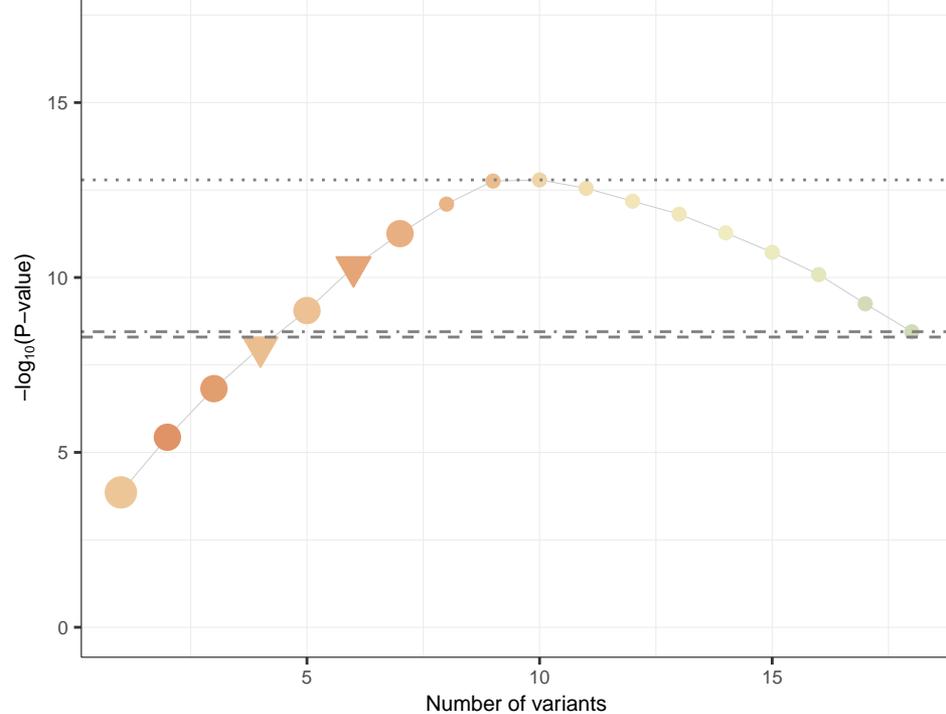
- missense
- ▽ splicing



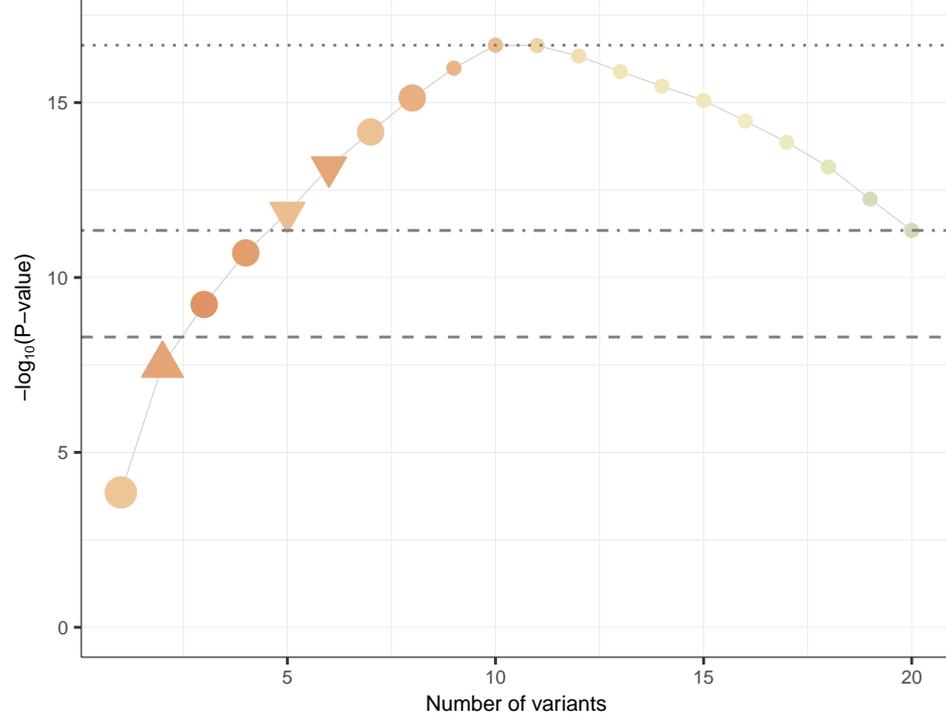
- >0.05
- <0.05
- <1e-3

- Significance Threshold
- Total P-value
- ⋯ Lowest P-value

2-methylbutyrylcarnitine (C5) in plasma at ACADSB (LoF_mis)



2-methylbutyrylcarnitine (C5) in plasma at ACADSB (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



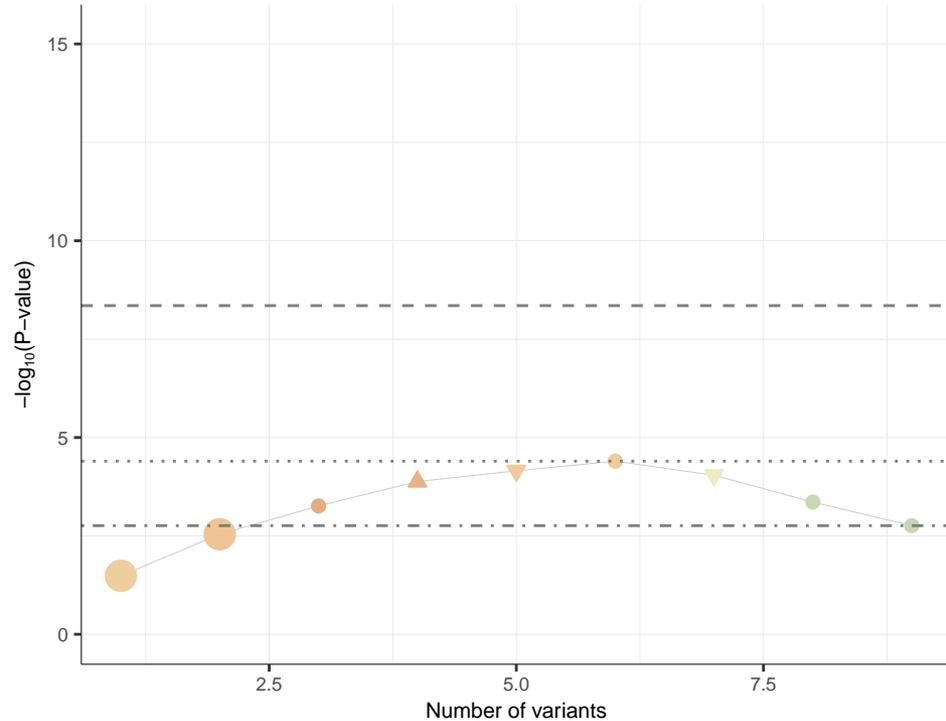
P-value

- >0.05
- <0.05
- <1e-3

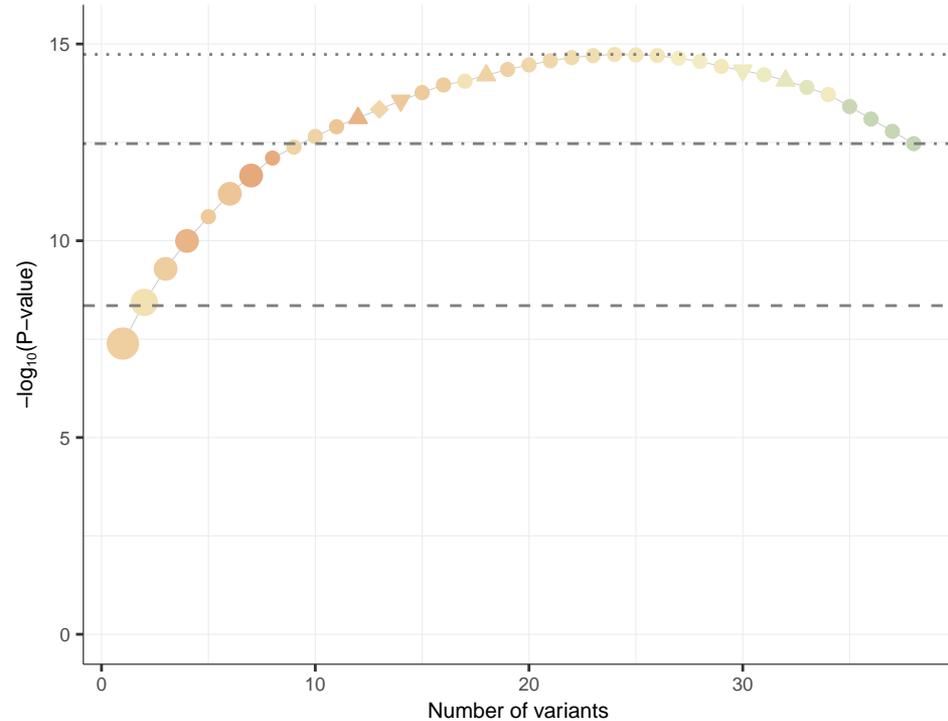
Thresholds

- - - Significance Threshold
- · - Total P-value
- · · Lowest P-value

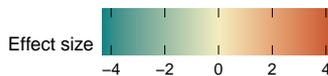
ethylmalonate in urine at ACSF3 (LoF_mis)



ethylmalonate in urine at ACSF3 (HI_mis)

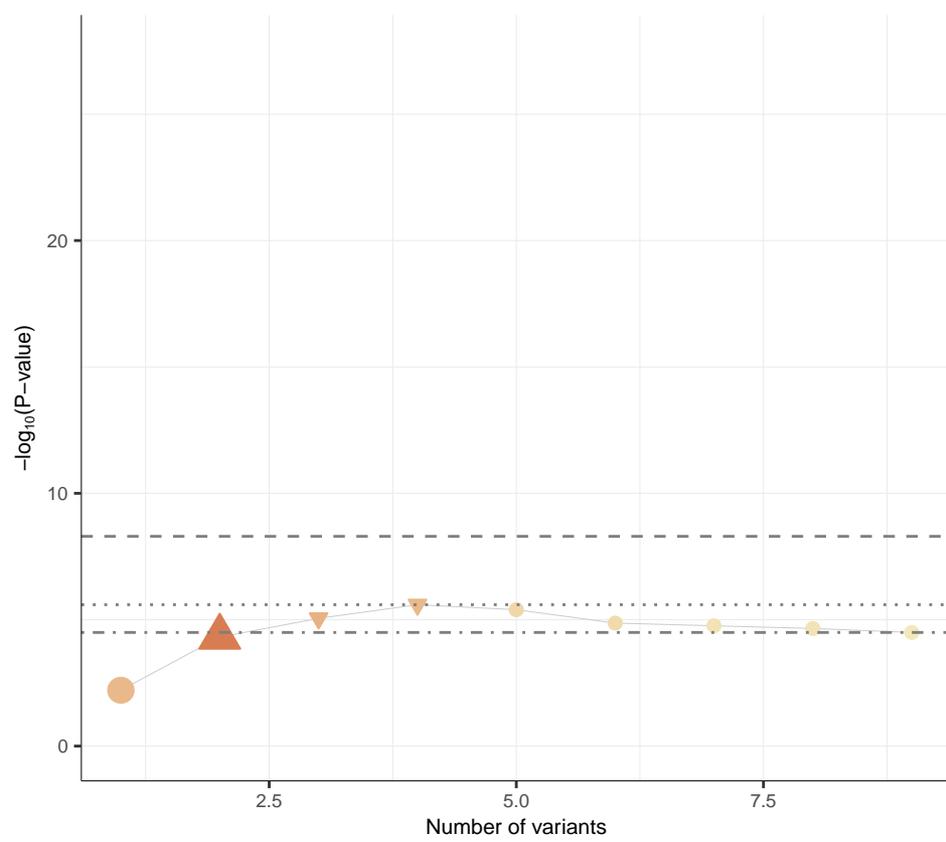


- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - △ stop gained

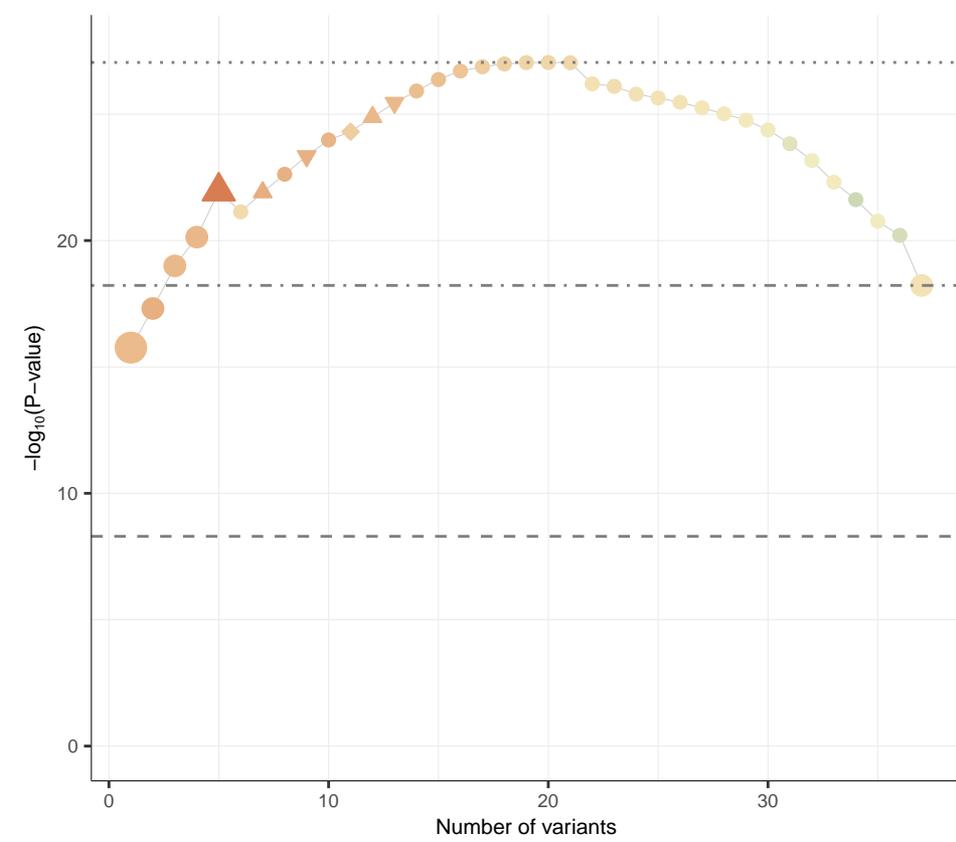


- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
- Thresholds
- - Significance Threshold
 - - - Total P-value
 - ... Lowest P-value

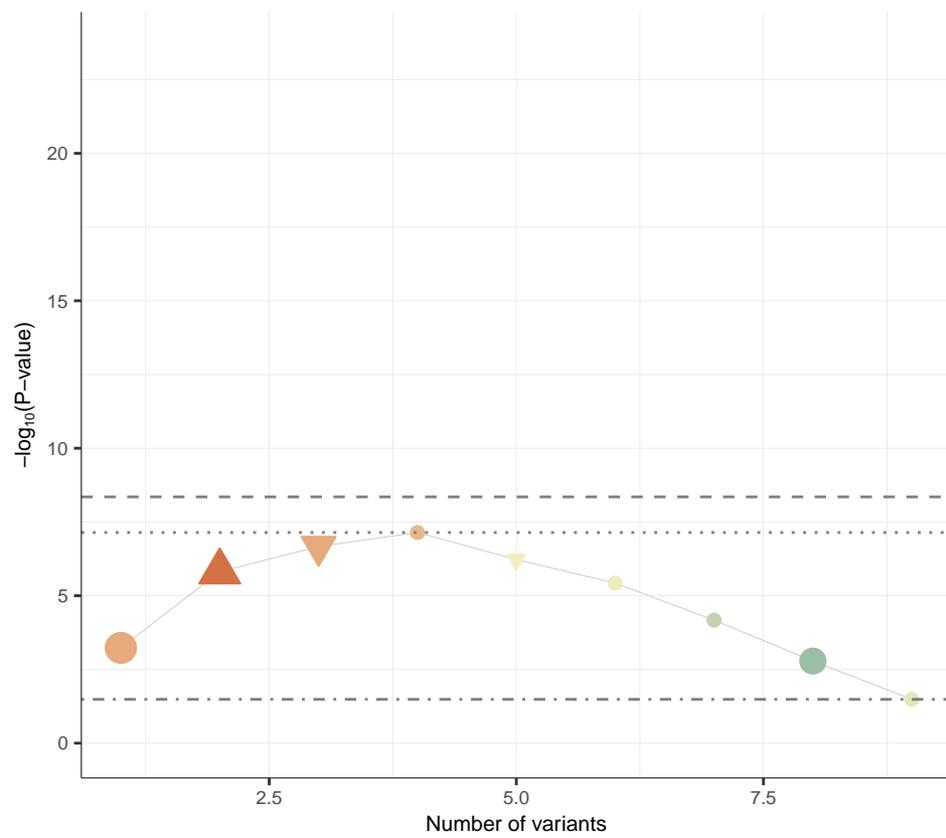
methylmalonate (MMA) in plasma at ACSF3 (LoF_mis)



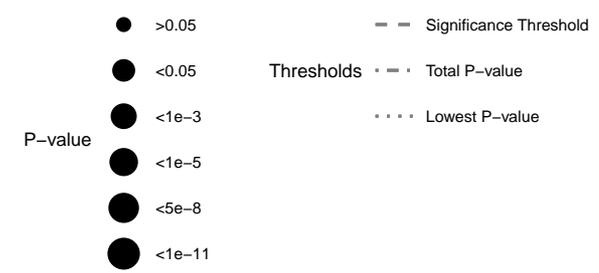
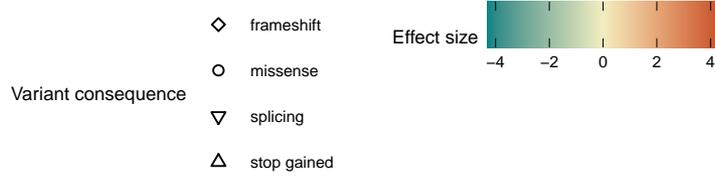
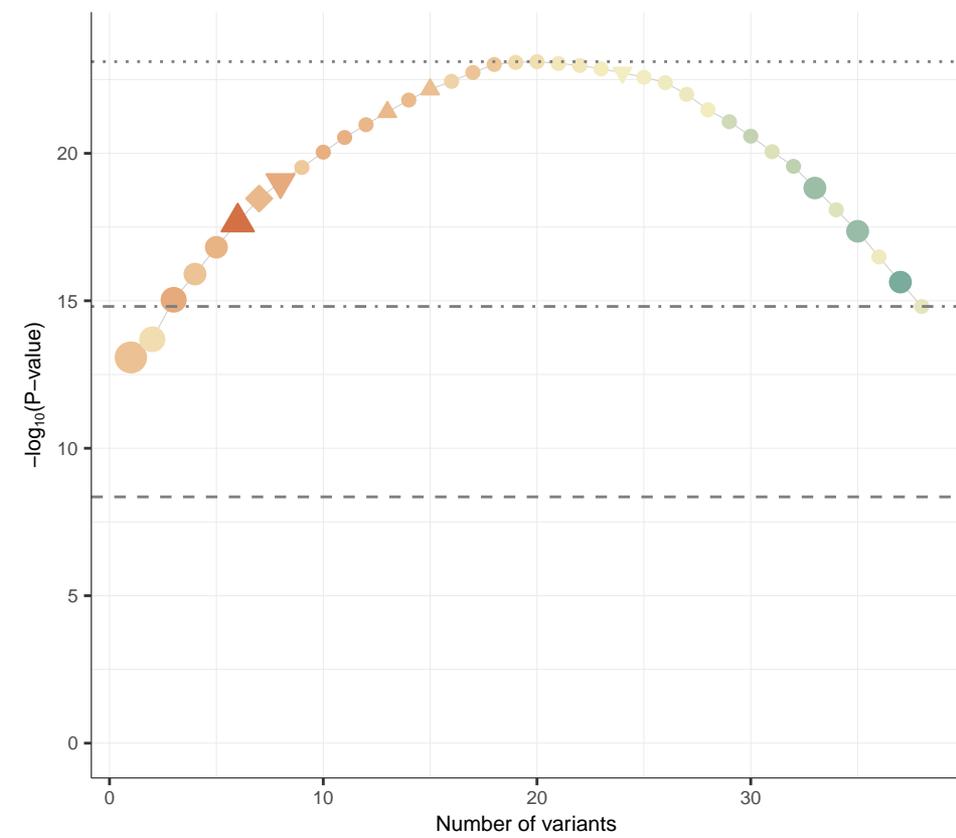
methylmalonate (MMA) in plasma at ACSF3 (HI_mis)



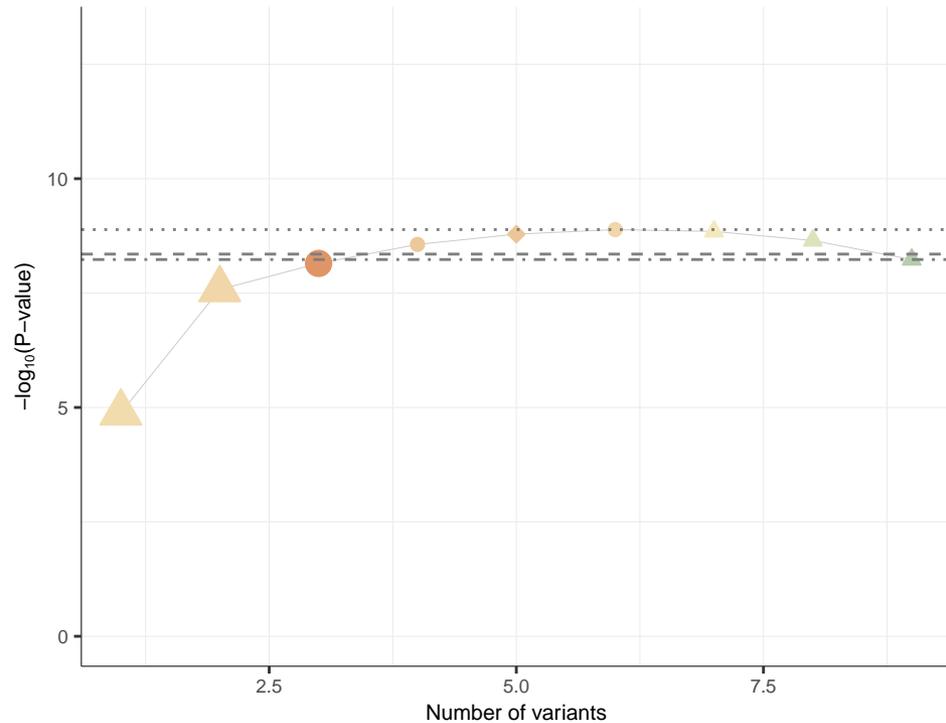
methylmalonate (MMA) in urine at ACSF3 (LoF_mis)



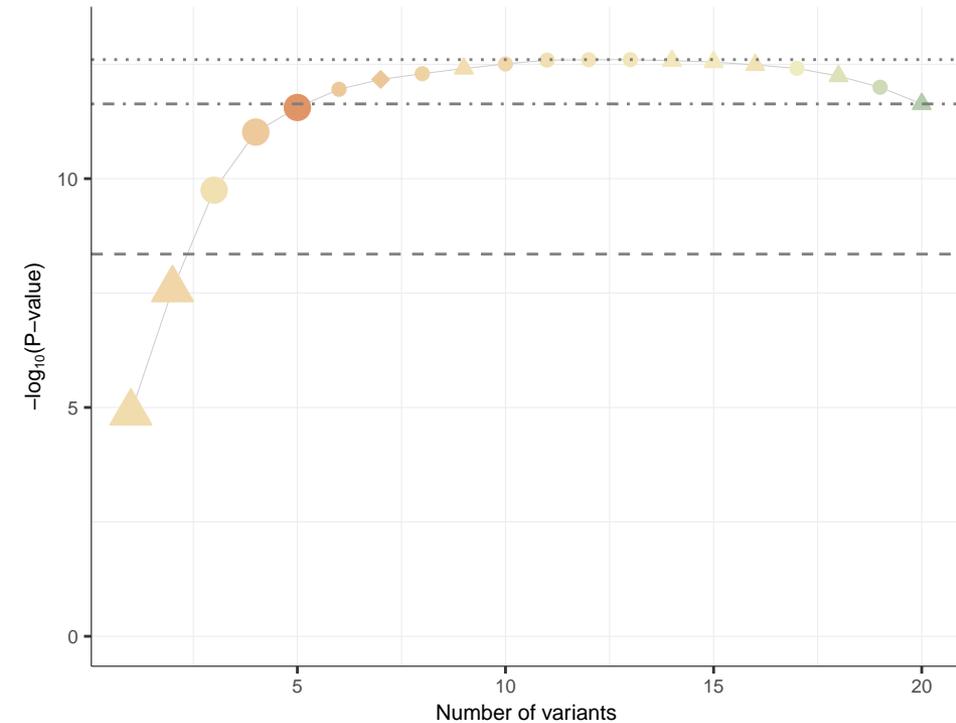
methylmalonate (MMA) in urine at ACSF3 (HI_mis)



3-(3-hydroxyphenyl)propionate in urine at ACSM2A (LoF_mis)

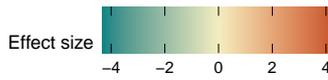


3-(3-hydroxyphenyl)propionate in urine at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



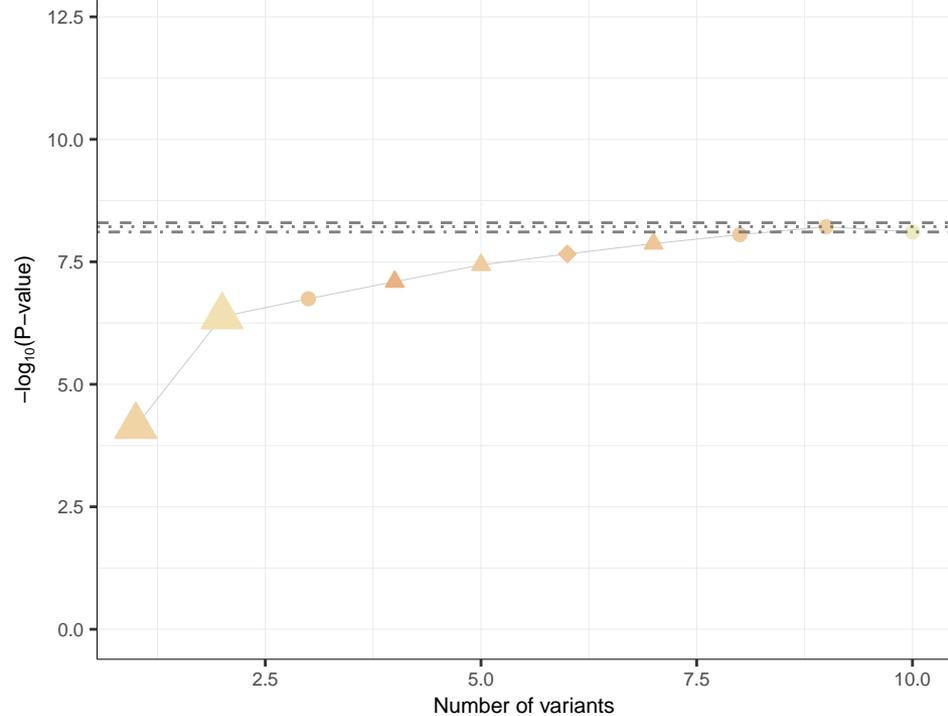
P-value

- >0.05
- <0.05
- <1e-3

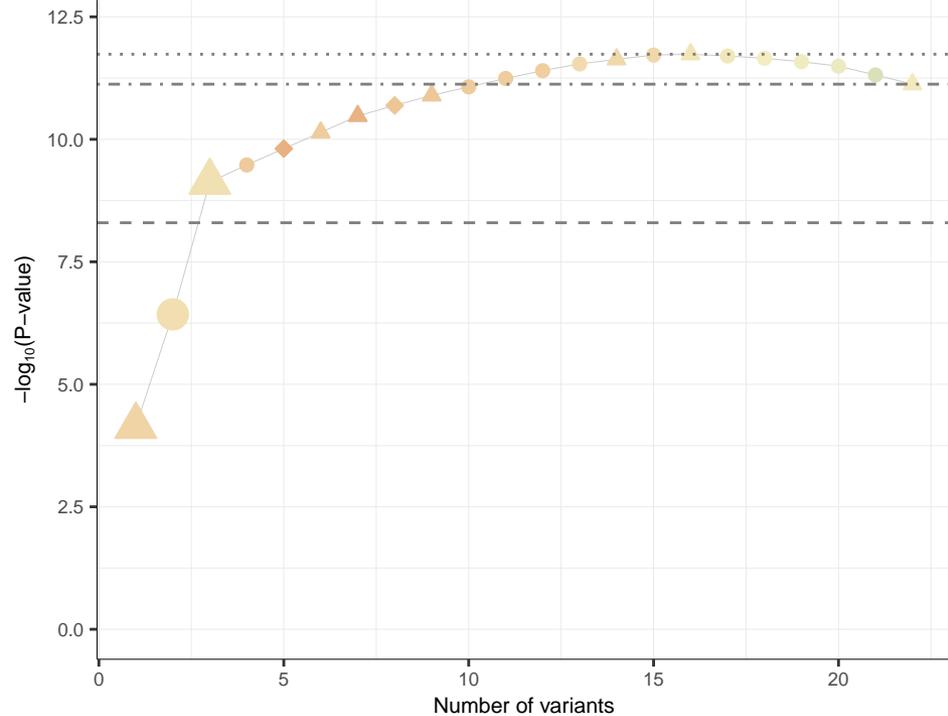
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

3-hydroxyhexanoate in plasma at ACSM2A (LoF_mis)



3-hydroxyhexanoate in plasma at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



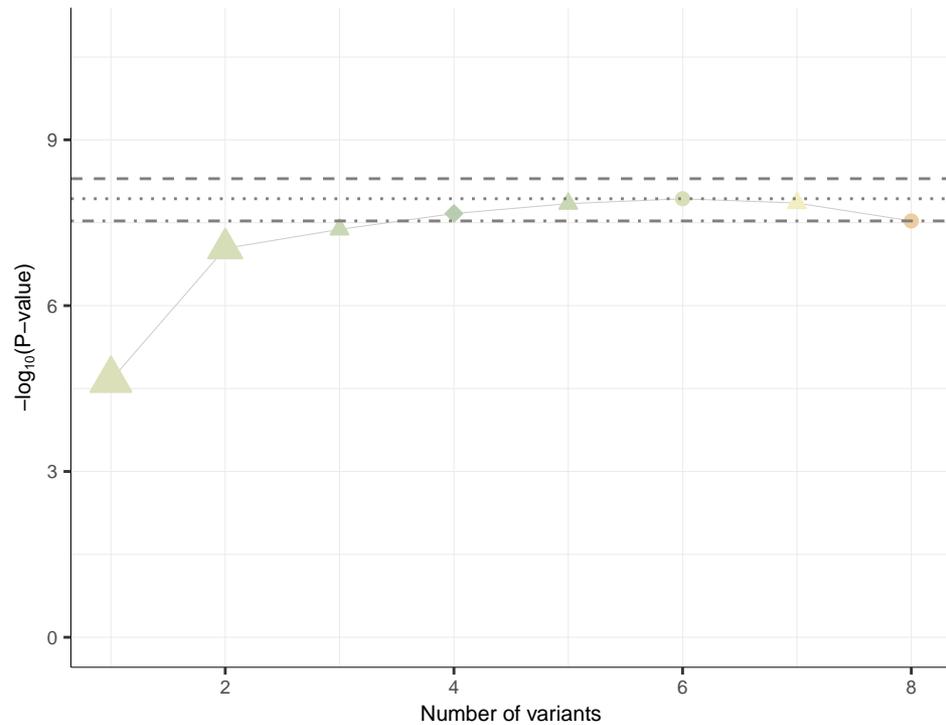
P-value

- >0.05
- <0.05
- <1e-3

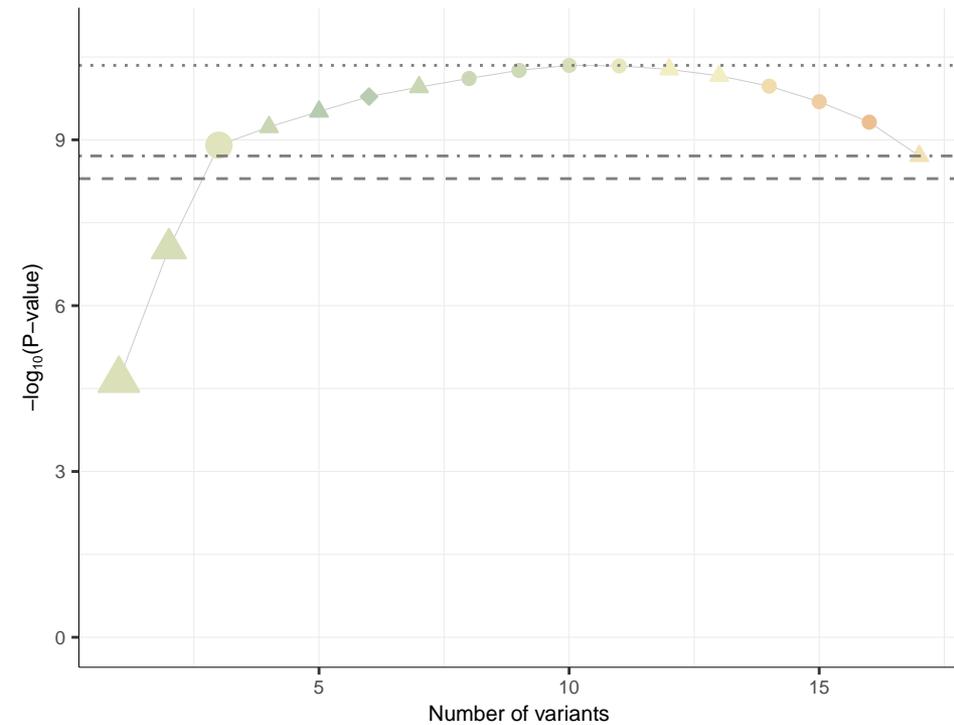
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

indoleacetyl carnitine* in plasma at ACSM2A (LoF_mis)

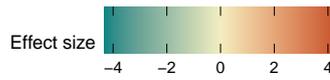


indoleacetyl carnitine* in plasma at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



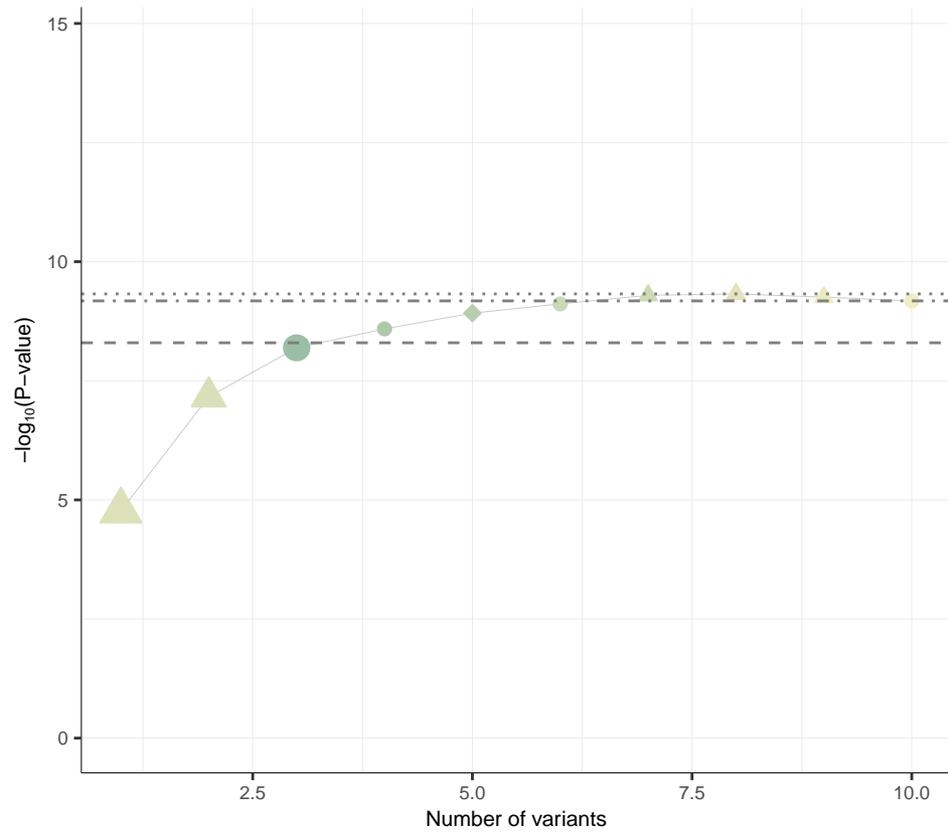
P-value

- >0.05
- <0.05
- <1e-3

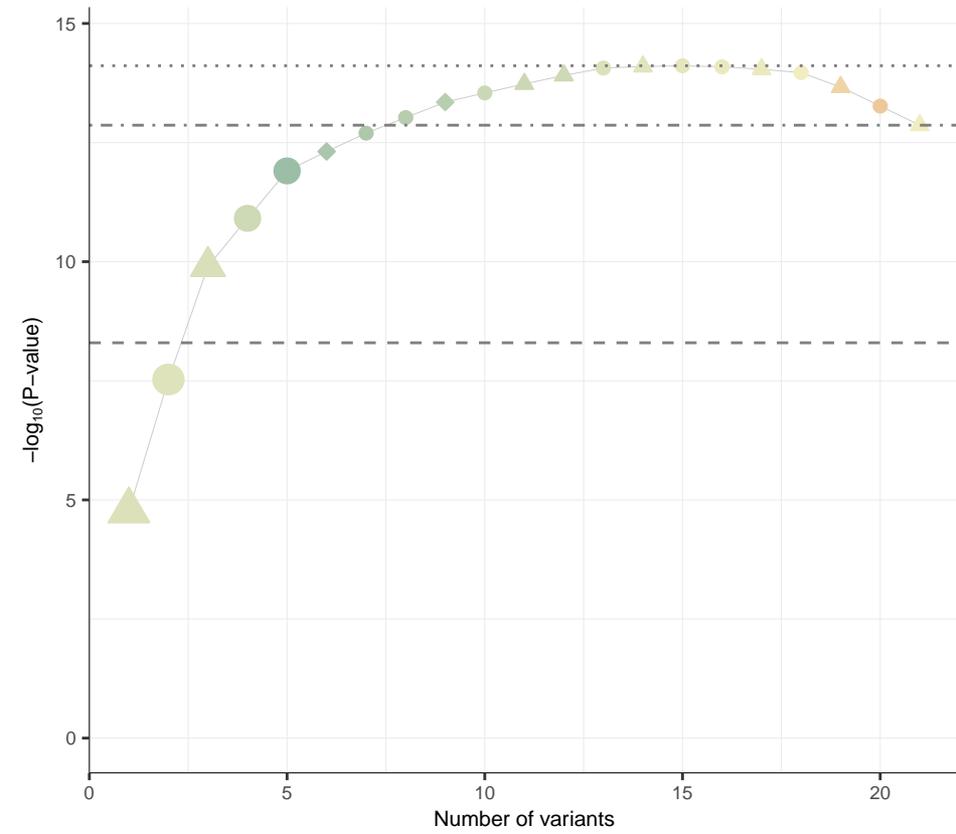
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

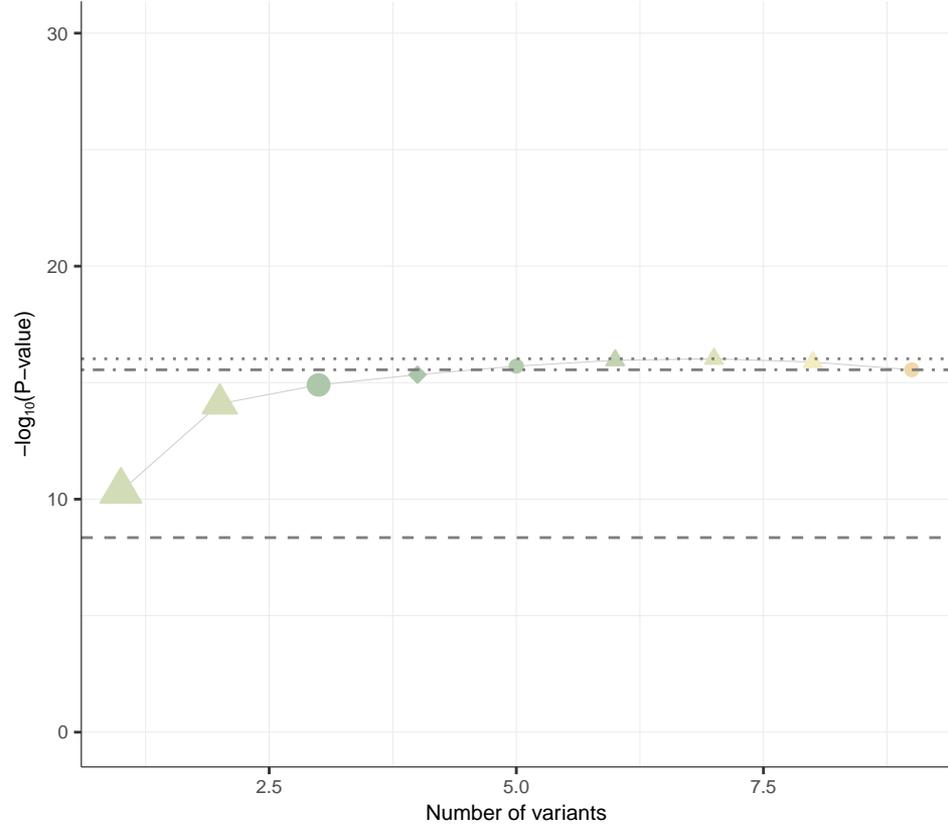
indoleacetylglutamine in plasma at ACSM2A (LoF_mis)



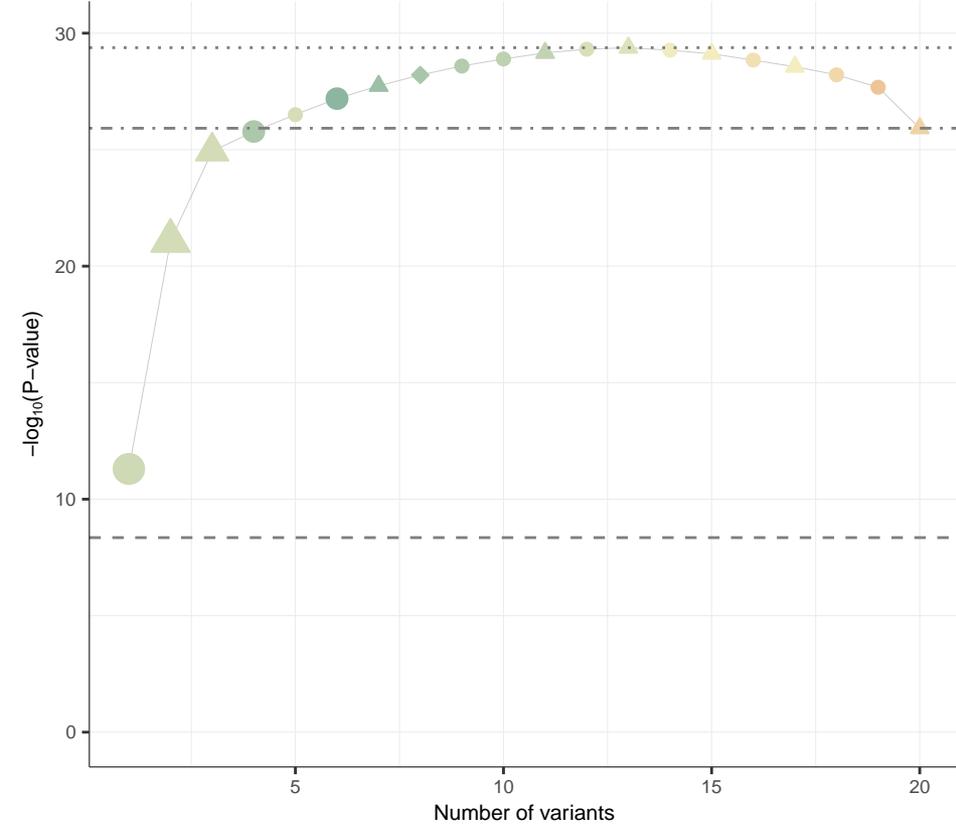
indoleacetylglutamine in plasma at ACSM2A (HI_mis)



indoleacetylglutamine in urine at ACSM2A (LoF_mis)

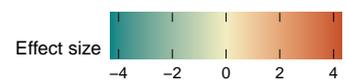


indoleacetylglutamine in urine at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



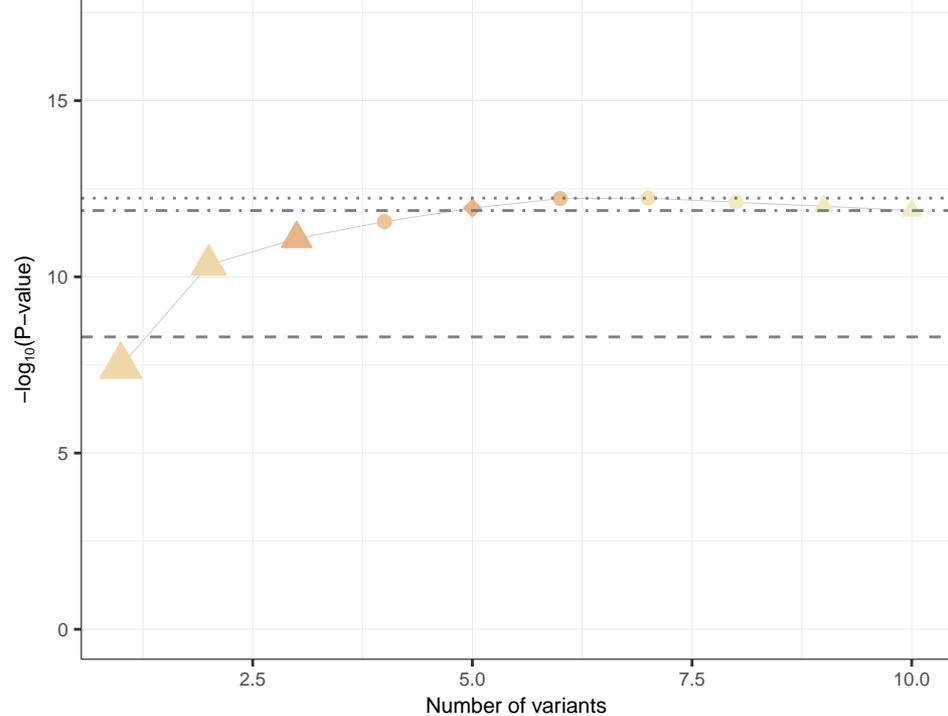
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

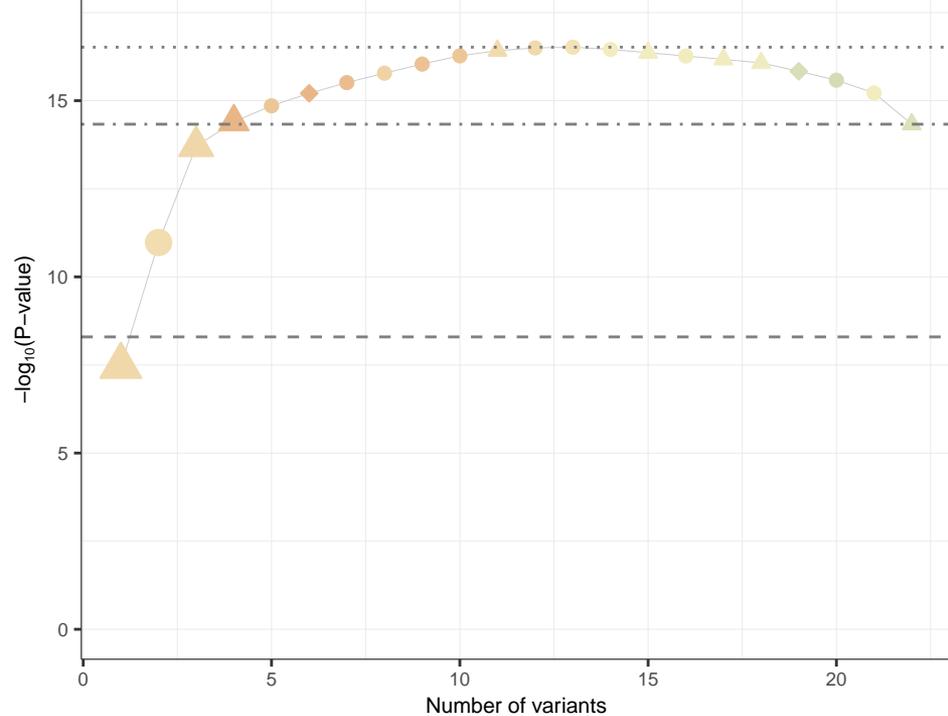
Thresholds

- Significance Threshold
- · - Total P-value
- Lowest P-value

indolepropionate in plasma at ACSM2A (LoF_mis)

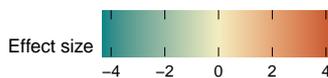


indolepropionate in plasma at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



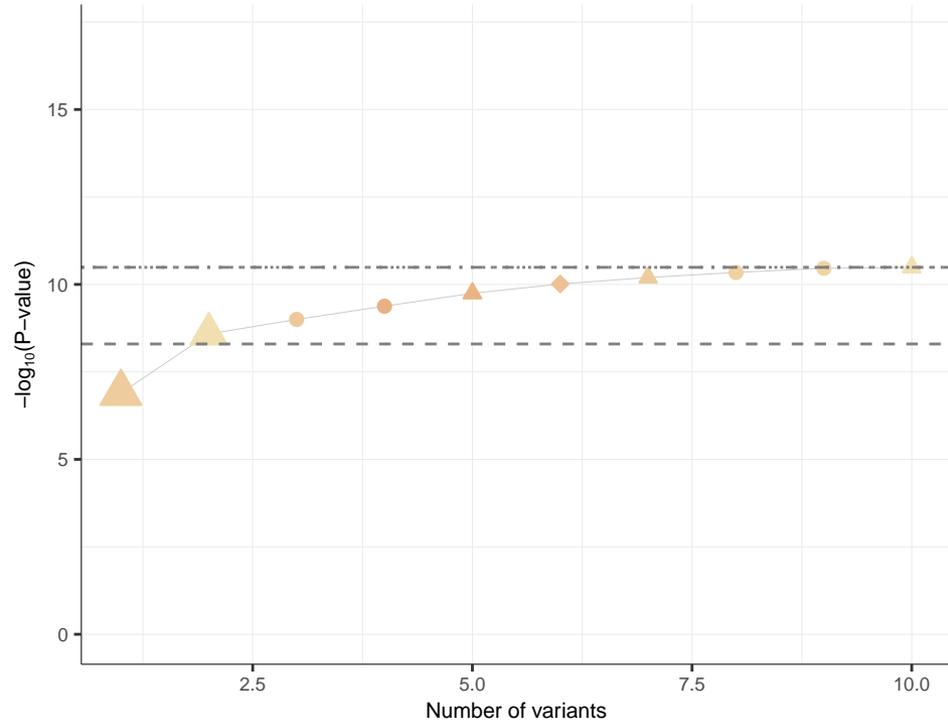
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

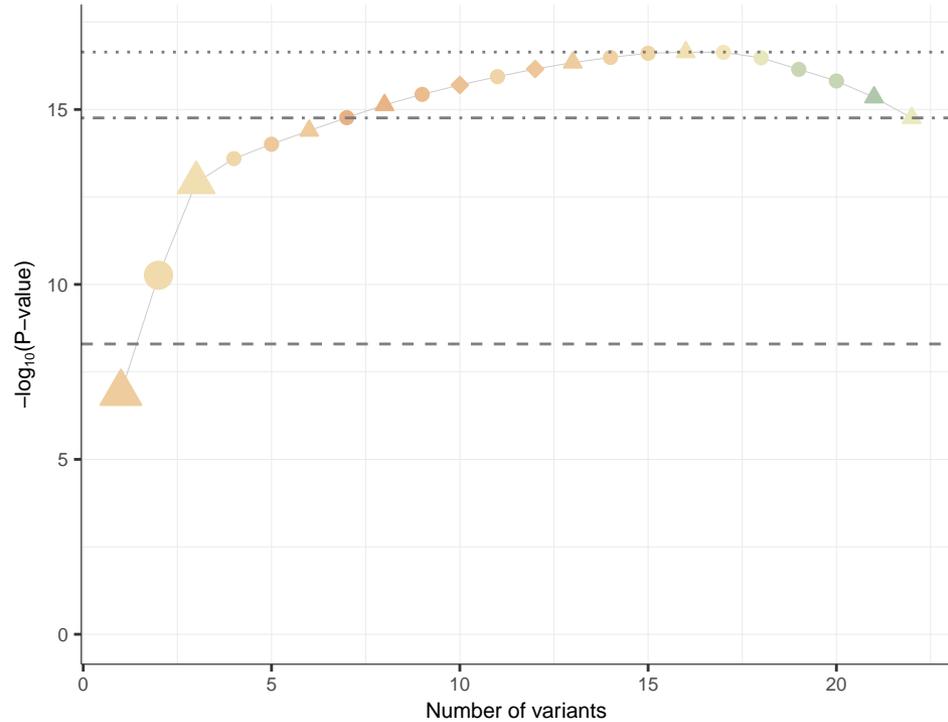
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

X - 11478 in plasma at ACSM2A (LoF_mis)

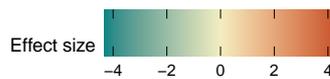


X - 11478 in plasma at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



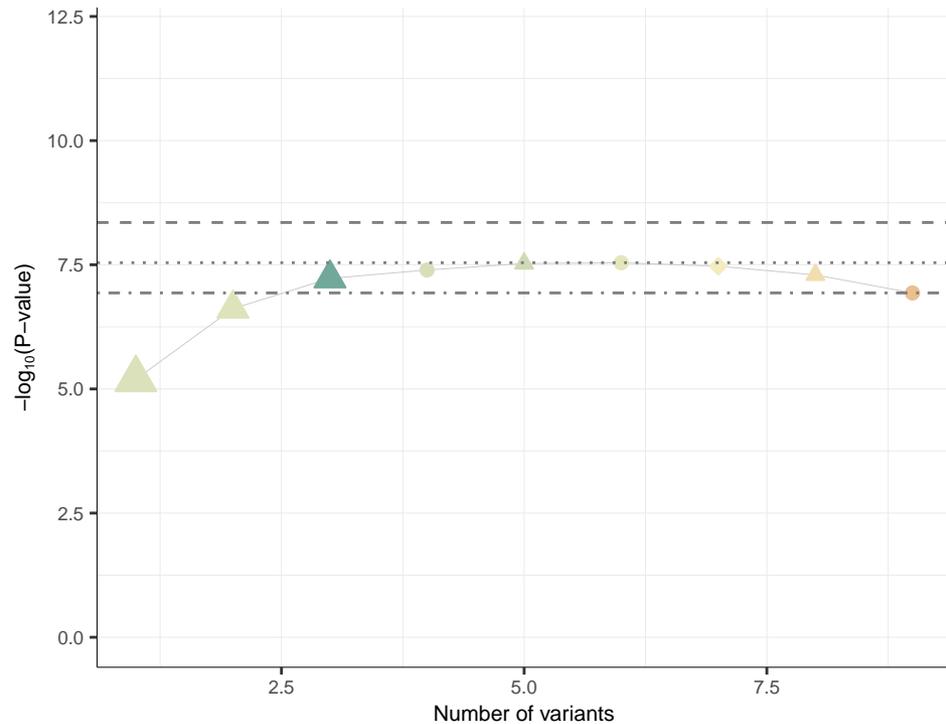
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

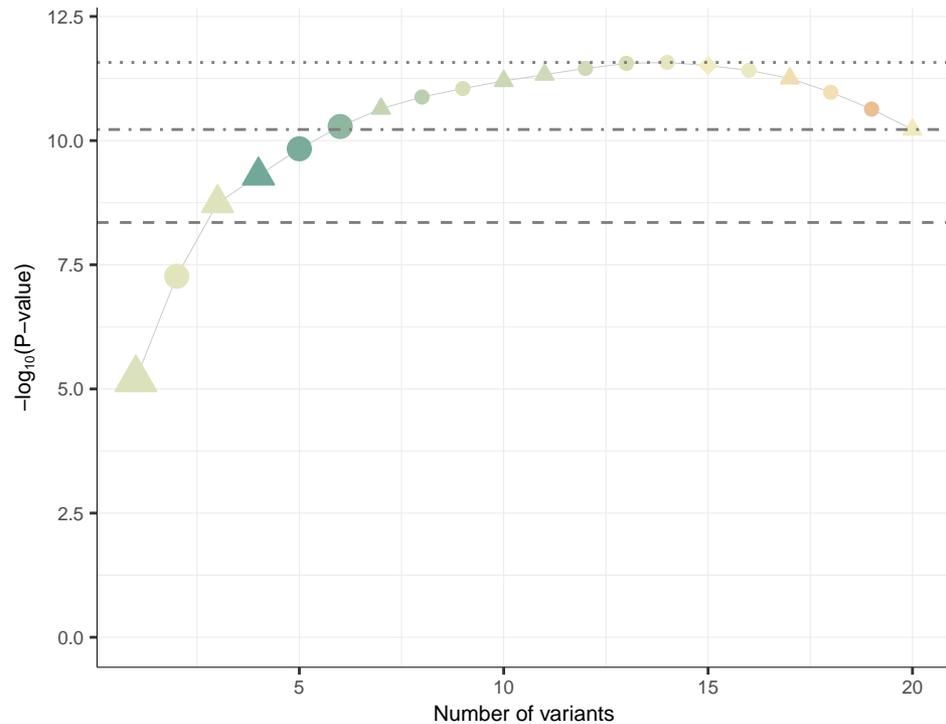
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

X - 17328 in urine at ACSM2A (LoF_mis)

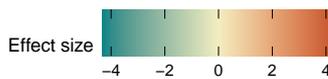


X - 17328 in urine at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



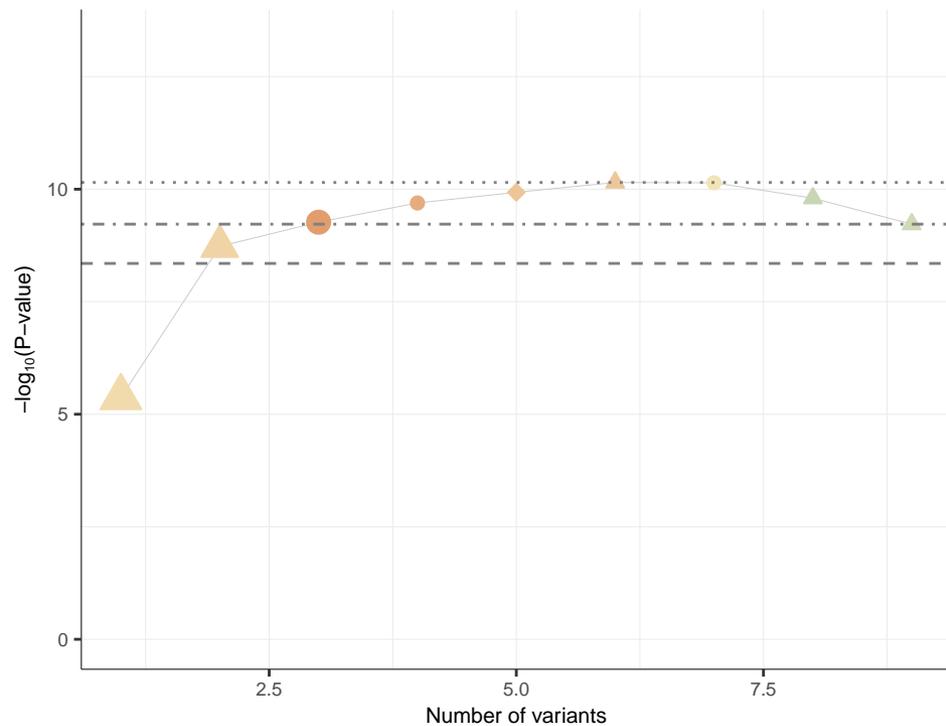
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

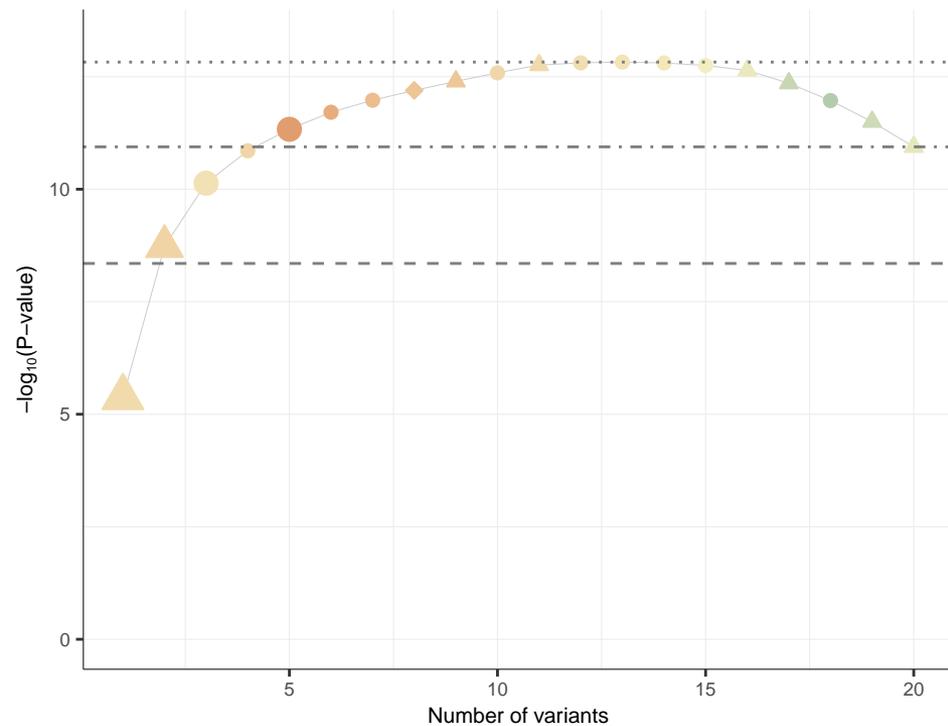
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

X - 24270 in urine at ACSM2A (LoF_mis)

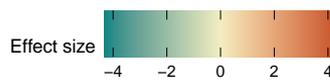


X - 24270 in urine at ACSM2A (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



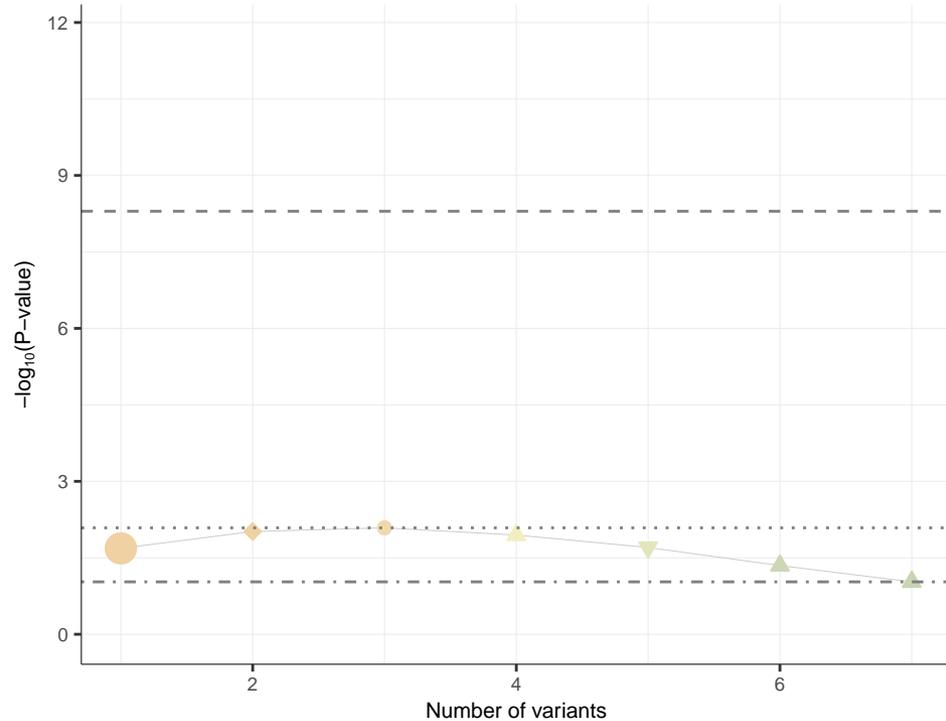
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

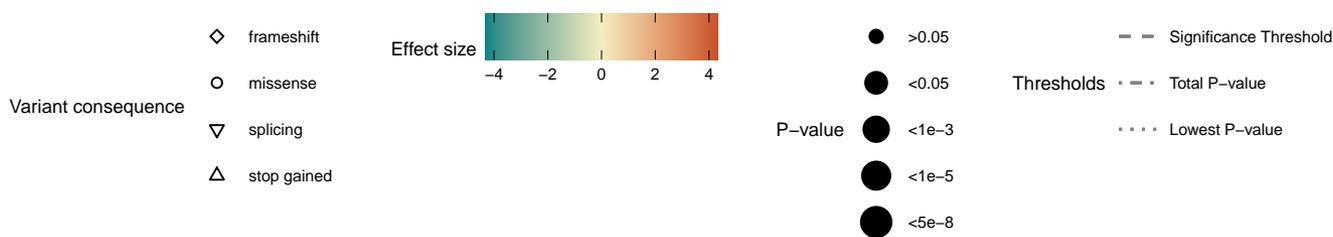
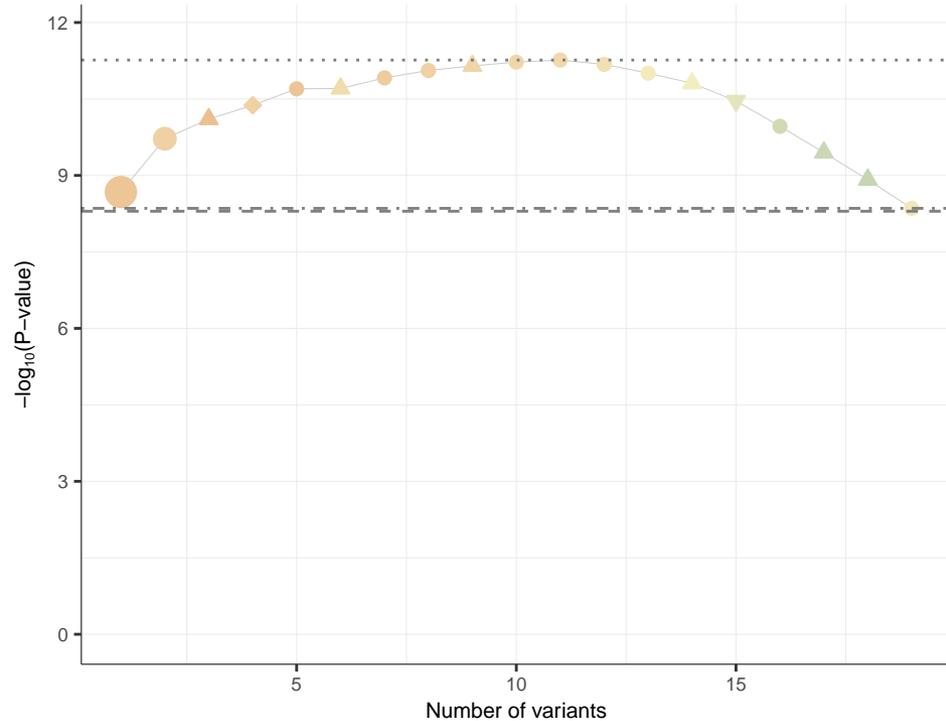
Thresholds

- - Significance Threshold
- - Total P-value
- ... Lowest P-value

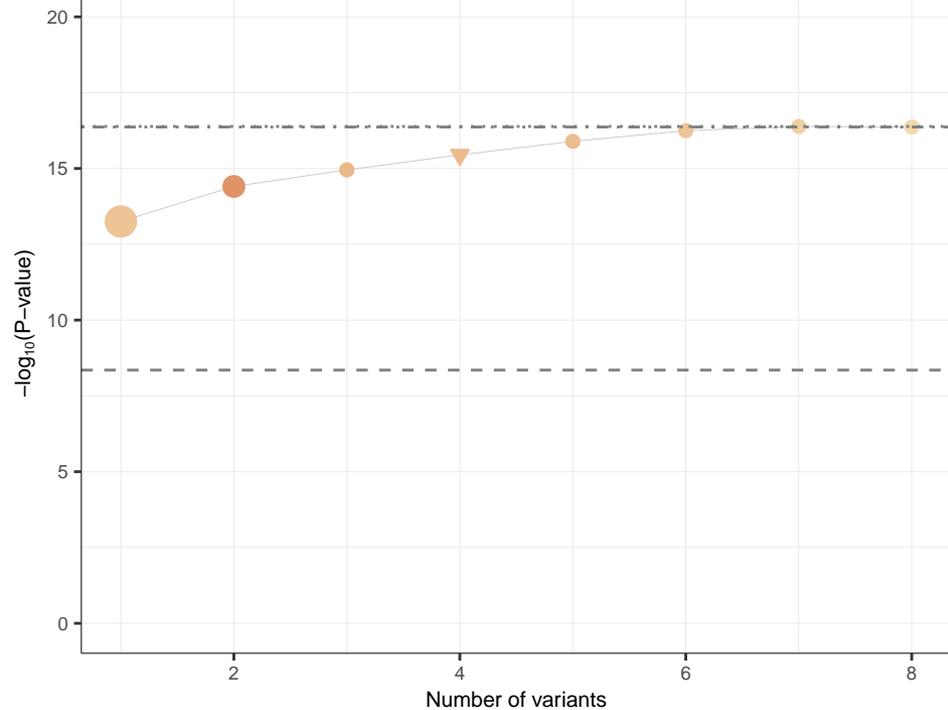
picolinate in plasma at *ACSM2B* (LoF_mis)



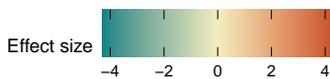
picolinate in plasma at *ACSM2B* (HI_mis)



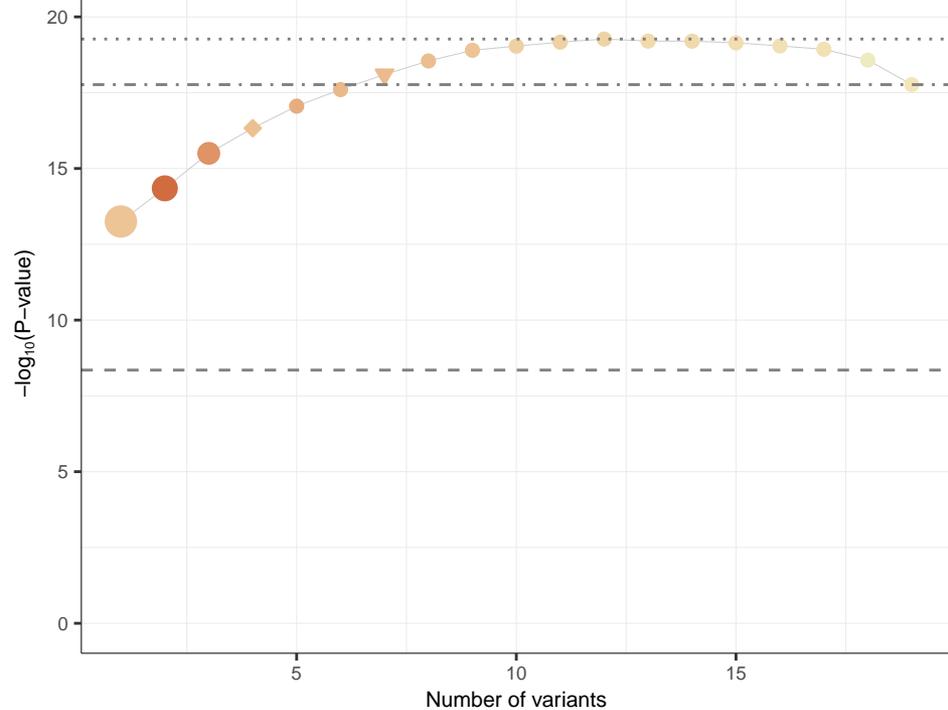
2-butenoylglycine in urine at ACY1 (LoF_mis)



- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing

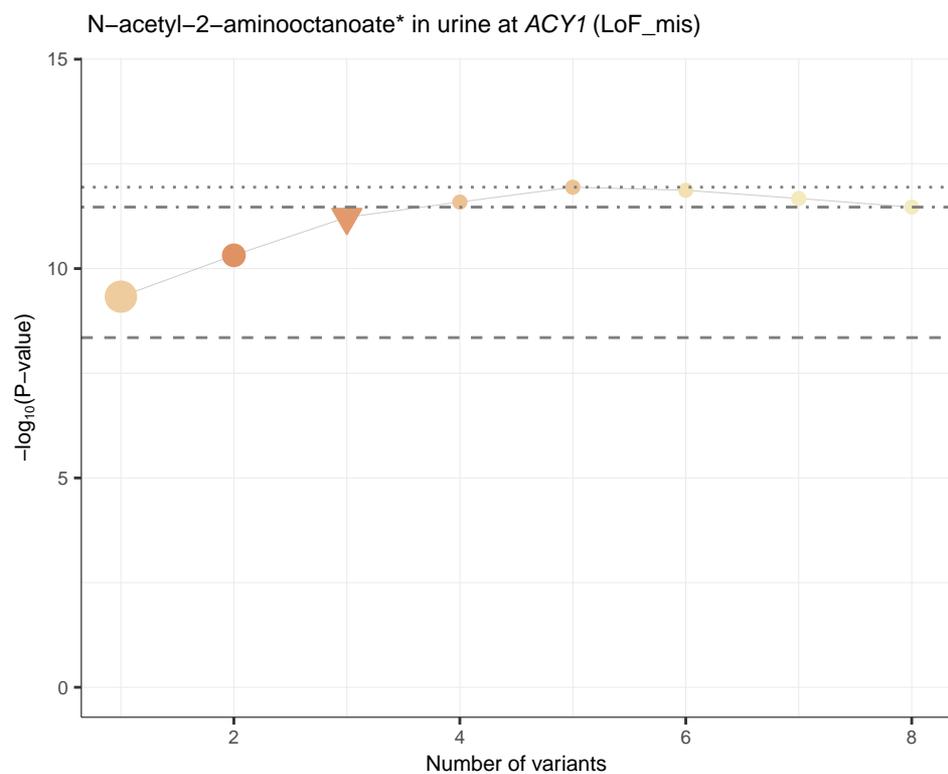


2-butenoylglycine in urine at ACY1 (HI_mis)



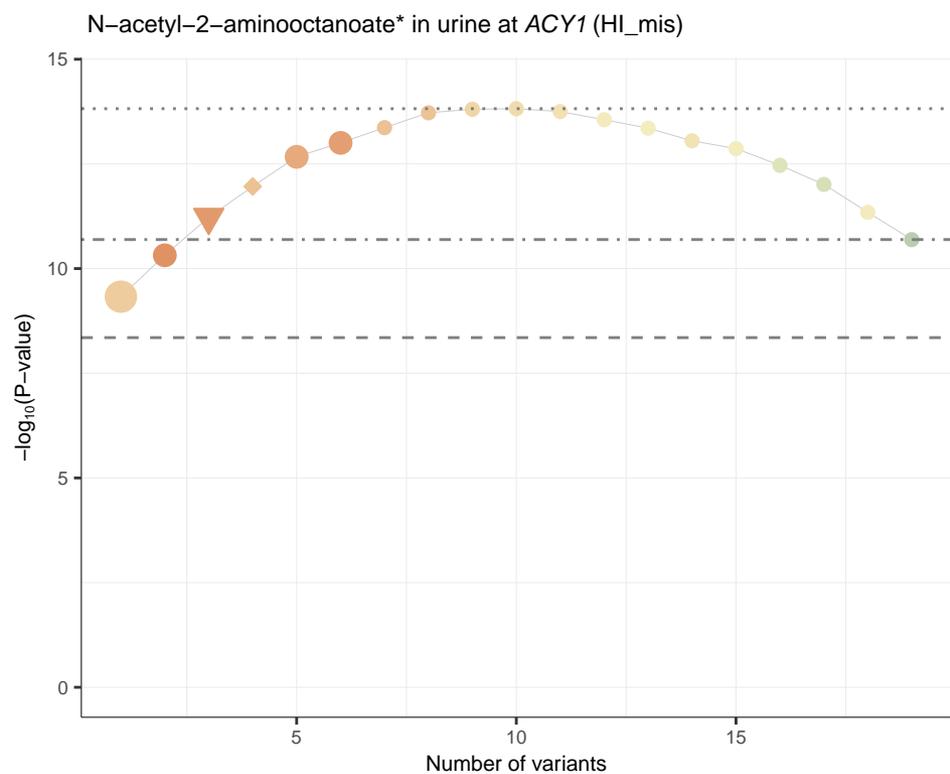
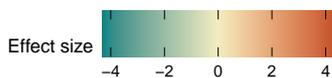
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

- Thresholds
- - - Significance Threshold
 - · - Total P-value
 - · · Lowest P-value



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



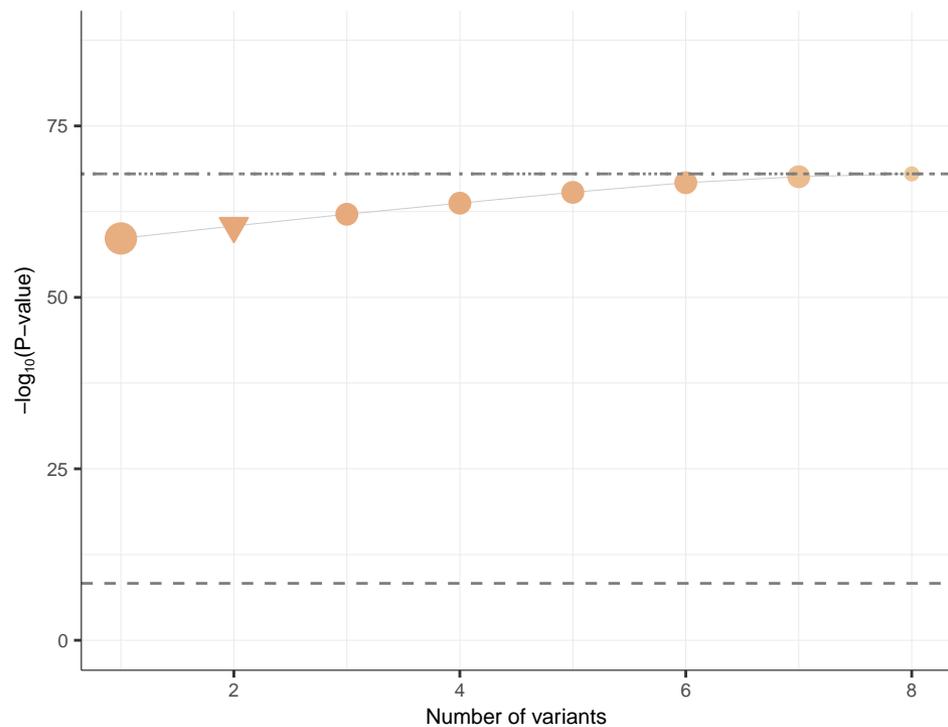
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

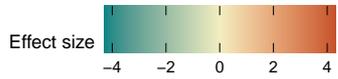
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

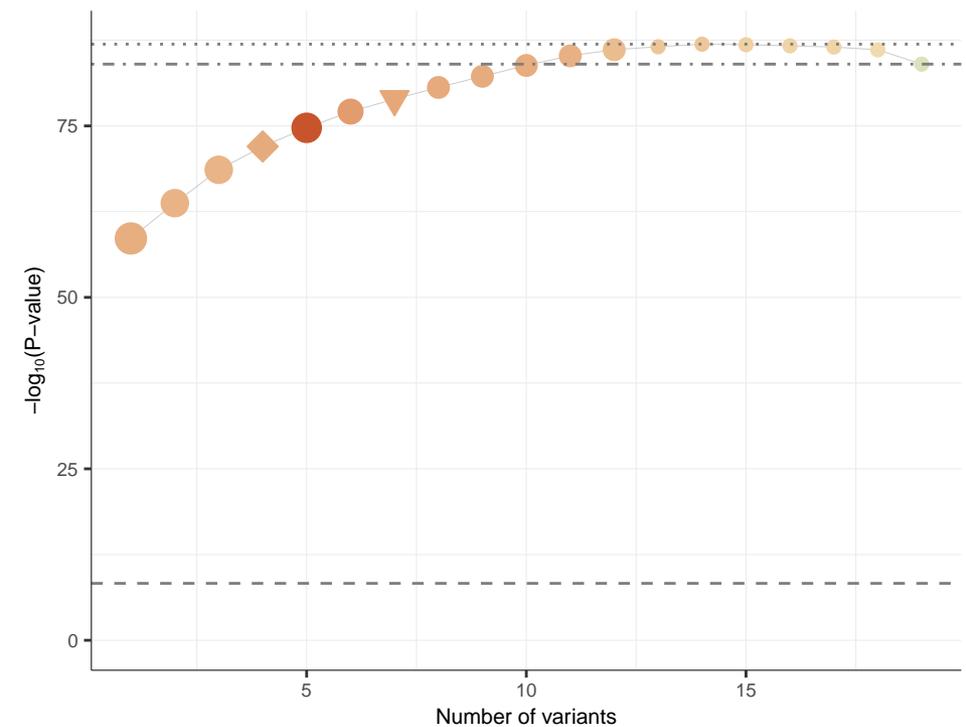
N-acetylalanine in plasma at ACY1 (LoF_mis)



- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing



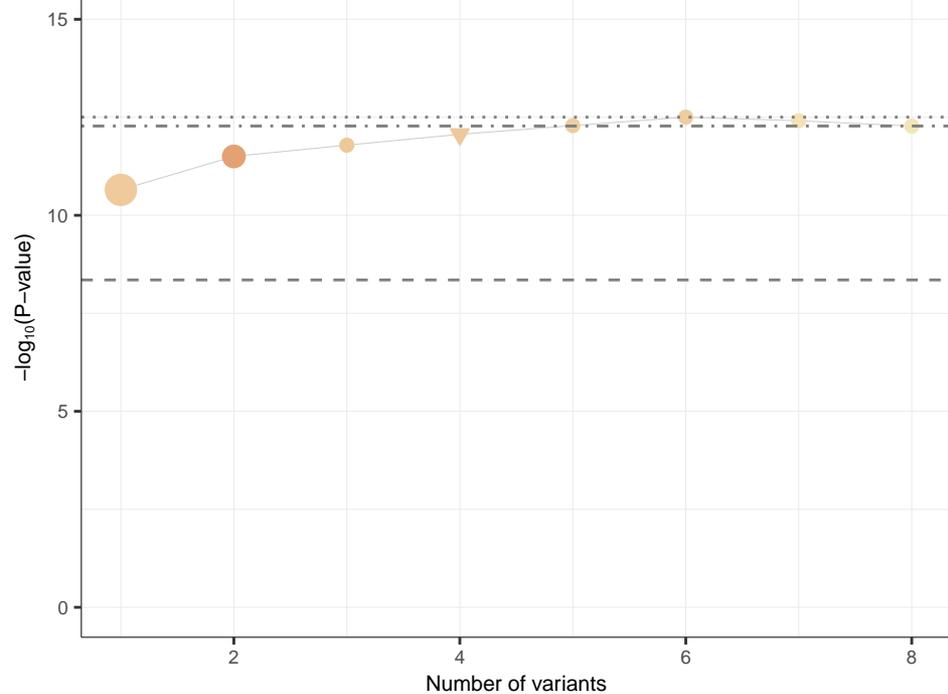
N-acetylalanine in plasma at ACY1 (HI_mis)



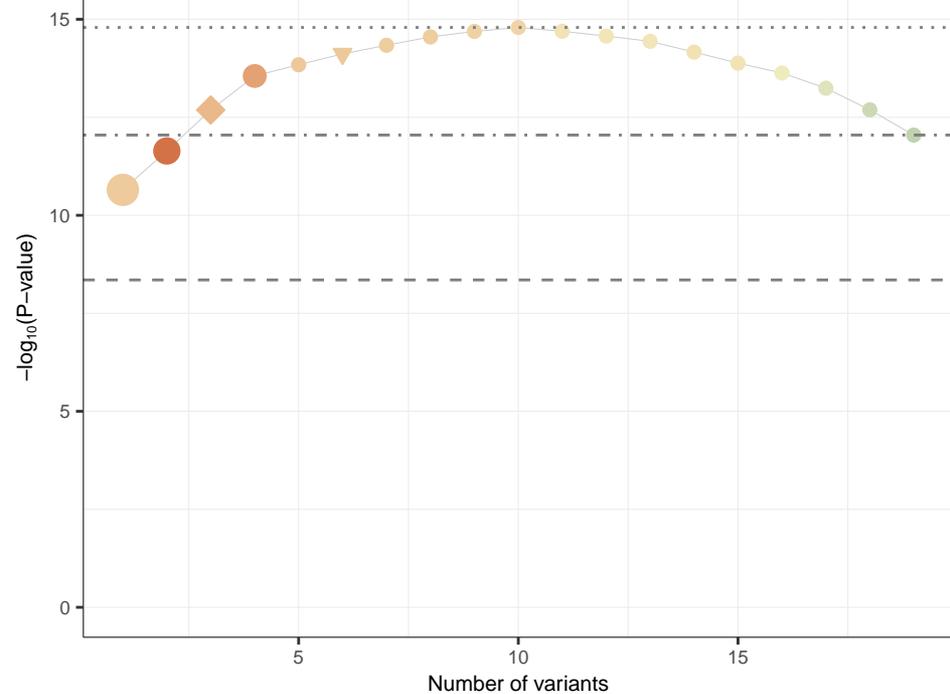
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

- Thresholds
- - Significance Threshold
 - . - Total P-value
 - Lowest P-value

N-acetylasparagine in urine at ACY1 (LoF_mis)

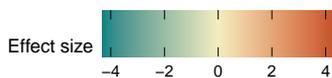


N-acetylasparagine in urine at ACY1 (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



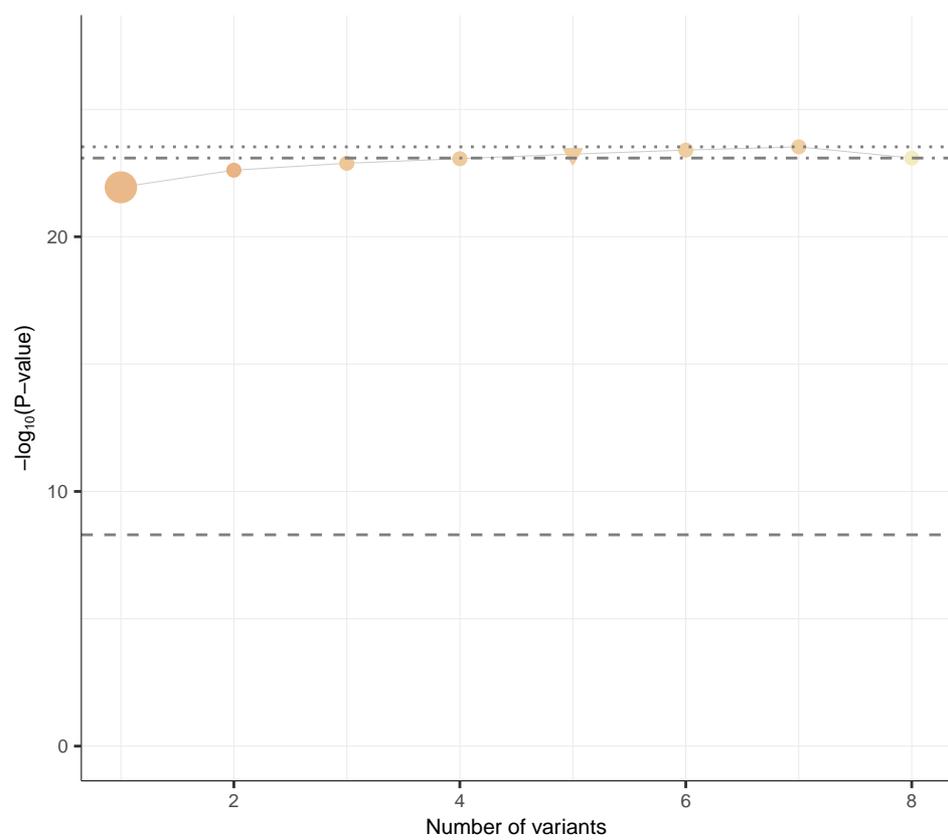
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

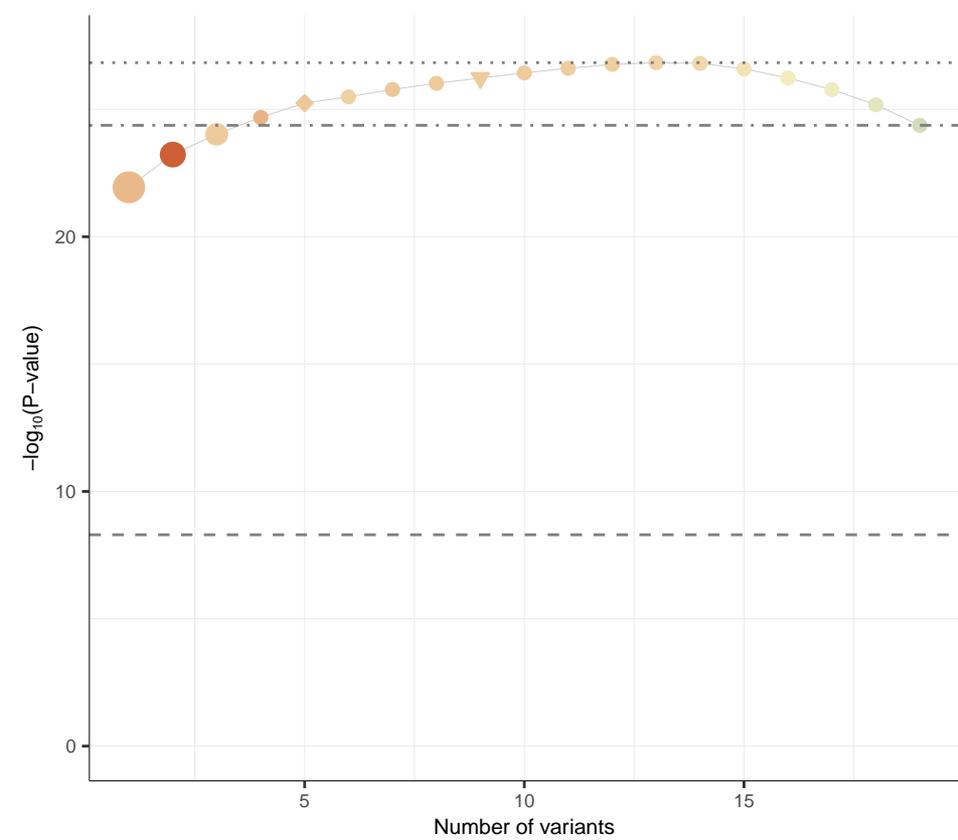
Thresholds

- - Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

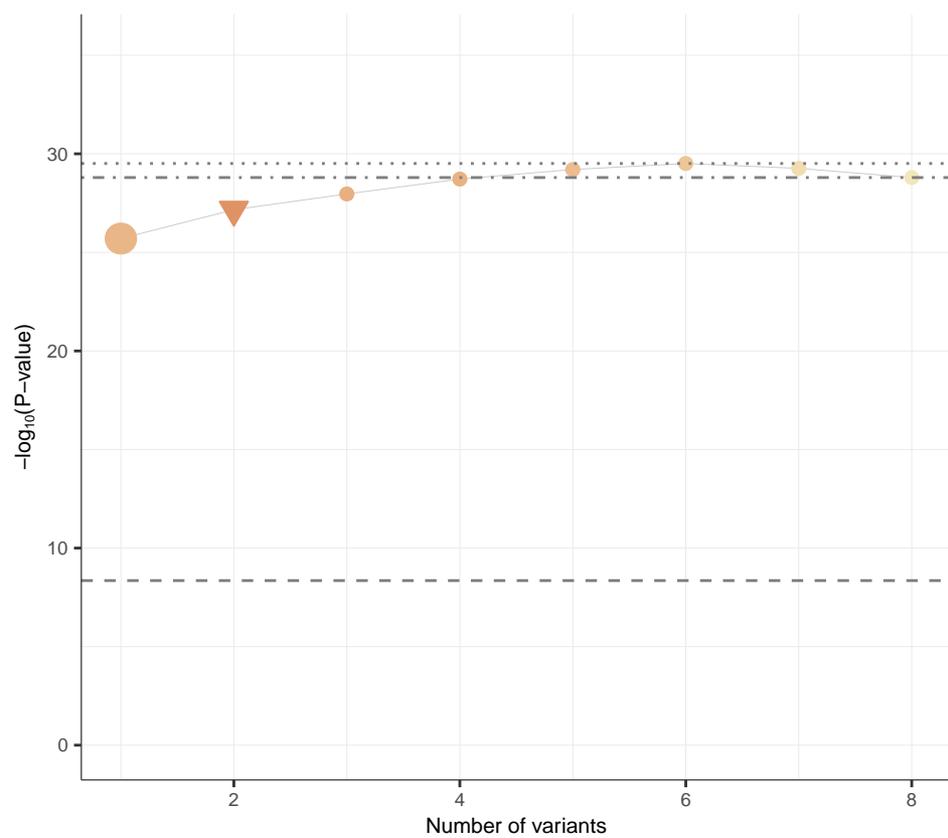
N-acetylglutamate in plasma at ACY1 (LoF_mis)



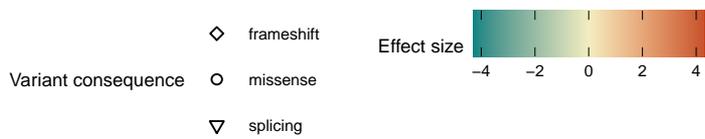
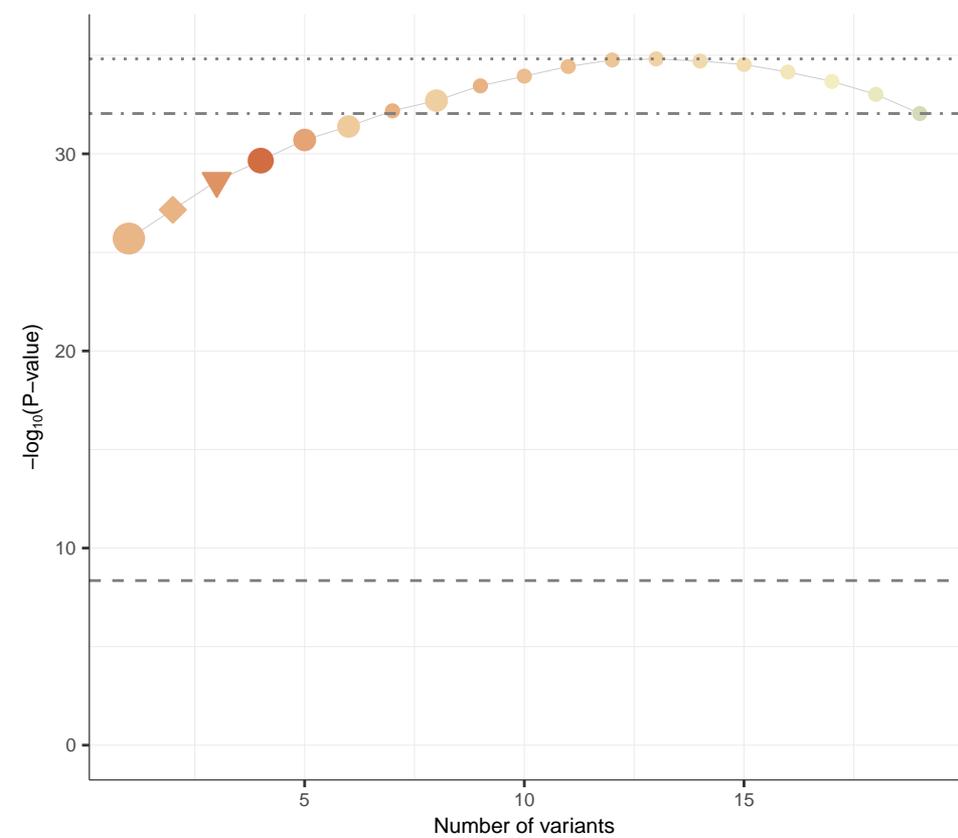
N-acetylglutamate in plasma at ACY1 (HI_mis)



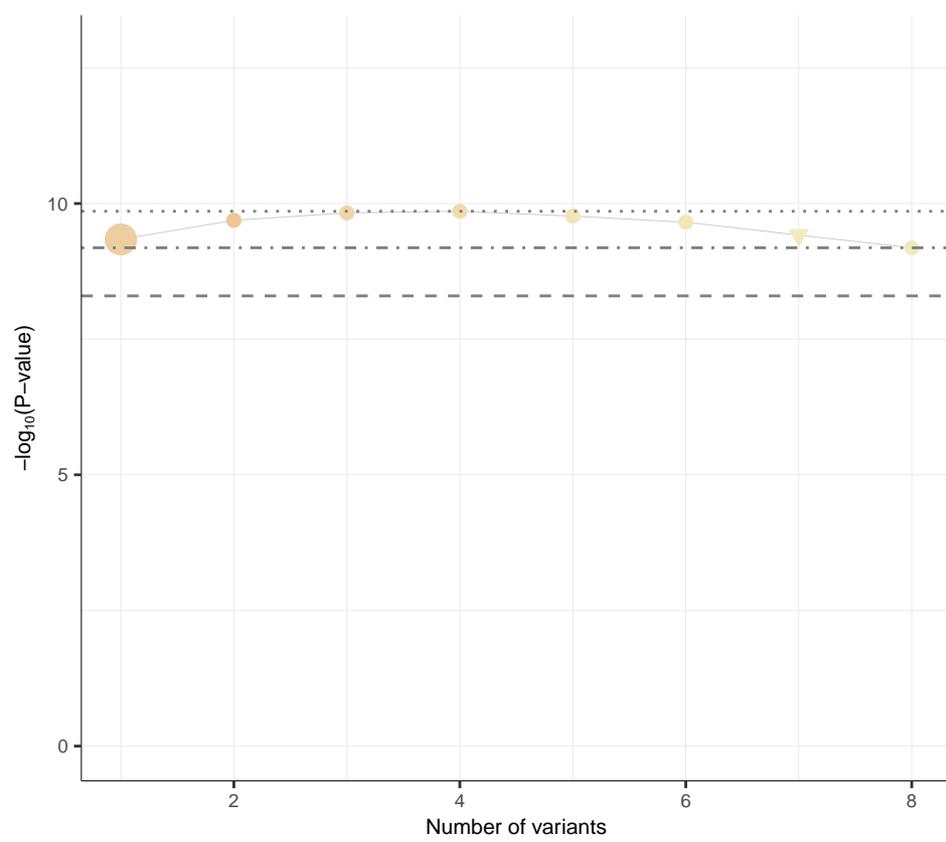
N-acetylglutamate in urine at ACY1 (LoF_mis)



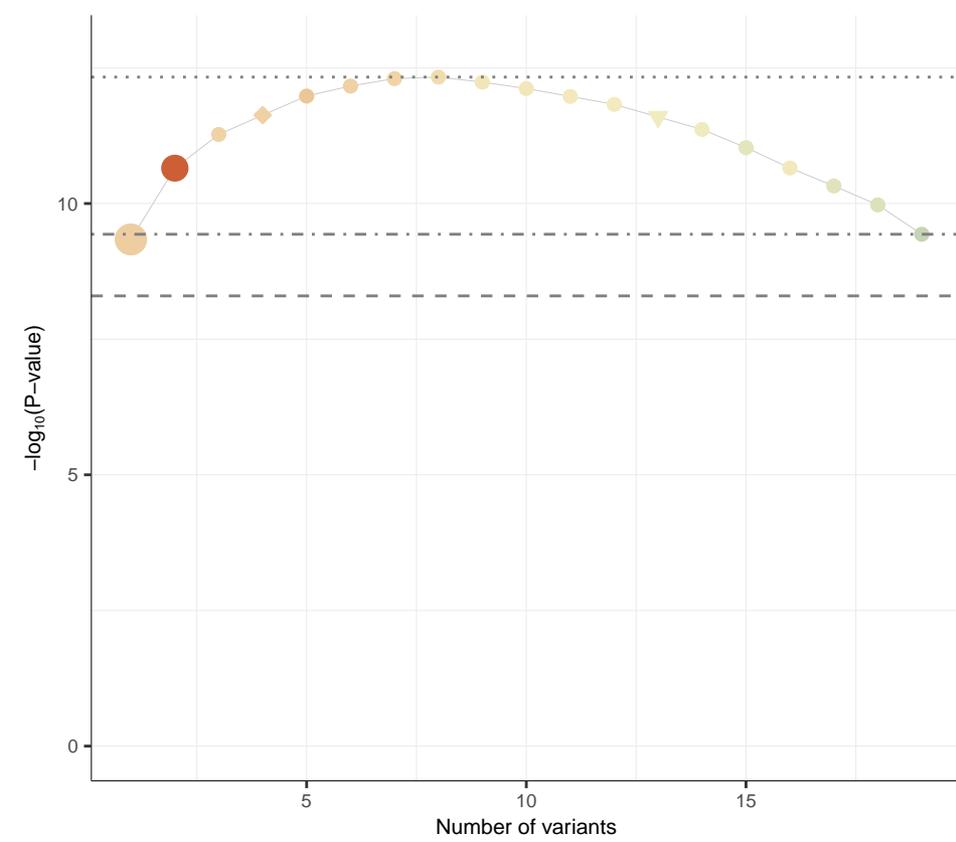
N-acetylglutamate in urine at ACY1 (HI_mis)



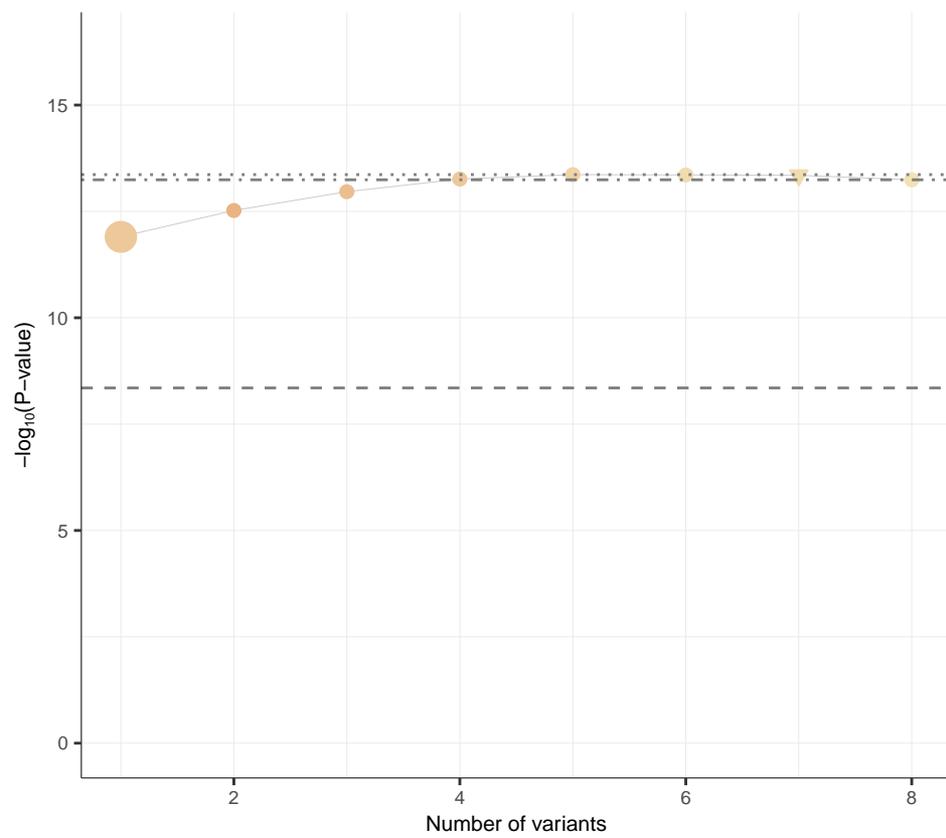
N-acetylglutamine in plasma at ACY1 (LoF_mis)



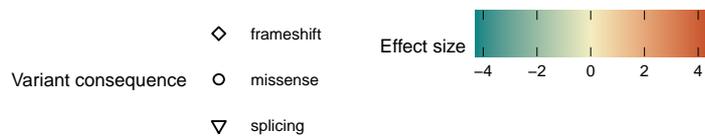
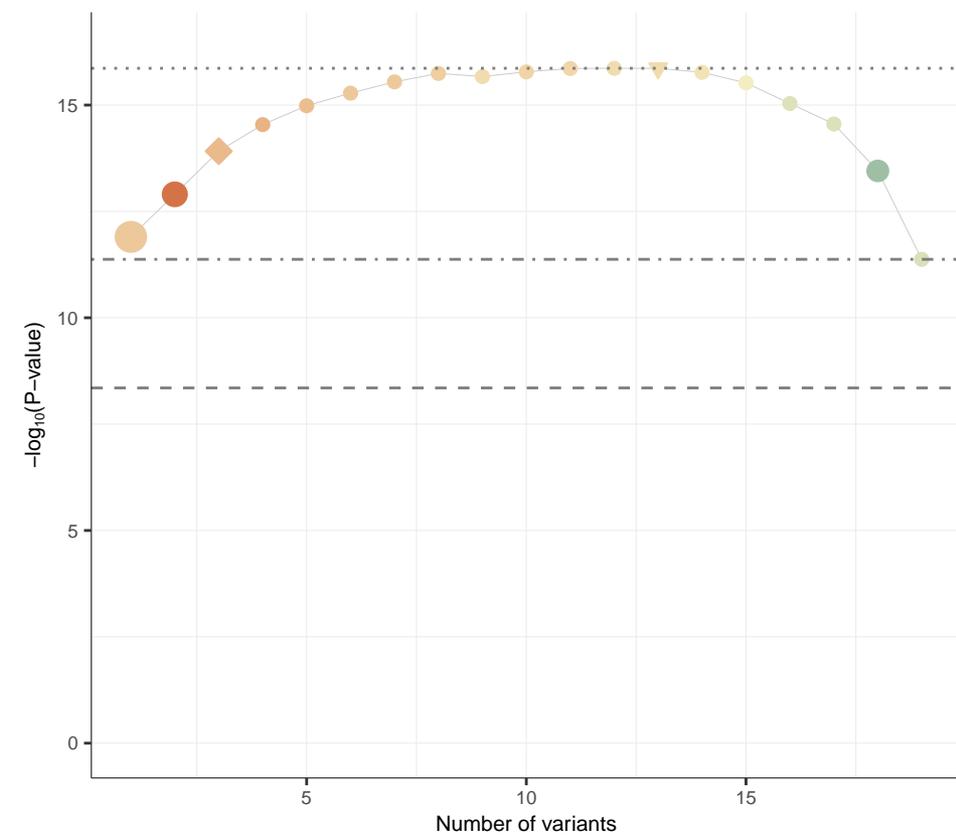
N-acetylglutamine in plasma at ACY1 (HI_mis)



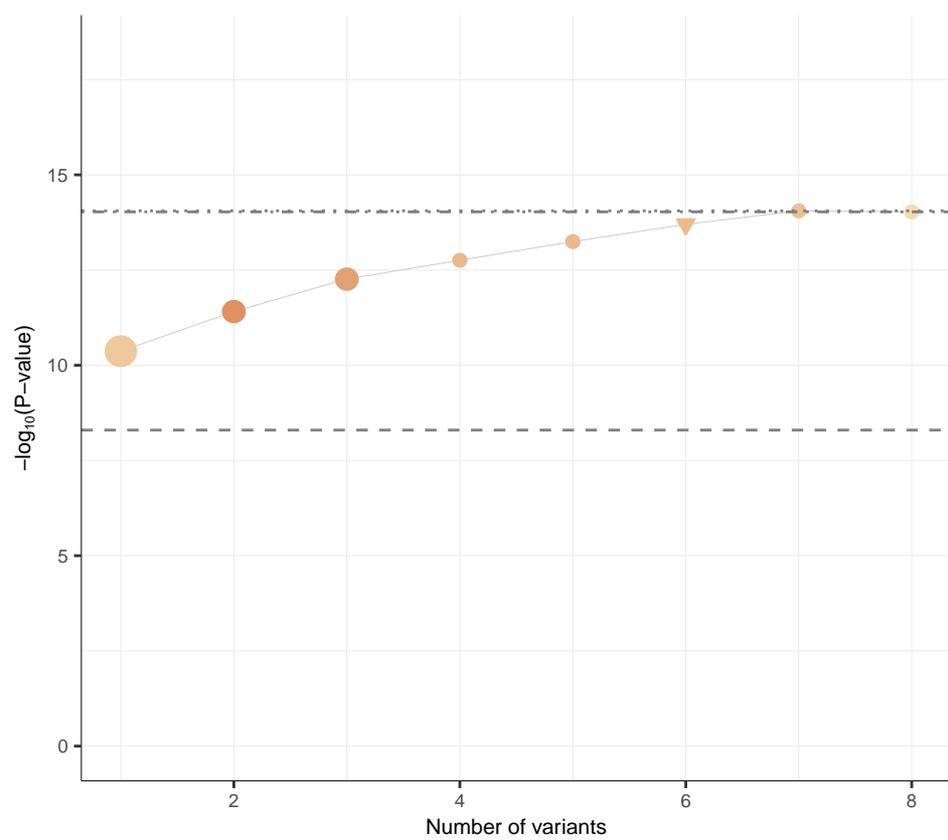
N-acetylglutamine in urine at ACY1 (LoF_mis)



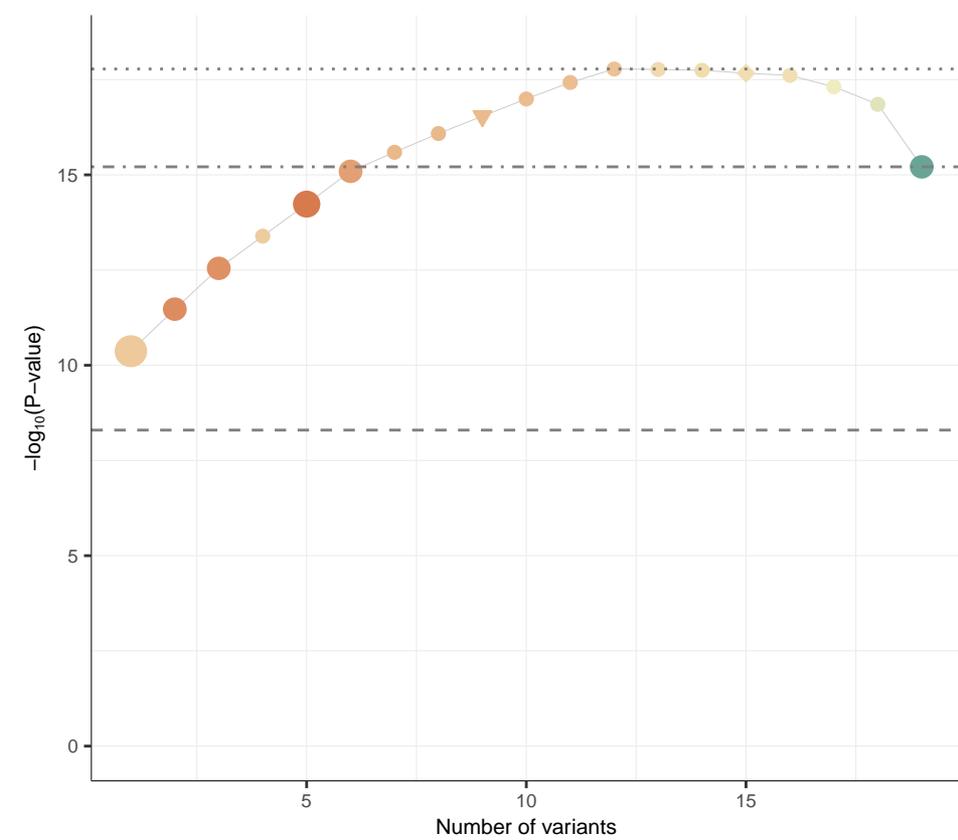
N-acetylglutamine in urine at ACY1 (HI_mis)



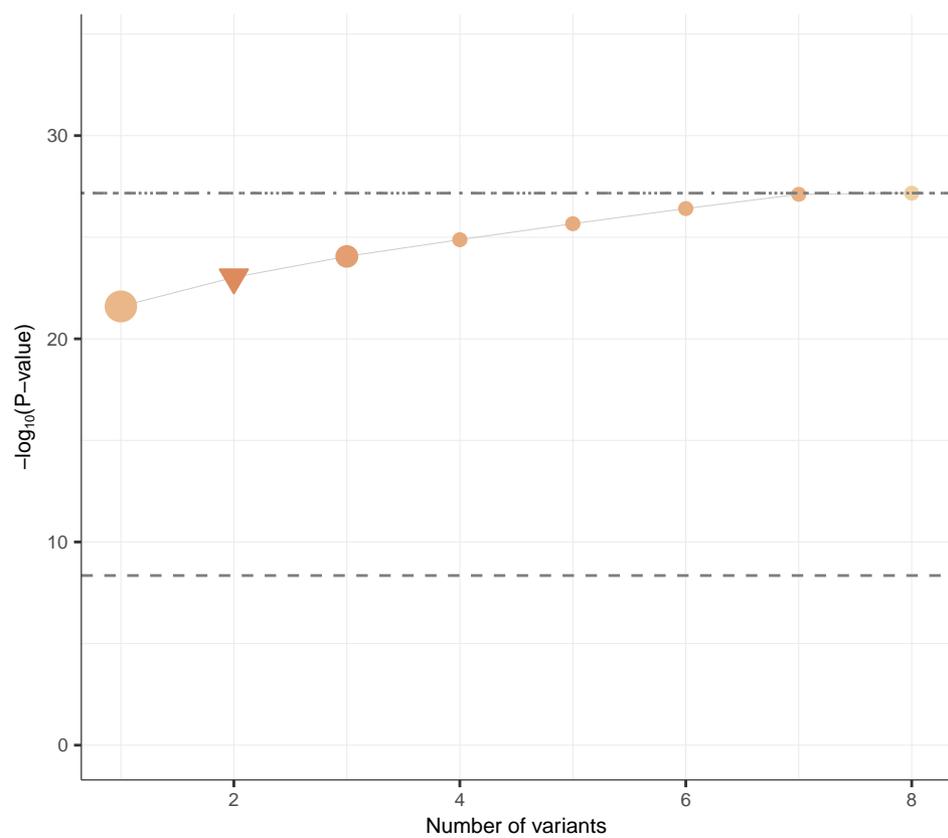
N-acetylglycine in plasma at *ACY1* (LoF_mis)



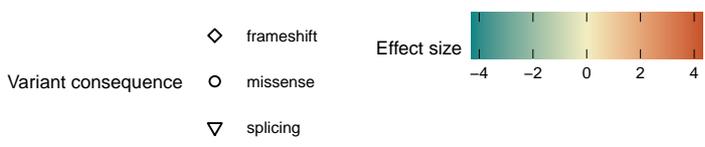
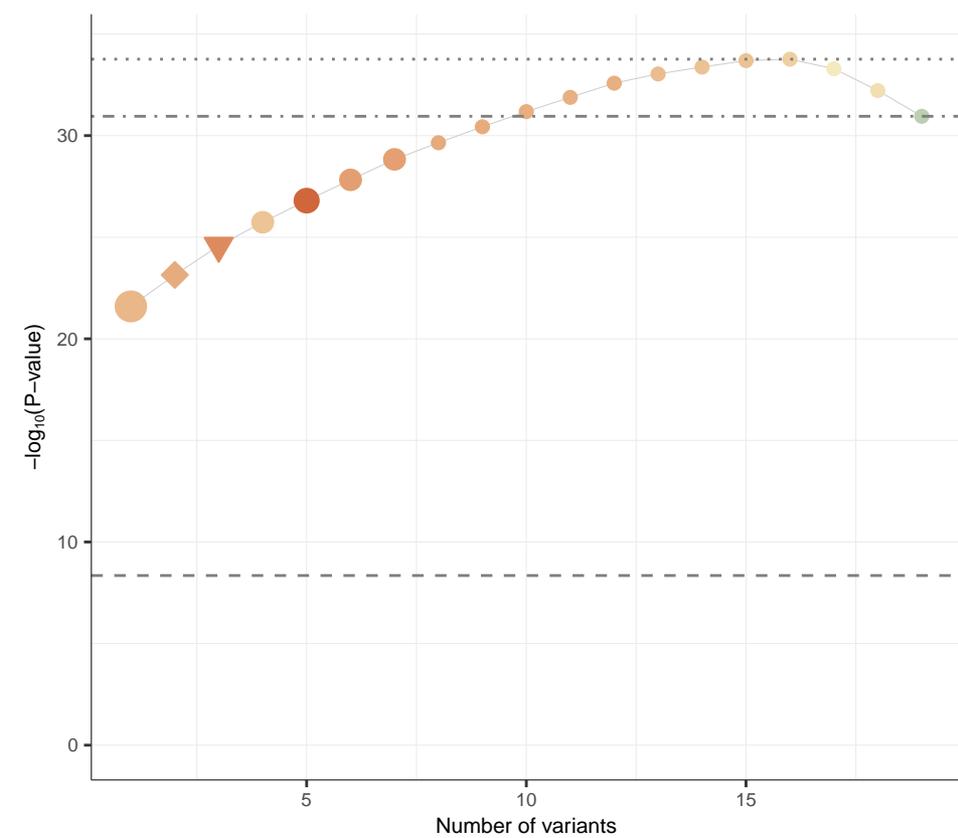
N-acetylglycine in plasma at *ACY1* (HI_mis)



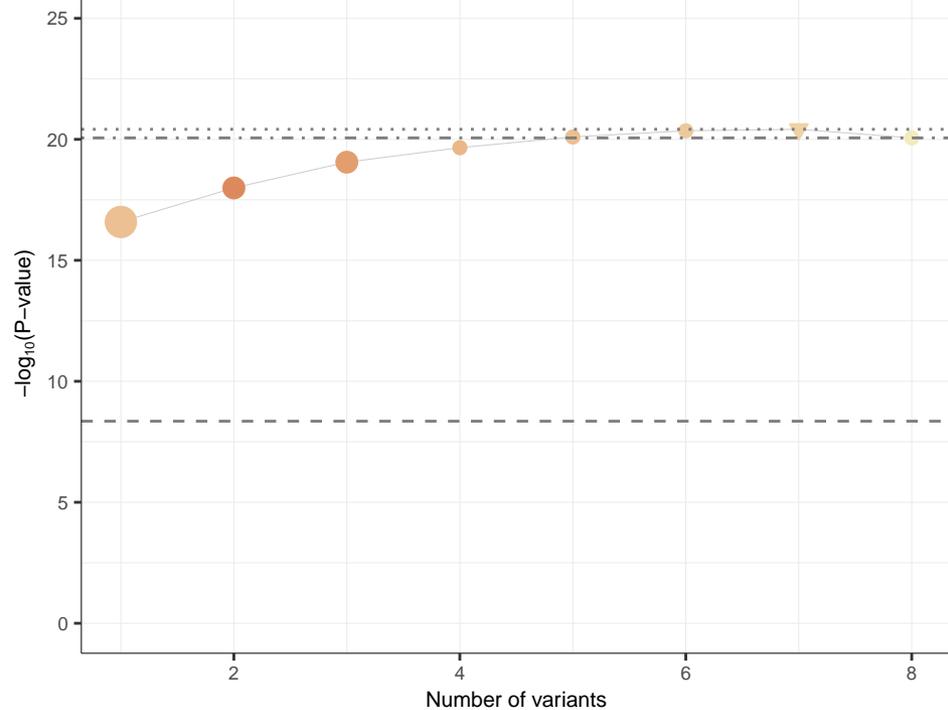
N-acetylglycine in urine at *ACY1* (LoF_mis)



N-acetylglycine in urine at *ACY1* (HI_mis)

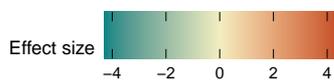


N-acetylisoleucine in urine at ACY1 (LoF_mis)

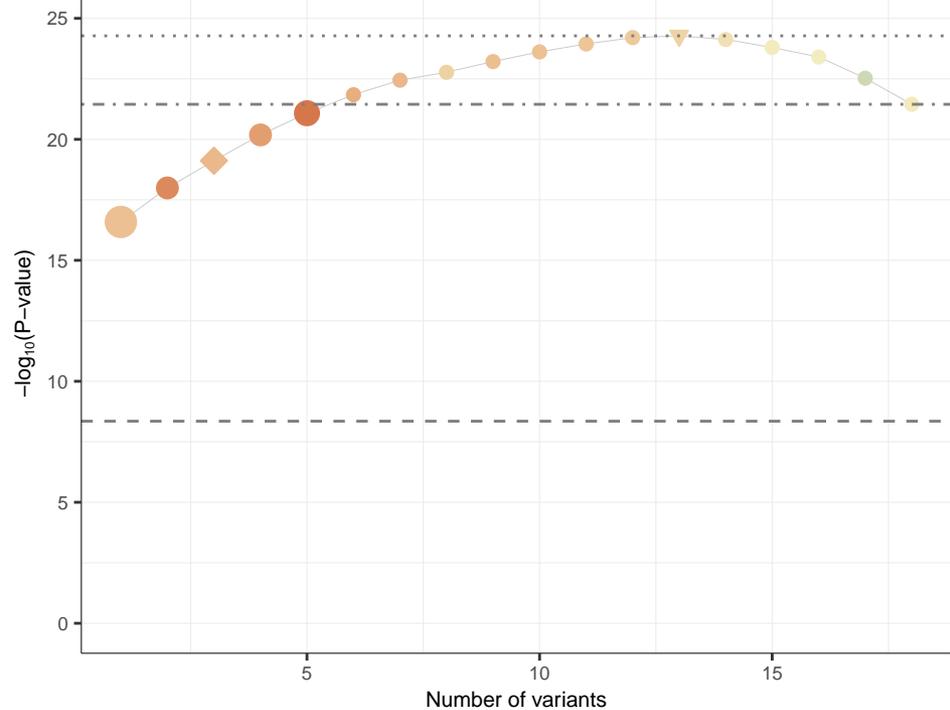


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



N-acetylisoleucine in urine at ACY1 (HI_mis)



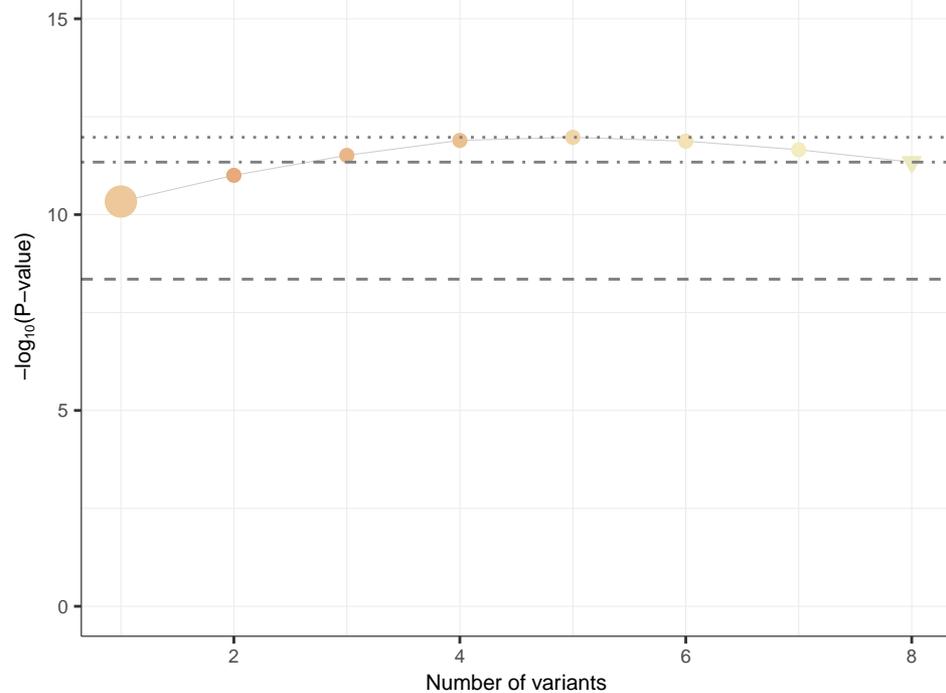
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

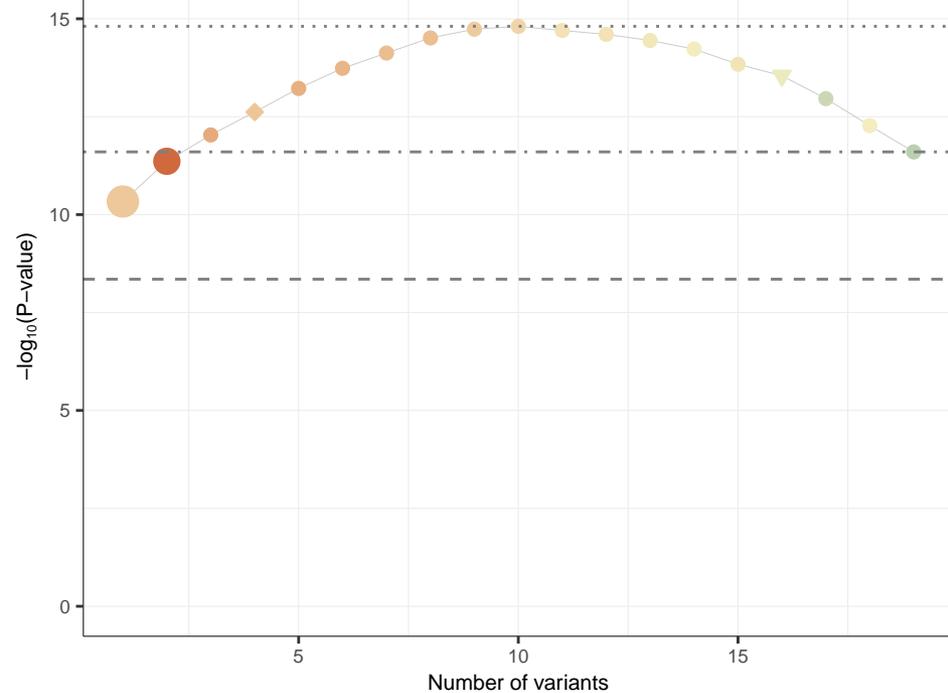
Thresholds

- - Significance Threshold
- · - Total P-value
- · · Lowest P-value

N-acetyllecucine in urine at ACY1 (LoF_mis)

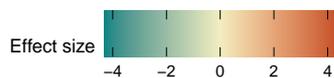


N-acetyllecucine in urine at ACY1 (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



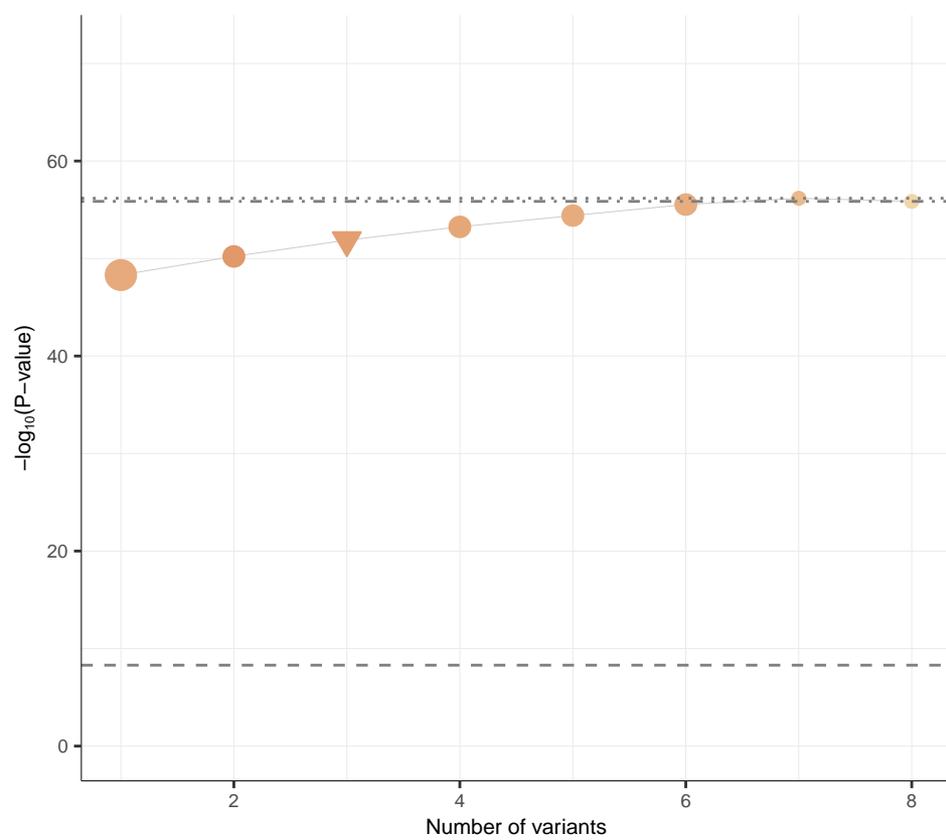
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

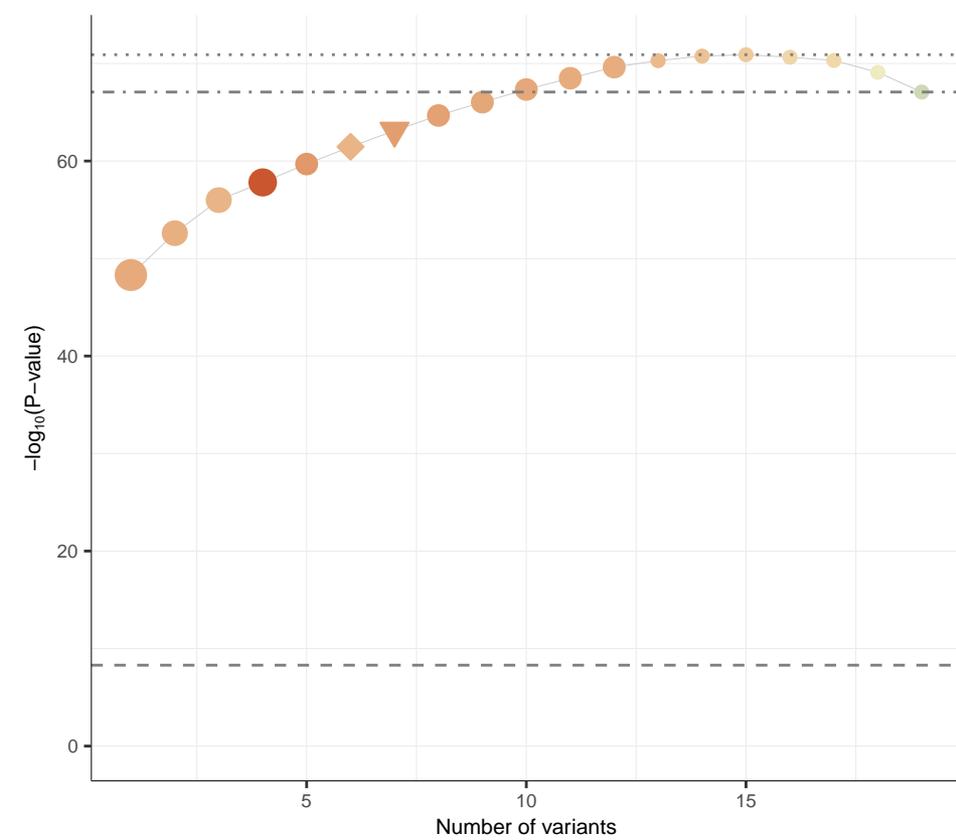
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

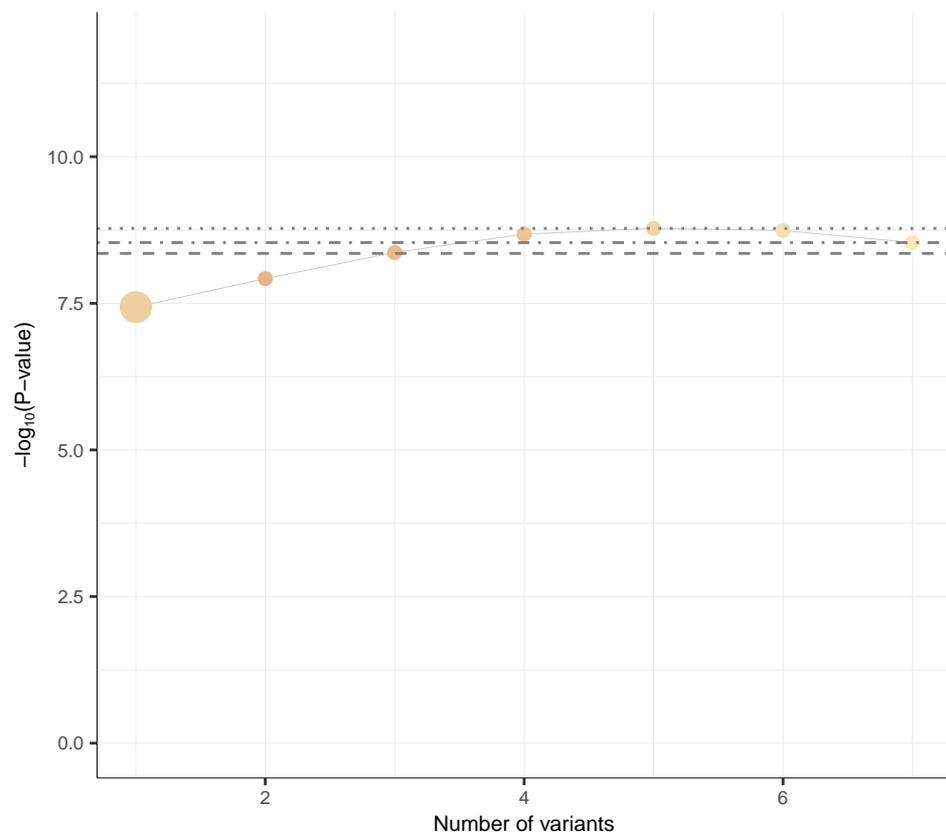
N-acetylmethionine in plasma at ACY1 (LoF_mis)



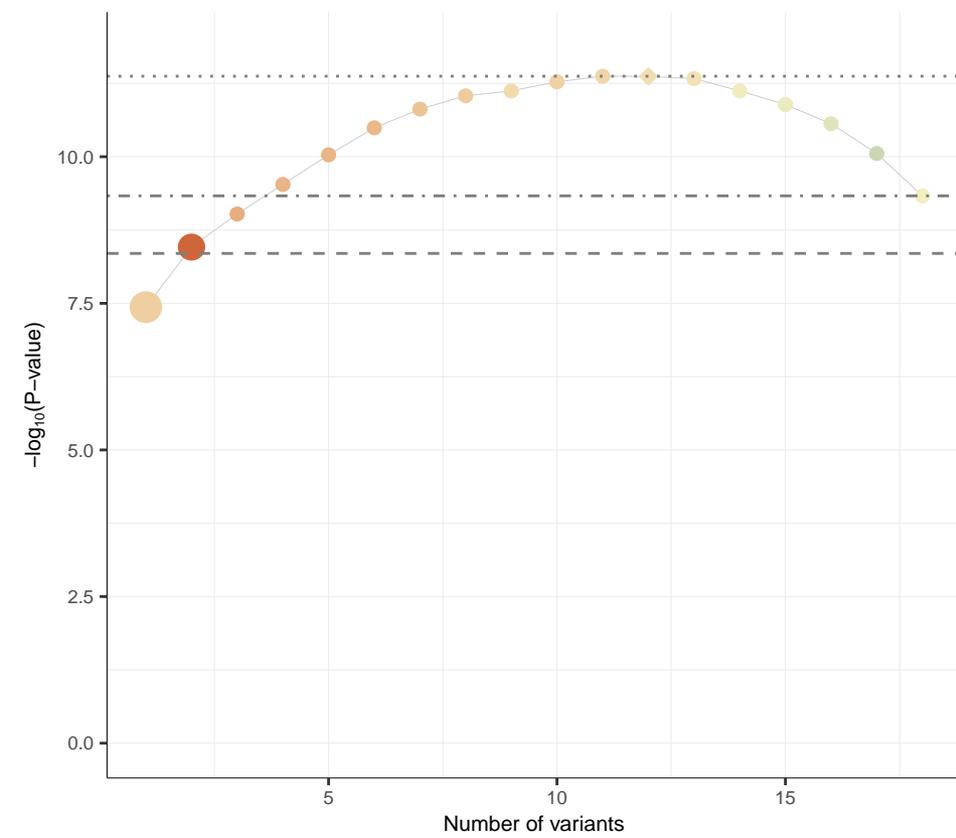
N-acetylmethionine in plasma at ACY1 (HI_mis)



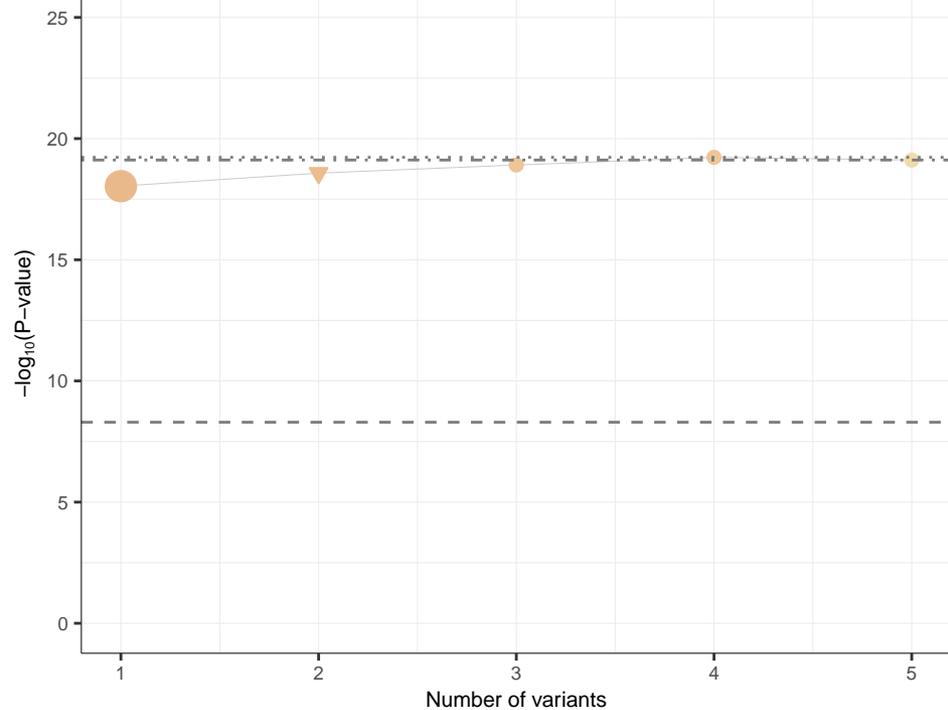
N-acetylmethionine in urine at ACY1 (LoF_mis)



N-acetylmethionine in urine at ACY1 (HI_mis)

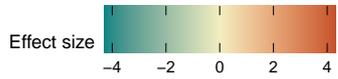


N-acetylmethionine sulfoxide in plasma at *ACY1* (LoF_mis)

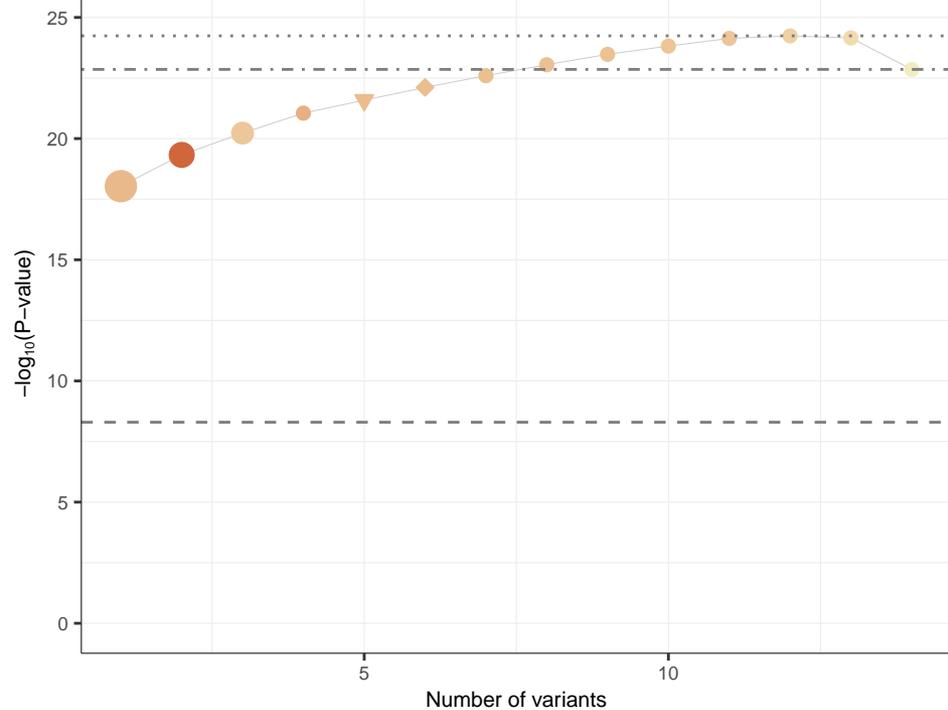


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



N-acetylmethionine sulfoxide in plasma at *ACY1* (HI_mis)



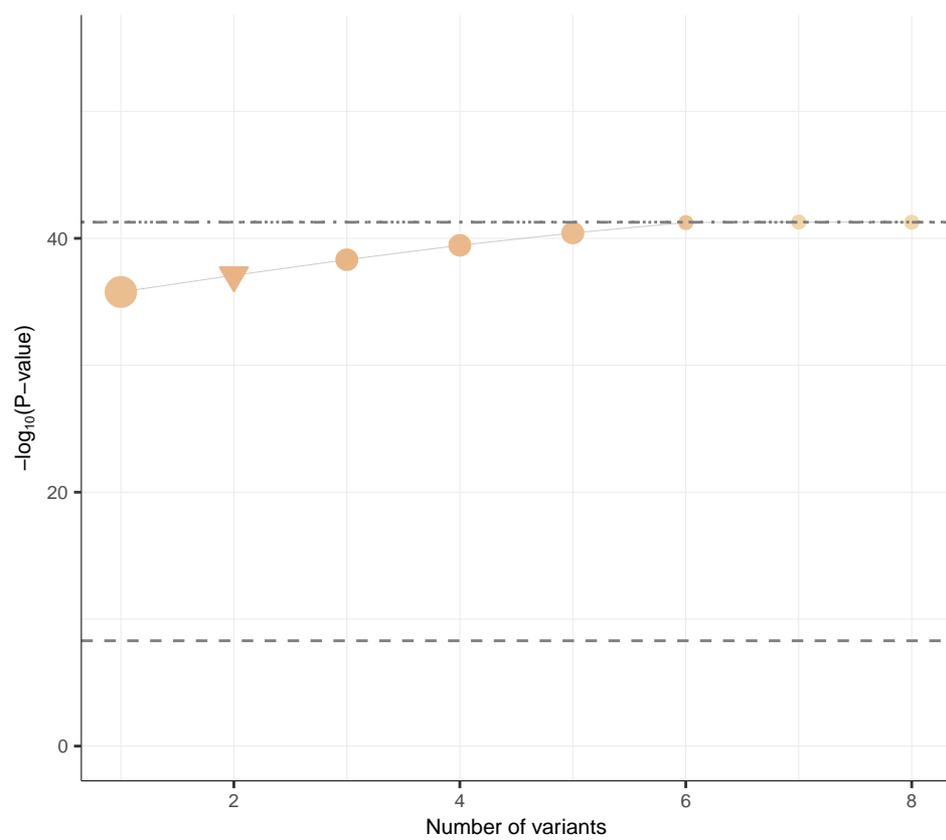
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

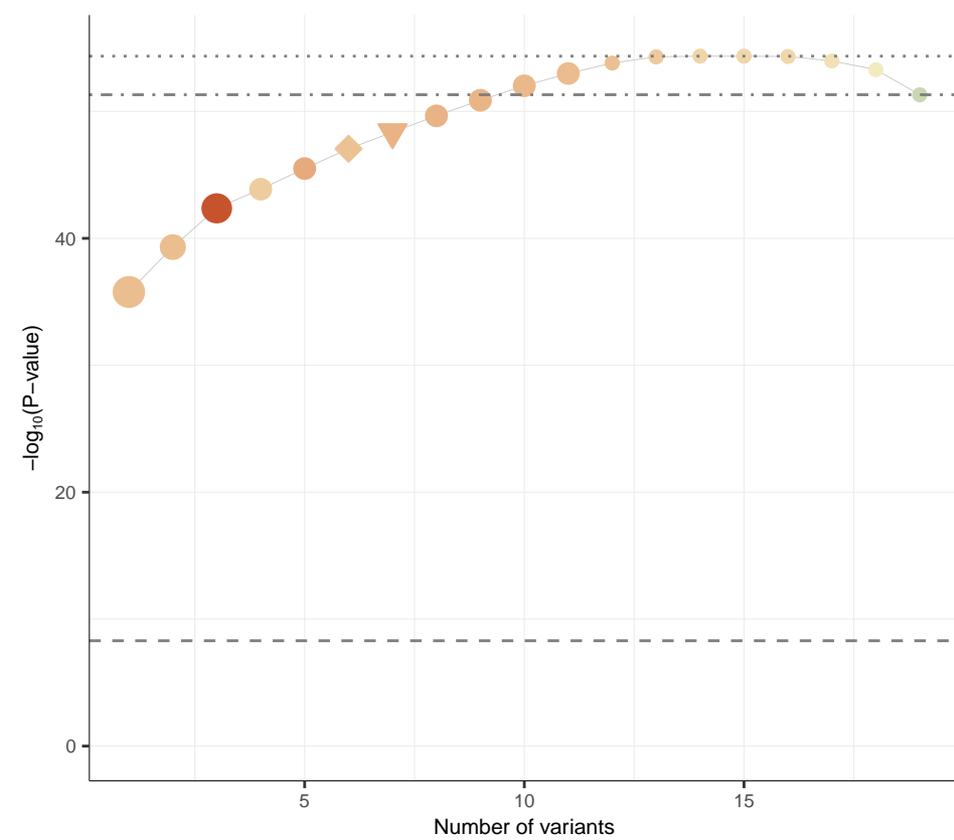
Thresholds

- - - Significance Threshold
- · - Total P-value
- · · Lowest P-value

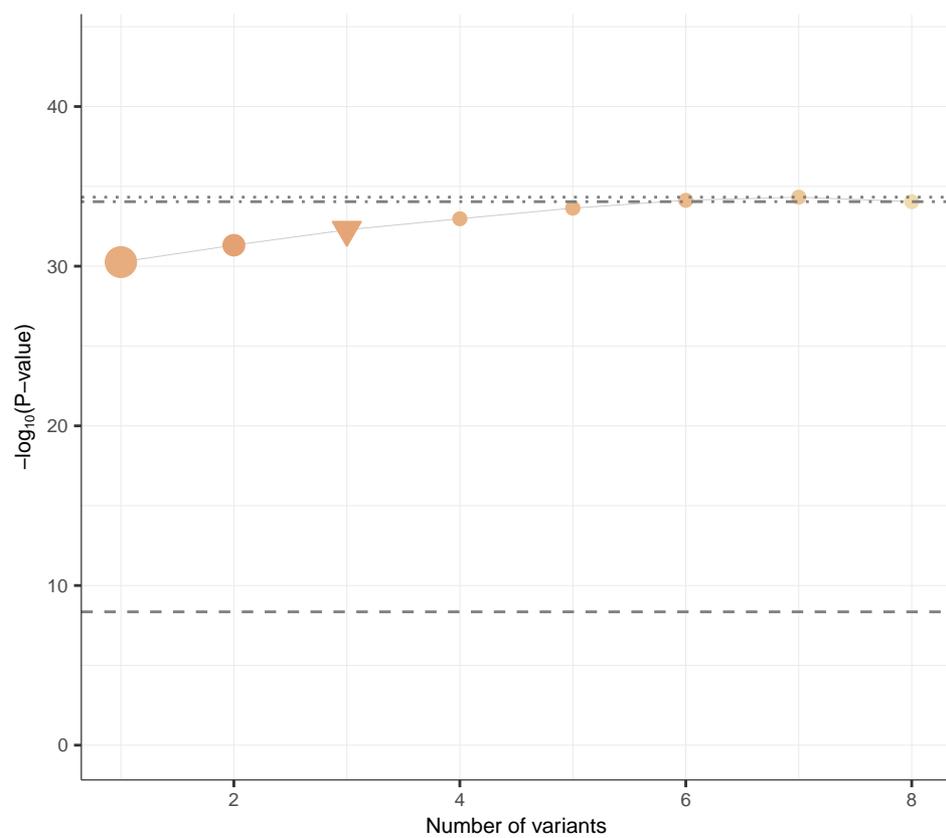
N-acetylserine in plasma at ACY1 (LoF_mis)



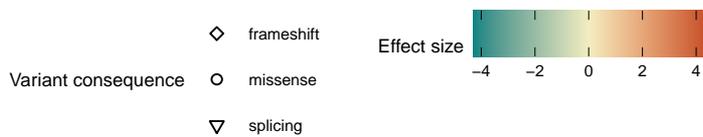
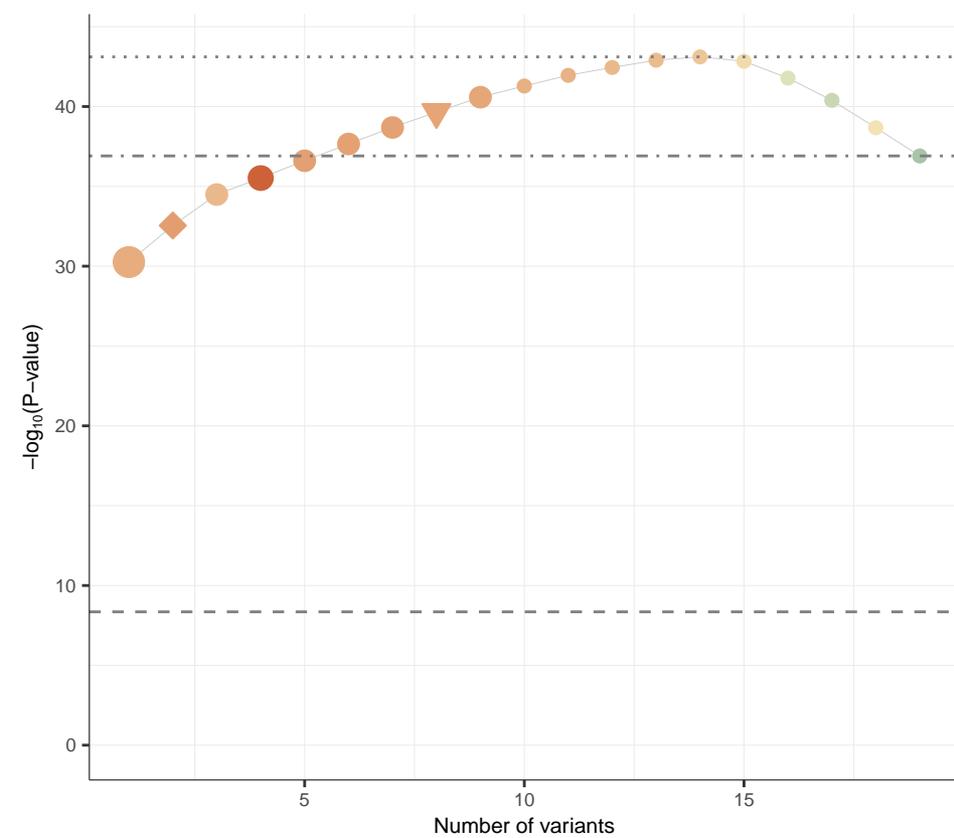
N-acetylserine in plasma at ACY1 (HI_mis)



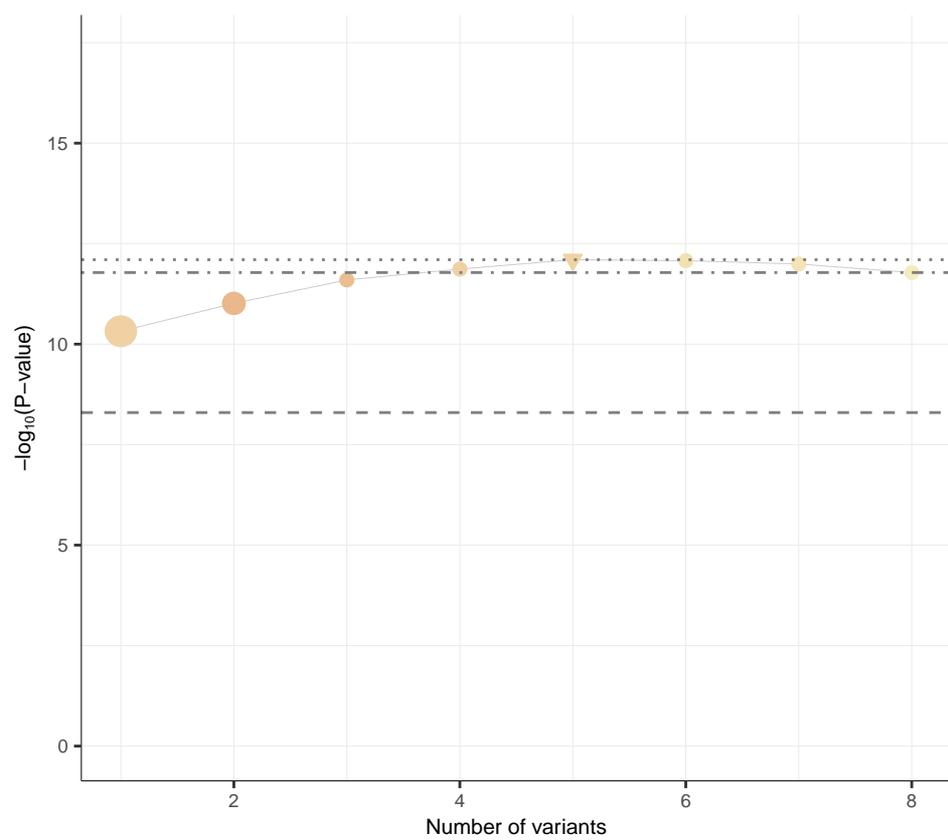
N-acetylserine in urine at ACY1 (LoF_mis)



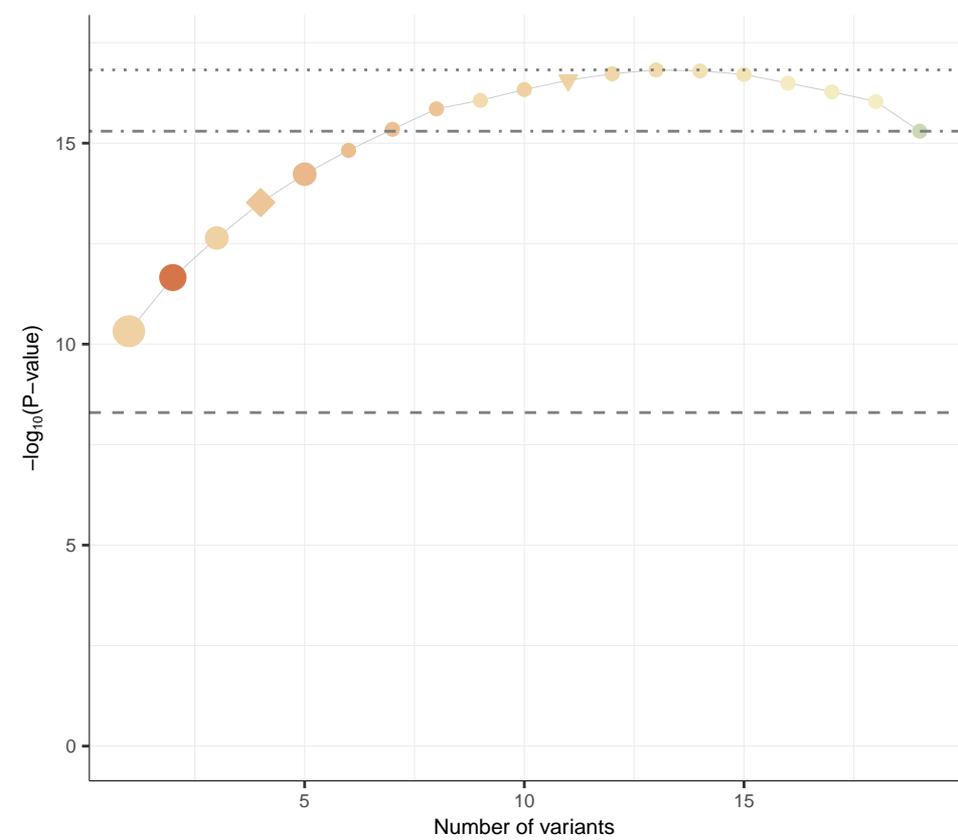
N-acetylserine in urine at ACY1 (HI_mis)



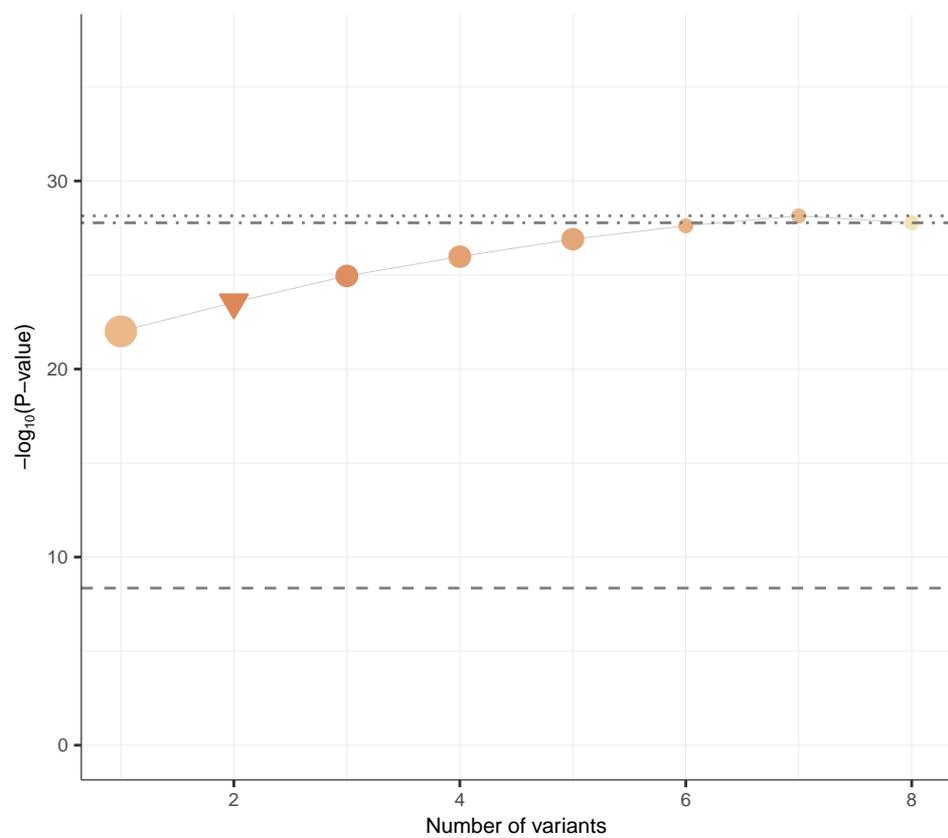
N-acetylthreonine in plasma at ACY1 (LoF_mis)



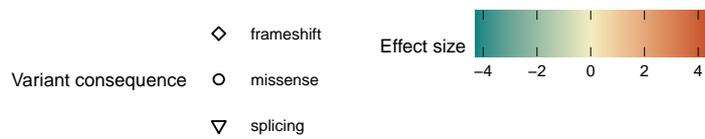
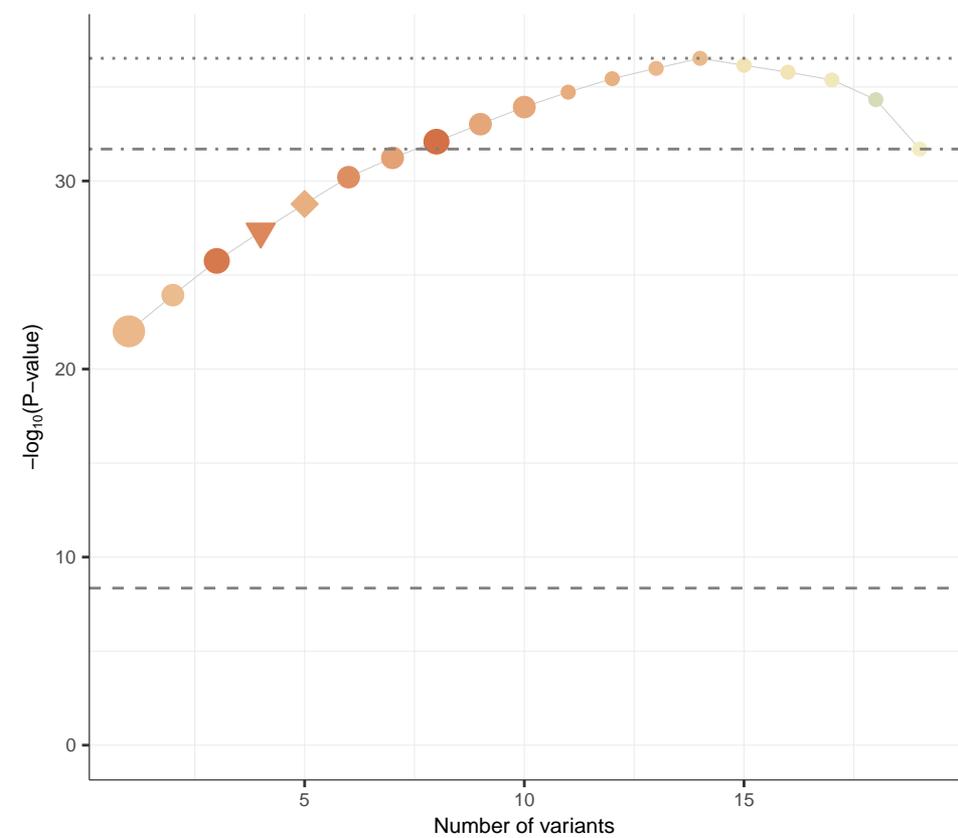
N-acetylthreonine in plasma at ACY1 (HI_mis)



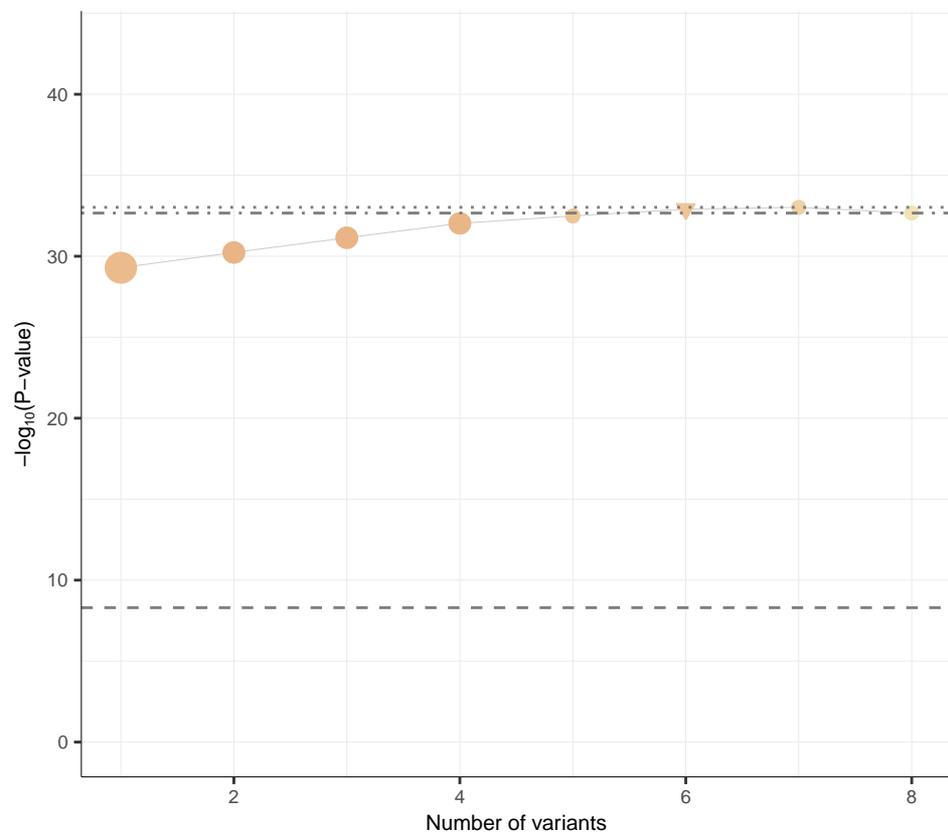
N-acetylthreonine in urine at ACY1 (LoF_mis)



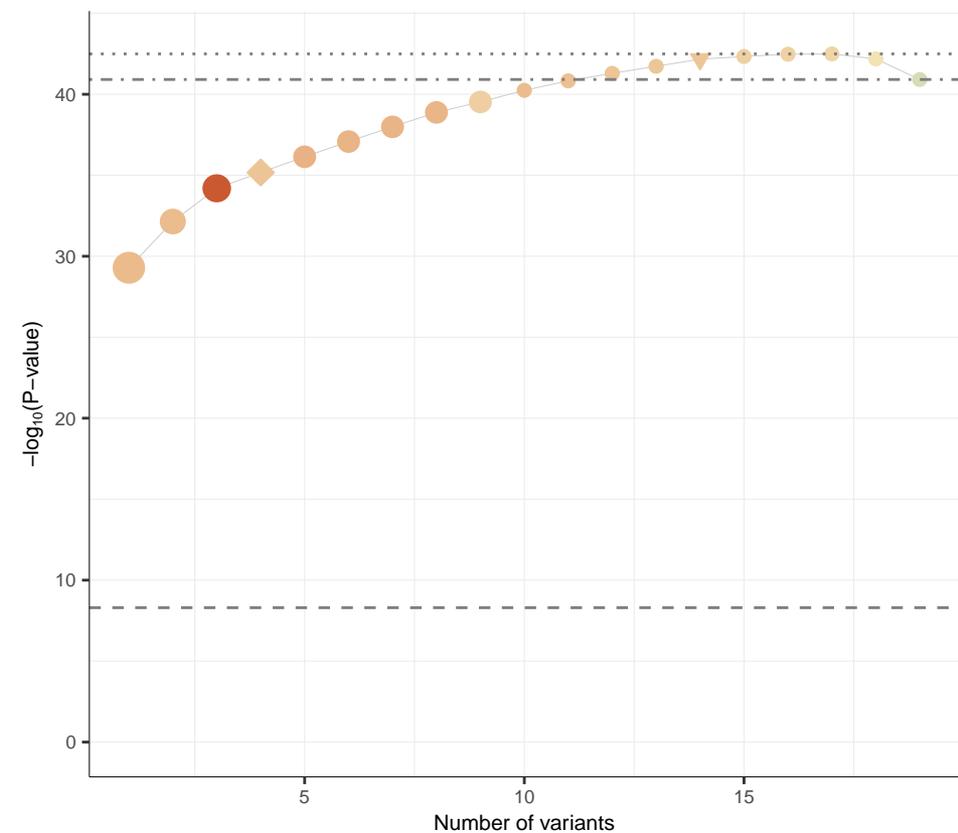
N-acetylthreonine in urine at ACY1 (HI_mis)



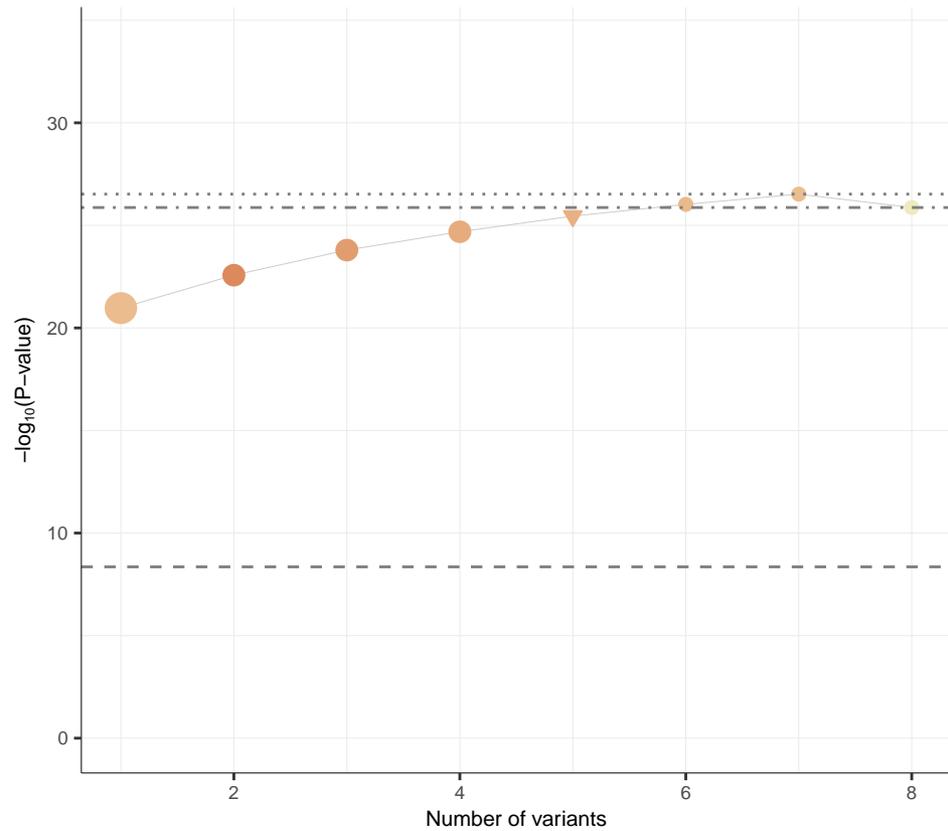
N-acetylvaline in plasma at ACY1 (LoF_mis)



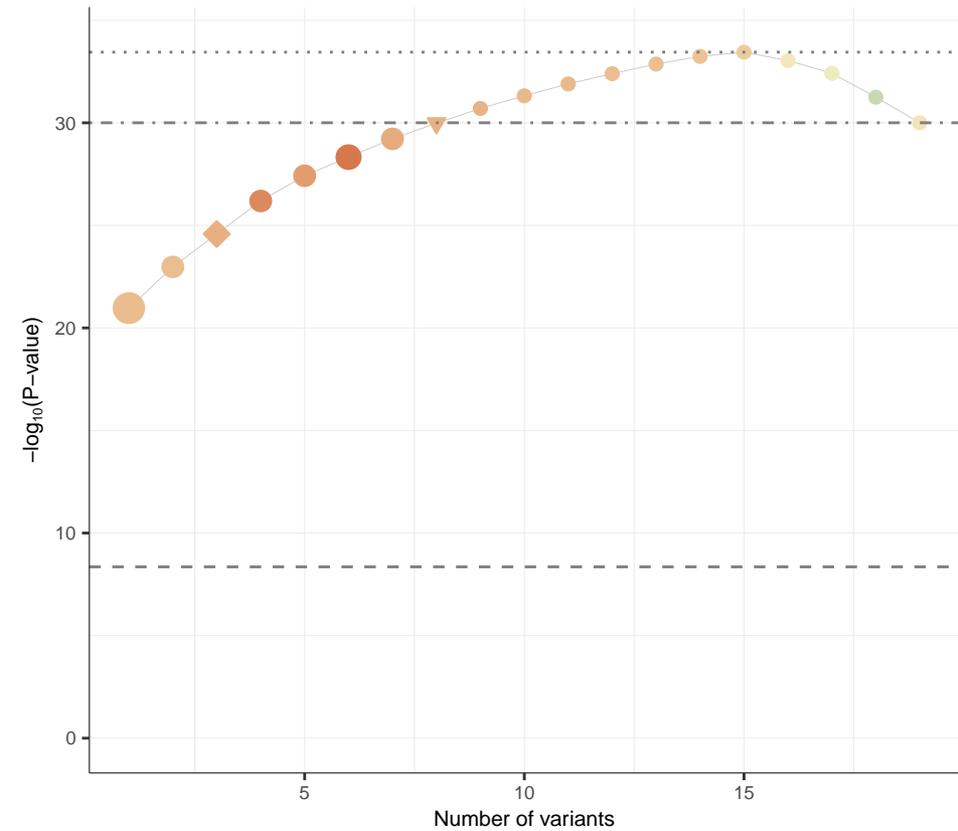
N-acetylvaline in plasma at ACY1 (HI_mis)



N-acetylvaline in urine at ACY1 (LoF_mis)

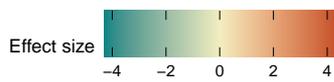


N-acetylvaline in urine at ACY1 (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



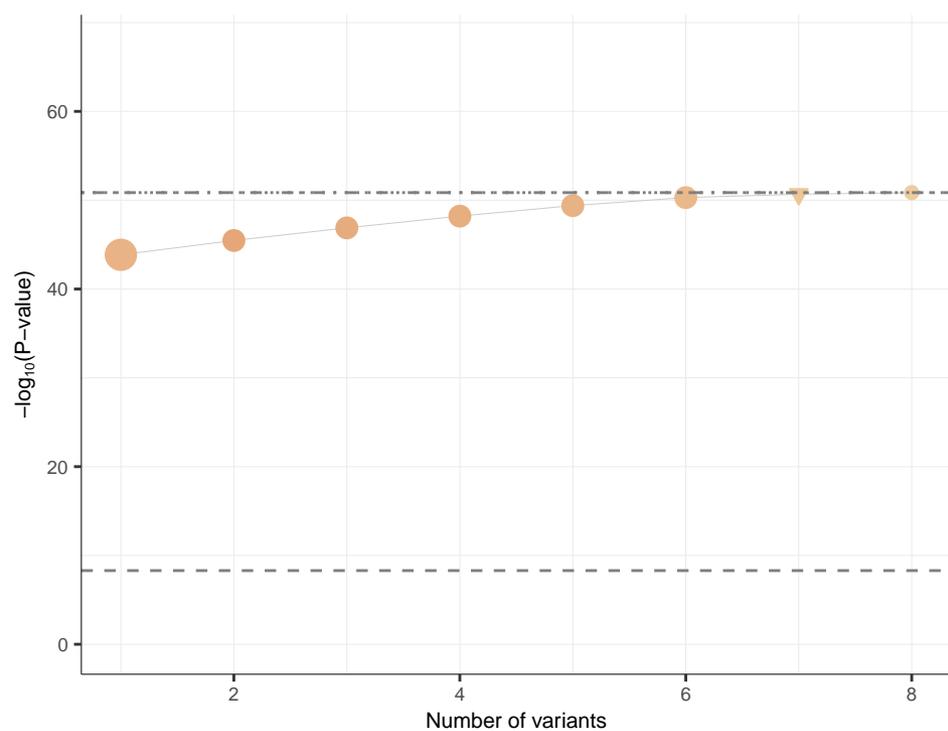
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

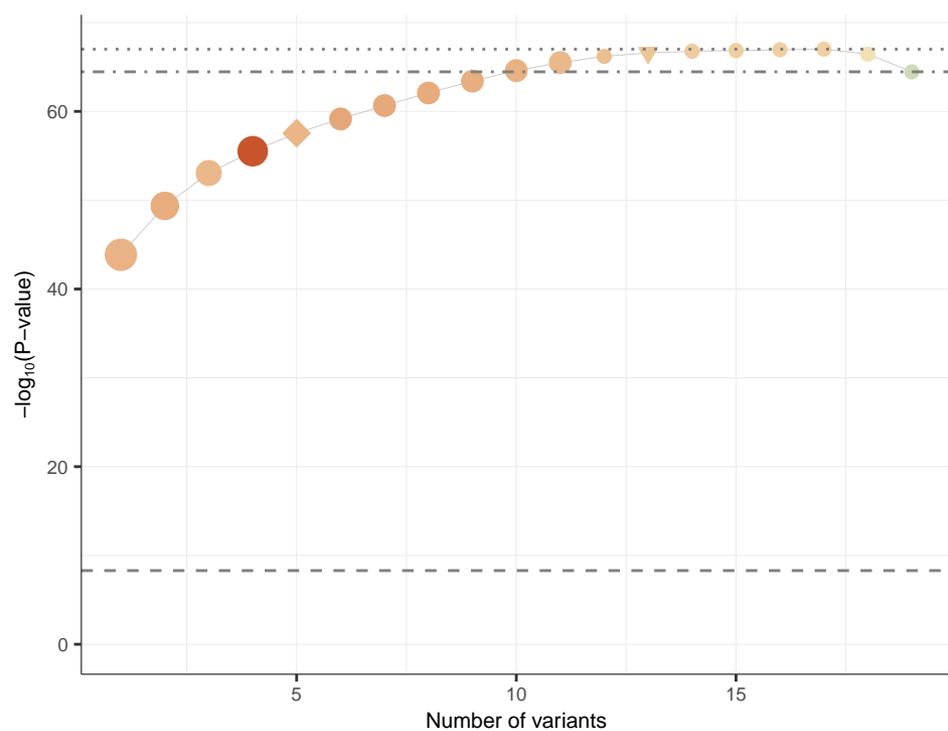
Thresholds

- - Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

N-formylmethionine in plasma at *ACY1* (LoF_mis)

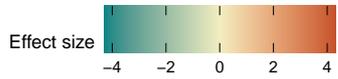


N-formylmethionine in plasma at *ACY1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



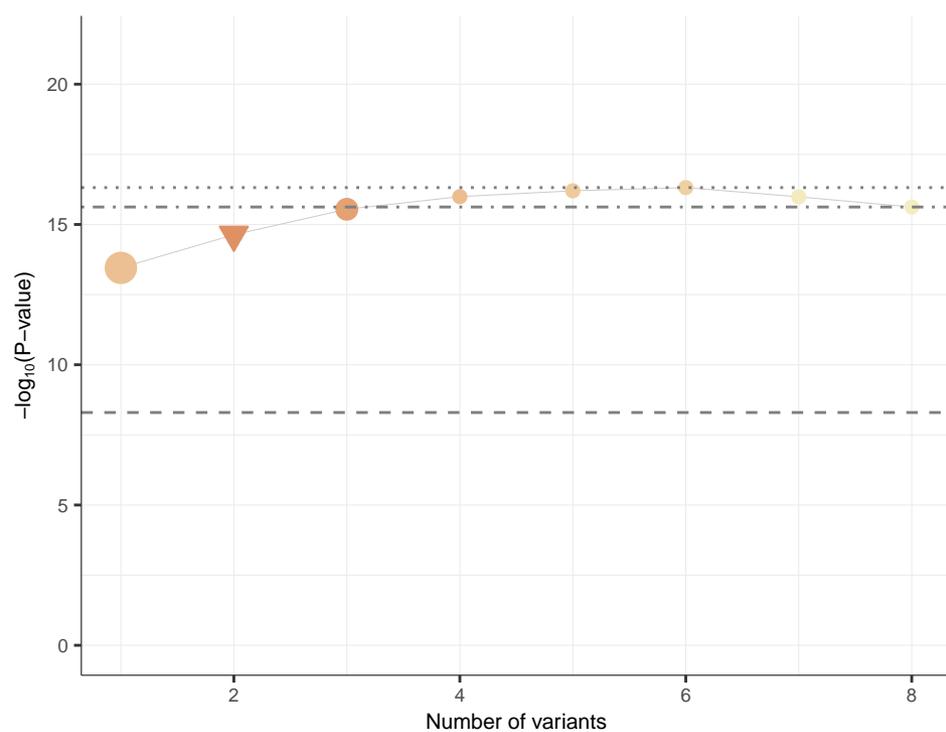
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

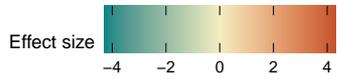
- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

propionylglycine in plasma at ACY1 (LoF_mis)

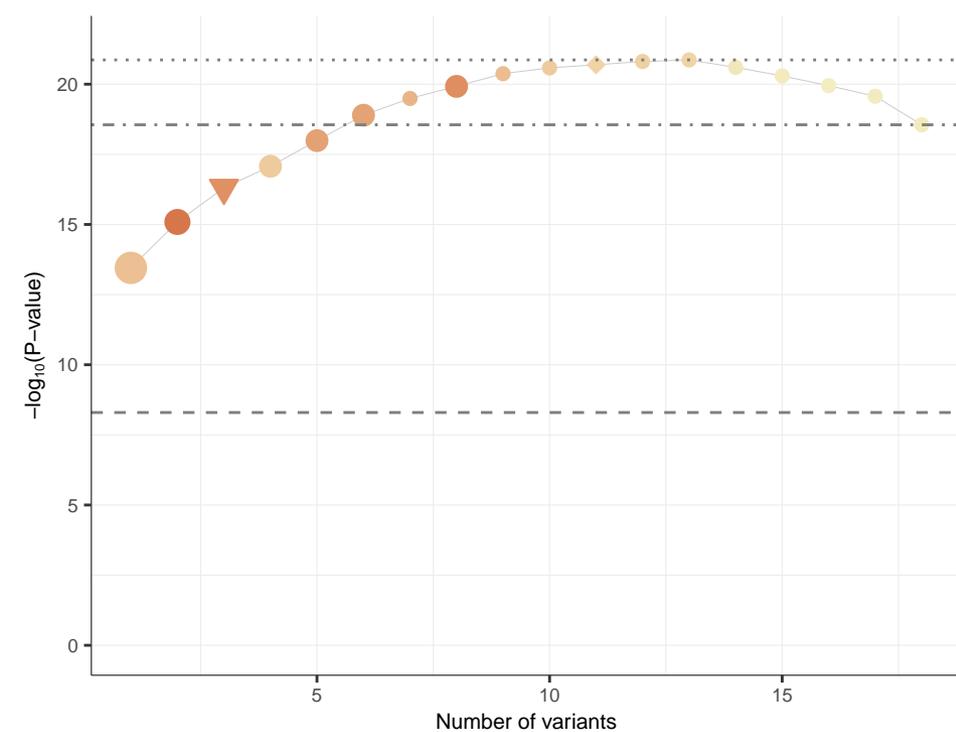


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



propionylglycine in plasma at ACY1 (HI_mis)



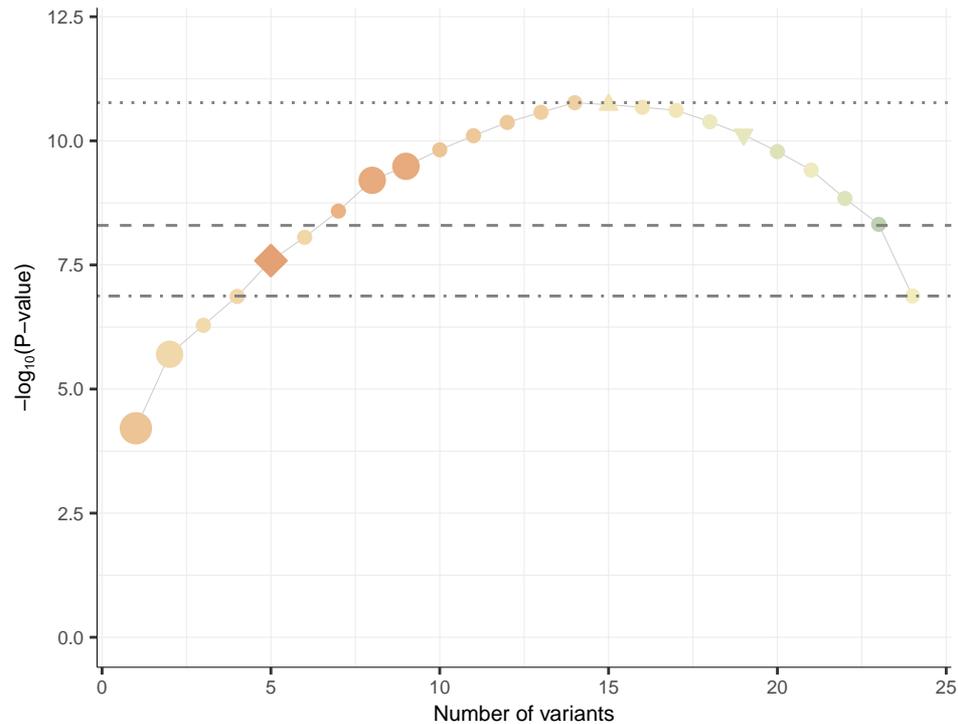
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

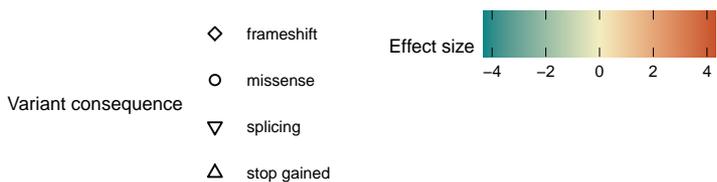
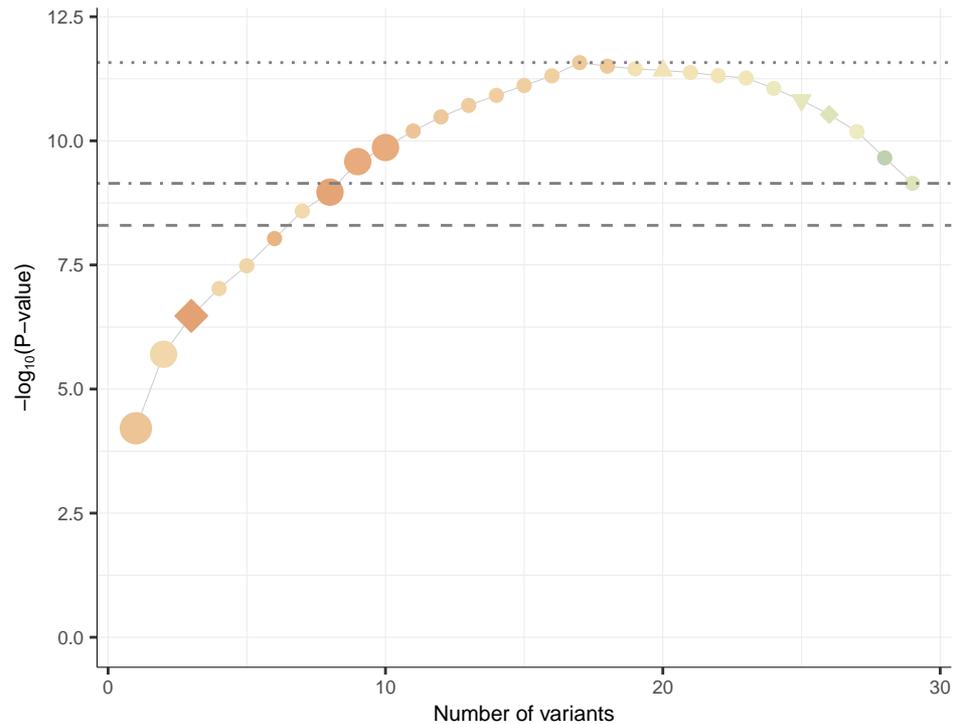
Thresholds

- - Significance Threshold
- - - Total P-value
- ... Lowest P-value

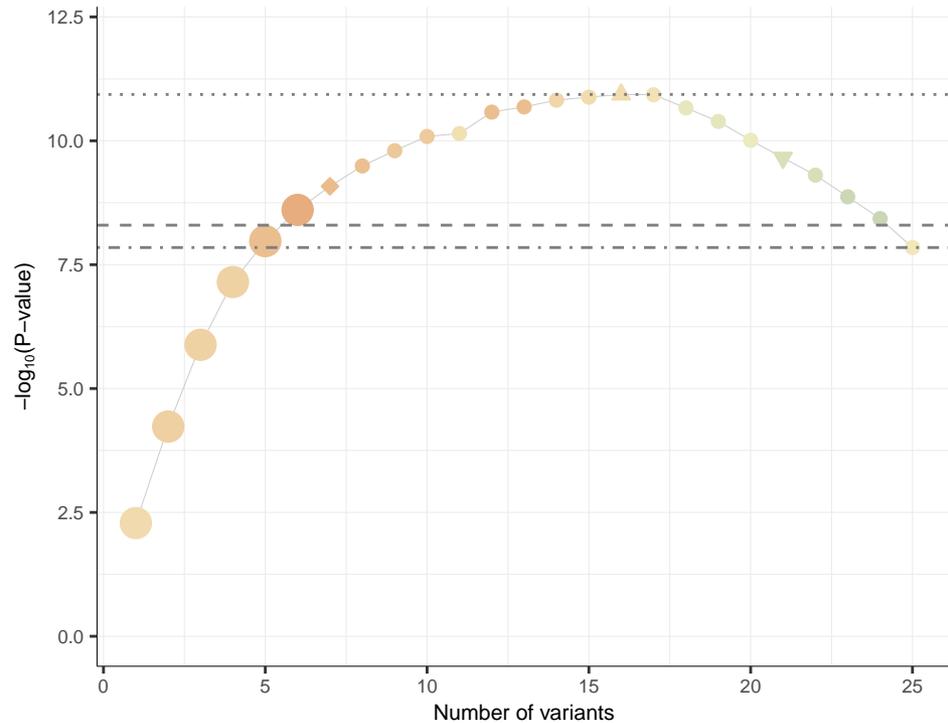
N-acetylkynurenine (2) in plasma at ACY3 (LoF_mis)



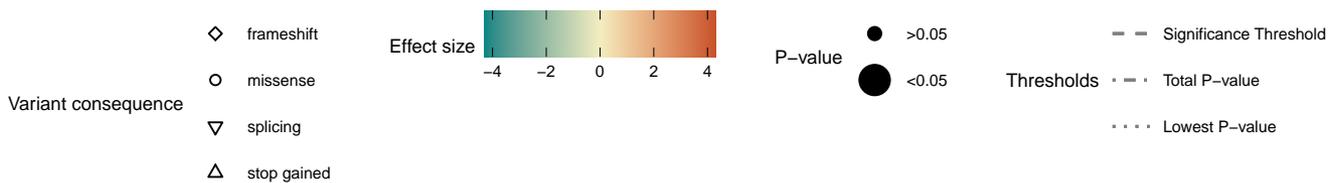
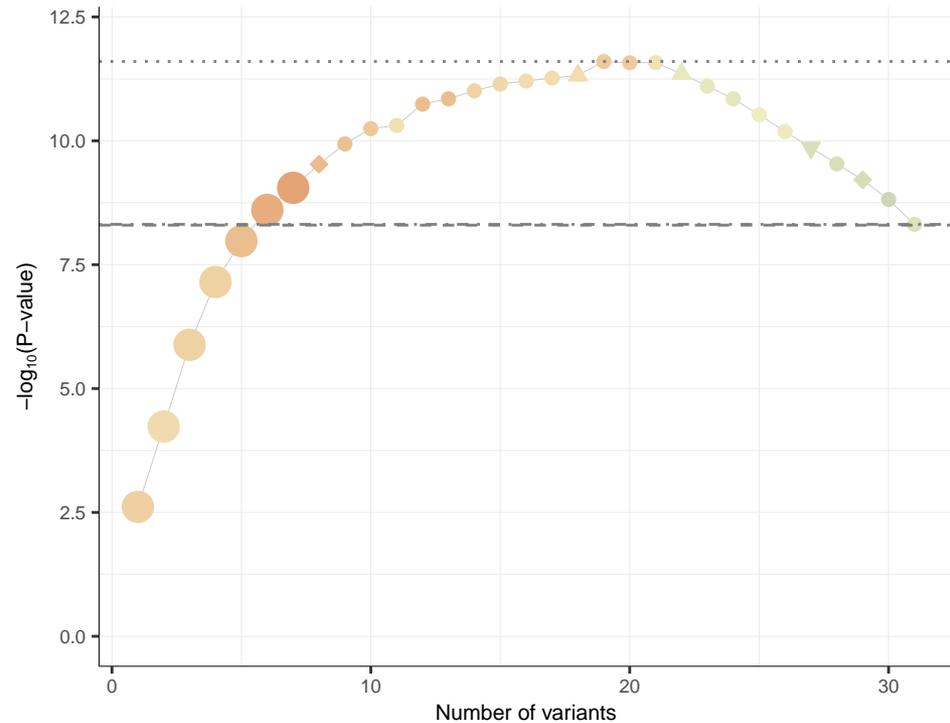
N-acetylkynurenine (2) in plasma at ACY3 (HI_mis)



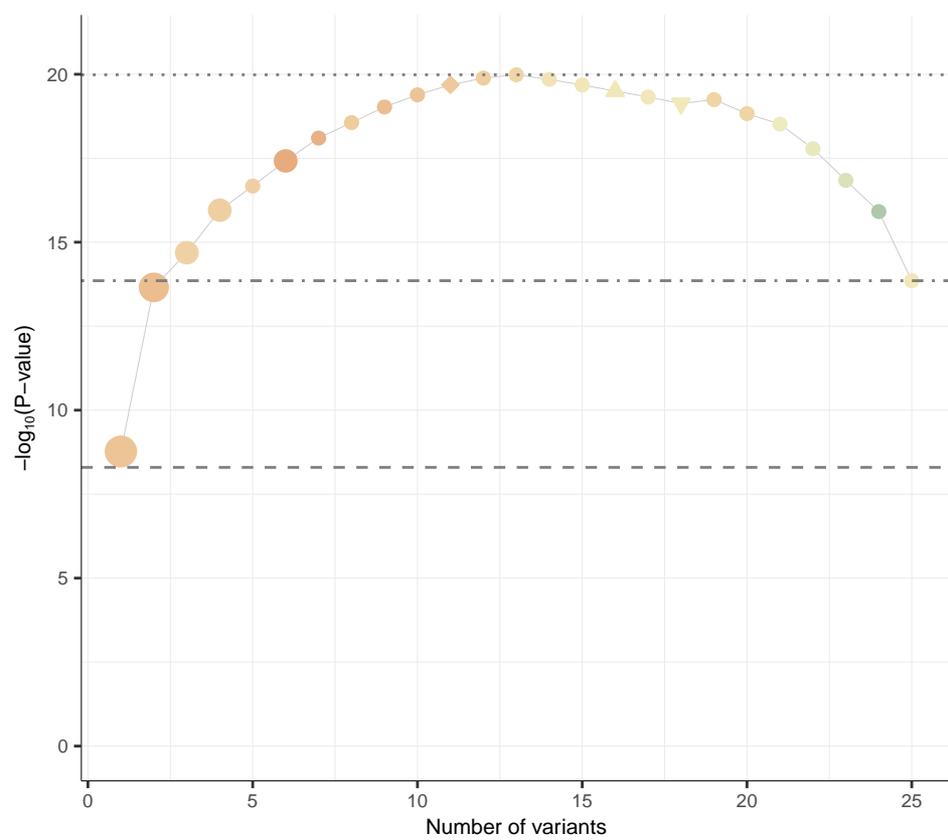
N-acetylphenylalanine in plasma at ACY3 (LoF_mis)



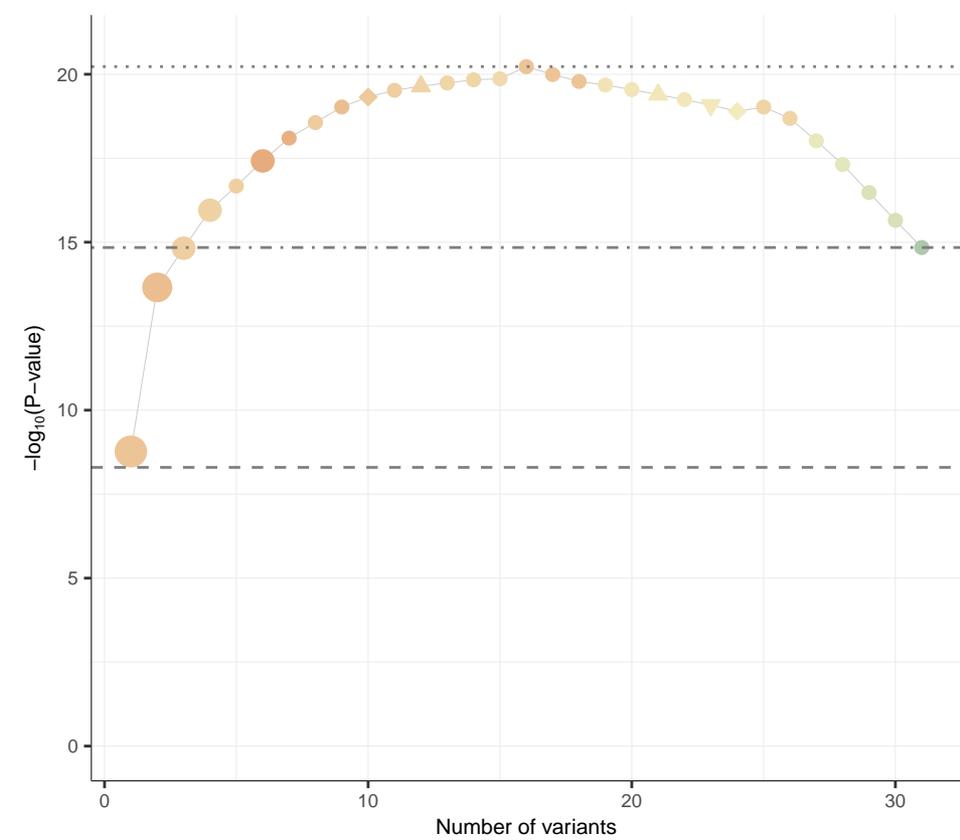
N-acetylphenylalanine in plasma at ACY3 (HI_mis)



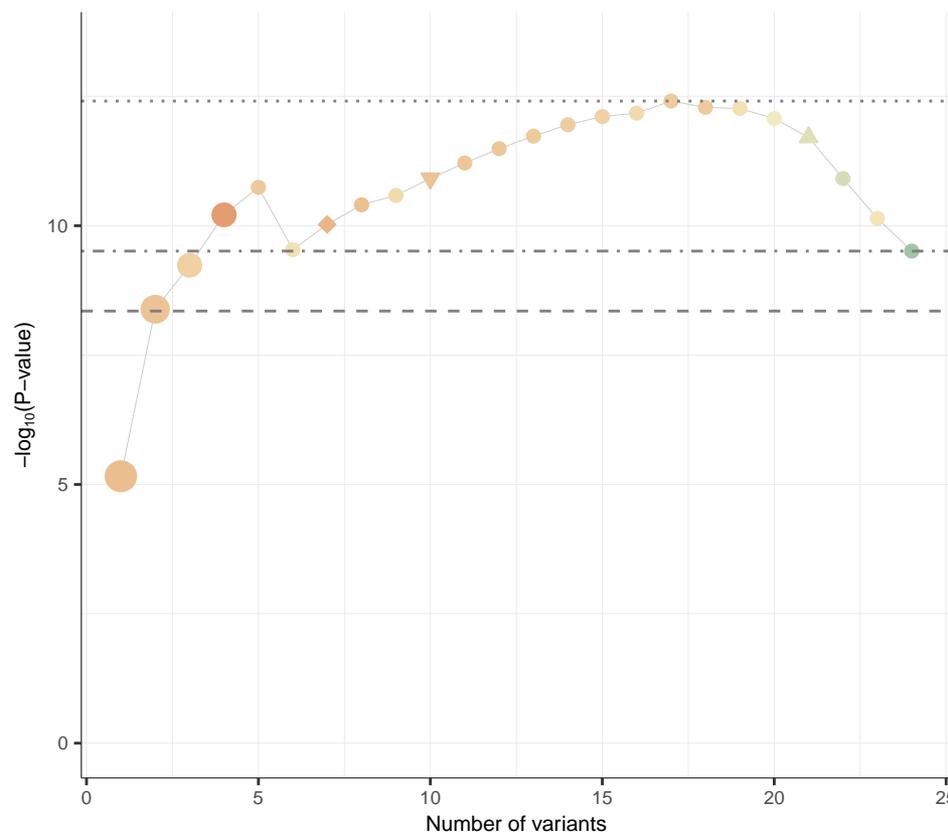
N-acetyltryptophan in plasma at ACY3 (LoF_mis)



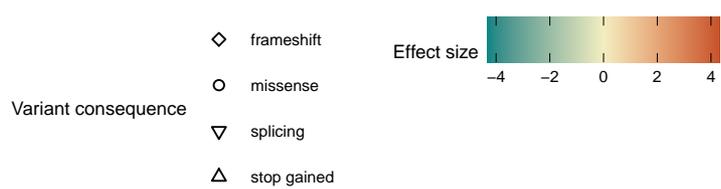
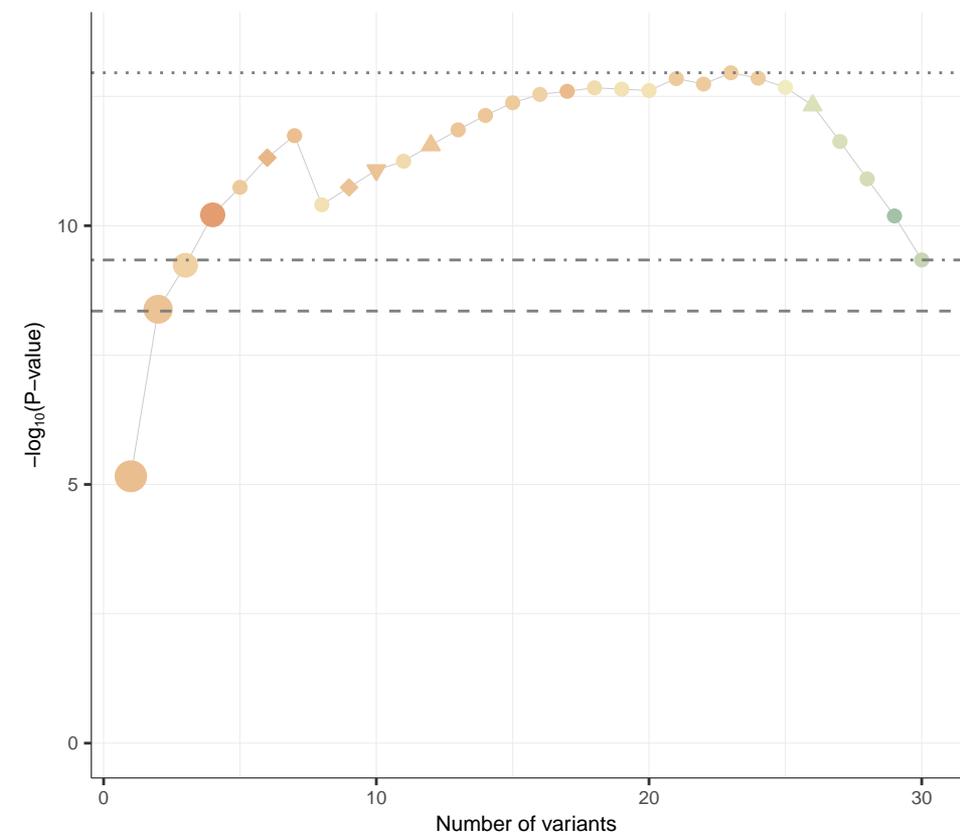
N-acetyltryptophan in plasma at ACY3 (HI_mis)



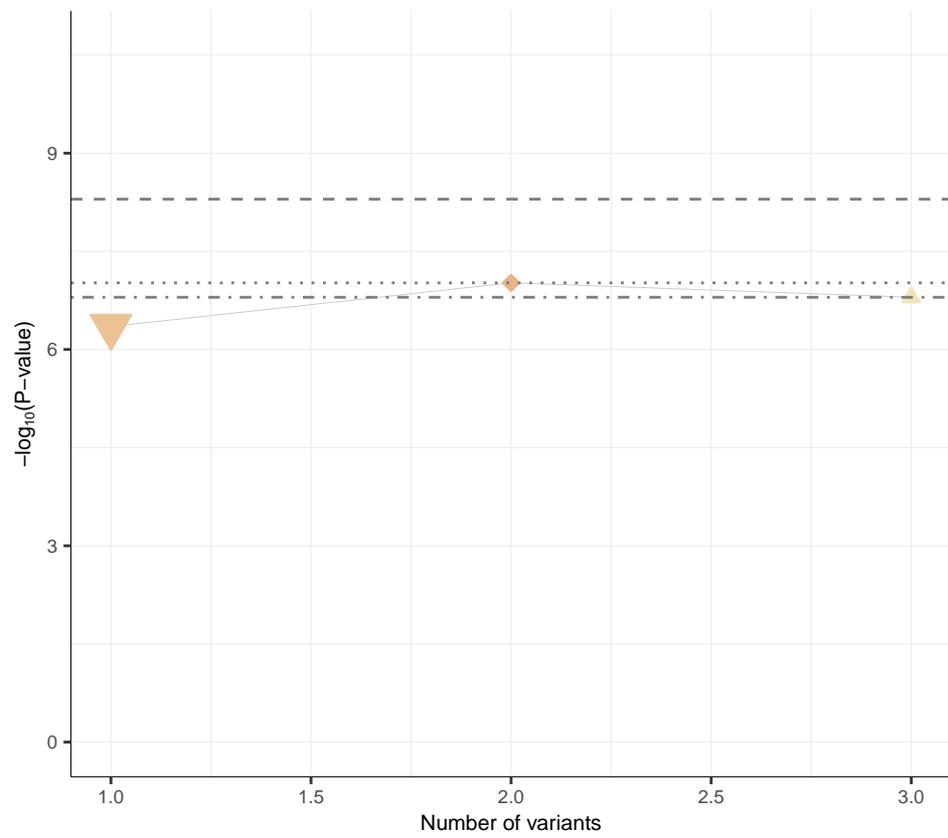
N-acetyltryptophan in urine at ACY3 (LoF_mis)



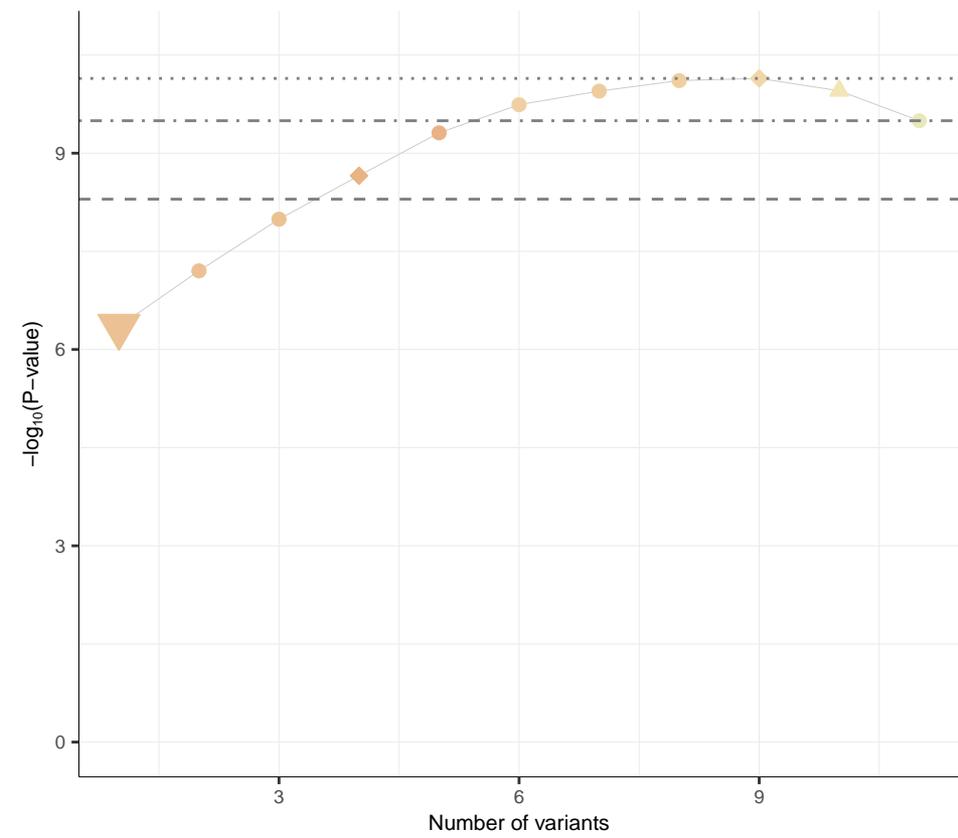
N-acetyltryptophan in urine at ACY3 (HI_mis)



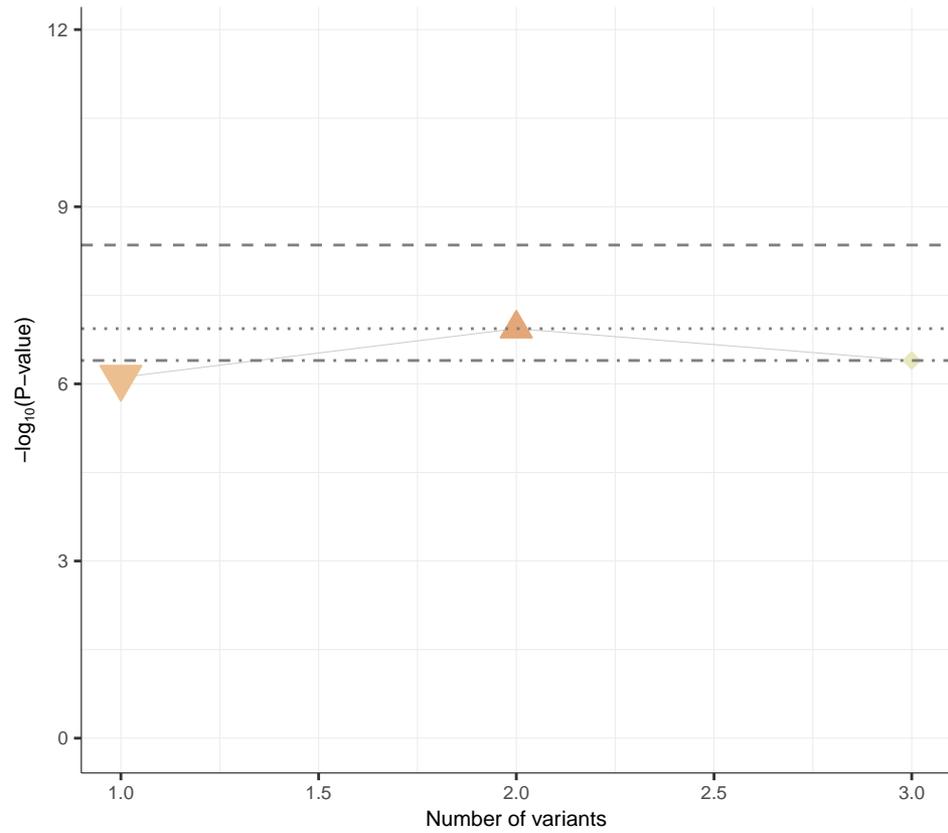
N-formylanthranilic acid in plasma at *AFMID* (LoF_mis)



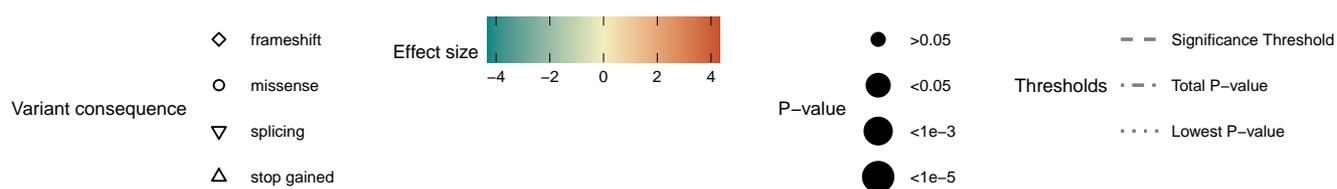
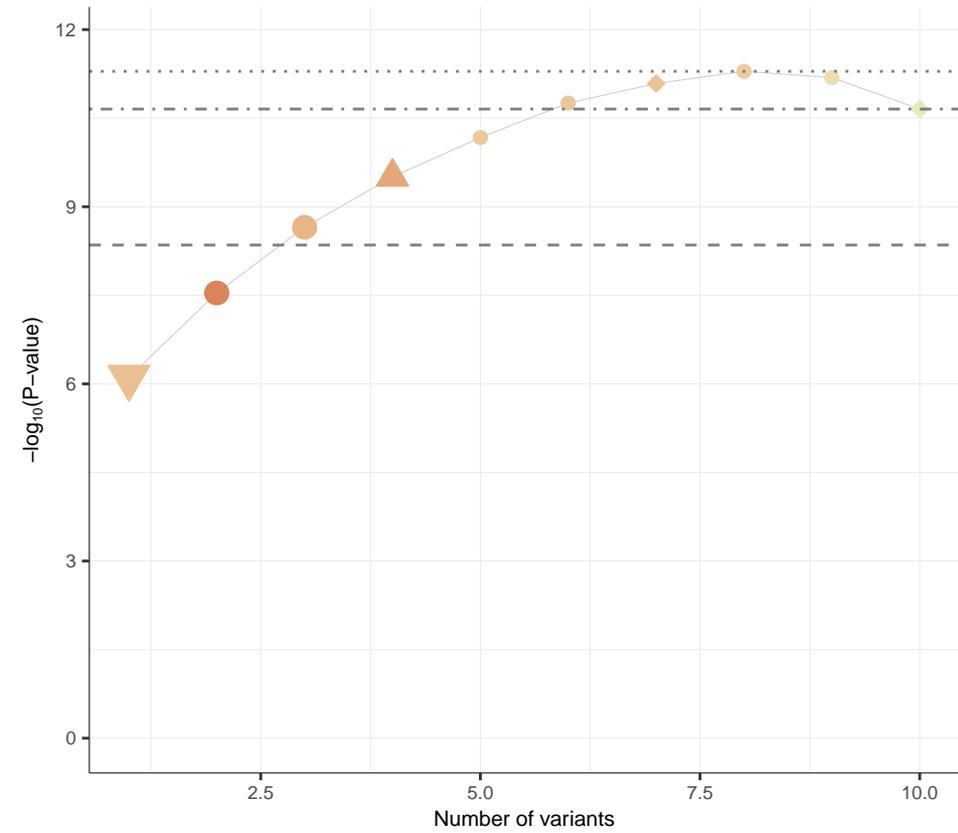
N-formylanthranilic acid in plasma at *AFMID* (HI_mis)



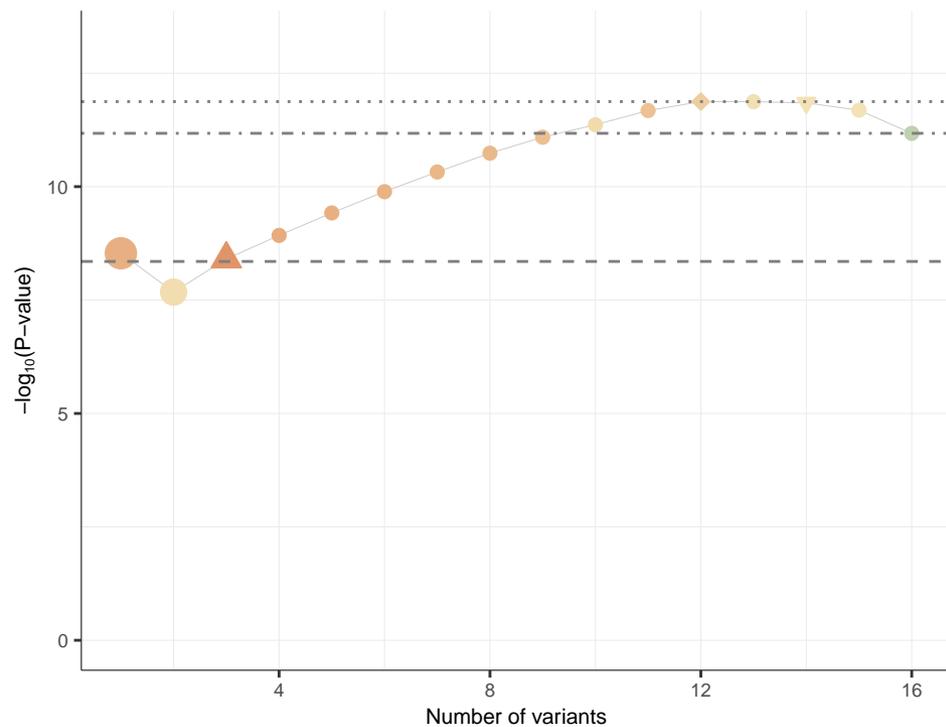
N-formylanthranilic acid in urine at *AFMID* (LoF_mis)



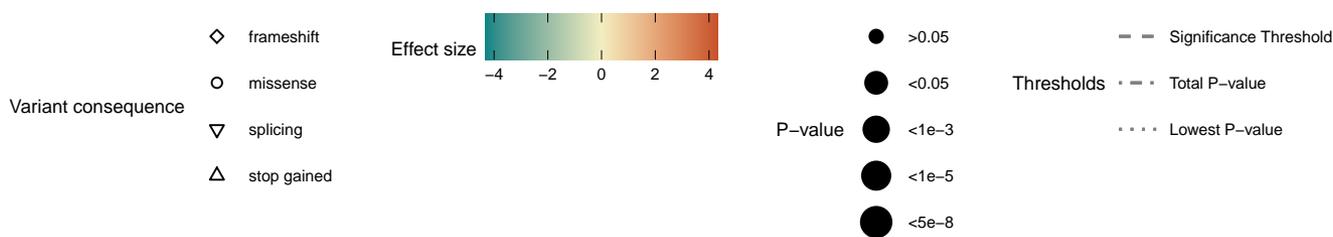
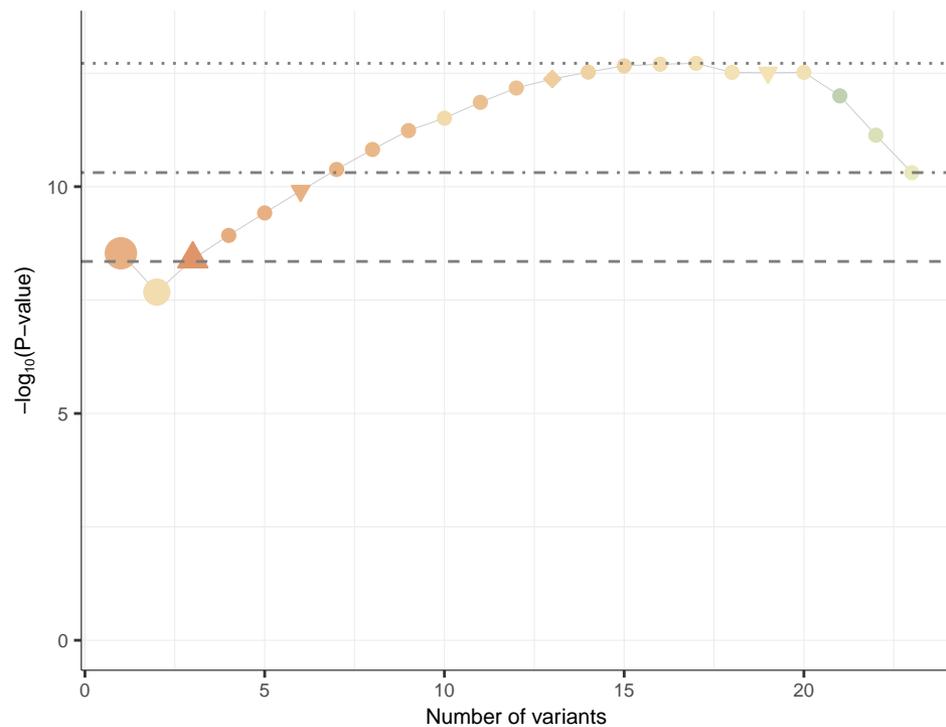
N-formylanthranilic acid in urine at *AFMID* (HI_mis)



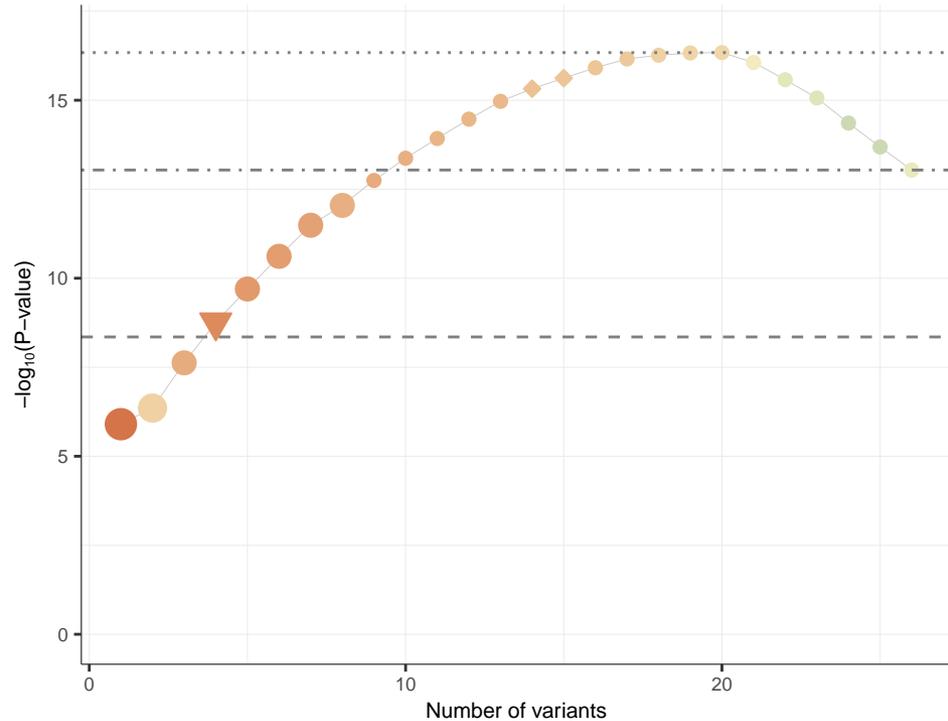
3-hydroxyisobutyrate in urine at *ALDH6A1* (LoF_mis)



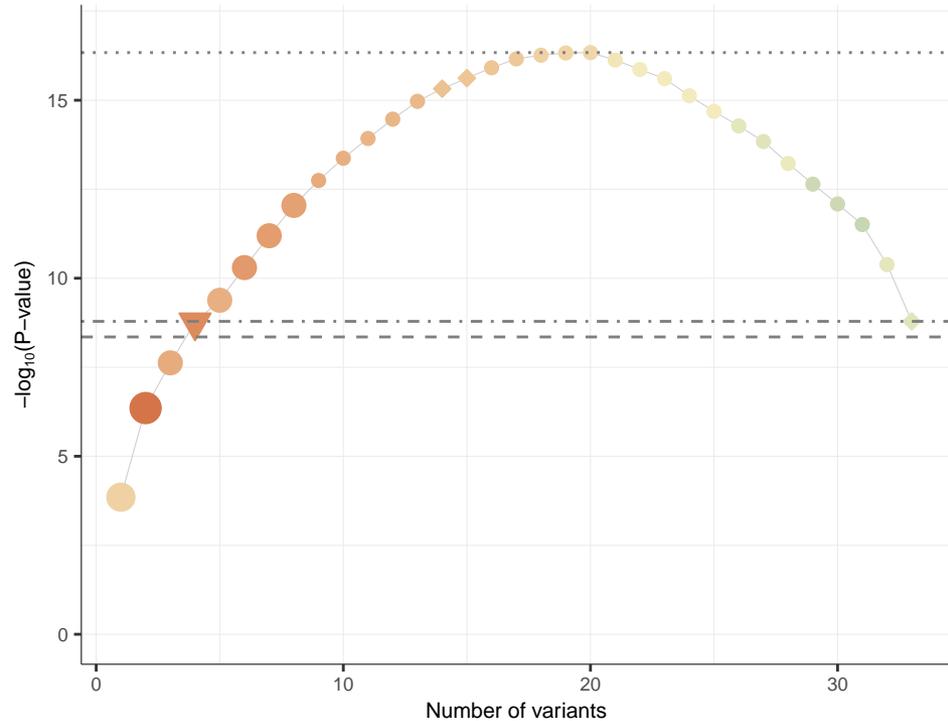
3-hydroxyisobutyrate in urine at *ALDH6A1* (HI_mis)



3-phosphoglycerate in urine at *ALPL* (LoF_mis)

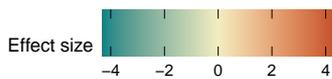


3-phosphoglycerate in urine at *ALPL* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



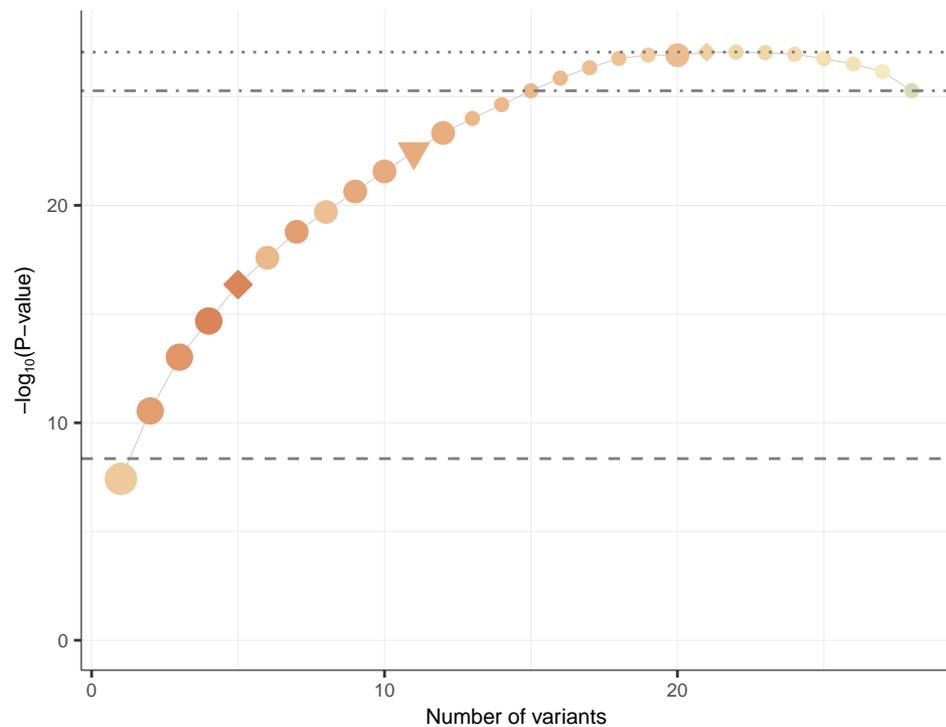
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

Thresholds

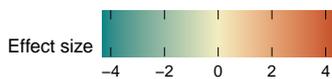
- - Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

choline phosphate in urine at *ALPL* (LoF_mis)

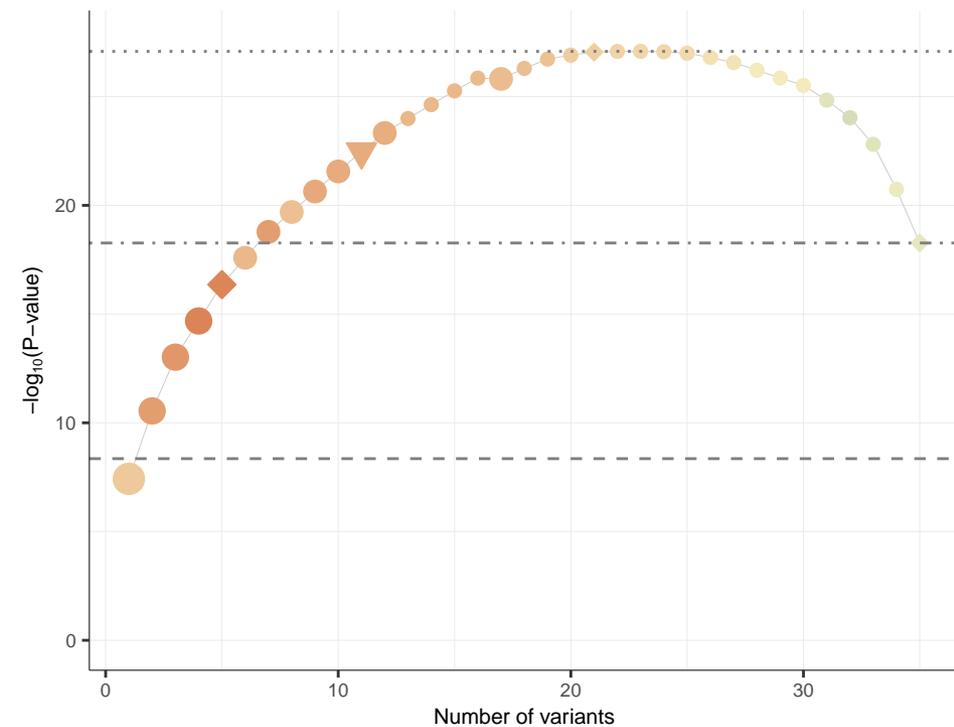


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



choline phosphate in urine at *ALPL* (HI_mis)



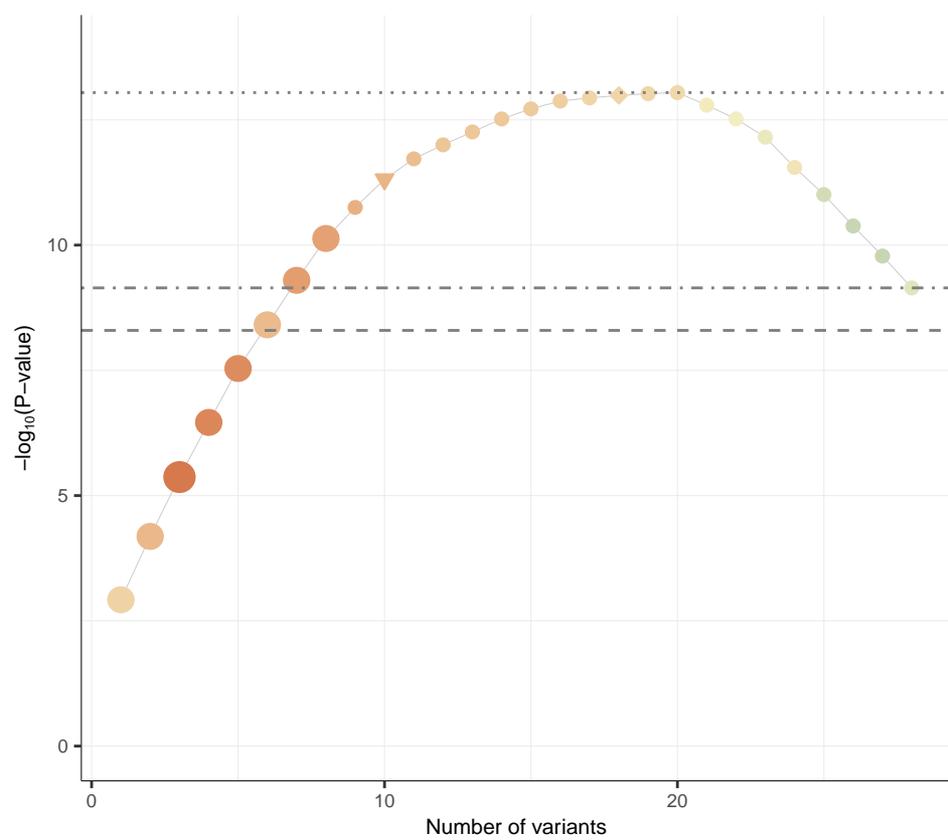
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

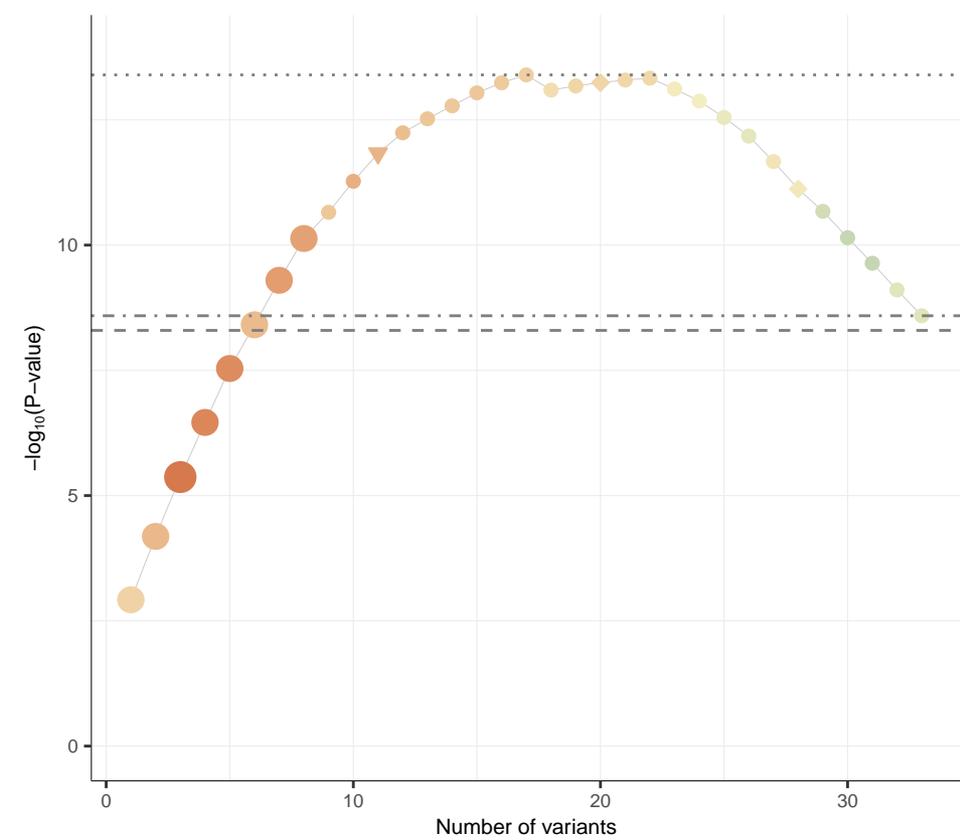
Thresholds

- - Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

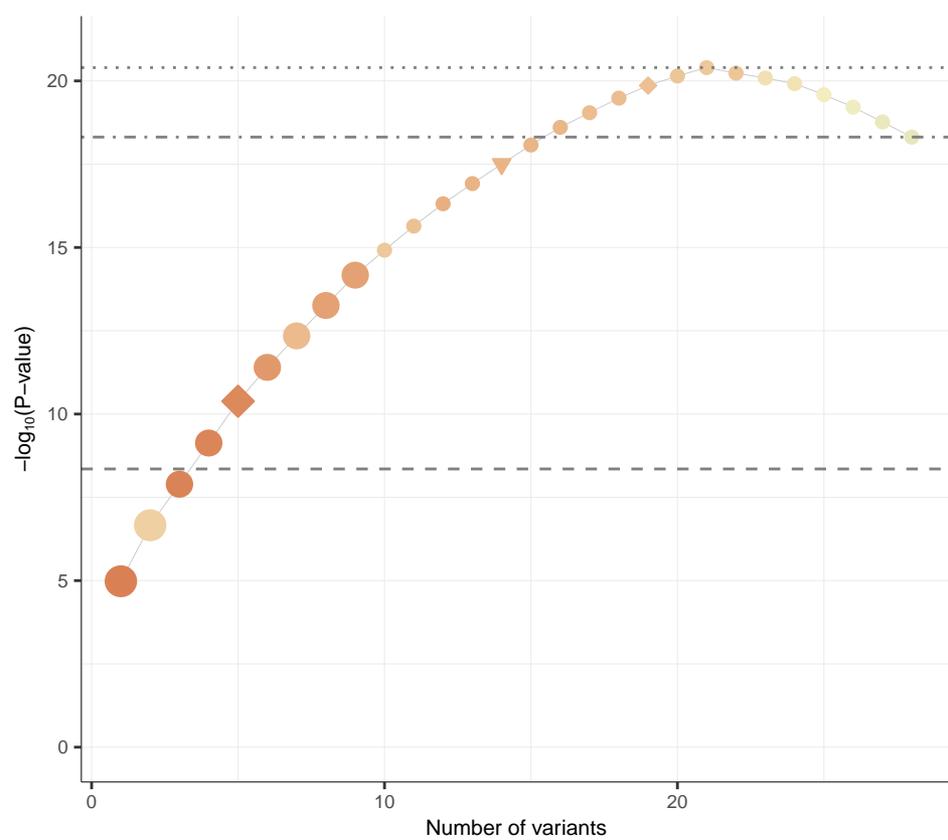
glycerol 3-phosphate in plasma at *ALPL* (LoF_mis)



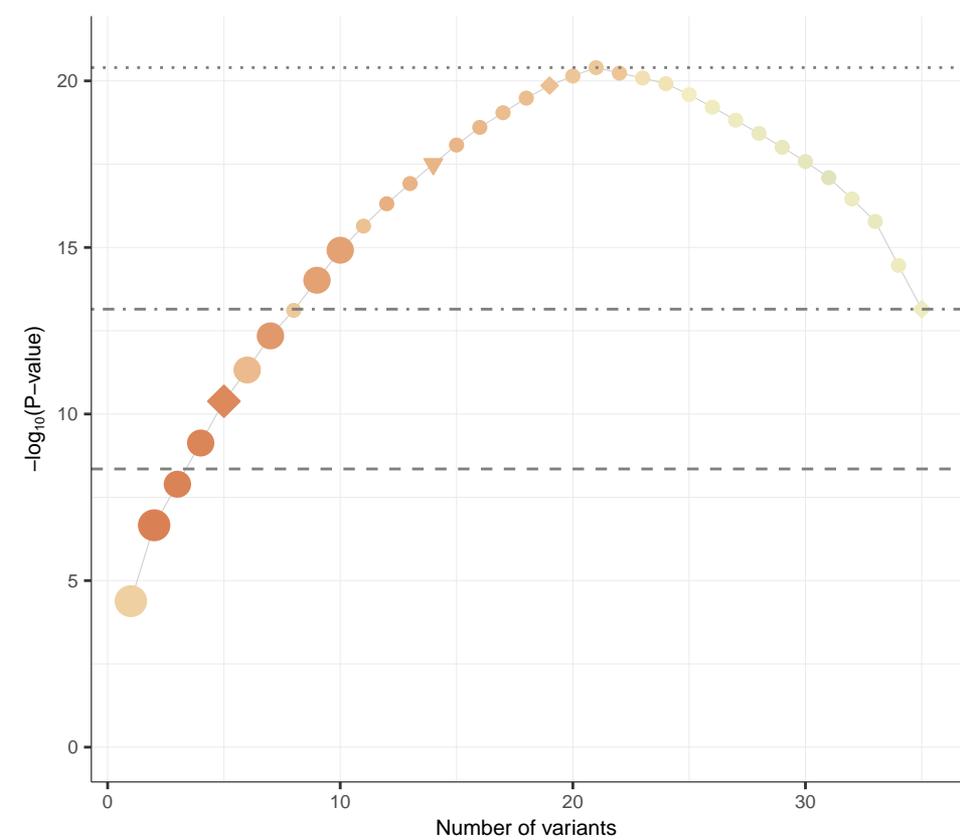
glycerol 3-phosphate in plasma at *ALPL* (HI_mis)



glycerol 3-phosphate in urine at *ALPL* (LoF_mis)



glycerol 3-phosphate in urine at *ALPL* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



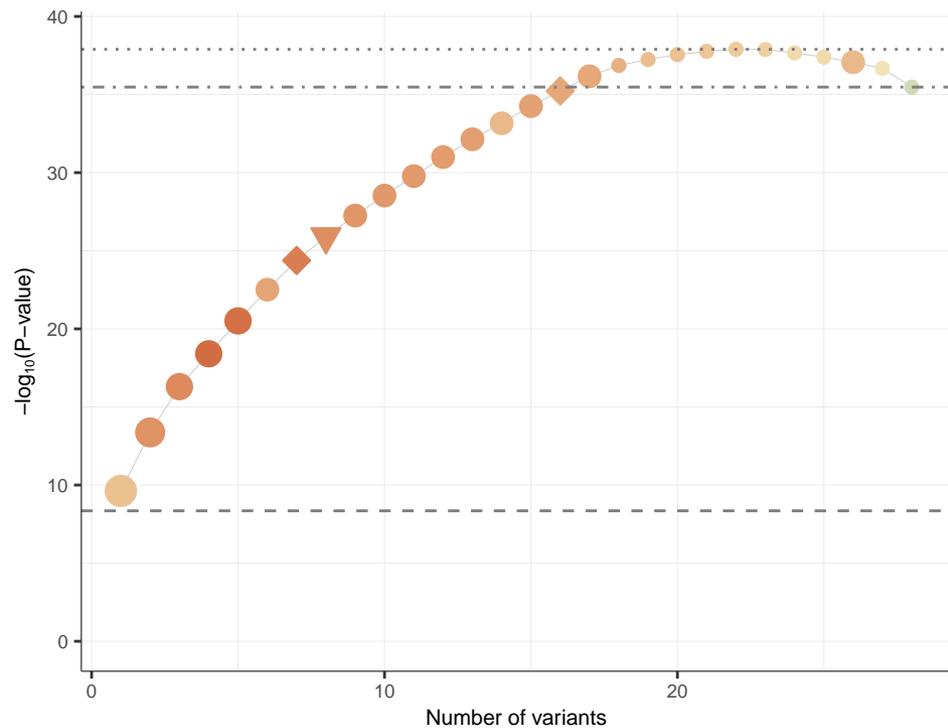
P-value

- >0.05
- <0.05
- <1e-3

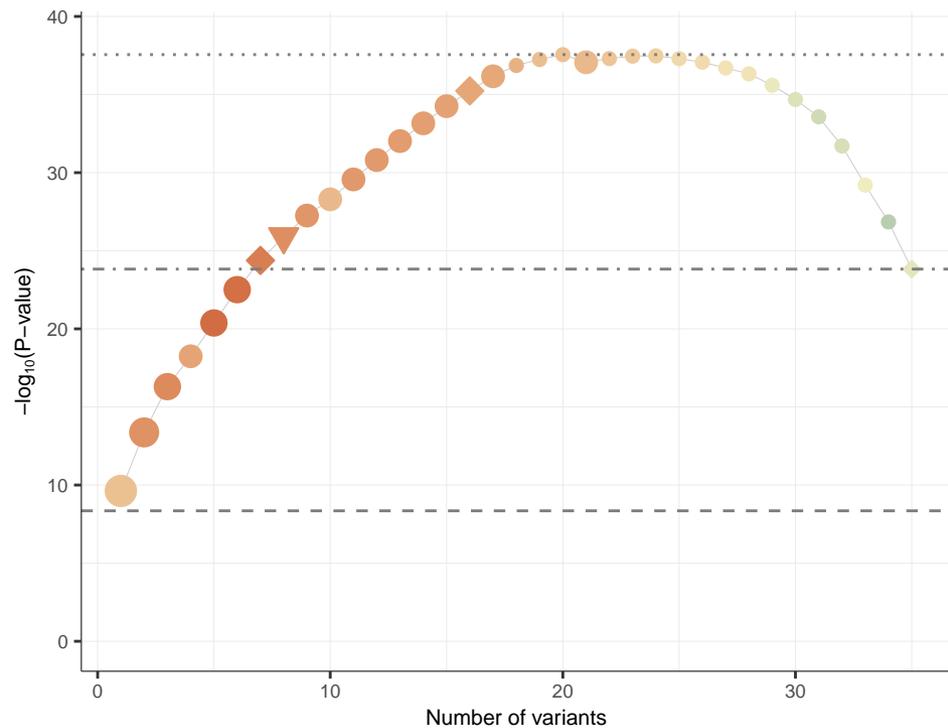
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

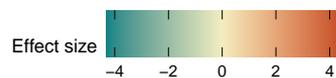
phosphoethanolamine in urine at *ALPL* (LoF_mis)



phosphoethanolamine in urine at *ALPL* (HI_mis)



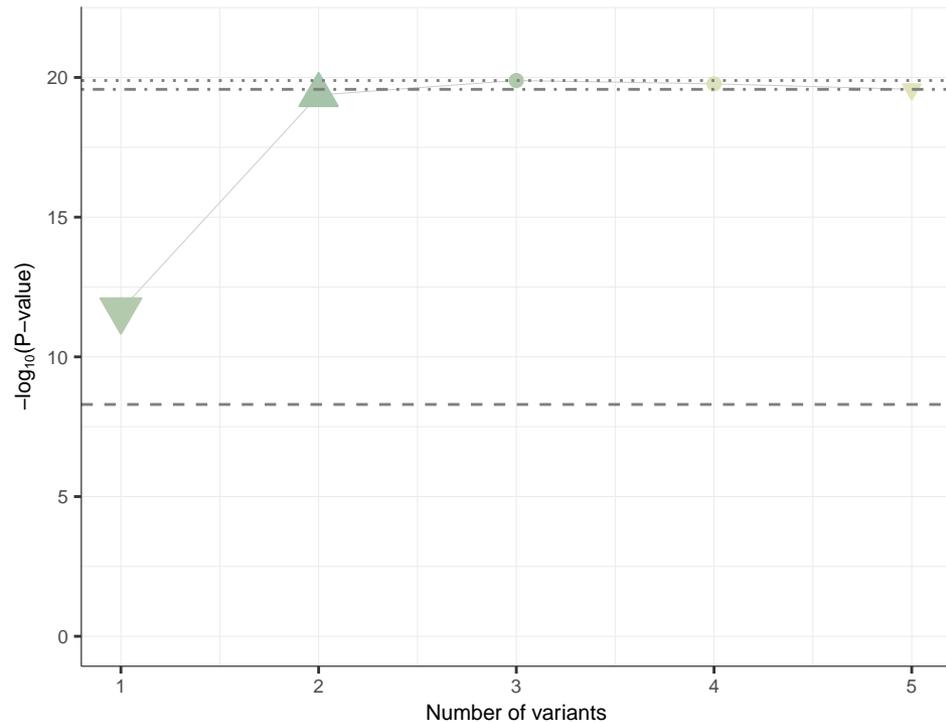
- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing



- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8

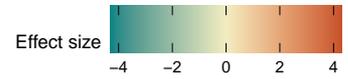
- Thresholds
- Significance Threshold
 - - - Total P-value
 - ⋯ Lowest P-value

1-oleoyl-2-arachidonoyl-GPE (18:1/20:4)* in plasma at APOC3 (LoF_mis)

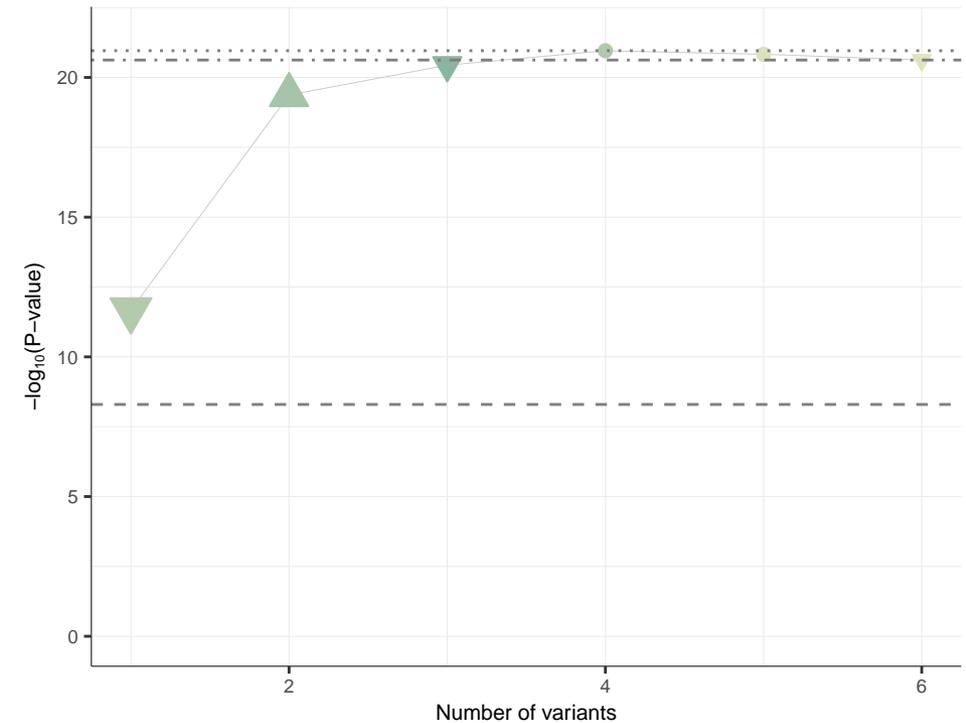


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-oleoyl-2-arachidonoyl-GPE (18:1/20:4)* in plasma at APOC3 (HI_mis)



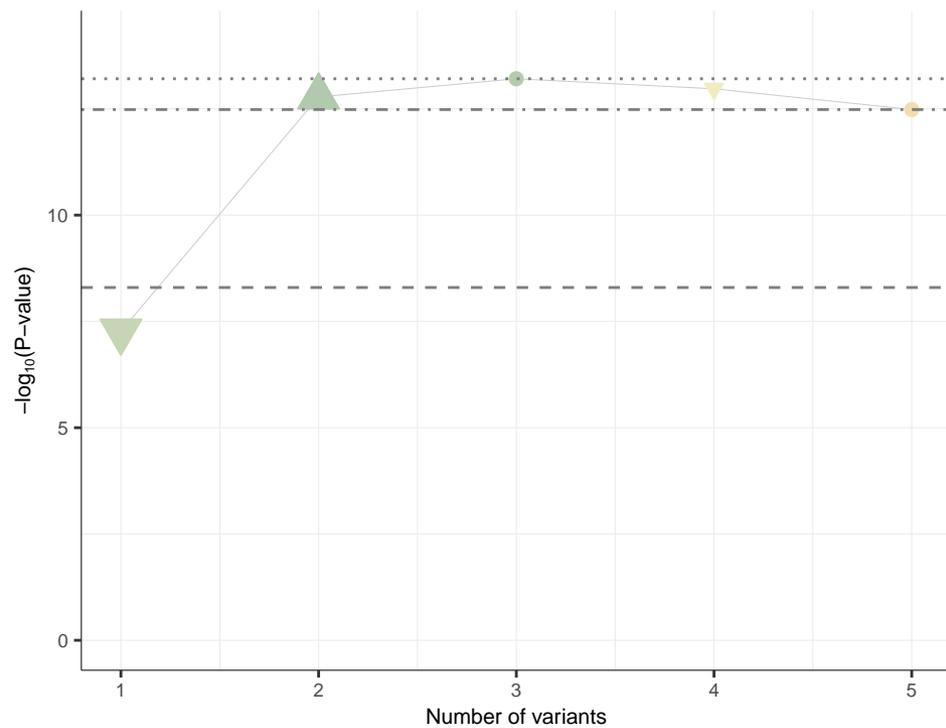
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

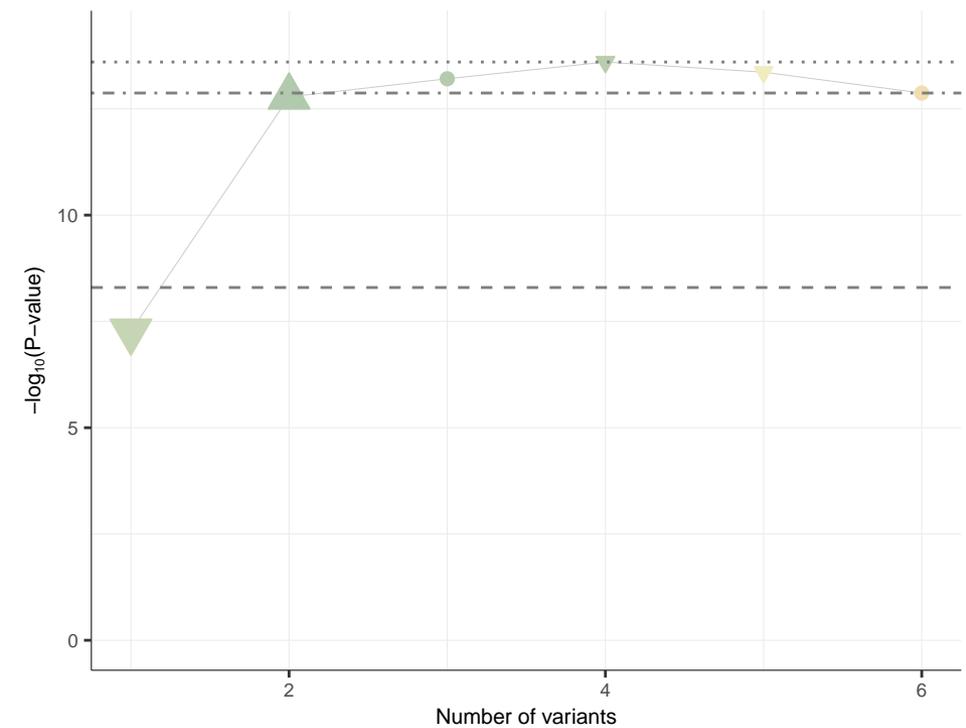
Thresholds

- - - Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-oleoyl-2-linoleoyl-GPE (18:1/18:2)* in plasma at APOC3 (LoF_mis)

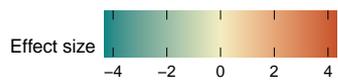


1-oleoyl-2-linoleoyl-GPE (18:1/18:2)* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



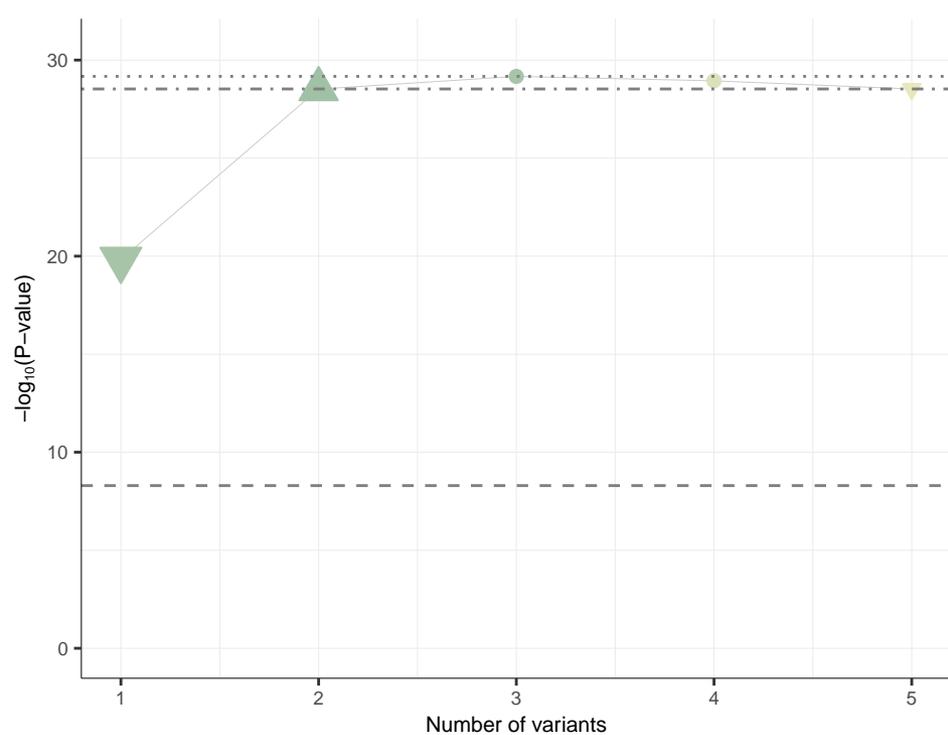
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

Thresholds

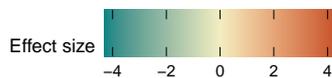
- Significance Threshold
- - - Total P-value
- ... Lowest P-value

1-palmitoyl-2-arachidonoyl-GPE (16:0/20:4)* in plasma at APOC3 (LoF_mis)

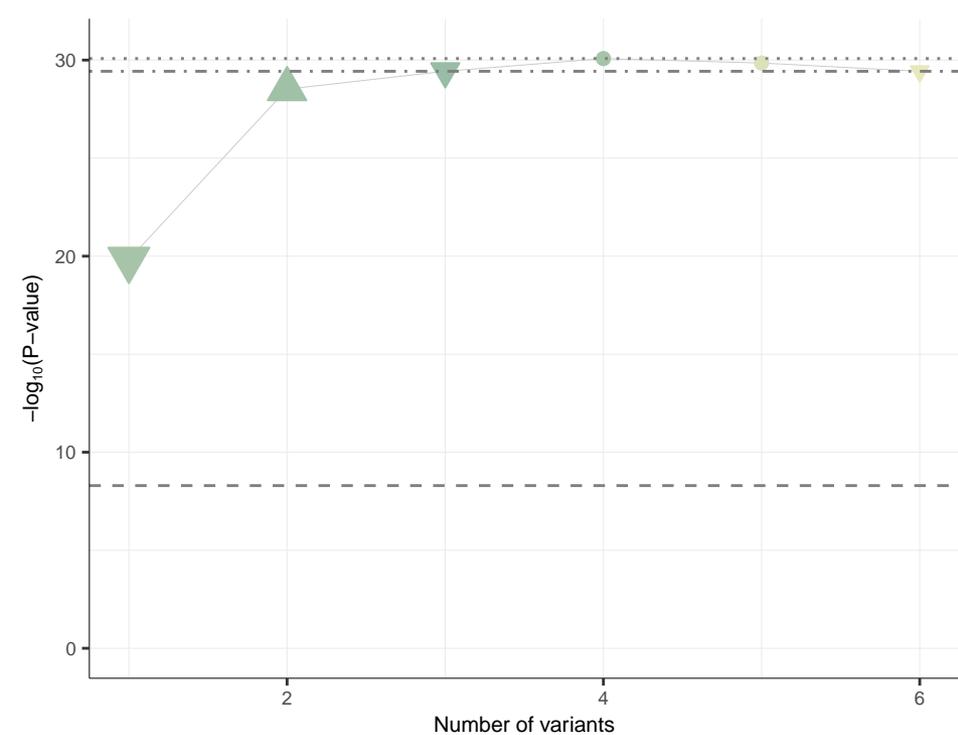


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-palmitoyl-2-arachidonoyl-GPE (16:0/20:4)* in plasma at APOC3 (HI_mis)



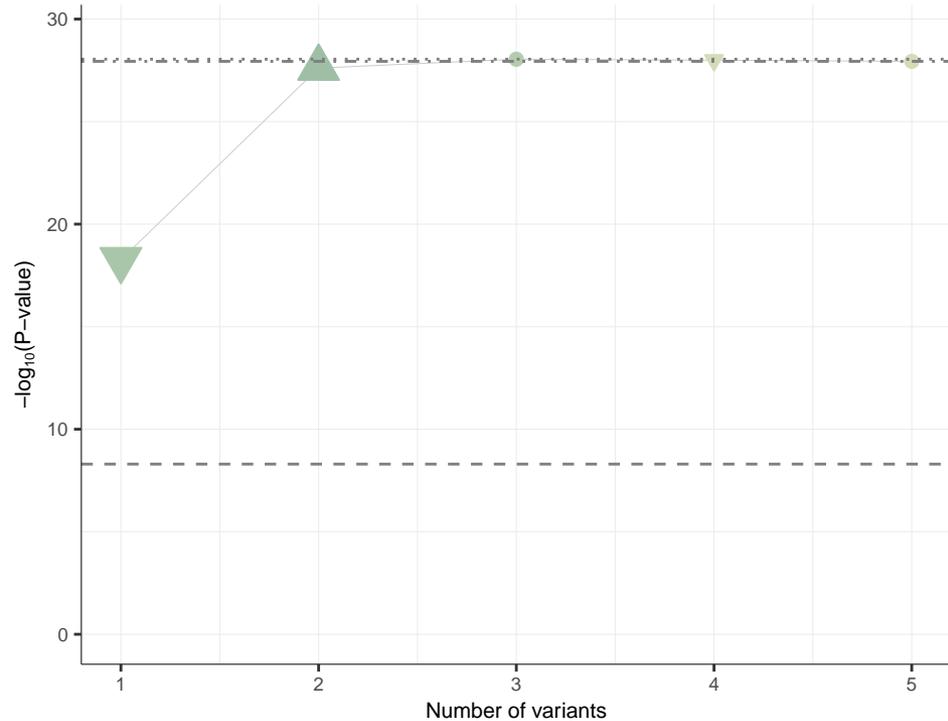
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

- Significance Threshold
- · - Total P-value
- · · · Lowest P-value

1-palmitoyl-2-docosahexaenoyl-GPE (16:0/22:6)* in plasma at APOC3 (LoF_mis)

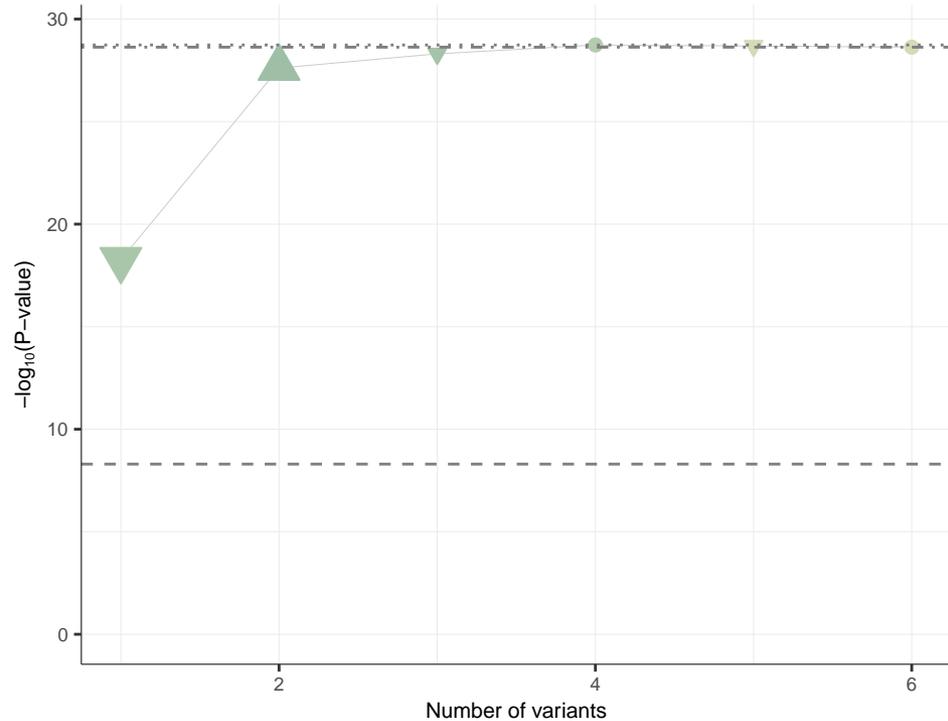


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-palmitoyl-2-docosahexaenoyl-GPE (16:0/22:6)* in plasma at APOC3 (HI_mis)



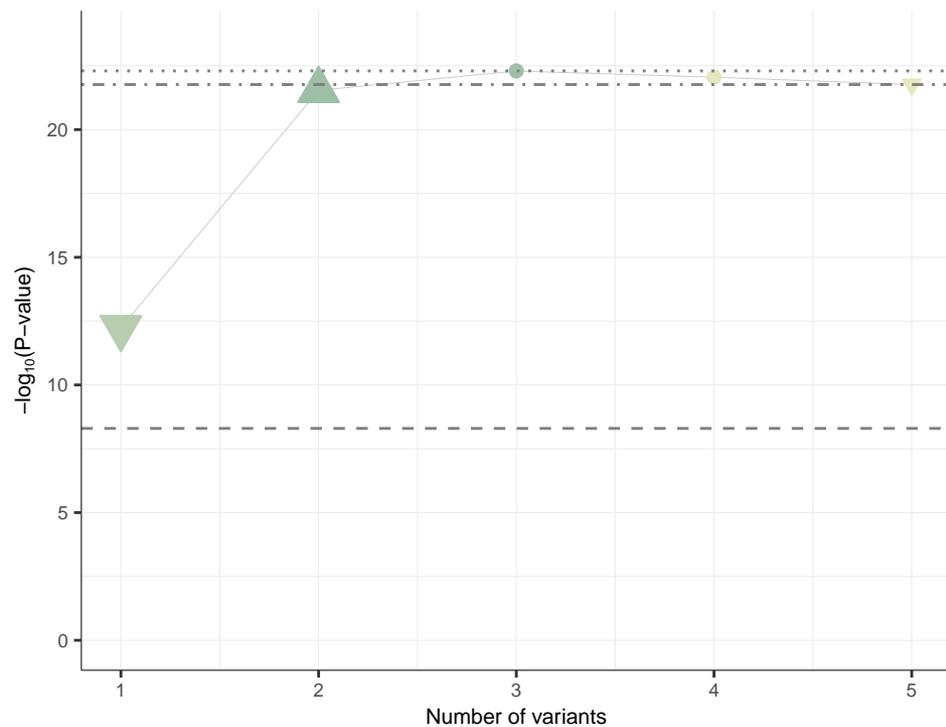
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

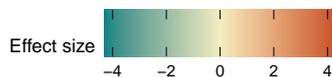
- Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-palmitoyl-2-linoleoyl-GPE (16:0/18:2) in plasma at APOC3 (LoF_mis)

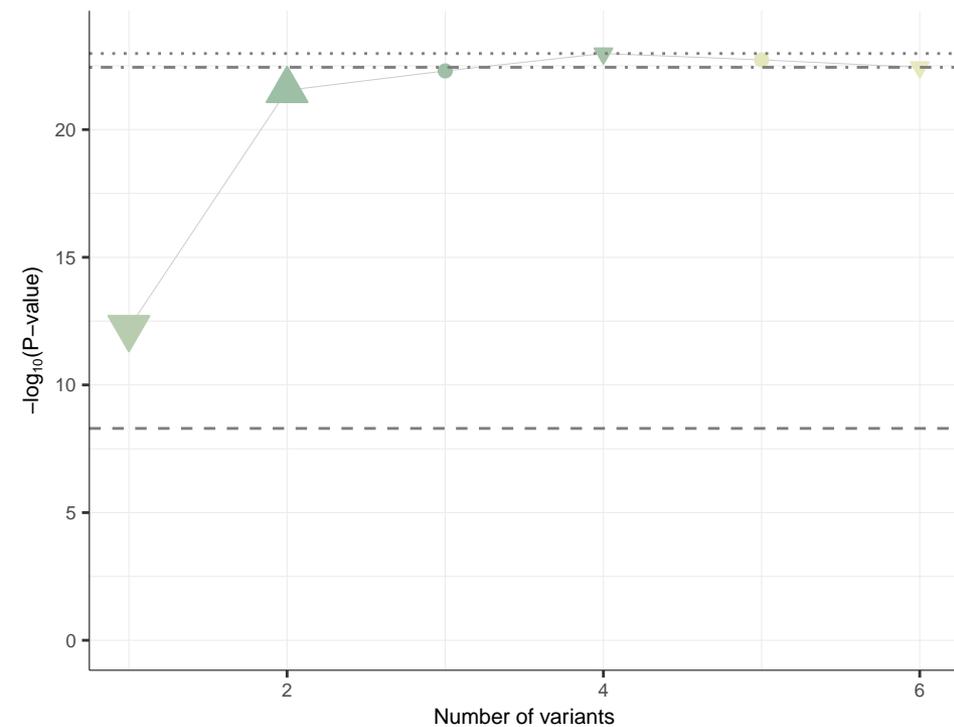


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-palmitoyl-2-linoleoyl-GPE (16:0/18:2) in plasma at APOC3 (HI_mis)



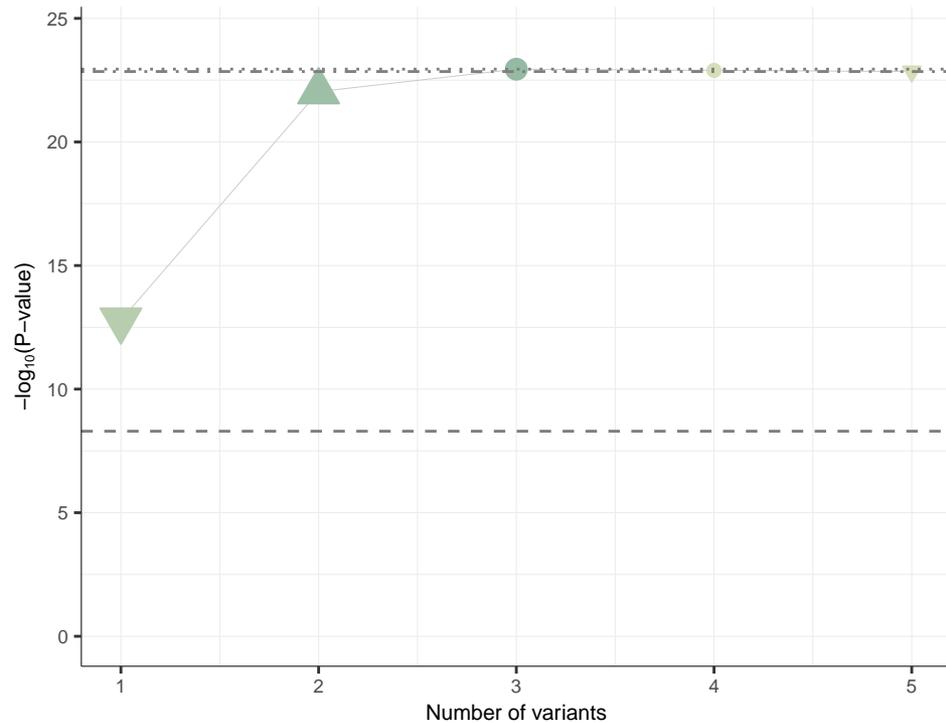
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

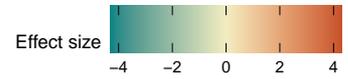
- Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-palmitoyl-2-oleoyl-GPE (16:0/18:1) in plasma at APOC3 (LoF_mis)

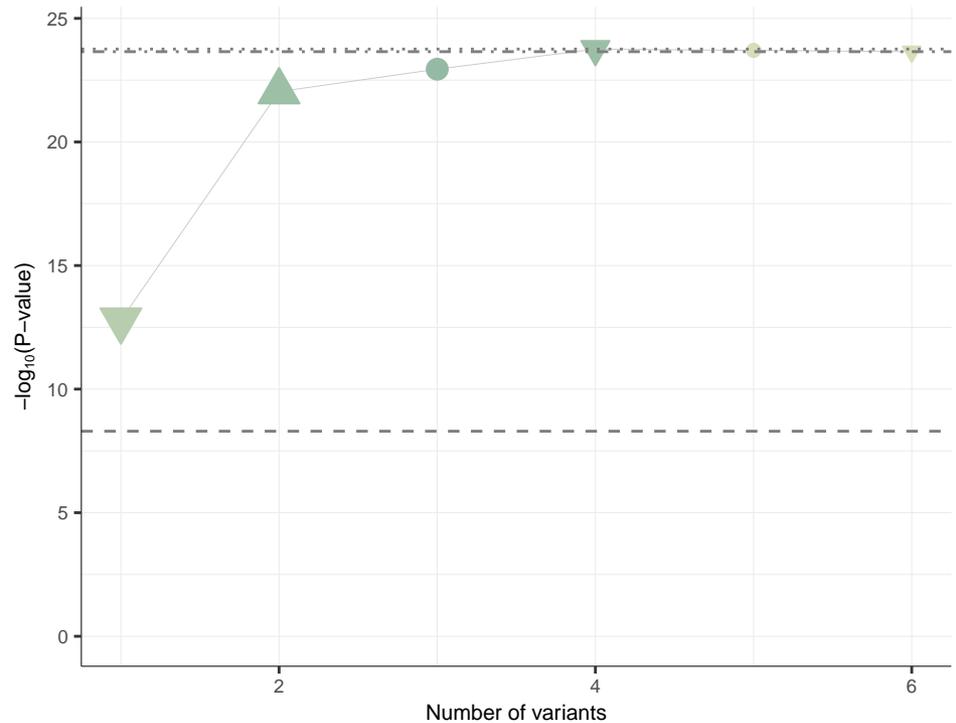


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-palmitoyl-2-oleoyl-GPE (16:0/18:1) in plasma at APOC3 (HI_mis)



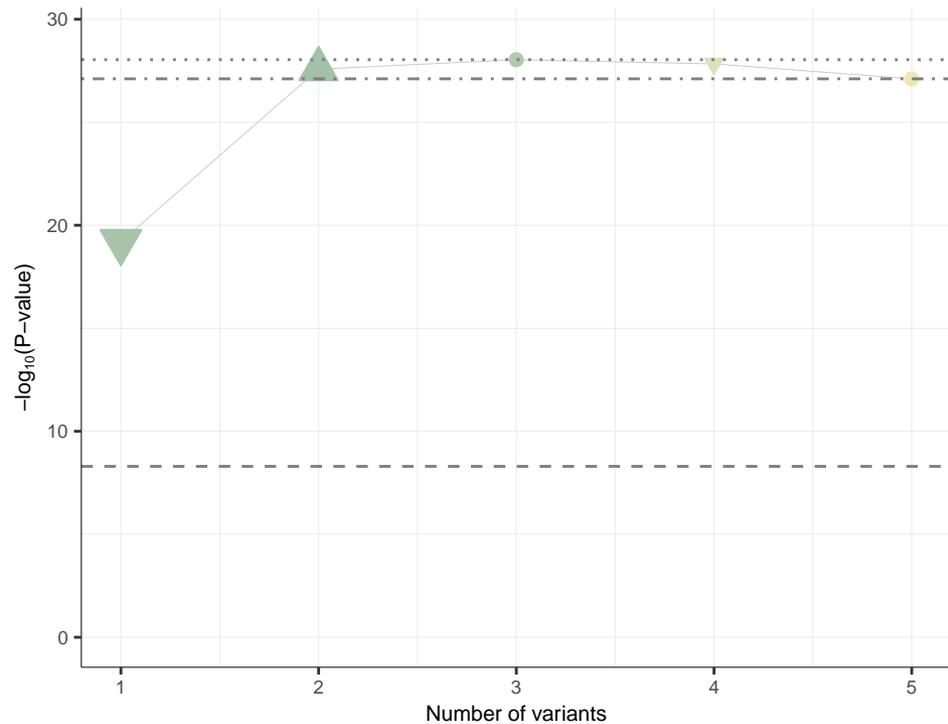
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

- - - Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-stearoyl-2-arachidonoyl-GPE (18:0/20:4) in plasma at APOC3 (LoF_mis)

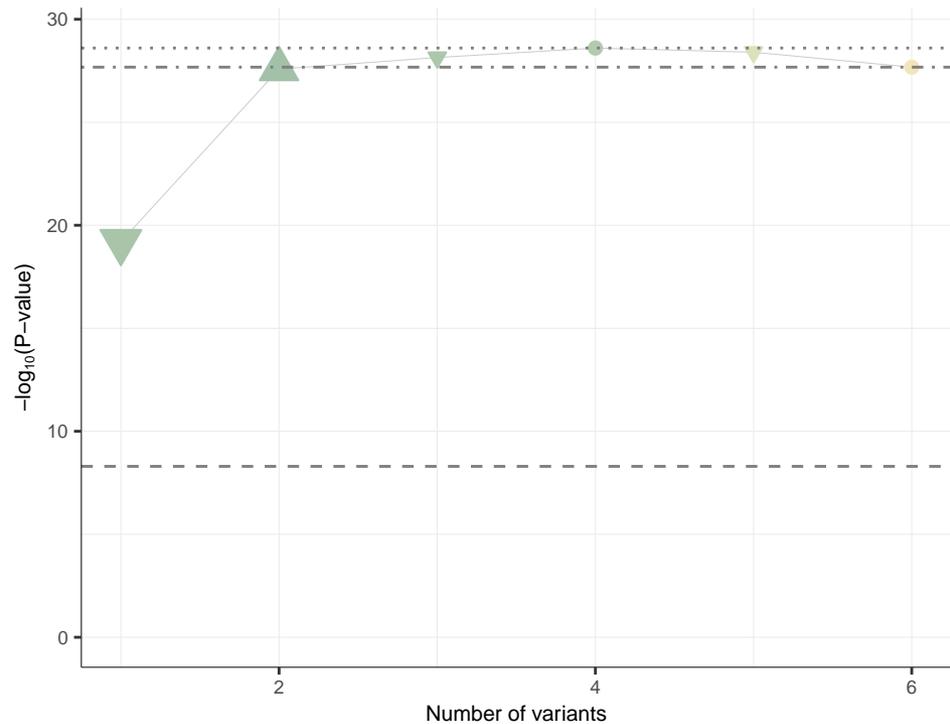


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-stearoyl-2-arachidonoyl-GPE (18:0/20:4) in plasma at APOC3 (HI_mis)



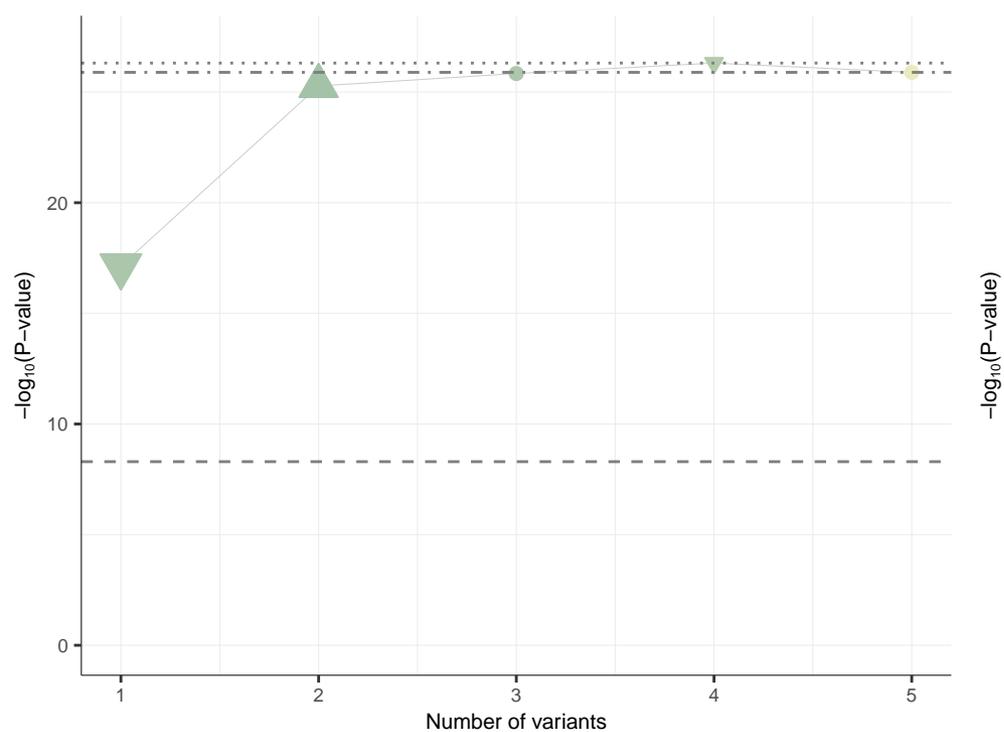
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

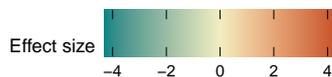
- Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-stearoyl-2-docosahexaenoyl-GPE (18:0/22:6)* in plasma at APOC3 (LoF_mis)

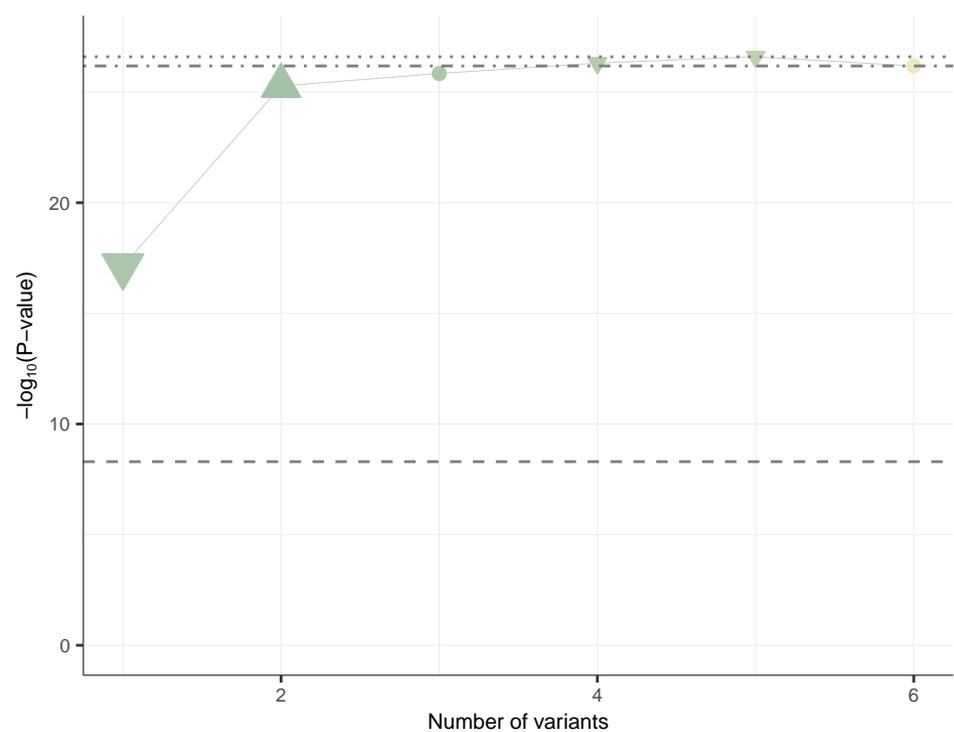


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-stearoyl-2-docosahexaenoyl-GPE (18:0/22:6)* in plasma at APOC3 (HI_mis)



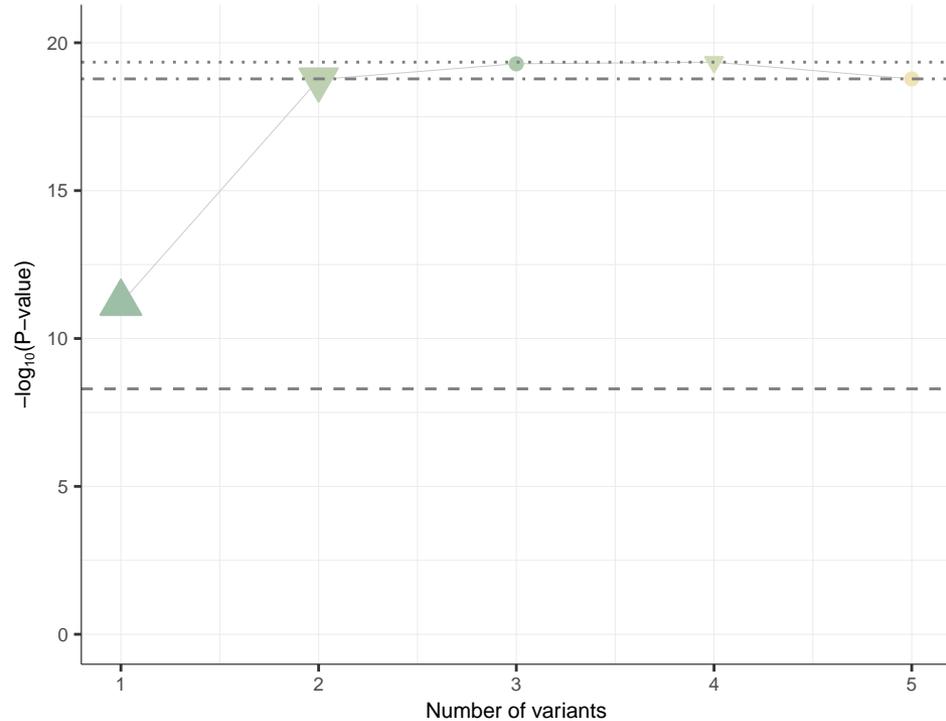
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

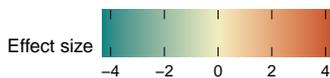
- Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-stearoyl-2-linoleoyl-GPE (18:0/18:2)* in plasma at APOC3 (LoF_mis)

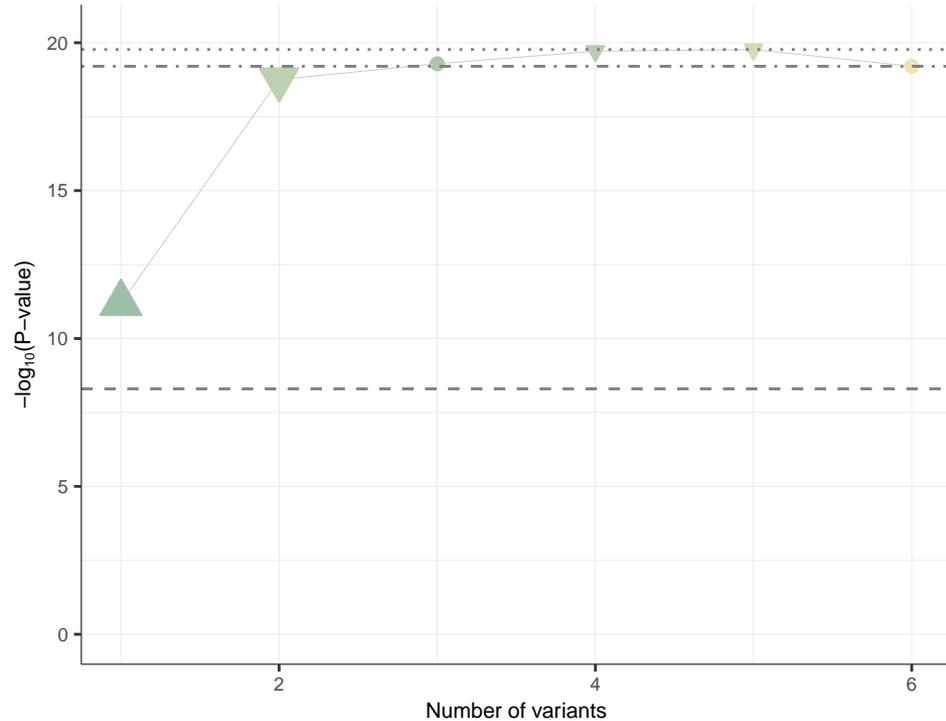


Variant consequence

- missense
- ▽ splicing
- △ stop gained



1-stearoyl-2-linoleoyl-GPE (18:0/18:2)* in plasma at APOC3 (HI_mis)



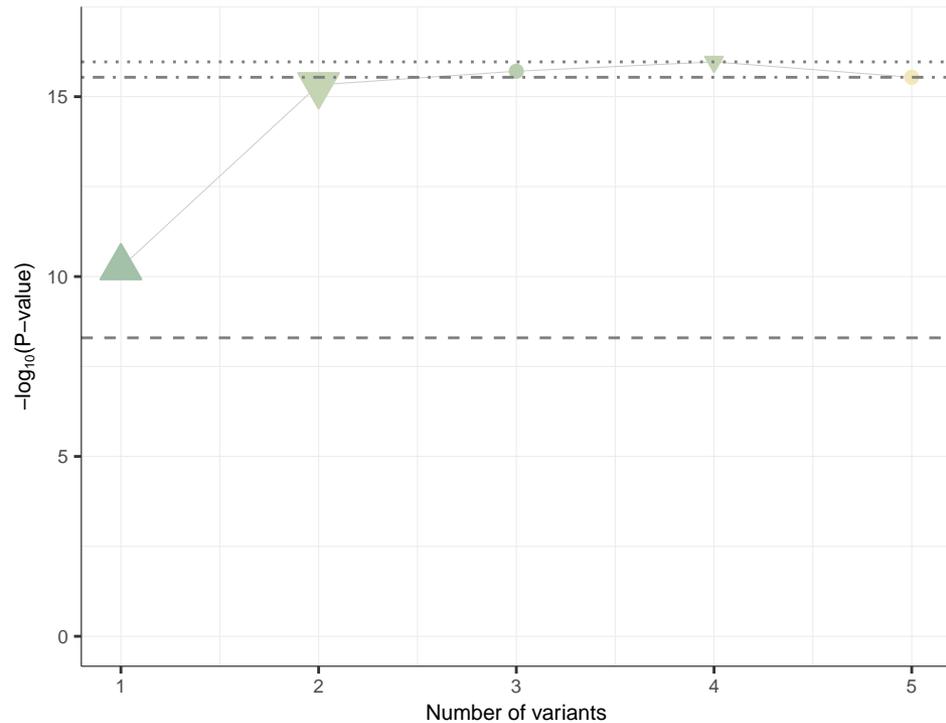
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

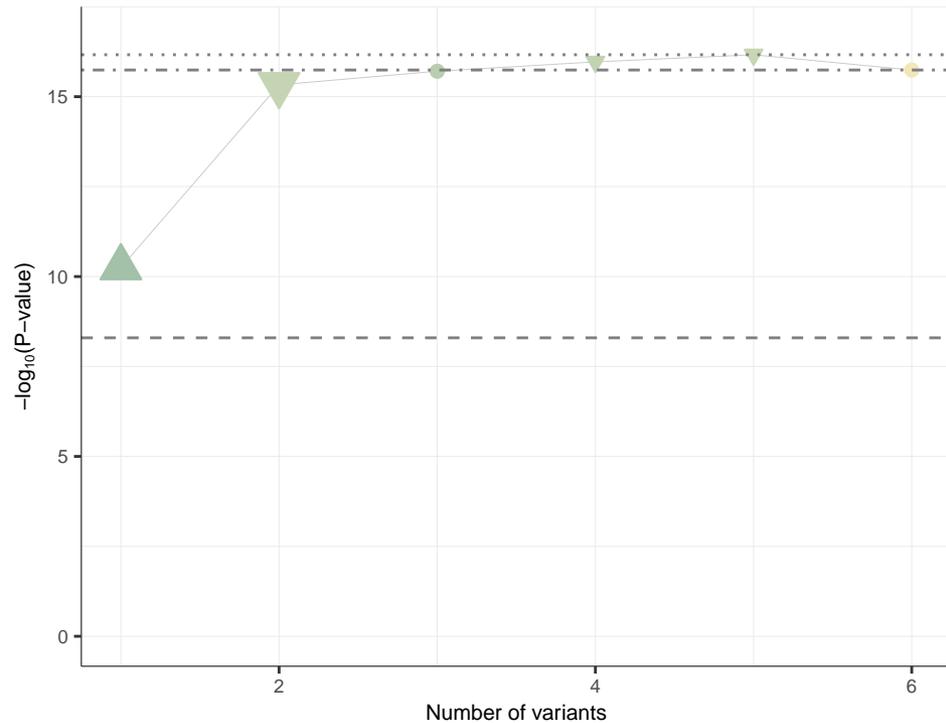
Thresholds

- Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-stearoyl-2-oleoyl-GPE (18:0/18:1) in plasma at APOC3 (LoF_mis)

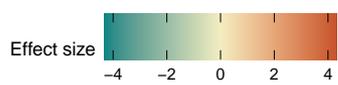


1-stearoyl-2-oleoyl-GPE (18:0/18:1) in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



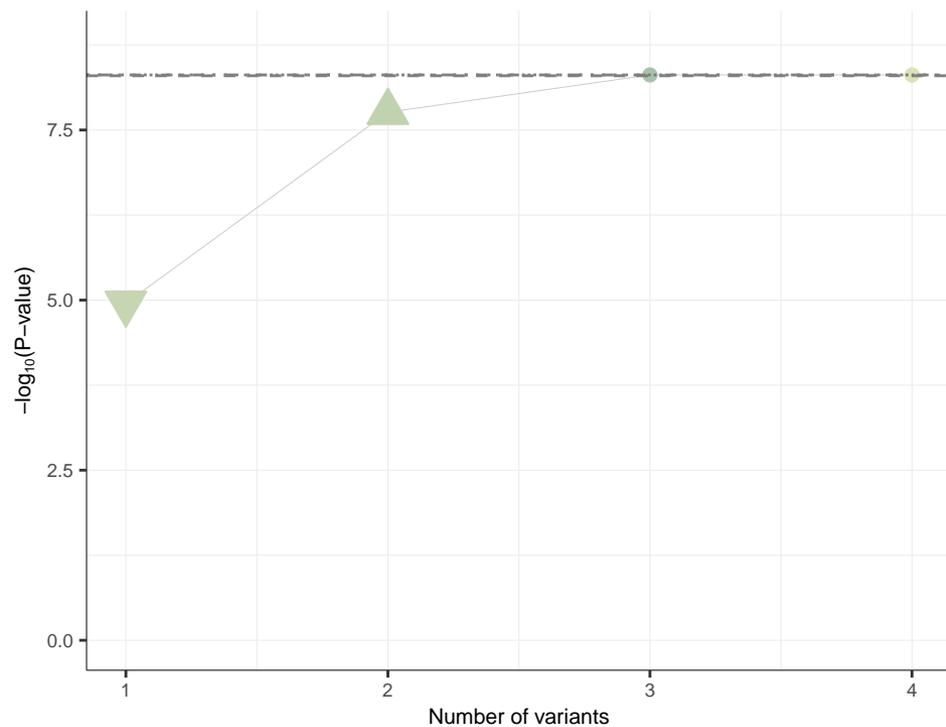
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

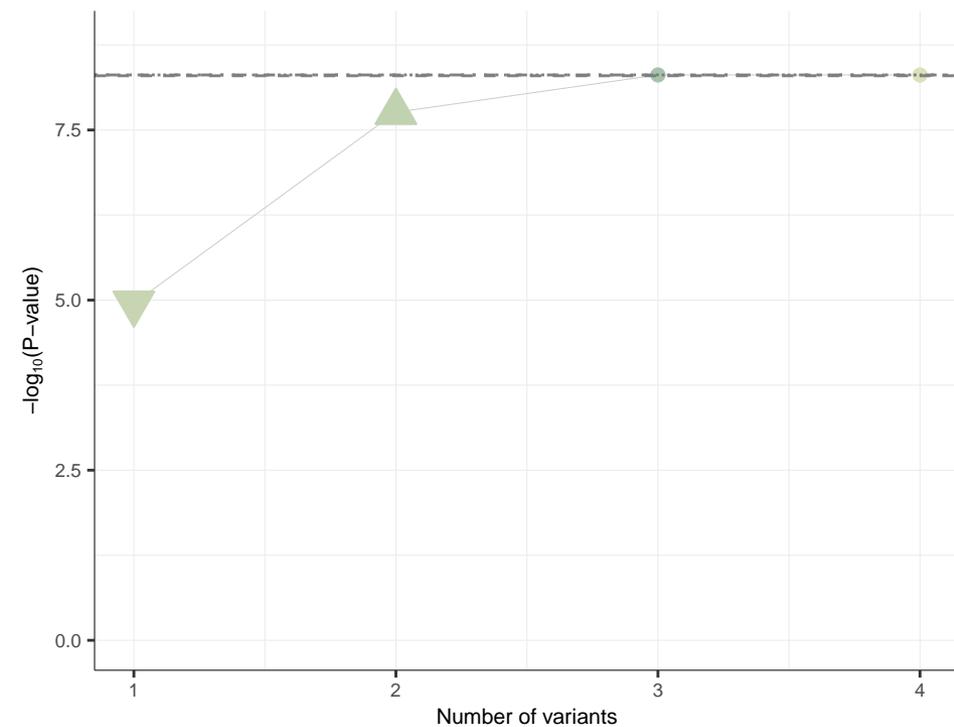
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

diacylglycerol (16:1/18:2 [2], 16:0/18:3 [1])* in plasma at APOC3 (LoF_mis)

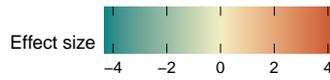


diacylglycerol (16:1/18:2 [2], 16:0/18:3 [1])* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



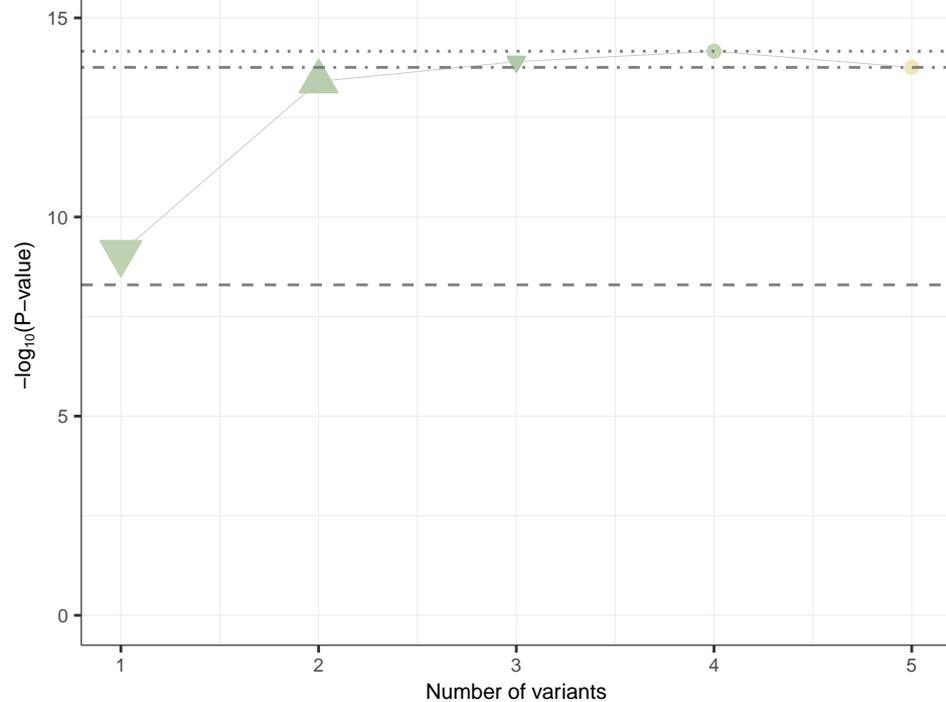
P-value

- >0.05
- <0.05
- <1e-3

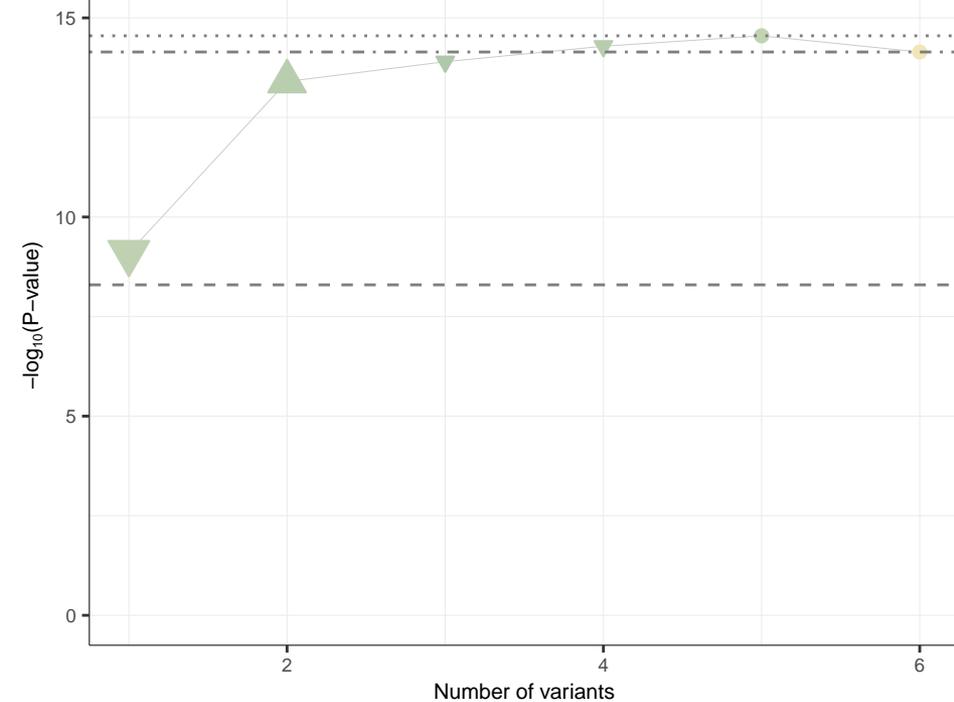
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

linoleoyl–linoleoyl–glycerol (18:2/18:2) [1]* in plasma at APOC3 (LoF_mis)

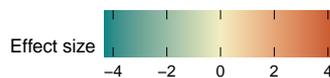


linoleoyl–linoleoyl–glycerol (18:2/18:2) [1]* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



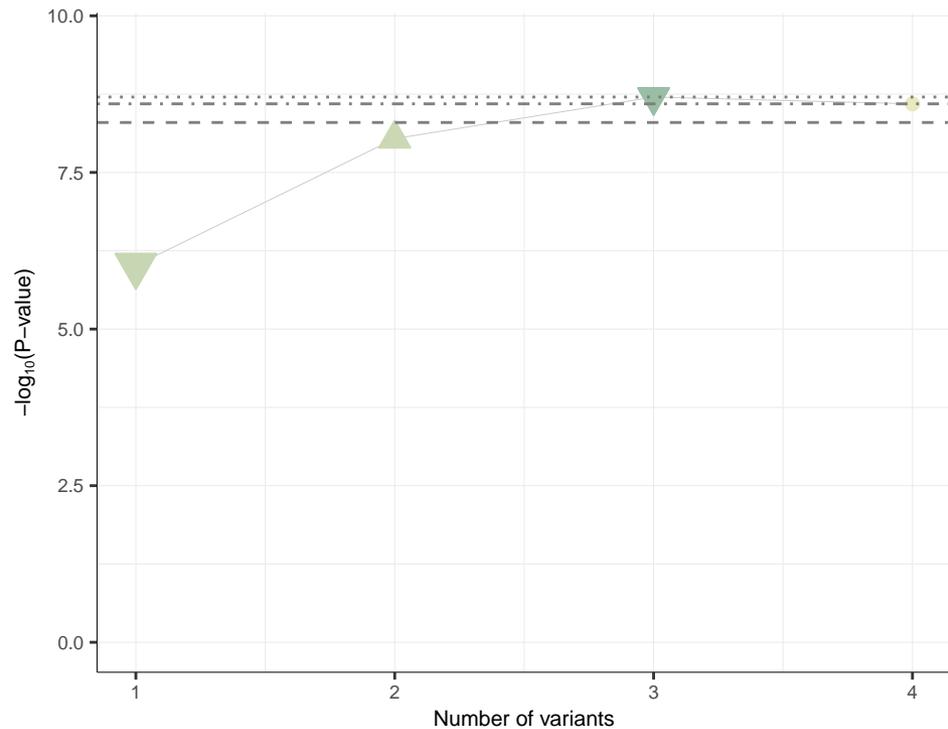
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

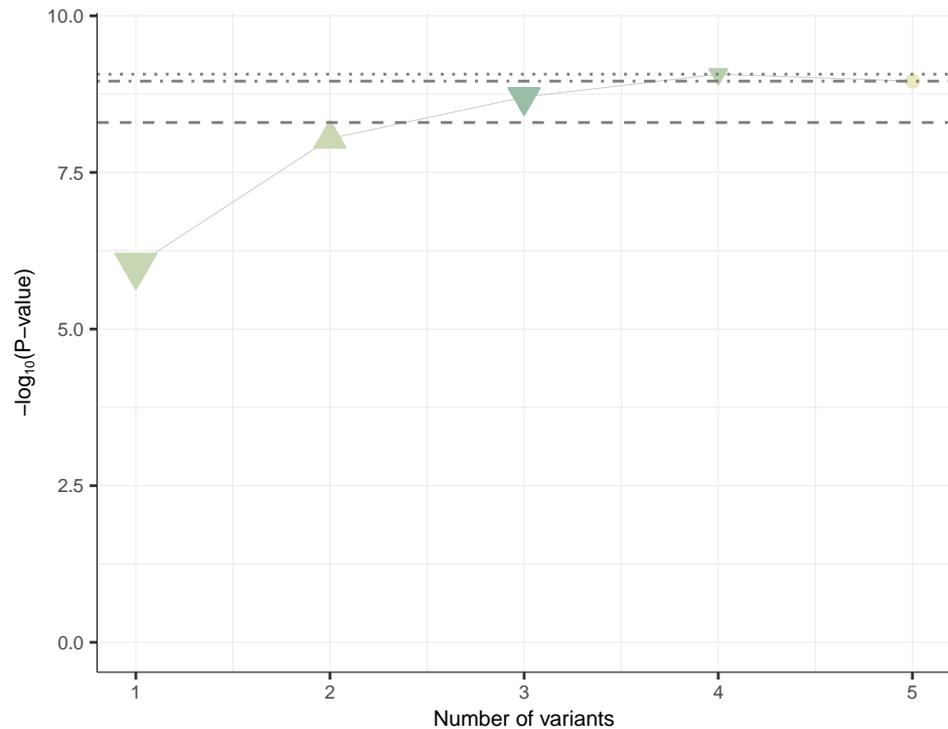
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

oleoyl–arachidonoyl–glycerol (18:1/20:4) [1]* in plasma at APOC3 (LoF_mis)

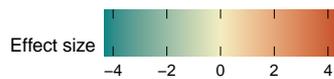


oleoyl–arachidonoyl–glycerol (18:1/20:4) [1]* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



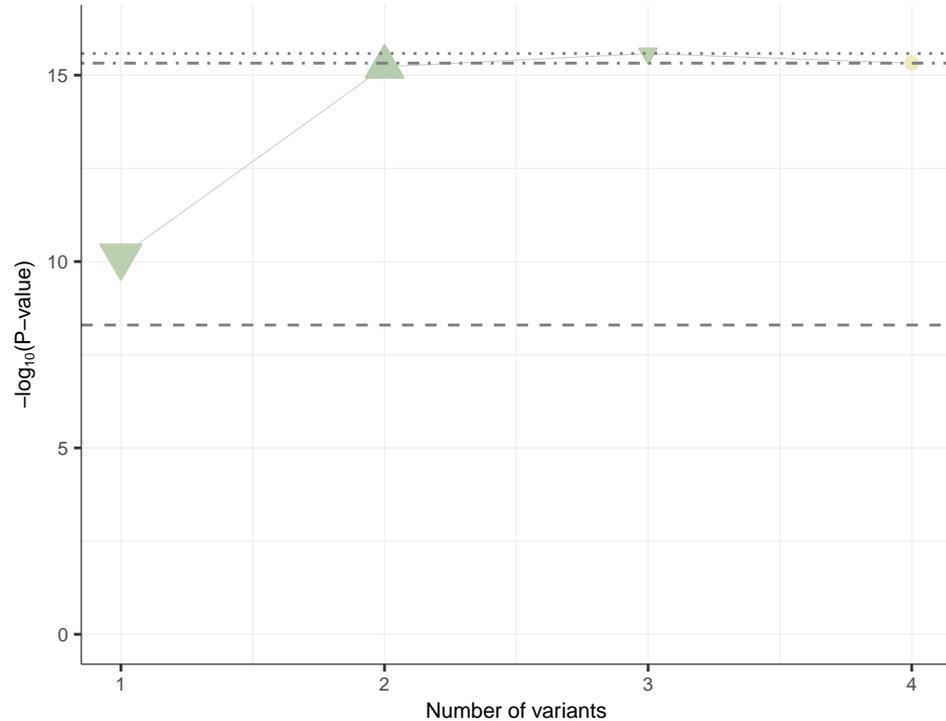
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

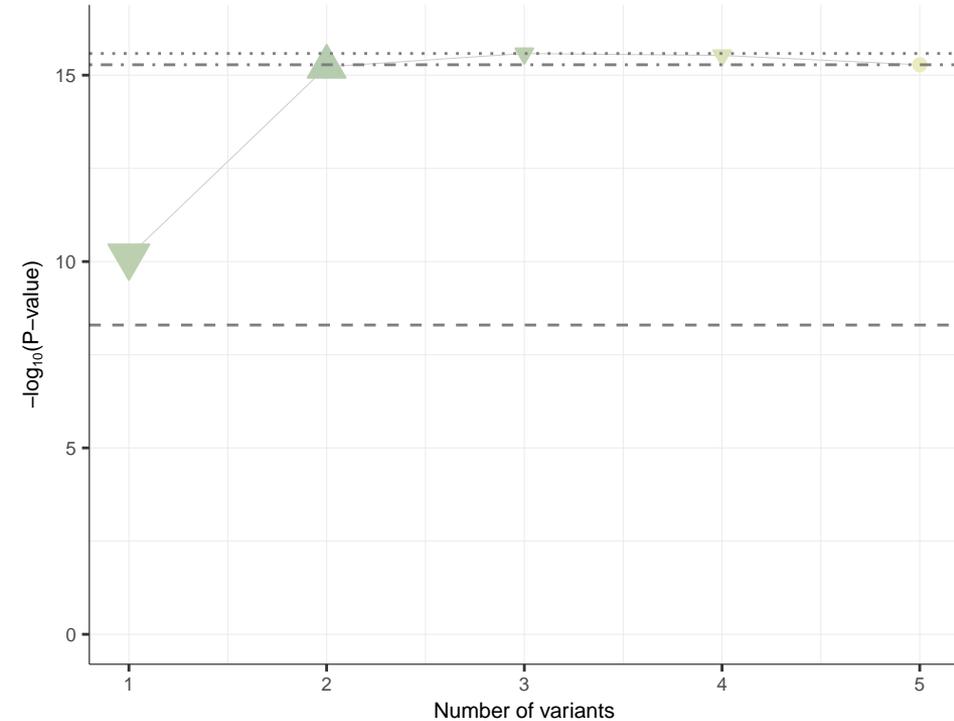
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

oleoyl–linoleoyl–glycerol (18:1/18:2) [1] in plasma at APOC3 (LoF_mis)

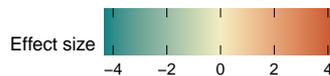


oleoyl–linoleoyl–glycerol (18:1/18:2) [1] in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



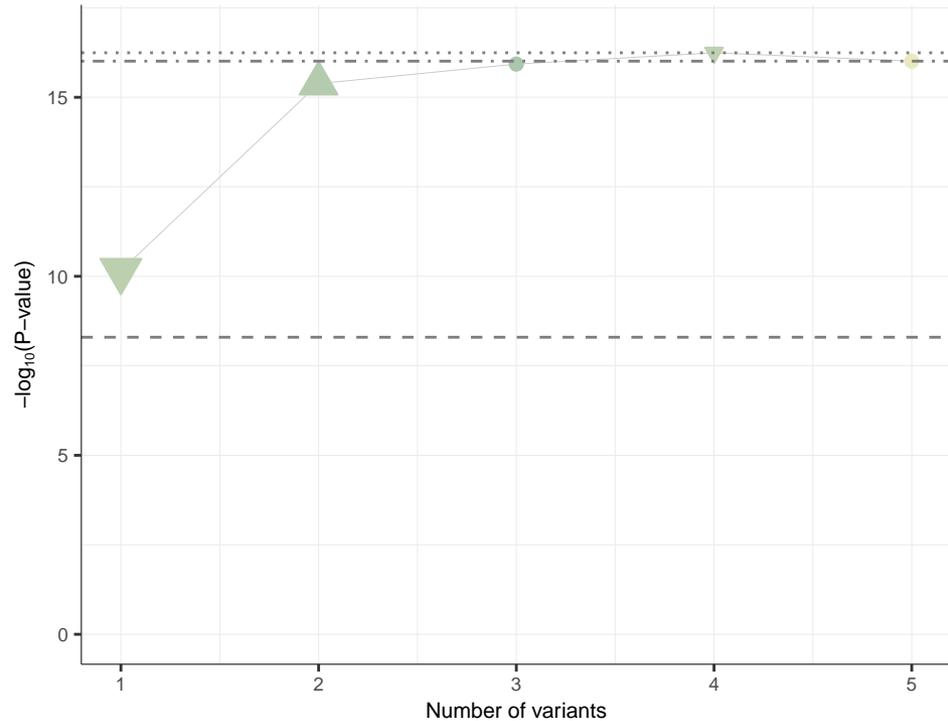
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

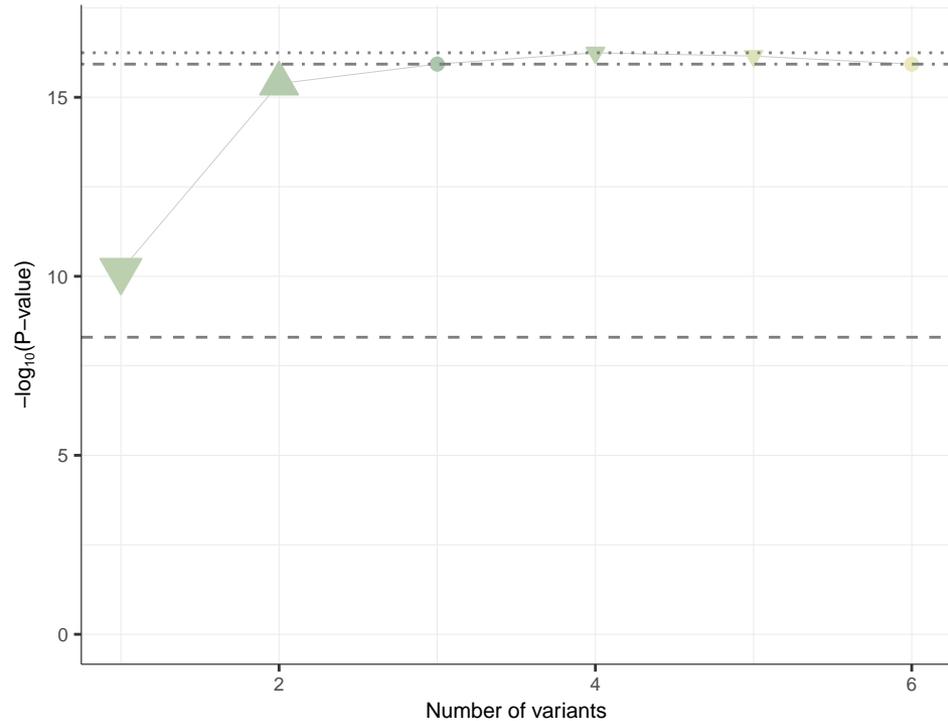
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

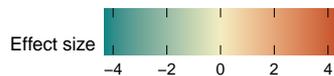
oleoyl-linoleoyl-glycerol (18:1/18:2) [2] in plasma at APOC3 (LoF_mis)



oleoyl-linoleoyl-glycerol (18:1/18:2) [2] in plasma at APOC3 (HI_mis)



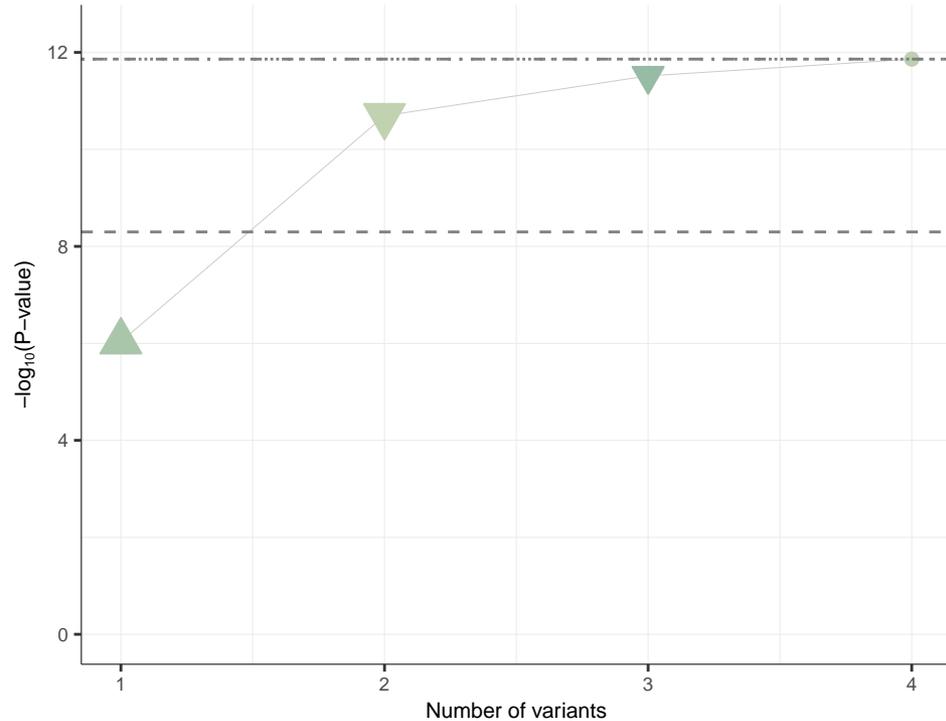
○ missense
 ▽ splicing
 △ stop gained



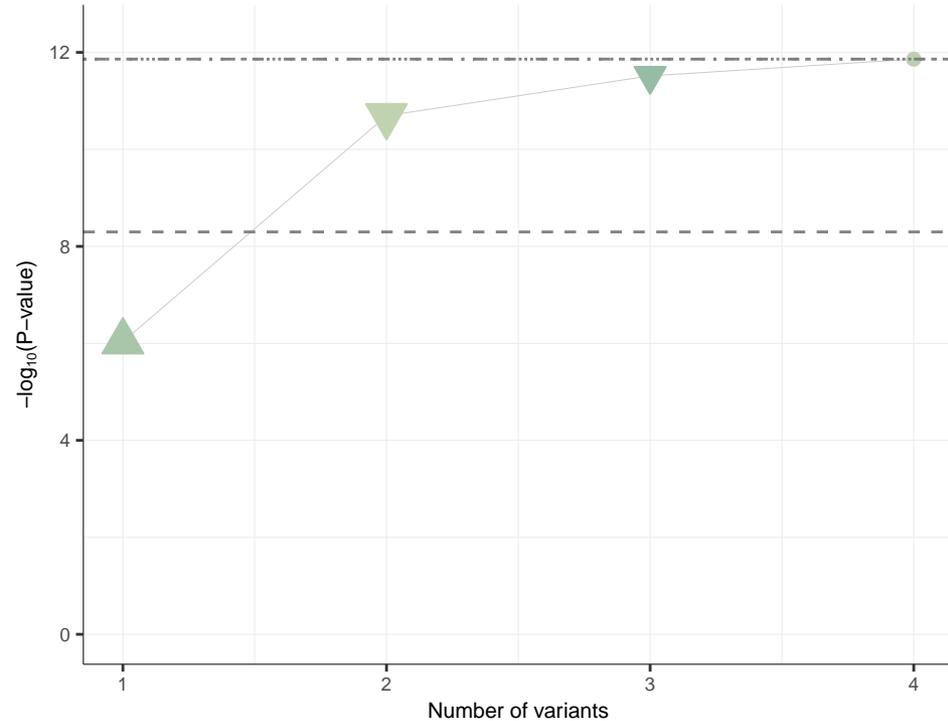
● >0.05
 ● <0.05
 ● <1e-3
 ● <1e-5
 ● <5e-8

--- Significance Threshold
 - - - Total P-value
 Lowest P-value

oleoyl-oleoyl-glycerol (18:1/18:1) [1]* in plasma at APOC3 (LoF_mis)

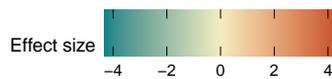


oleoyl-oleoyl-glycerol (18:1/18:1) [1]* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



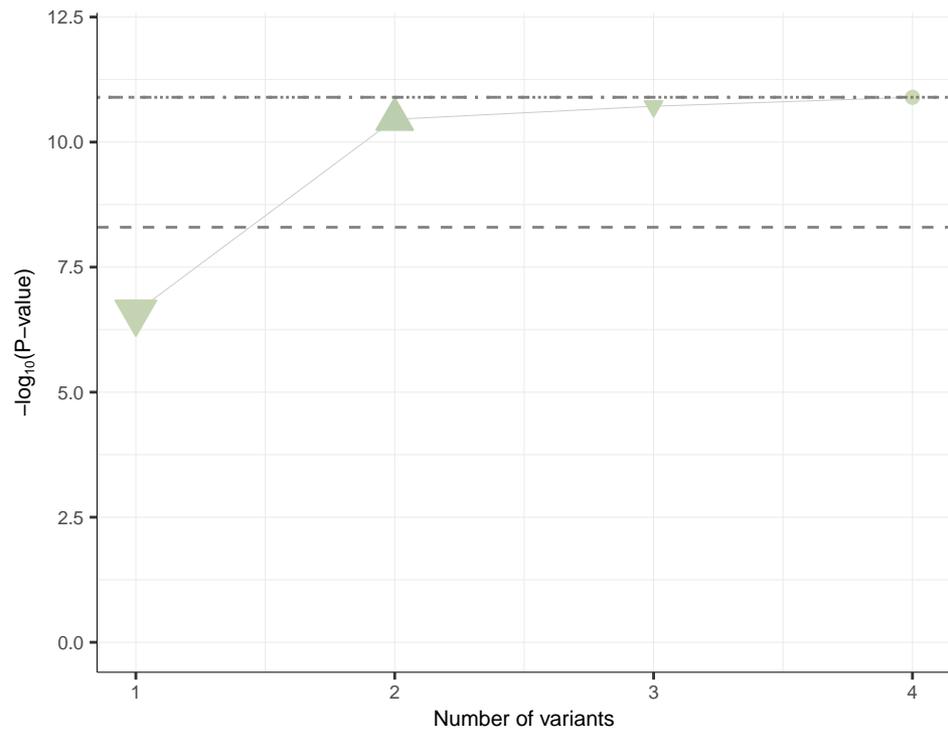
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

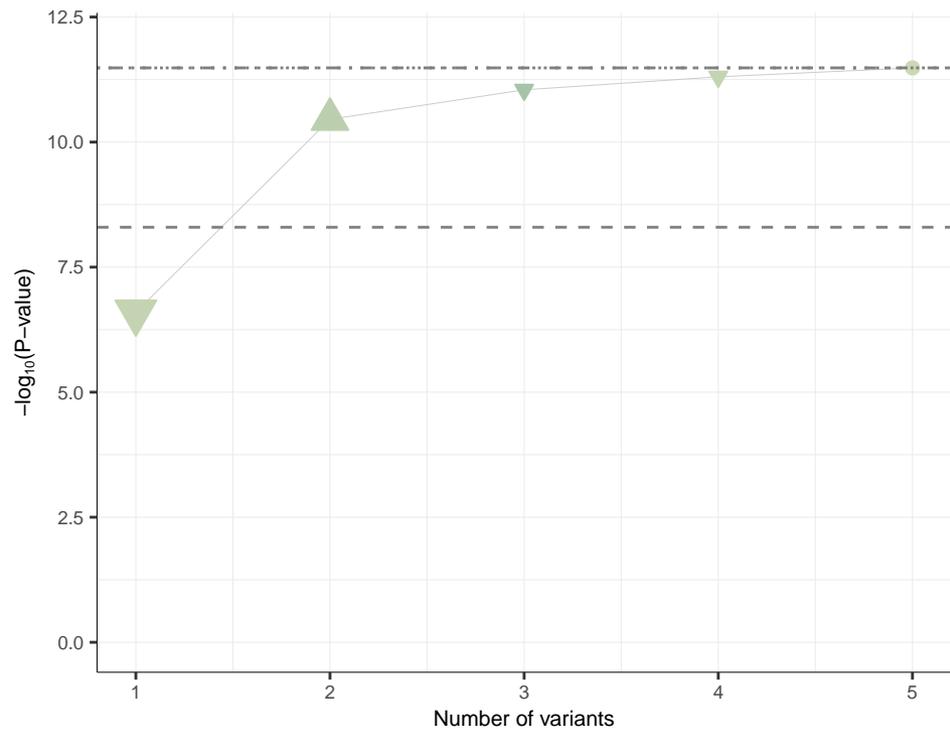
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

oleoyl-oleoyl-glycerol (18:1/18:1) [2]* in plasma at APOC3 (LoF_mis)

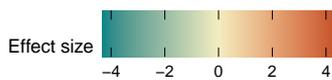


oleoyl-oleoyl-glycerol (18:1/18:1) [2]* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



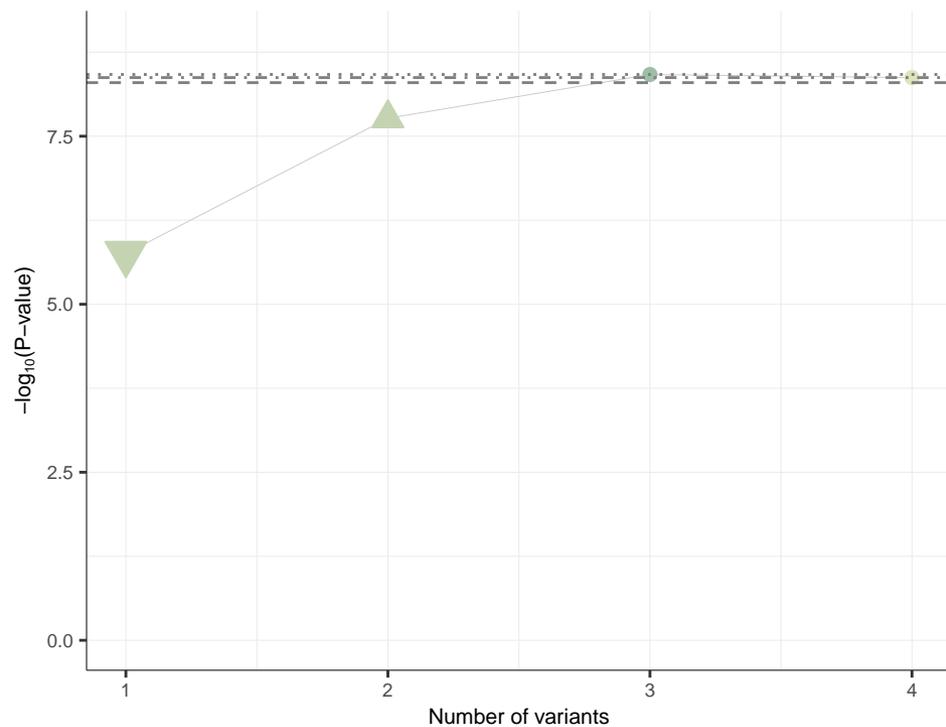
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

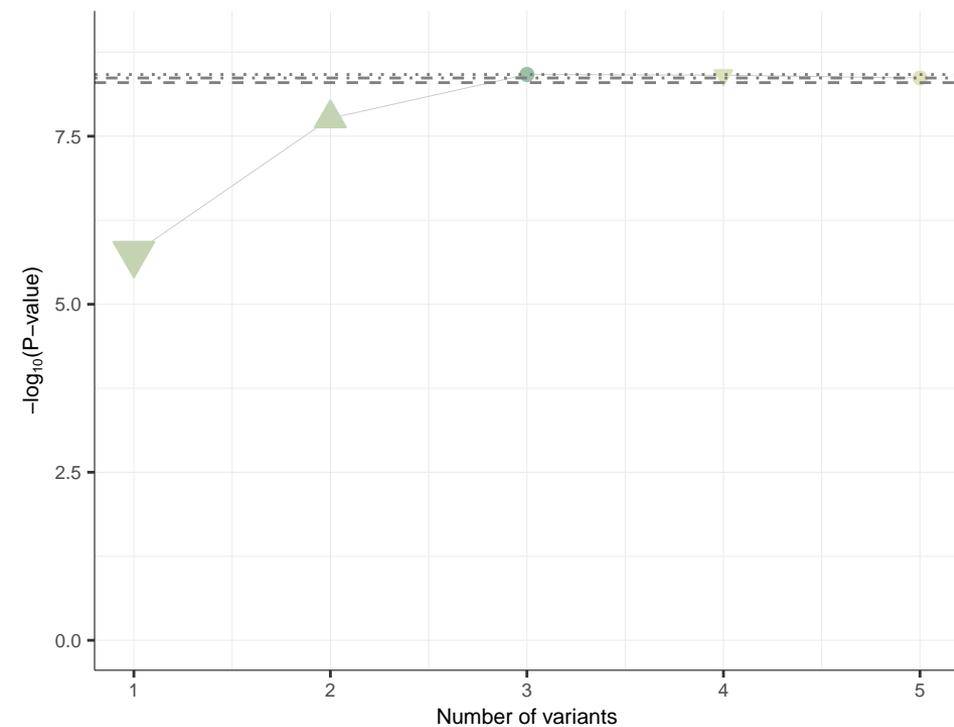
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

palmitoleoyl–linoleoyl–glycerol (16:1/18:2) [1]* in plasma at APOC3 (LoF_mis)

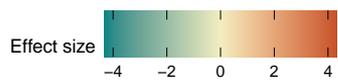


palmitoleoyl–linoleoyl–glycerol (16:1/18:2) [1]* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



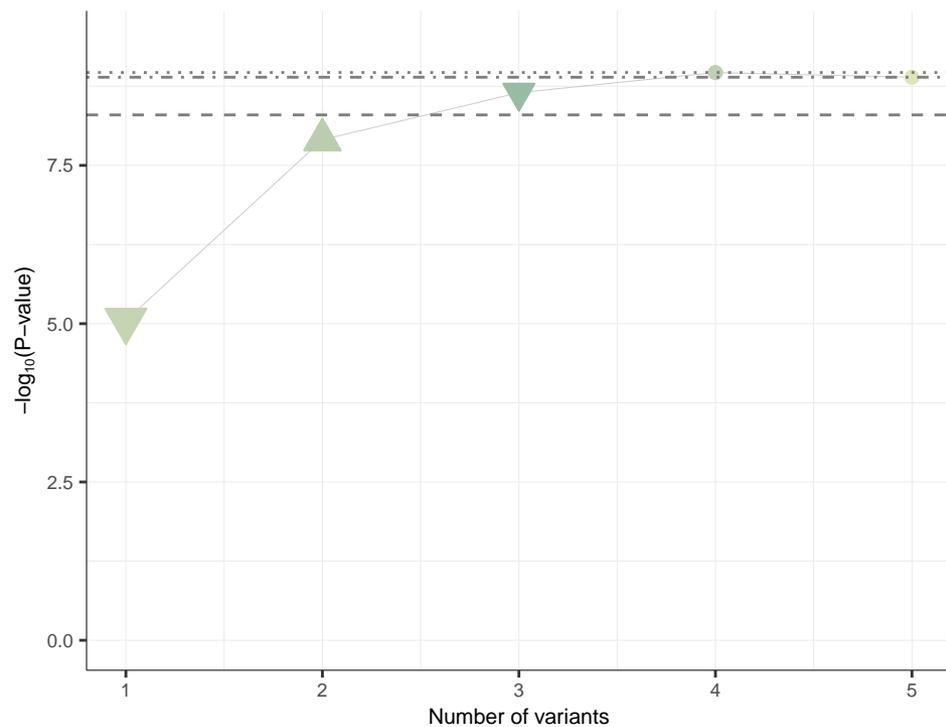
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

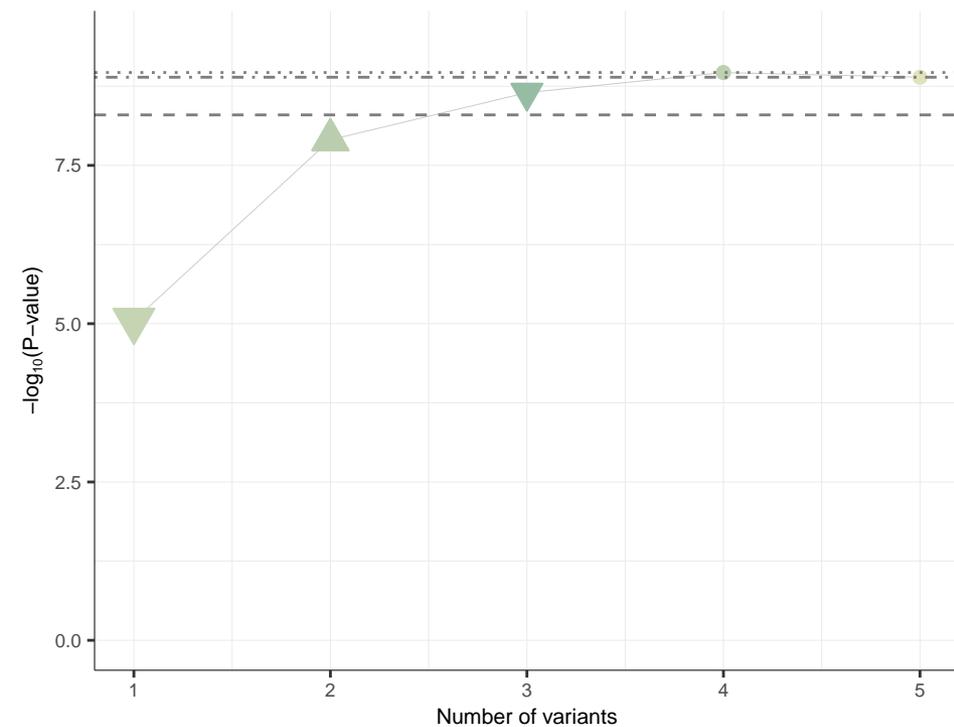
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

palmitoyl–linoleoyl–glycerol (16:0/18:2) [1]* in plasma at APOC3 (LoF_mis)

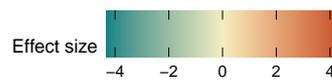


palmitoyl–linoleoyl–glycerol (16:0/18:2) [1]* in plasma at APOC3 (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



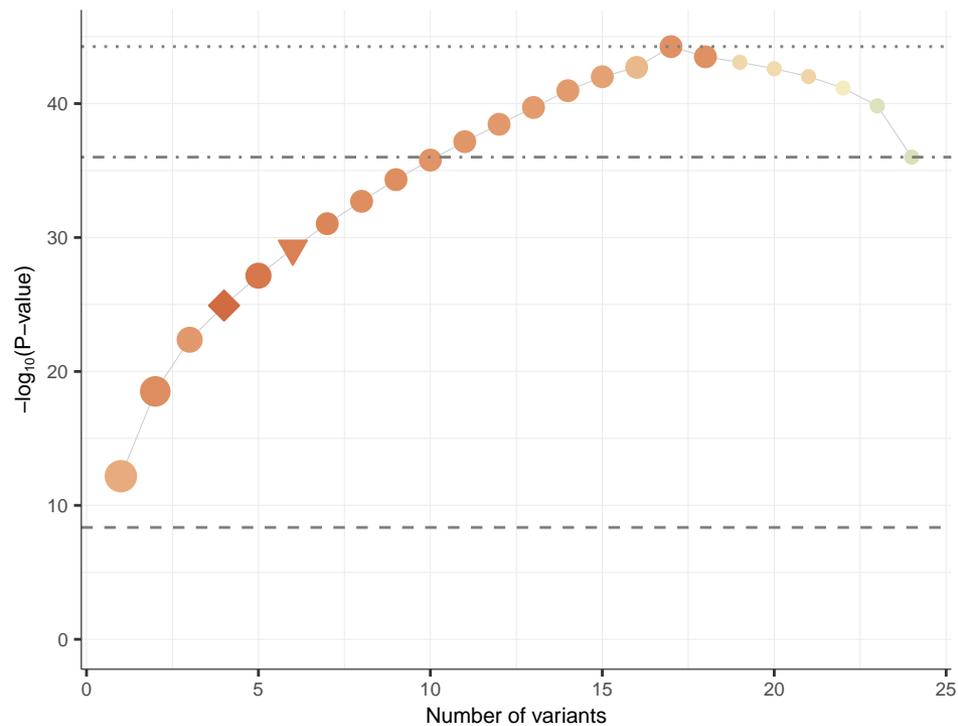
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

Thresholds

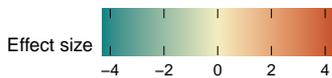
- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

argininosuccinate in urine at ASL (LoF_mis)

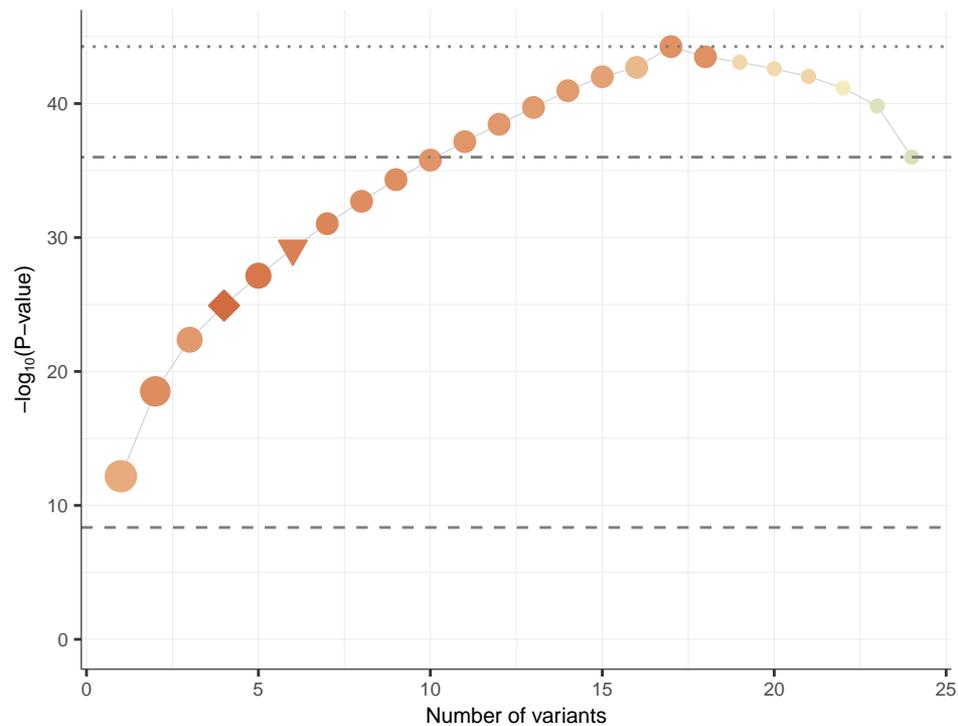


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



argininosuccinate in urine at ASL (HI_mis)

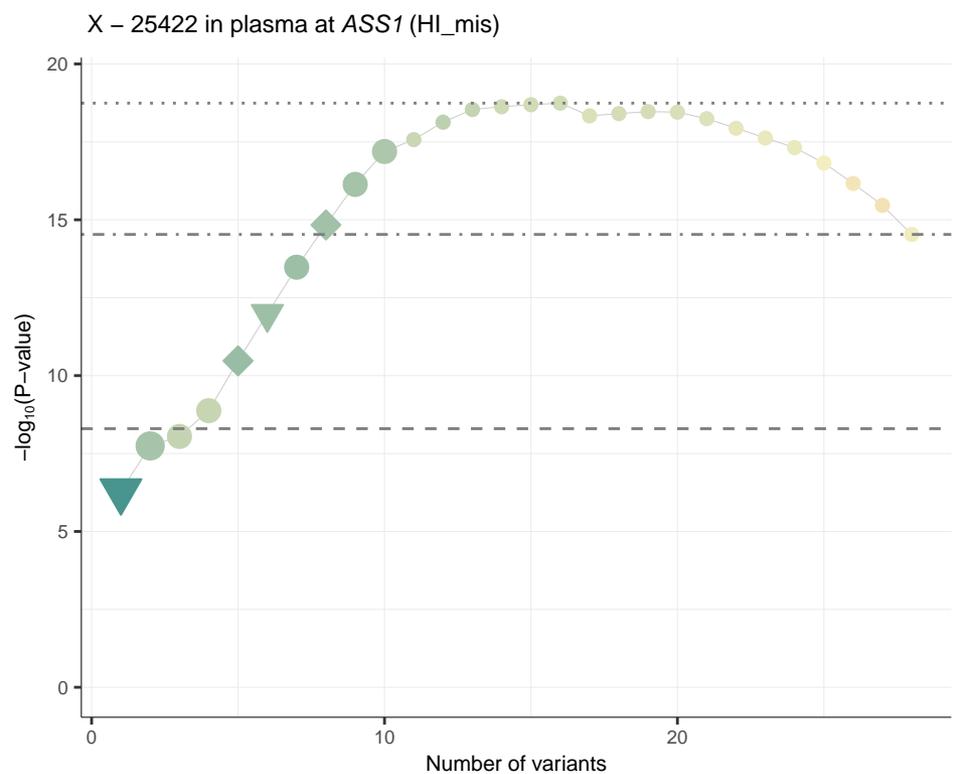
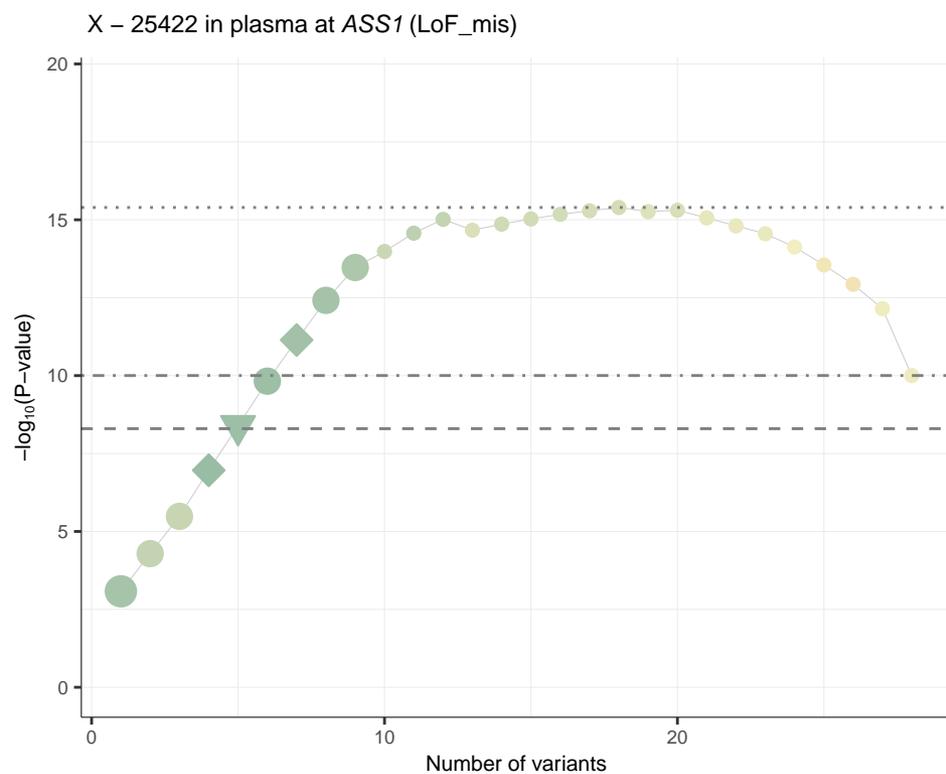


P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

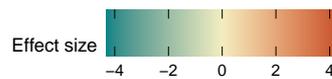
Thresholds

- Significance Threshold
- - - Total P-value
- Lowest P-value



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing



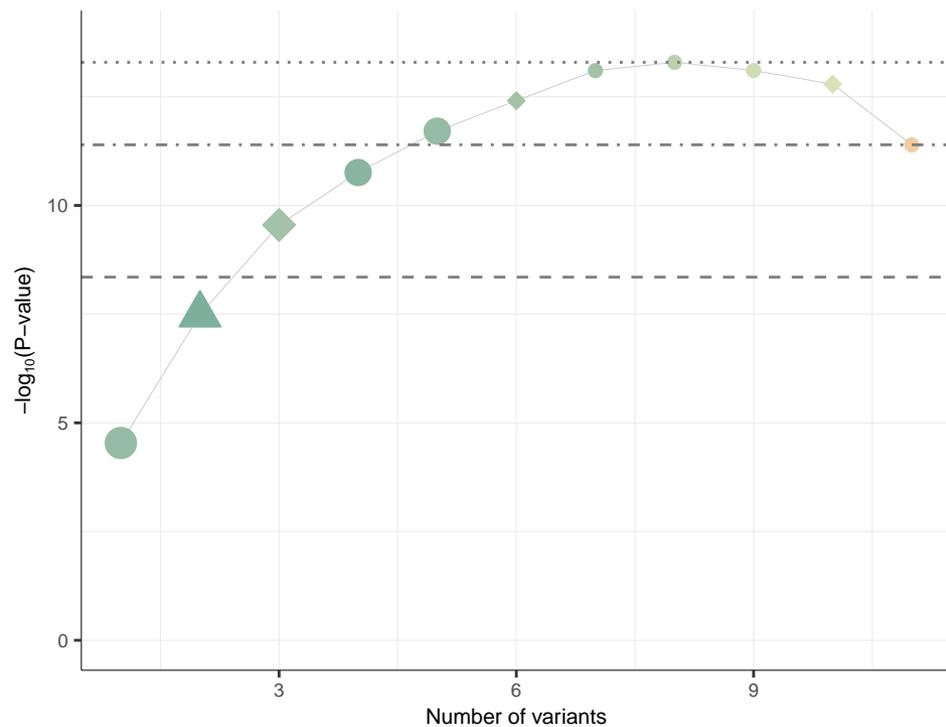
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

Thresholds

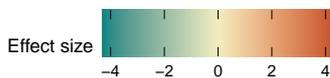
- - Significance Threshold
- - - Total P-value
- ... Lowest P-value

X - 23654 in urine at *BBOX1* (LoF_mis)

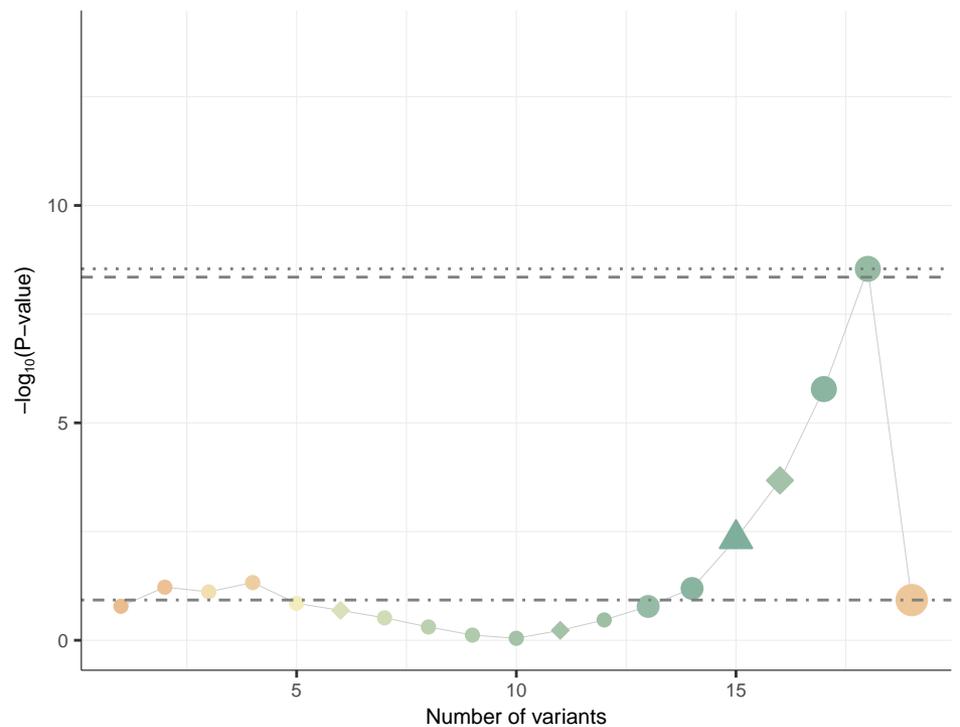


Variant consequence

- ◇ frameshift
- missense
- △ stop gained



X - 23654 in urine at *BBOX1* (HI_mis)



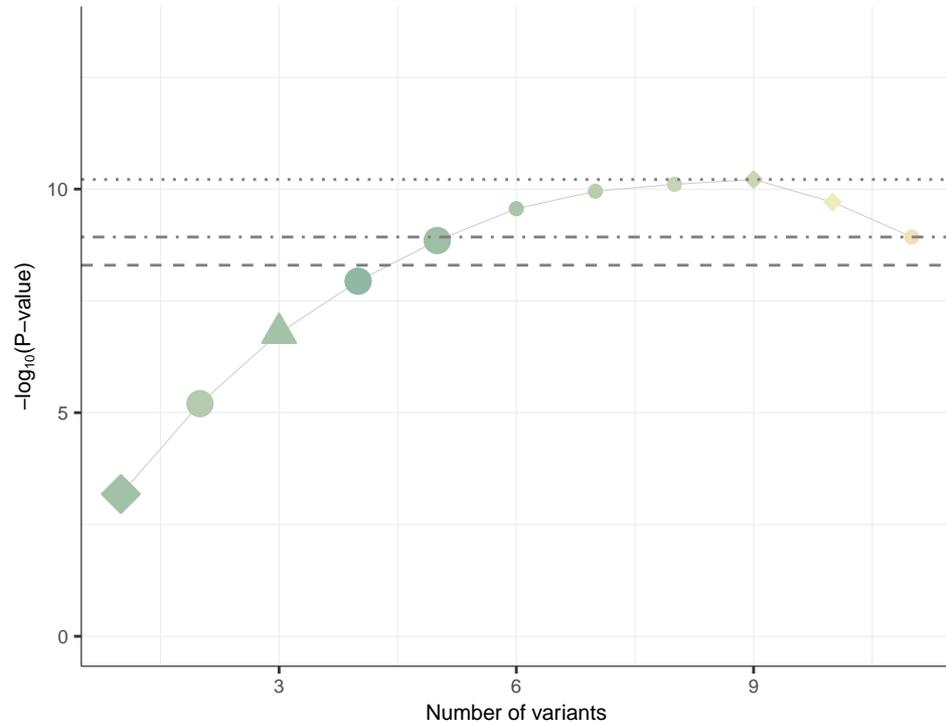
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

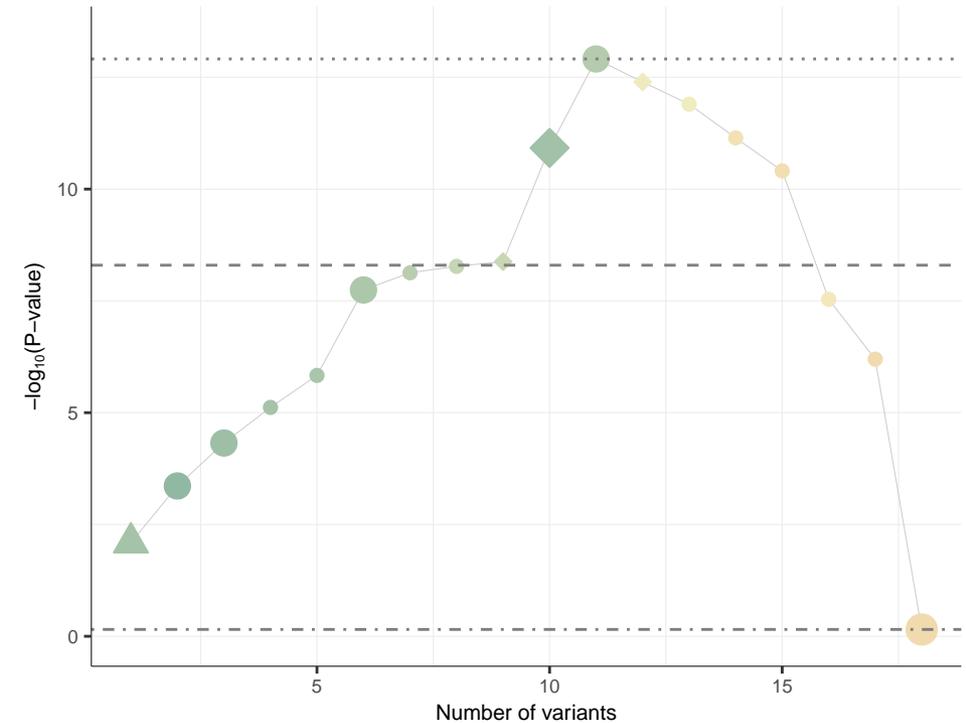
Thresholds

- Significance Threshold
- - - Total P-value
- Lowest P-value

X - 24801 in plasma at *BBOX1* (LoF_mis)

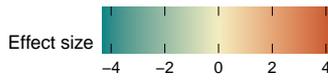


X - 24801 in plasma at *BBOX1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



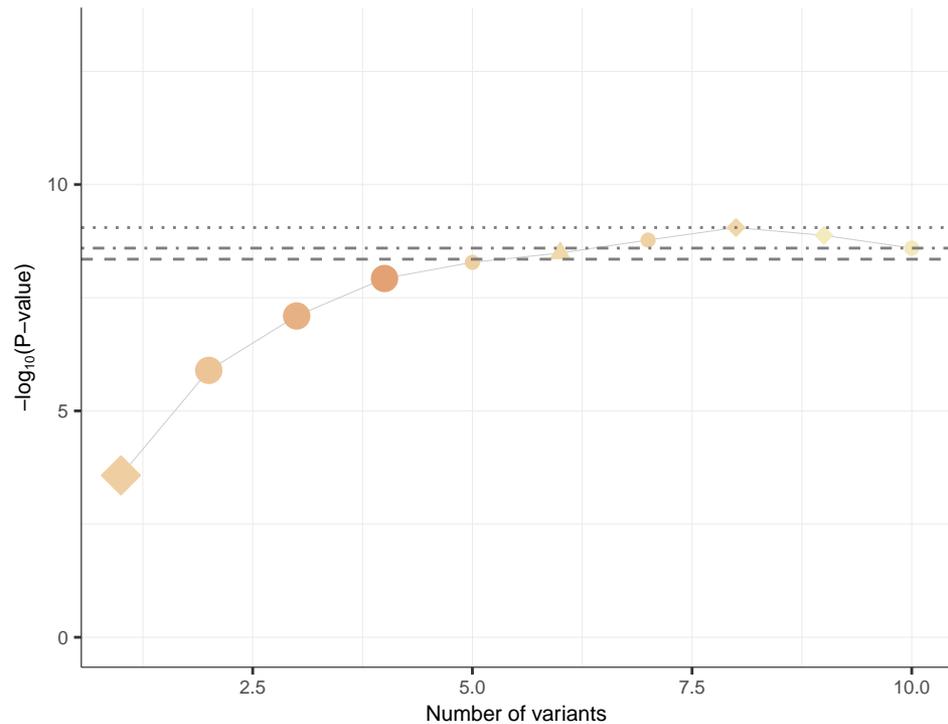
P-value

- >0.05
- <0.05
- <1e-3

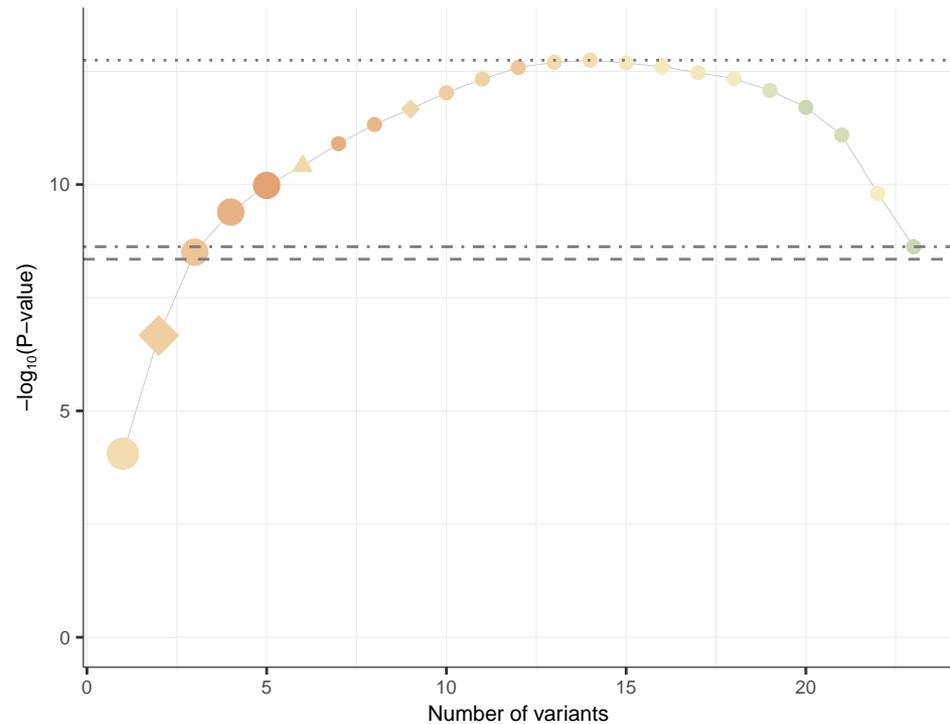
Thresholds

- — Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

carnosine in urine at *CNDP1* (LoF_mis)



carnosine in urine at *CNDP1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



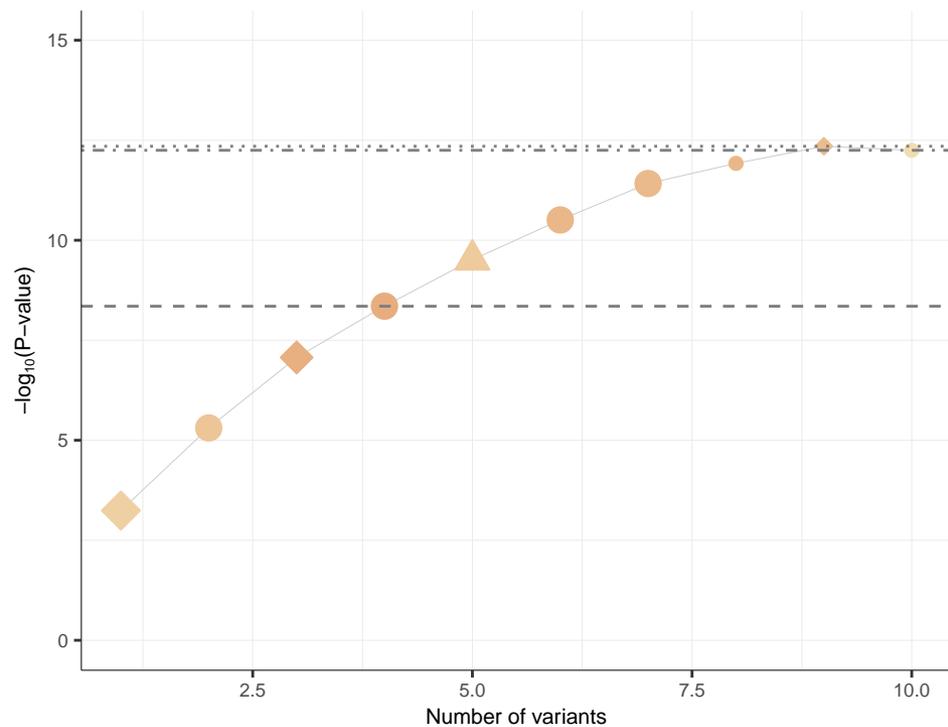
P-value

- >0.05
- <0.05
- <1e-3

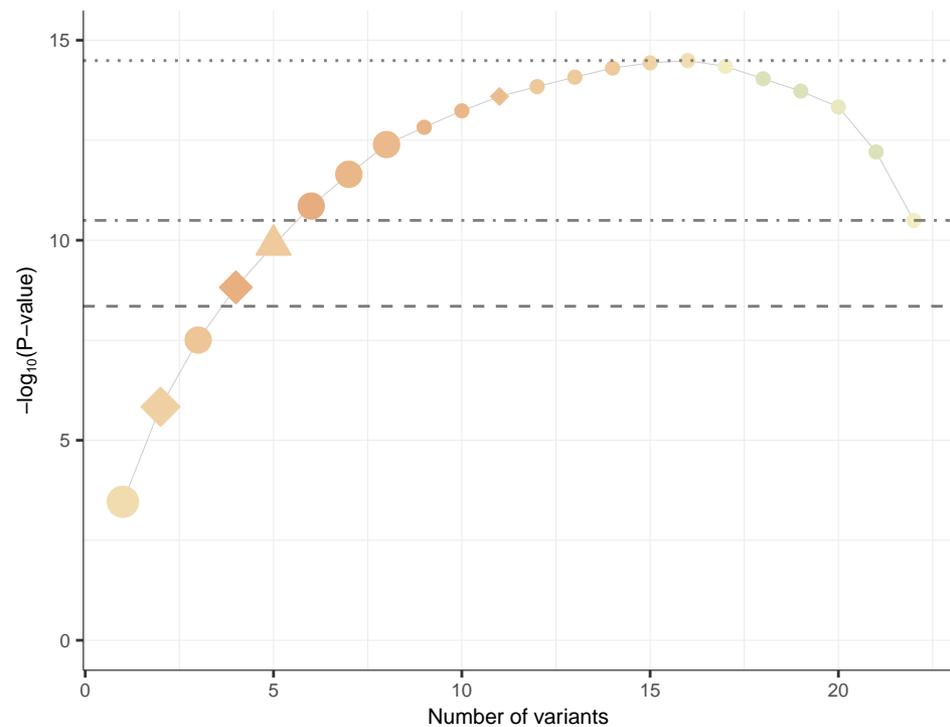
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

homocarnosine in urine at *CNDP1* (LoF_mis)



homocarnosine in urine at *CNDP1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



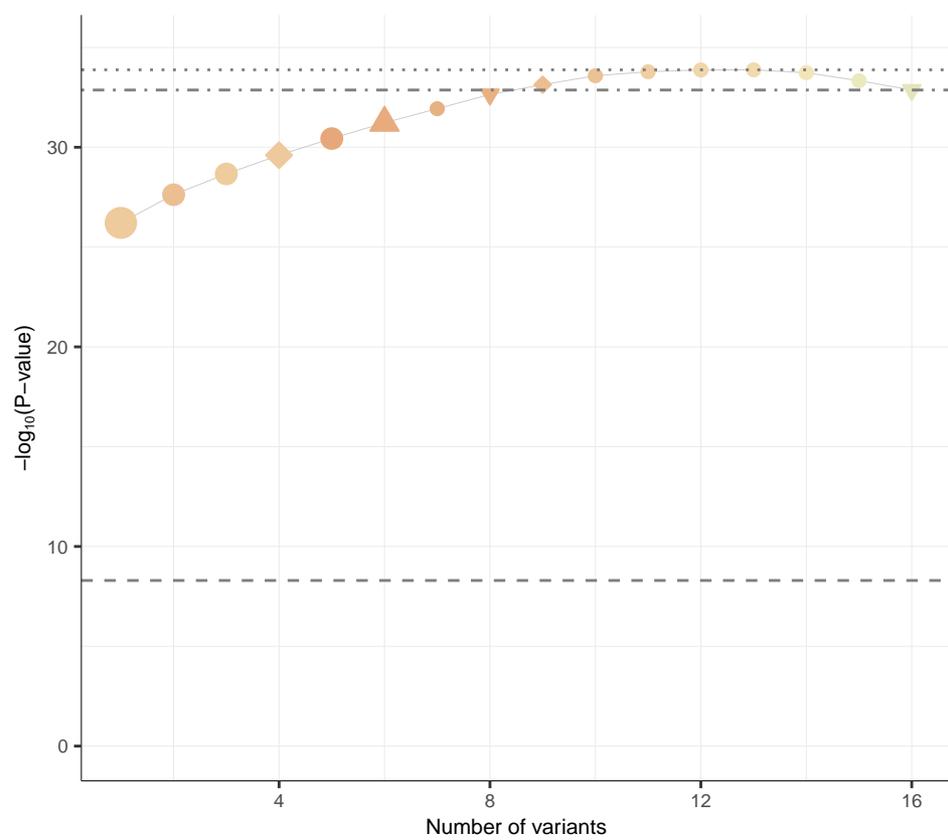
P-value

- >0.05
- <0.05
- <1e-3

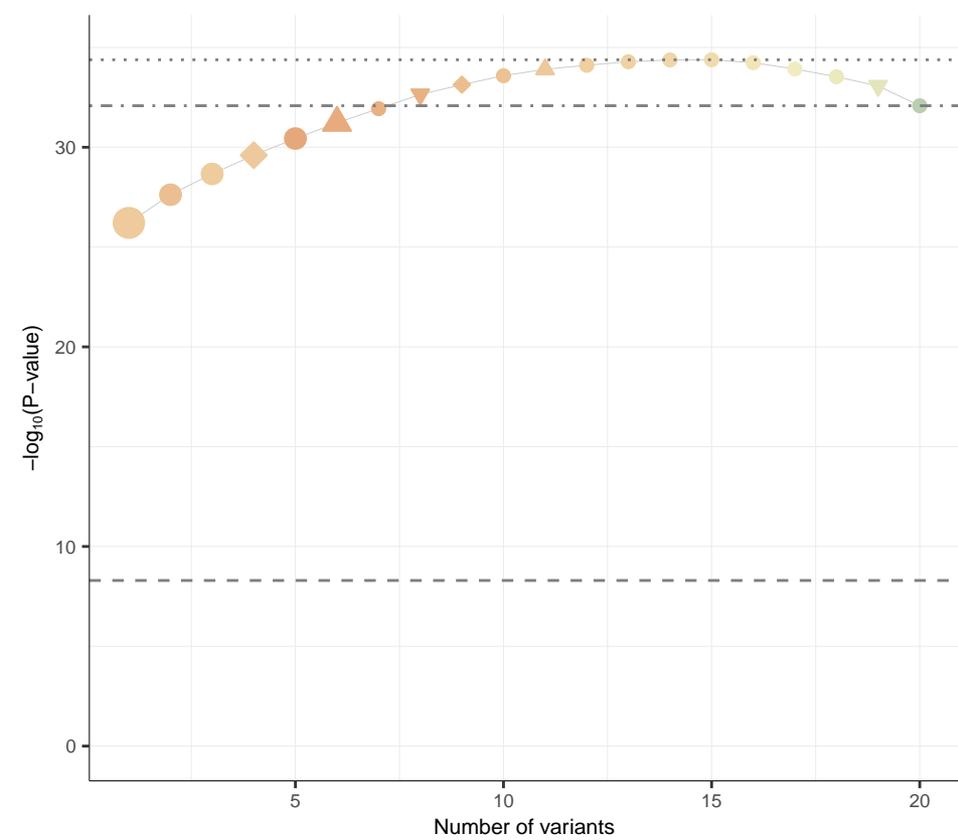
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

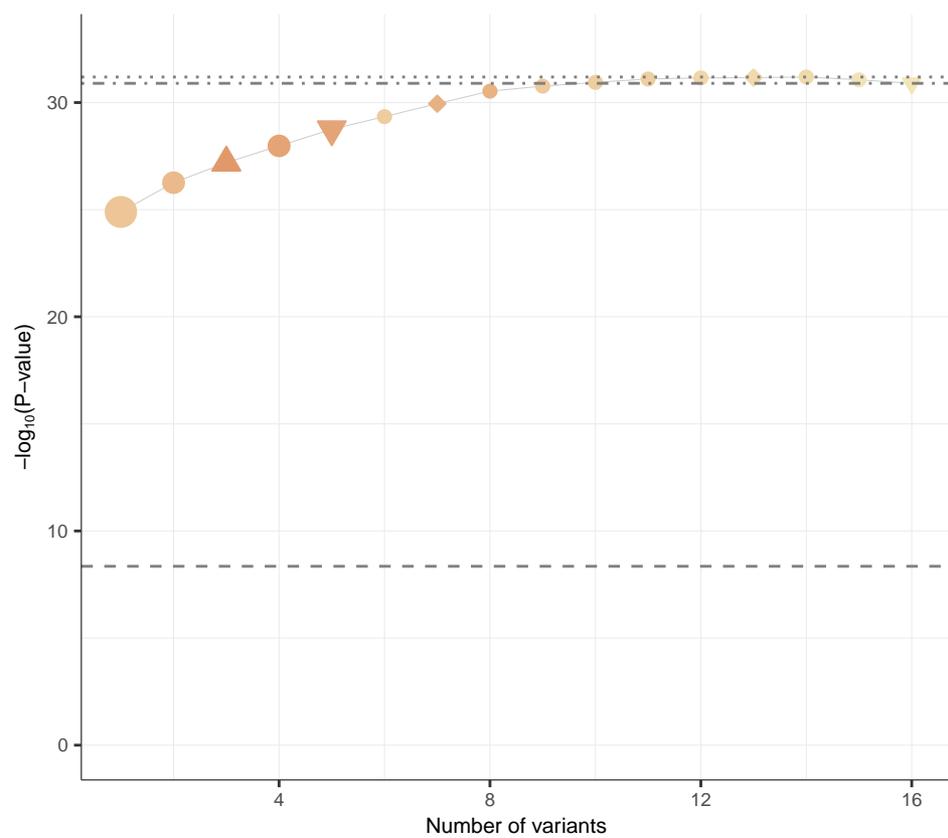
cystathionine in plasma at *CTH* (LoF_mis)



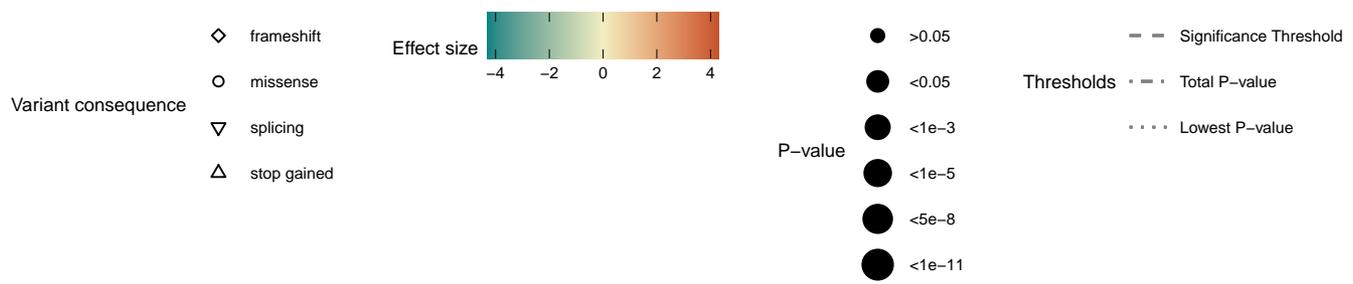
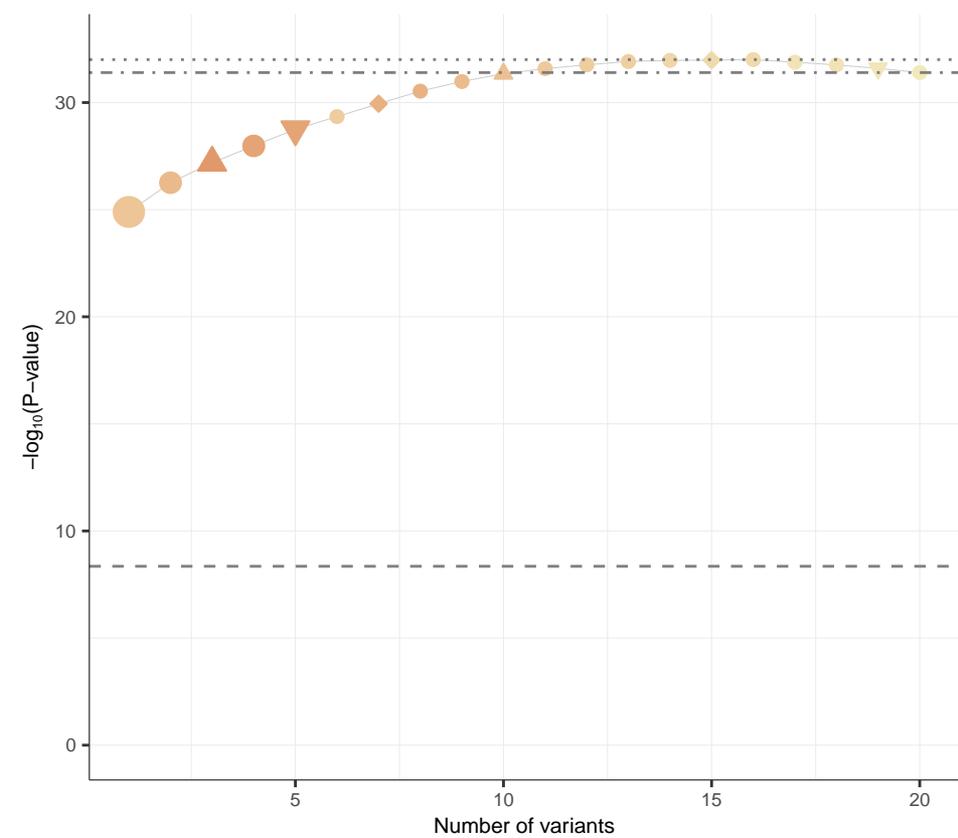
cystathionine in plasma at *CTH* (HI_mis)



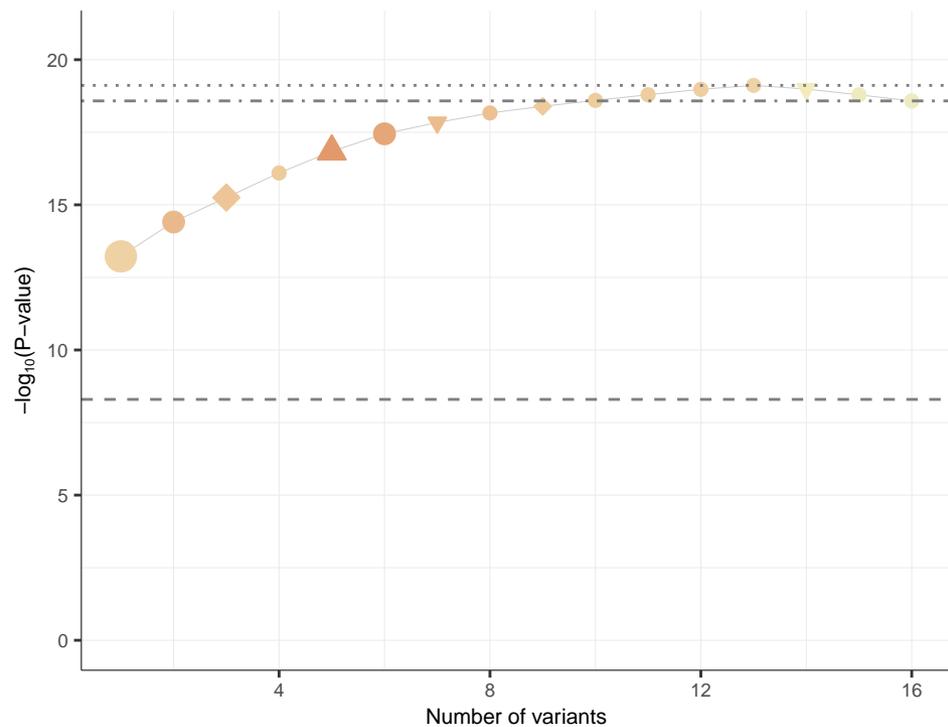
cystathionine in urine at *CTH* (LoF_mis)



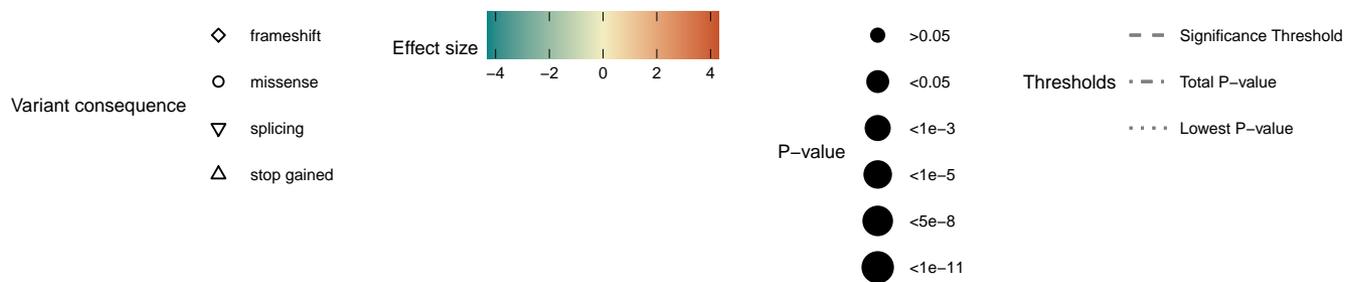
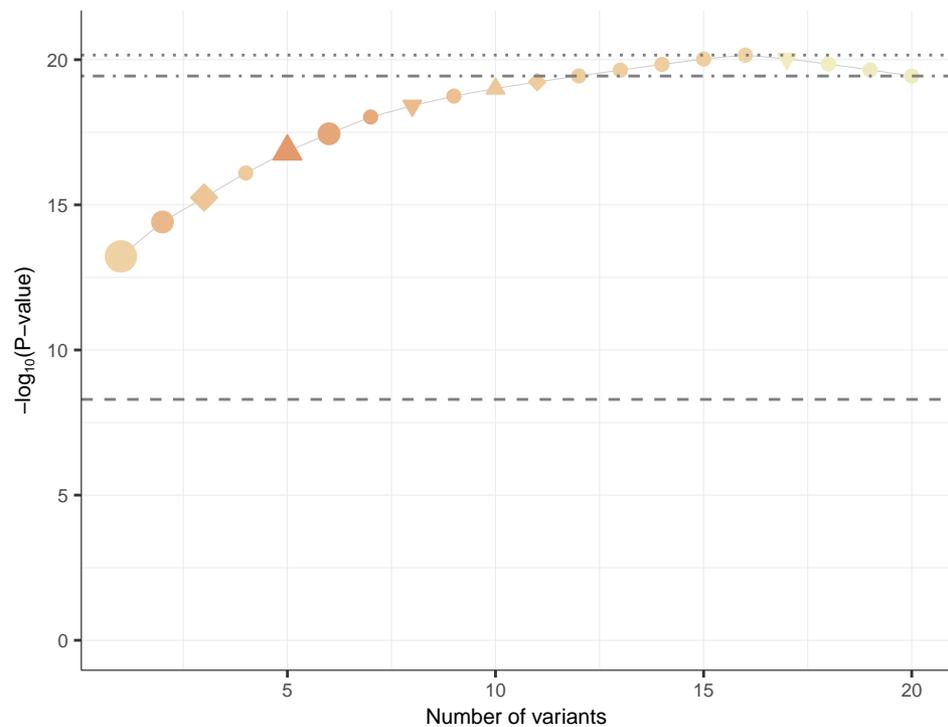
cystathionine in urine at *CTH* (HI_mis)



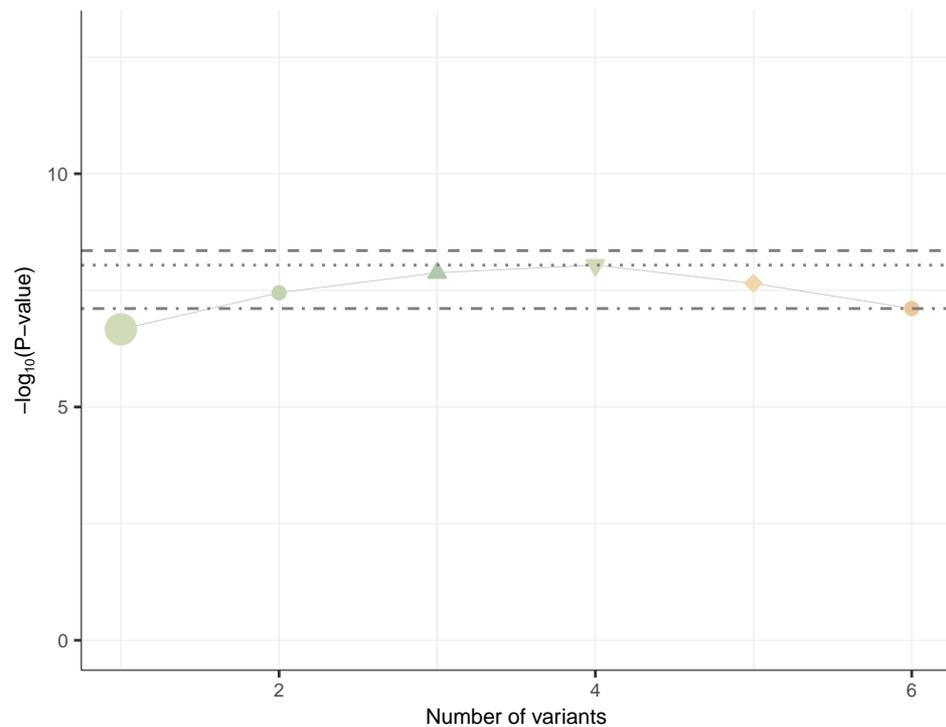
X - 11795 in plasma at *CTH* (LoF_mis)



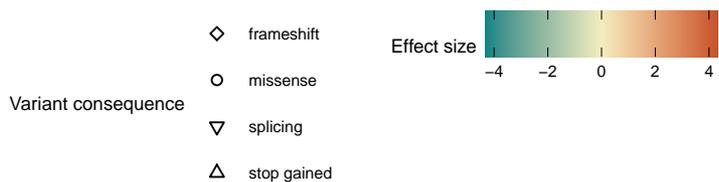
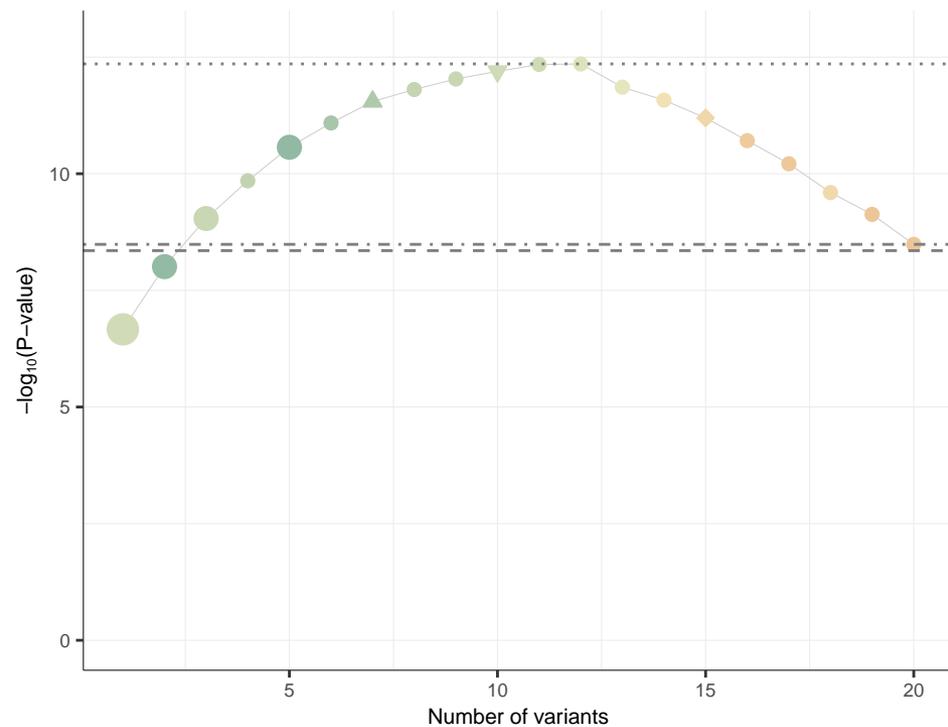
X - 11795 in plasma at *CTH* (HI_mis)

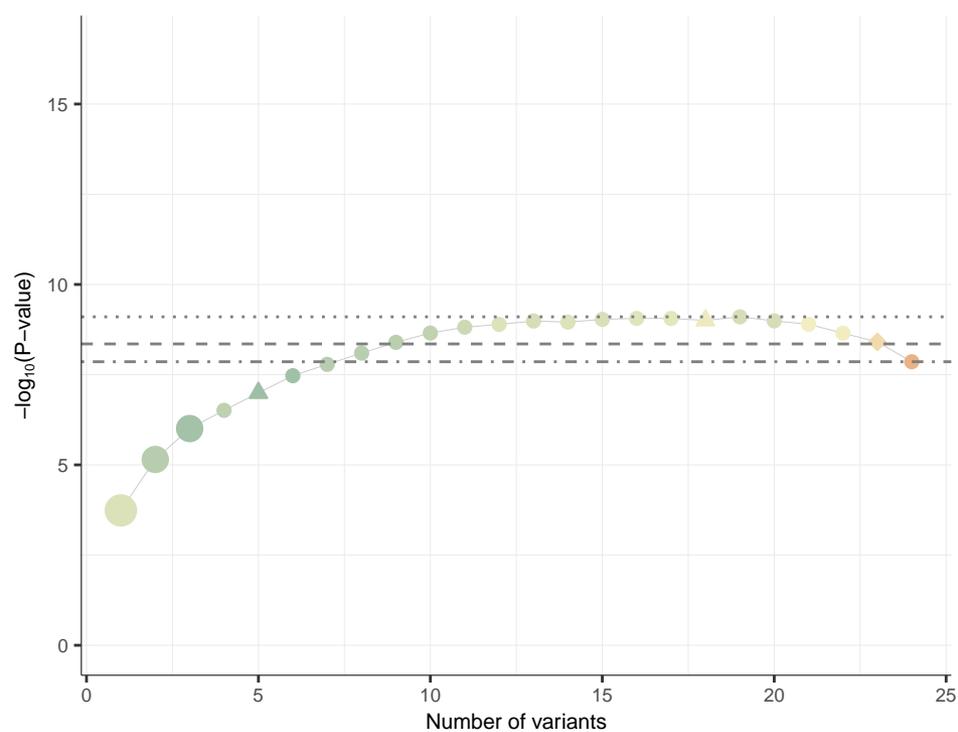
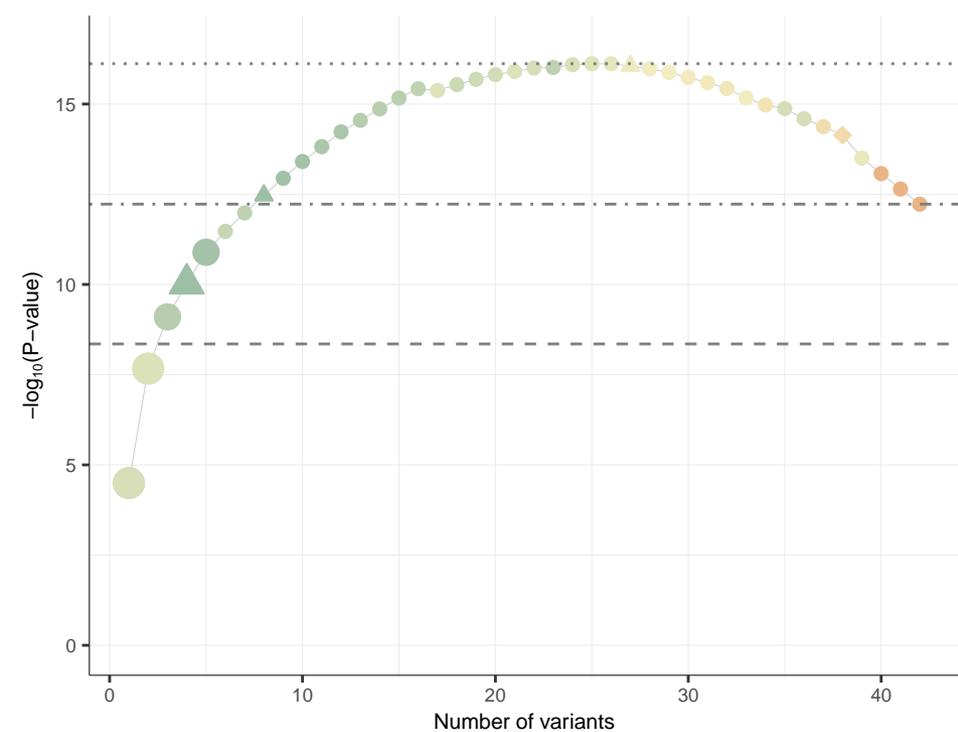


X - 24339 in urine at *DECR2* (LoF_mis)



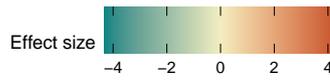
X - 24339 in urine at *DECR2* (HI_mis)



4-ureidobutyrate in urine at *DHTKD1* (LoF_mis)4-ureidobutyrate in urine at *DHTKD1* (HI_mis)

Variant consequence

- ◇ frameshift
- missense
- △ stop gained



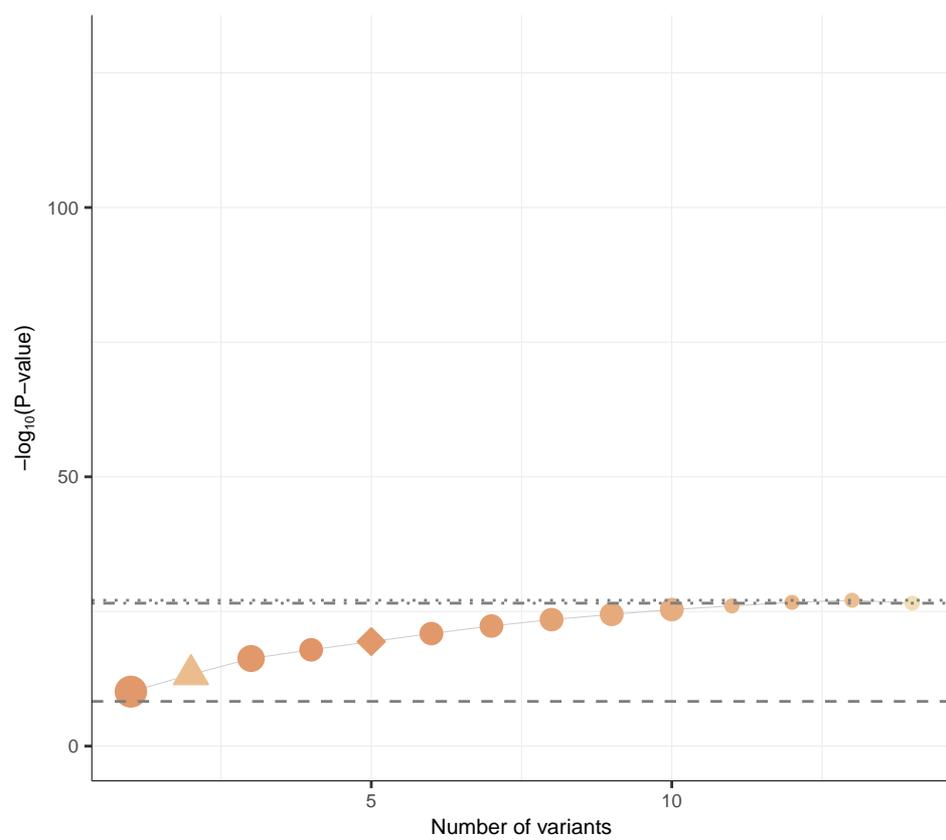
P-value

- >0.05
- <0.05
- <1e-3

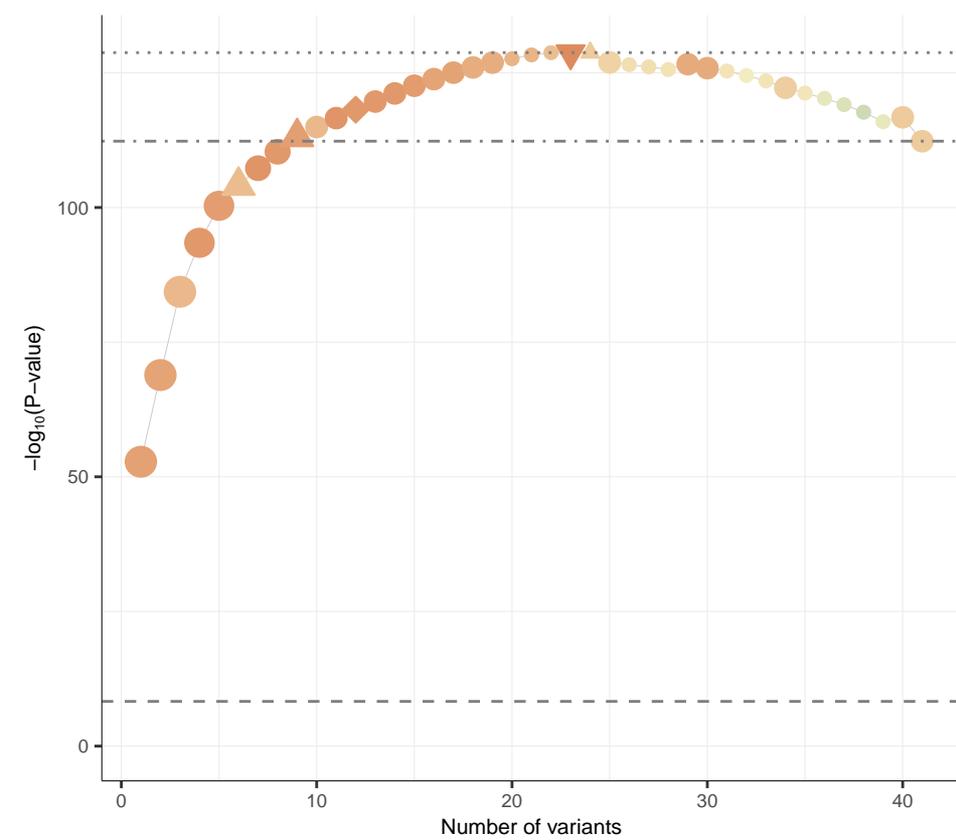
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

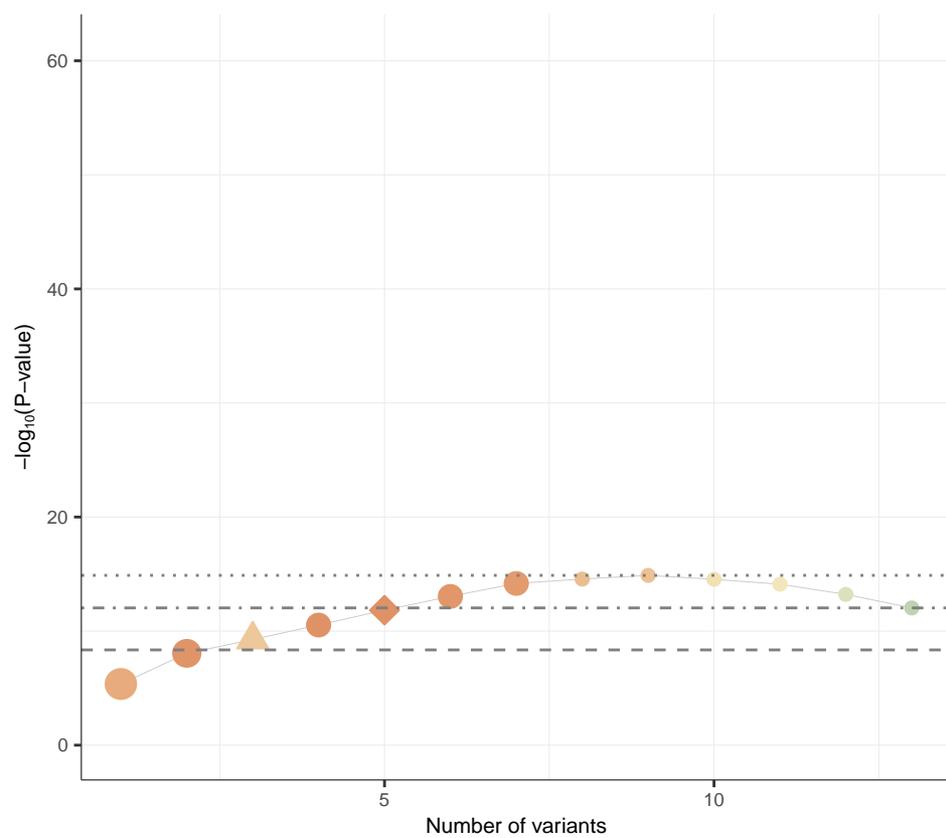
dimethylglycine in plasma at *DMGDH* (LoF_mis)



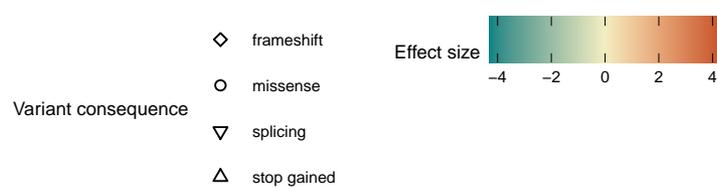
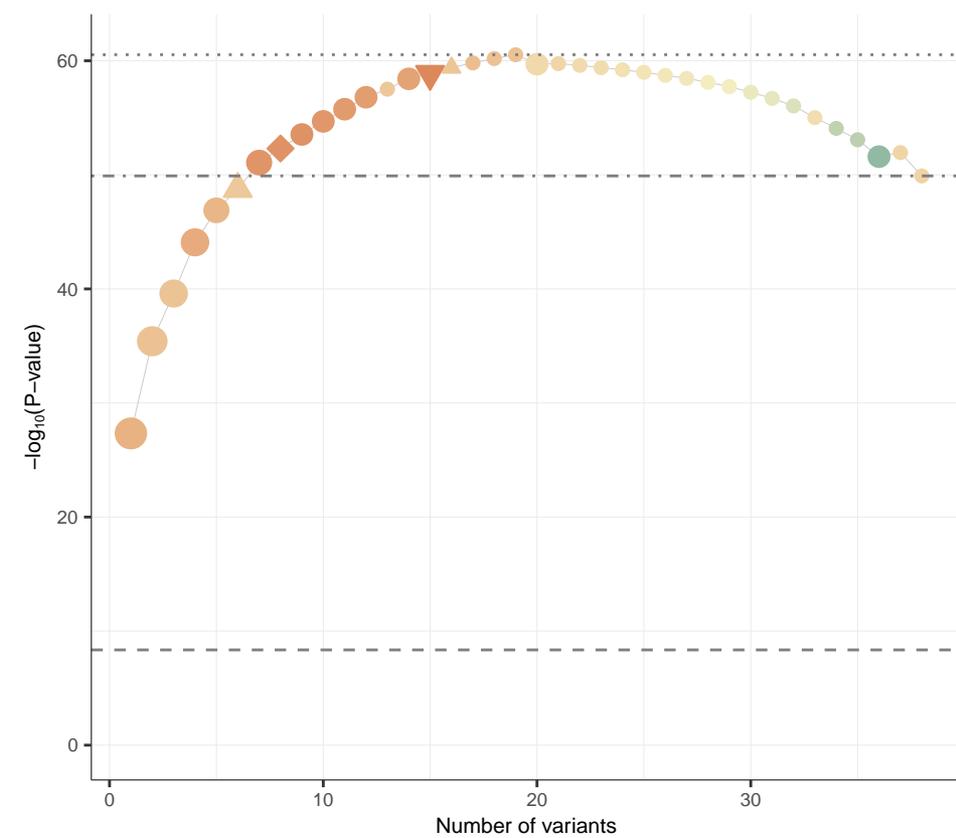
dimethylglycine in plasma at *DMGDH* (HI_mis)



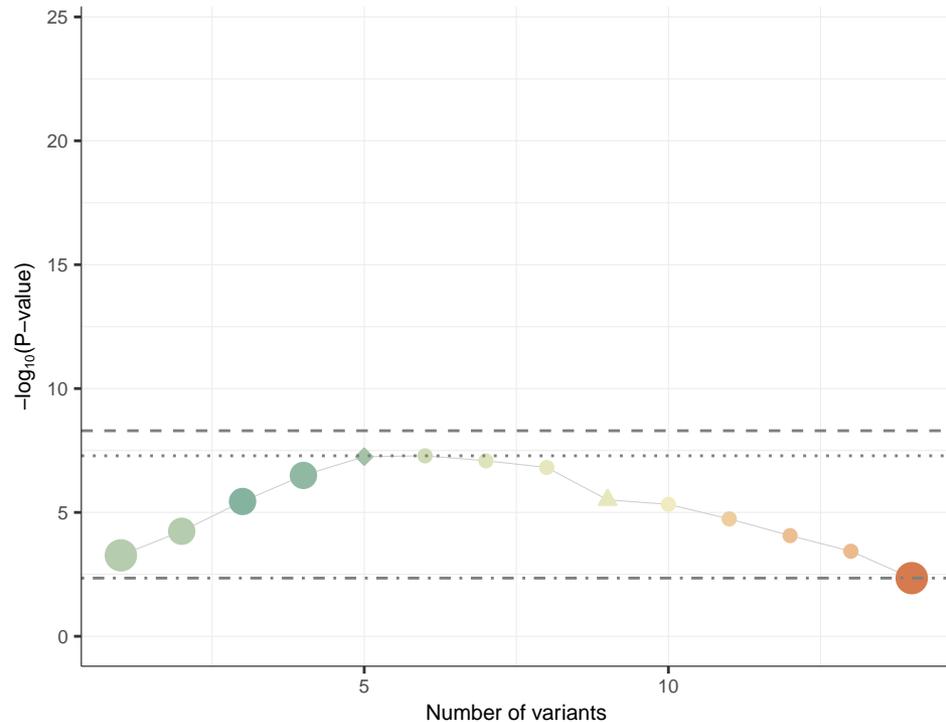
dimethylglycine in urine at *DMGDH* (LoF_mis)



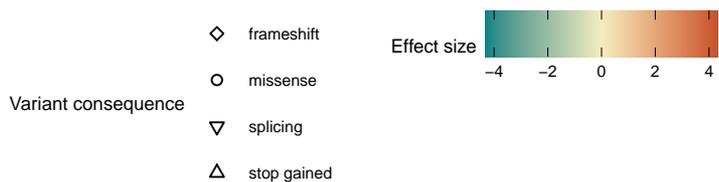
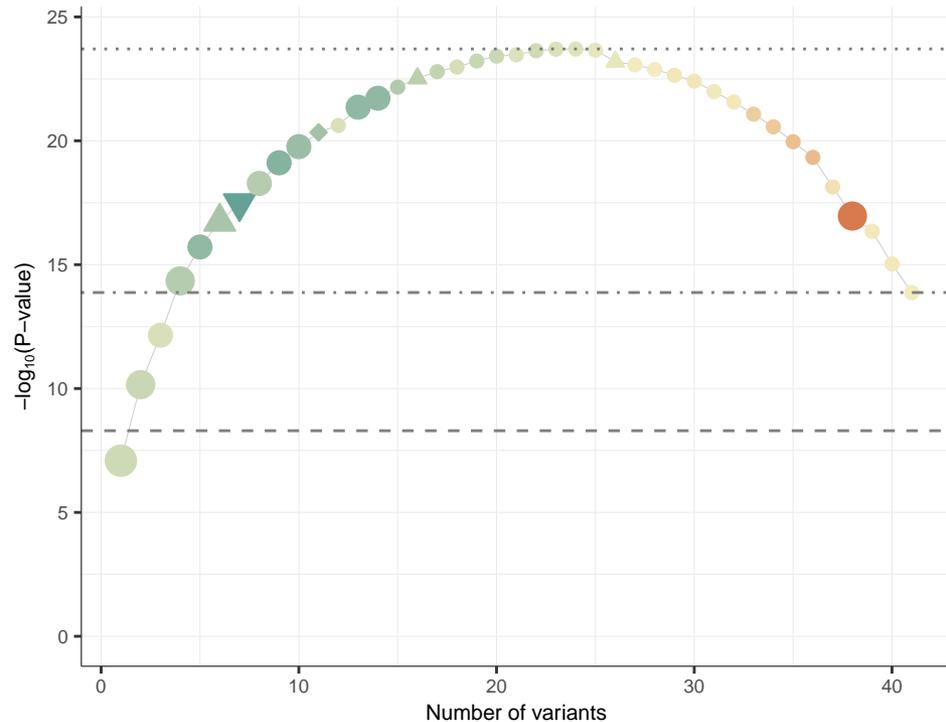
dimethylglycine in urine at *DMGDH* (HI_mis)



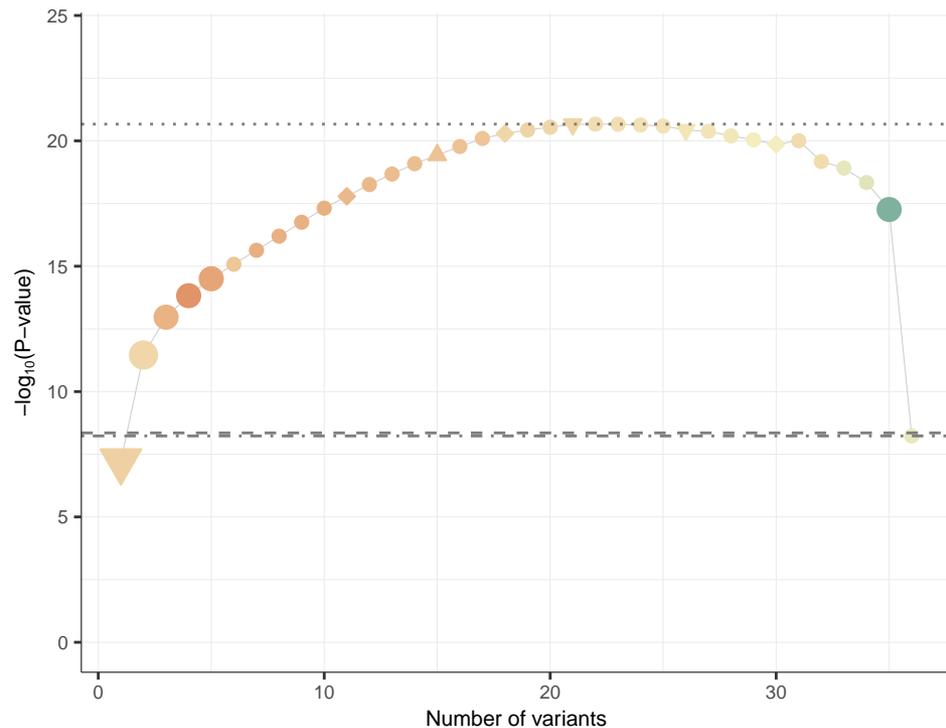
X - 23636 in plasma at *DMGDH* (LoF_mis)



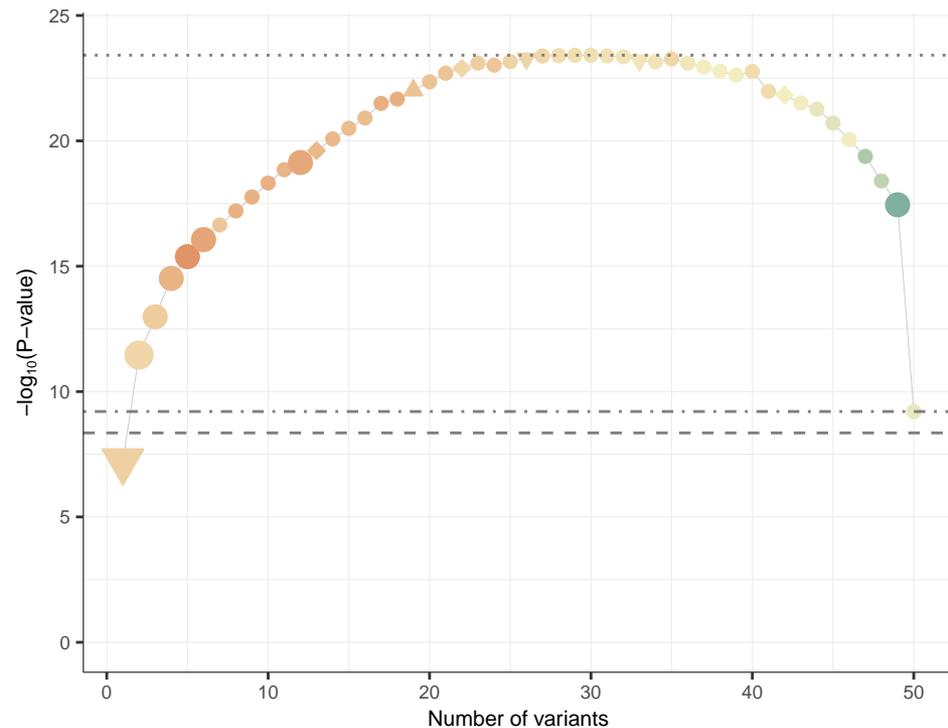
X - 23636 in plasma at *DMGDH* (HI_mis)



thymine in urine at *DPYD* (LoF_mis)

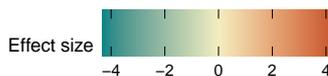


thymine in urine at *DPYD* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



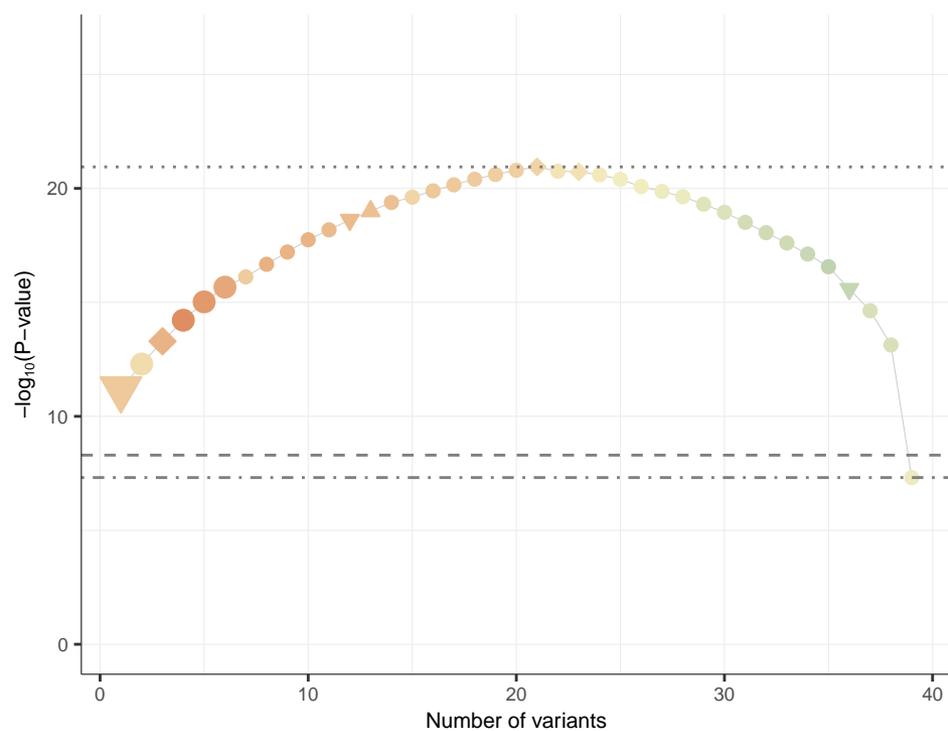
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

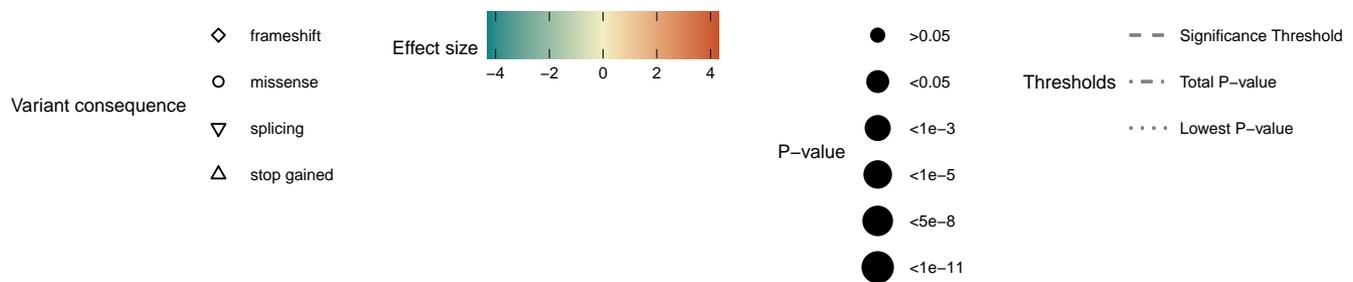
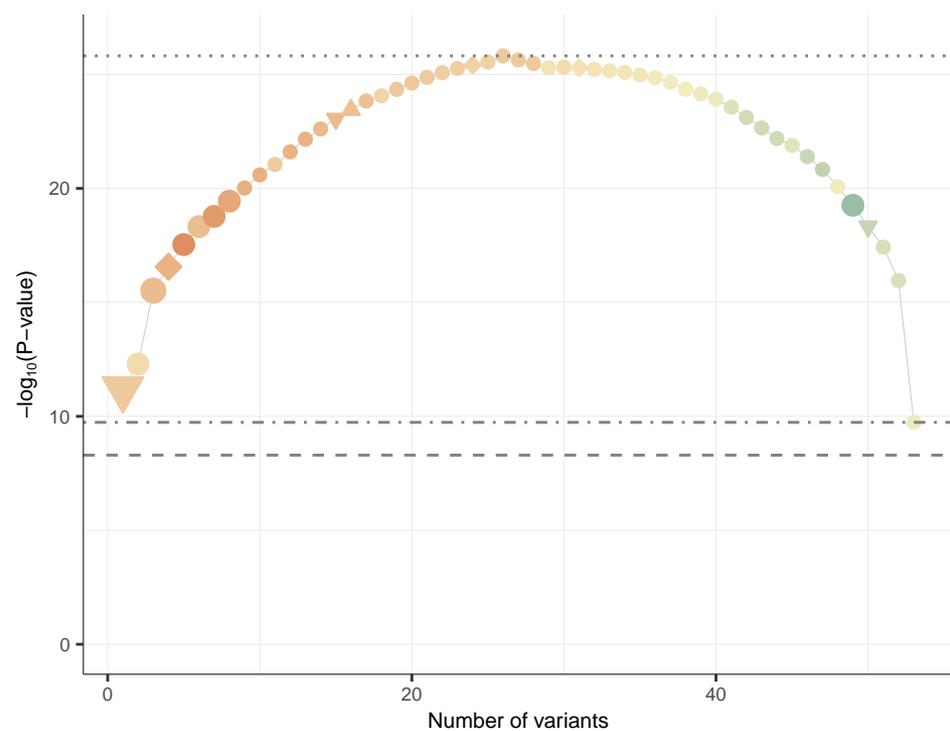
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

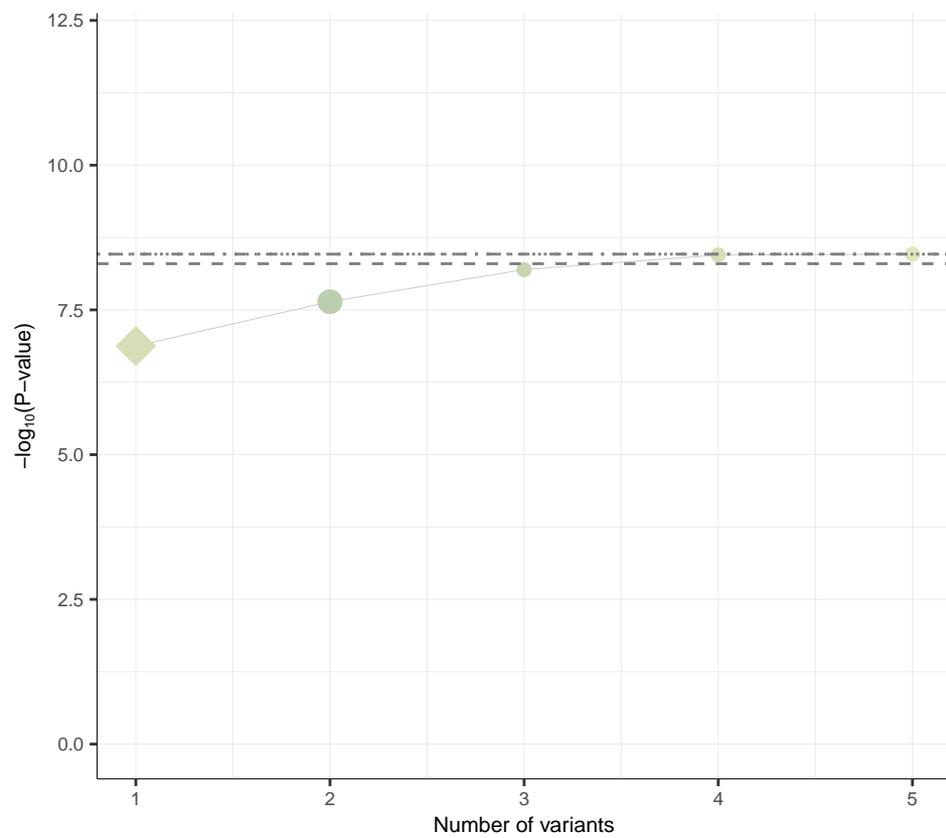
uracil in plasma at *DPYD* (LoF_mis)



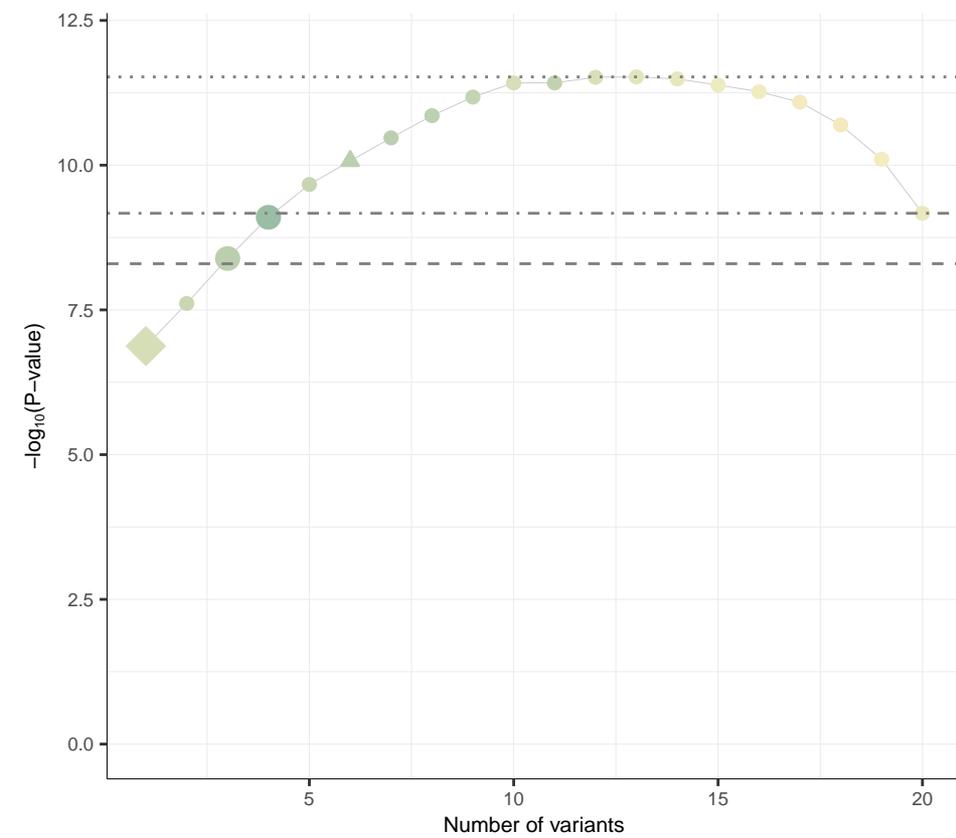
uracil in plasma at *DPYD* (HI_mis)



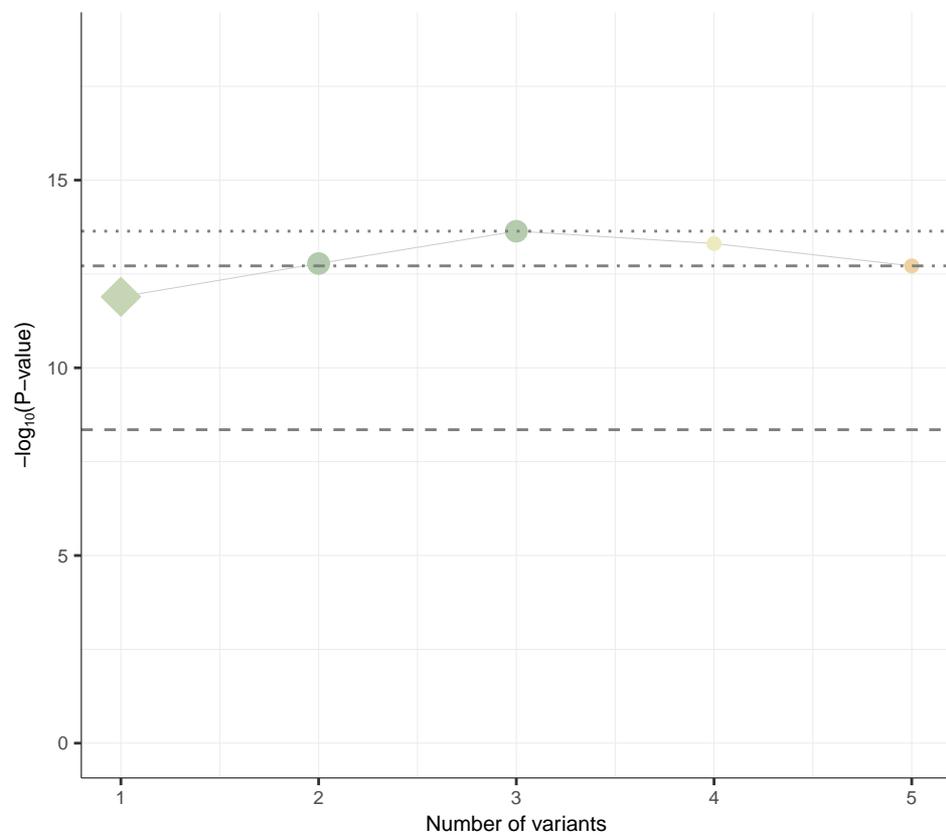
3-methylglutaconate in plasma at *ECHDC2* (LoF_mis)



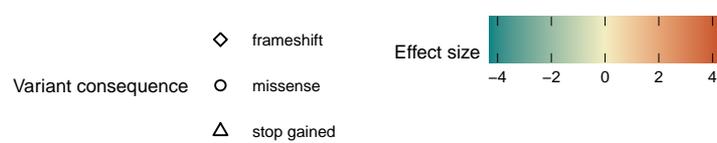
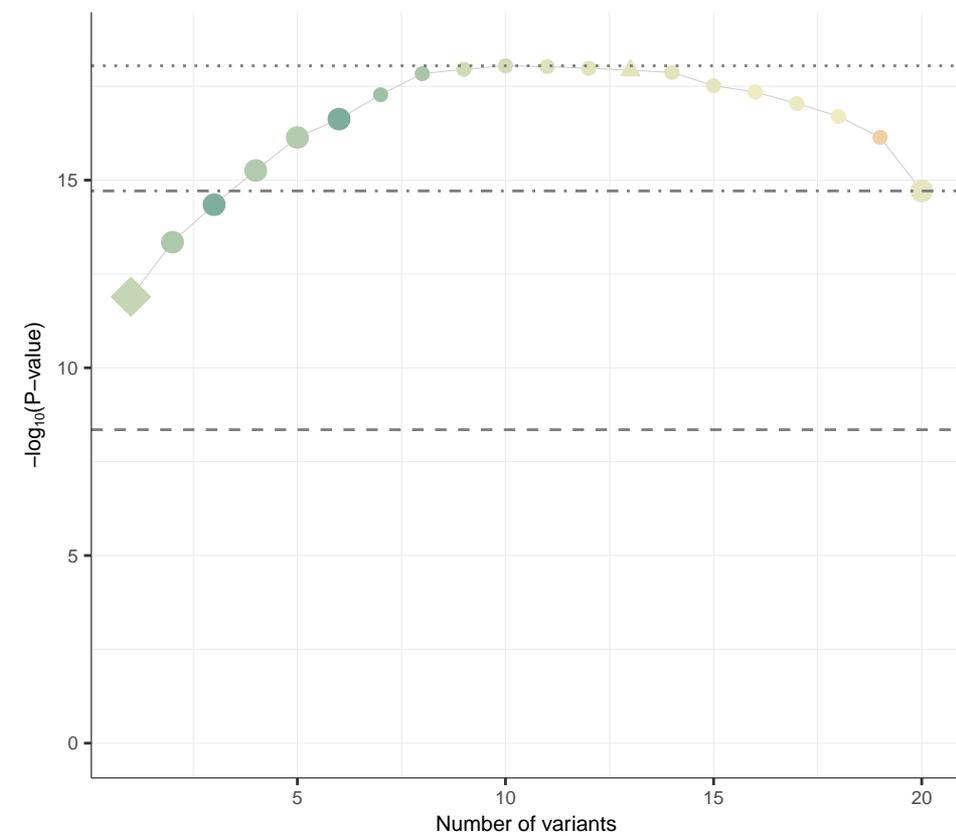
3-methylglutaconate in plasma at *ECHDC2* (HI_mis)



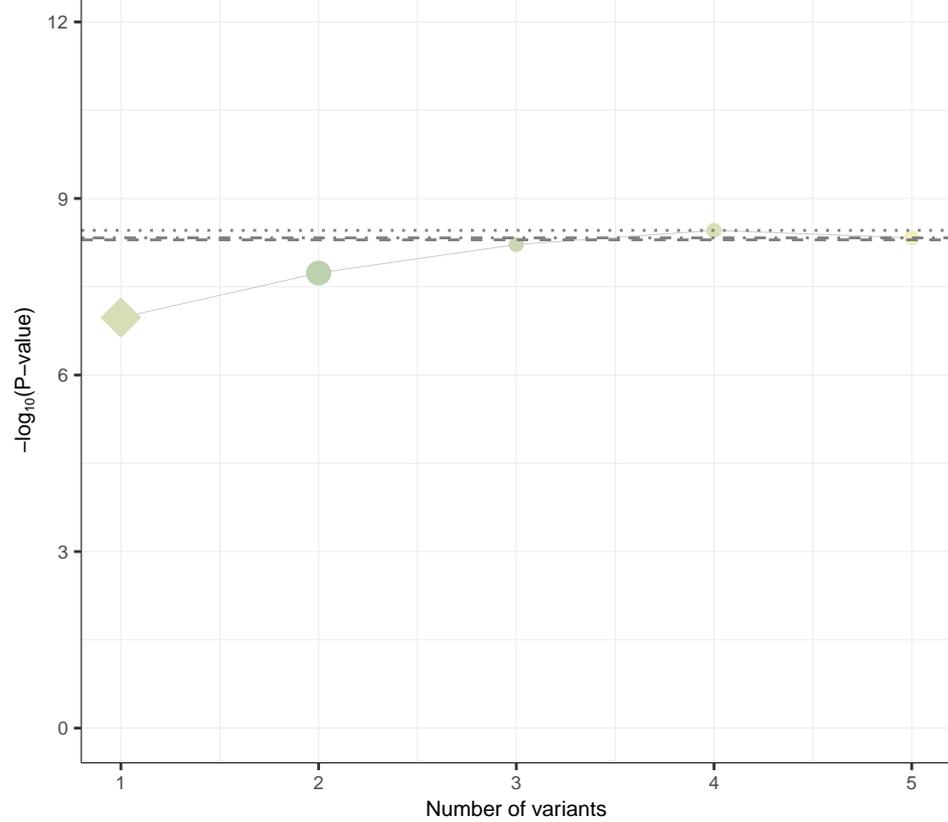
3-methylglutaconate in urine at *ECHDC2* (LoF_mis)



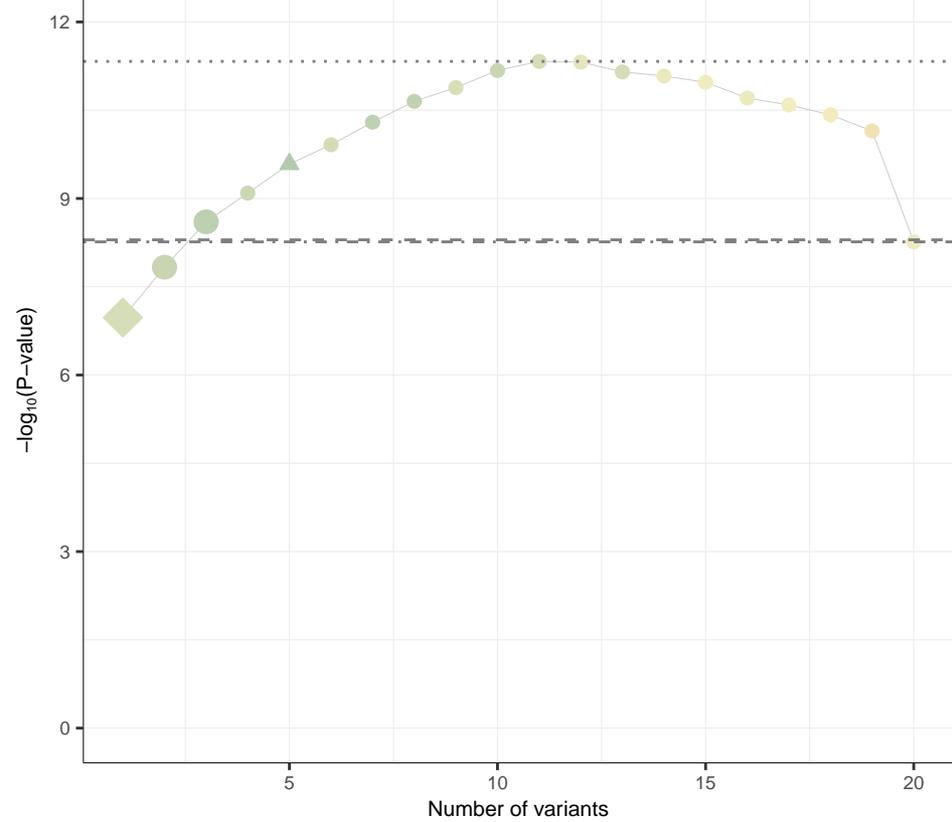
3-methylglutaconate in urine at *ECHDC2* (HI_mis)



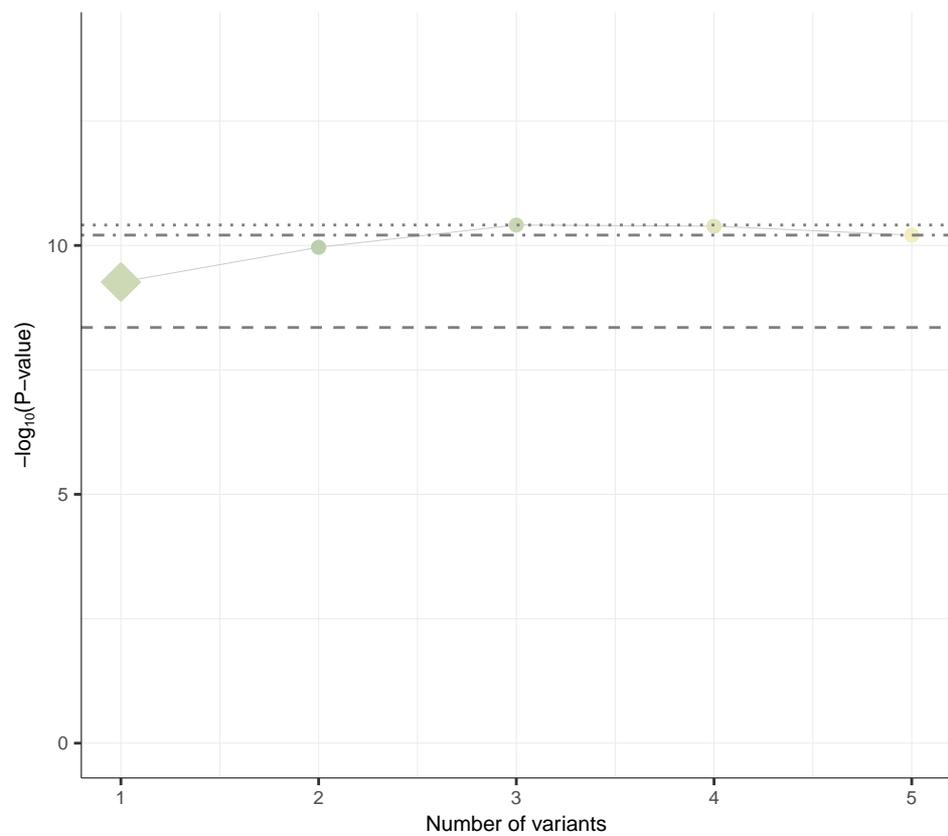
3-methylglutaryl carnitine (2) in plasma at *ECHDC2* (LoF_mis)



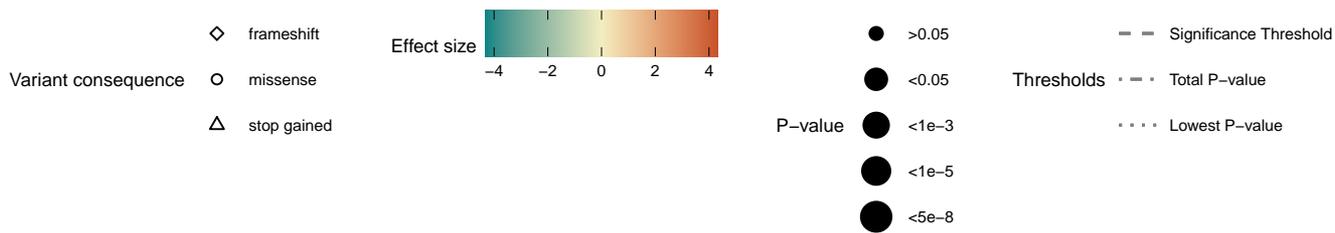
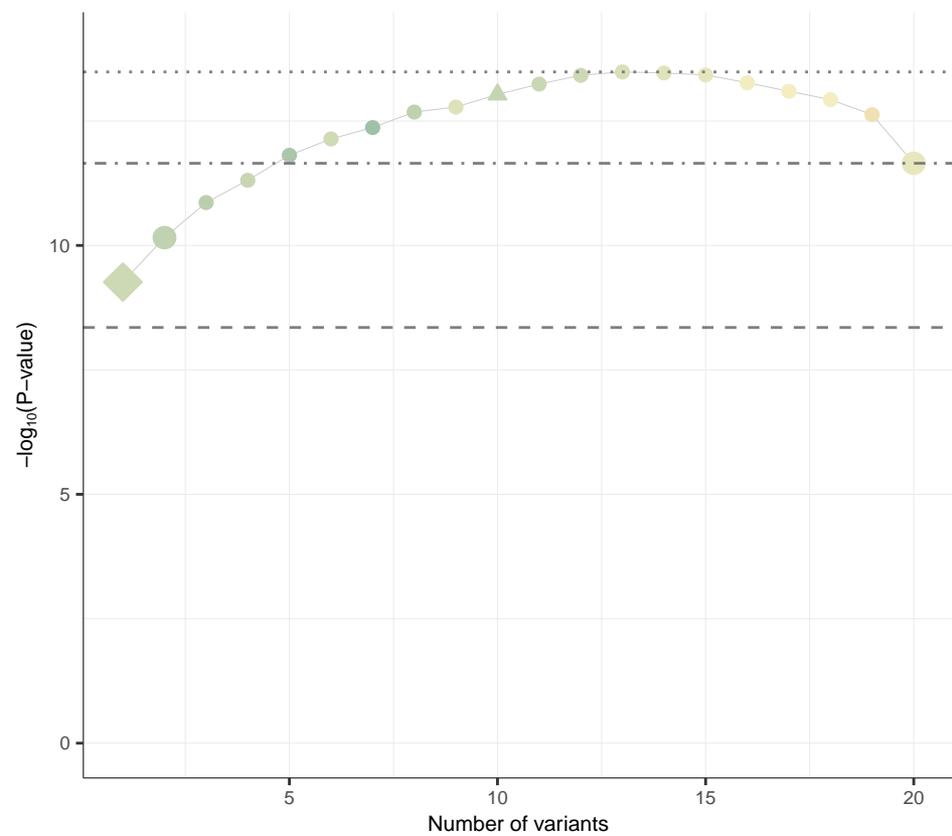
3-methylglutaryl carnitine (2) in plasma at *ECHDC2* (HI_mis)



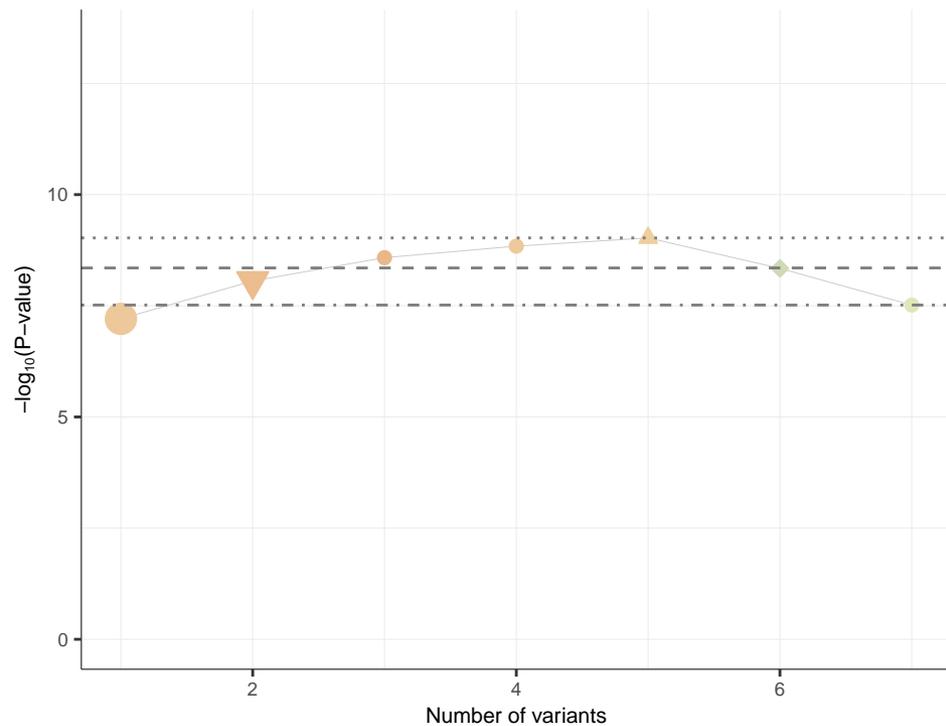
3-methylglutaryl carnitine (2) in urine at *ECHDC2* (LoF_mis)



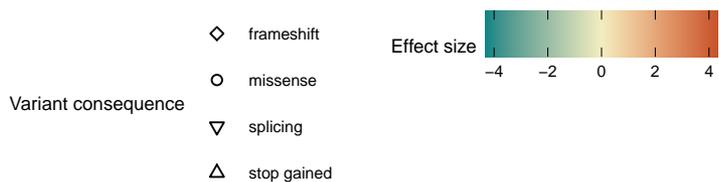
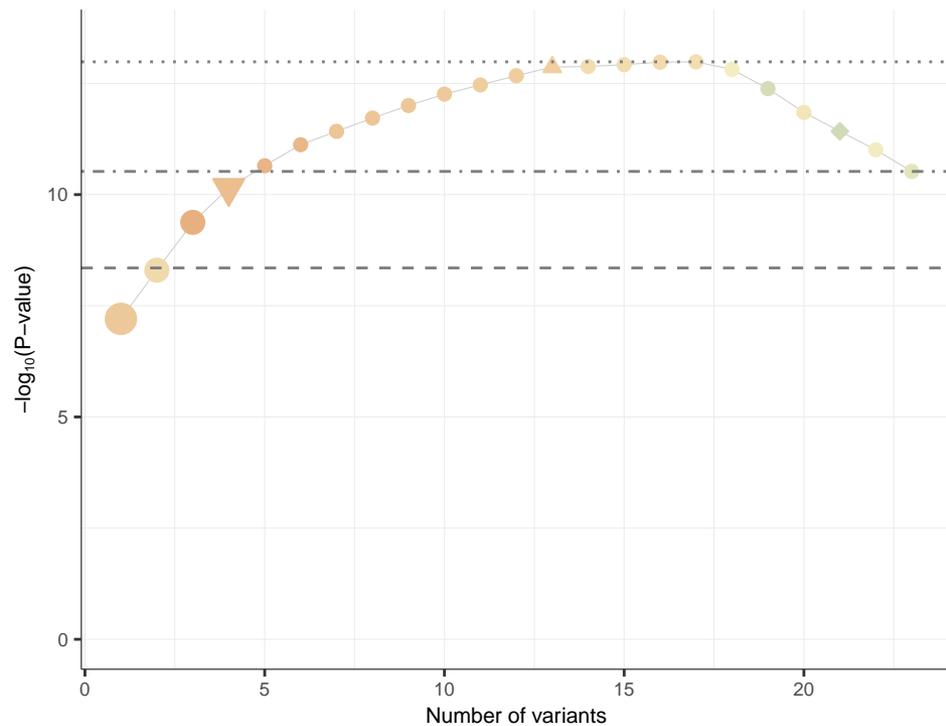
3-methylglutaryl carnitine (2) in urine at *ECHDC2* (HI_mis)



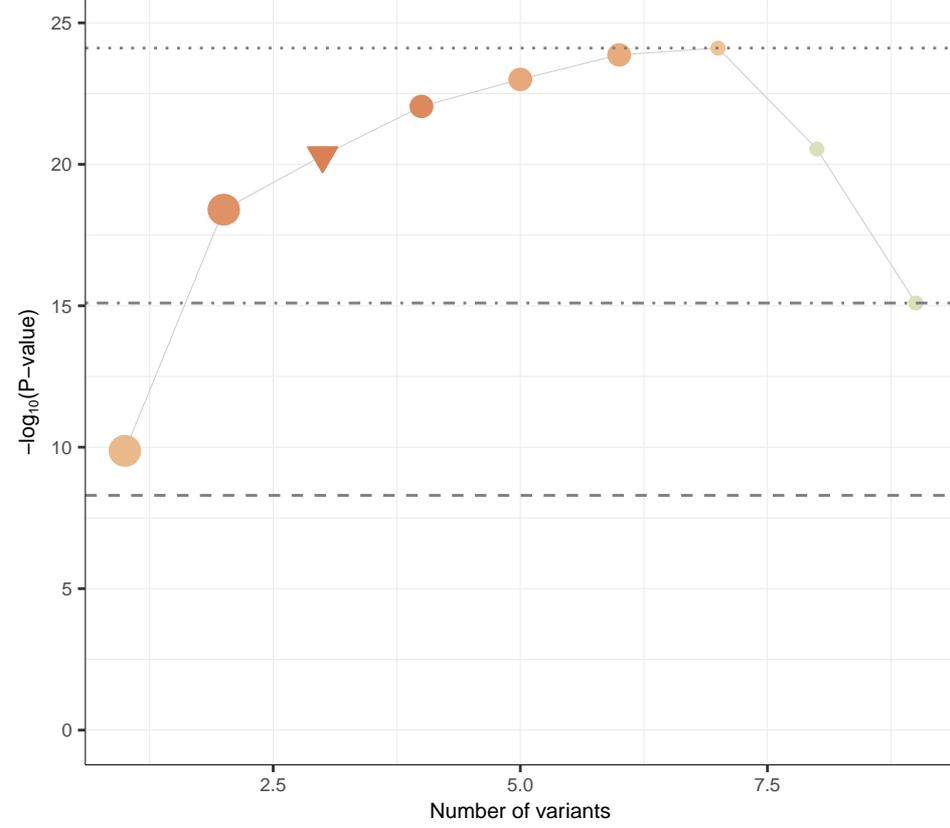
ribonate in urine at *ENOSF1* (LoF_mis)



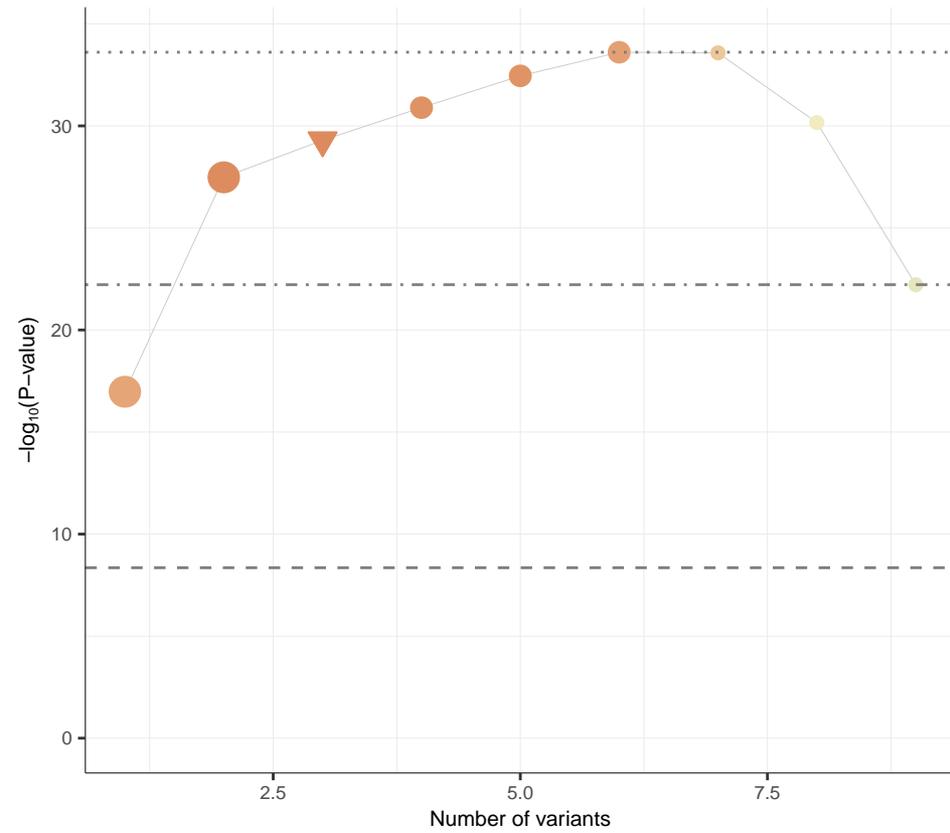
ribonate in urine at *ENOSF1* (HI_mis)



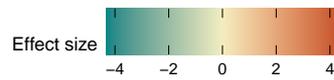
N-acetyl-aspartyl-glutamate (NAAG) in plasma at *FOLH1* (HI_mis)



N-acetyl-aspartyl-glutamate (NAAG) in urine at *FOLH1* (HI_mis)



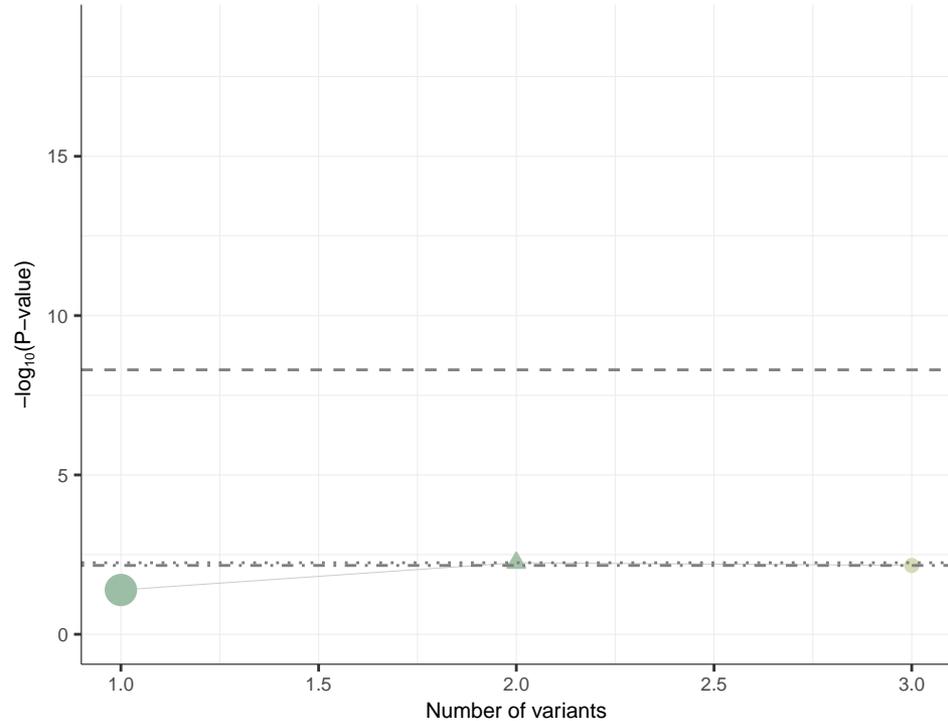
Variant consequence
 ○ missense
 ▽ splicing



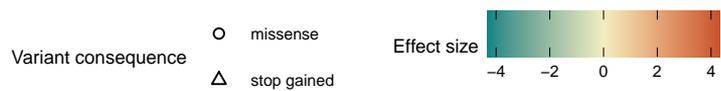
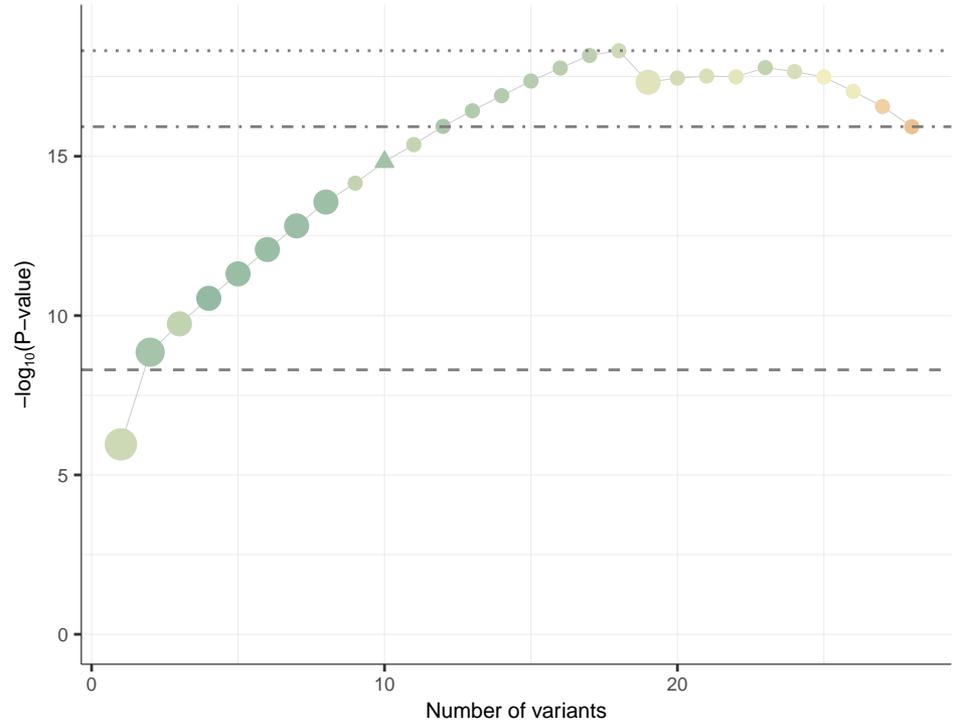
P-value
 ● >0.05
 ● <0.05
 ● <1e-3
 ● <1e-5
 ● <5e-8
 ● <1e-11

Thresholds
 - - Significance Threshold
 - · - Total P-value
 · · · Lowest P-value

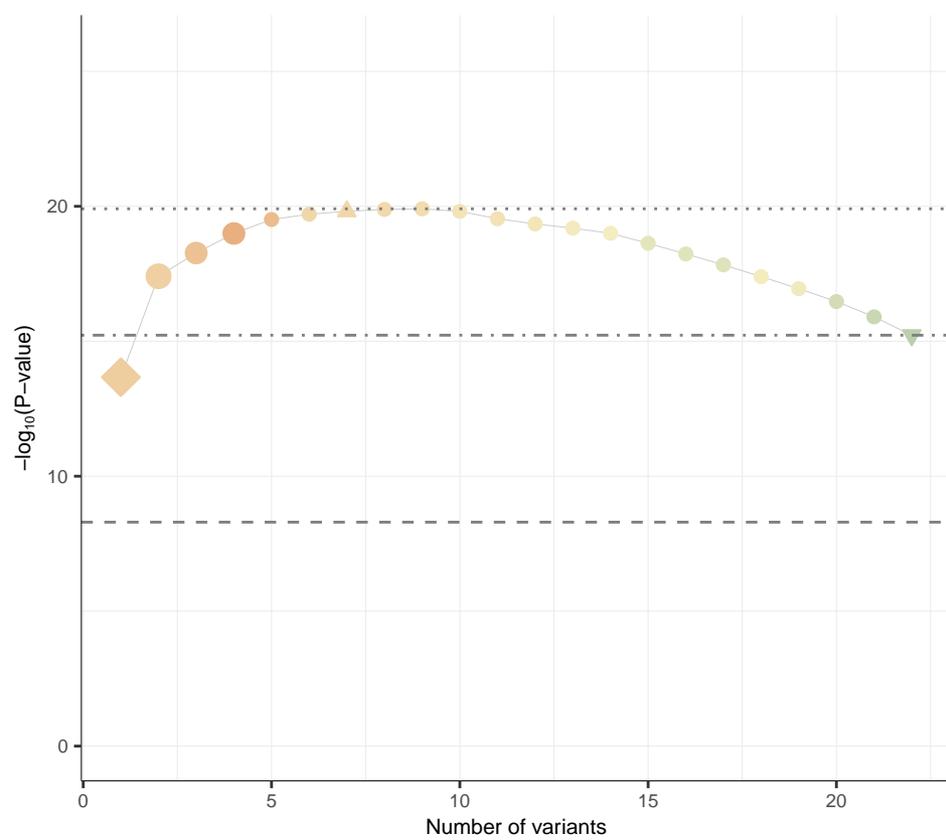
6-bromotryptophan in plasma at *FOXRED2* (LoF_mis)



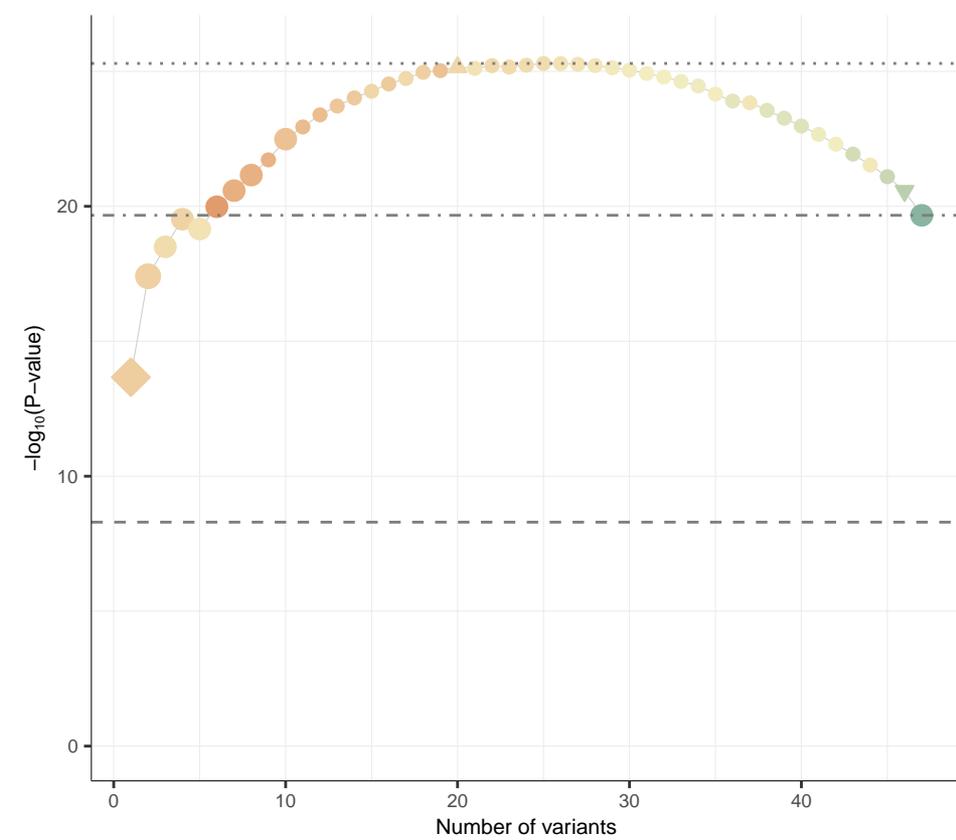
6-bromotryptophan in plasma at *FOXRED2* (HI_mis)



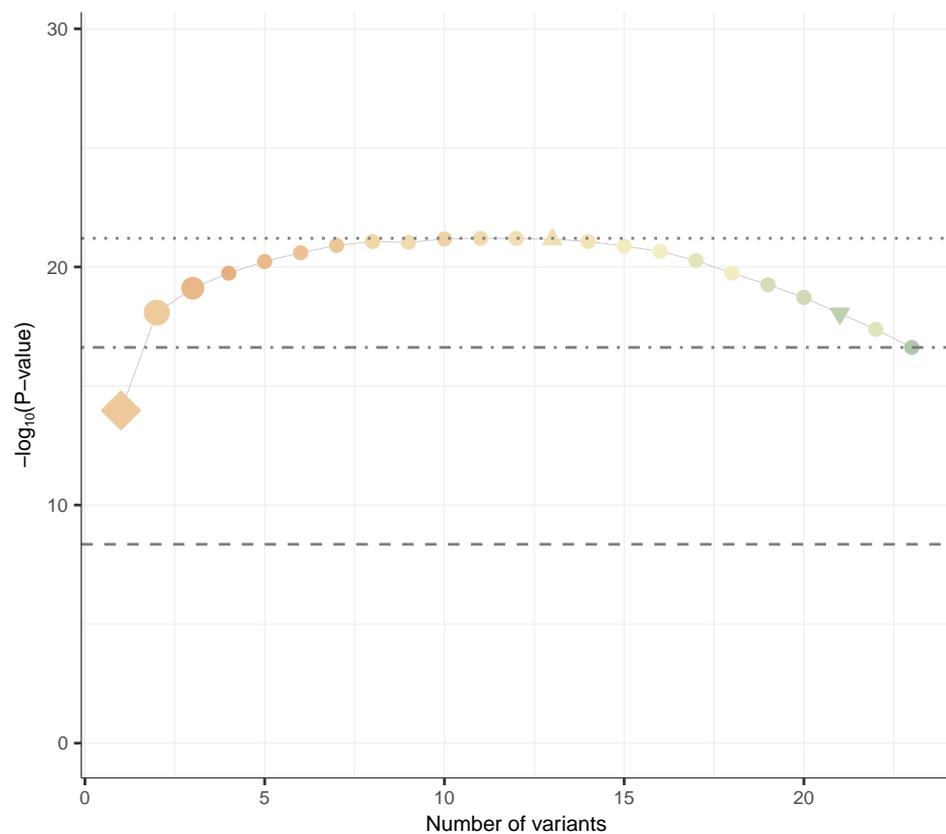
formiminoglutamate in plasma at *FTCD* (LoF_mis)



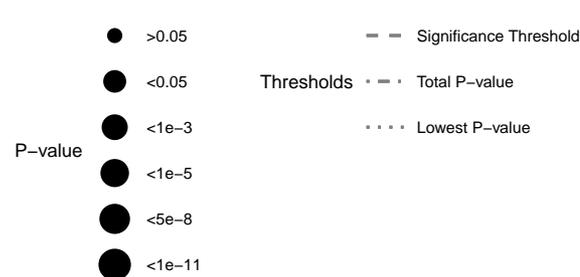
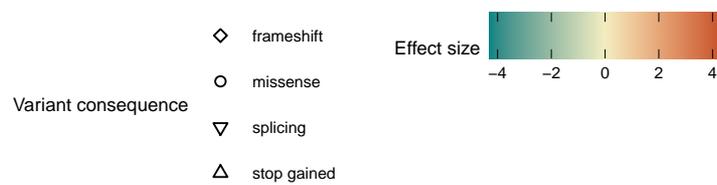
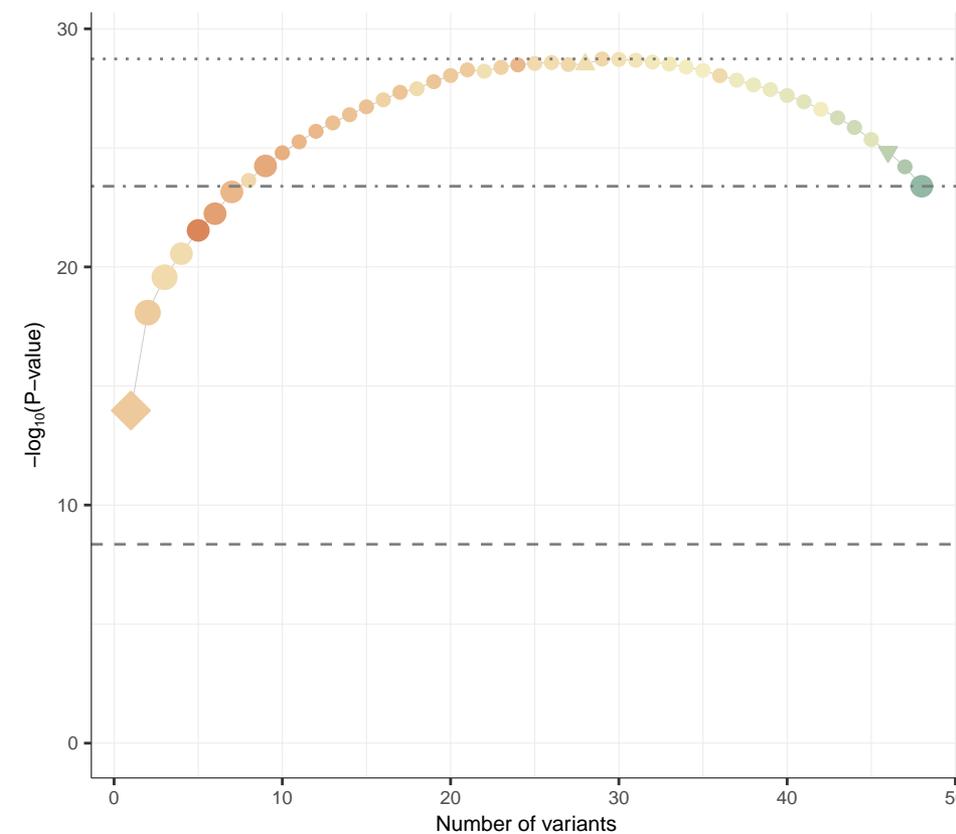
formiminoglutamate in plasma at *FTCD* (HI_mis)



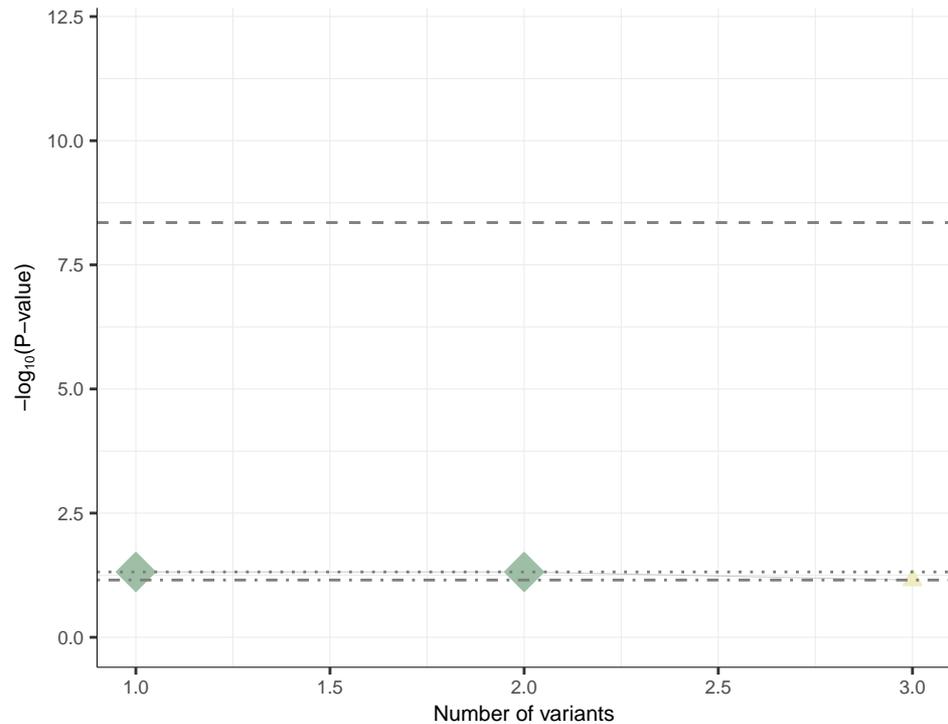
formiminoglutamate in urine at *FTCD* (LoF_mis)



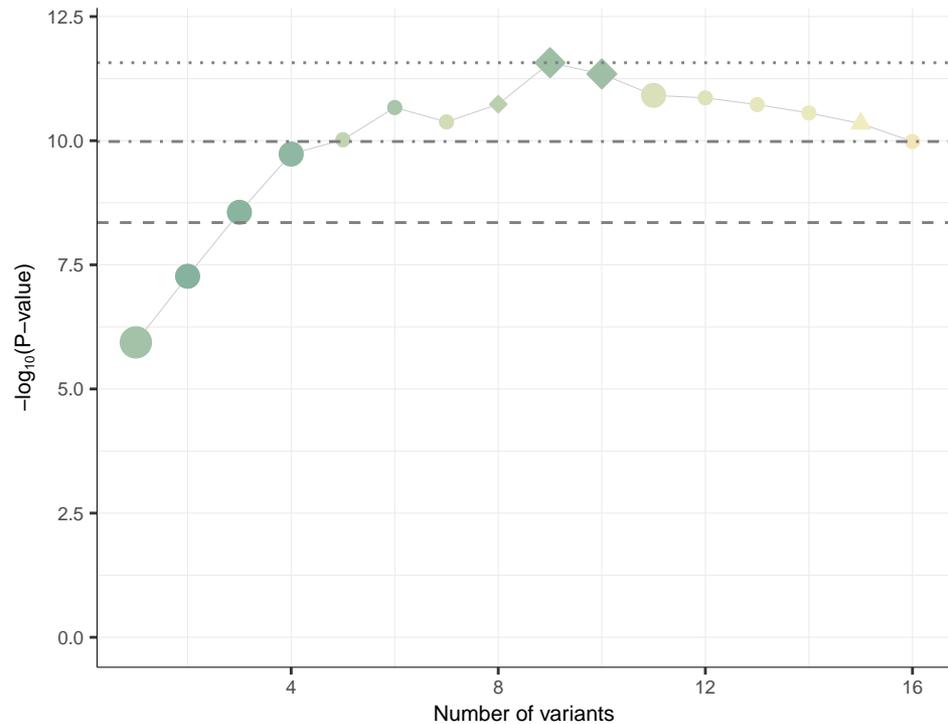
formiminoglutamate in urine at *FTCD* (HI_mis)



tigloylglycine in urine at *GLYAT* (LoF_mis)

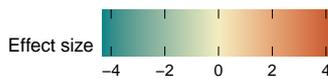


tigloylglycine in urine at *GLYAT* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



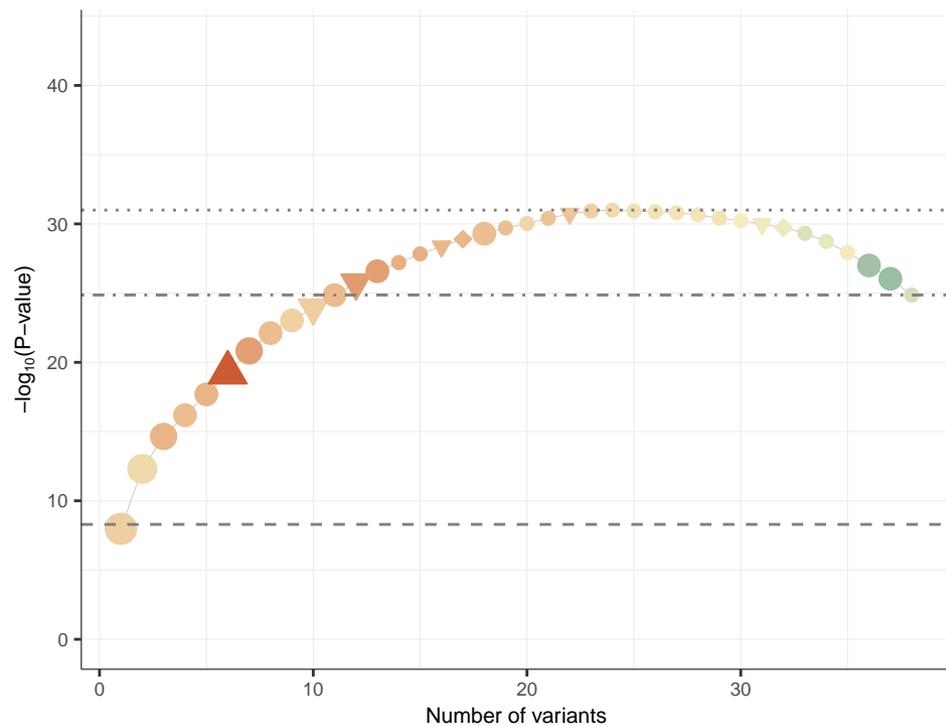
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

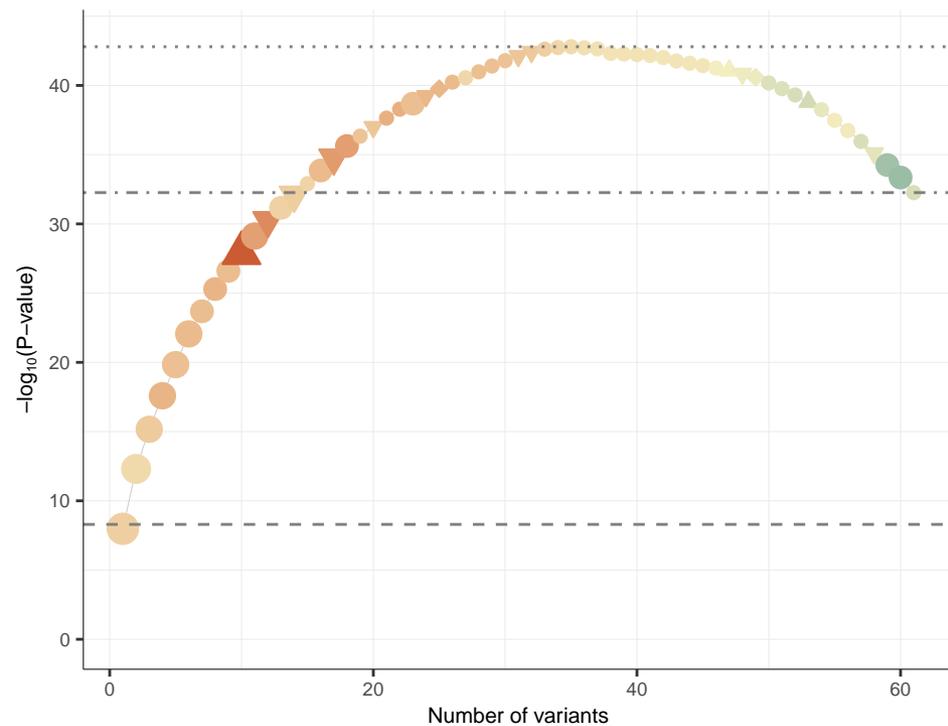
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

gamma-glutamylhistidine in plasma at HAL (LoF_mis)

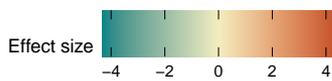


gamma-glutamylhistidine in plasma at HAL (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



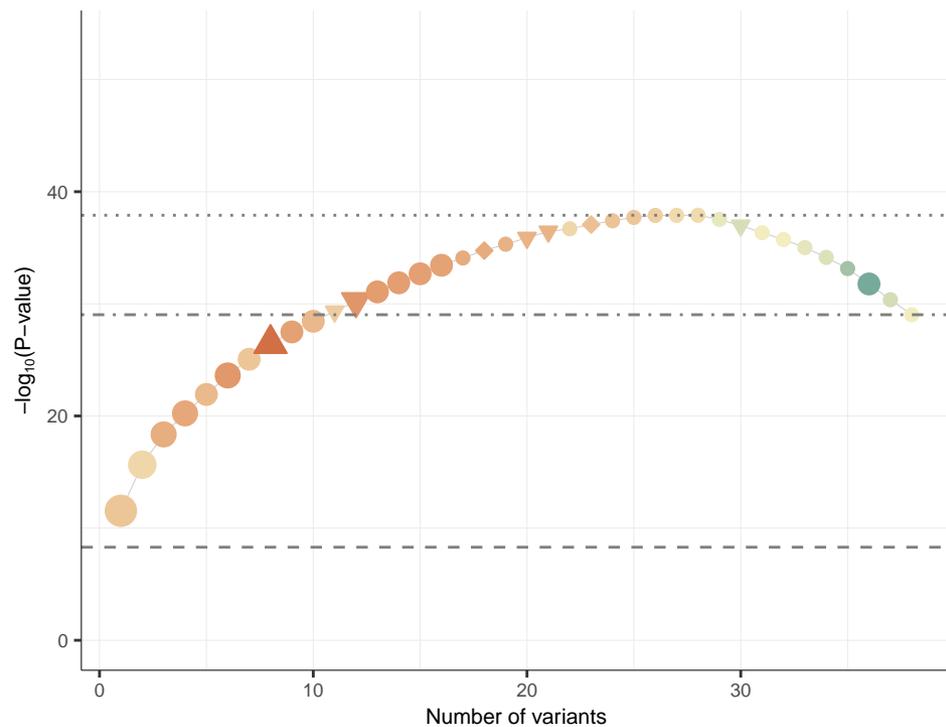
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

Thresholds

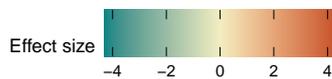
- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

histidine in plasma at *HAL* (LoF_mis)

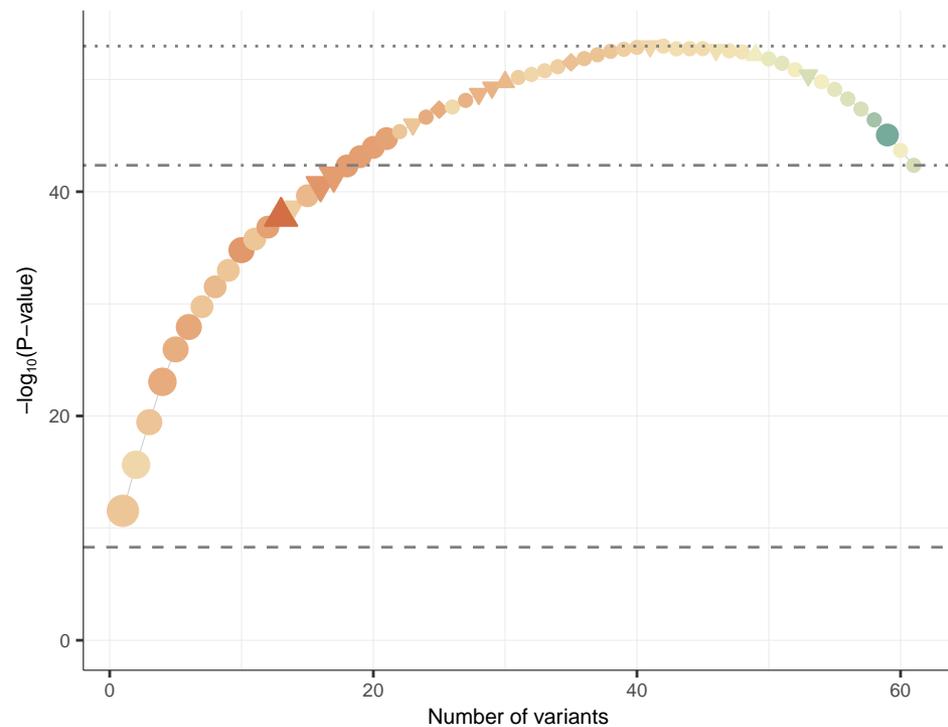


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



histidine in plasma at *HAL* (HI_mis)



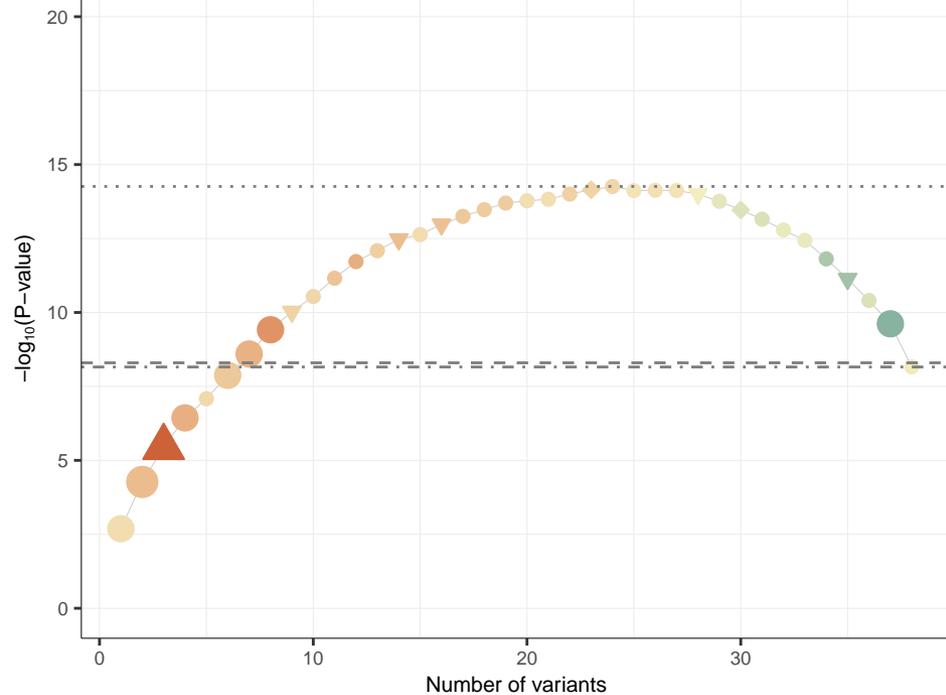
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

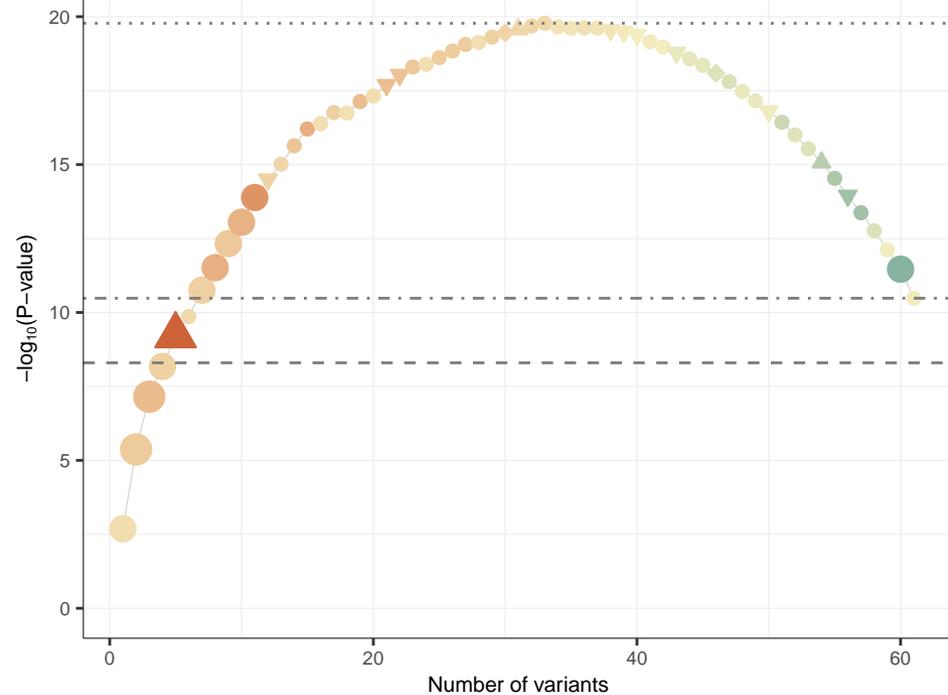
Thresholds

- - Significance Threshold
- · - Total P-value
- · · Lowest P-value

imidazole lactate in plasma at *HAL* (LoF_mis)

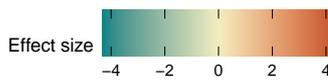


imidazole lactate in plasma at *HAL* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



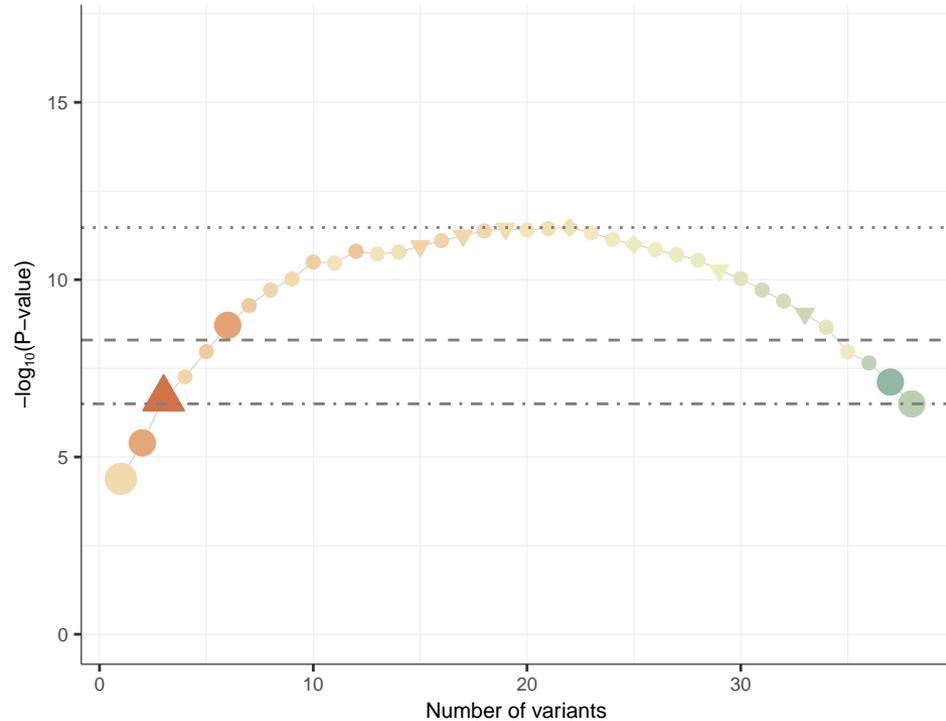
P-value

- >0.05
- <0.05
- <1e-3

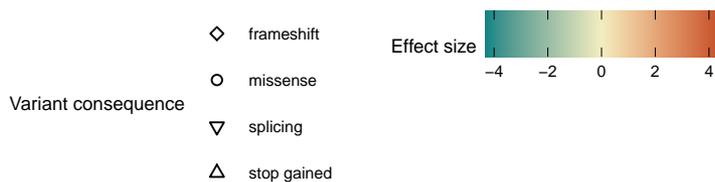
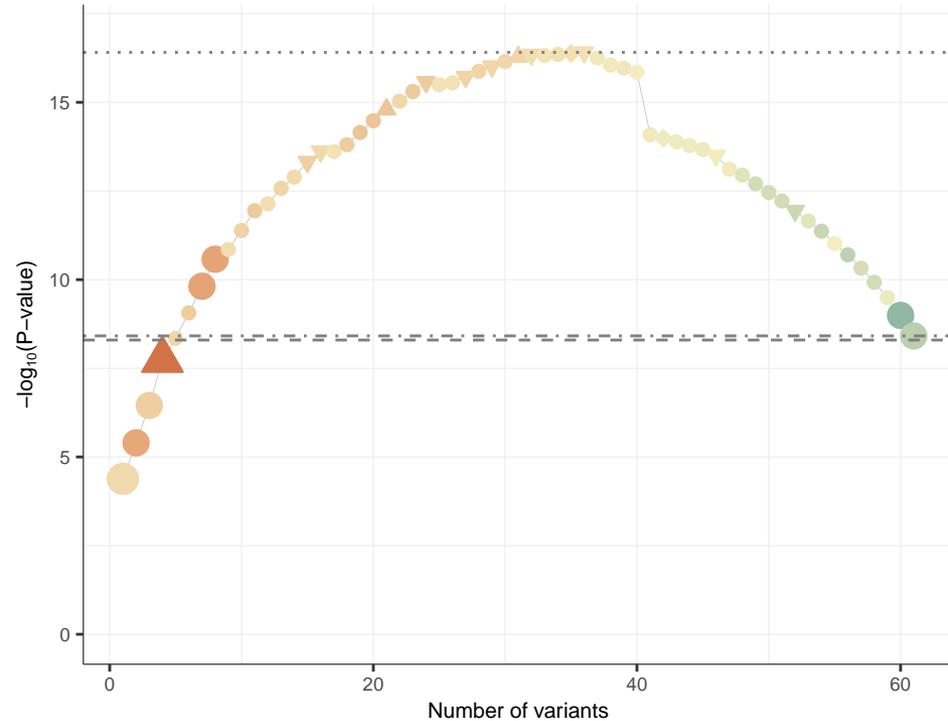
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

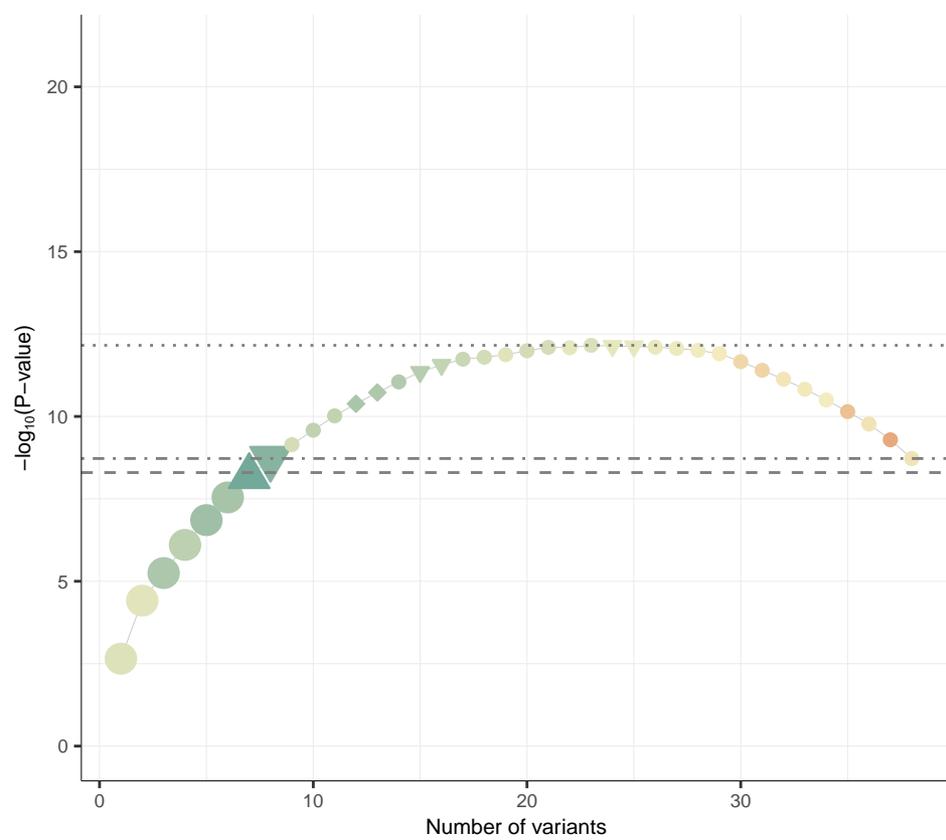
N-acetylhistidine in plasma at *HAL* (LoF_mis)



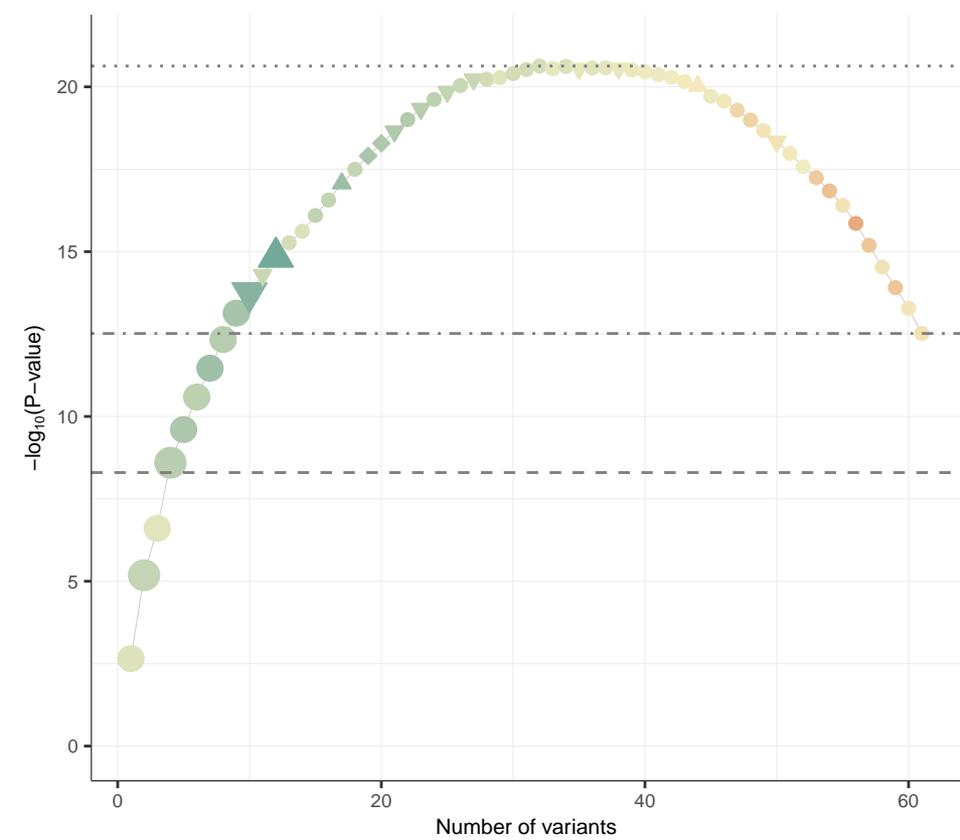
N-acetylhistidine in plasma at *HAL* (HI_mis)



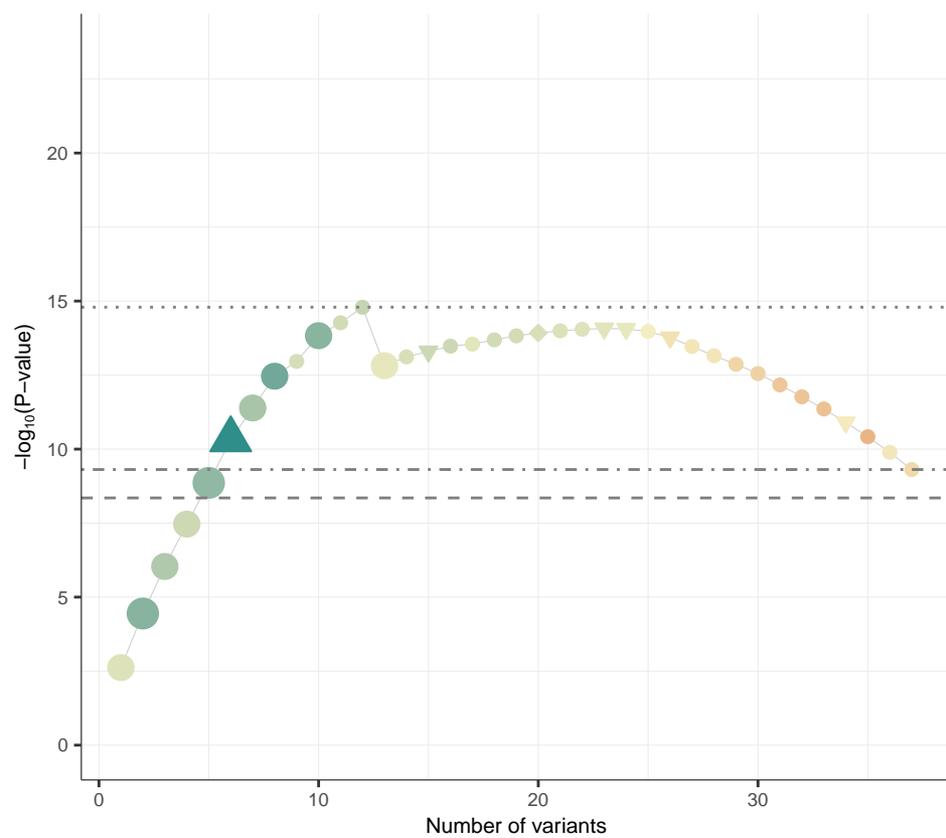
trans-urocanate in plasma at HAL (LoF_mis)



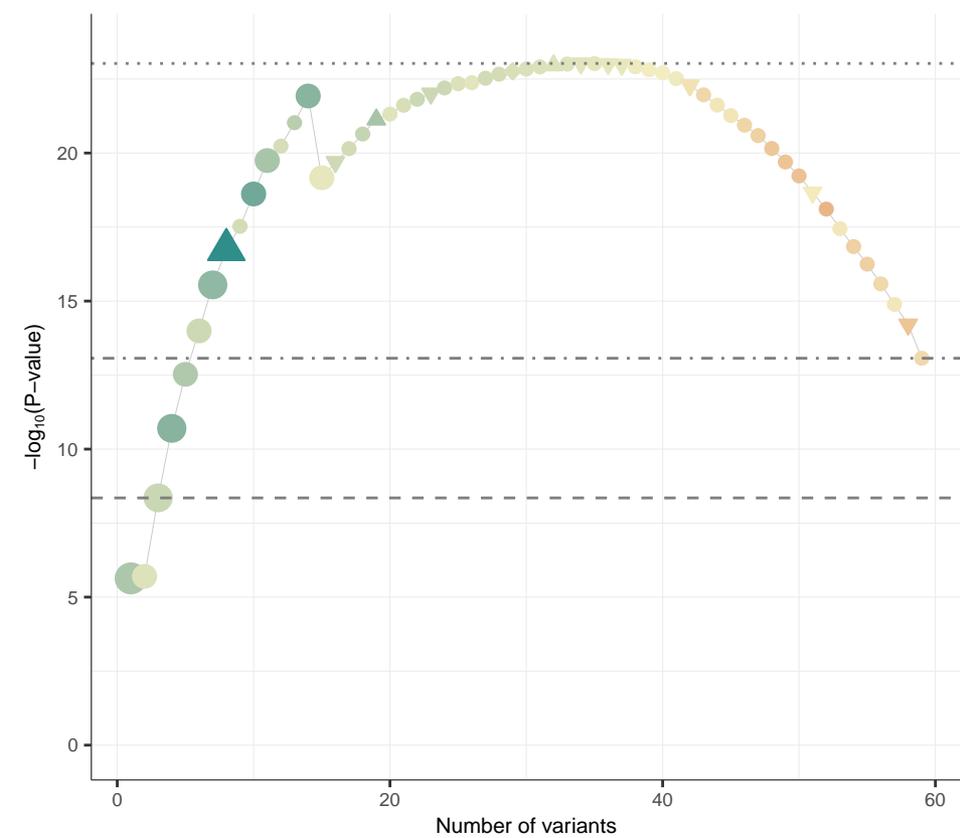
trans-urocanate in plasma at HAL (HI_mis)



trans-urocanate in urine at HAL (LoF_mis)



trans-urocanate in urine at HAL (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained

Effect size

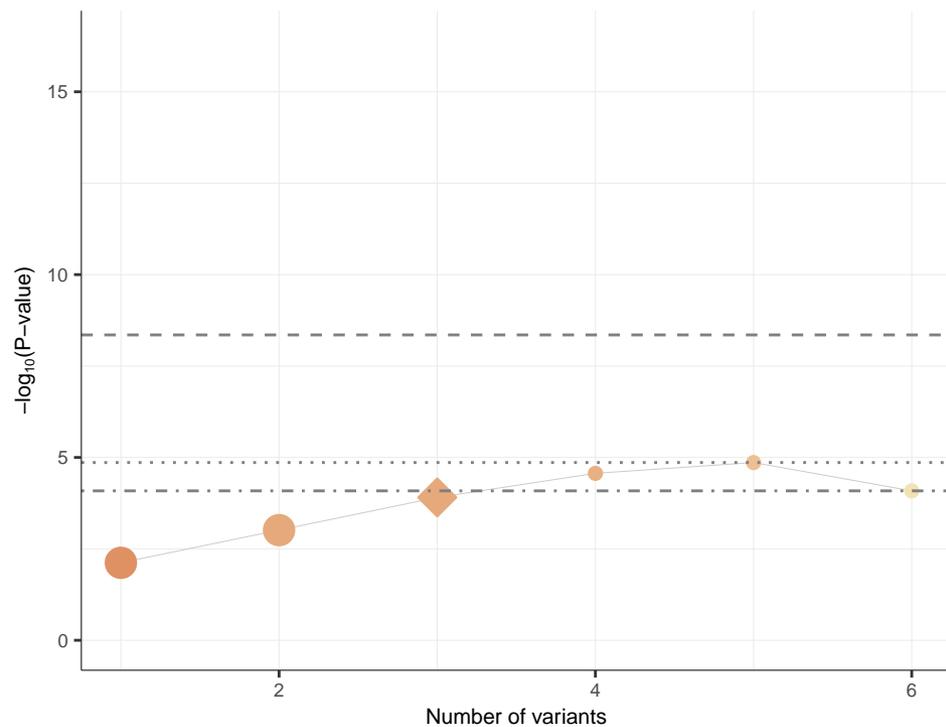
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

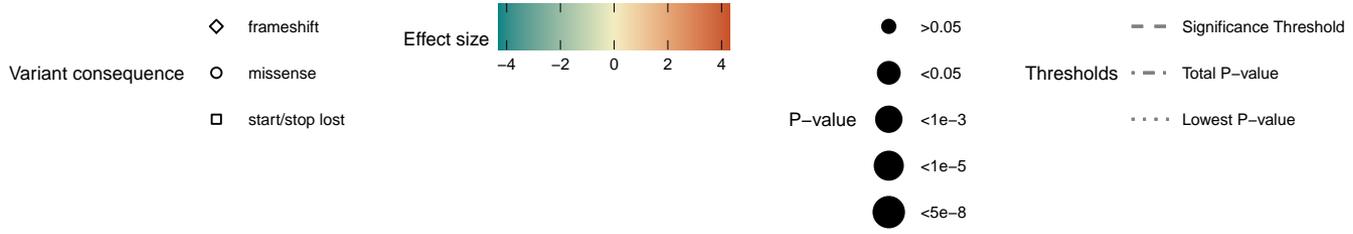
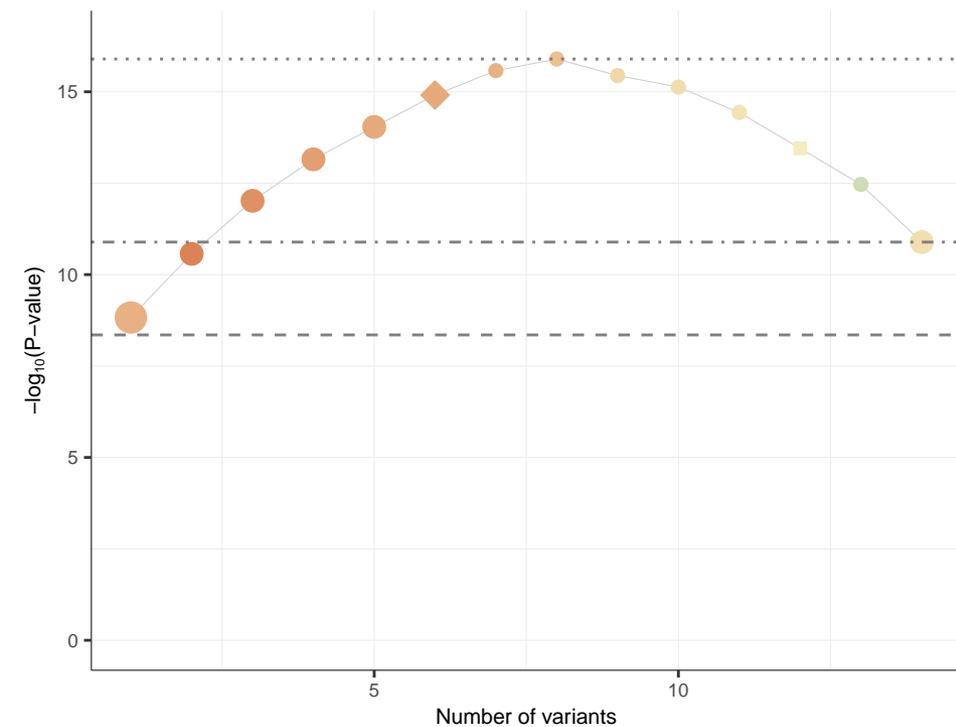
Thresholds

- Significance Threshold
- - - Total P-value
- Lowest P-value

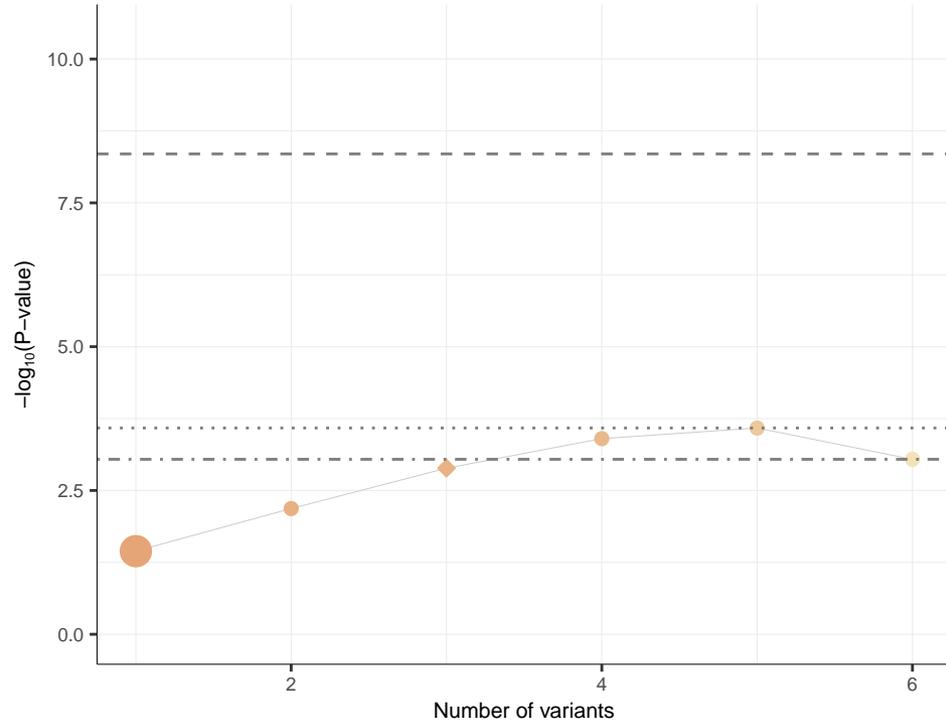
3-(4-hydroxyphenyl)lactate in urine at *HAO2* (LoF_mis)



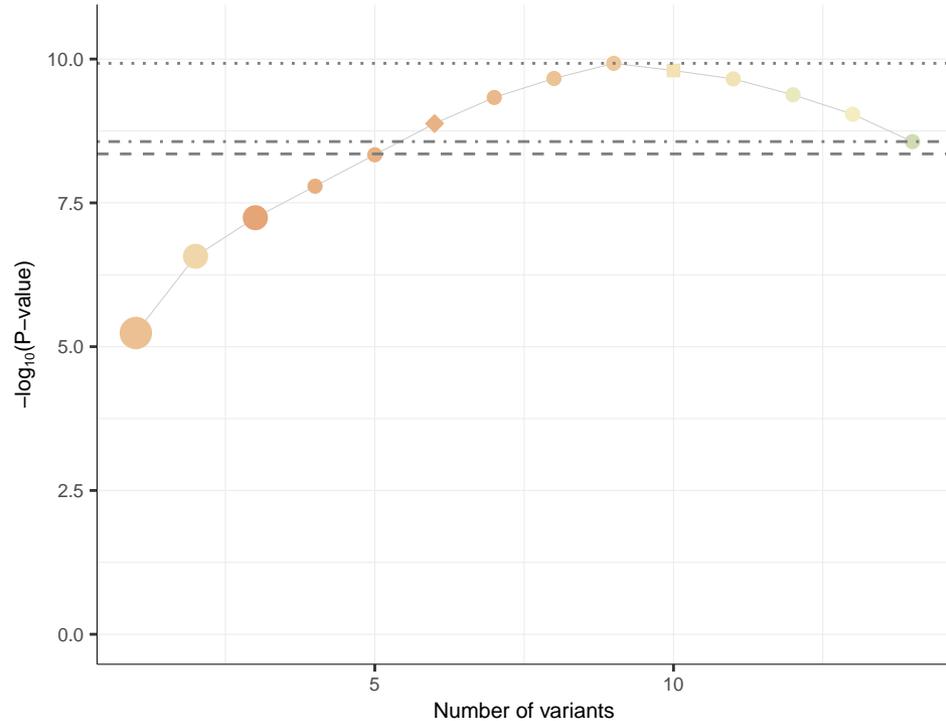
3-(4-hydroxyphenyl)lactate in urine at *HAO2* (HI_mis)



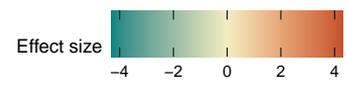
indolelactate in urine at *HAO2* (LoF_mis)



indolelactate in urine at *HAO2* (HI_mis)



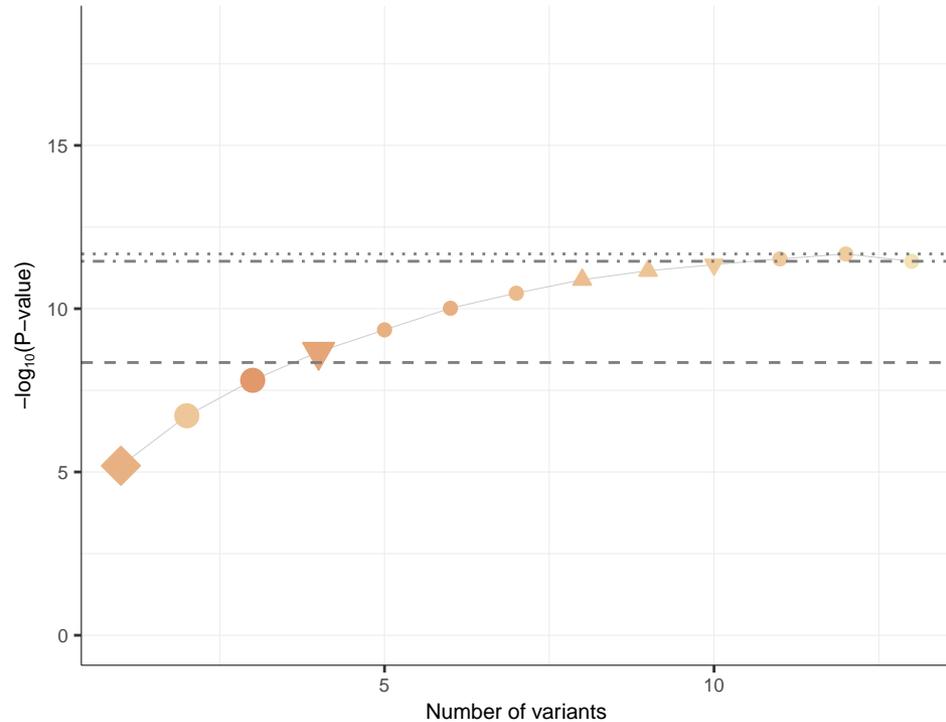
- Variant consequence
- ◇ frameshift
 - missense
 - start/stop lost



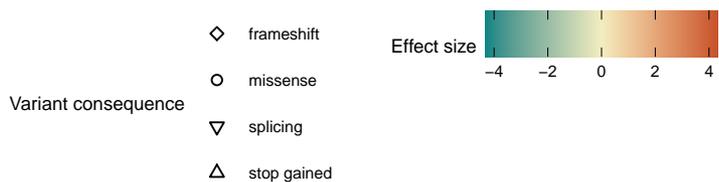
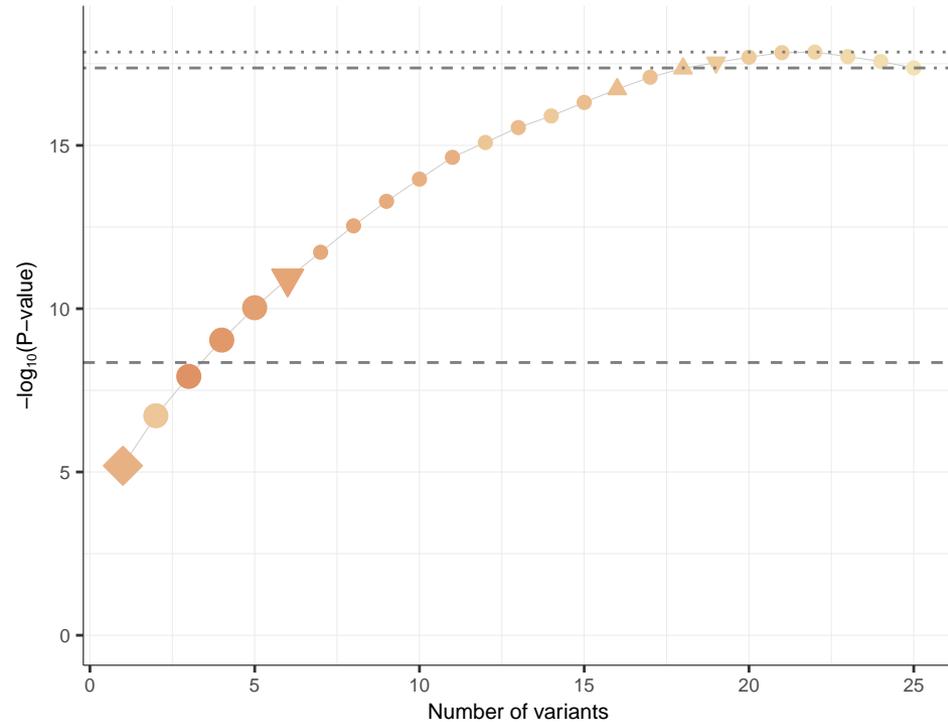
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5

- Thresholds
- Significance Threshold
 - - - Total P-value
 - ⋯ Lowest P-value

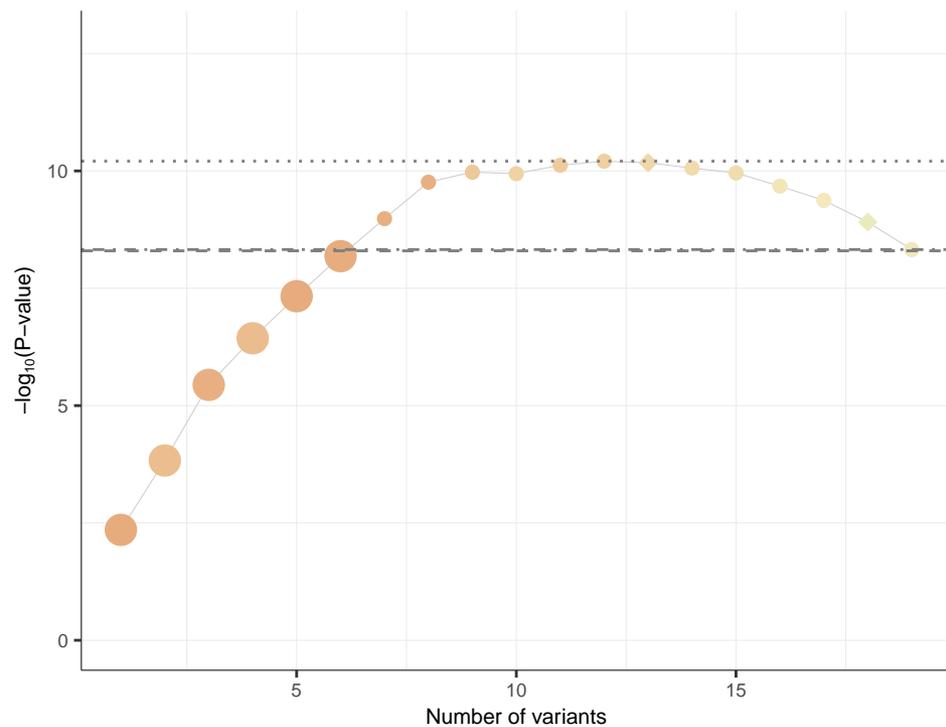
diacetylpermidine* in urine at *HDAC10* (LoF_mis)



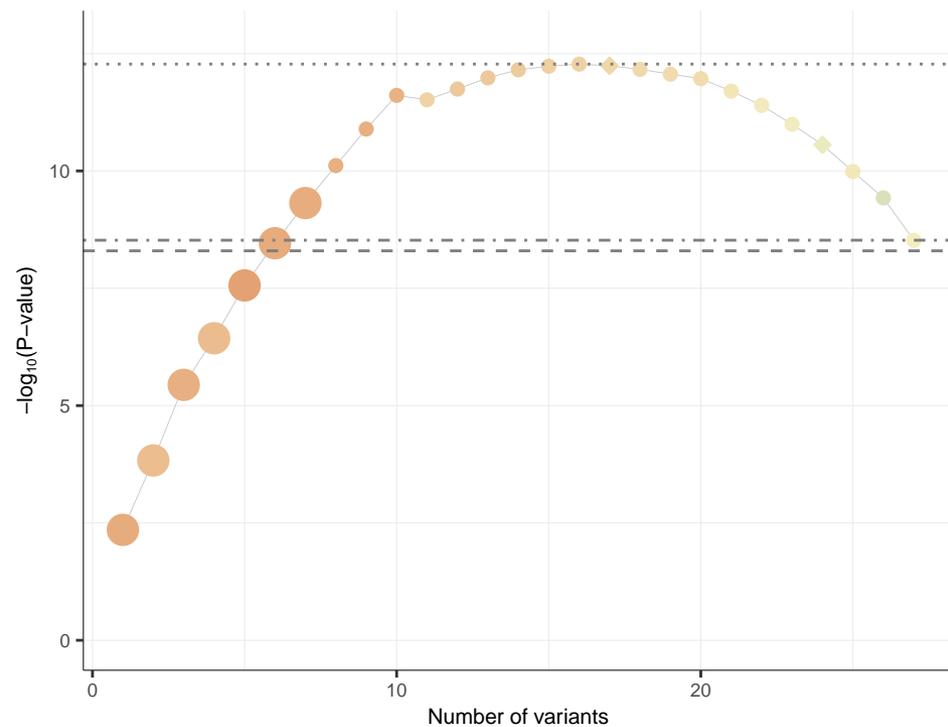
diacetylpermidine* in urine at *HDAC10* (HI_mis)



3-(4-hydroxyphenyl)lactate in plasma at *KYAT1* (LoF_mis)



3-(4-hydroxyphenyl)lactate in plasma at *KYAT1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense



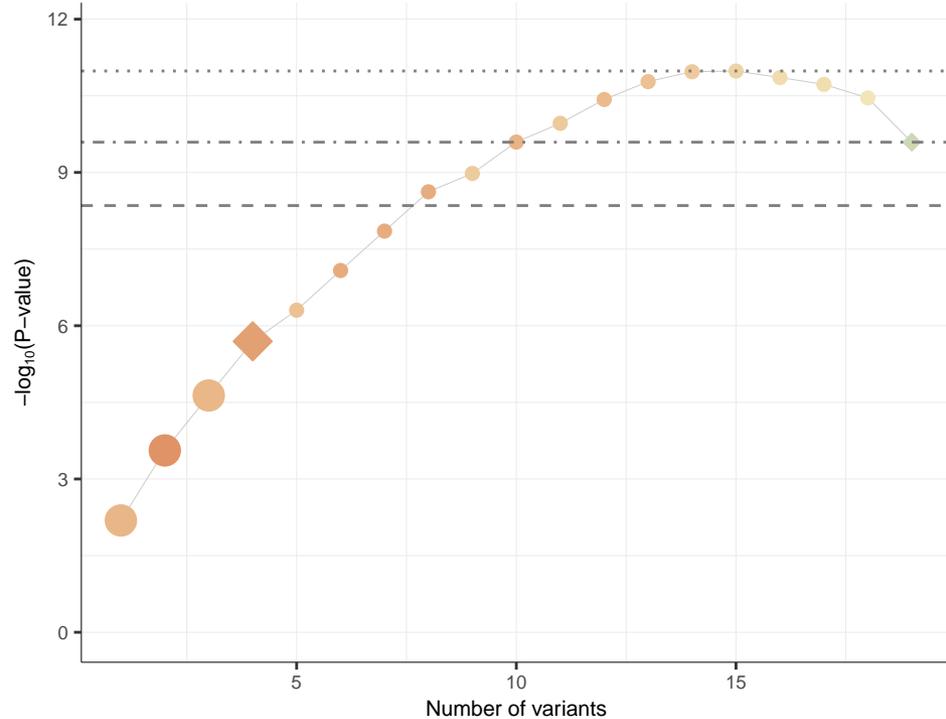
P-value

- >0.05
- <0.05

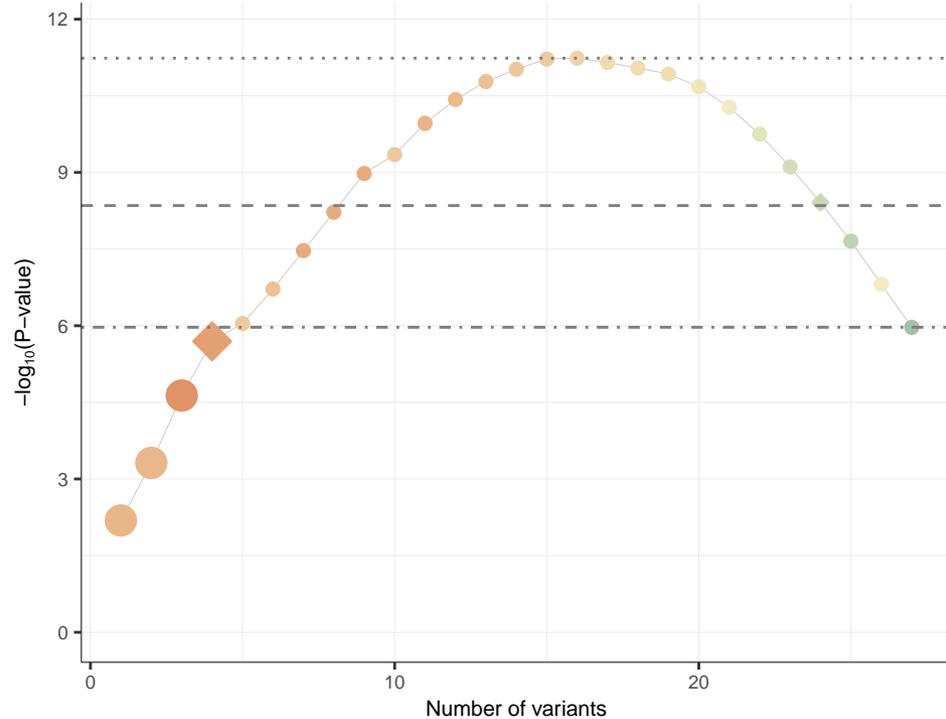
Thresholds

- - Significance Threshold
- · - Total P-value
- · · Lowest P-value

3-formylindole in urine at *KYAT1* (LoF_mis)

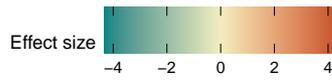


3-formylindole in urine at *KYAT1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense



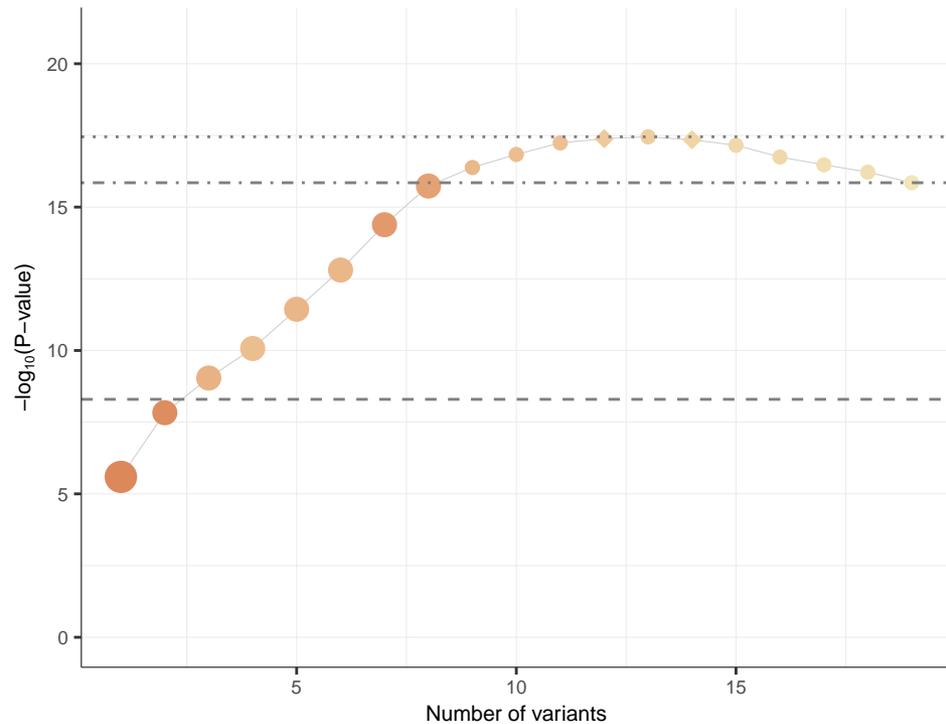
P-value

- >0.05
- <0.05

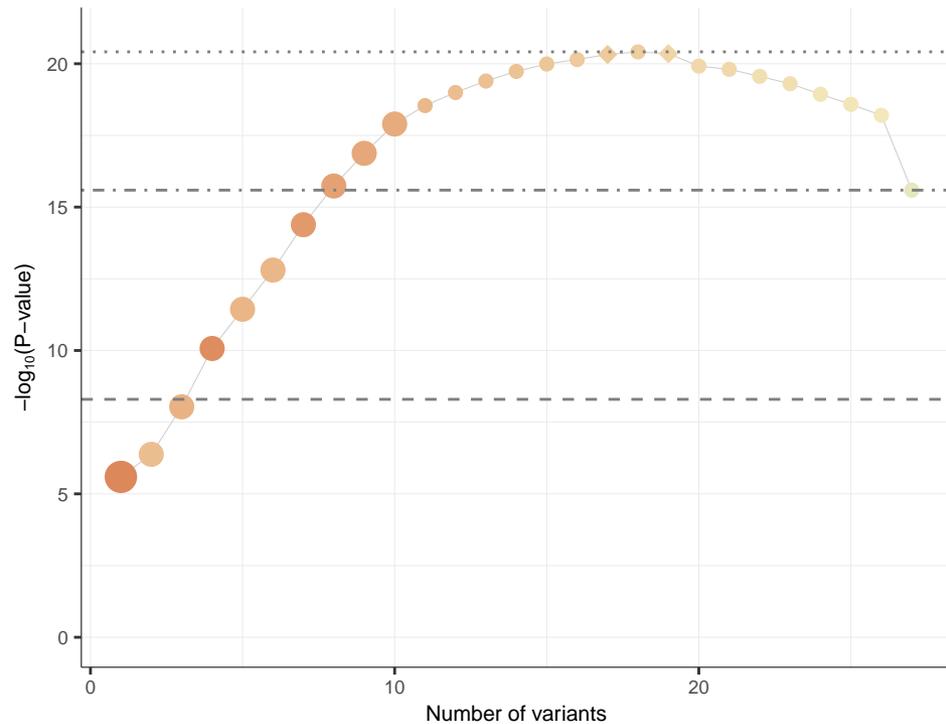
Thresholds

- — Significance Threshold
- · - Total P-value
- · · Lowest P-value

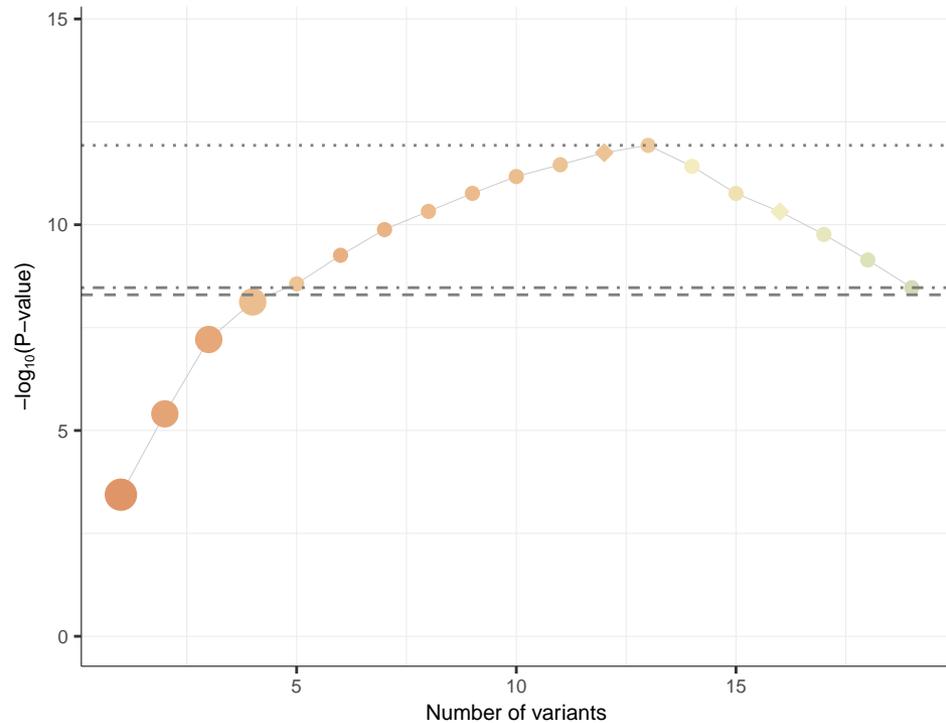
indolelactate in plasma at *KYAT1* (LoF_mis)



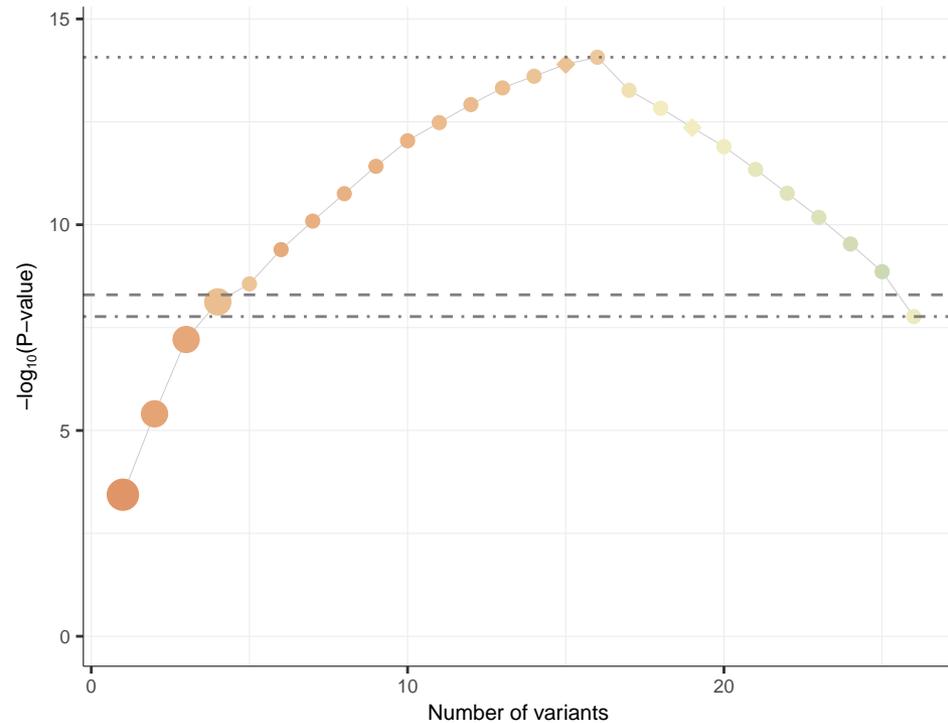
indolelactate in plasma at *KYAT1* (HI_mis)



phenylpyruvate in plasma at *KYAT1* (LoF_mis)



phenylpyruvate in plasma at *KYAT1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense



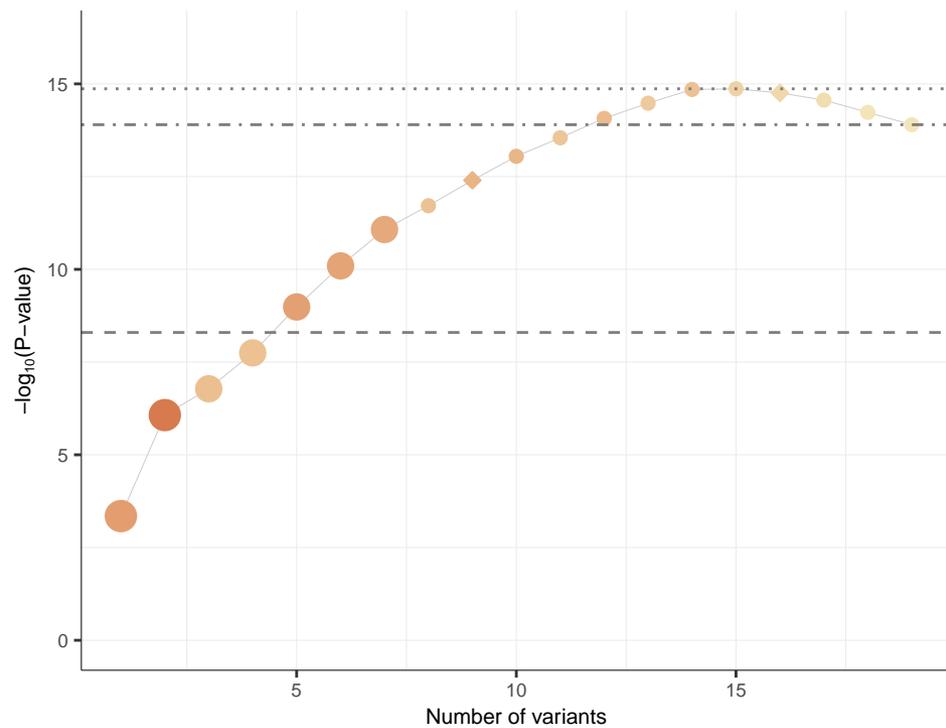
P-value

- >0.05
- <0.05
- <1e-3

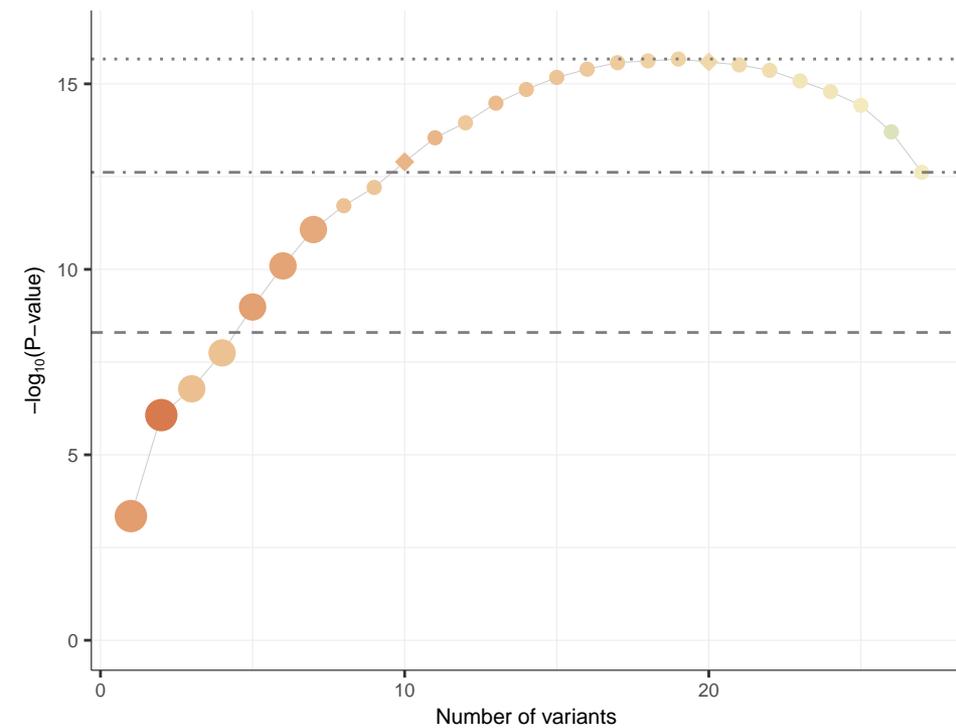
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

X - 24585 in plasma at *KYAT1* (LoF_mis)



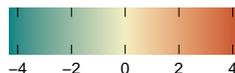
X - 24585 in plasma at *KYAT1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense

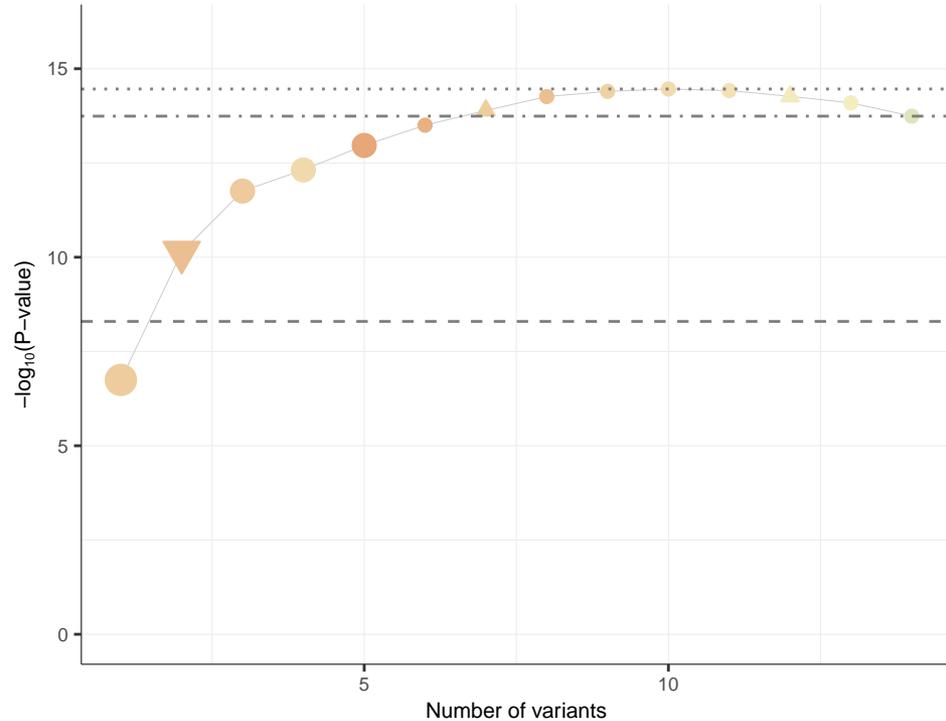
Effect size



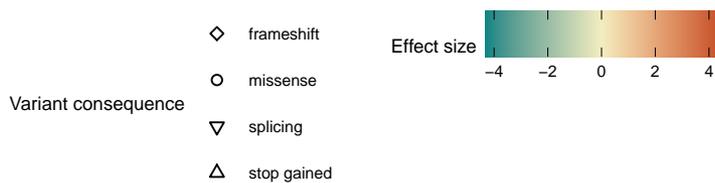
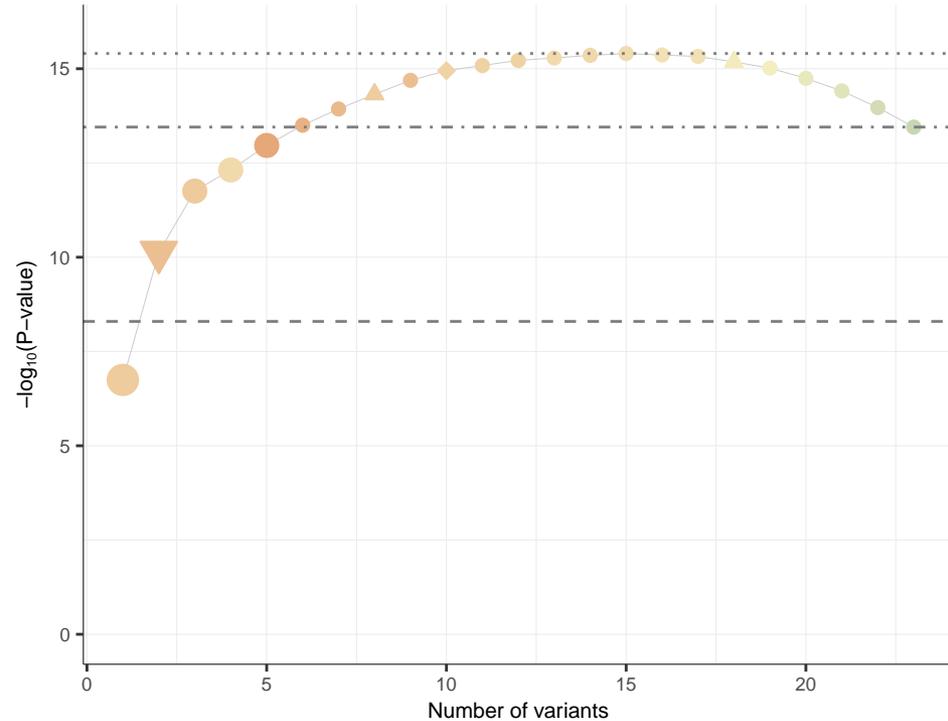
- P-value
- >0.05
 - <0.05
 - <1e-3

- Thresholds
- Significance Threshold
 - - - Total P-value
 - ⋯ Lowest P-value

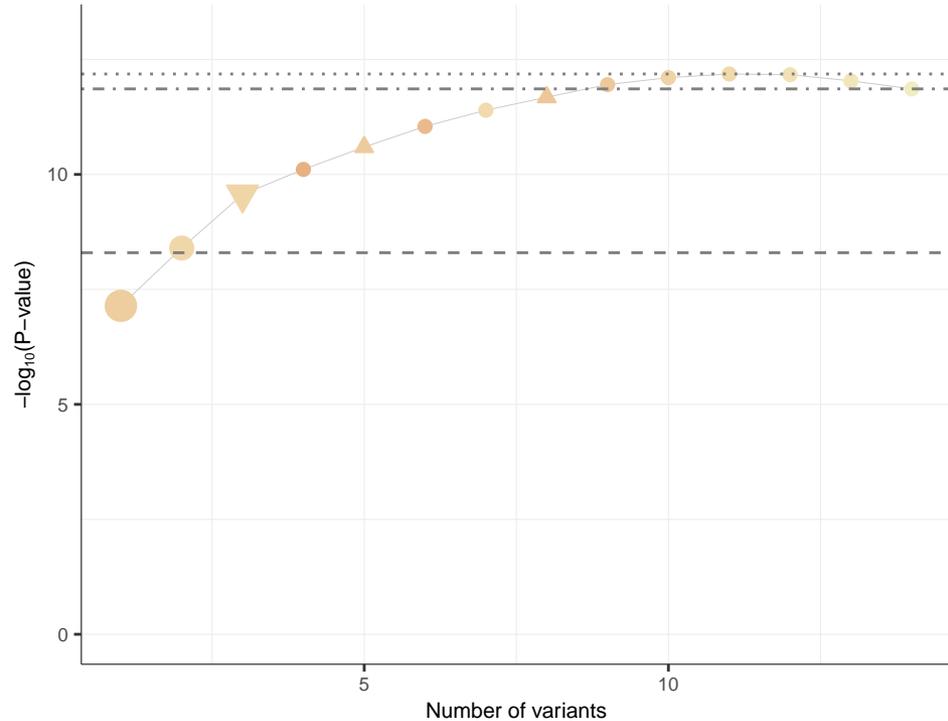
2-hydroxy-4-(methylthio)butanoic acid in plasma at KYAT3 (LoF_mis)



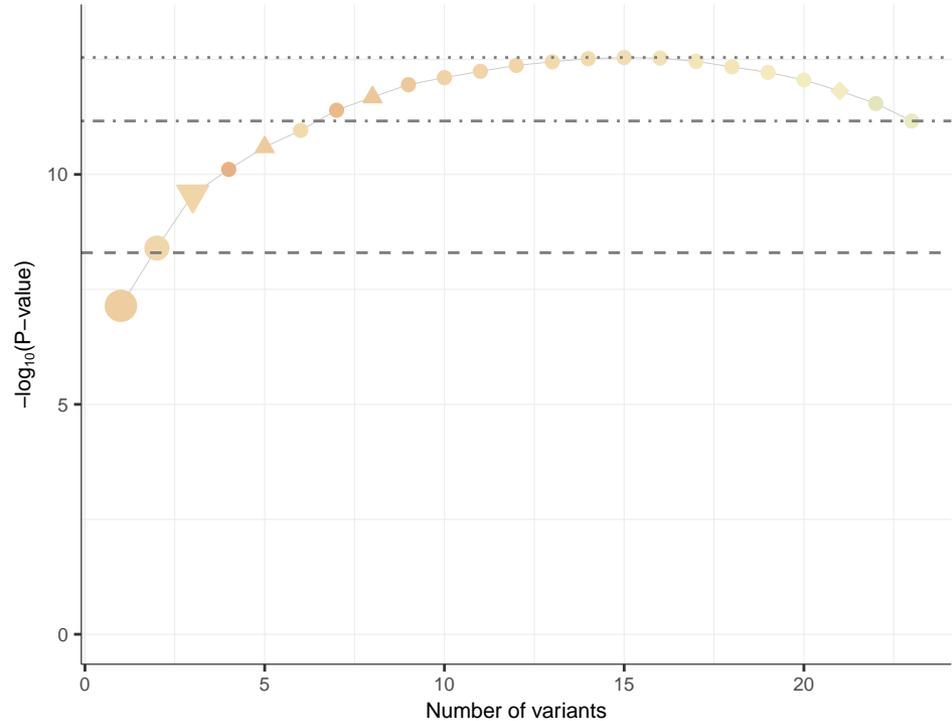
2-hydroxy-4-(methylthio)butanoic acid in plasma at KYAT3 (HI_mis)



imidazole lactate in plasma at KYAT3 (LoF_mis)

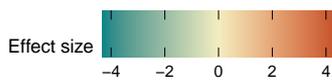


imidazole lactate in plasma at KYAT3 (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



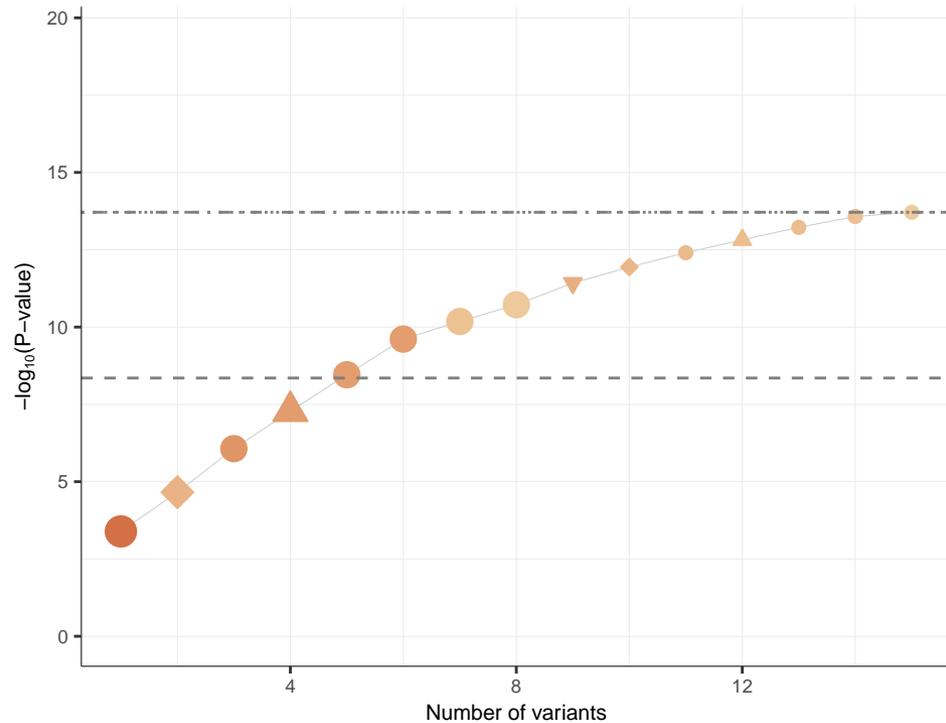
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

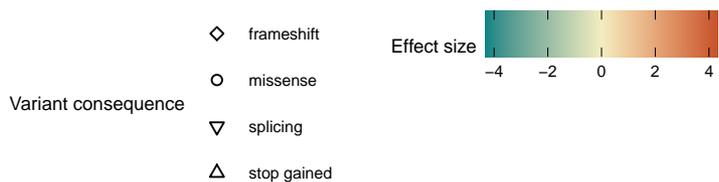
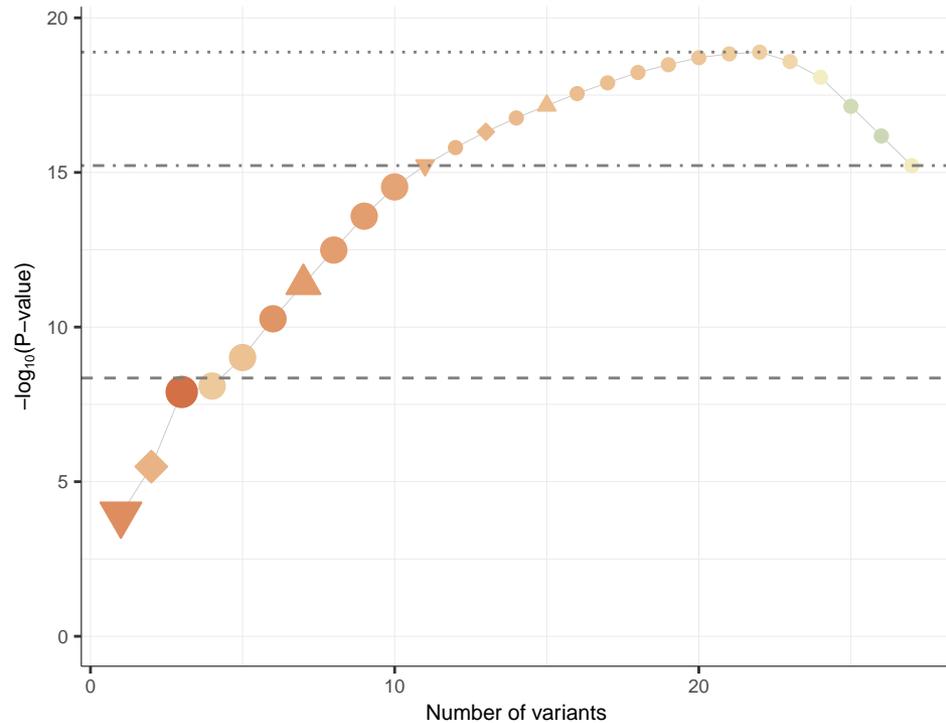
Thresholds

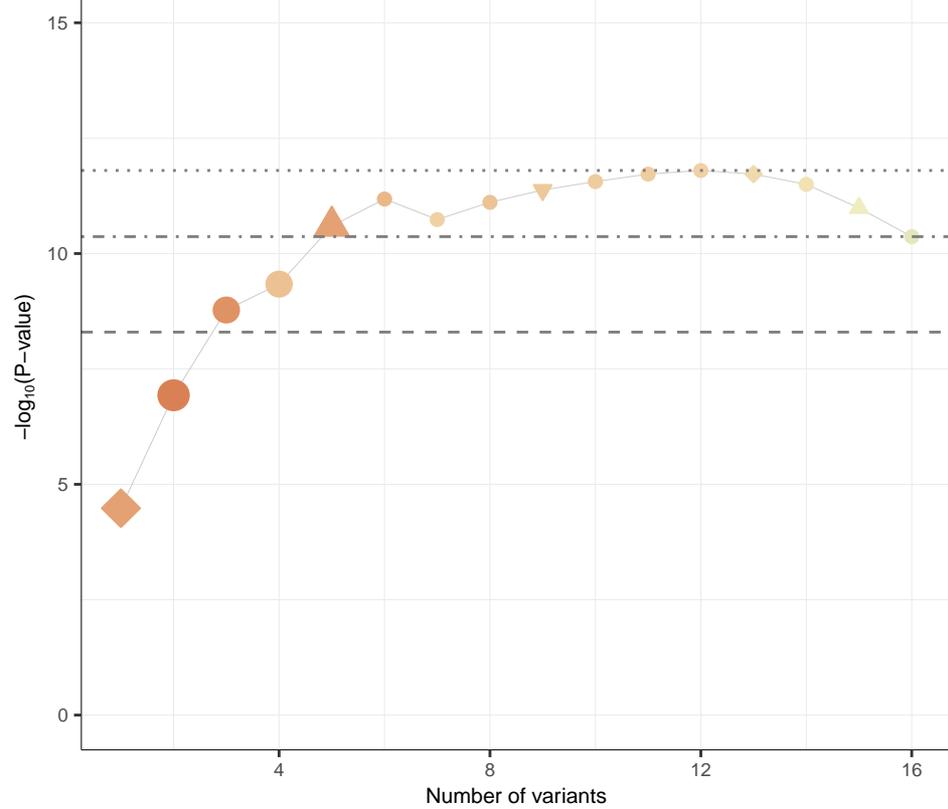
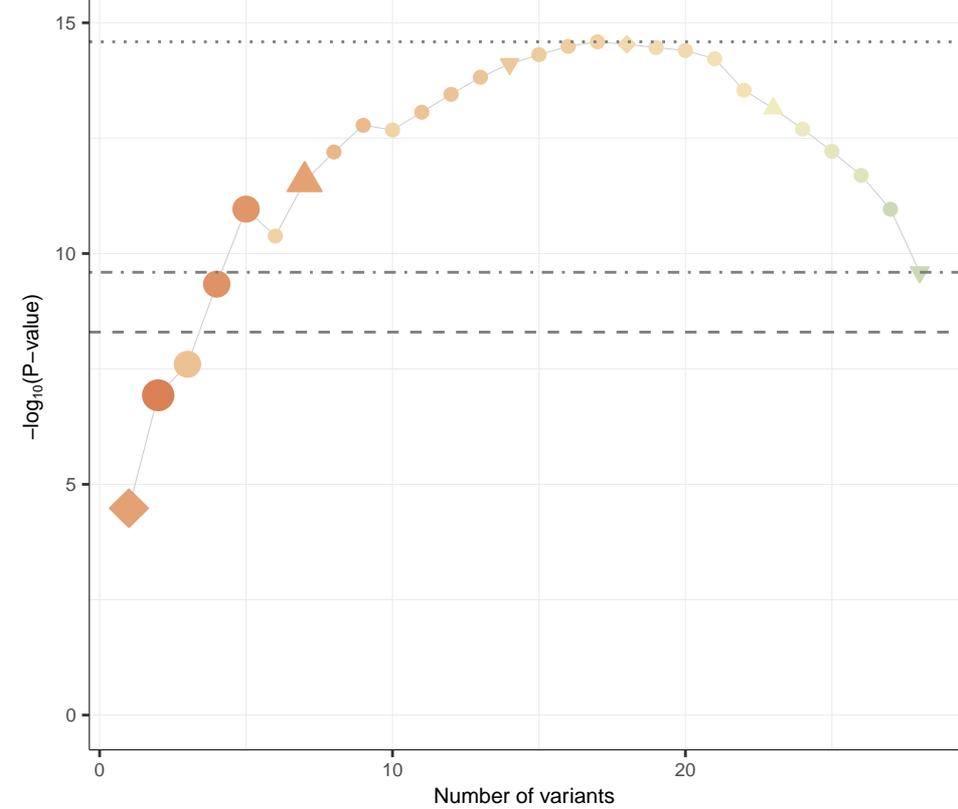
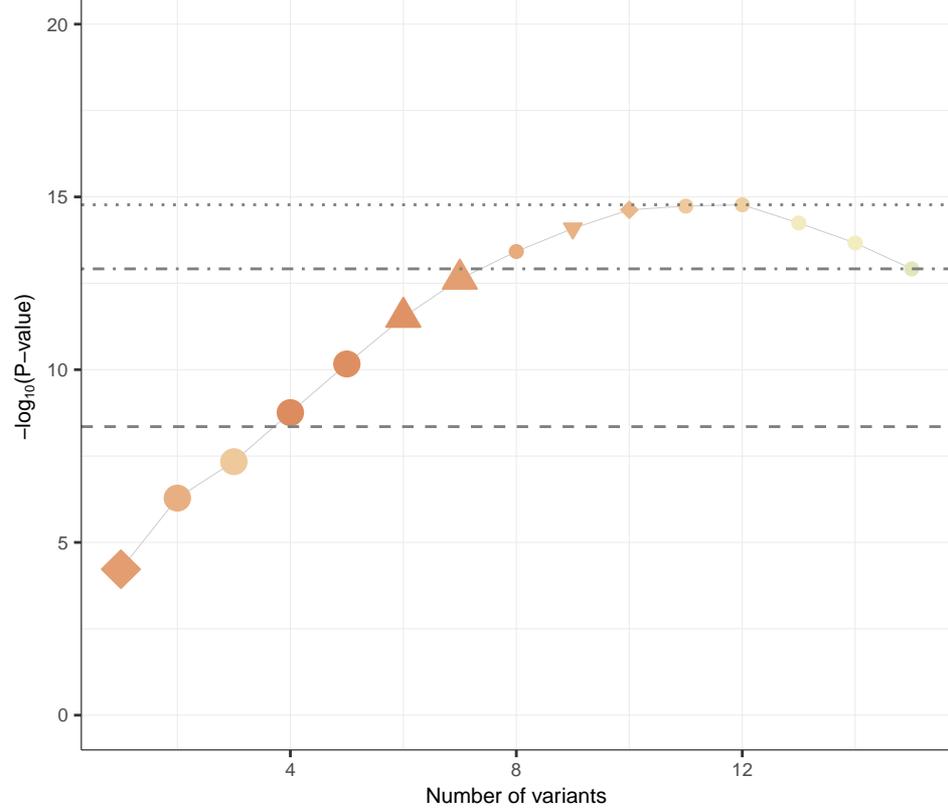
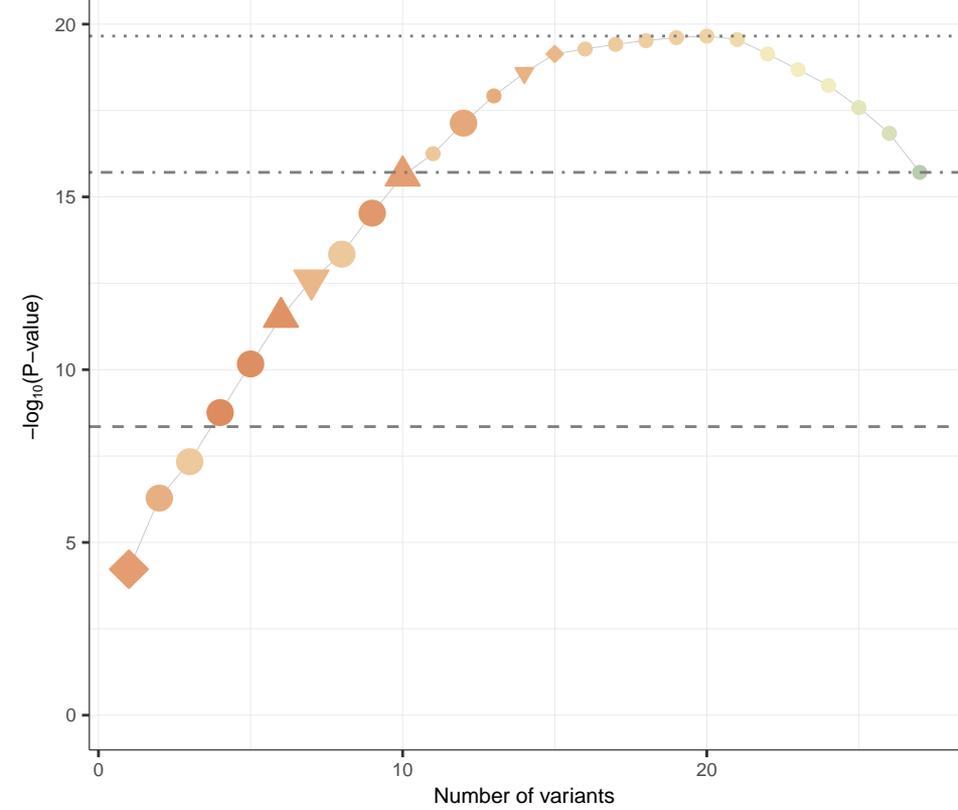
- Significance Threshold
- - - Total P-value
- ... Lowest P-value

3-hydroxykynurenine in urine at *KYNU* (LoF_mis)



3-hydroxykynurenine in urine at *KYNU* (HI_mis)



8-methoxykynurenate in plasma at *KYNU* (LoF_mis)8-methoxykynurenate in plasma at *KYNU* (HI_mis)8-methoxykynurenate in urine at *KYNU* (LoF_mis)8-methoxykynurenate in urine at *KYNU* (HI_mis)

Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained

Effect size

-4 -2 0 2 4

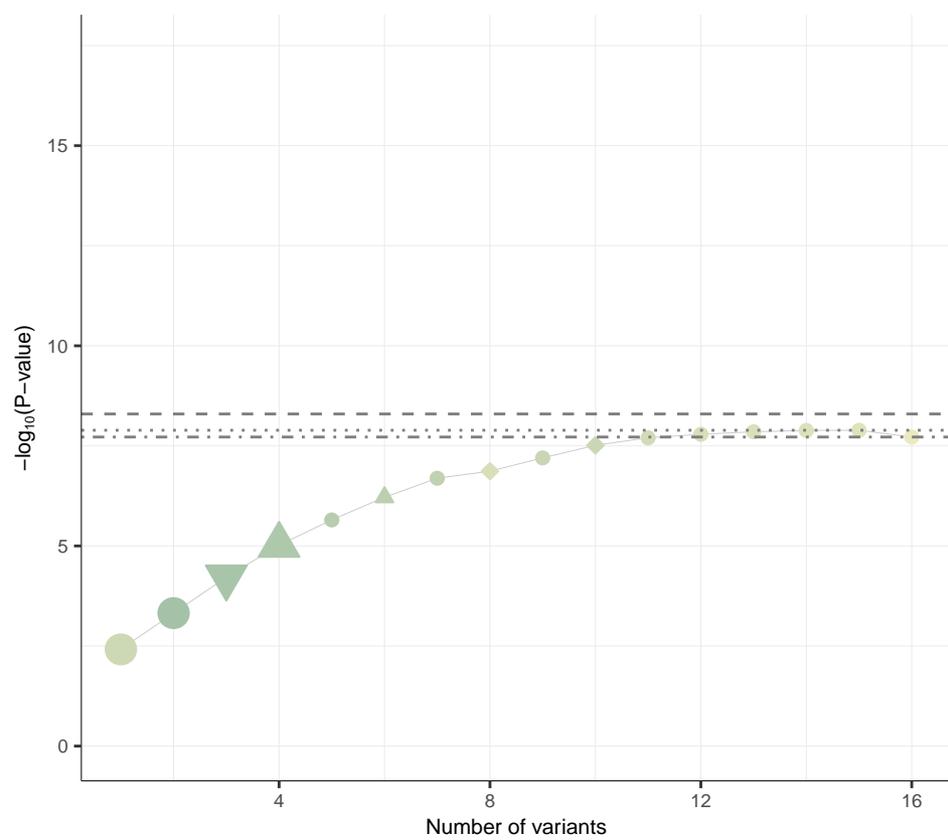
P-value

- >0.05
- <0.05
- <1e-3

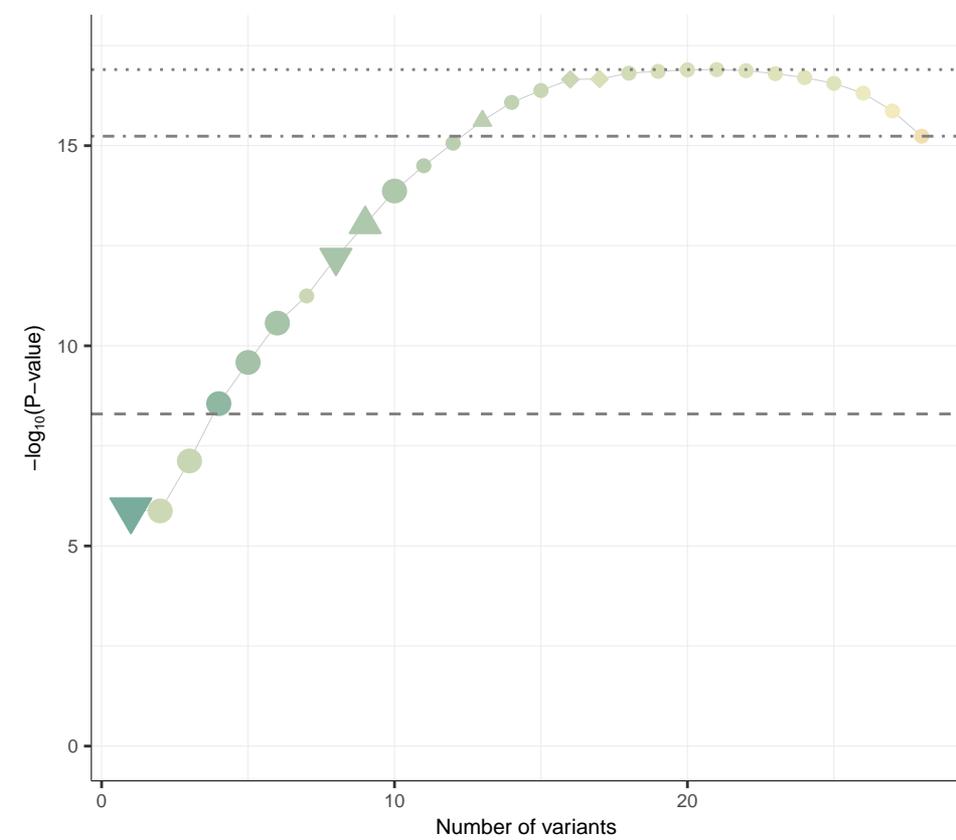
Thresholds

- - Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

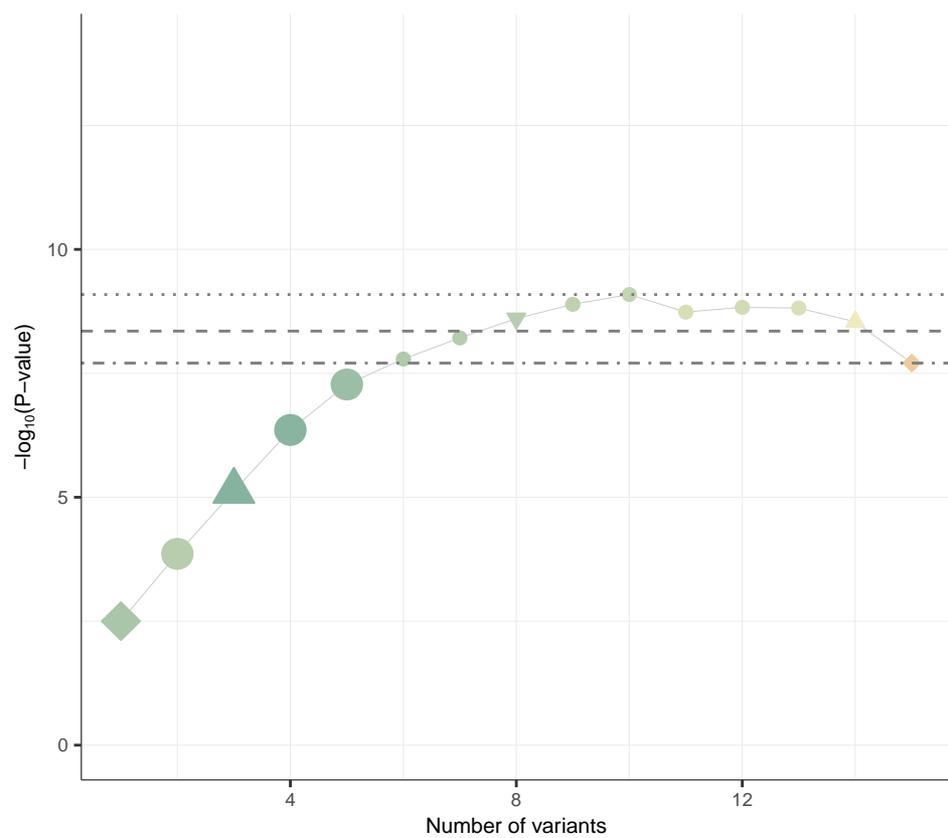
X – 15503 in plasma at *KYNU* (LoF_mis)



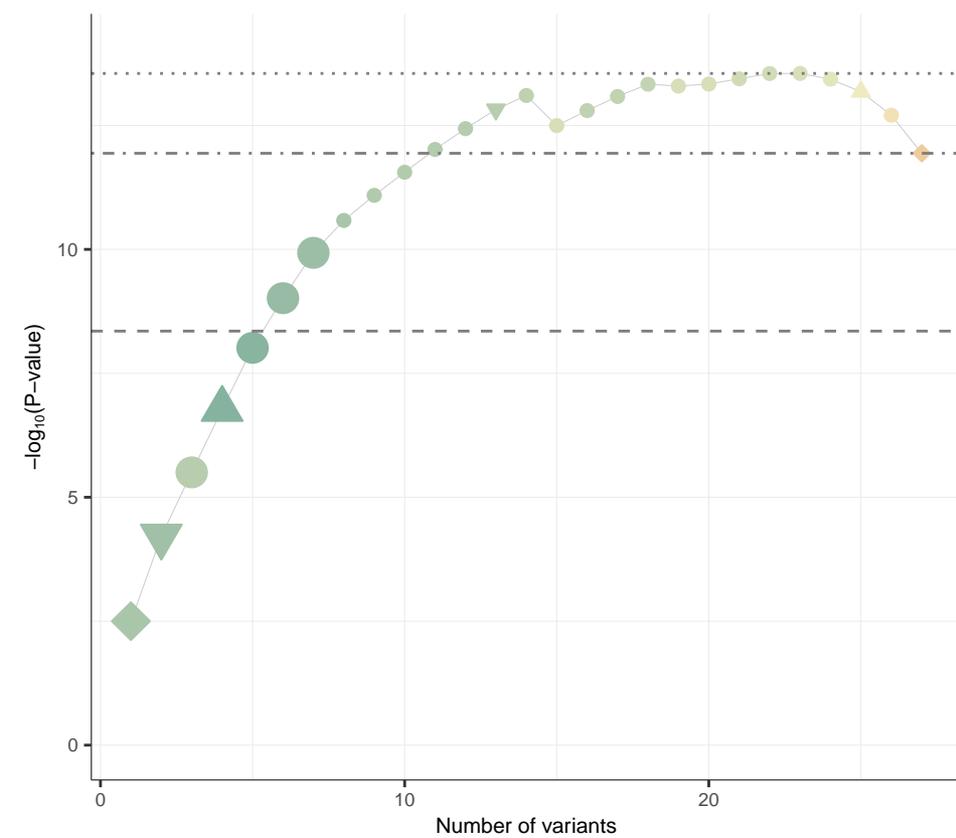
X – 15503 in plasma at *KYNU* (HI_mis)



X – 15503 in urine at *KYNU* (LoF_mis)



X – 15503 in urine at *KYNU* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained

Effect size

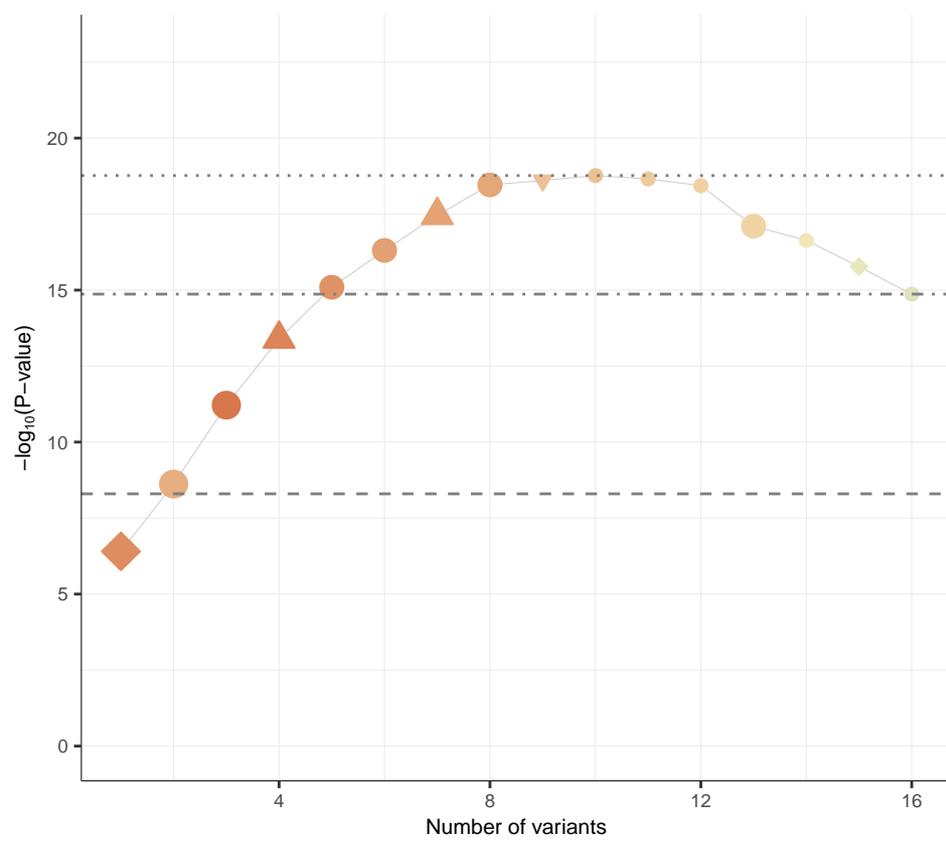
P-value

- >0.05
- <0.05

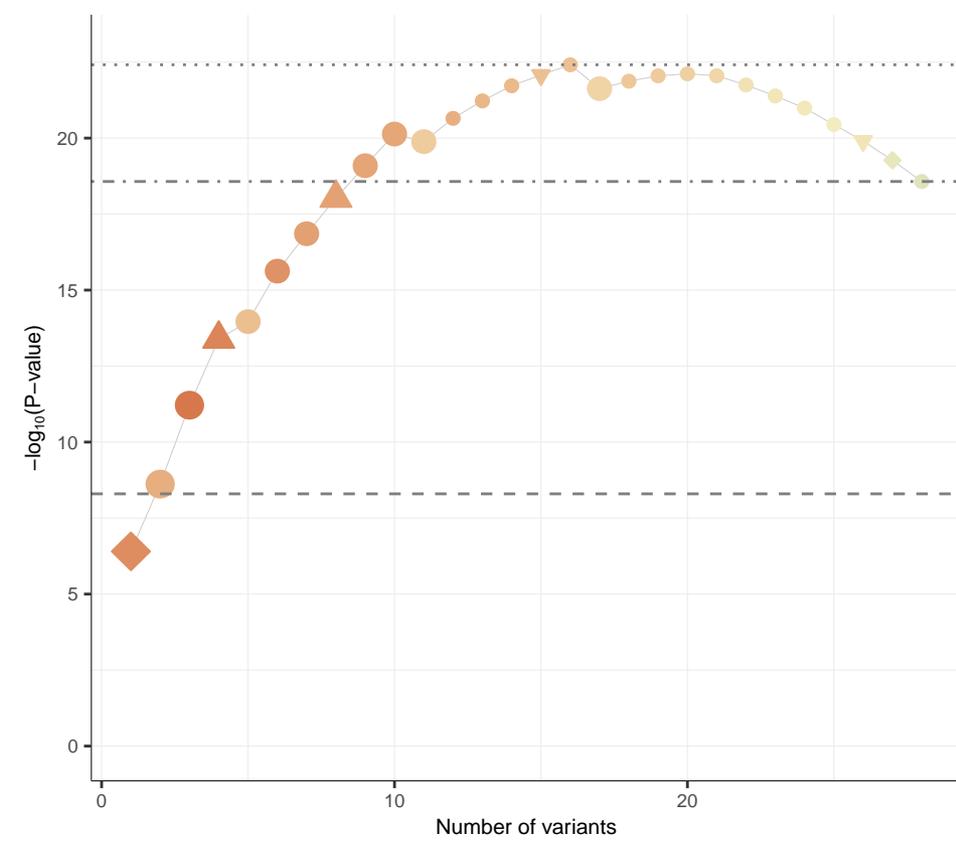
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

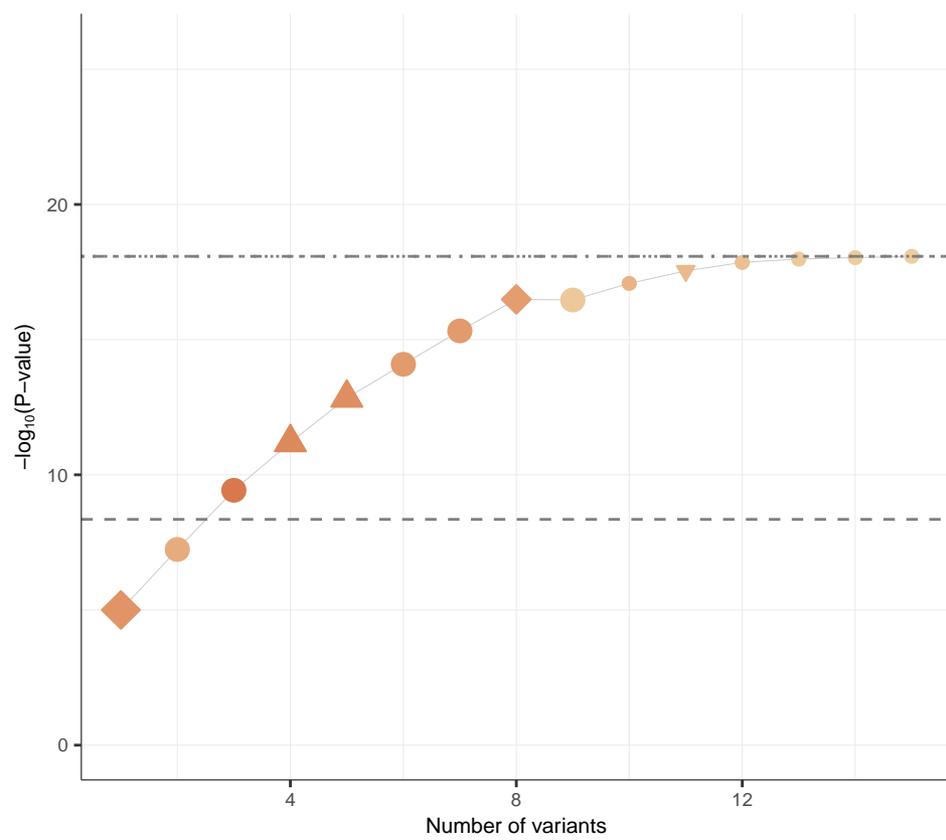
xanthurenate in plasma at *KYNU* (LoF_mis)



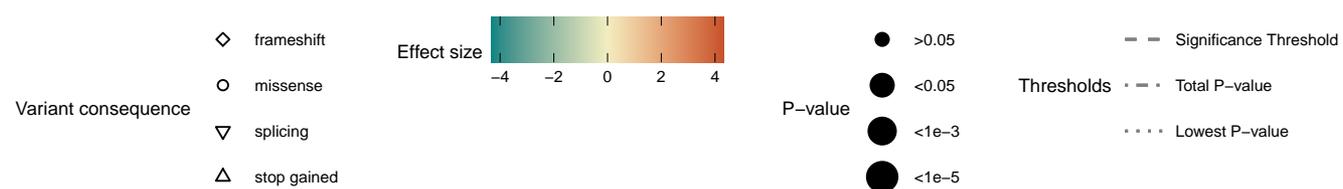
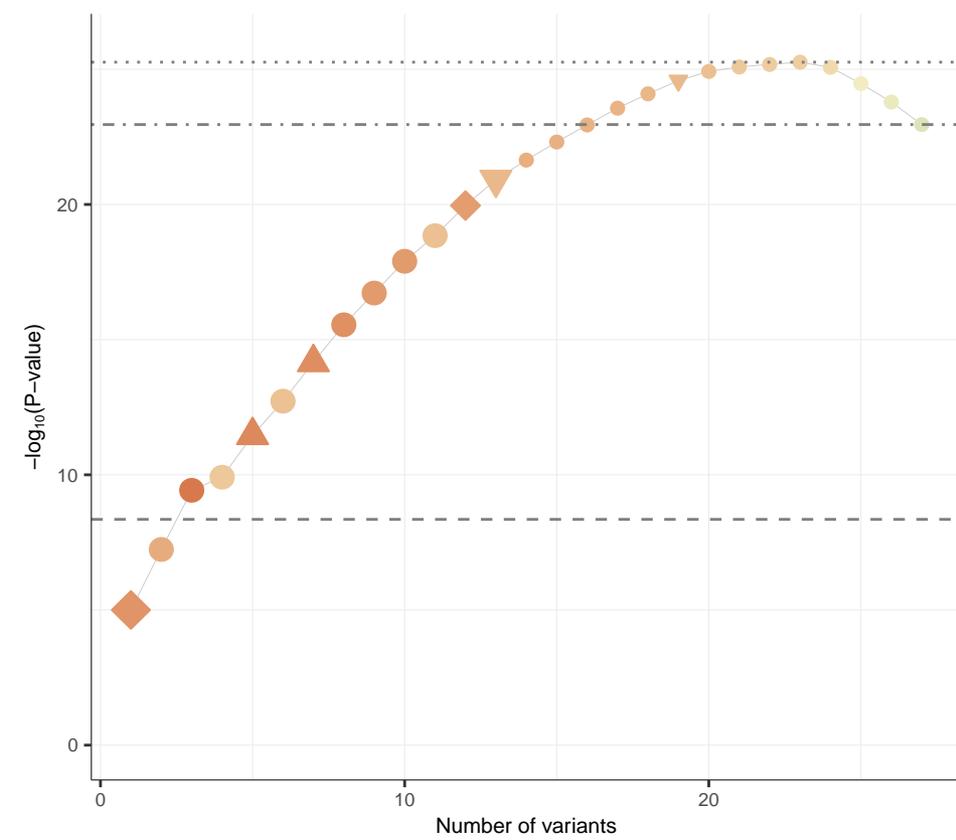
xanthurenate in plasma at *KYNU* (HI_mis)



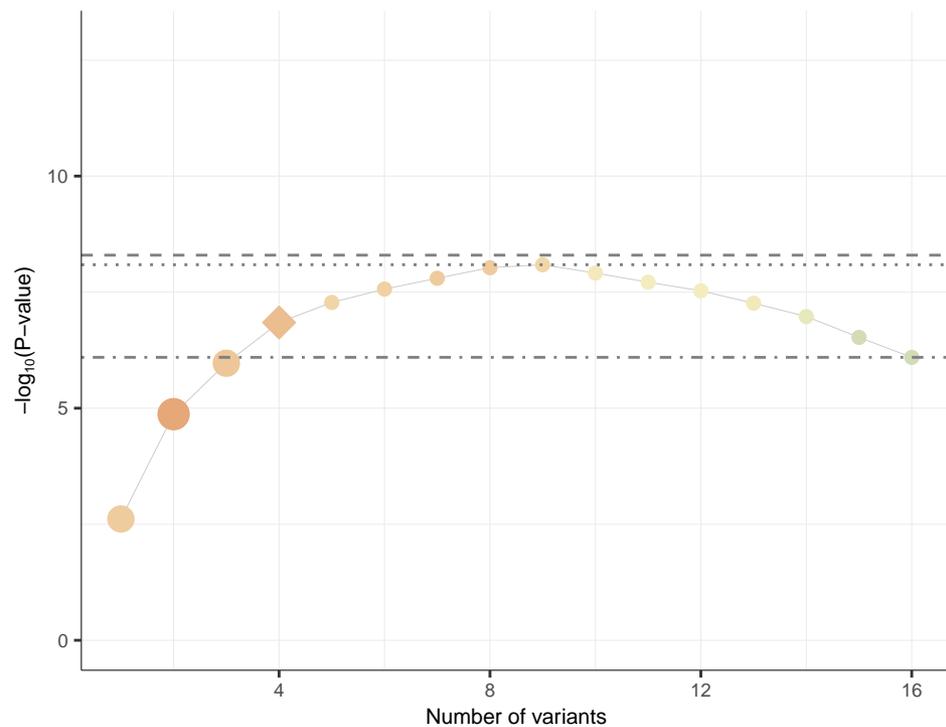
xanthurenate in urine at *KYNU* (LoF_mis)



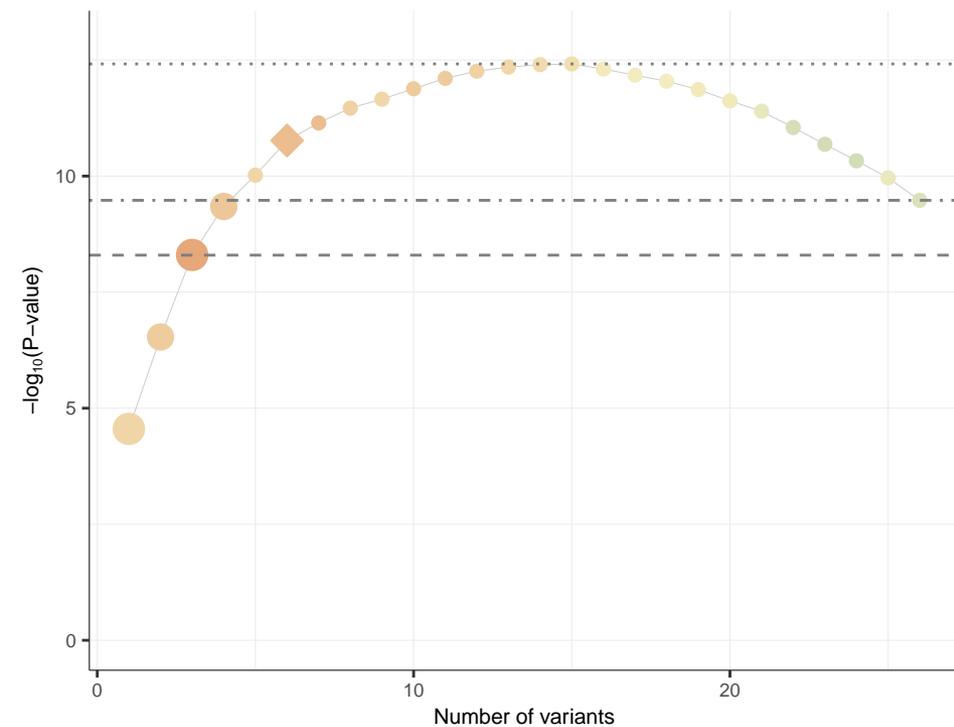
xanthurenate in urine at *KYNU* (HI_mis)



1-palmitoyl-2-arachidonoyl-GPE (16:0/20:4)* in plasma at *LIPC* (LoF_mis)

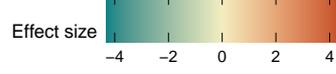


1-palmitoyl-2-arachidonoyl-GPE (16:0/20:4)* in plasma at *LIPC* (HI_mis)



Variant consequence

- ◇ frameshift
- missense



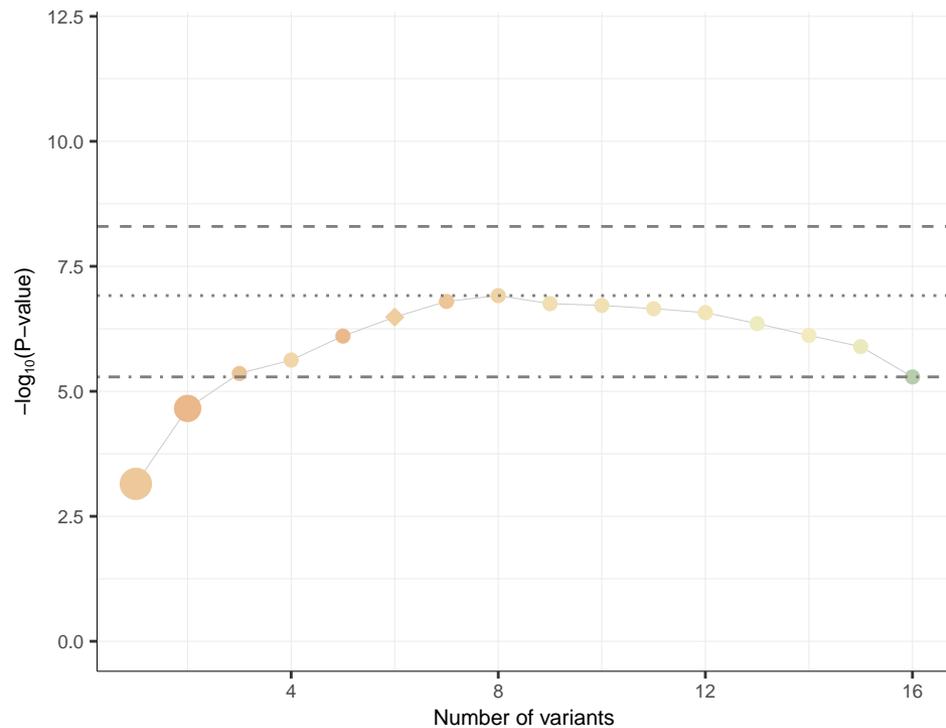
P-value

- >0.05
- <0.05
- <1e-3

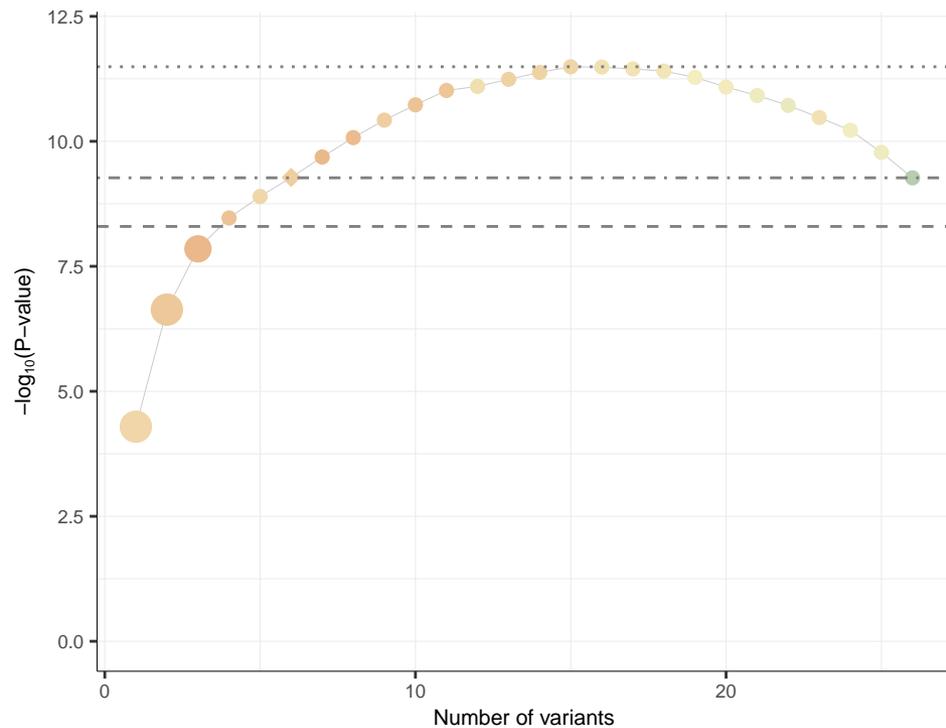
Thresholds

- - Significance Threshold
- · - Total P-value
- · · Lowest P-value

1-palmitoyl-2-docosahexaenoyl-GPE (16:0/22:6)* in plasma at *LIPC* (LoF_mis)

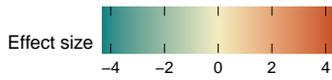


1-palmitoyl-2-docosahexaenoyl-GPE (16:0/22:6)* in plasma at *LIPC* (HI_mis)



Variant consequence

- ◇ frameshift
- missense



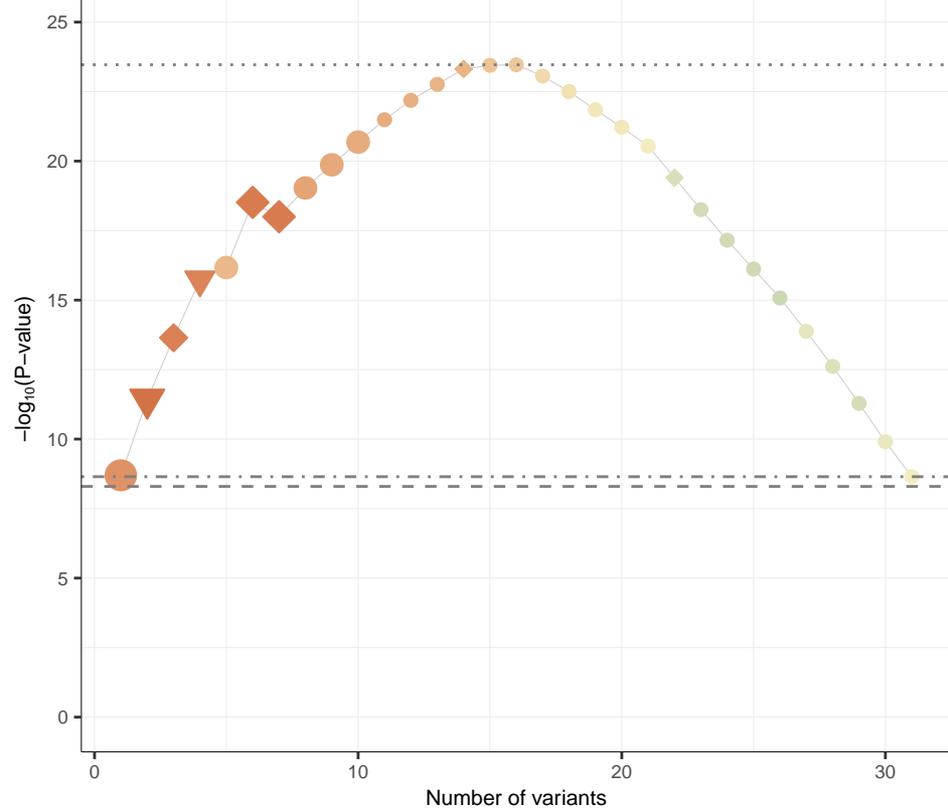
P-value

- >0.05
- <0.05
- <1e-3

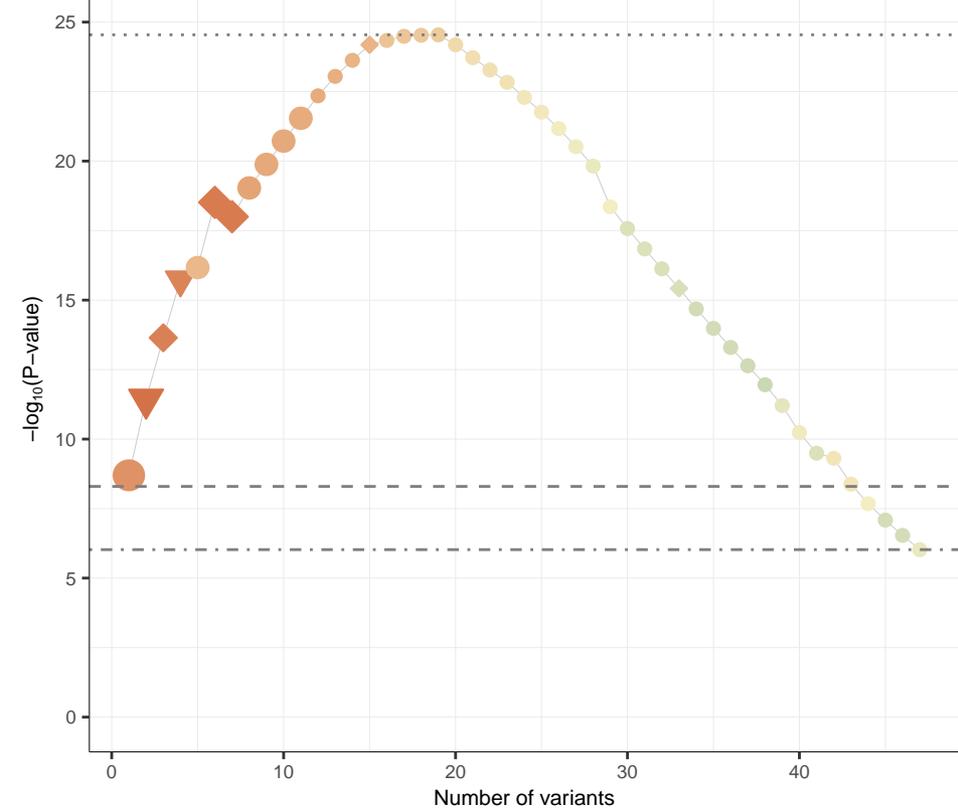
Thresholds

- - Significance Threshold
- . - Total P-value
- Lowest P-value

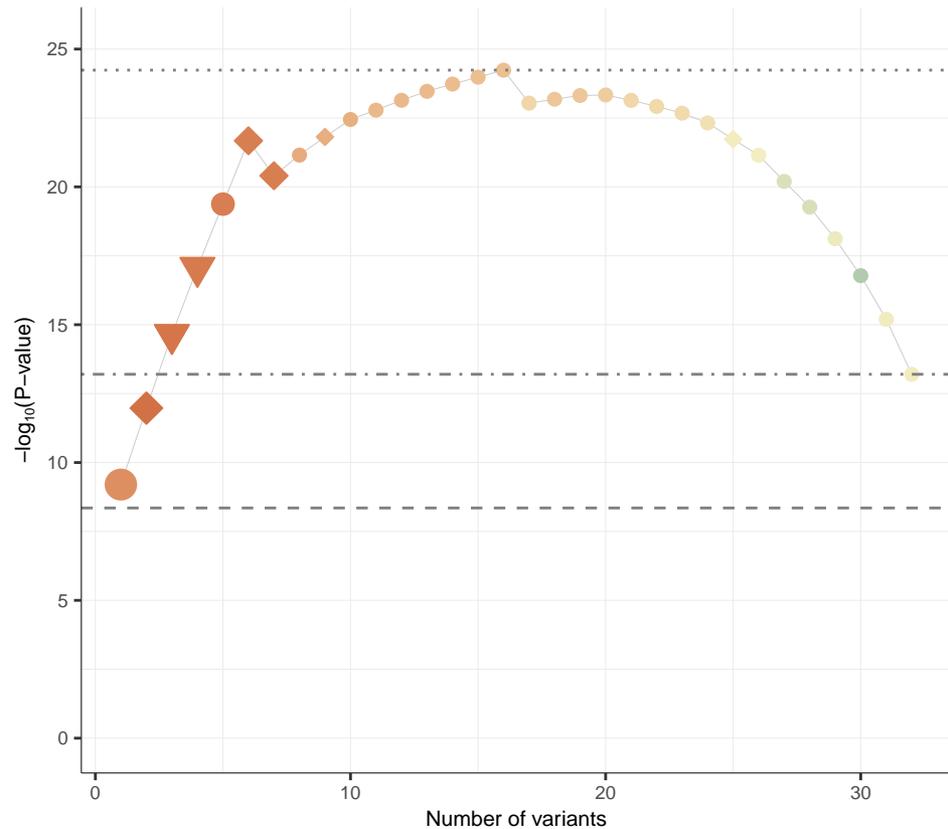
3-methylcrotonylglycine in plasma at *MCCC1* (LoF_mis)



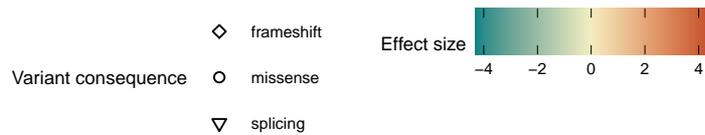
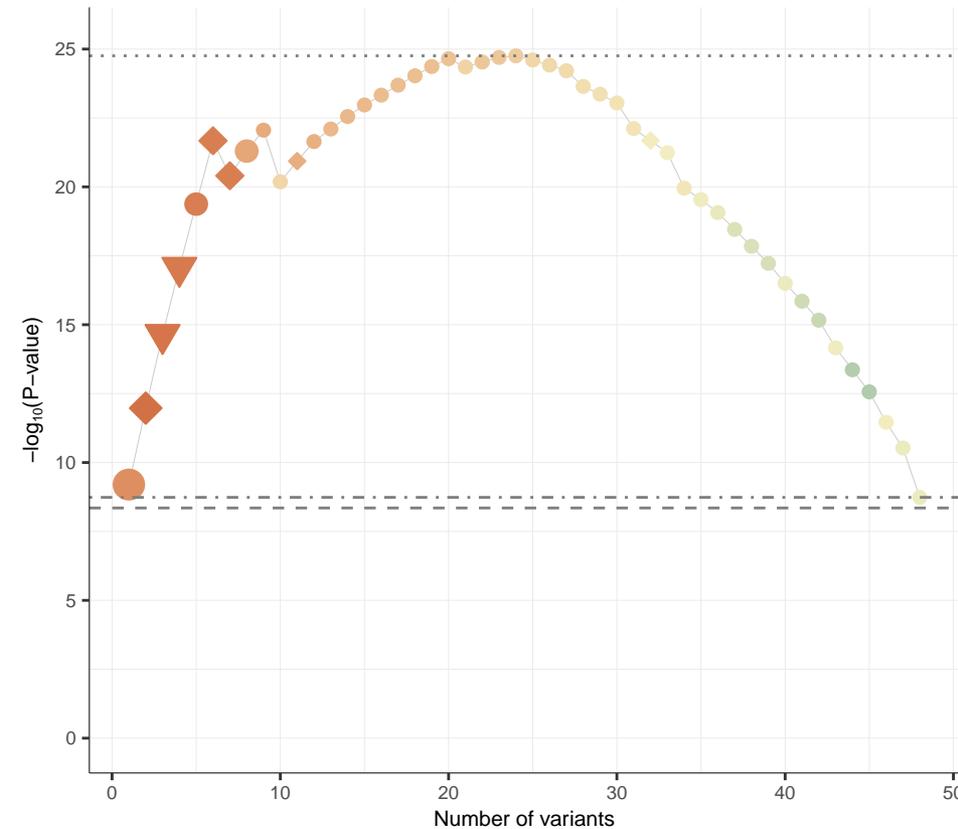
3-methylcrotonylglycine in plasma at *MCCC1* (HI_mis)



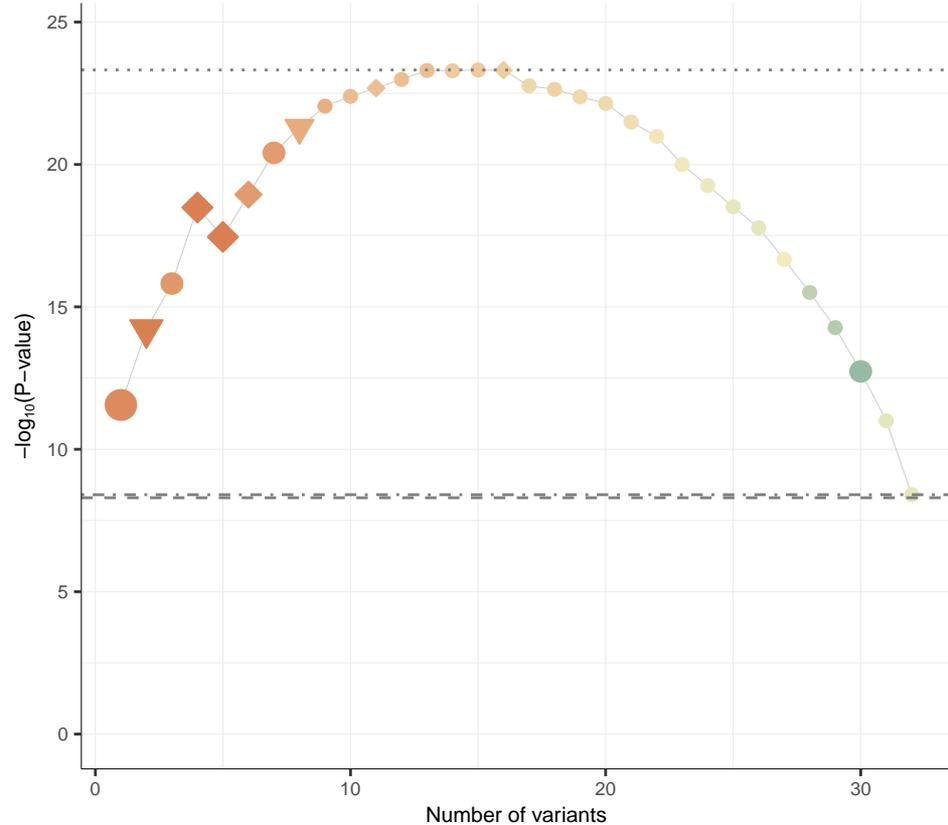
3-methylcrotonylglycine in urine at *MCCC1* (LoF_mis)



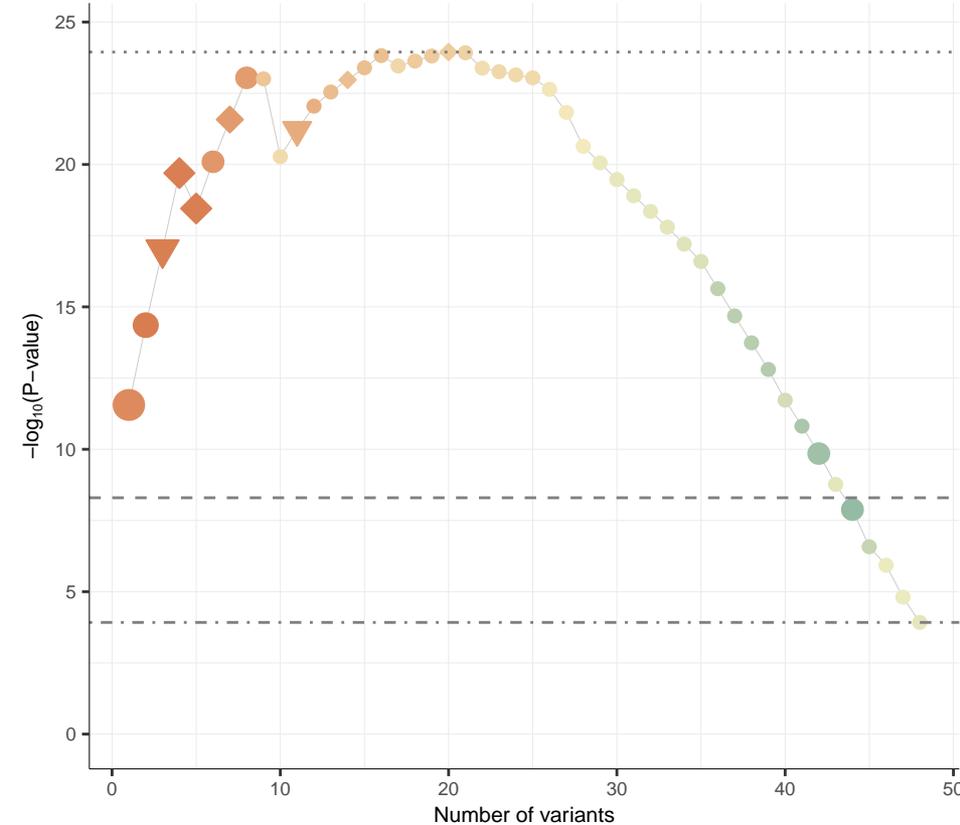
3-methylcrotonylglycine in urine at *MCCC1* (HI_mis)



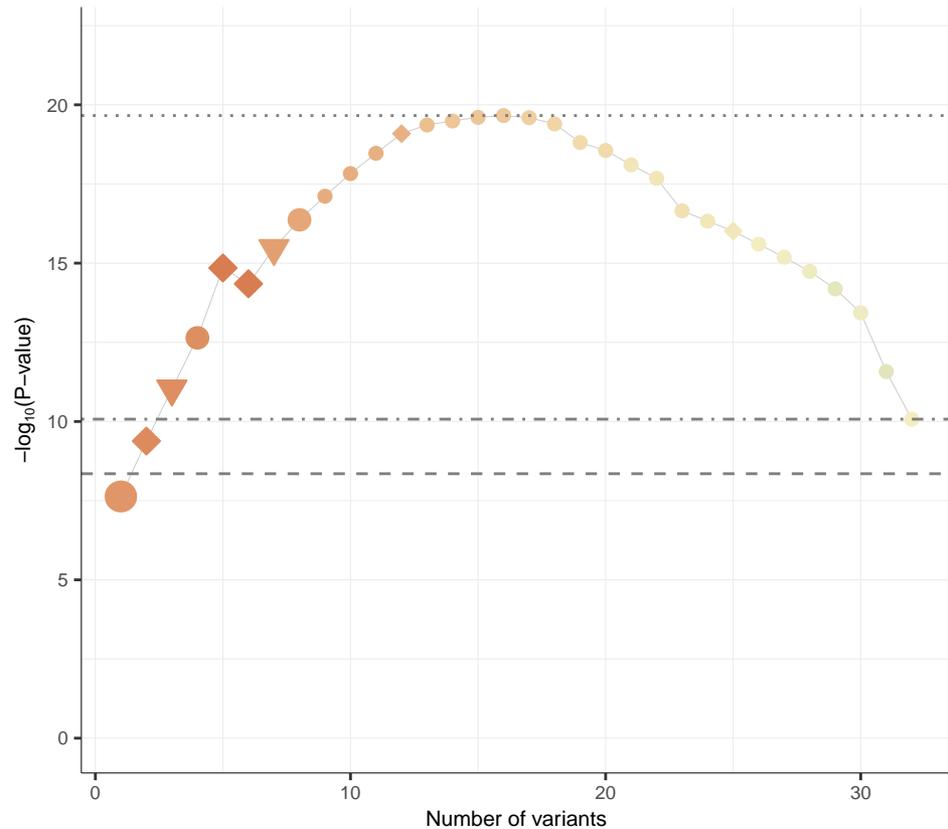
beta-hydroxyisovaleroylcarnitine in plasma at *MCCC1* (LoF_mis)



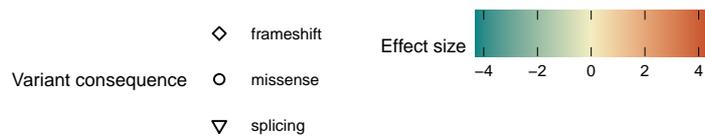
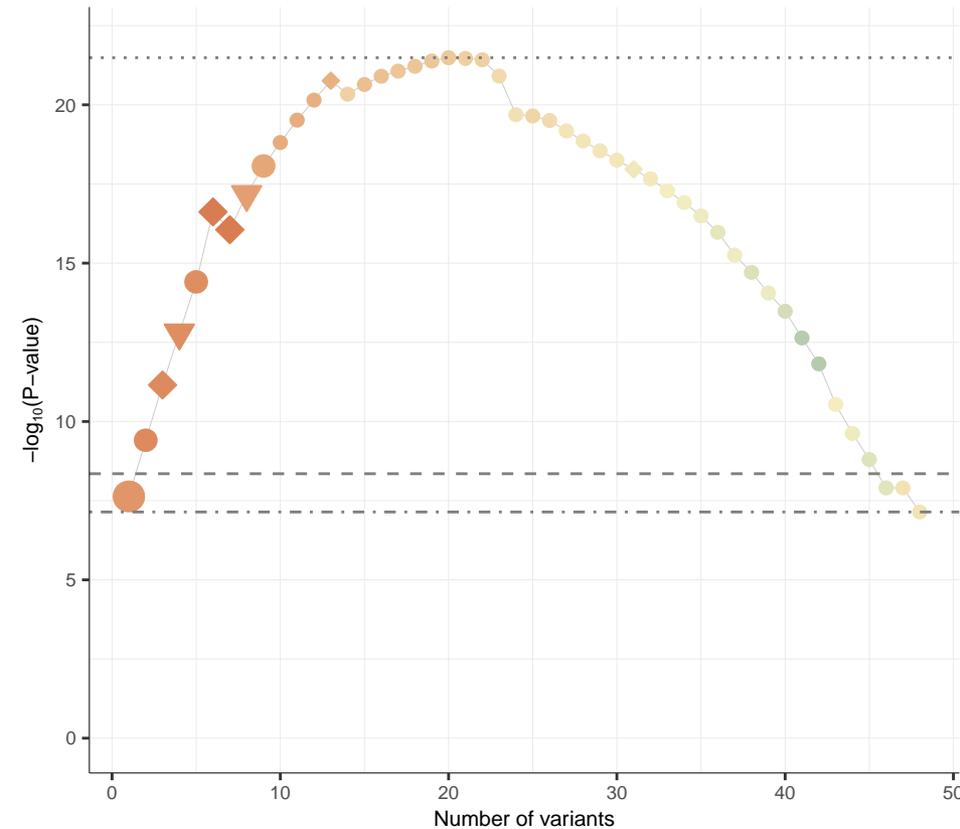
beta-hydroxyisovaleroylcarnitine in plasma at *MCCC1* (HI_mis)



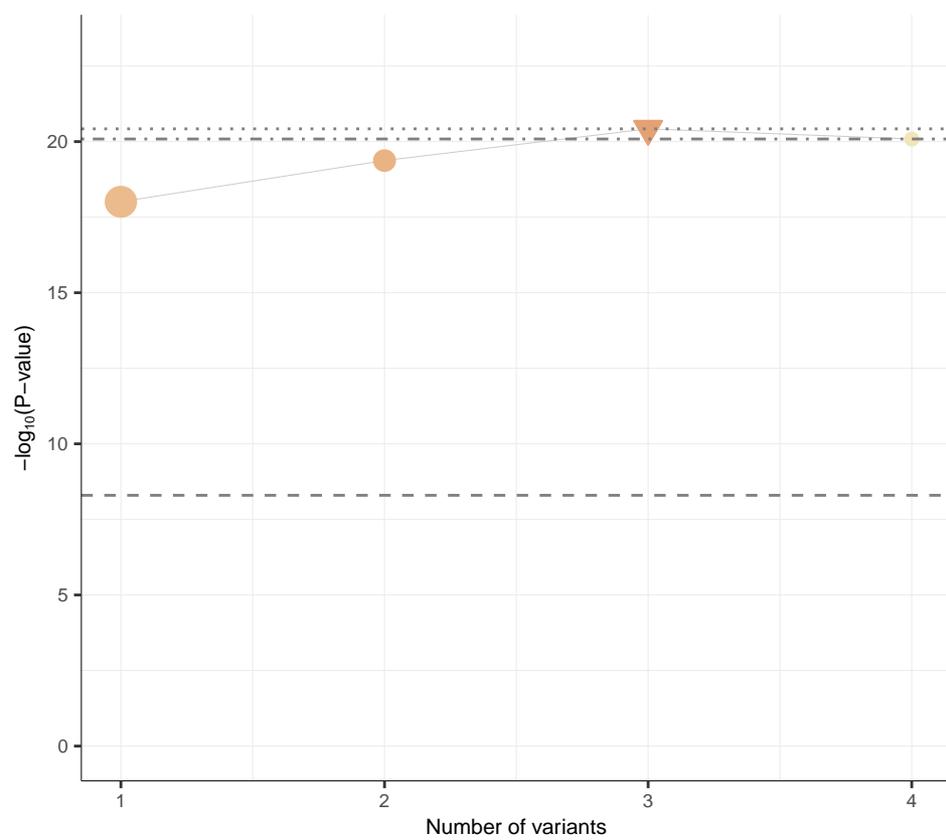
beta-hydroxyisovaleroylcarnitine in urine at *MCCC1* (LoF_mis)



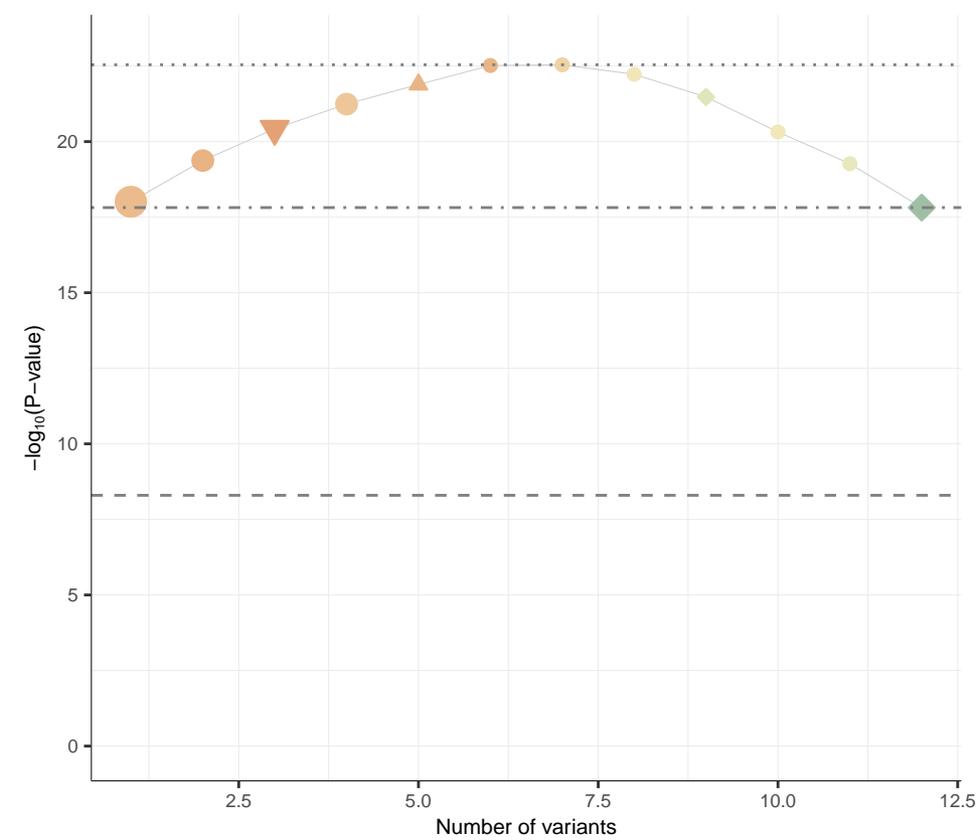
beta-hydroxyisovaleroylcarnitine in urine at *MCCC1* (HI_mis)



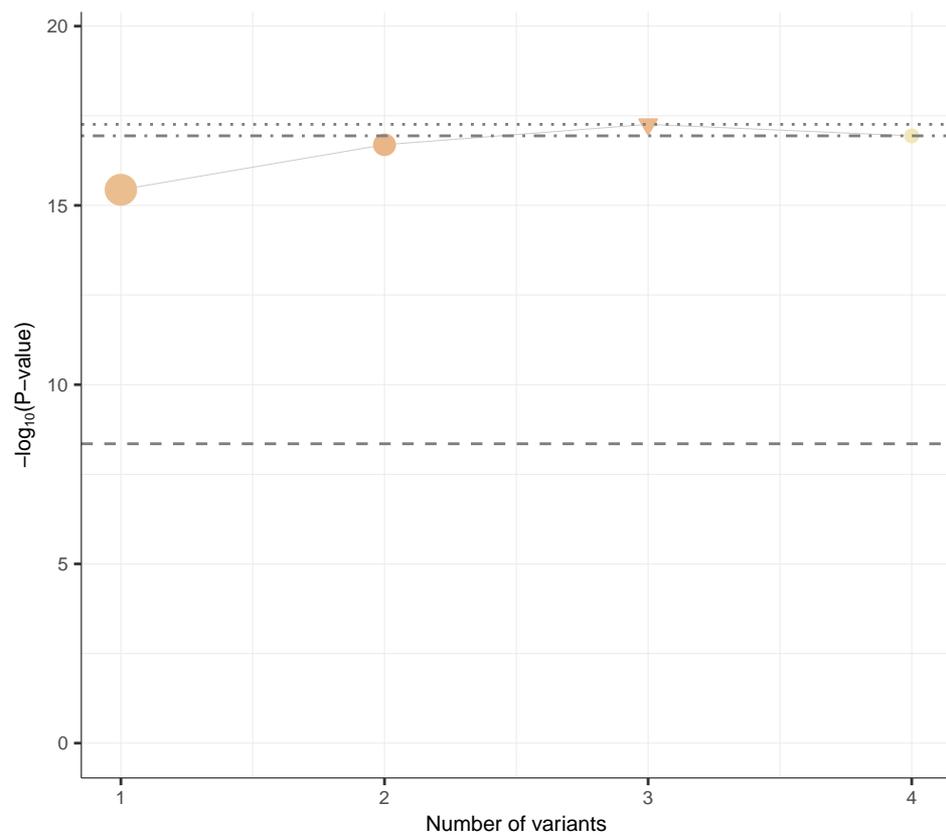
X - 13684 in plasma at MPST (LoF_mis)



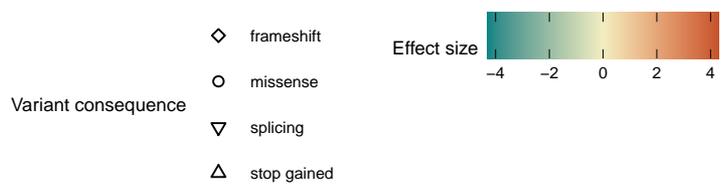
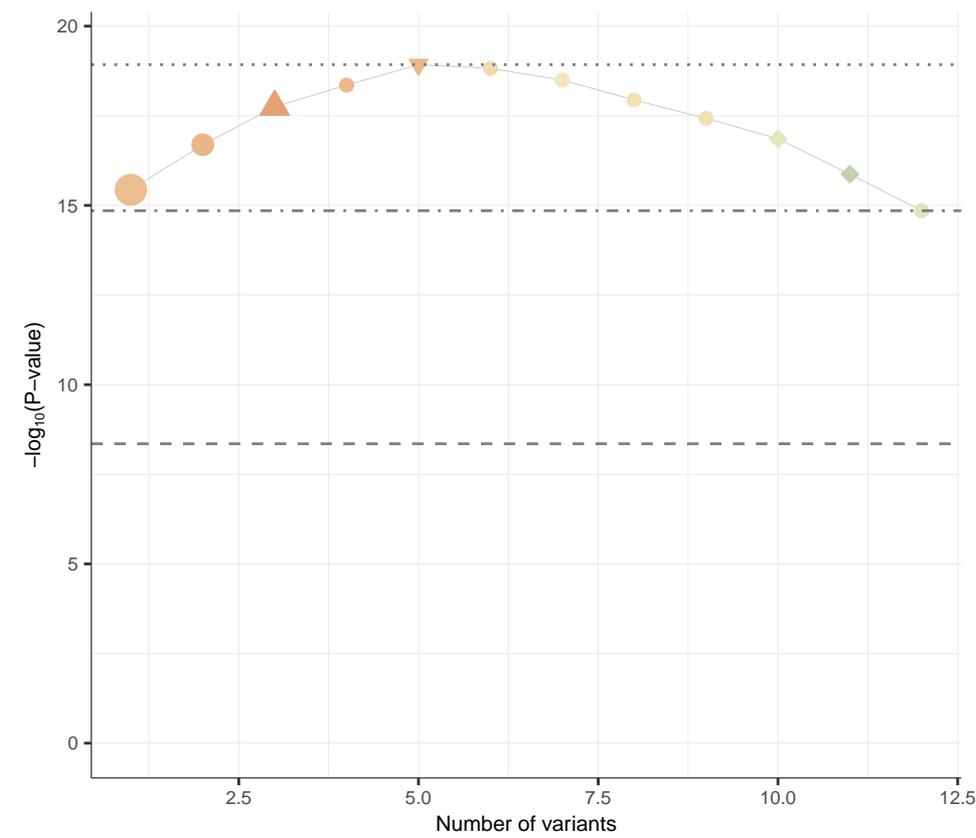
X - 13684 in plasma at MPST (HI_mis)



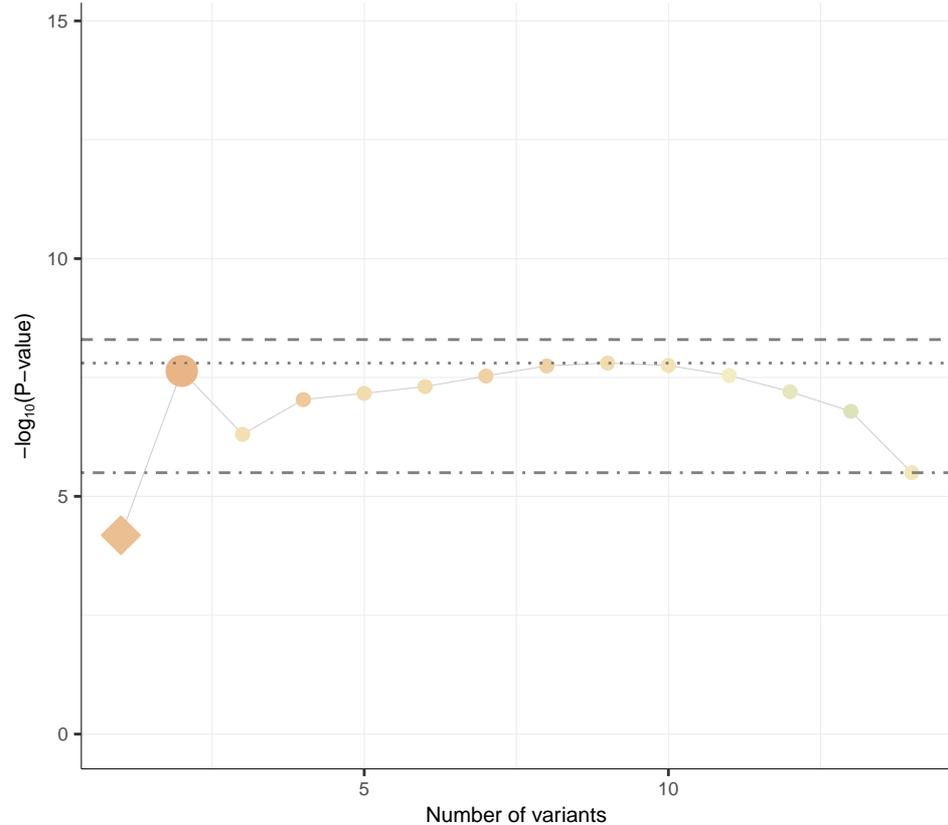
X - 13684 in urine at MPST (LoF_mis)



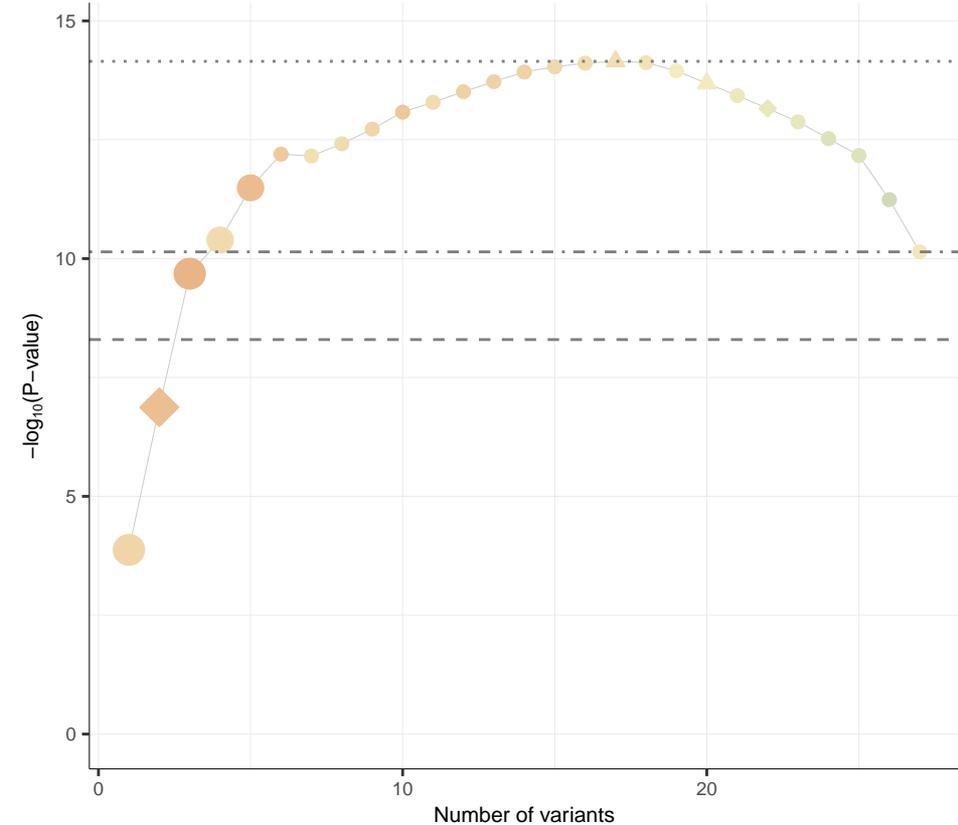
X - 13684 in urine at MPST (HI_mis)



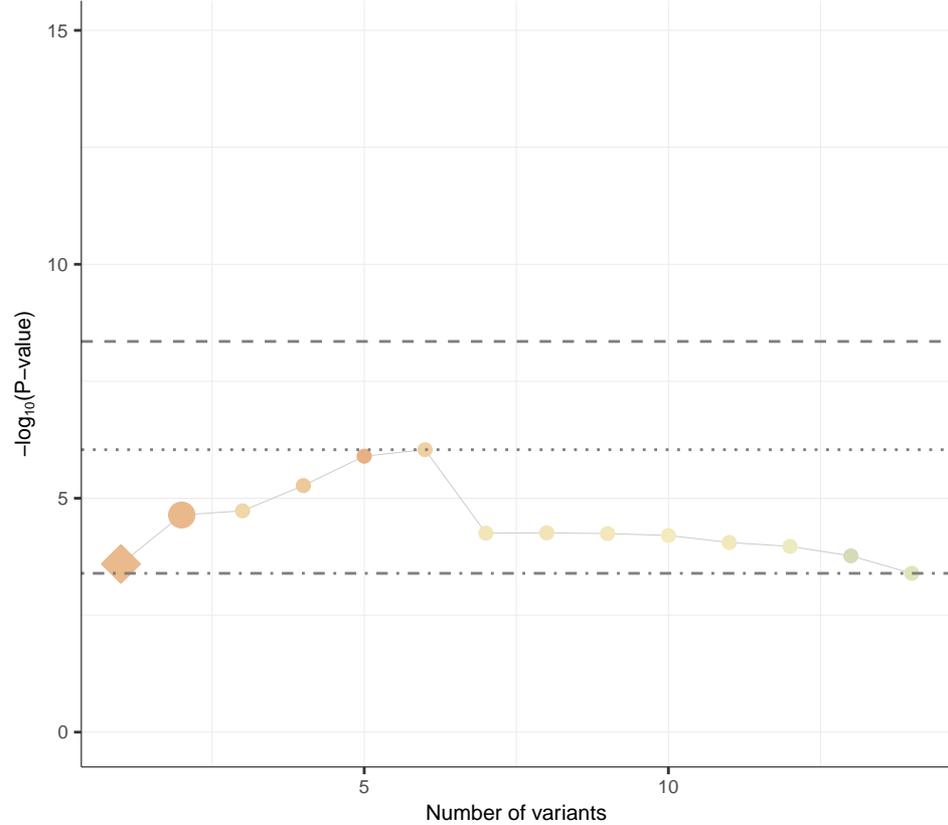
X - 12411 in plasma at *MRI1* (LoF_mis)



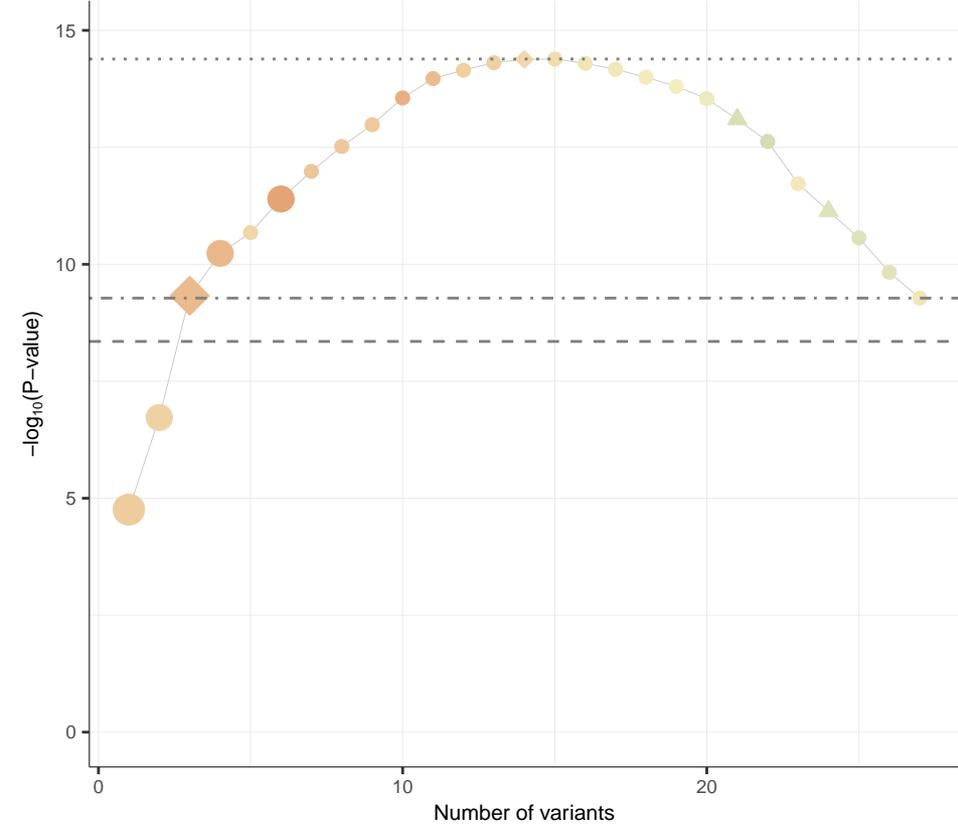
X - 12411 in plasma at *MRI1* (HI_mis)



X - 12411 in urine at *MRI1* (LoF_mis)

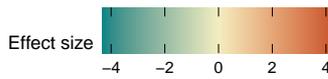


X - 12411 in urine at *MRI1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



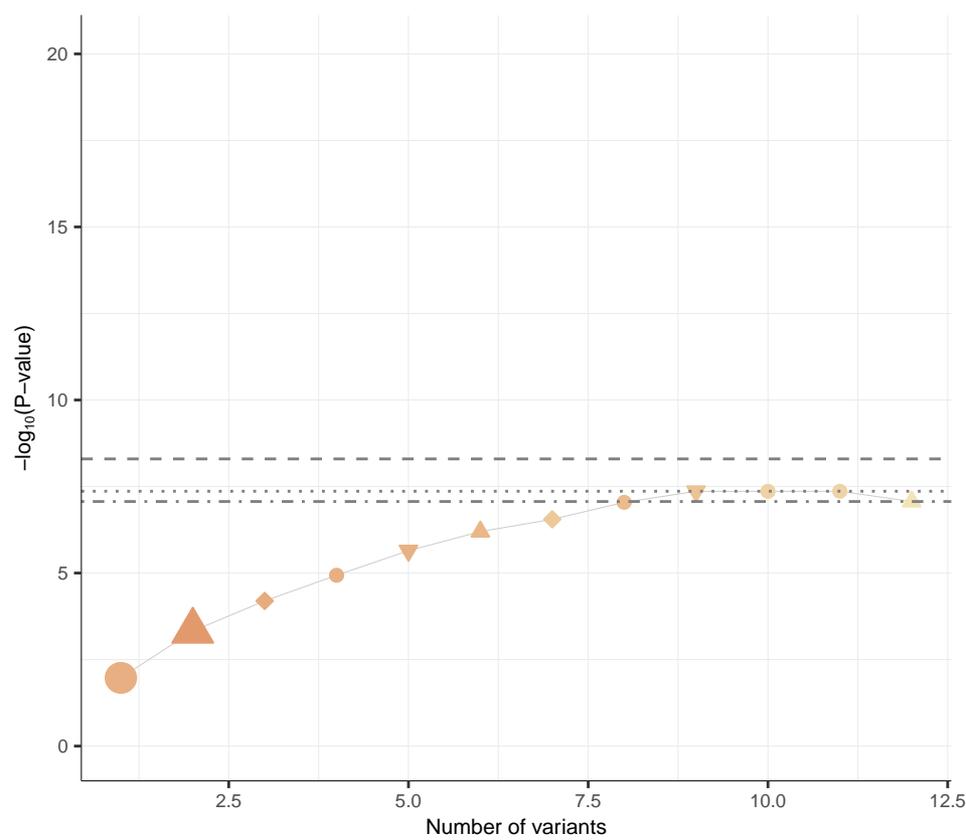
P-value

- >0.05
- <0.05
- <1e-3

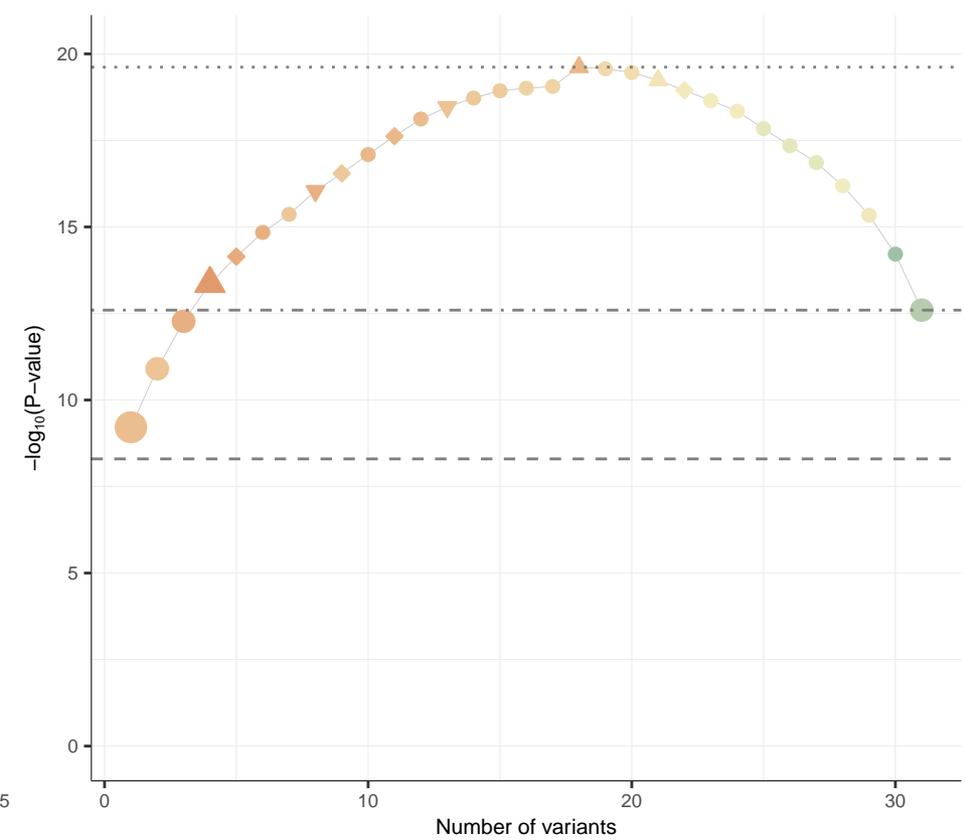
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

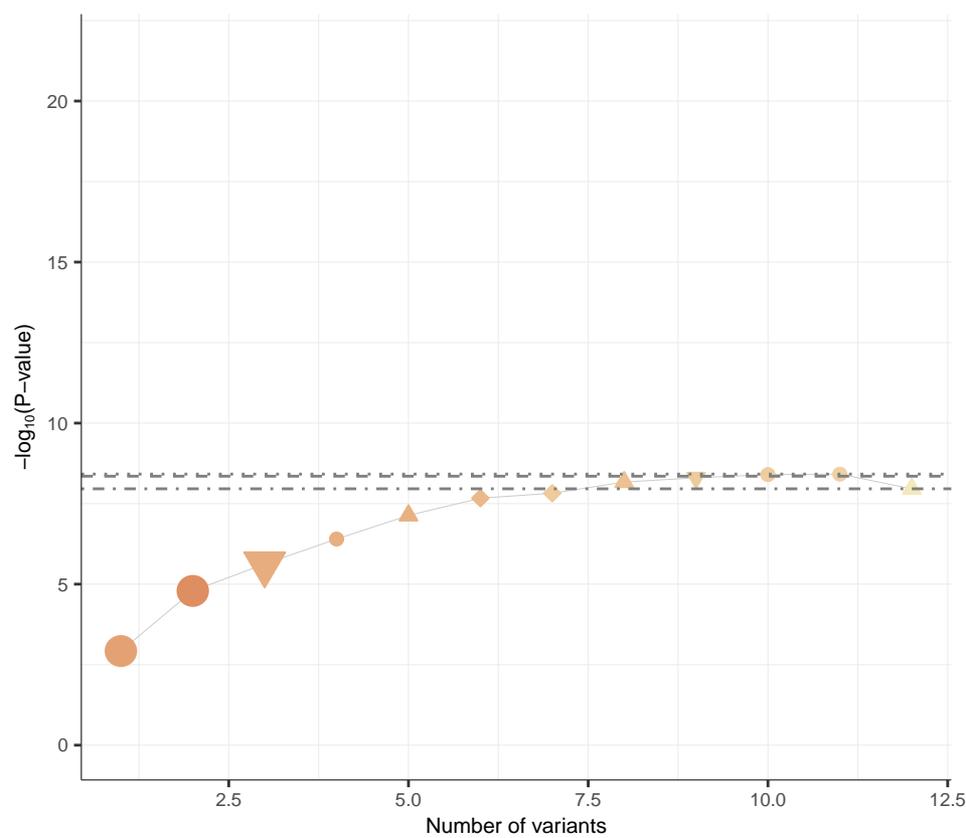
beta-citrylglutamate in plasma at NAALAD2 (LoF_mis)



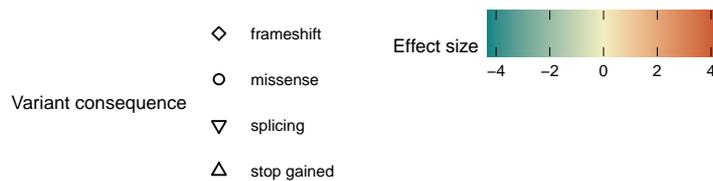
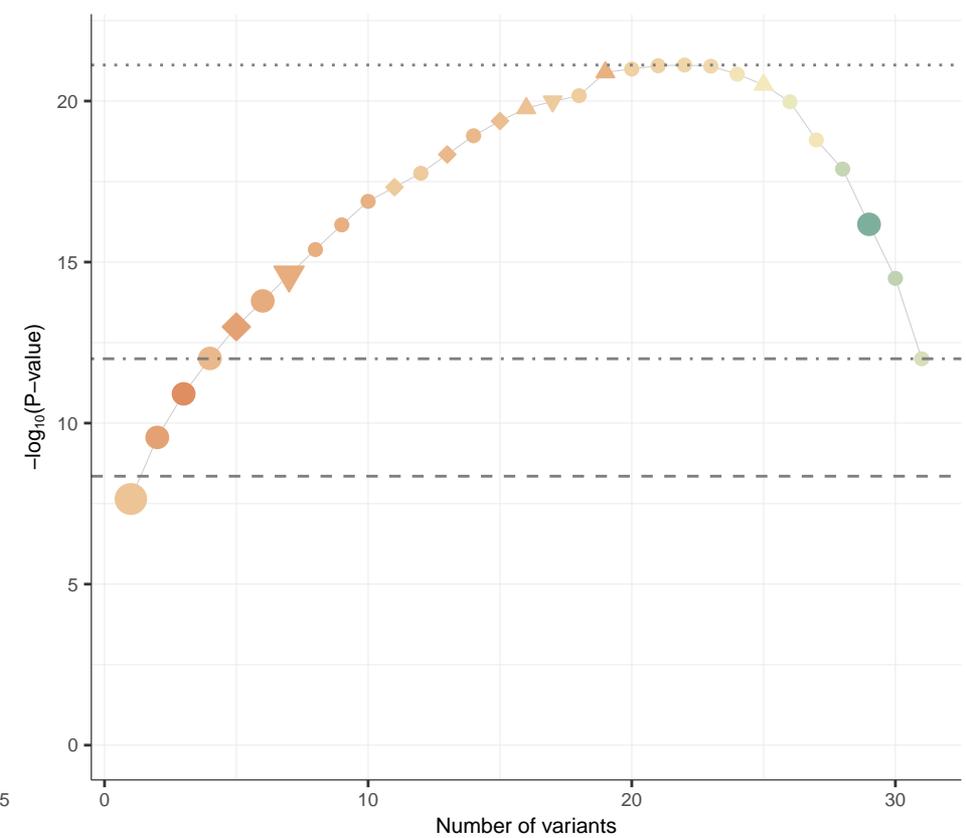
beta-citrylglutamate in plasma at NAALAD2 (HI_mis)



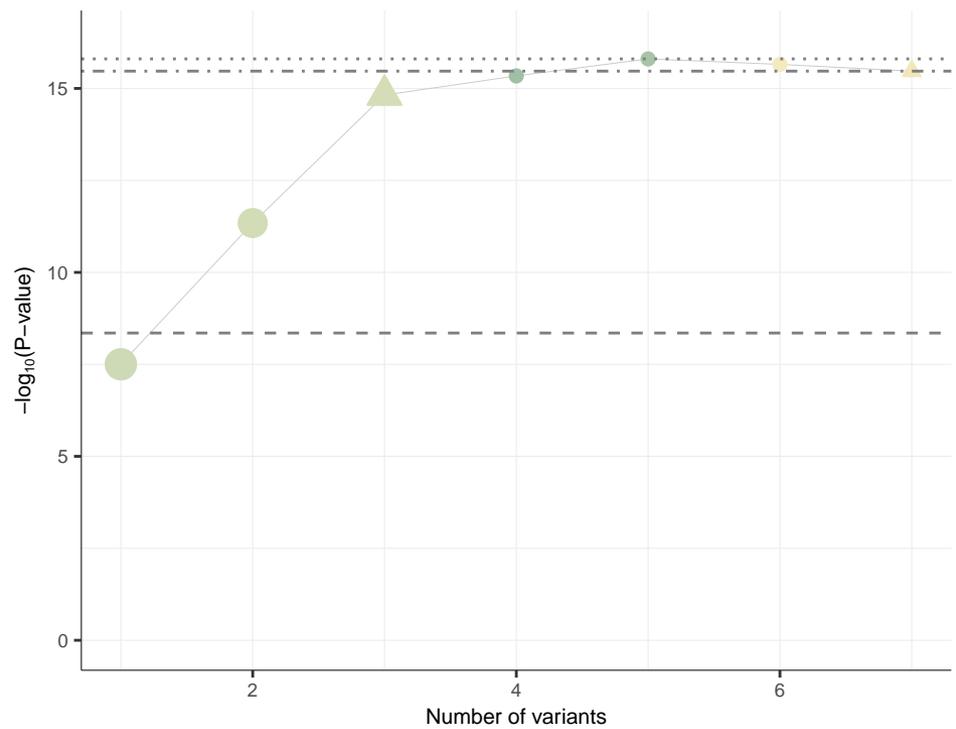
beta-citrylglutamate in urine at NAALAD2 (LoF_mis)



beta-citrylglutamate in urine at NAALAD2 (HI_mis)



X - 12410 in urine at NAT1 (HI_mis)



Variant consequence

- missense
- △ stop gained

Effect size

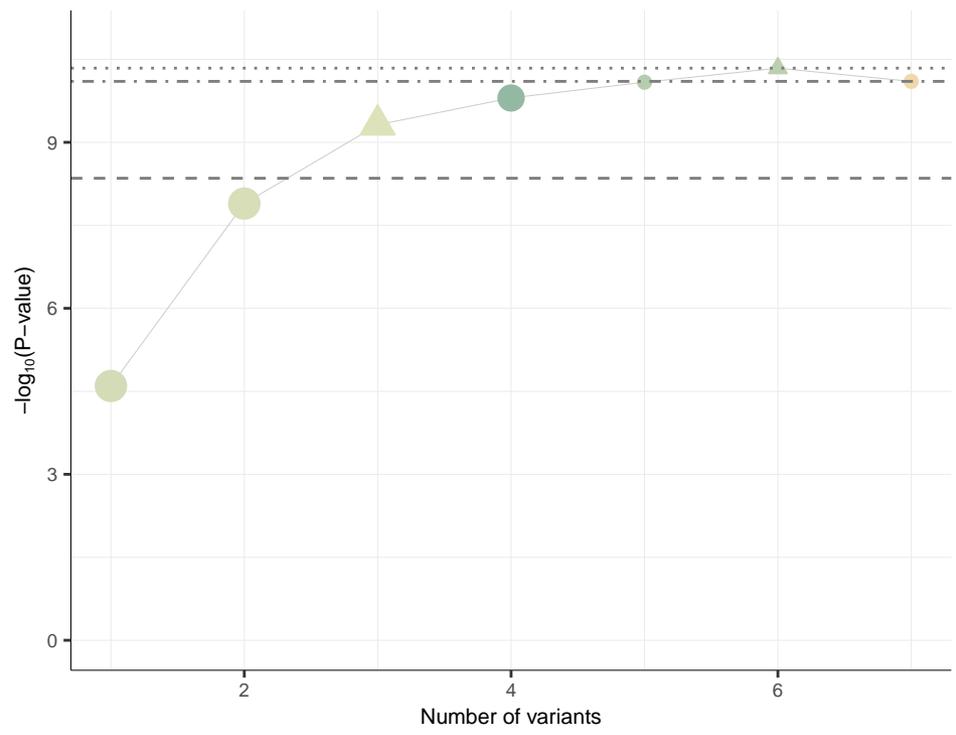
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

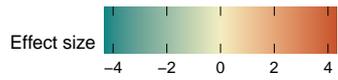
Thresholds

- - Significance Threshold
- . - Total P-value
- . . . Lowest P-value

X – 15461 in urine at *NAT1* (HI_mis)



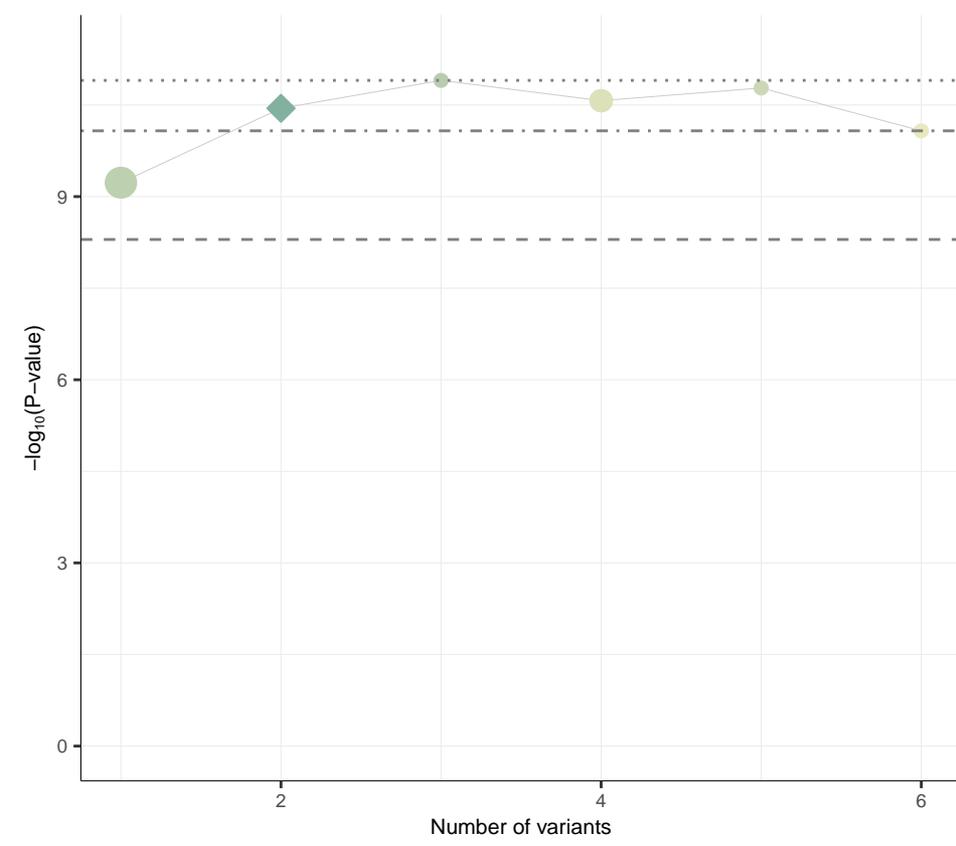
Variant consequence
 ○ missense
 △ stop gained



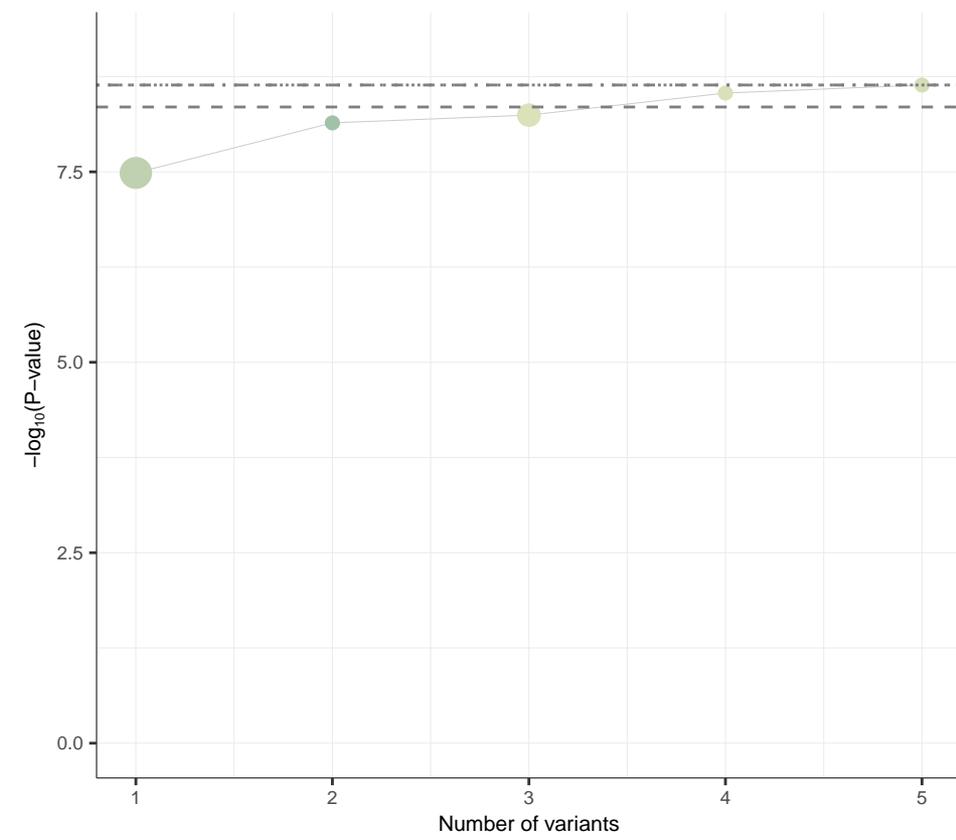
P-value
 ● >0.05
 ● <0.05
 ● <1e-3

Thresholds
 - - Significance Threshold
 - - - Total P-value
 . . . Lowest P-value

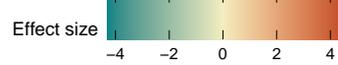
N-acetylarginine in plasma at NAT8 (HI_mis)



N-acetylarginine in urine at NAT8 (HI_mis)



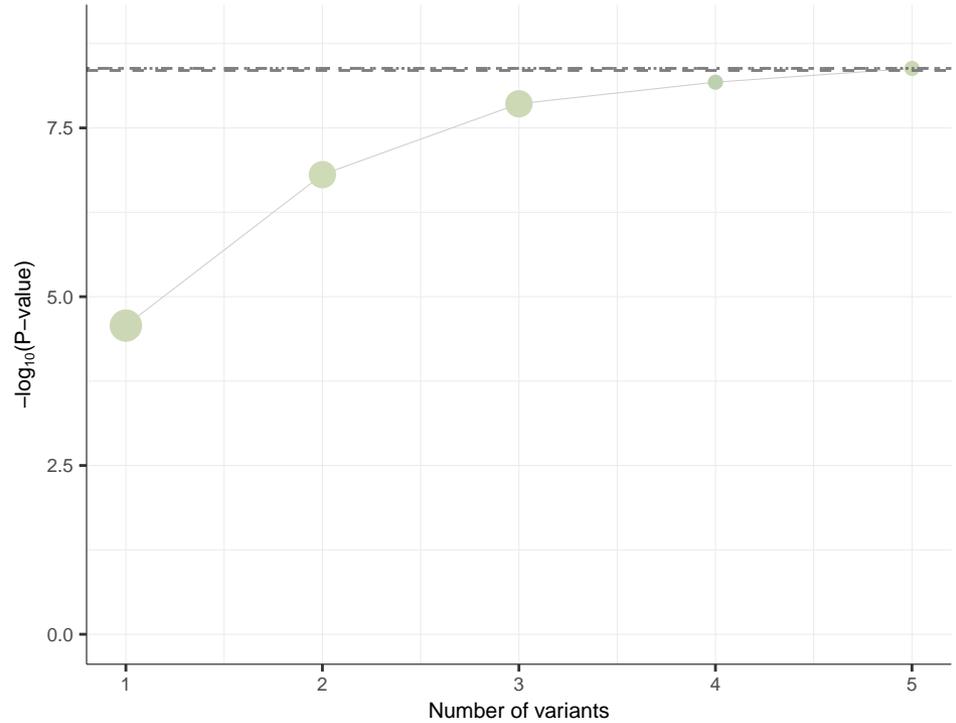
Variant consequence ○ missense



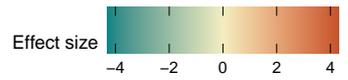
- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

- Significance Threshold
- Total P-value
- ... Lowest P-value

N-acetylhistidine in urine at NAT8 (HI_mis)



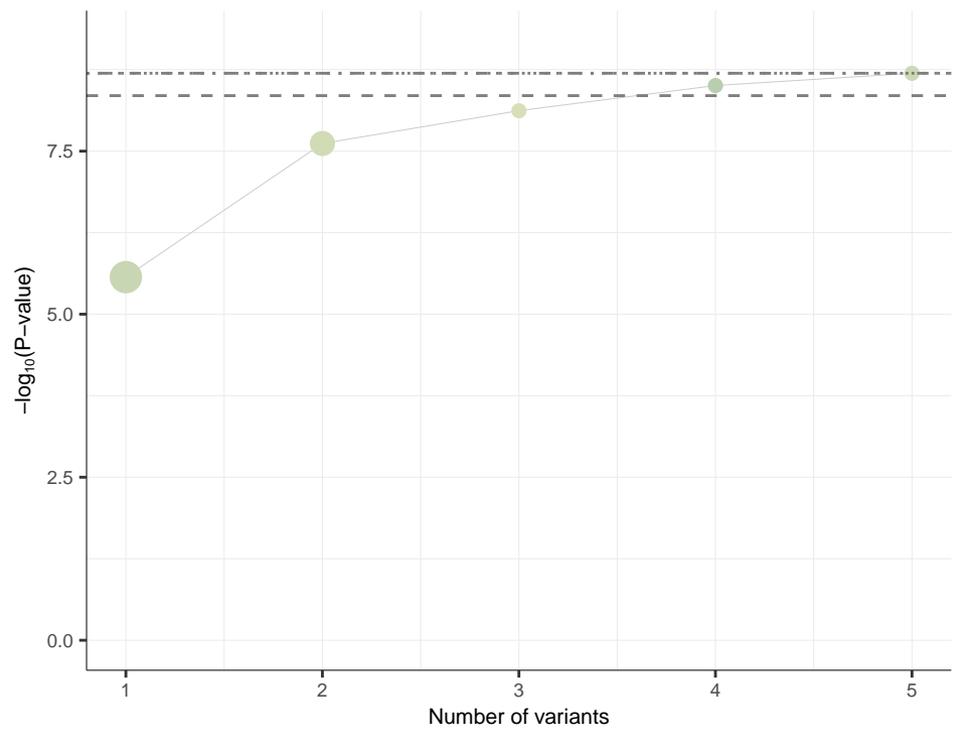
Variant consequence ○ missense



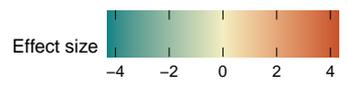
P-value ● >0.05
● <0.05
● <1e-3

Thresholds - - Significance Threshold
- · - Total P-value
· · · Lowest P-value

N-acetyliso-leucine in urine at NAT8 (HI_mis)



Variant consequence ○ missense



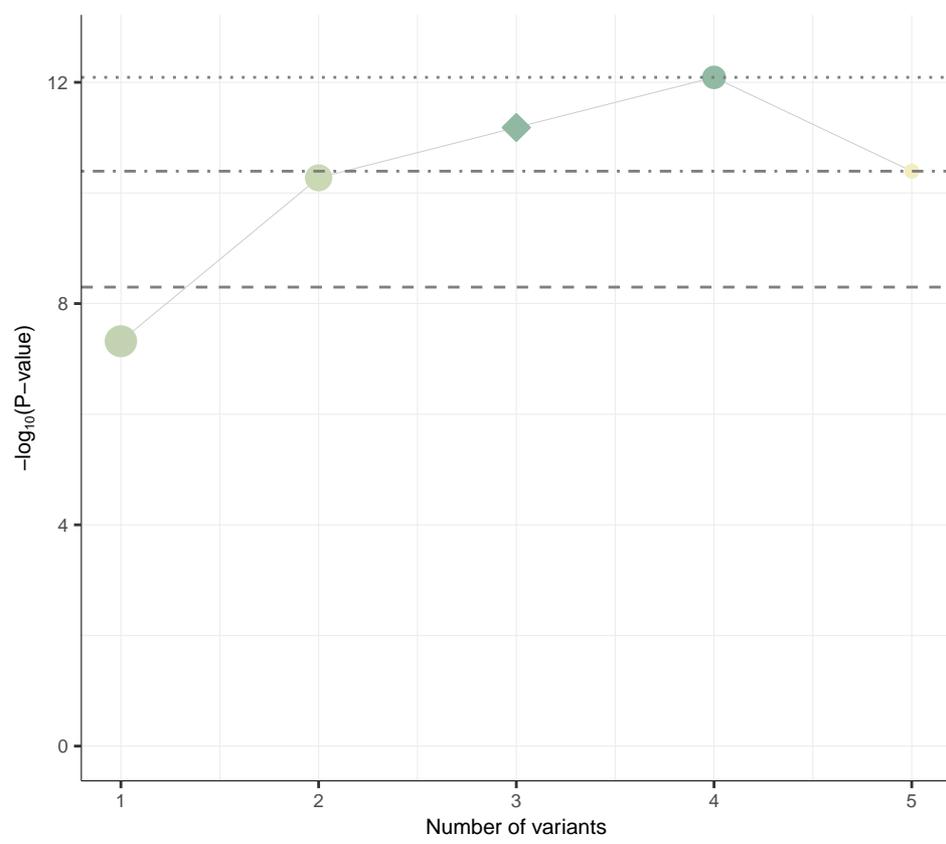
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

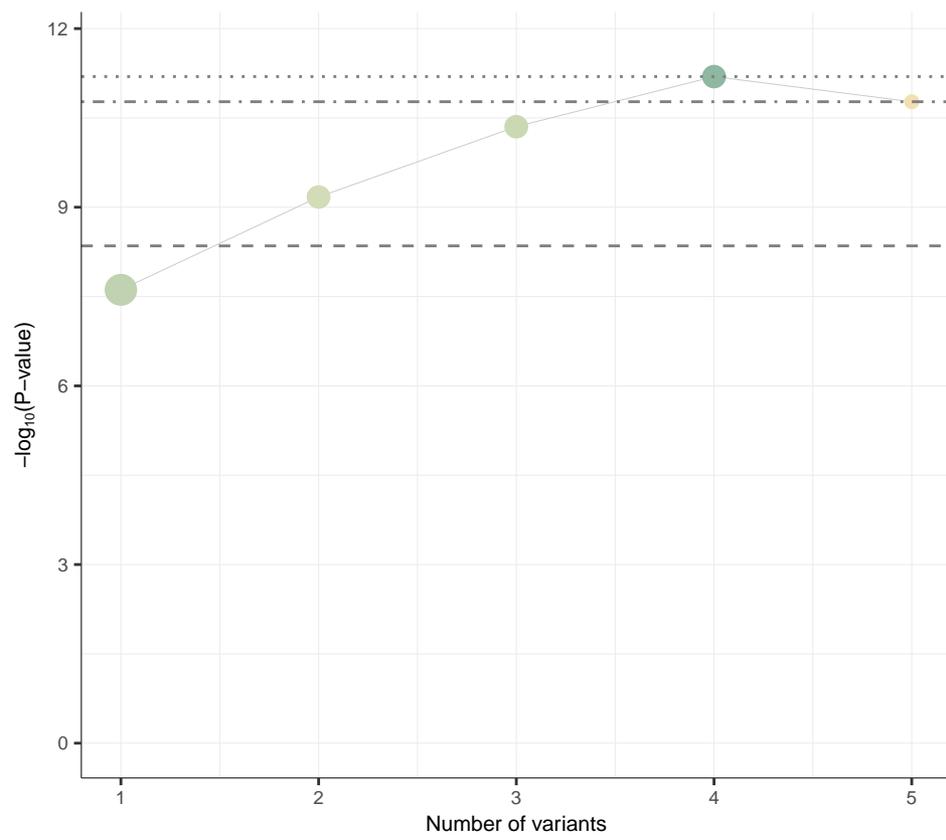
Thresholds

- Significance Threshold
- . - Total P-value
- Lowest P-value

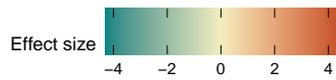
N-acetyltryptophan in plasma at *NAT8* (HI_mis)



N-acetyltryptophan in urine at *NAT8* (HI_mis)



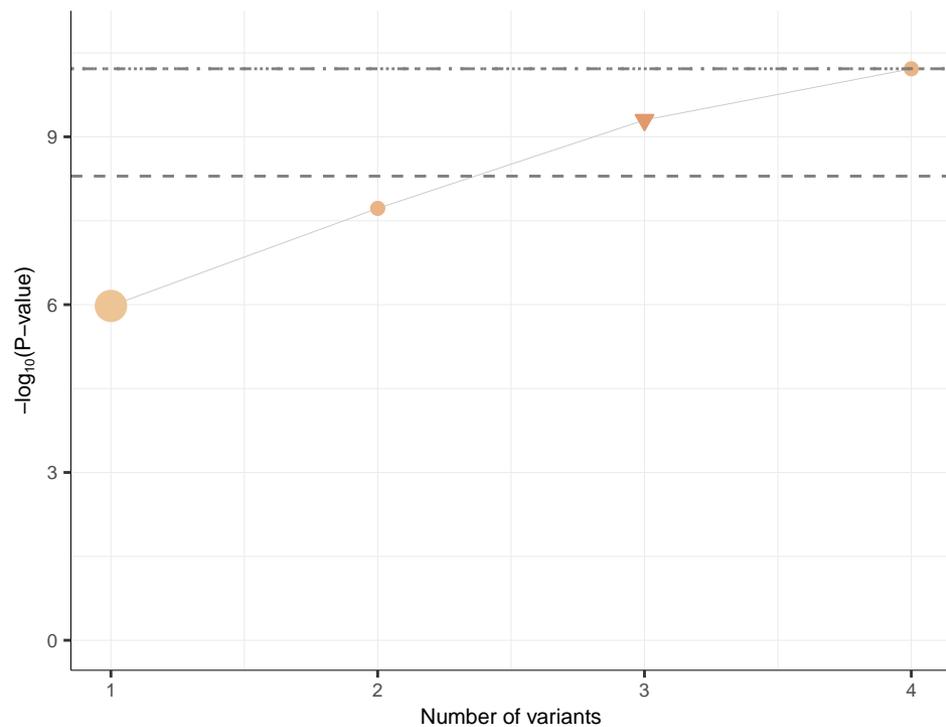
Variant consequence ○ missense



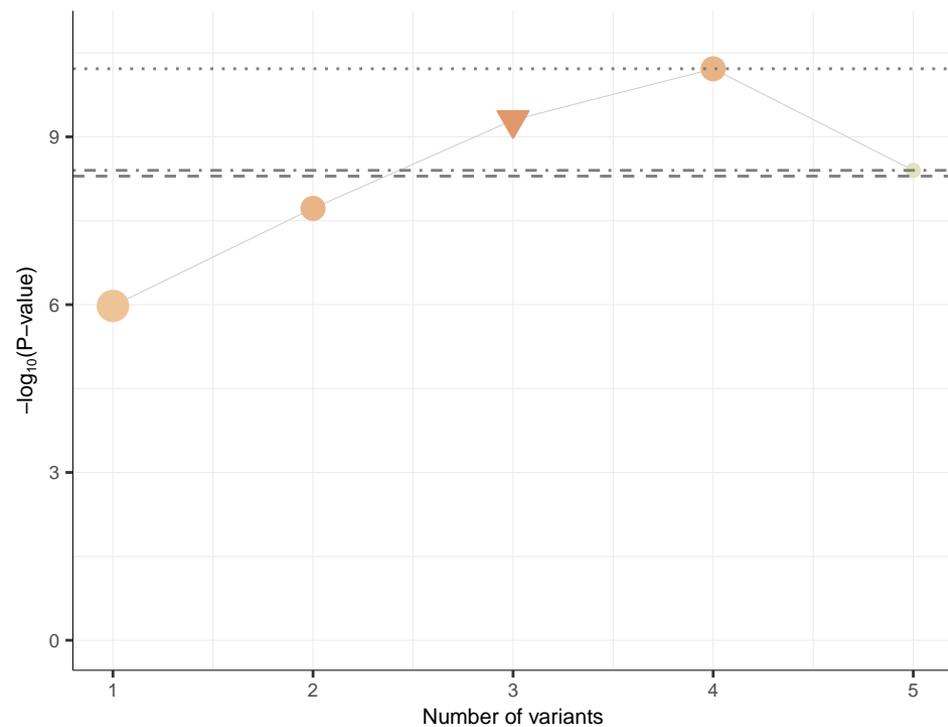
- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

- Significance Threshold
- Total P-value
- ... Lowest P-value

alpha-ketoglutaramate* in plasma at *NIT2* (LoF_mis)

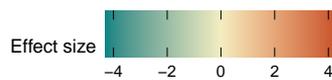


alpha-ketoglutaramate* in plasma at *NIT2* (HI_mis)



Variant consequence

- missense
- ▽ splicing



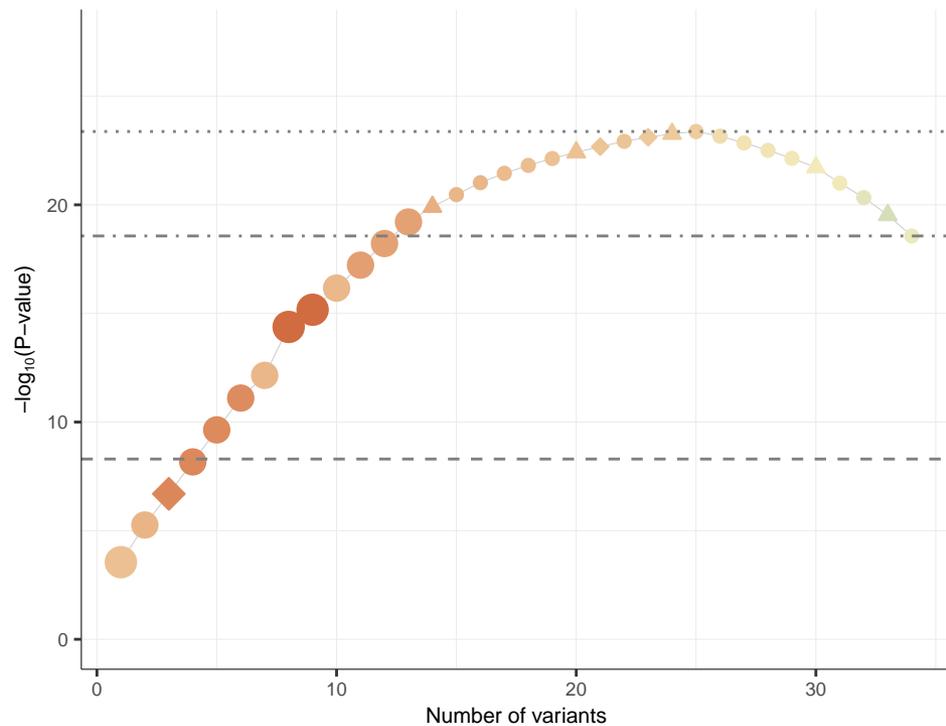
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

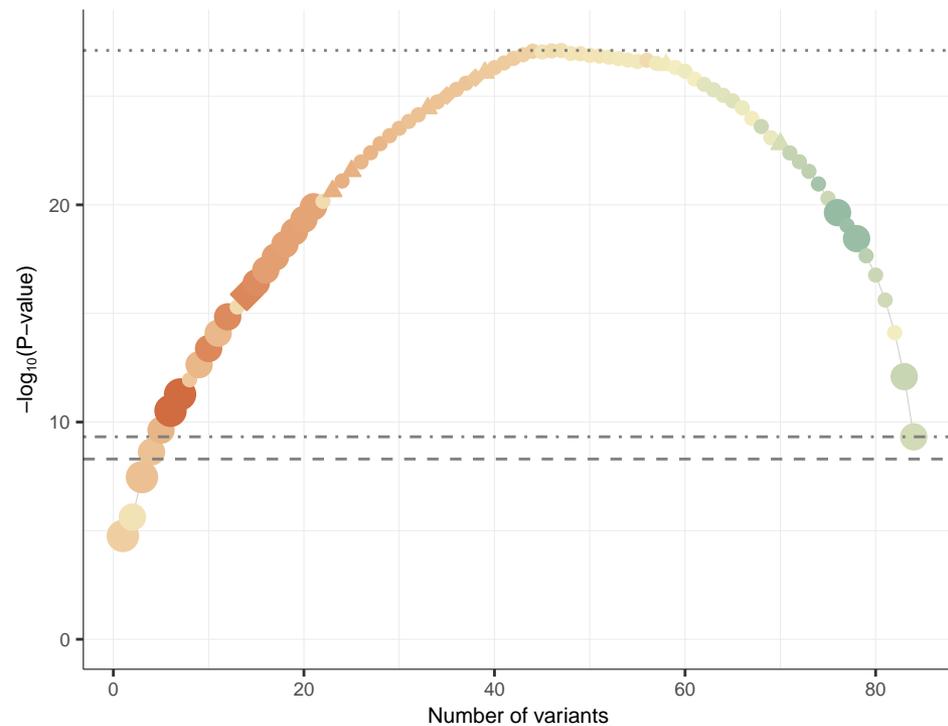
Thresholds

- - - Significance Threshold
- · - · Total P-value
- · · · Lowest P-value

5-oxoproline in plasma at *OPLAH* (LoF_mis)

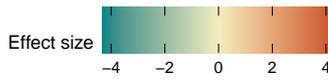


5-oxoproline in plasma at *OPLAH* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



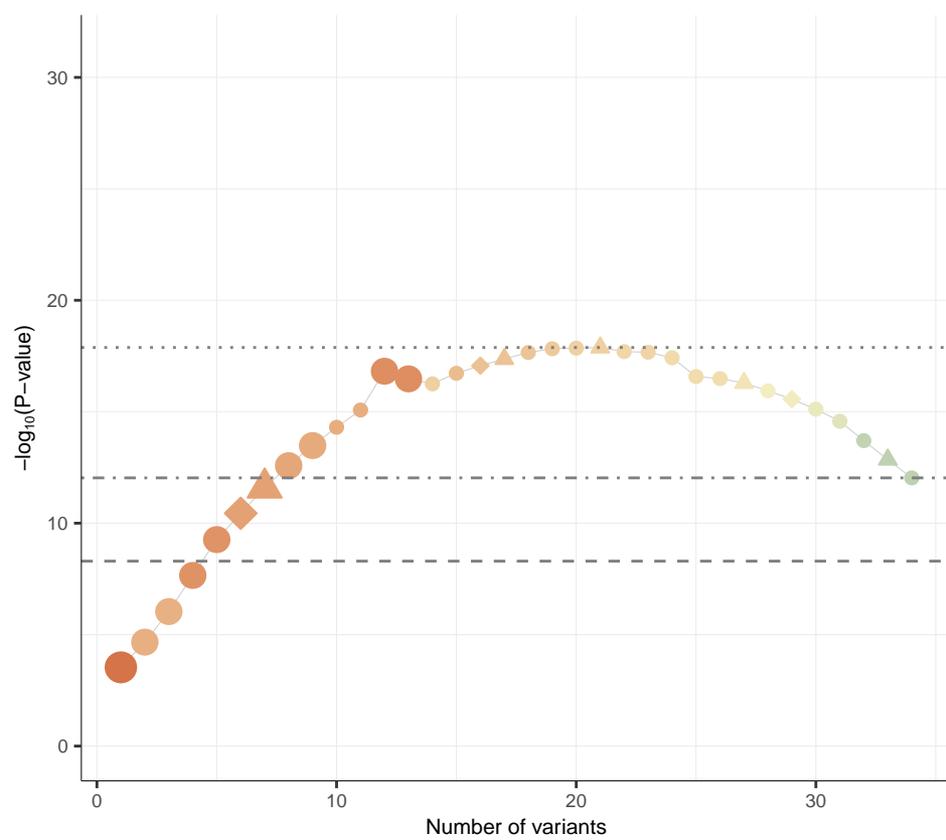
P-value

- >0.05
- <0.05
- <1e-3

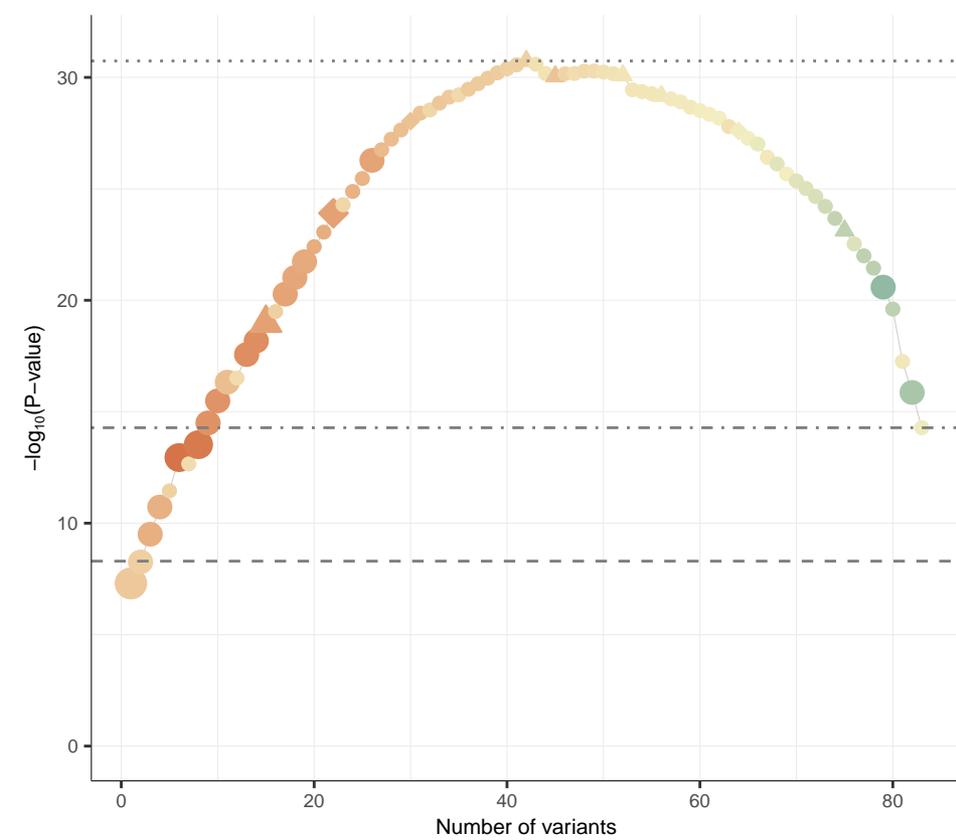
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

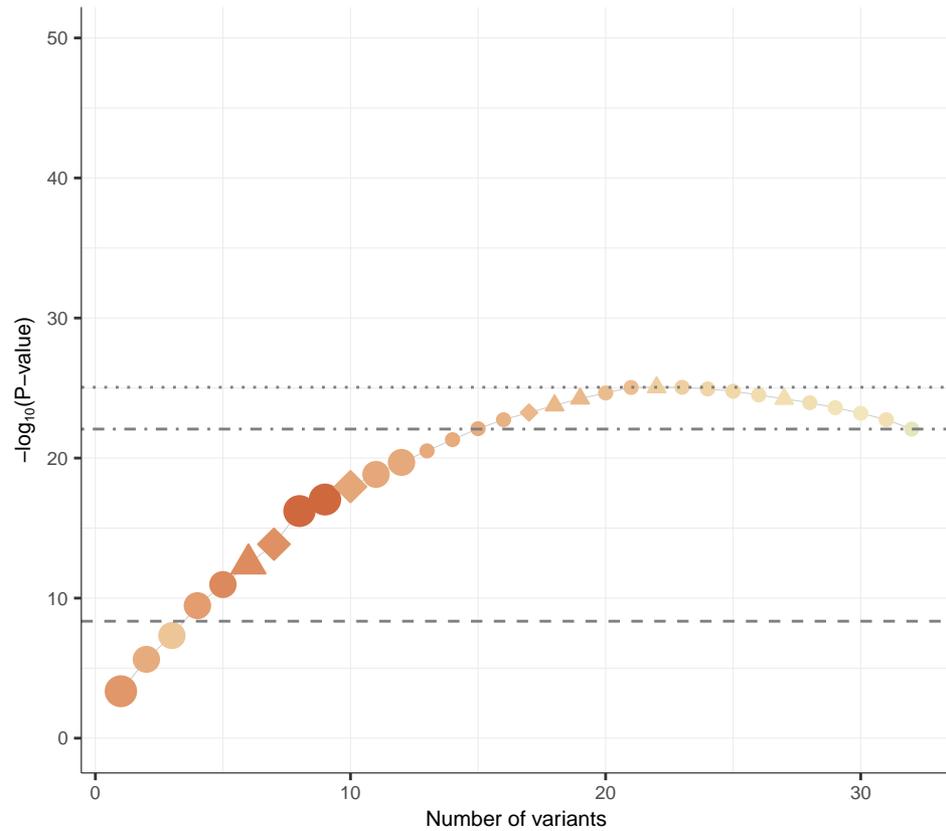
6-oxopiperidine-2-carboxylate in plasma at *OPLAH* (LoF_mis)



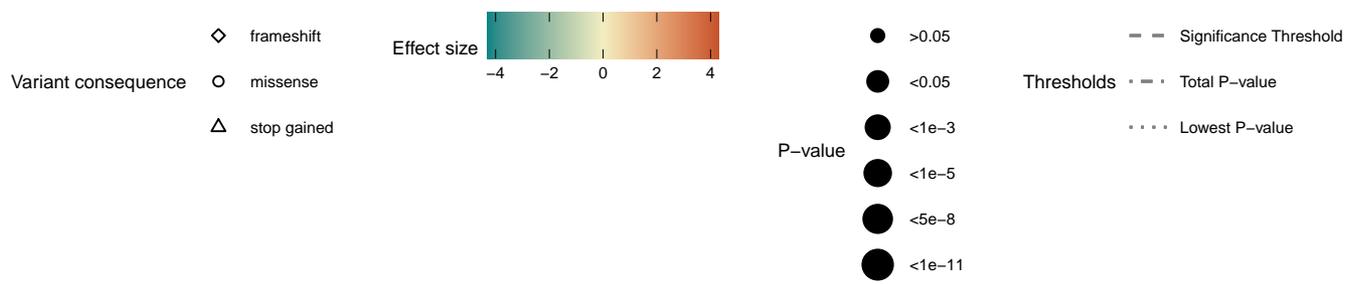
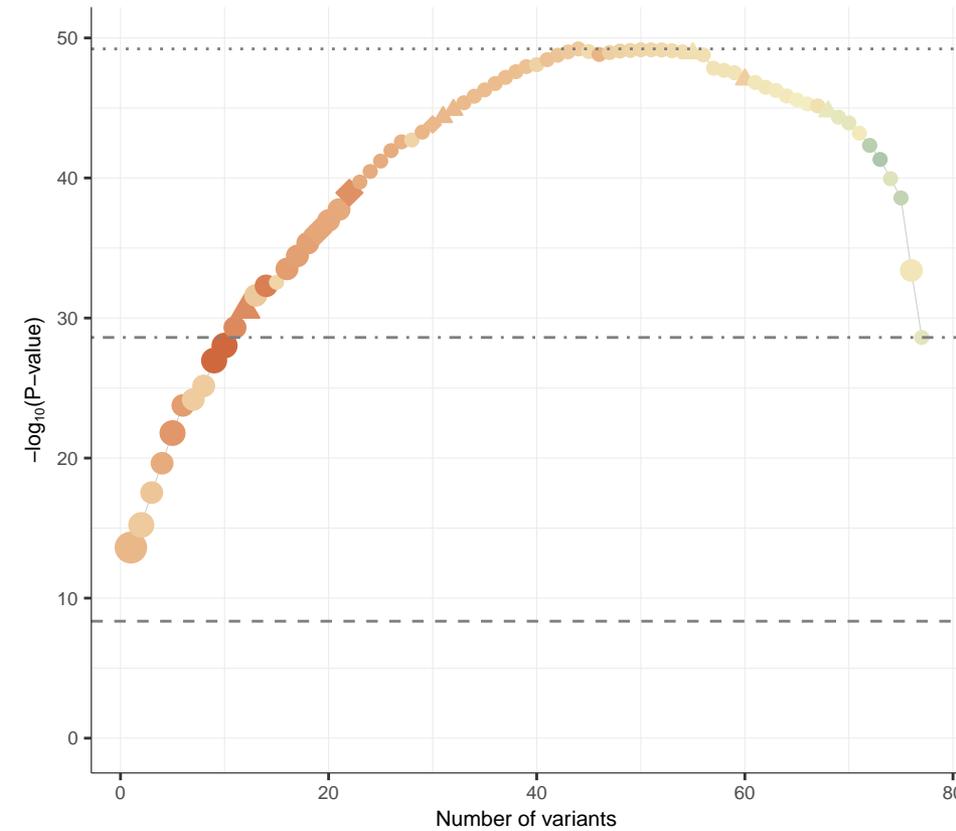
6-oxopiperidine-2-carboxylate in plasma at *OPLAH* (HI_mis)



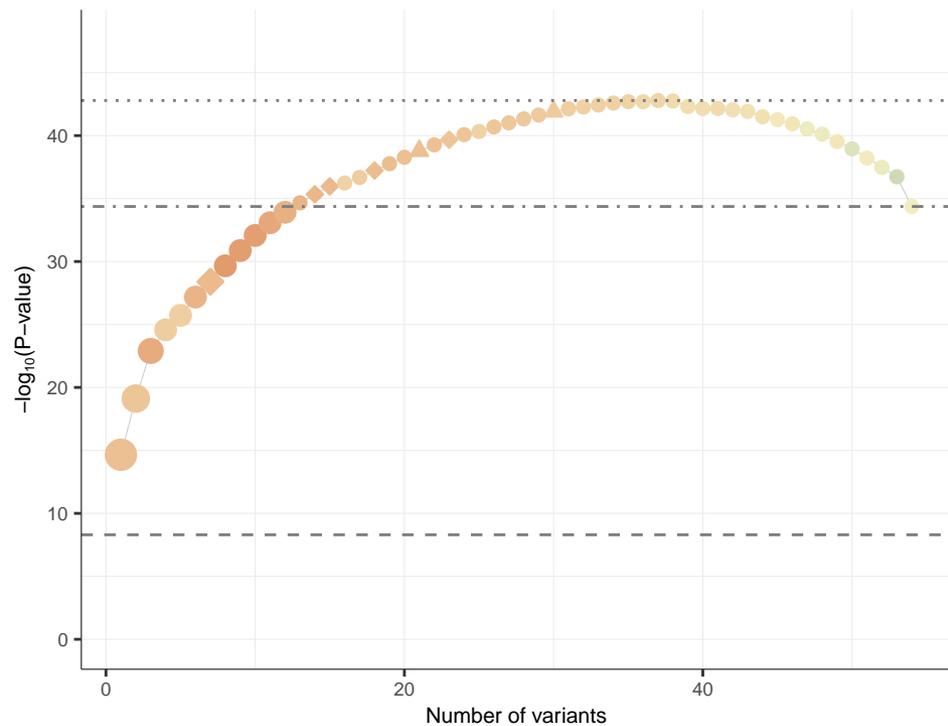
6-oxopiperidine-2-carboxylate in urine at *OPLAH* (LoF_mis)



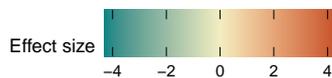
6-oxopiperidine-2-carboxylate in urine at *OPLAH* (HI_mis)



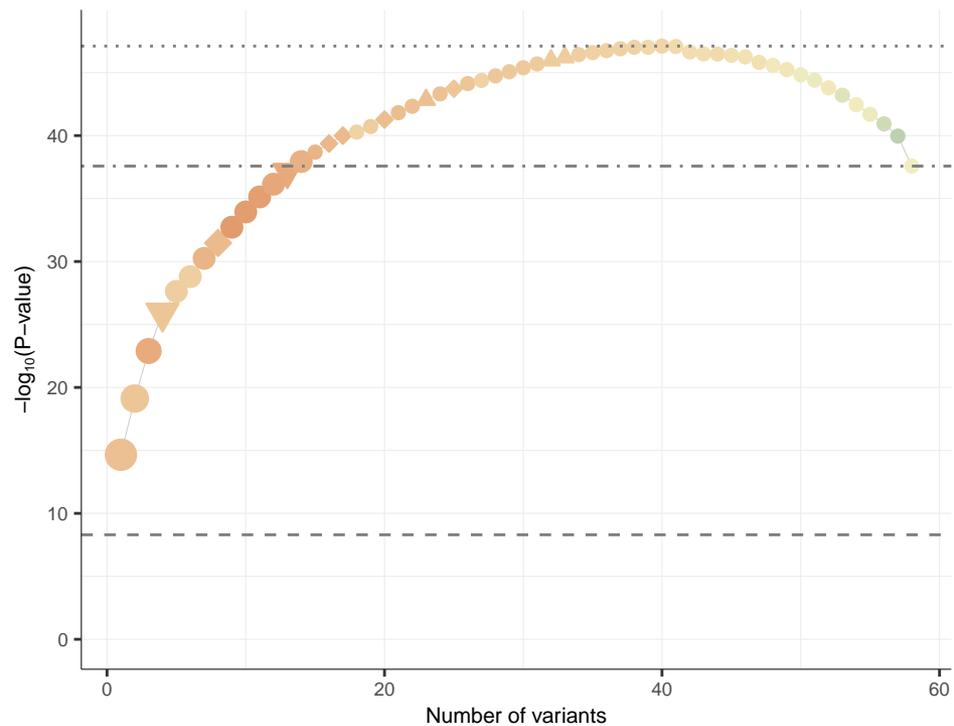
gamma-glutamylphenylalanine in plasma at PAH (LoF_mis)



- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - △ stop gained



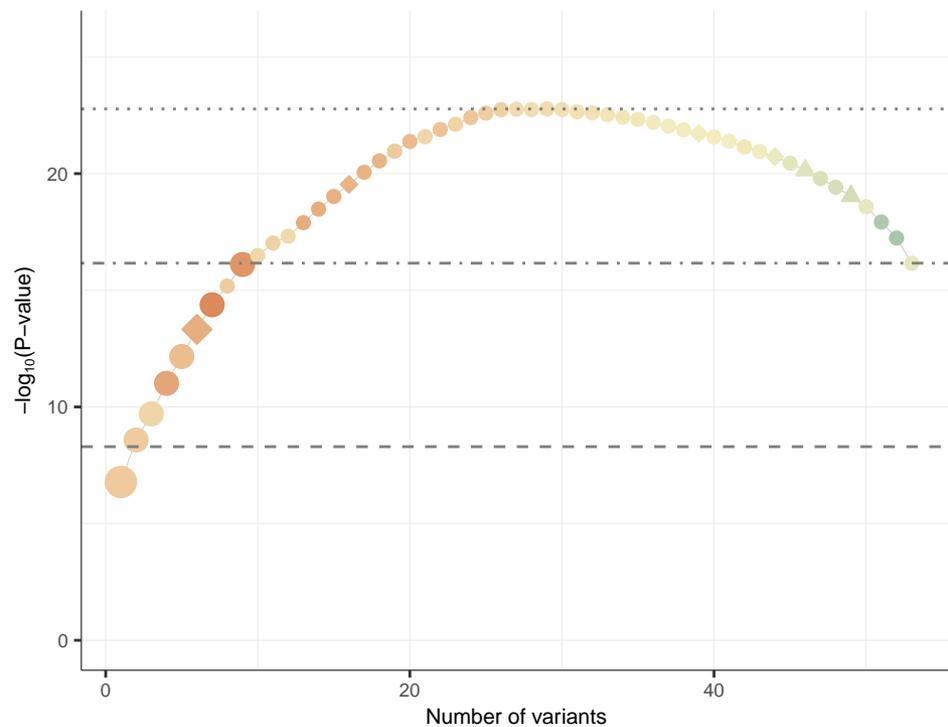
gamma-glutamylphenylalanine in plasma at PAH (HI_mis)



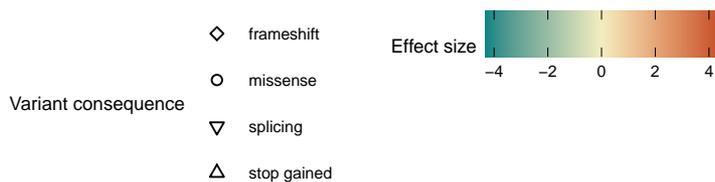
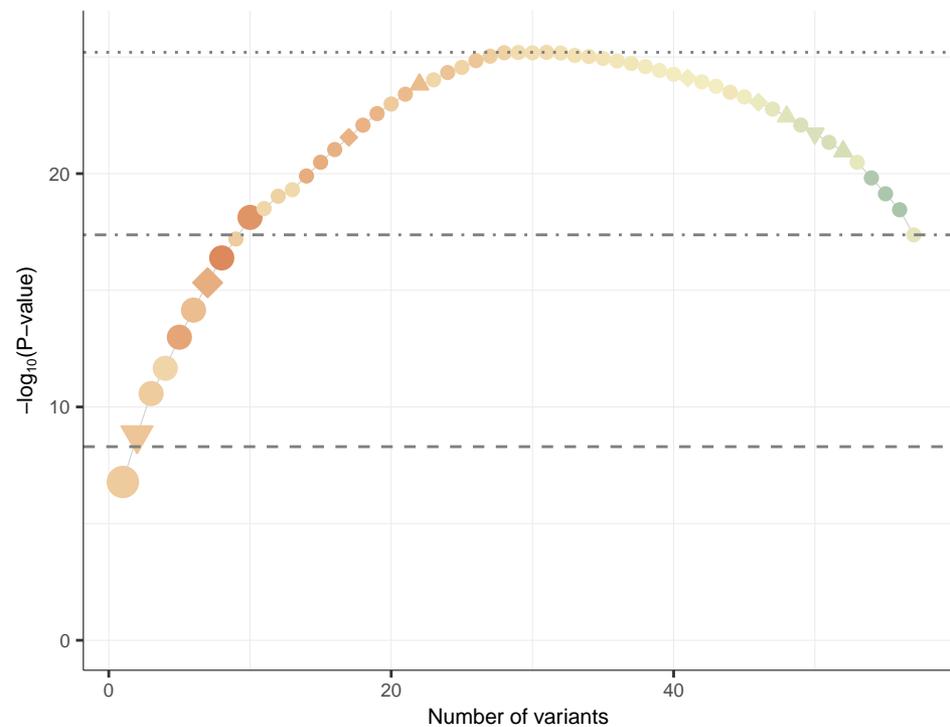
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

- Thresholds
- Significance Threshold
 - · - Total P-value
 - · · · · Lowest P-value

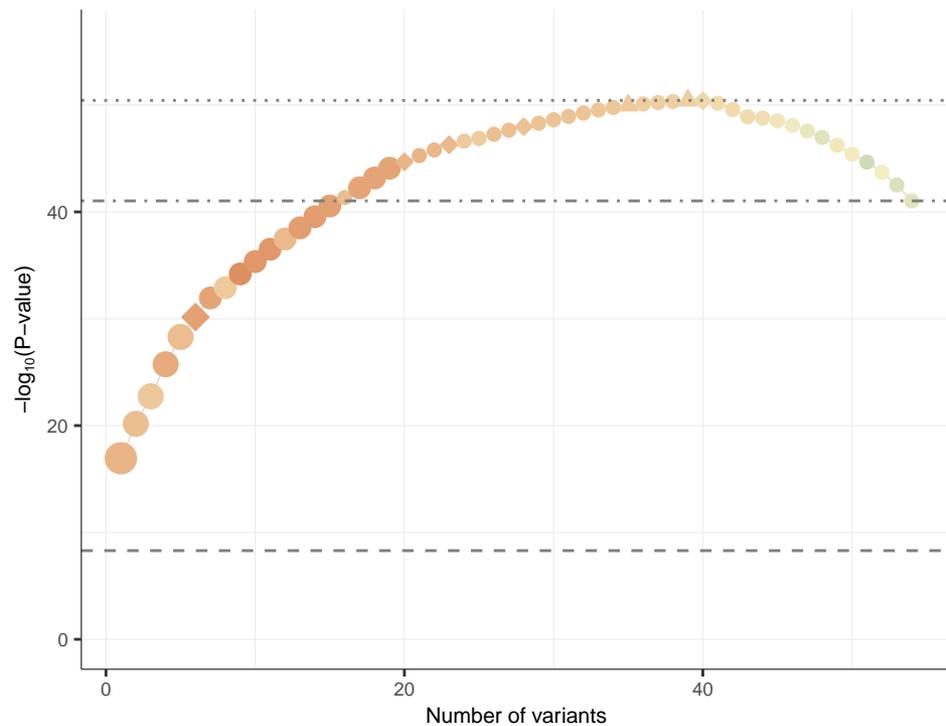
N-formylphenylalanine in plasma at PAH (LoF_mis)



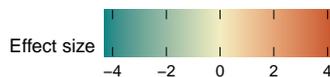
N-formylphenylalanine in plasma at PAH (HI_mis)



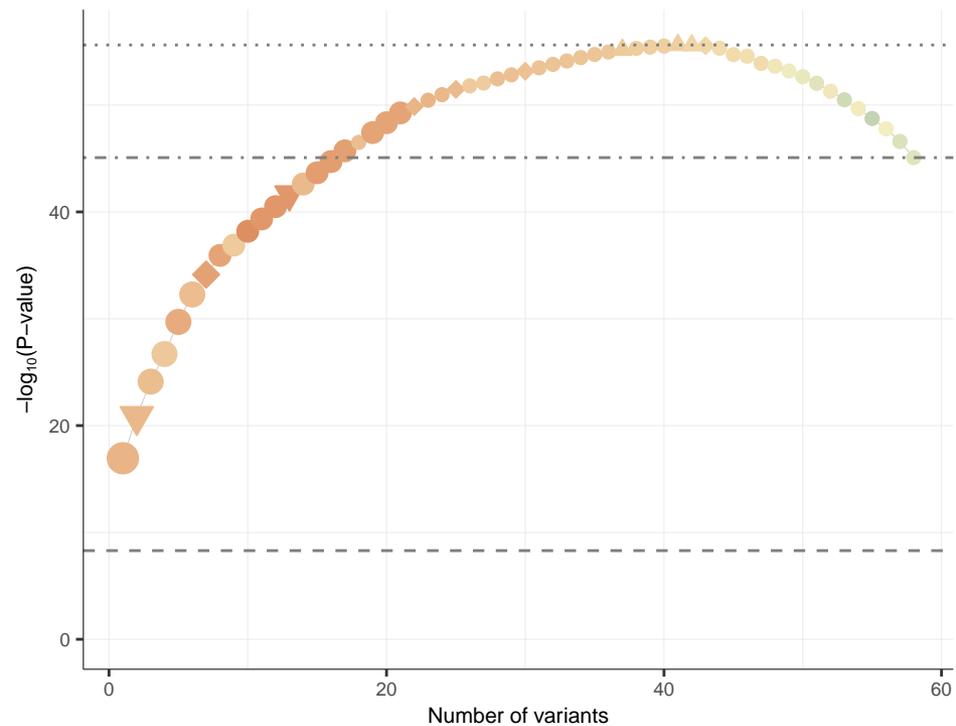
phenylalanine in plasma at PAH (LoF_mis)



- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - △ stop gained



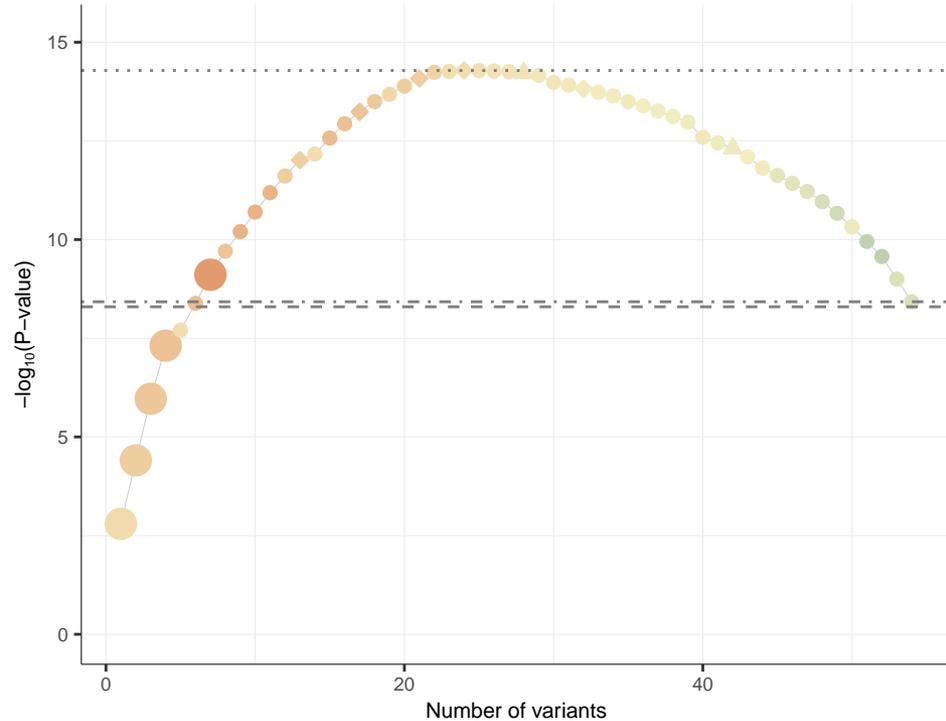
phenylalanine in plasma at PAH (HI_mis)



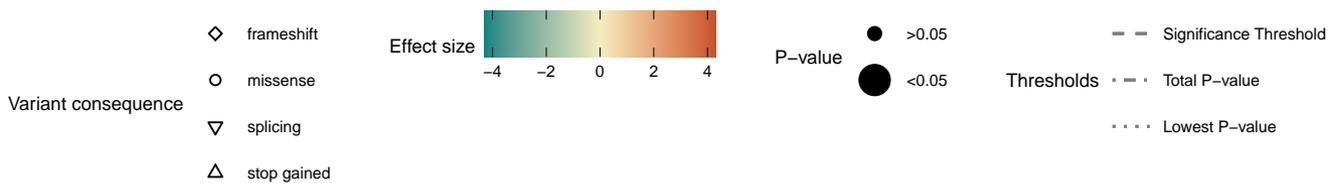
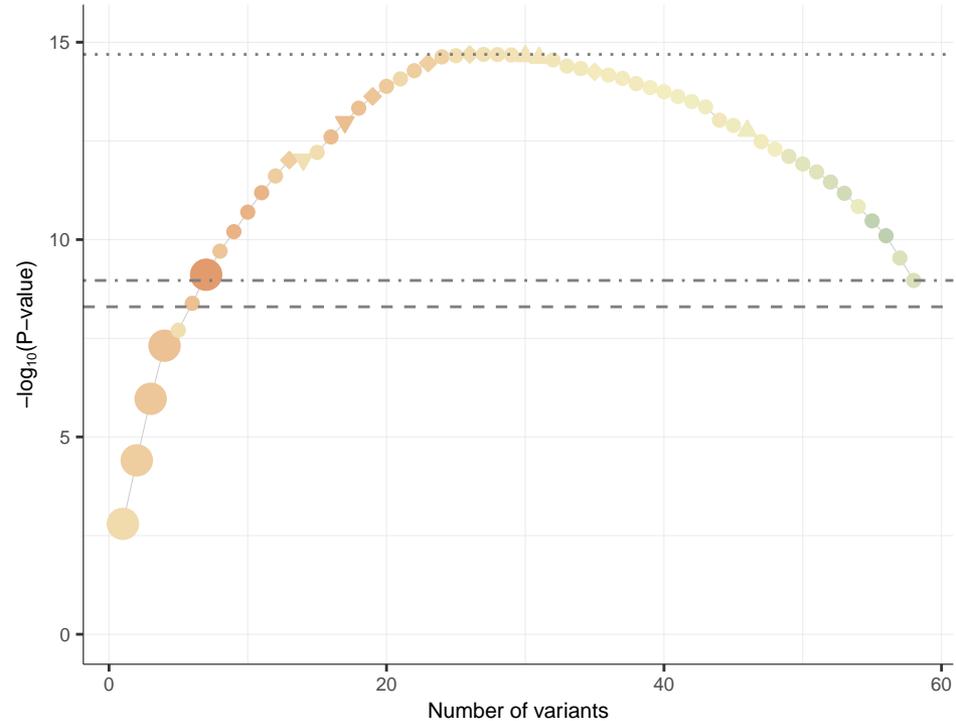
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

- Thresholds
- Significance Threshold
 - - - Total P-value
 - Lowest P-value

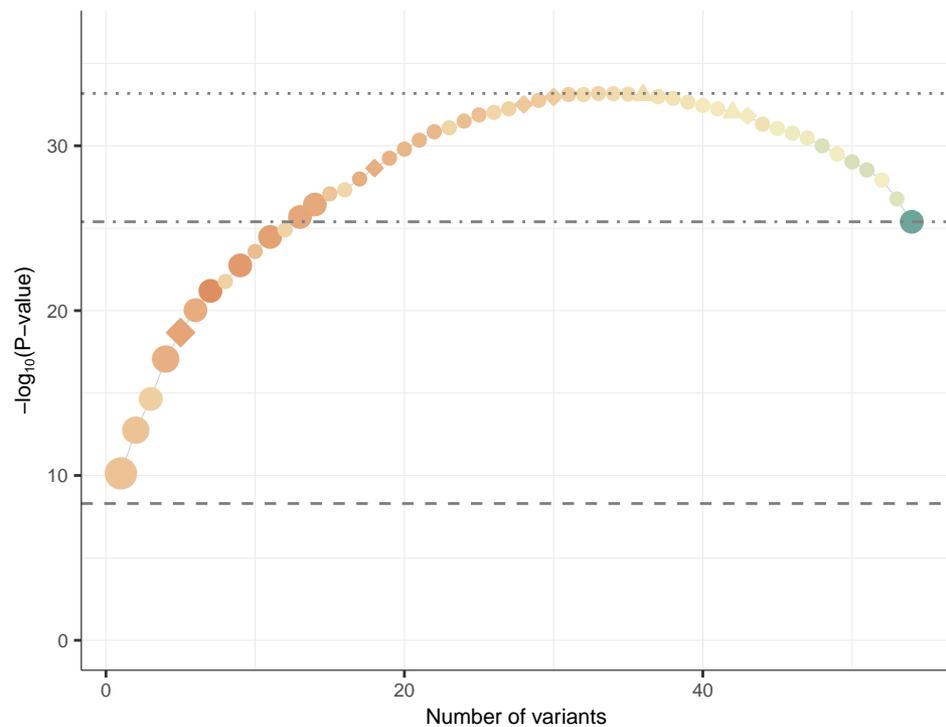
phenyllactate (PLA) in plasma at *PAH* (LoF_mis)



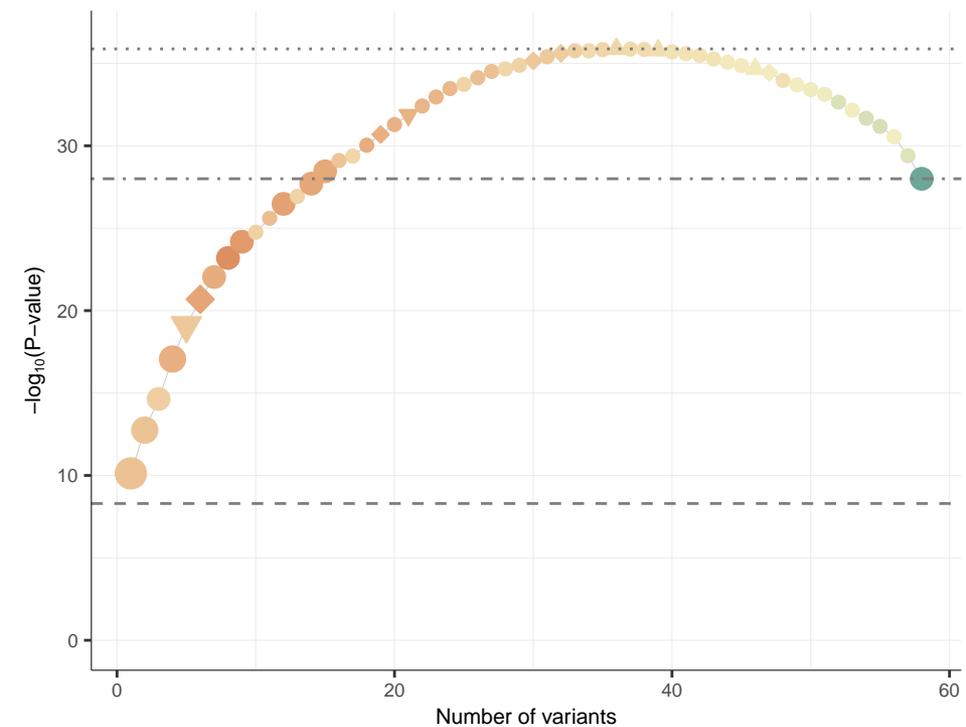
phenyllactate (PLA) in plasma at *PAH* (HI_mis)



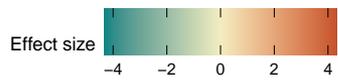
phenylpyruvate in plasma at PAH (LoF_mis)



phenylpyruvate in plasma at PAH (HI_mis)



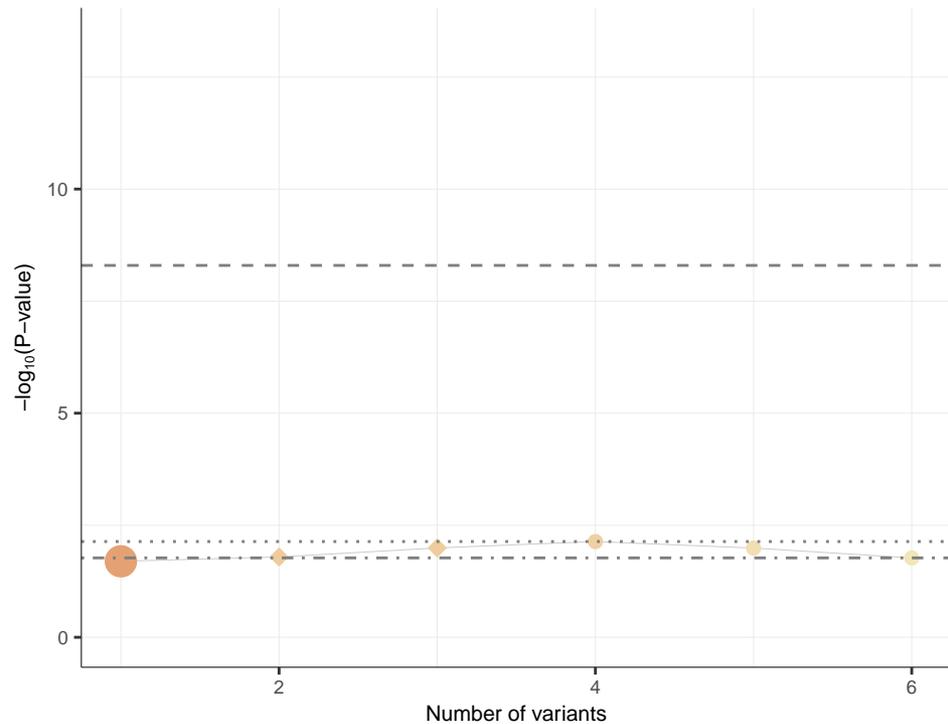
- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - △ stop gained



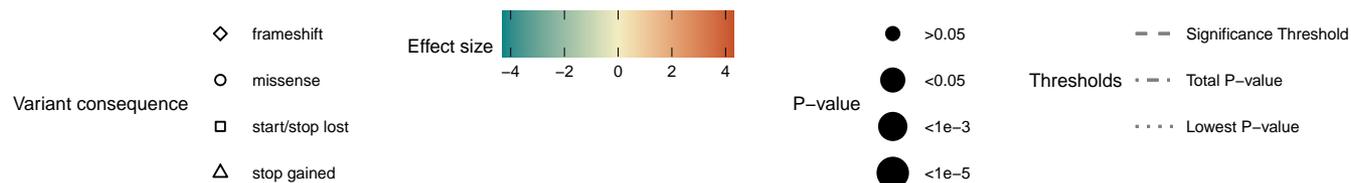
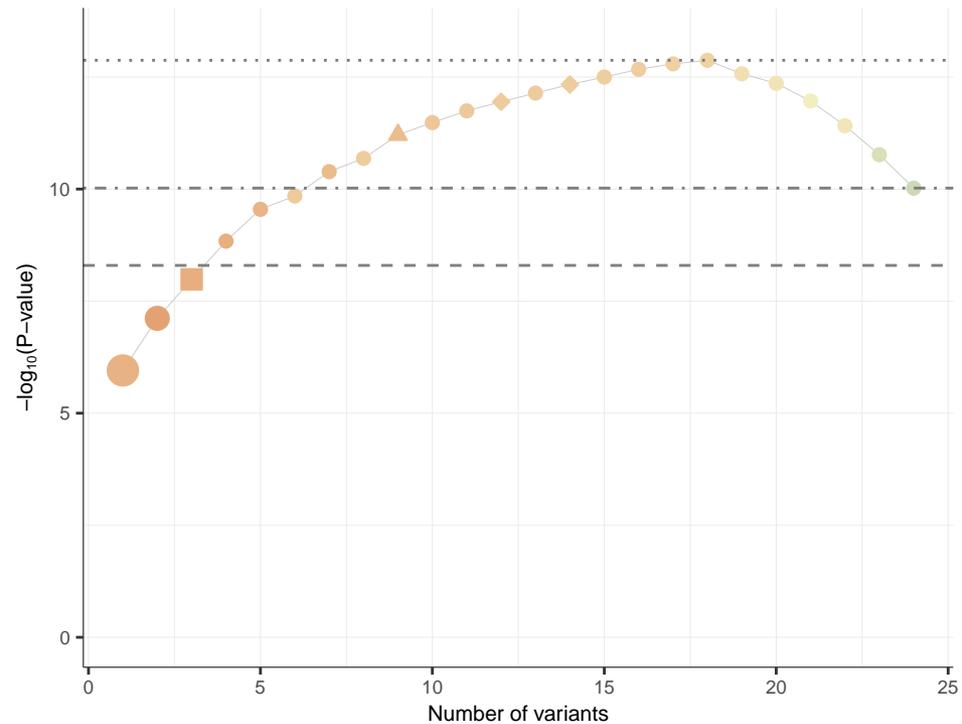
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8

- Thresholds
- - Significance Threshold
 - - - Total P-value
 - ⋯ Lowest P-value

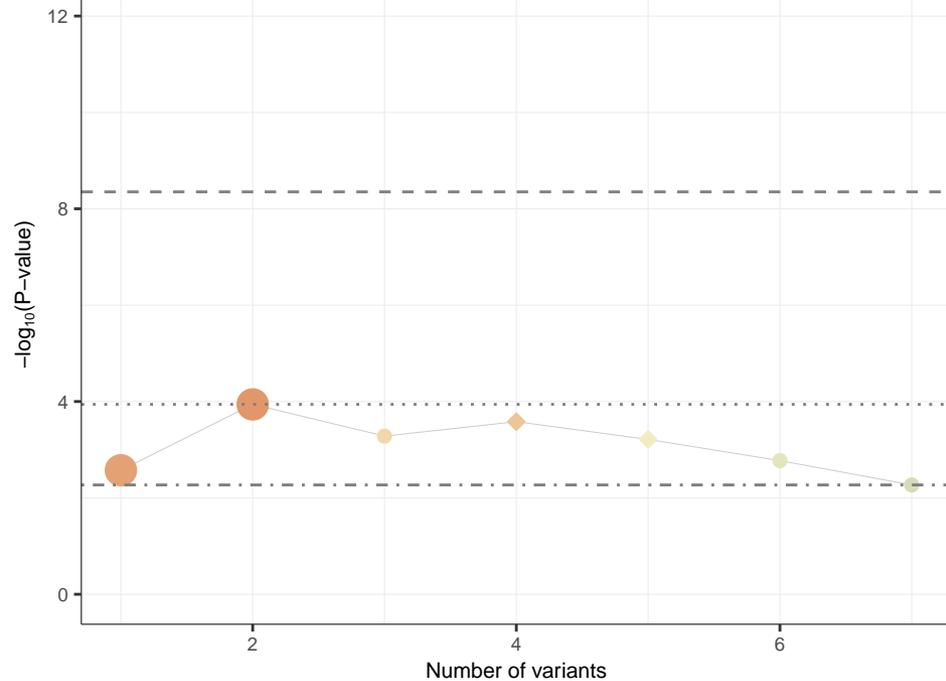
acisoga in plasma at PAOX (LoF_mis)



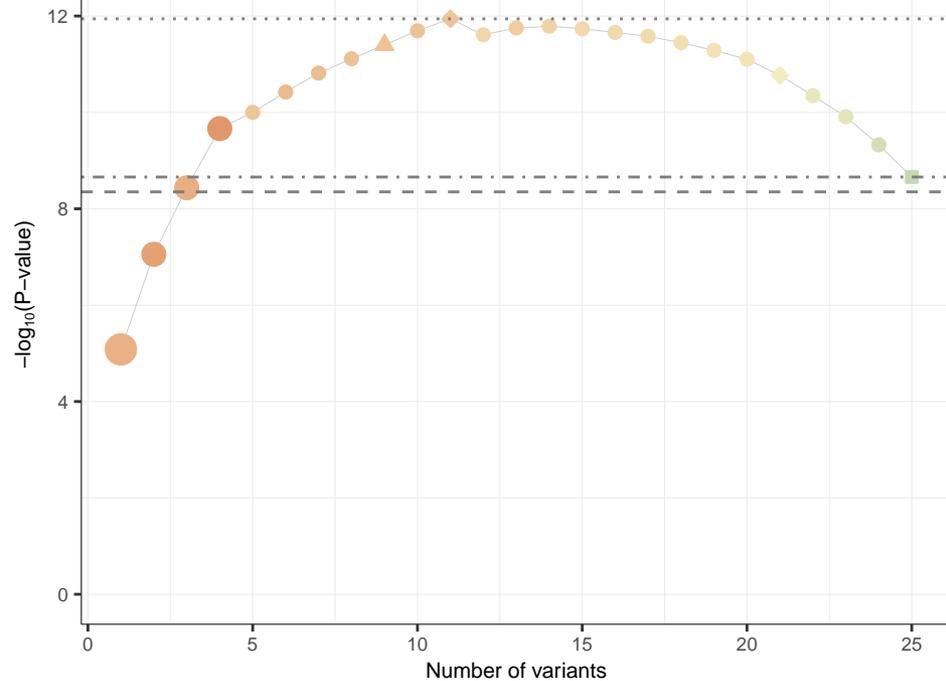
acisoga in plasma at PAOX (HI_mis)



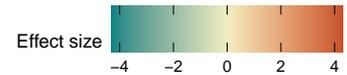
diacetylspermidine* in urine at PAOX (LoF_mis)



diacetylspermidine* in urine at PAOX (HI_mis)



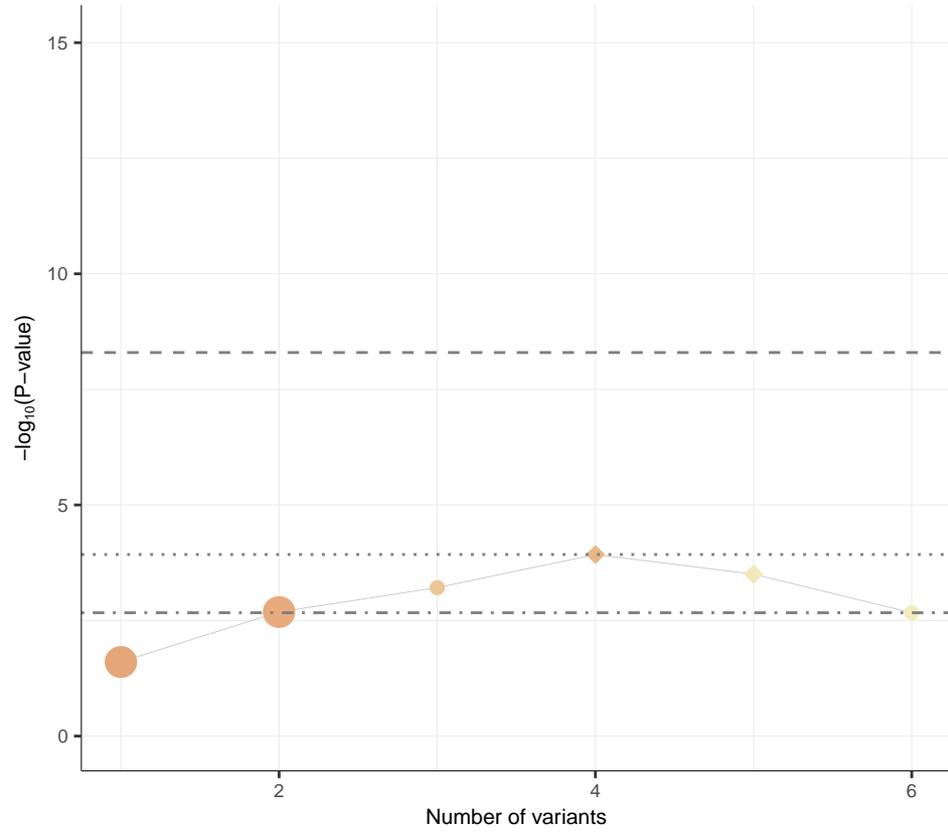
- Variant consequence
- ◇ frameshift
 - missense
 - start/stop lost
 - △ stop gained



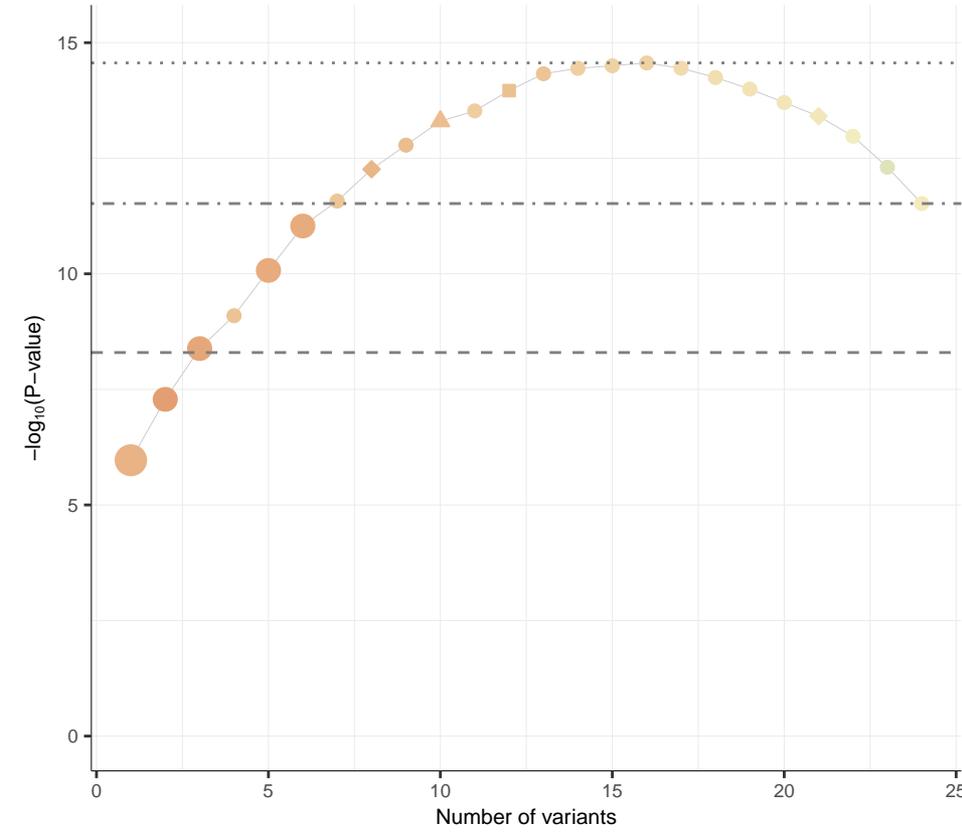
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5

- Thresholds
- Significance Threshold
 - - - Total P-value
 - ⋯⋯ Lowest P-value

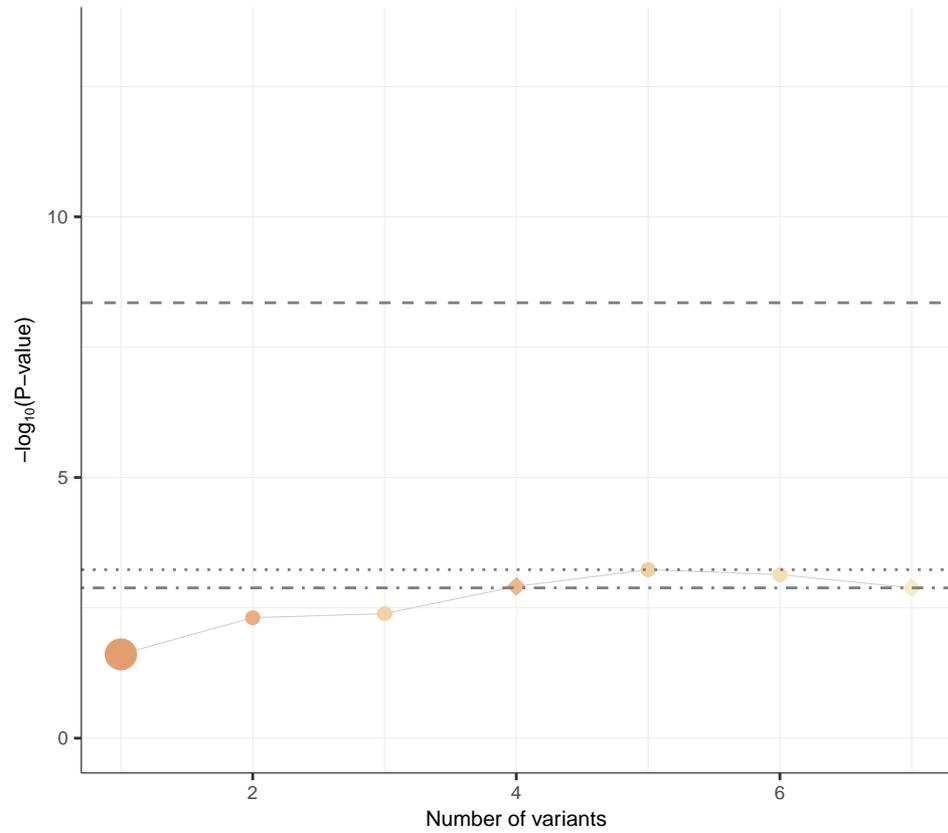
N-acetyl-isoptreanine in plasma at PAOX (LoF_mis)



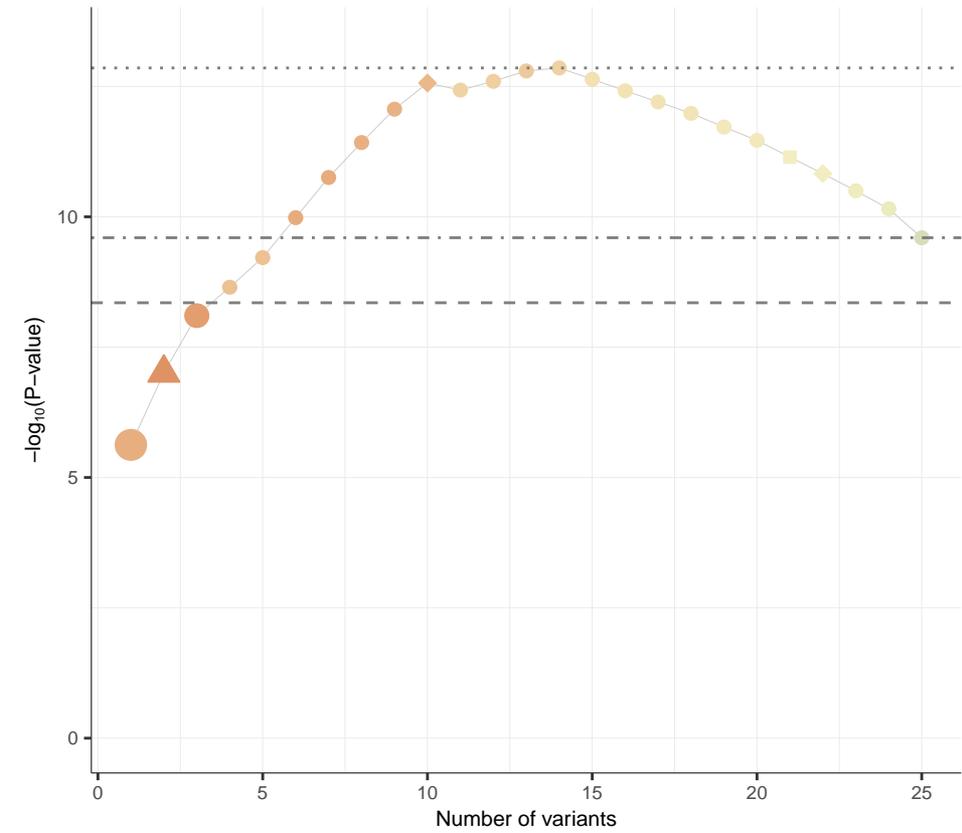
N-acetyl-isoptreanine in plasma at PAOX (HI_mis)



N-acetyl-isoptreanine in urine at PAOX (LoF_mis)



N-acetyl-isoptreanine in urine at PAOX (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- start/stop lost
- △ stop gained

Effect size

-4 -2 0 2 4

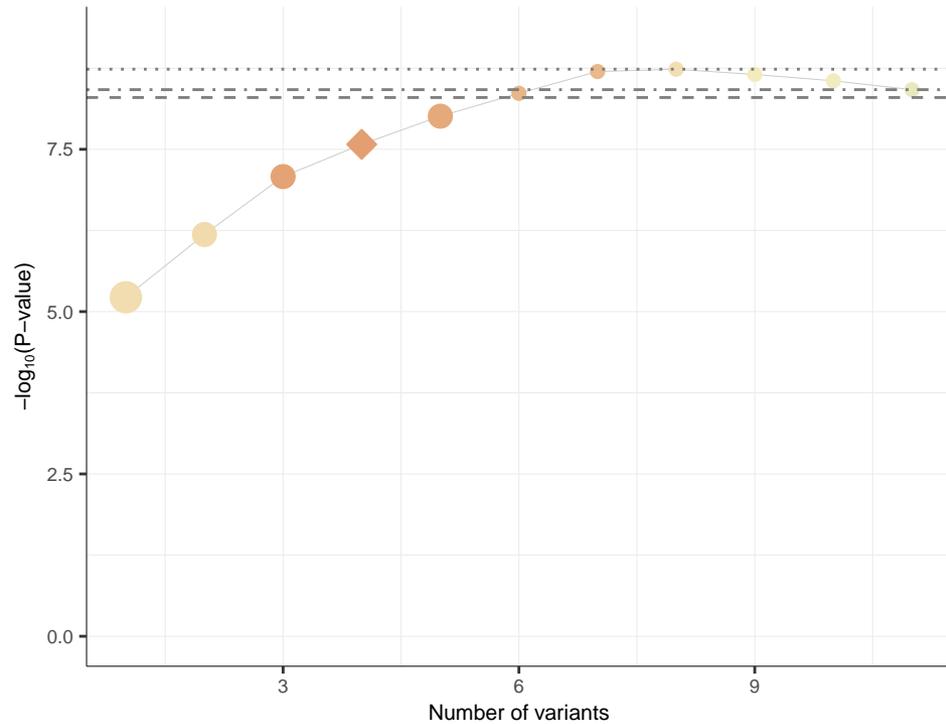
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

Thresholds

- - Significance Threshold
- · - Total P-value
- · · · · Lowest P-value

1-stearoyl-2-linoleoyl-GPI (18:0/18:2) in plasma at PAQR7 (HI_mis)



Variant consequence

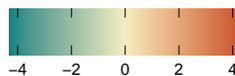


frameshift



missense

Effect size



P-value



>0.05



<0.05



<1e-3



<1e-5



Significance Threshold

Thresholds

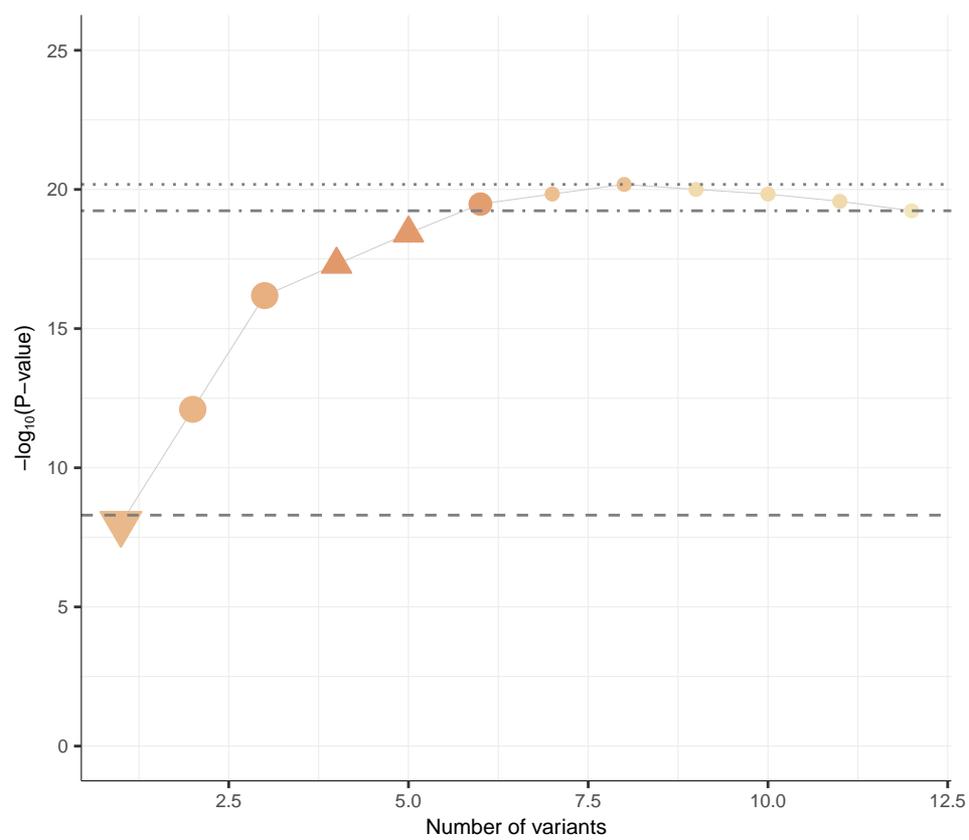


Total P-value

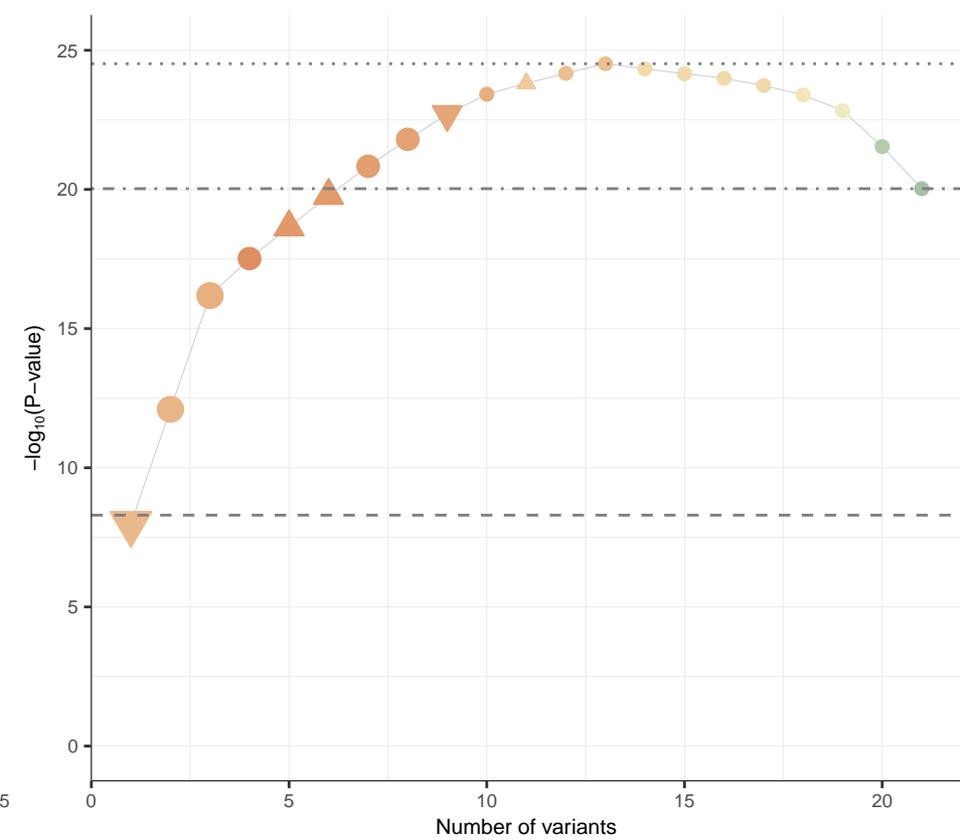


Lowest P-value

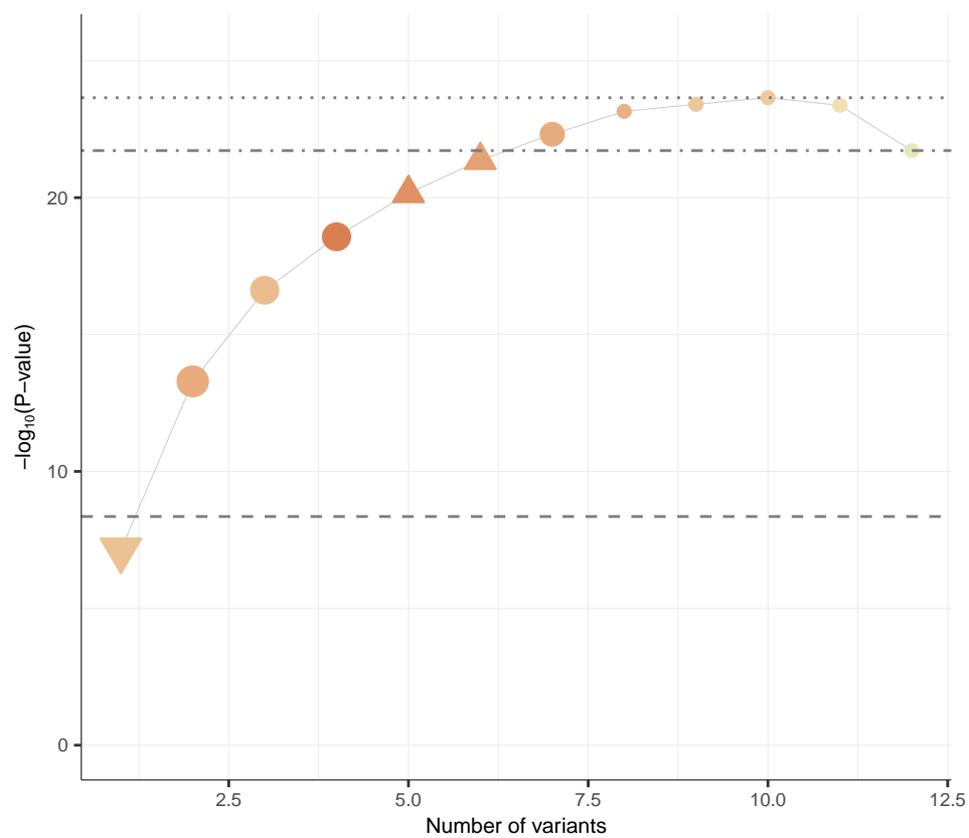
2'-O-methylcytidine in plasma at *PHYHD1* (LoF_mis)



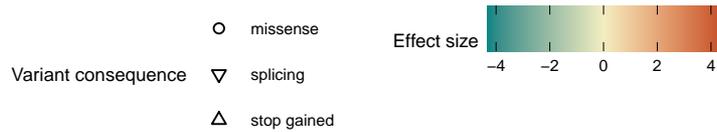
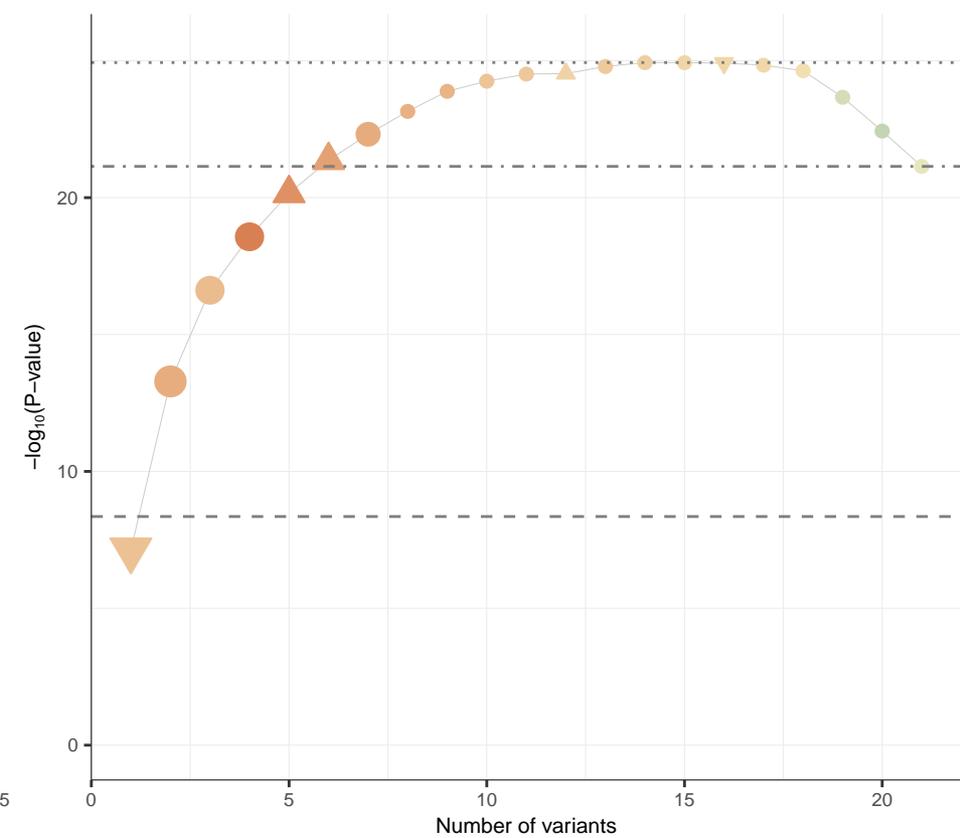
2'-O-methylcytidine in plasma at *PHYHD1* (HI_mis)



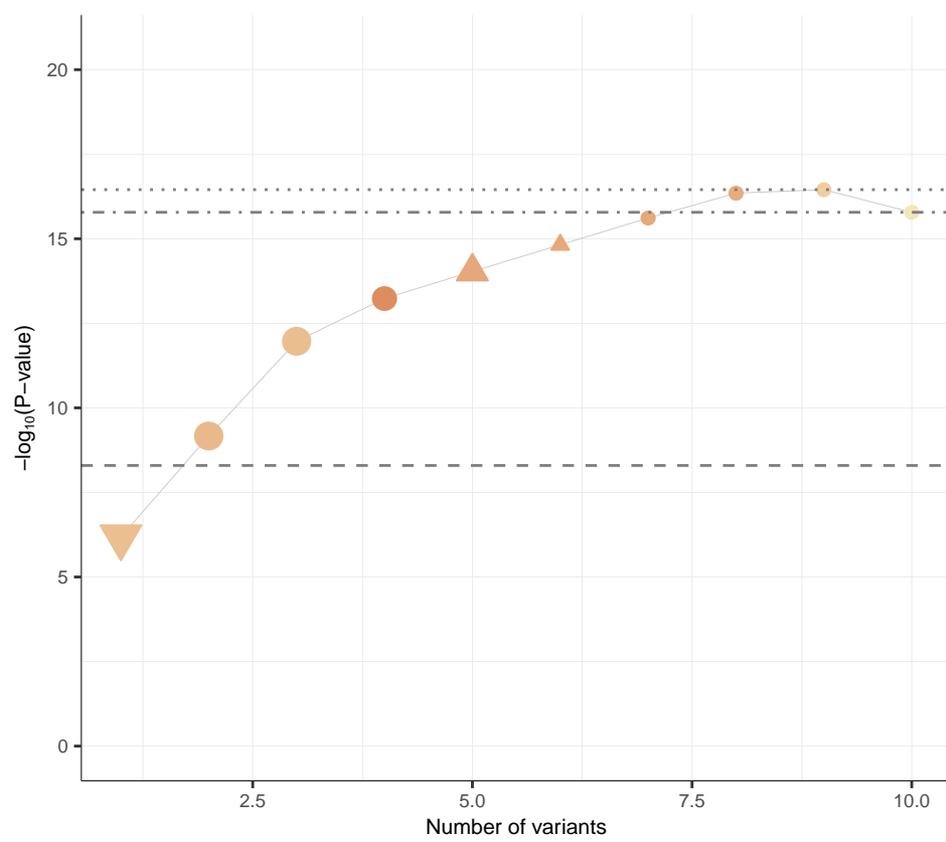
2'-O-methylcytidine in urine at *PHYHD1* (LoF_mis)



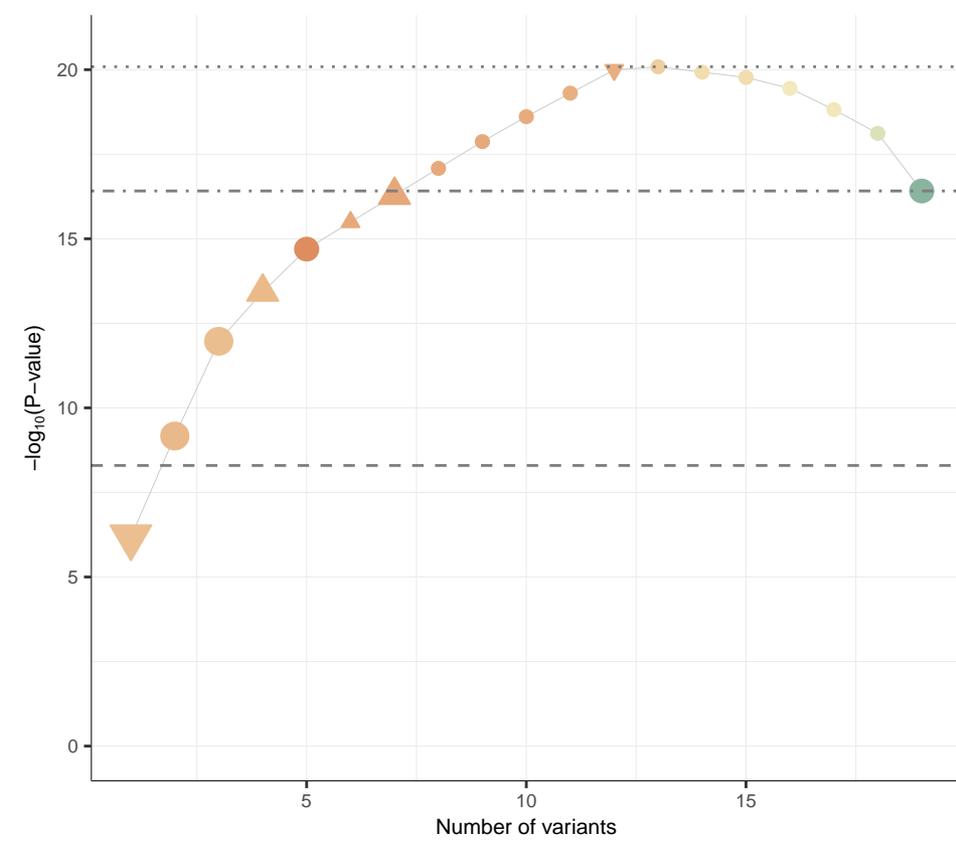
2'-O-methylcytidine in urine at *PHYHD1* (HI_mis)



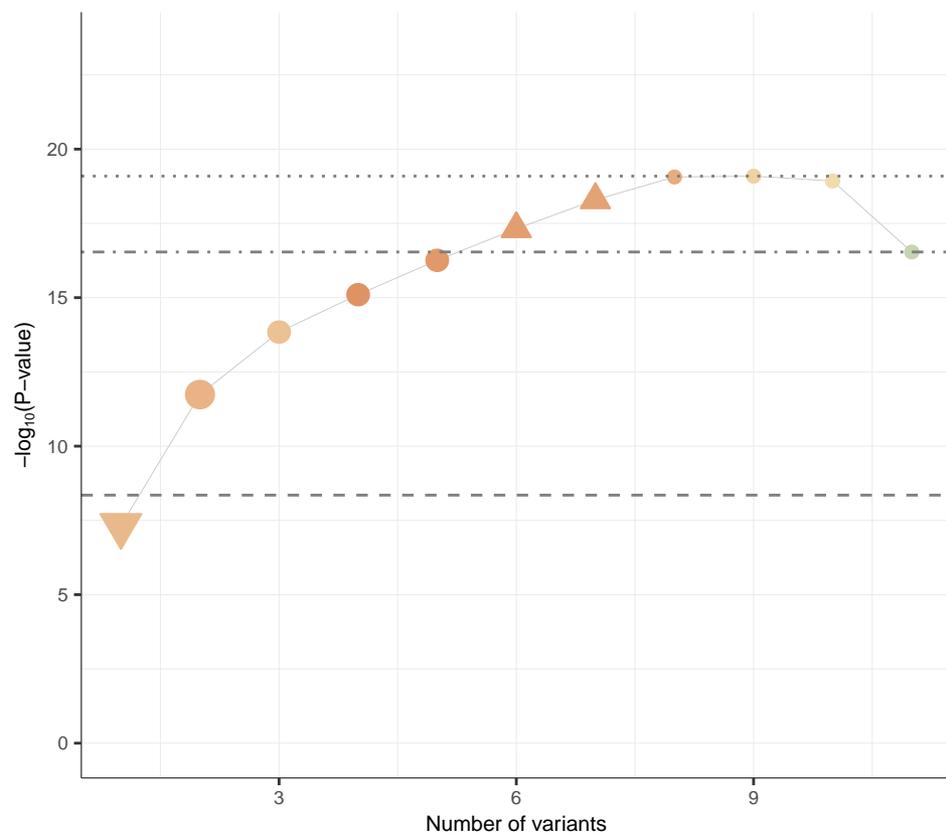
2'-O-methyluridine in plasma at *PHYHD1* (LoF_mis)



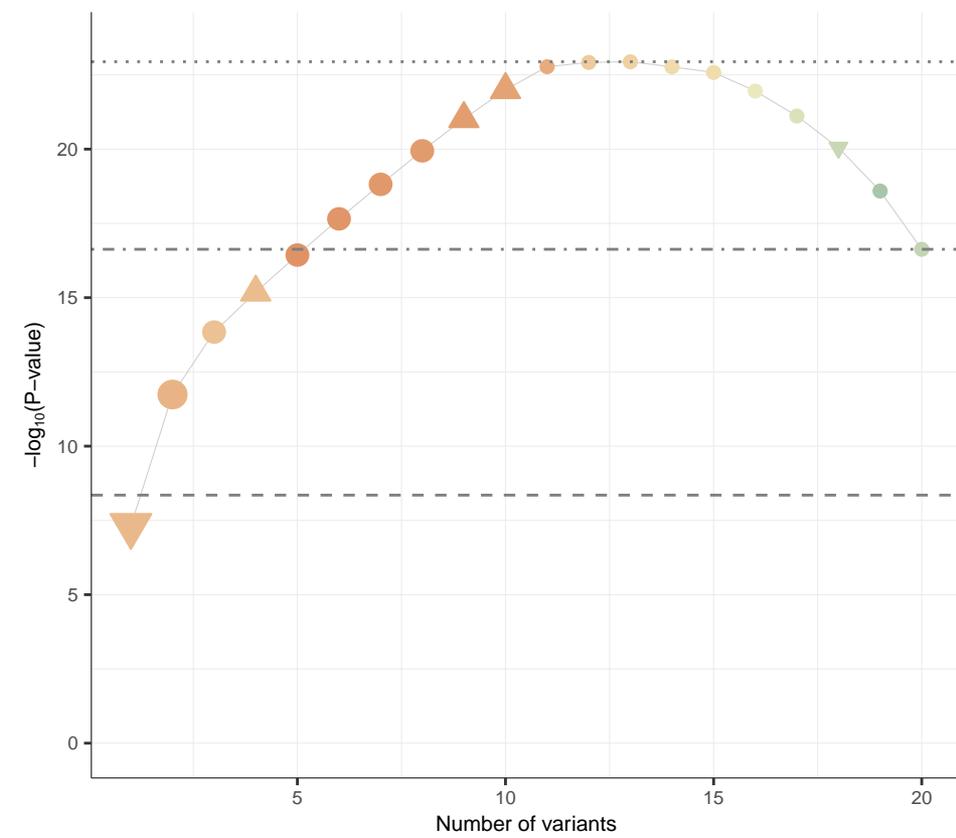
2'-O-methyluridine in plasma at *PHYHD1* (HI_mis)



2'-O-methyluridine in urine at *PHYHD1* (LoF_mis)

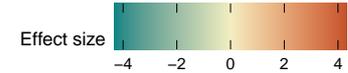


2'-O-methyluridine in urine at *PHYHD1* (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



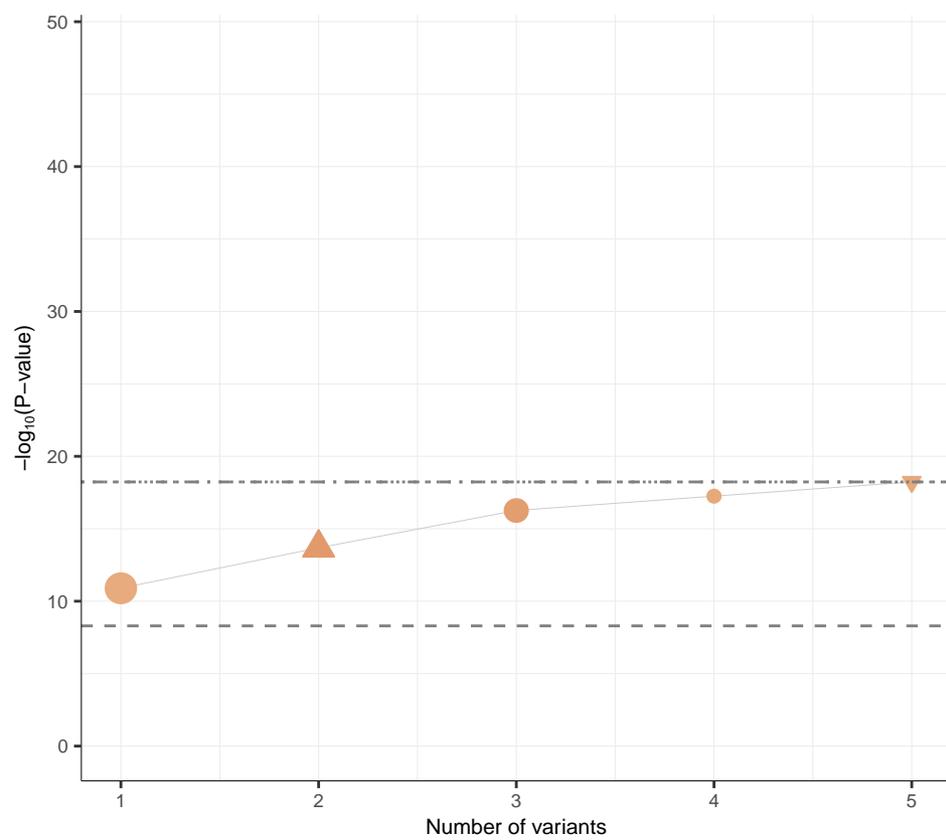
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

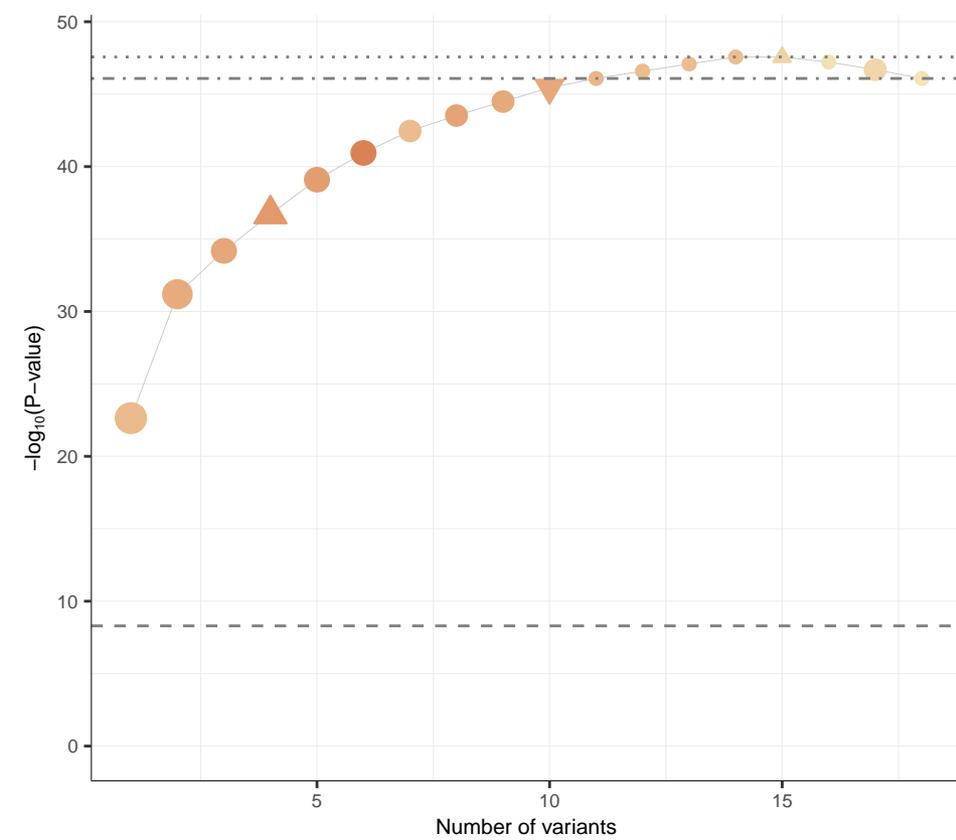
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

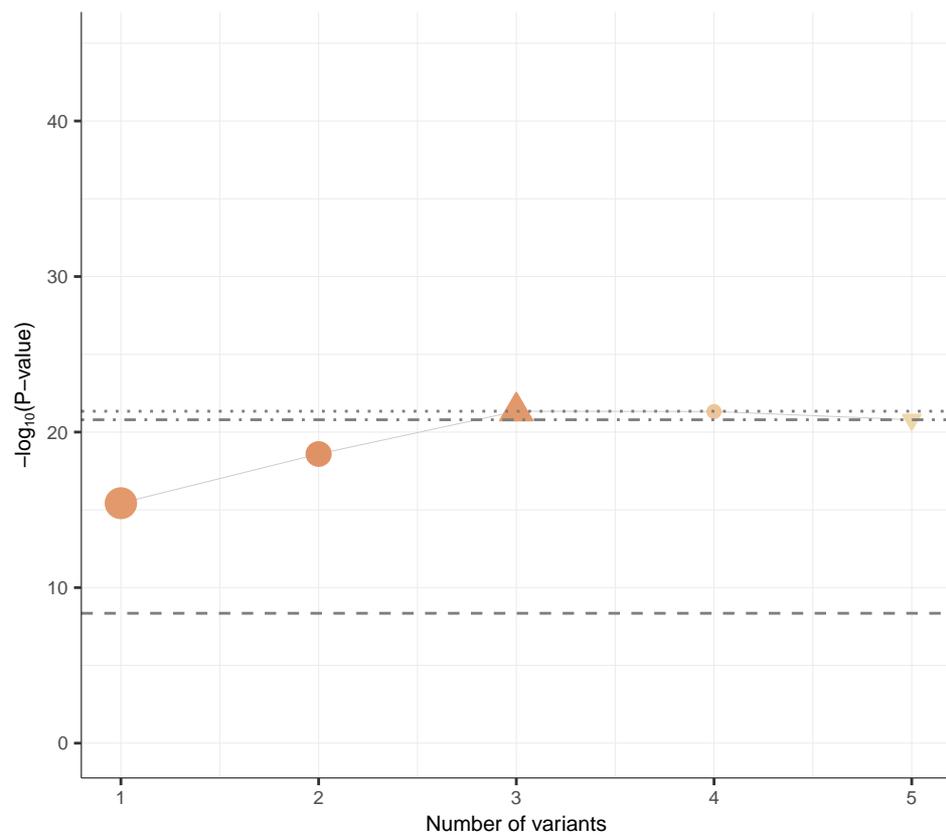
N-acetyl-beta-alanine in plasma at *PTER* (LoF_mis)



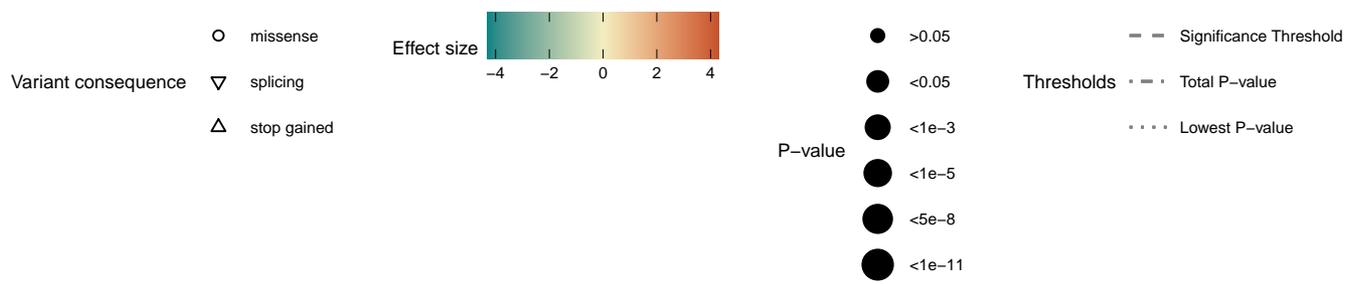
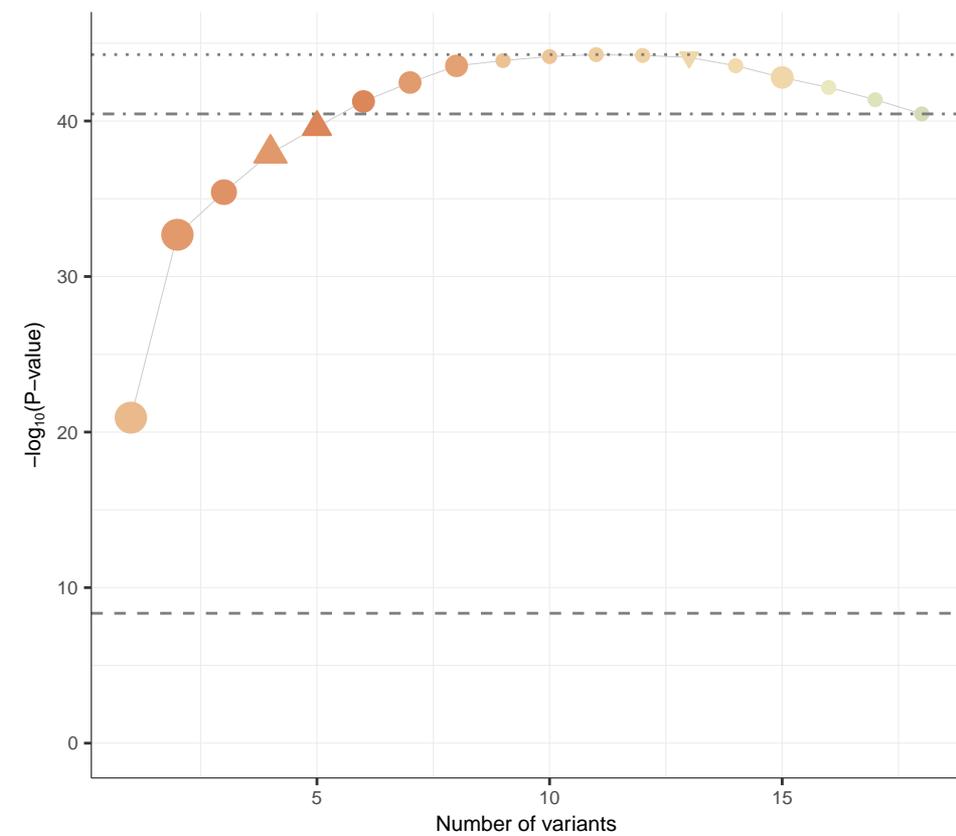
N-acetyl-beta-alanine in plasma at *PTER* (HI_mis)



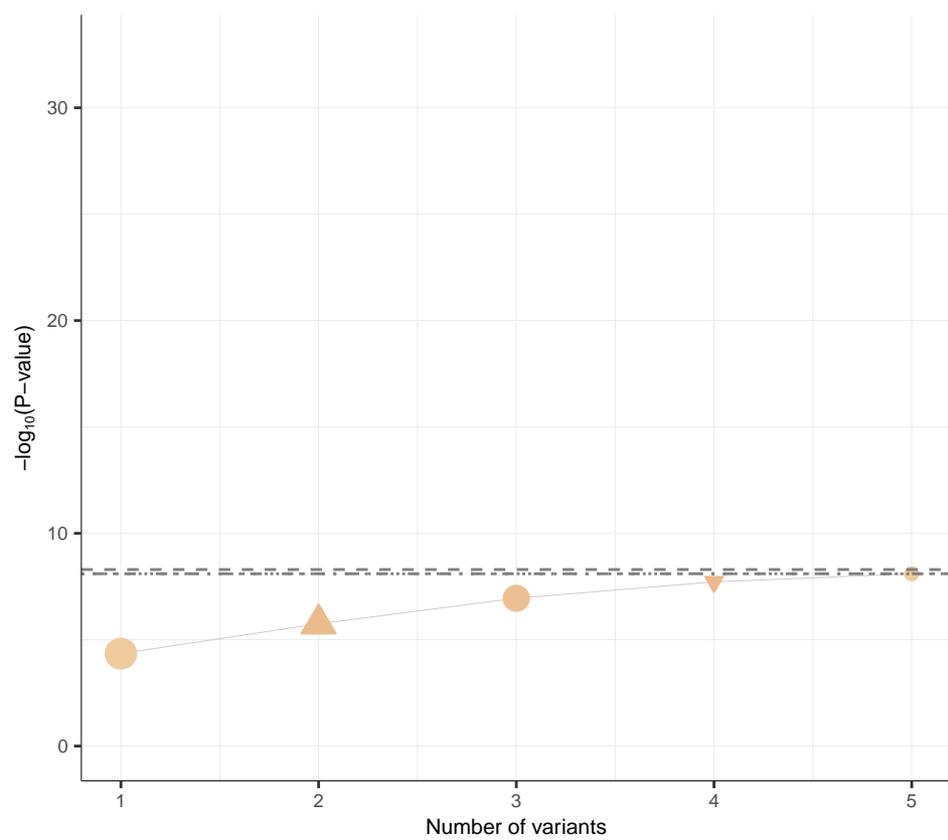
N-acetyl-beta-alanine in urine at *PTER* (LoF_mis)



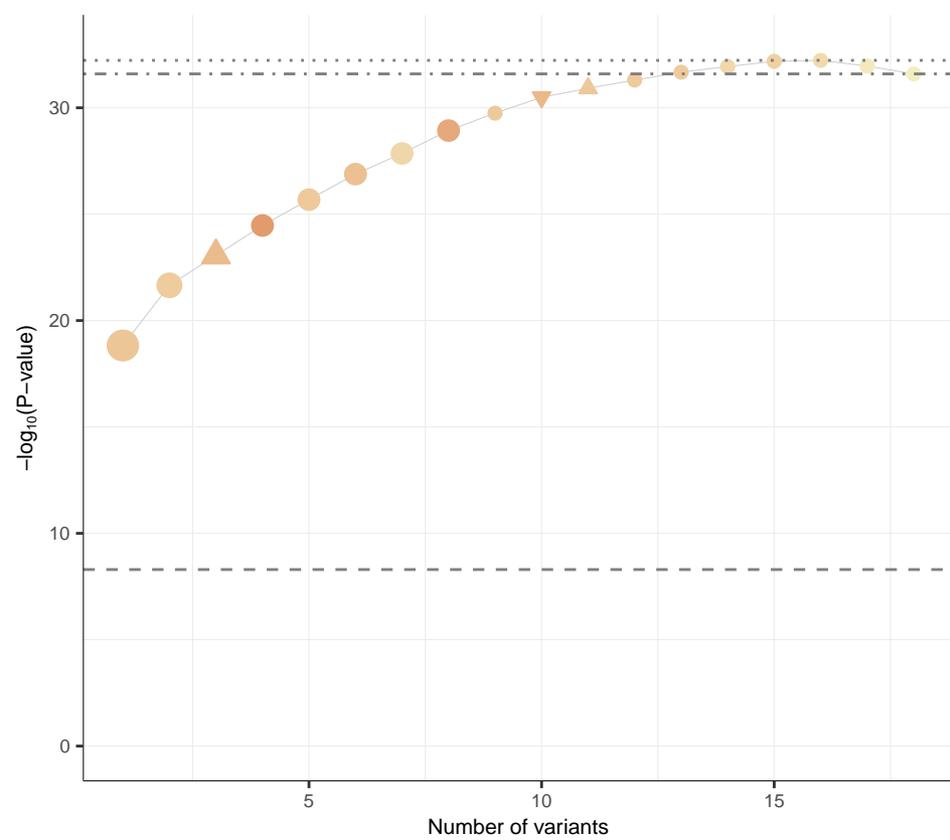
N-acetyl-beta-alanine in urine at *PTER* (HI_mis)



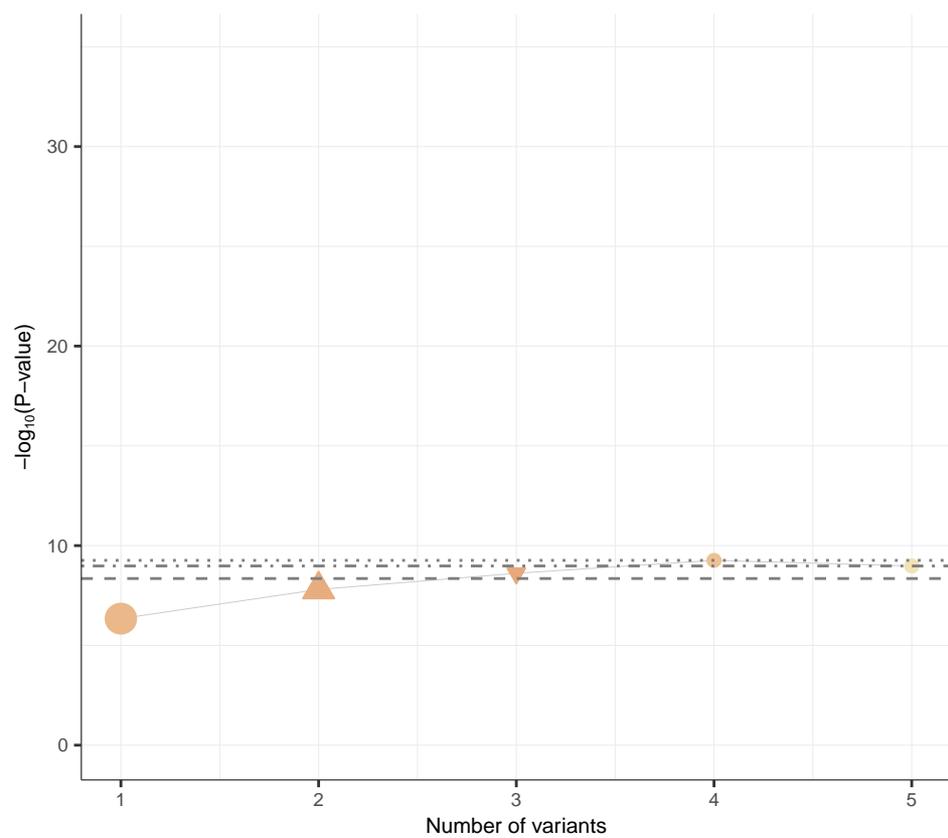
N-acetyltaurine in plasma at *PTER* (LoF_mis)



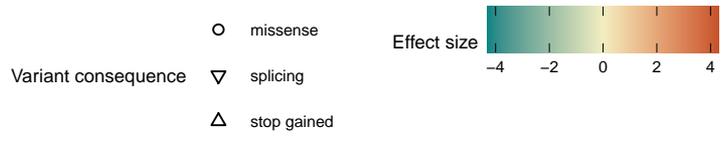
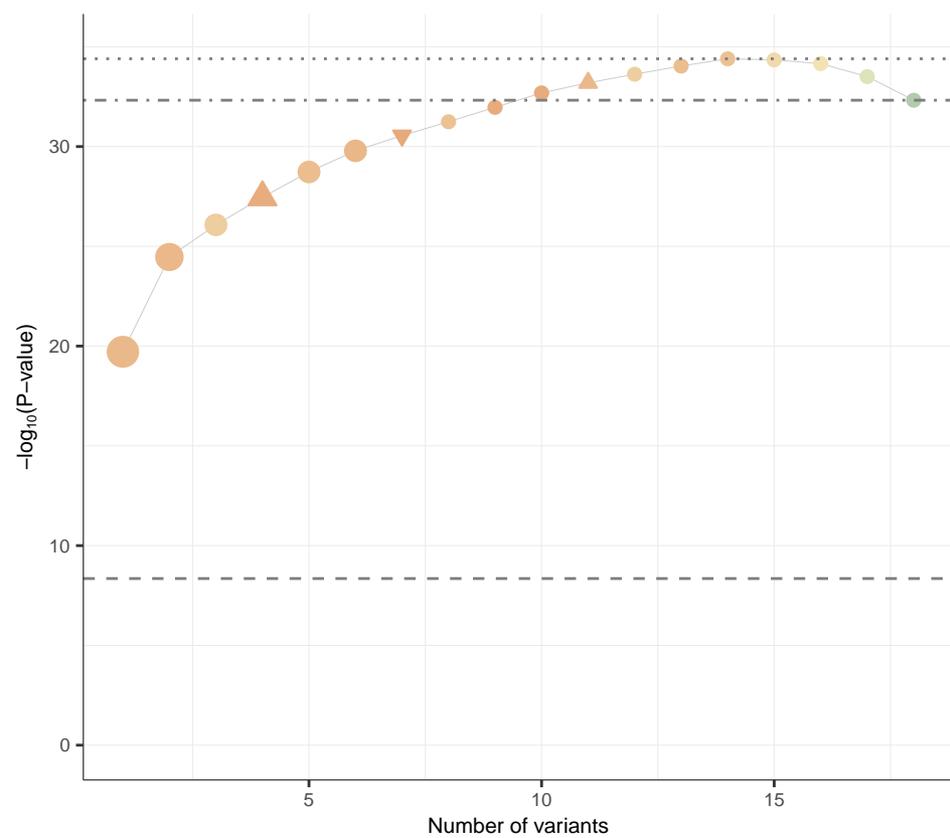
N-acetyltaurine in plasma at *PTER* (HI_mis)



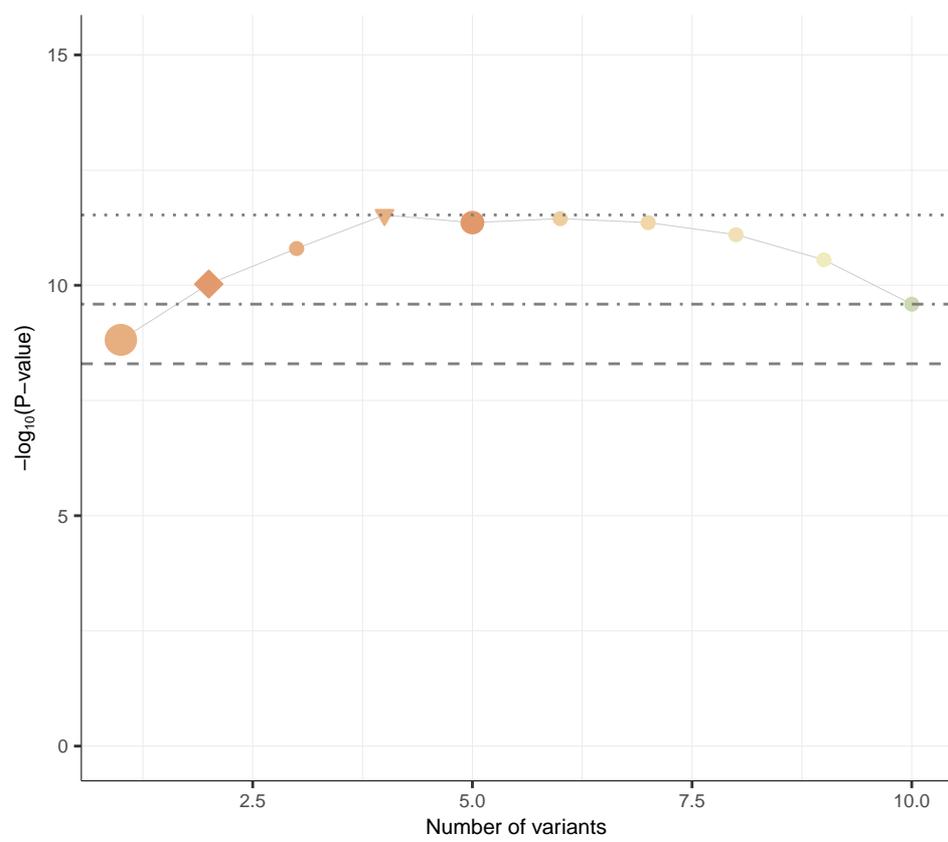
N-acetyltaurine in urine at *PTER* (LoF_mis)



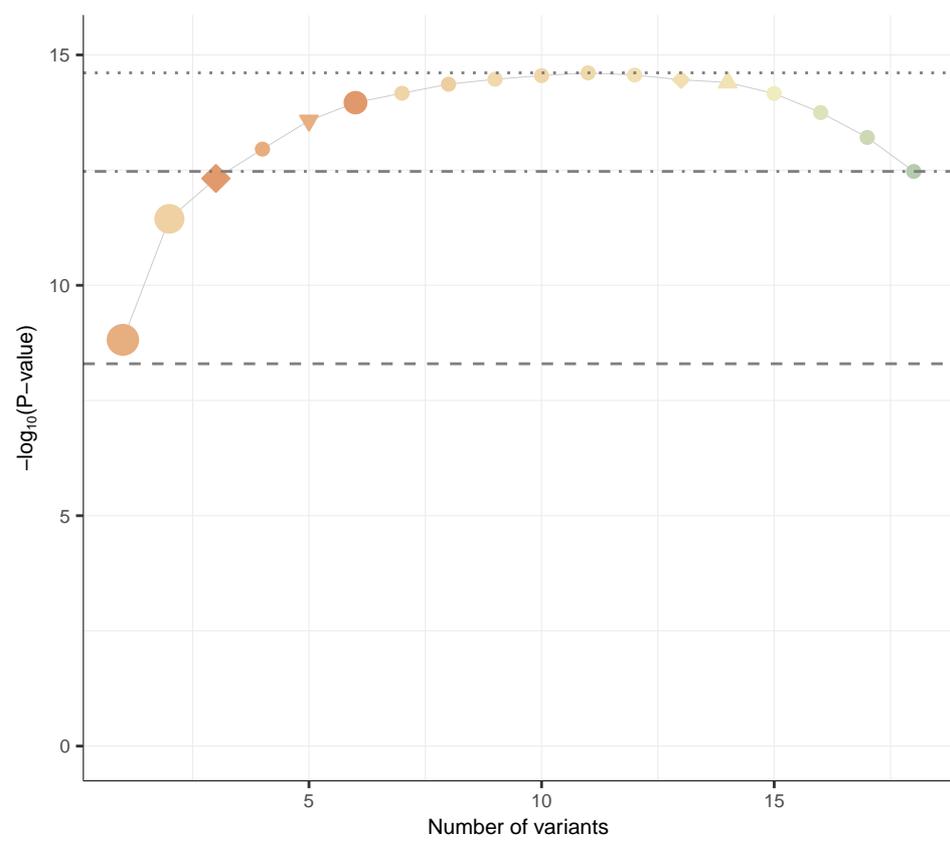
N-acetyltaurine in urine at *PTER* (HI_mis)



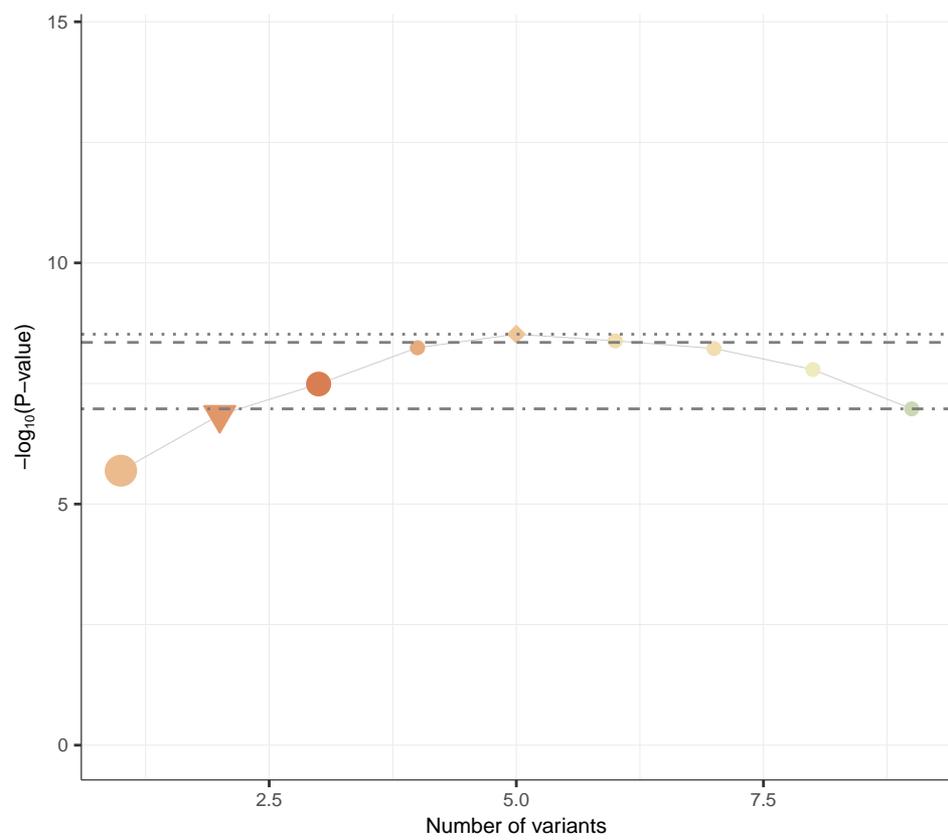
S-1-pyrroline-5-carboxylate in plasma at *PYCR3* (LoF_mis)



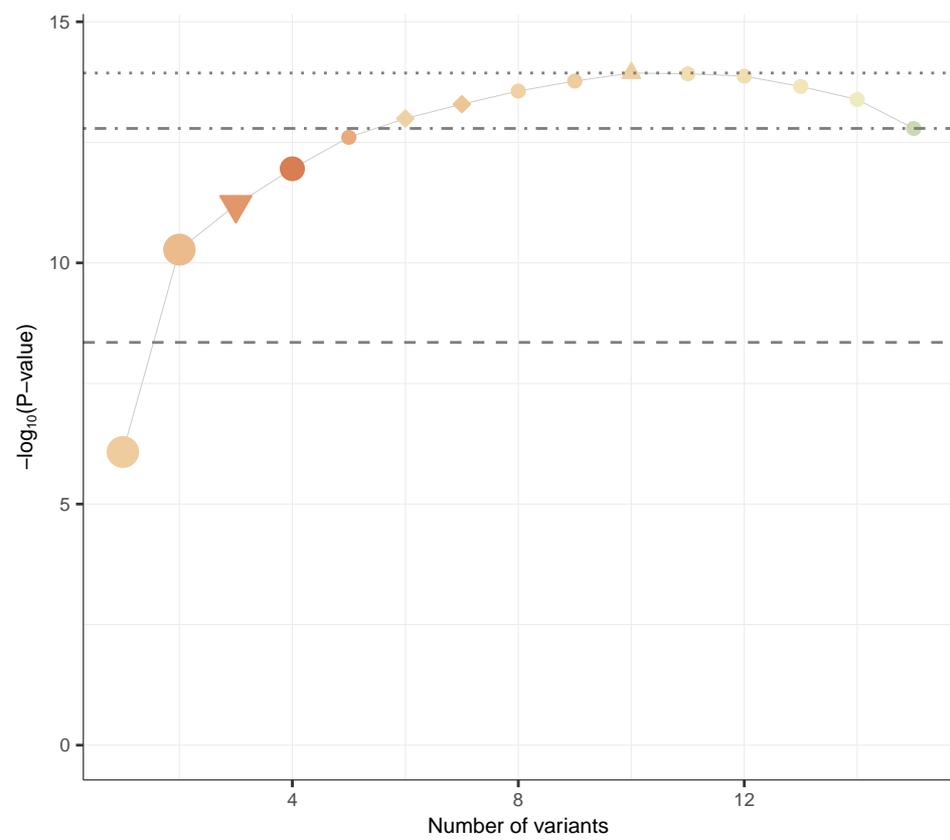
S-1-pyrroline-5-carboxylate in plasma at *PYCR3* (HI_mis)



S-1-pyrroline-5-carboxylate in urine at *PYCR3* (LoF_mis)



S-1-pyrroline-5-carboxylate in urine at *PYCR3* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained

Effect size

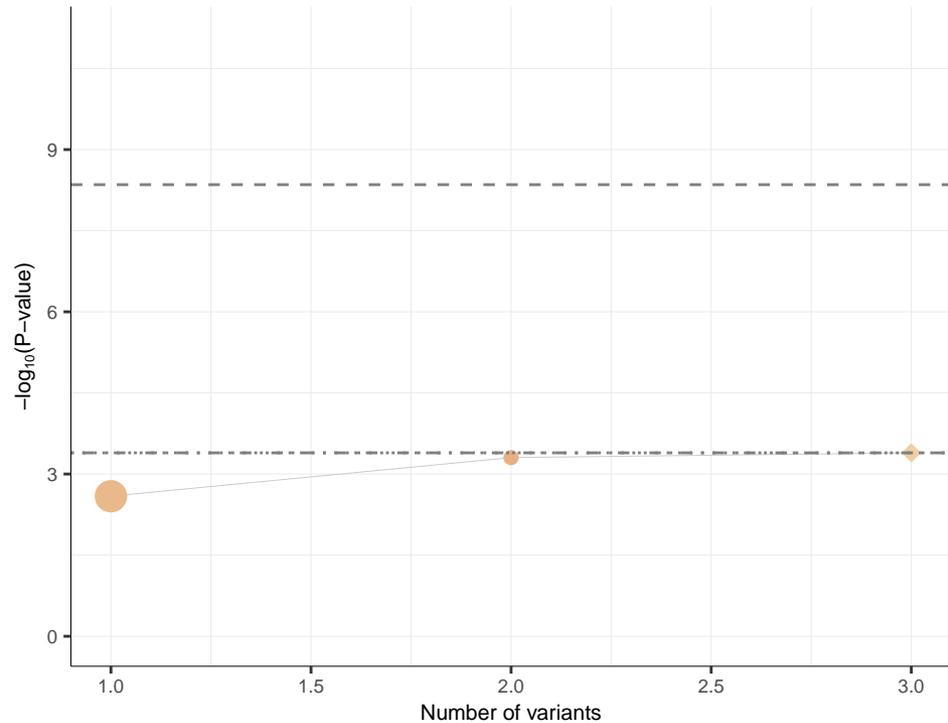
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

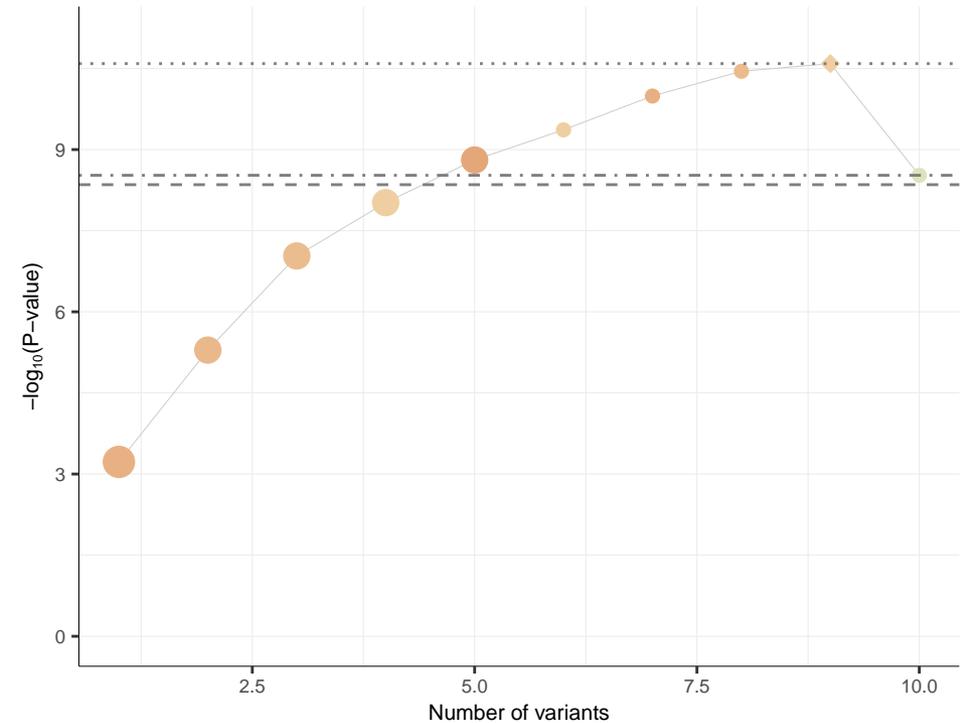
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

X - 23436 in urine at RGN (LoF_mis)

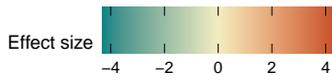


X - 23436 in urine at RGN (HI_mis)



Variant consequence

- ◇ frameshift
- missense



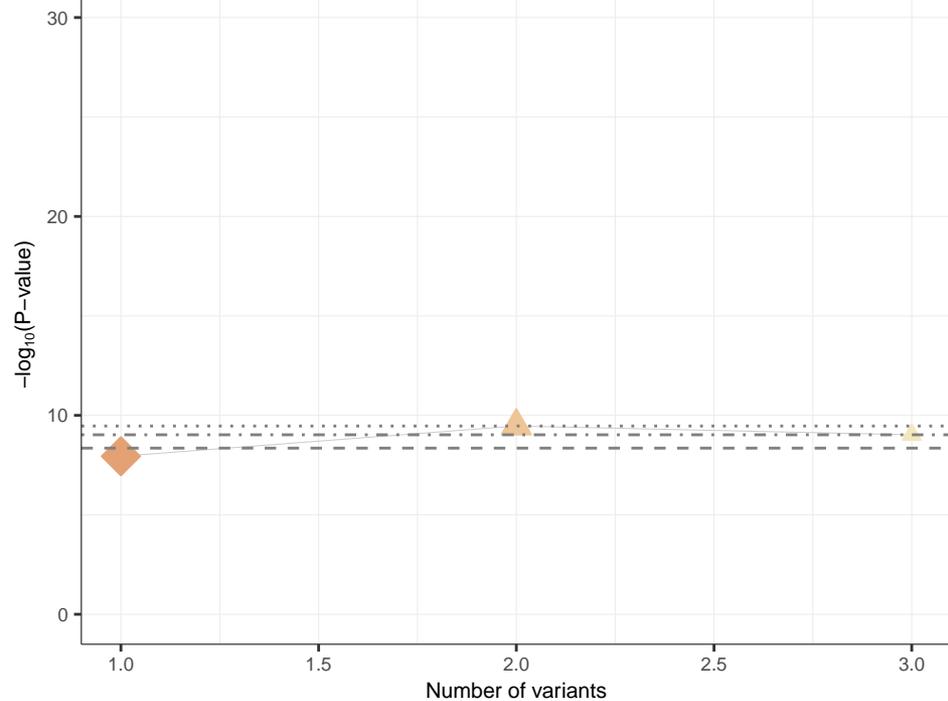
P-value

- >0.05
- <0.05
- <1e-3

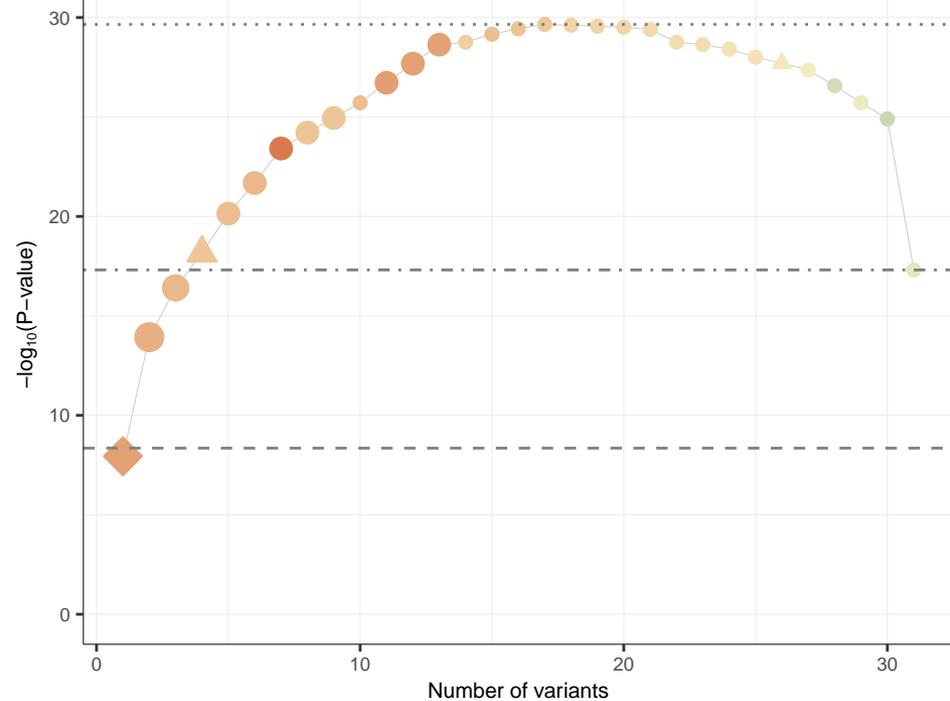
Thresholds

- - Significance Threshold
- . - Total P-value
- . . . Lowest P-value

X - 10457 in urine at RNPEP (LoF_mis)

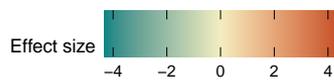


X - 10457 in urine at RNPEP (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



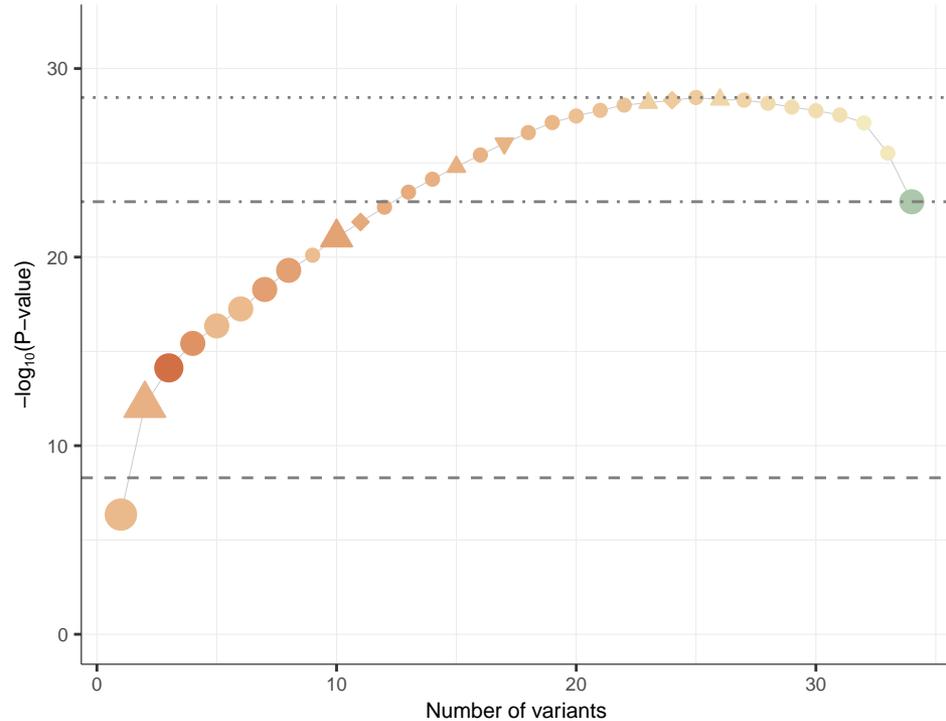
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

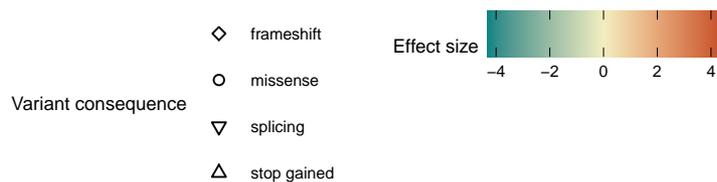
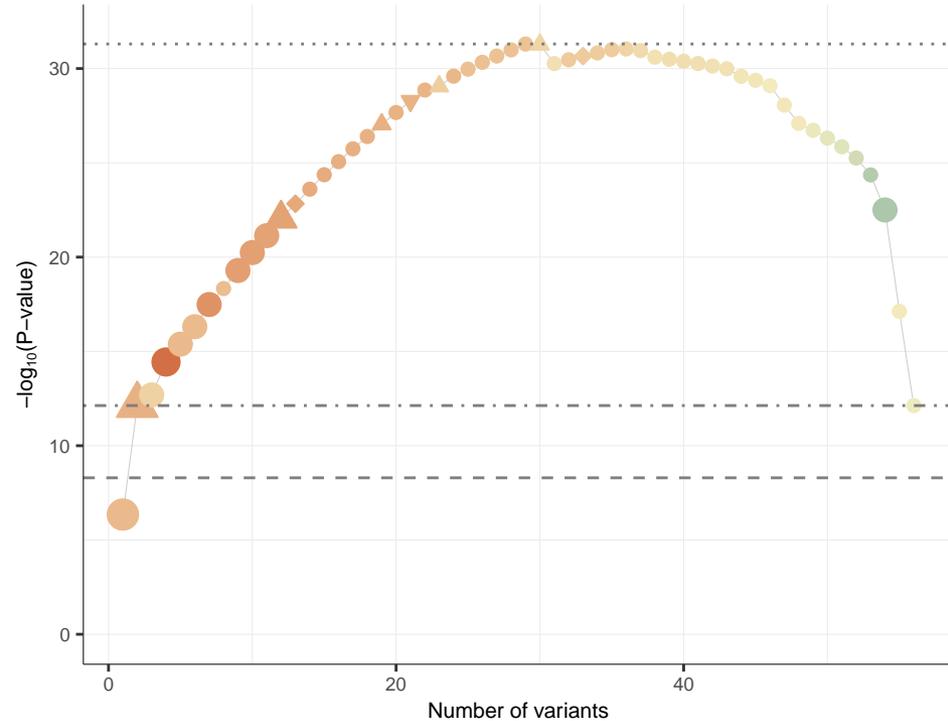
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

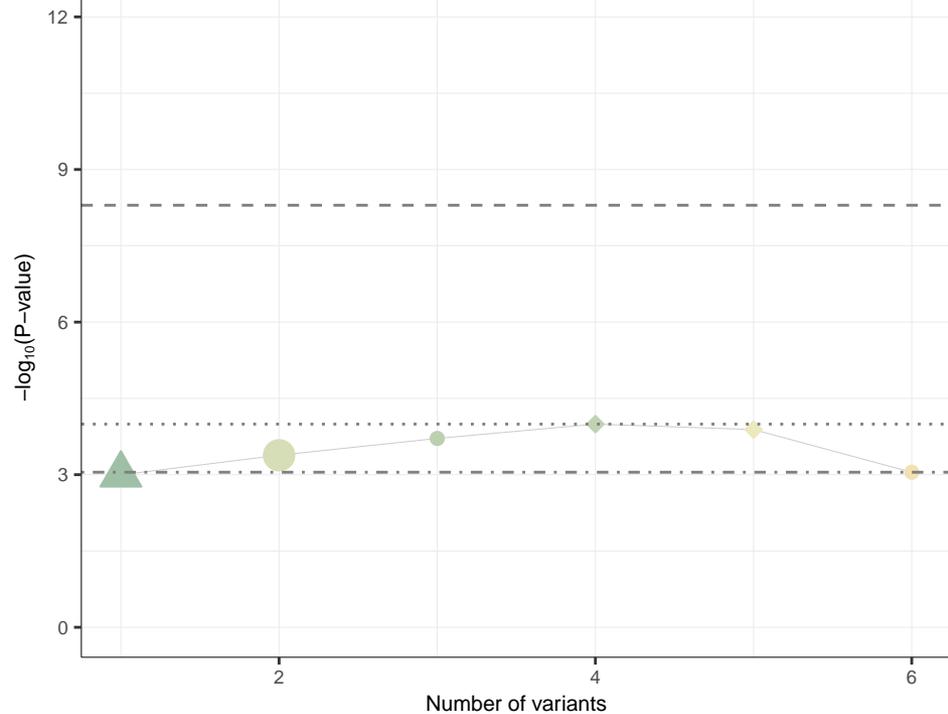
sarcosine in plasma at *SARDH* (LoF_mis)



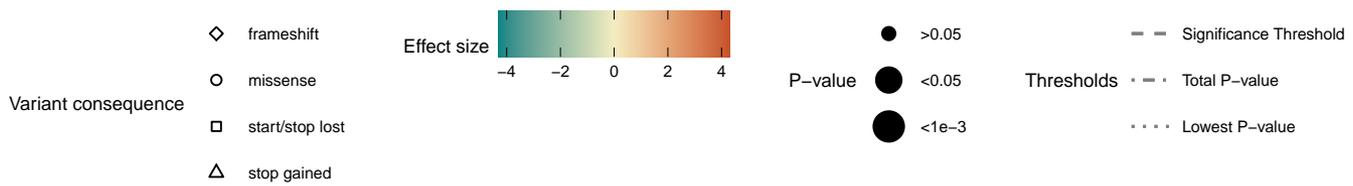
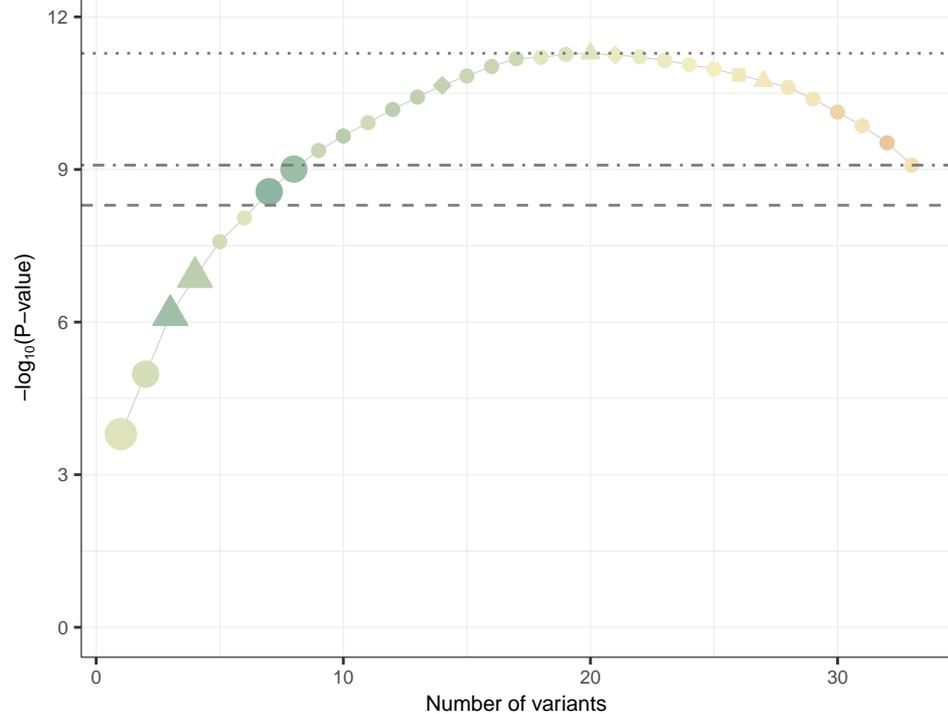
sarcosine in plasma at *SARDH* (HI_mis)

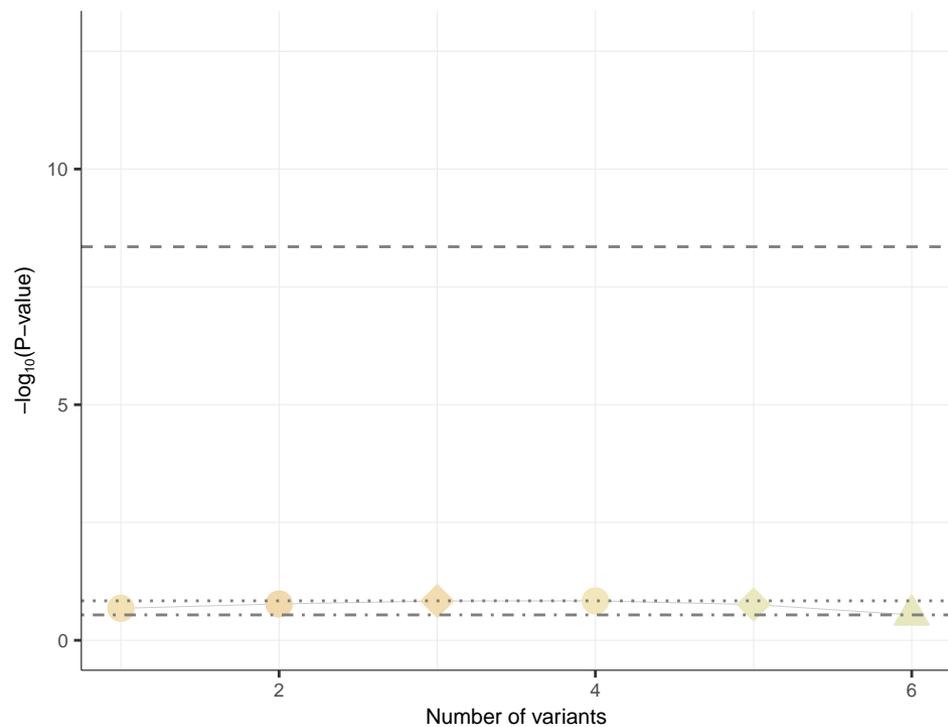


glycochenodeoxycholate 3-sulfate in plasma at *SLC10A2* (LoF_mis)



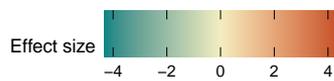
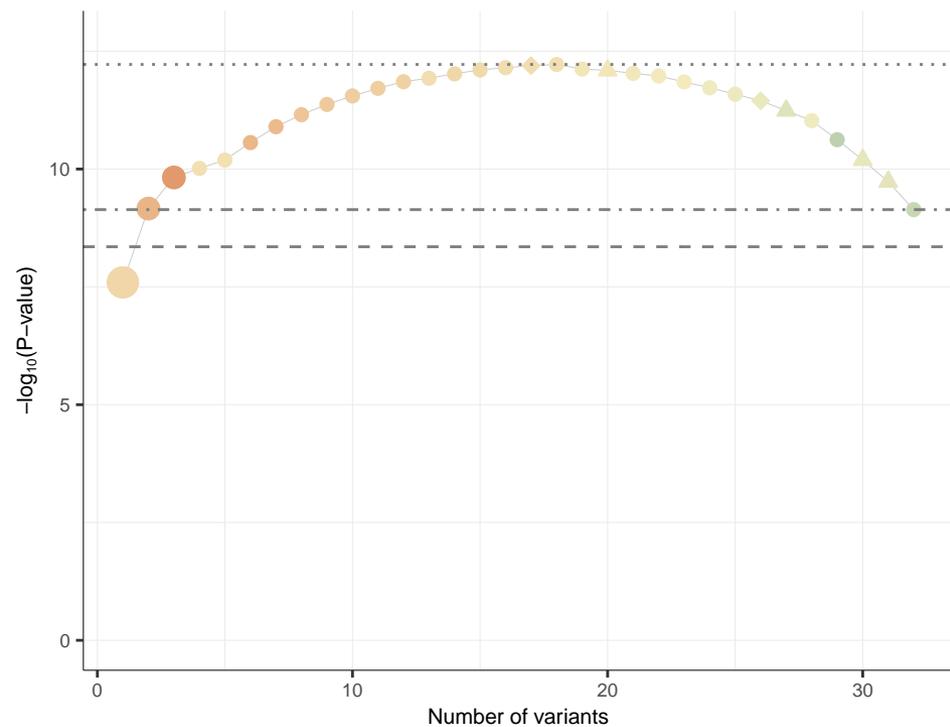
glycochenodeoxycholate 3-sulfate in plasma at *SLC10A2* (HI_mis)



glycocholate in urine at *SLC10A2* (LoF_mis)

Variant consequence

- ◇ frameshift
- missense
- △ stop gained

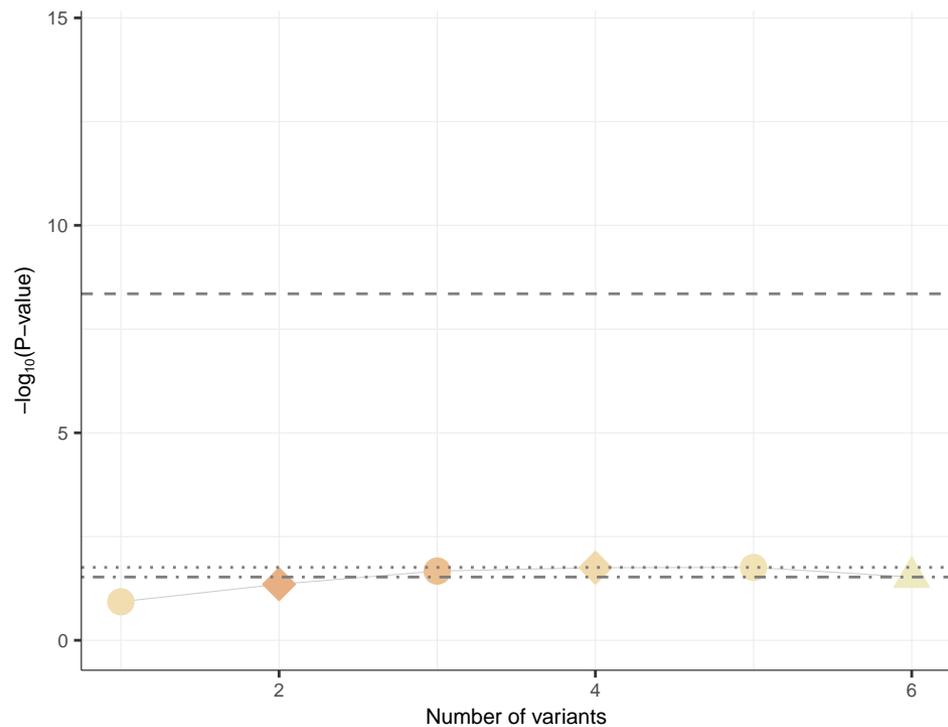
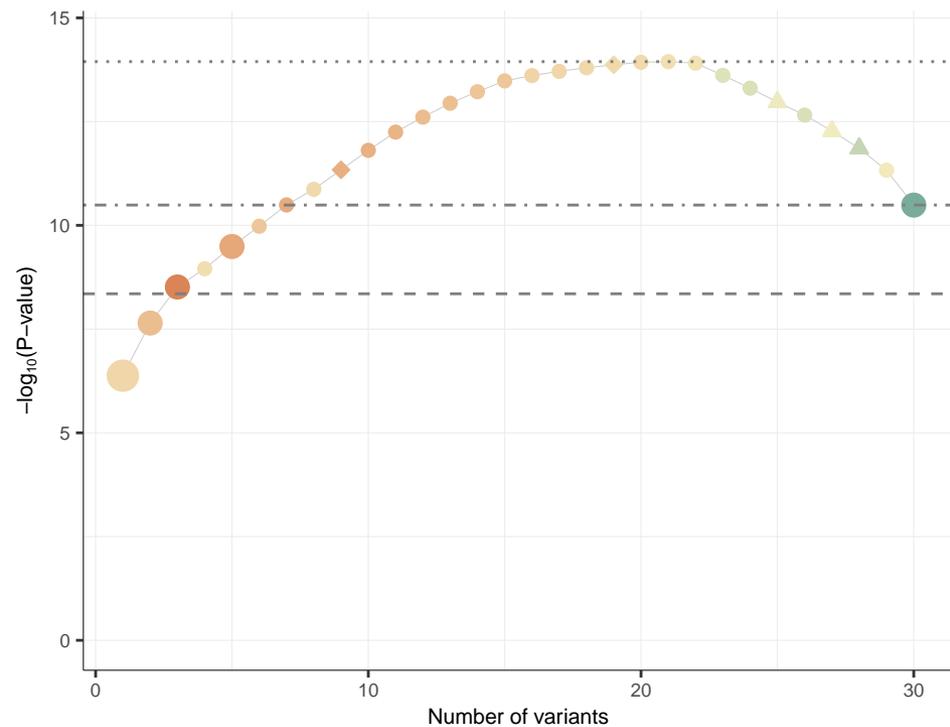
glycocholate in urine at *SLC10A2* (HI_mis)

P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

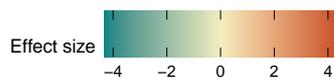
Thresholds

- Significance Threshold
- · - Total P-value
- Lowest P-value

glycoursodeoxycholate in urine at *SLC10A2* (LoF_mis)glycoursodeoxycholate in urine at *SLC10A2* (HI_mis)

Variant consequence

- ◇ frameshift
- missense
- △ stop gained



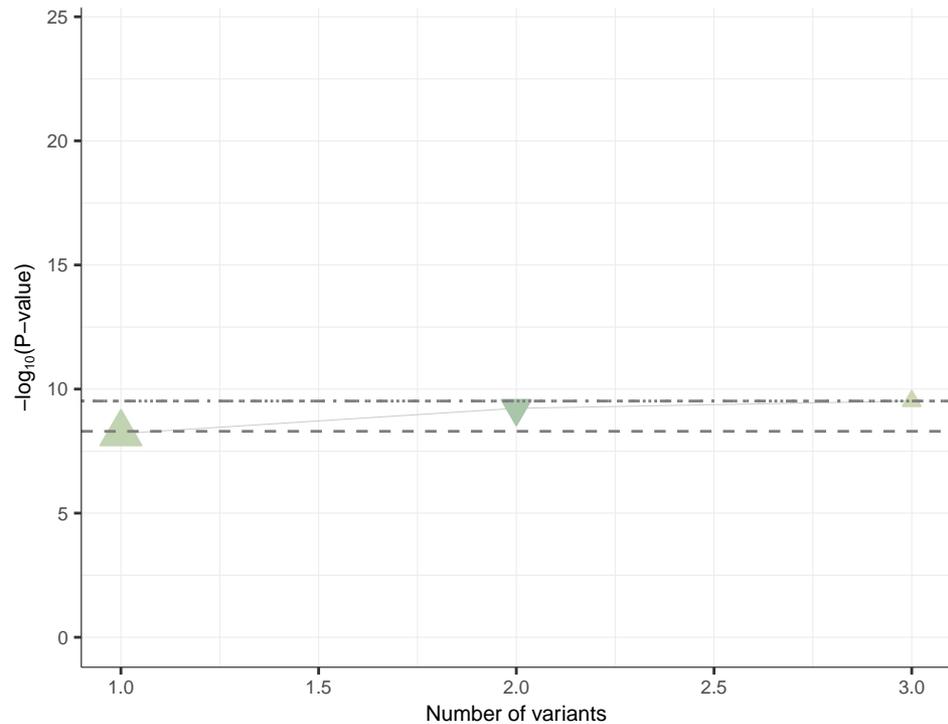
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

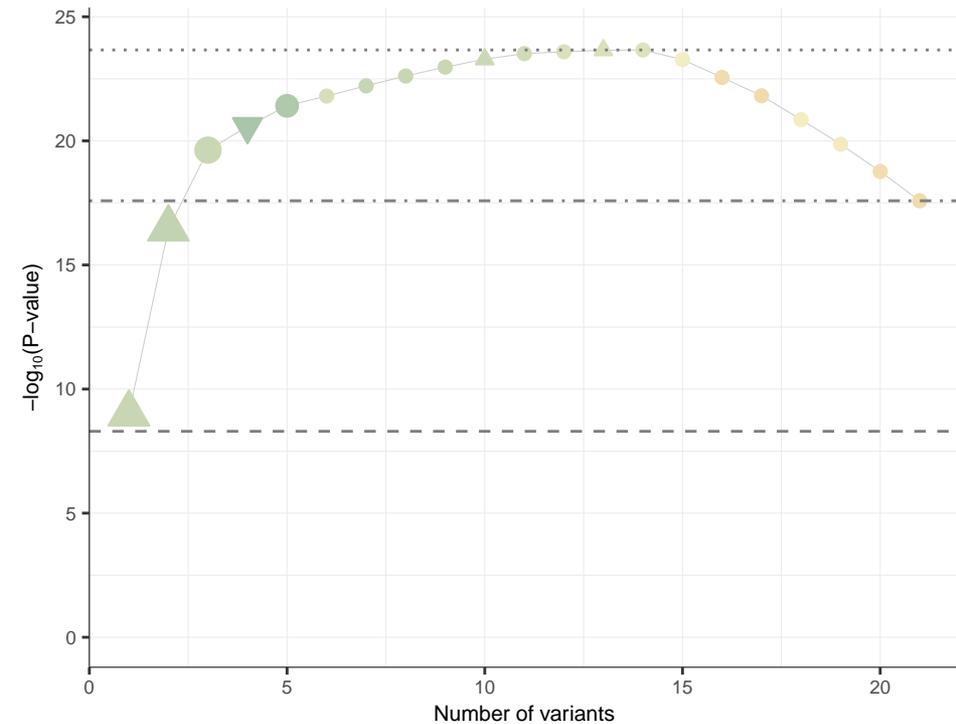
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

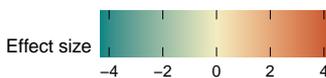
sulfate* in plasma at *SLC13A1* (LoF_mis)



sulfate* in plasma at *SLC13A1* (HI_mis)



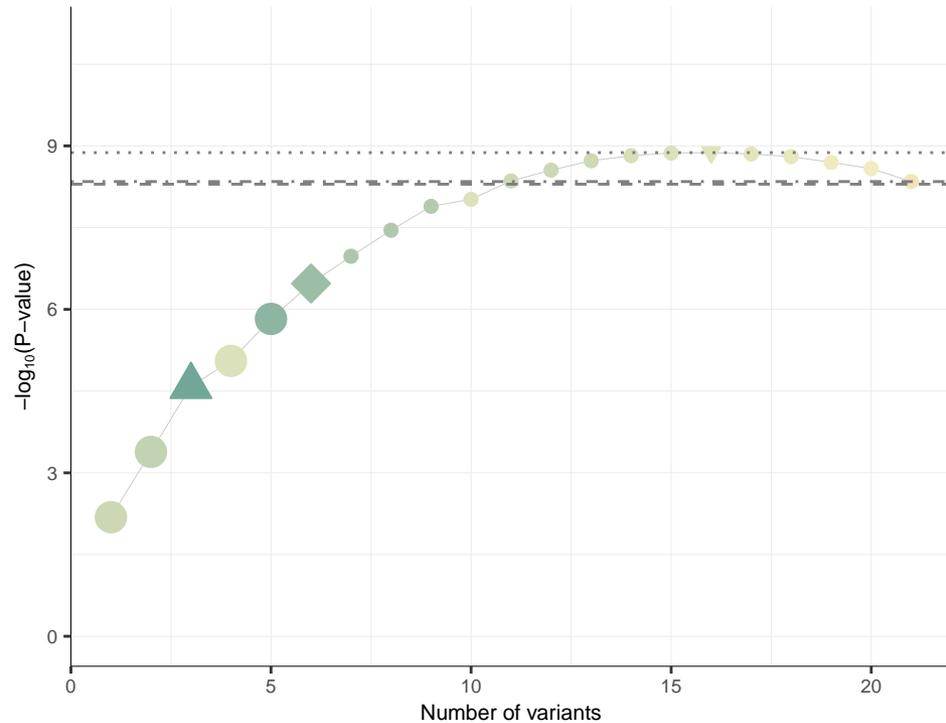
- Variant consequence
- missense
 - ▽ splicing
 - △ stop gained



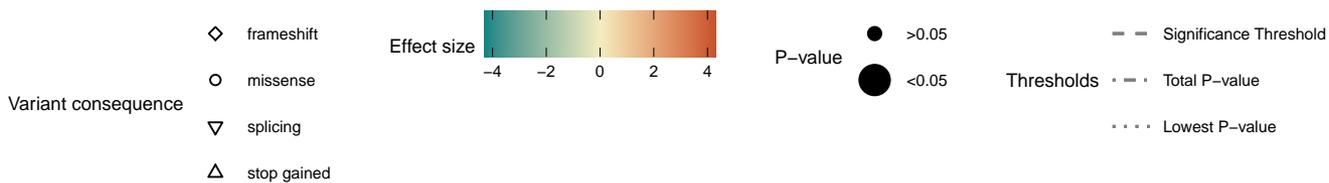
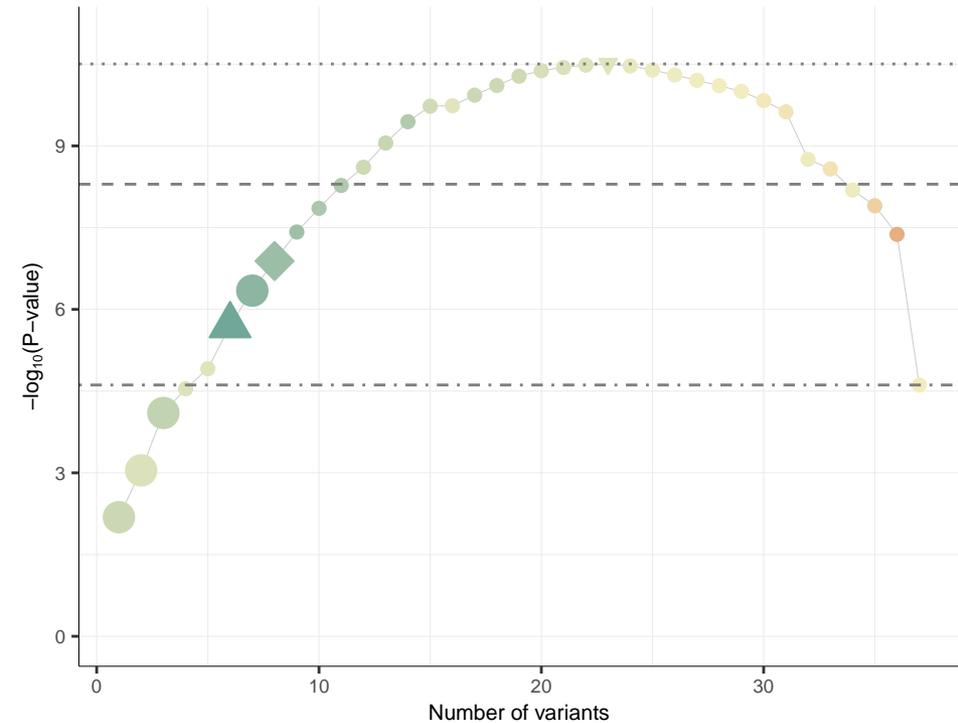
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8

- Thresholds
- - Significance Threshold
 - - - Total P-value
 - ⋯ Lowest P-value

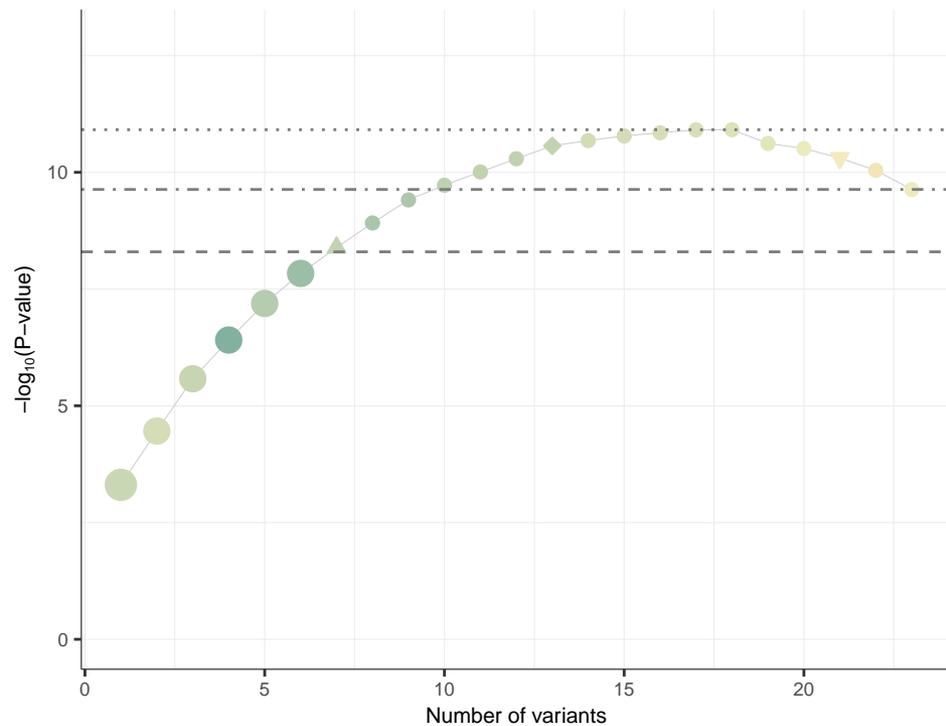
arachidonoylcarnitine (C20:4) in plasma at *SLC22A5* (LoF_mis)



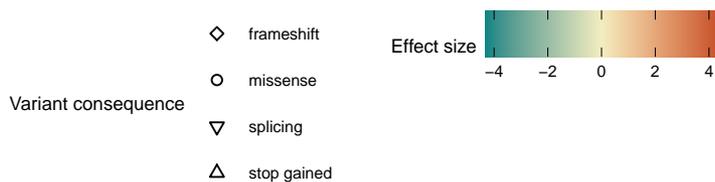
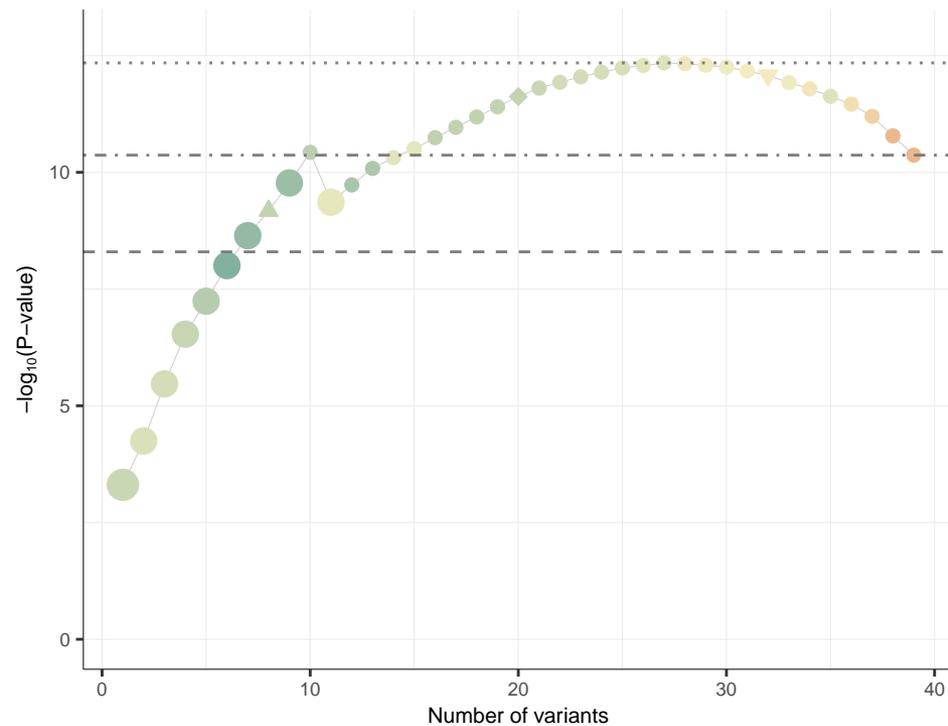
arachidonoylcarnitine (C20:4) in plasma at *SLC22A5* (HI_mis)



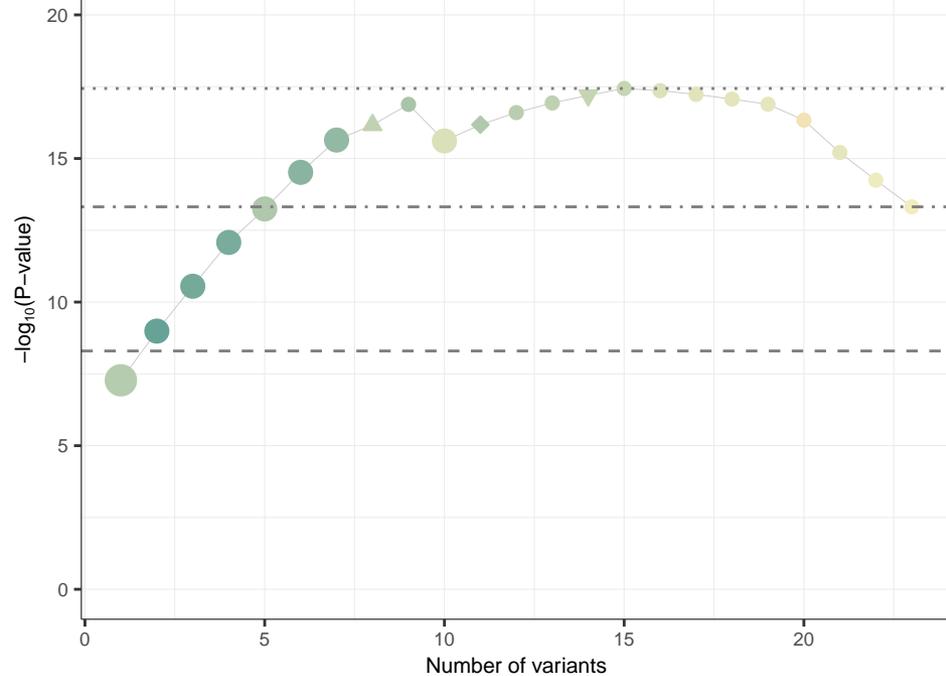
carnitine in plasma at SLC22A5 (LoF_mis)



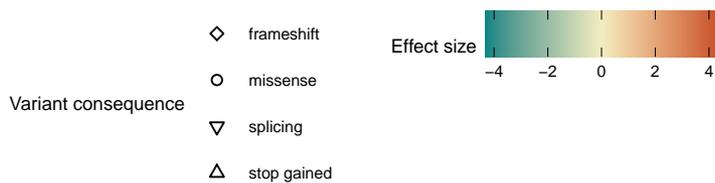
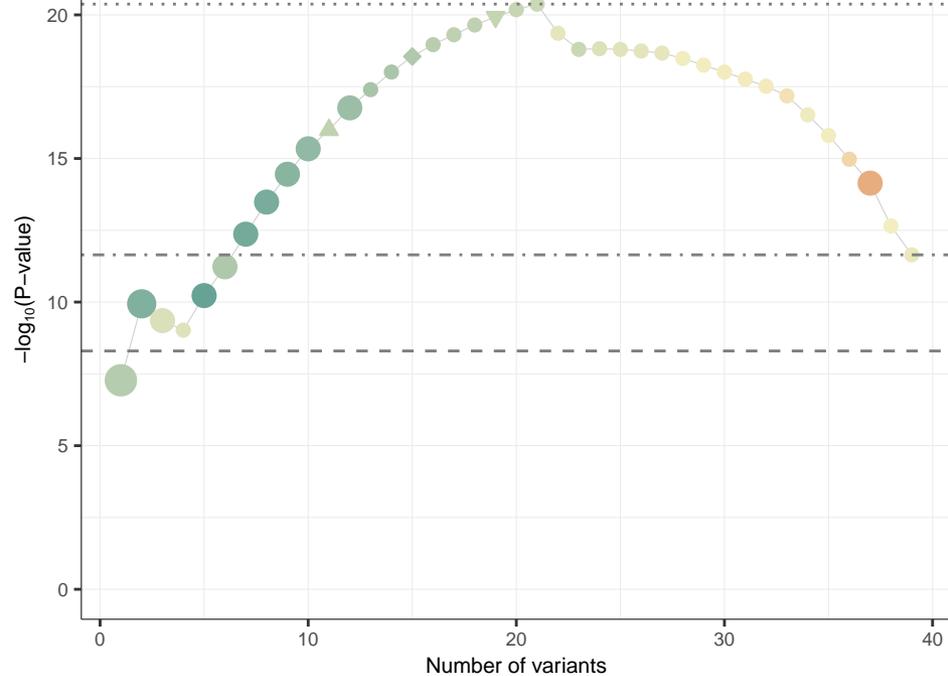
carnitine in plasma at SLC22A5 (HI_mis)



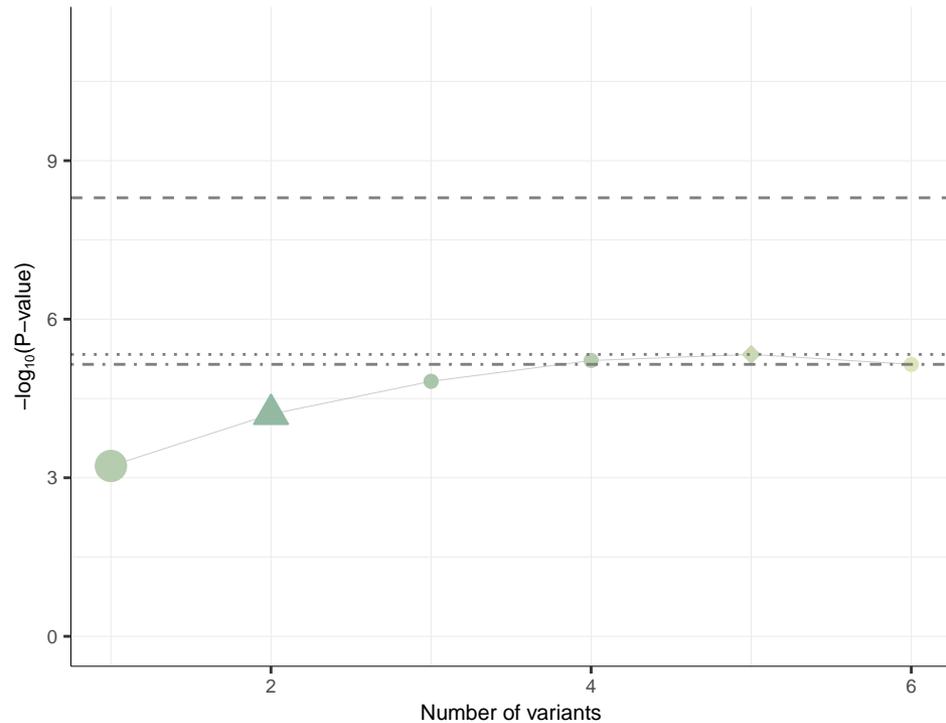
N,N,N-trimethyl-5-aminovalerate in plasma at *SLC22A5* (LoF_mis)



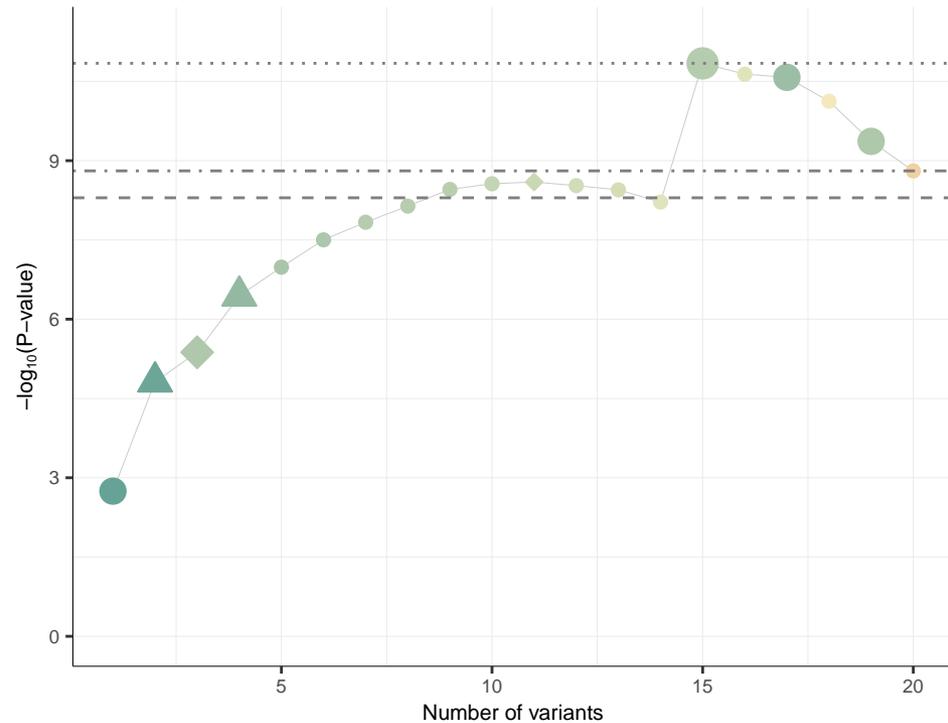
N,N,N-trimethyl-5-aminovalerate in plasma at *SLC22A5* (HI_mis)



gamma-glutamylglutamate in plasma at *SLC22A7* (LoF_mis)

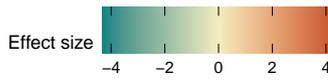


gamma-glutamylglutamate in plasma at *SLC22A7* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



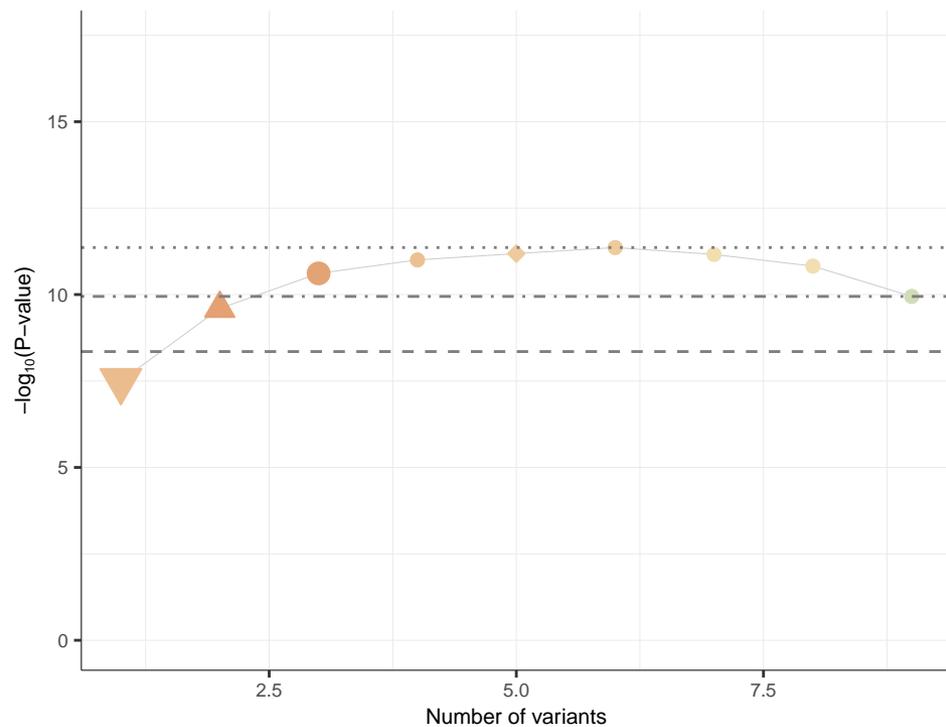
P-value

- >0.05
- <0.05
- <1e-3

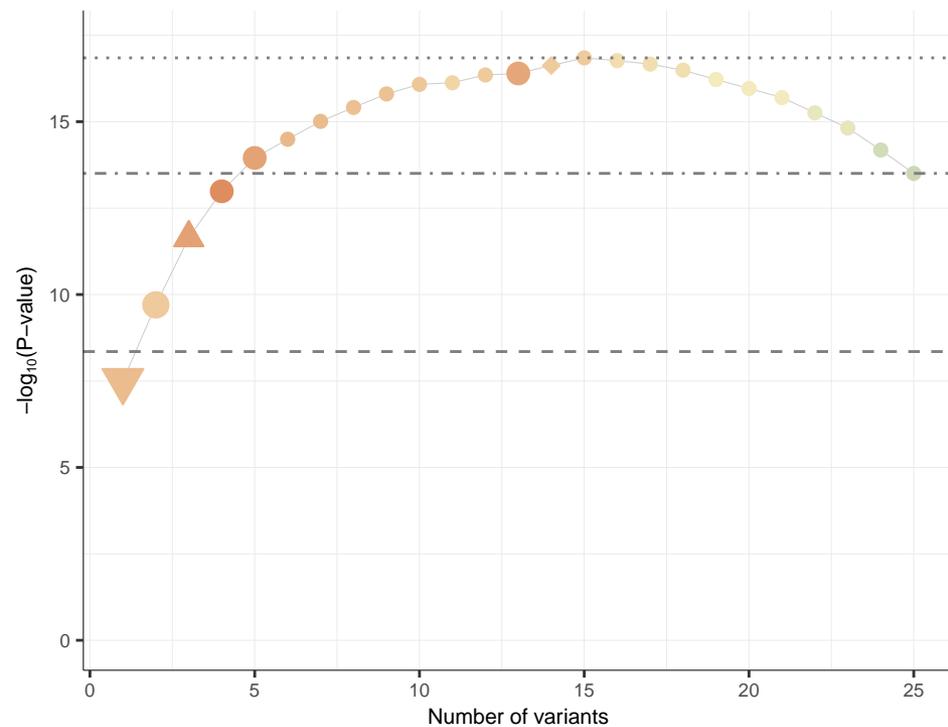
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

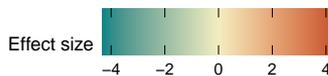
choline in urine at *SLC25A48* (LoF_mis)



choline in urine at *SLC25A48* (HI_mis)

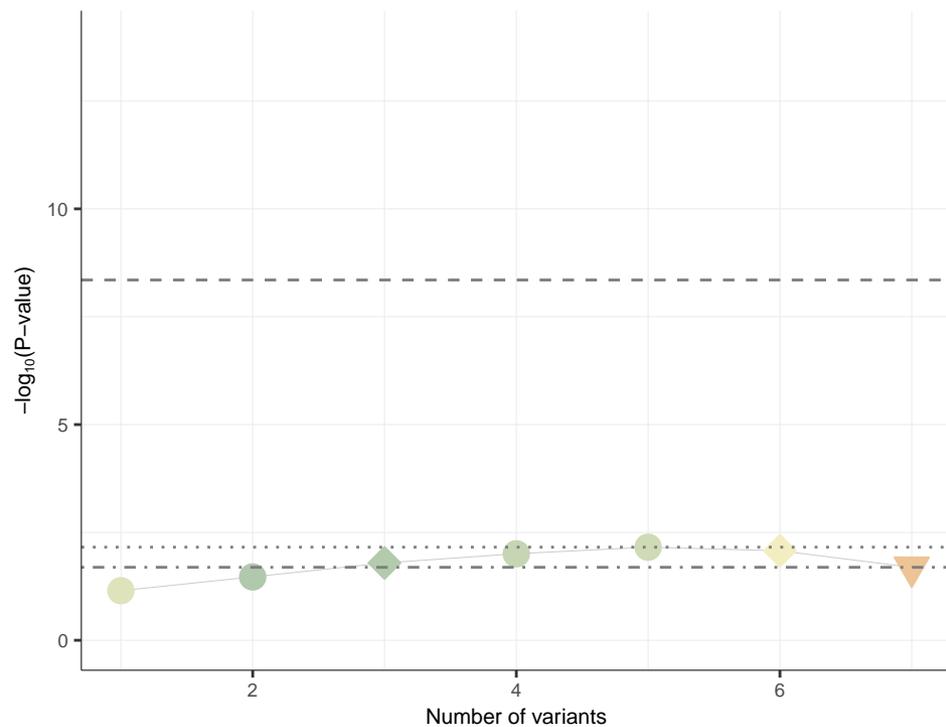


- Variant consequence
- ◇ frameshift
 - missense
 - ▽ splicing
 - △ stop gained

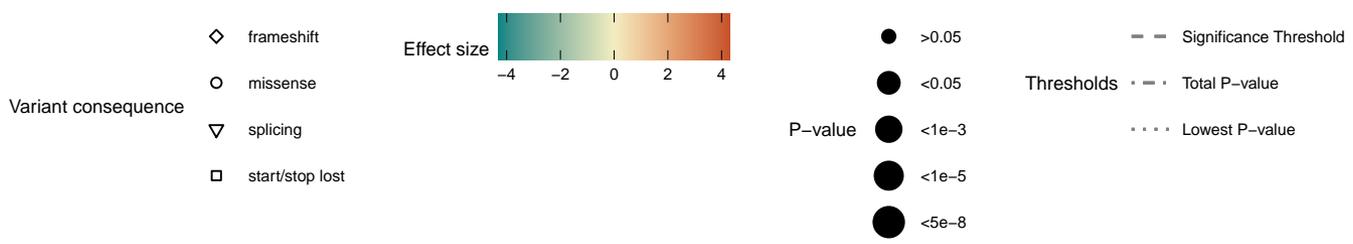
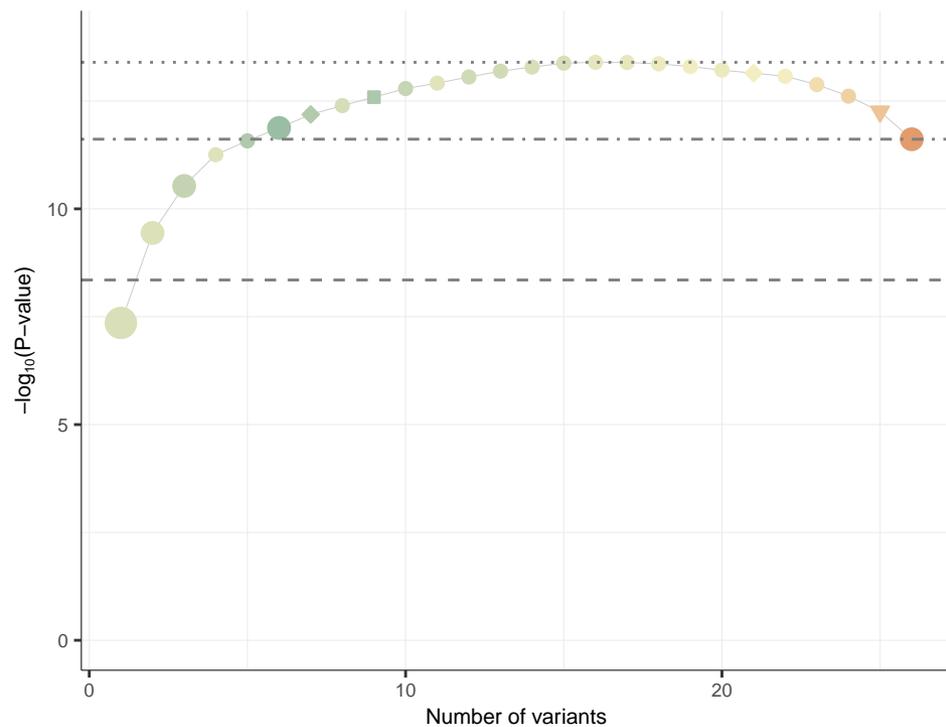


- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
- Thresholds
- Significance Threshold
 - - - Total P-value
 - ⋯ Lowest P-value

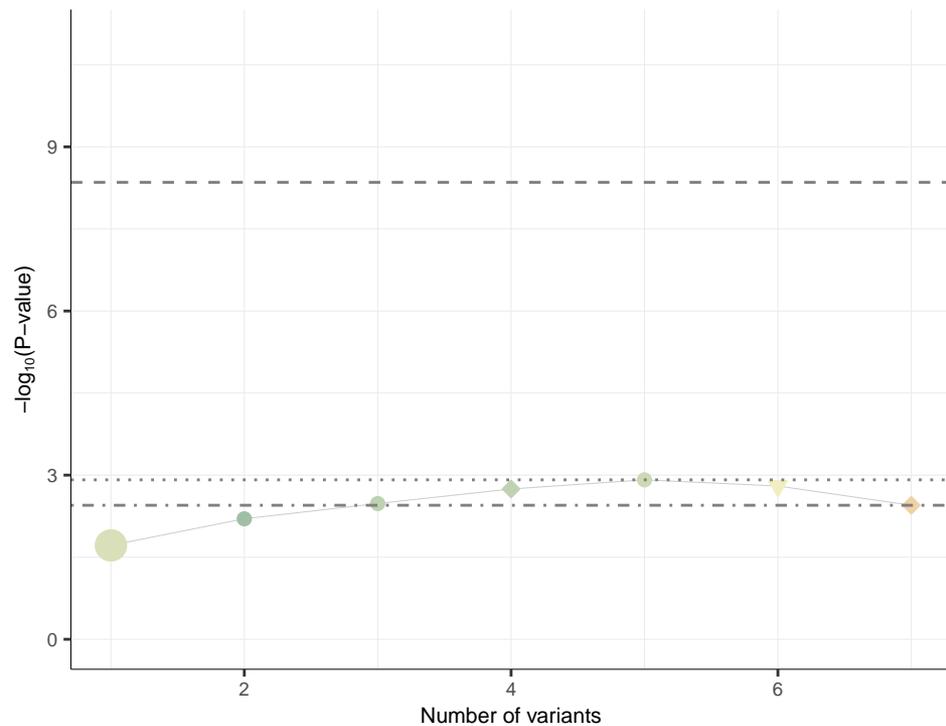
(N(1) + N(8))-acetylsermidine in urine at *SLC47A1* (LoF_mis)



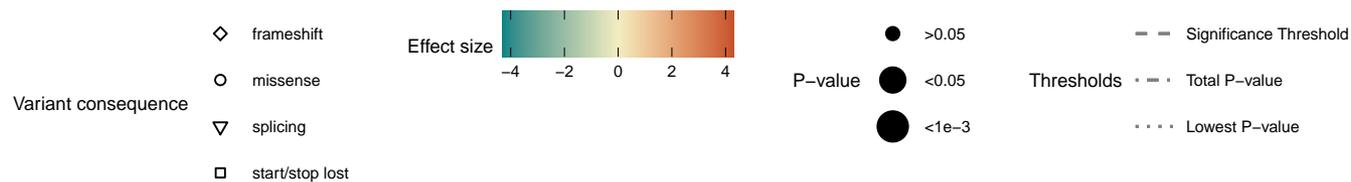
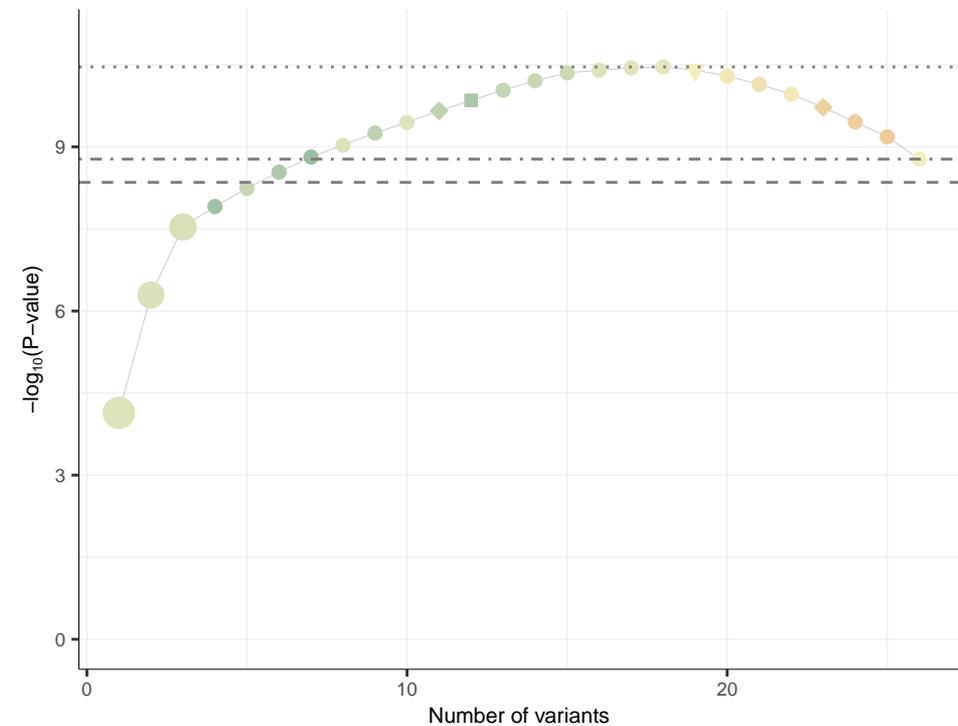
(N(1) + N(8))-acetylsermidine in urine at *SLC47A1* (HI_mis)



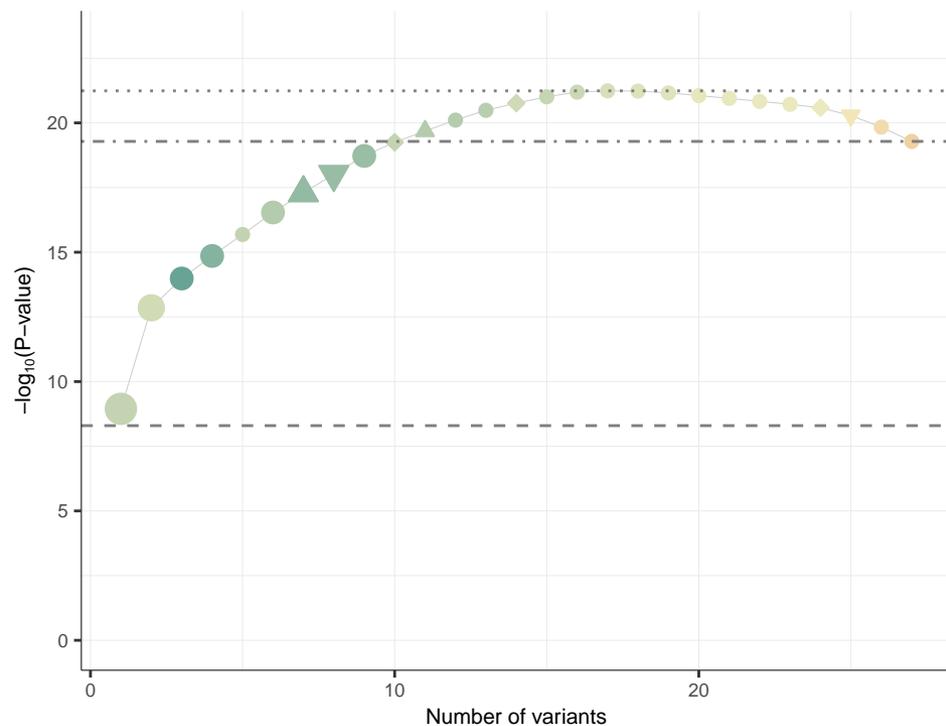
dopamine in urine at *SLC47A1* (LoF_mis)



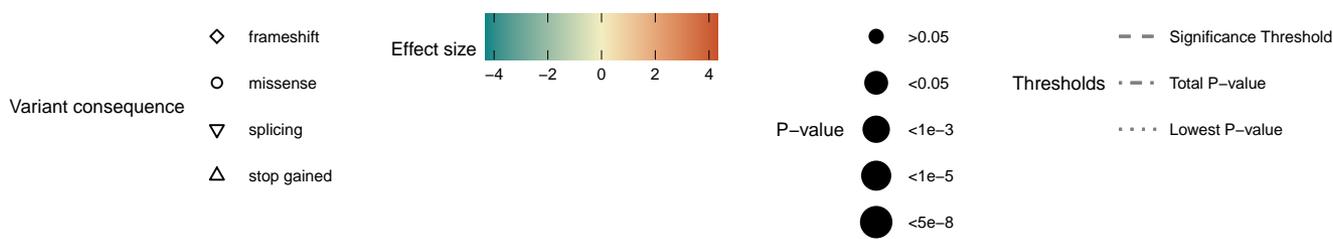
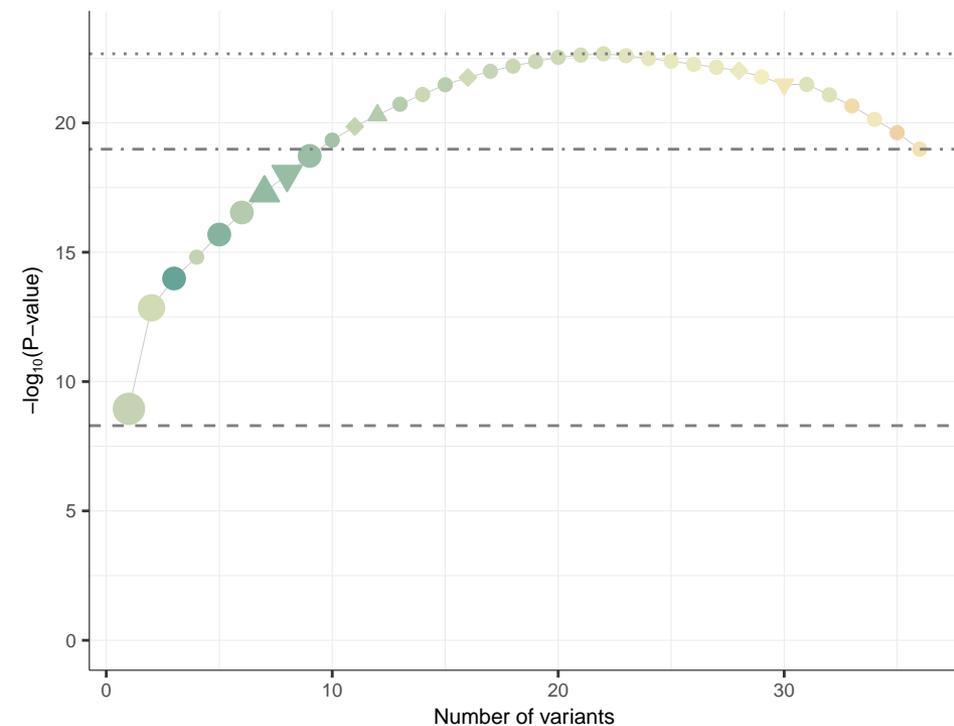
dopamine in urine at *SLC47A1* (HI_mis)



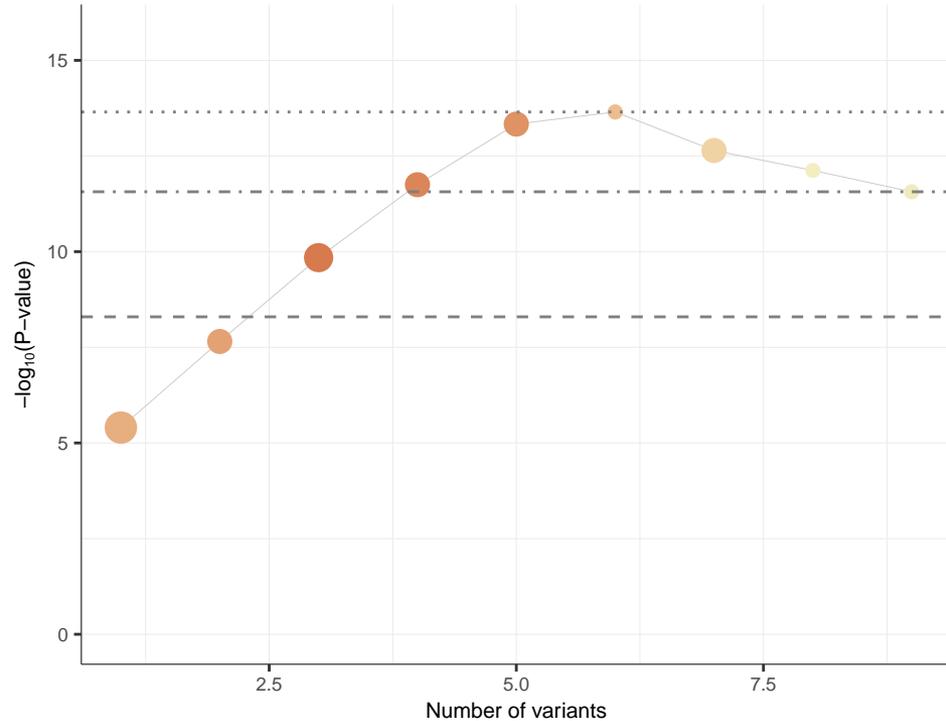
1,5-anhydroglucitol (1,5-AG) in plasma at *SLC5A10* (LoF_mis)



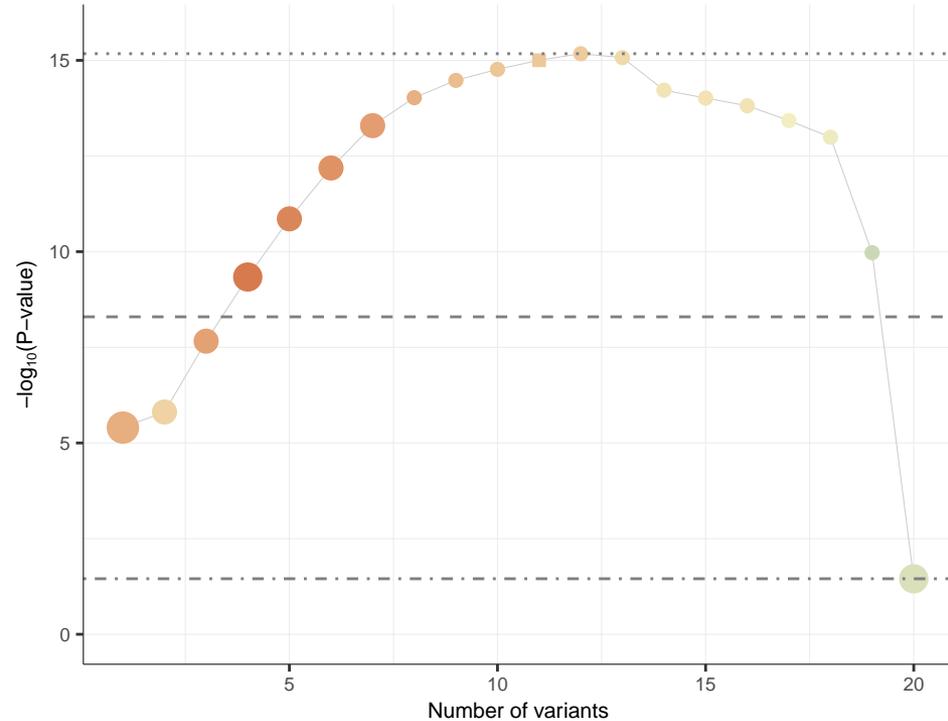
1,5-anhydroglucitol (1,5-AG) in plasma at *SLC5A10* (HI_mis)



betaine in plasma at *SLC6A12* (LoF_mis)



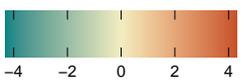
betaine in plasma at *SLC6A12* (HI_mis)



Variant consequence

- missense
- start/stop lost

Effect size



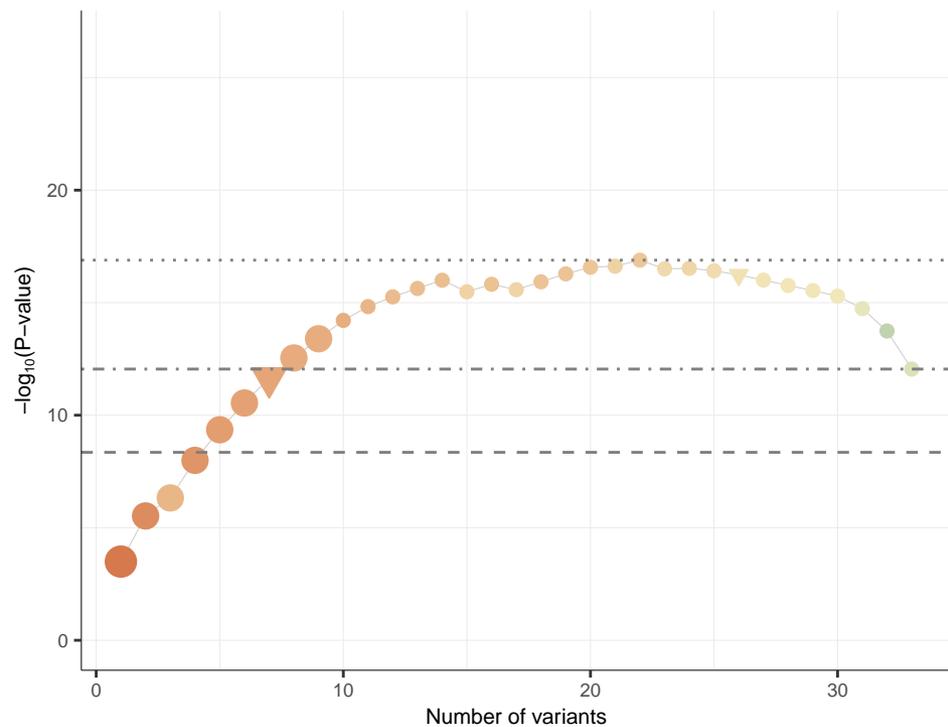
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

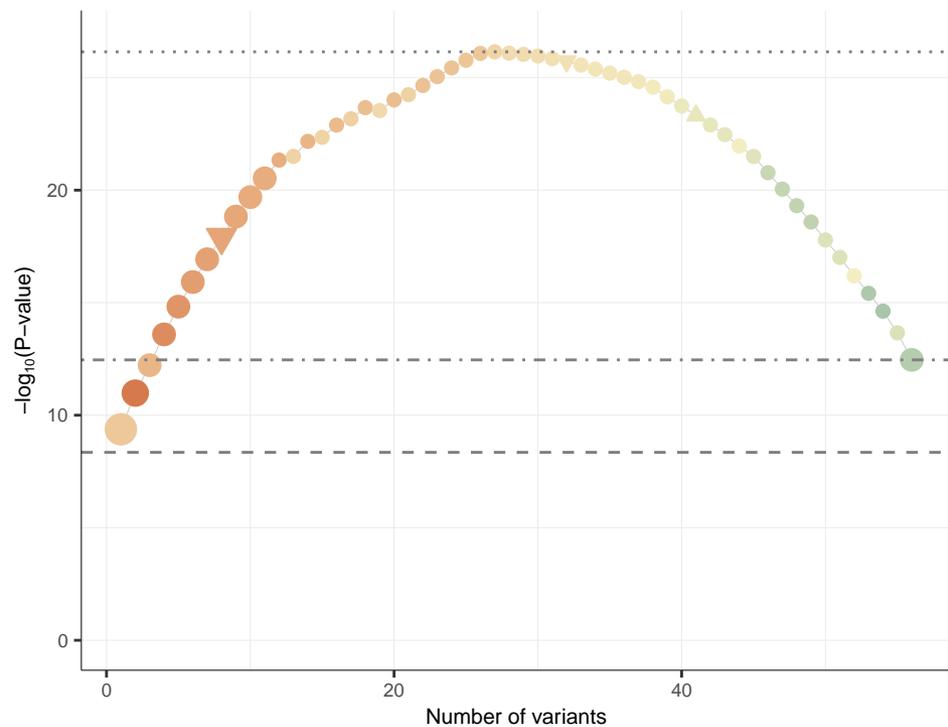
Thresholds

- Significance Threshold
- - - Total P-value
- ... Lowest P-value

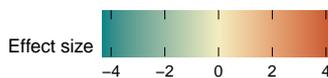
histidine in urine at *SLC6A19* (LoF_mis)



histidine in urine at *SLC6A19* (HI_mis)



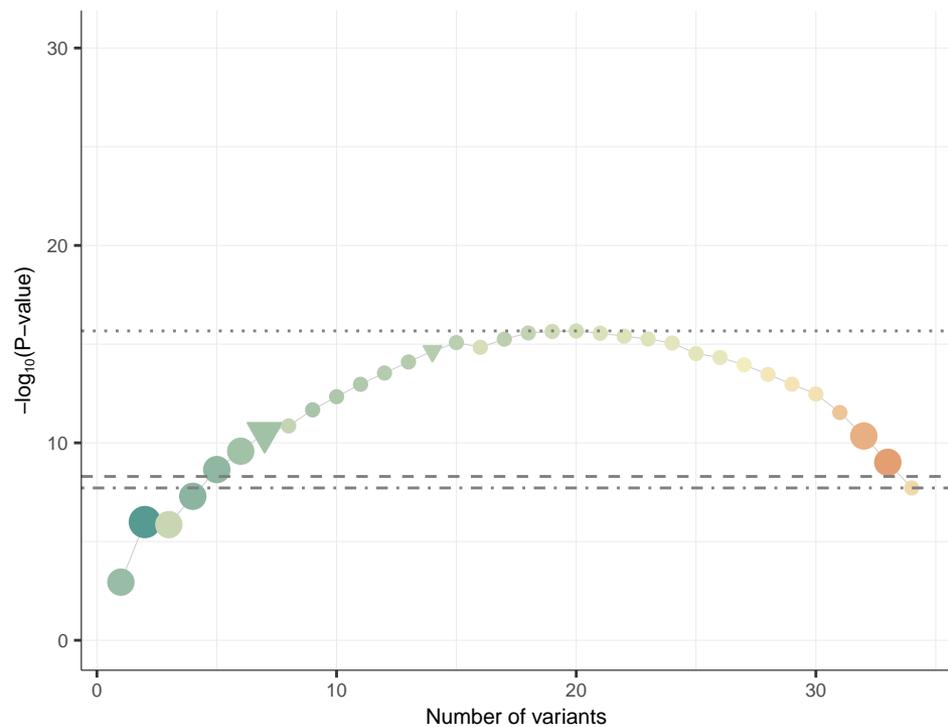
○ missense
 ▽ splicing
 △ stop gained



● >0.05
 ● <0.05
 P-value ● <1e-3
 ● <1e-5
 ● <5e-8

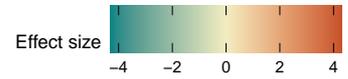
— Significance Threshold
 - - - Total P-value
 ···· Lowest P-value

methionine sulfone in plasma at *SLC6A19* (LoF_mis)

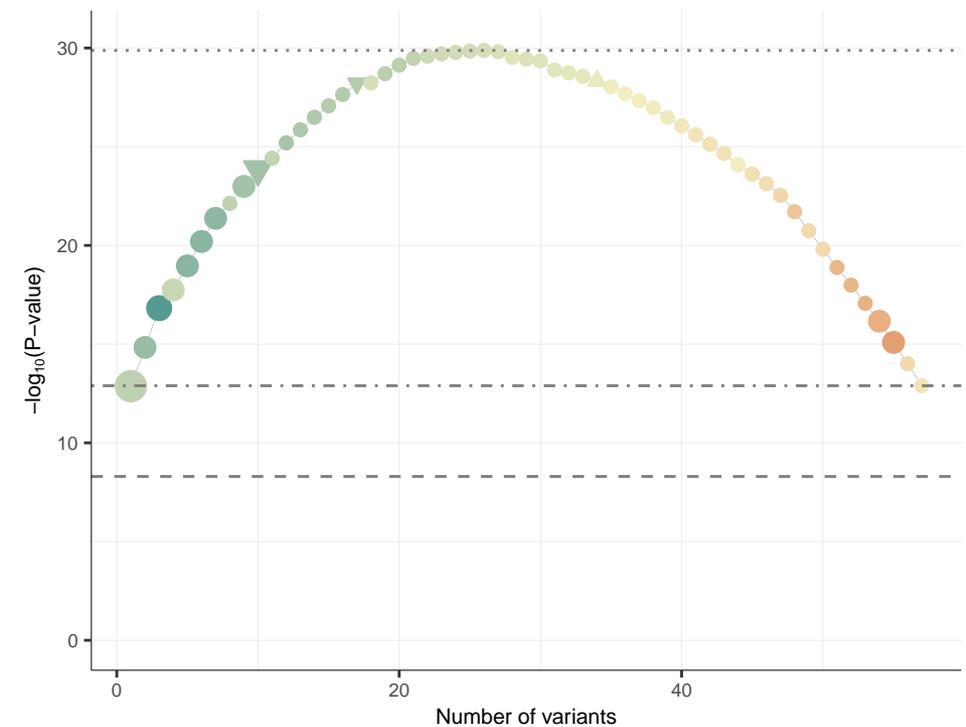


Variant consequence

- missense
- ▽ splicing
- △ stop gained



methionine sulfone in plasma at *SLC6A19* (HI_mis)



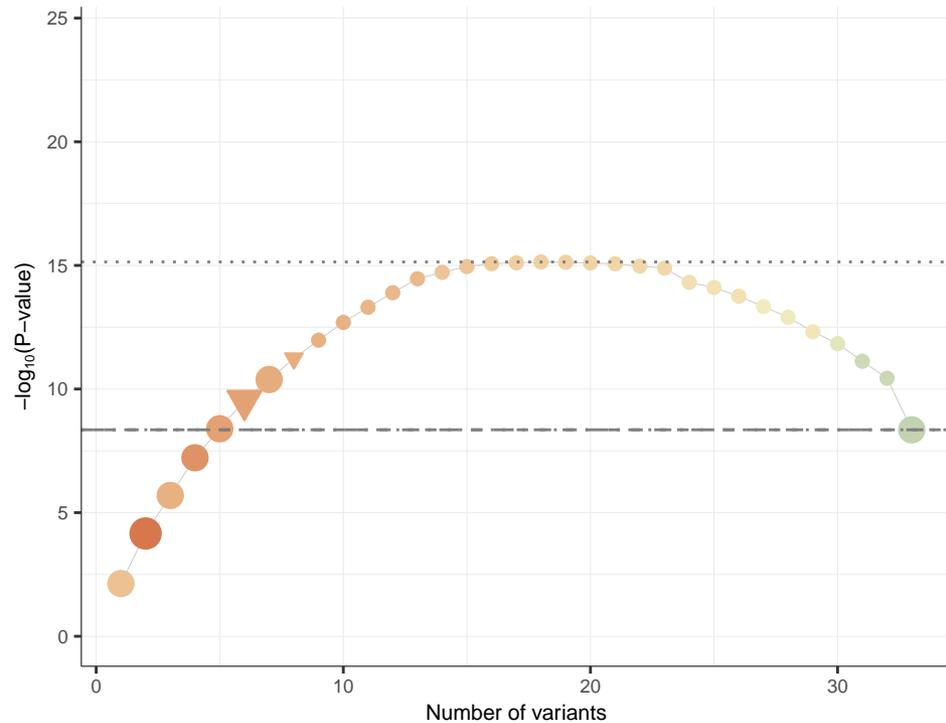
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

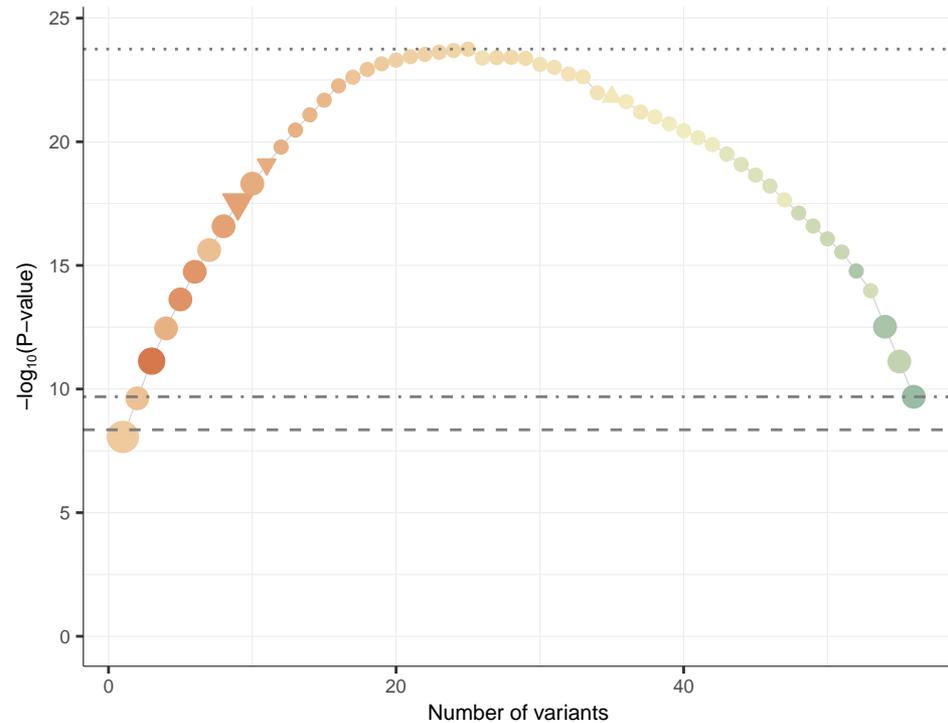
Thresholds

- Significance Threshold
- - - Total P-value
- Lowest P-value

tryptophan in urine at *SLC6A19* (LoF_mis)

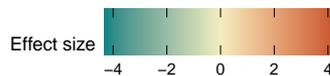


tryptophan in urine at *SLC6A19* (HI_mis)



○ missense
 ▽ splicing
 △ stop gained

Variant consequence

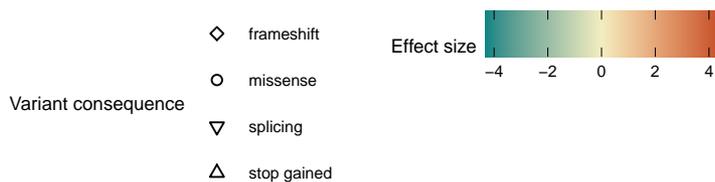
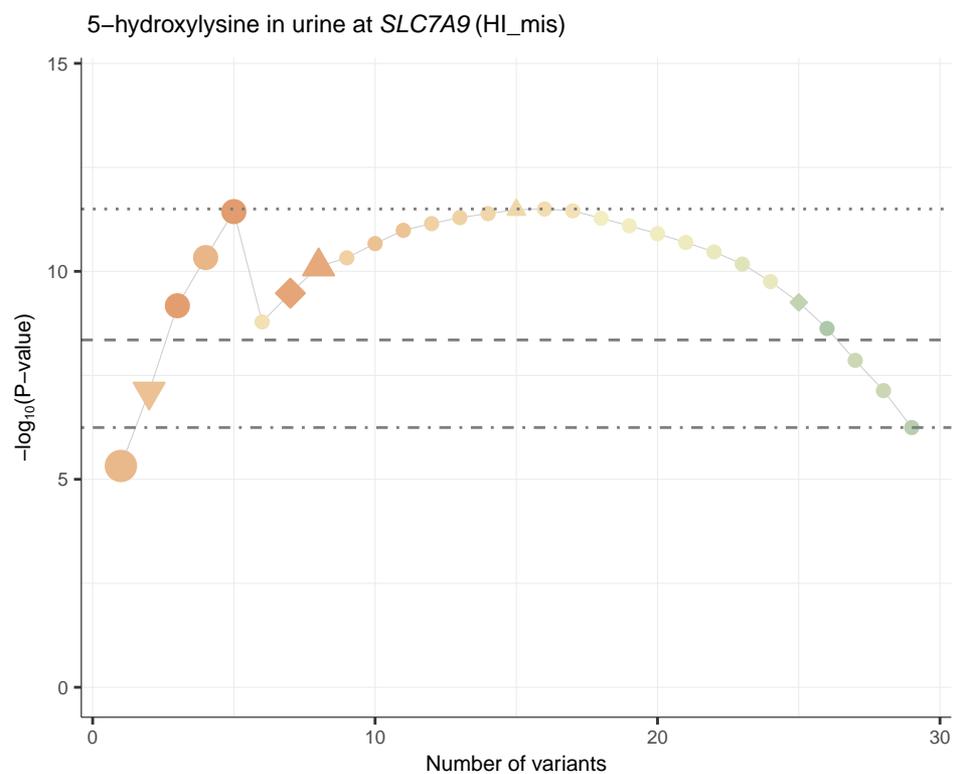
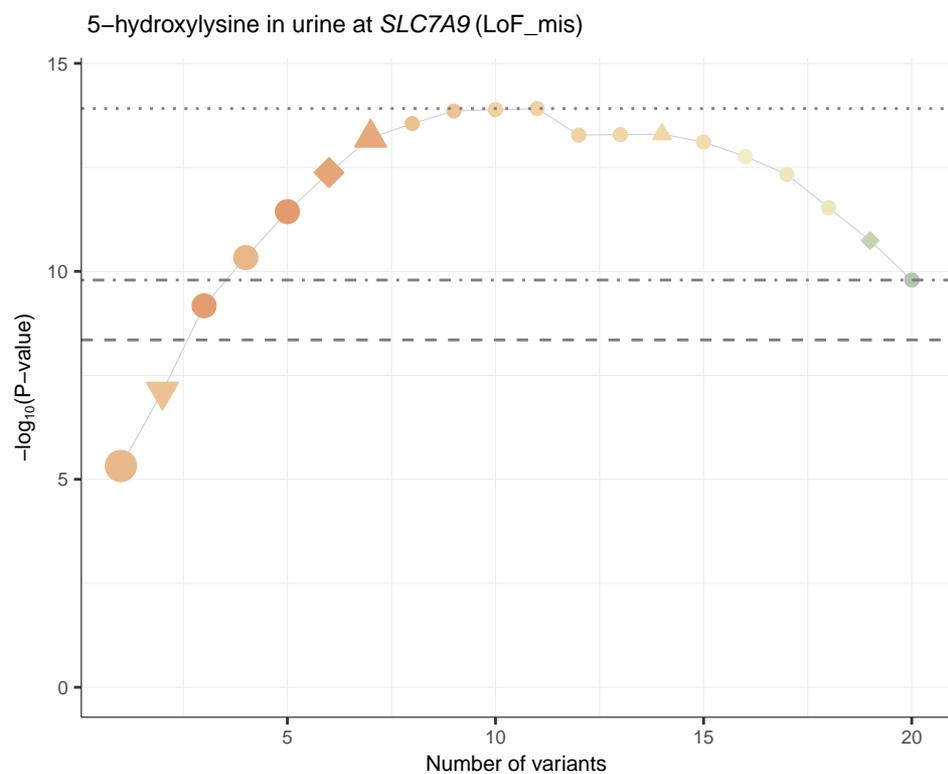


● >0.05
 ● <0.05
 ● <1e-3
 ● <1e-5
 ● <5e-8

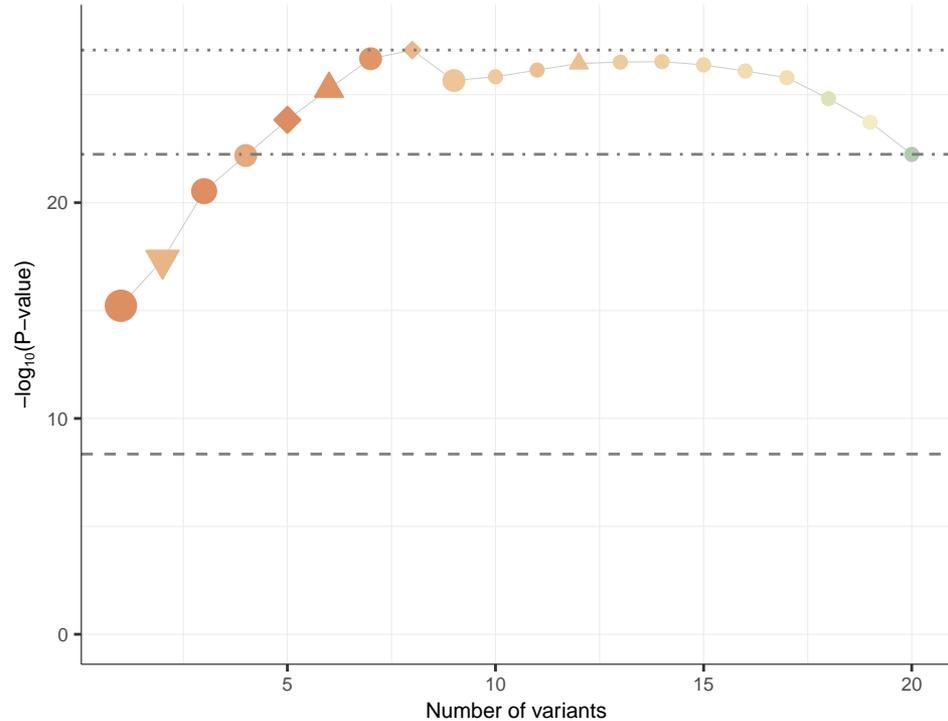
P-value

--- Significance Threshold
 - - - Total P-value
 ···· Lowest P-value

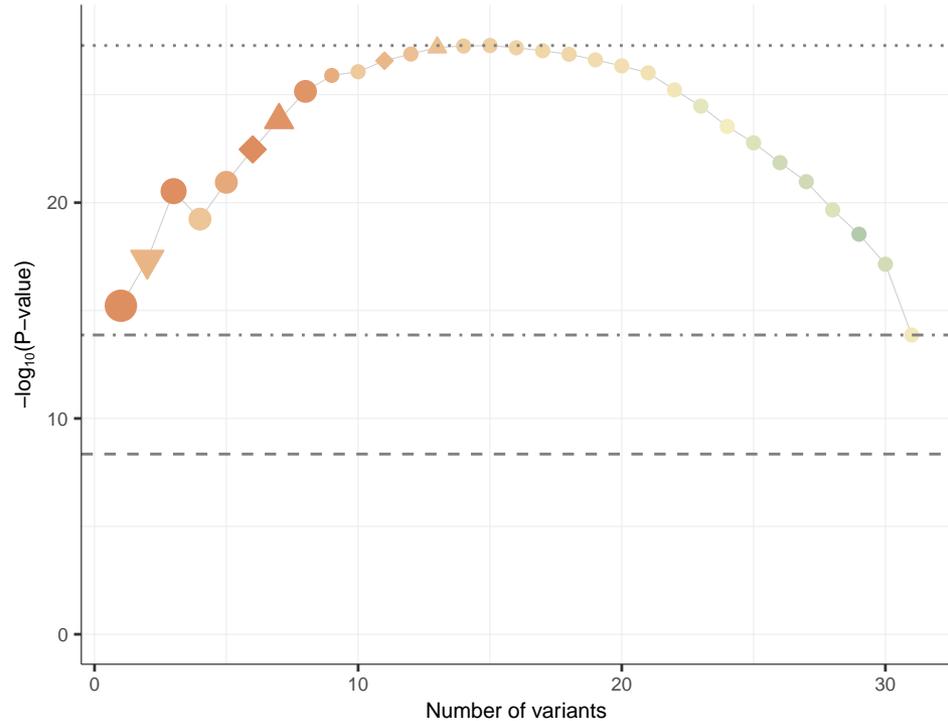
Thresholds



cystine in urine at *SLC7A9* (LoF_mis)

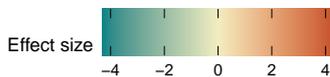


cystine in urine at *SLC7A9* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

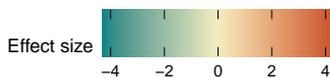
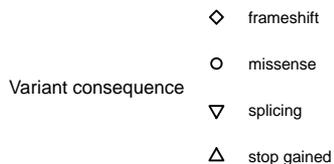
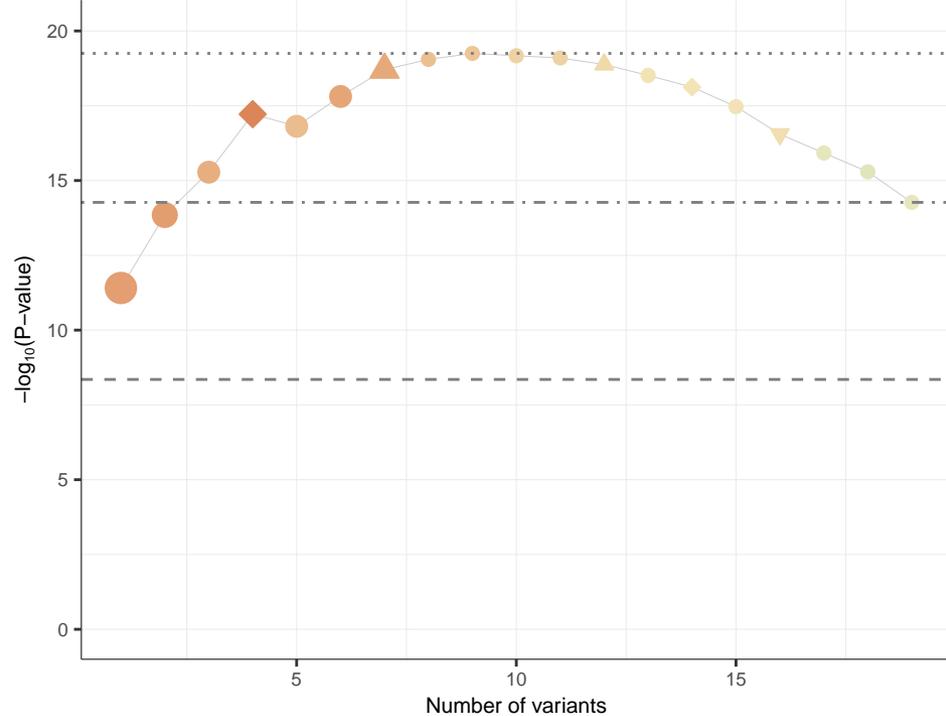
Significance Threshold

Total P-value

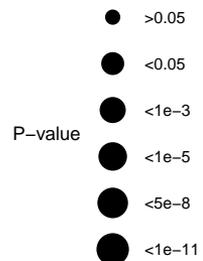
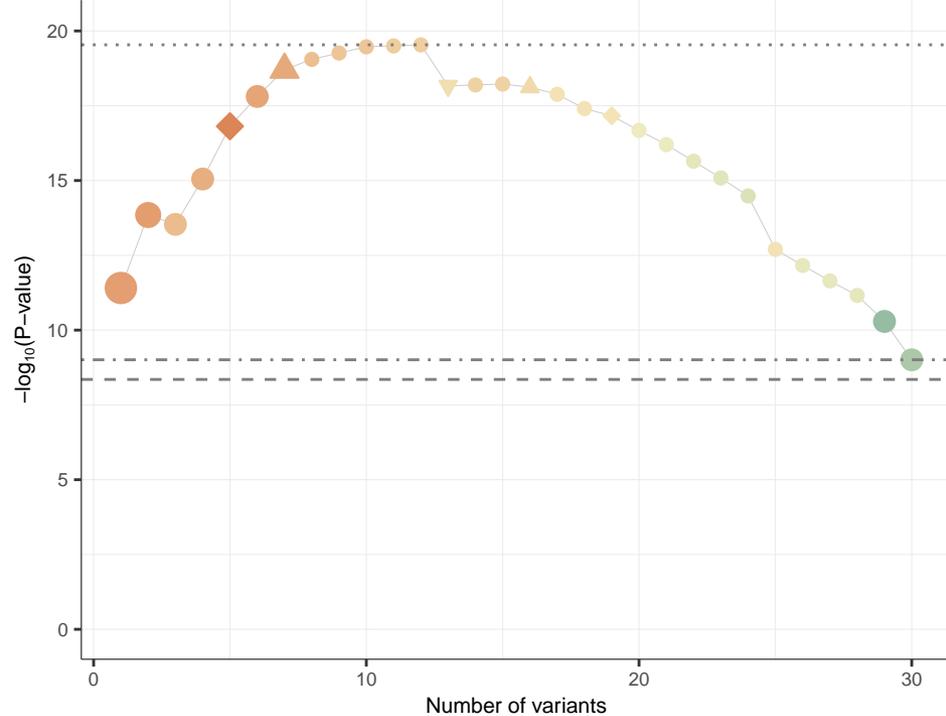
Lowest P-value

Thresholds

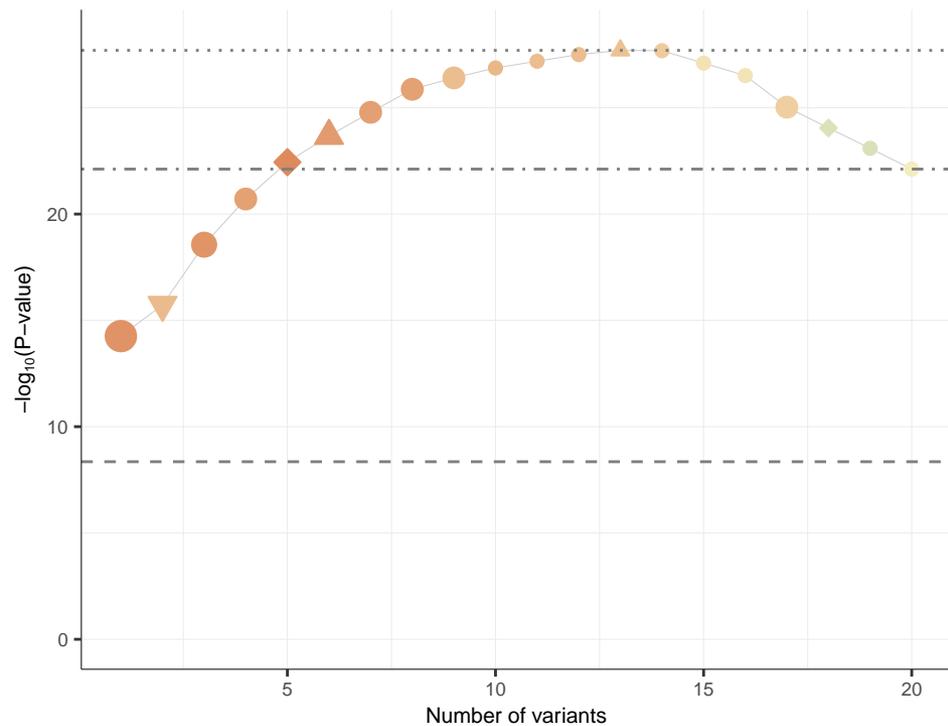
homoarginine in urine at *SLC7A9* (LoF_mis)



homoarginine in urine at *SLC7A9* (HI_mis)

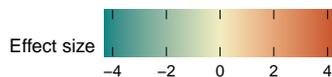


lysine in urine at SLC7A9 (LoF_mis)

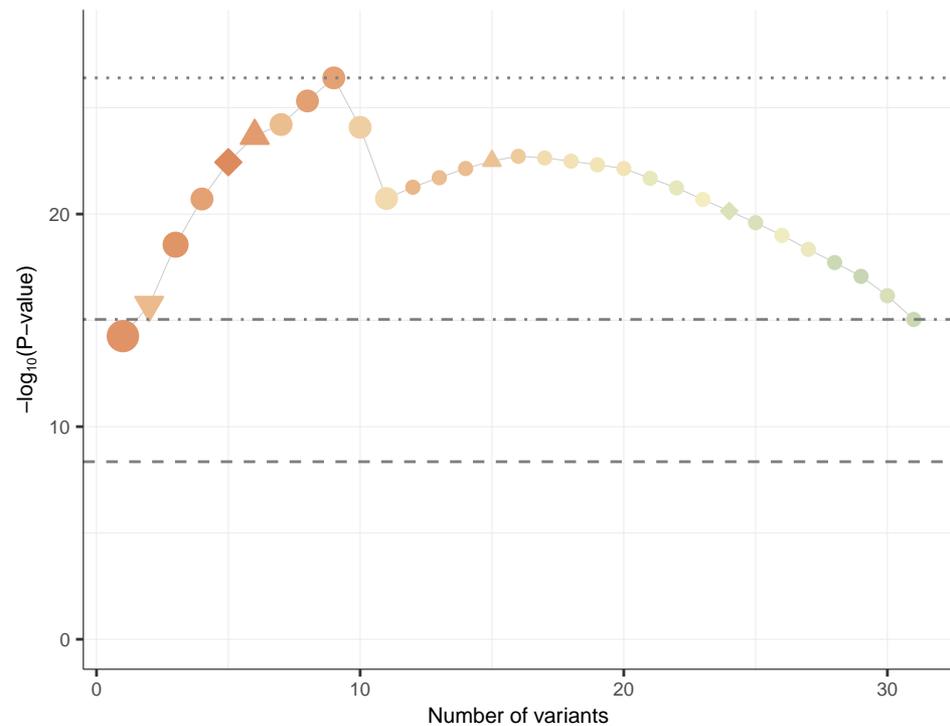


Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



lysine in urine at SLC7A9 (HI_mis)



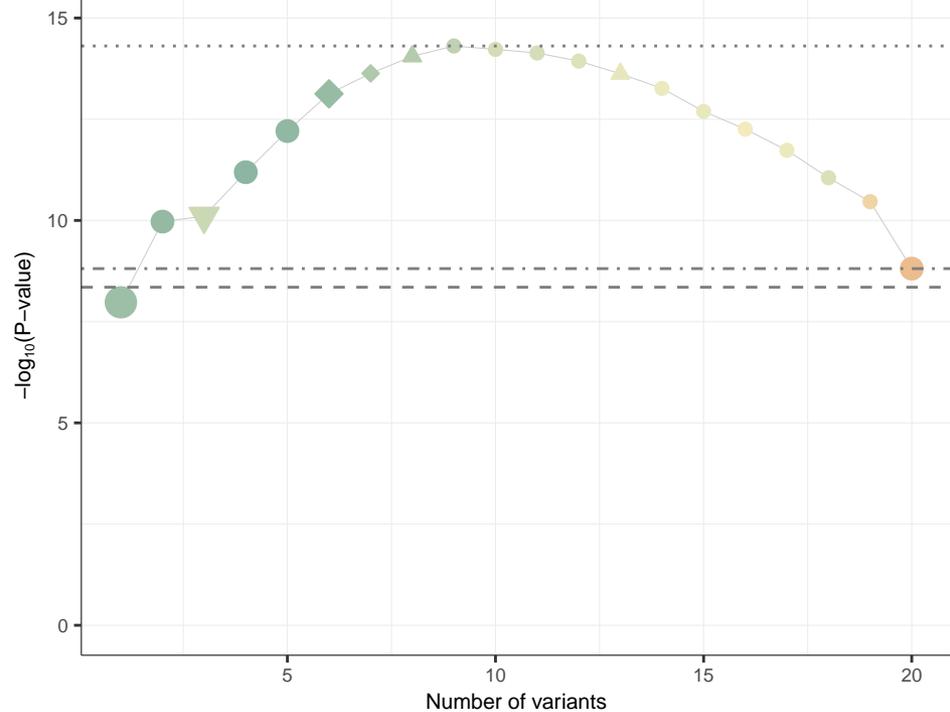
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

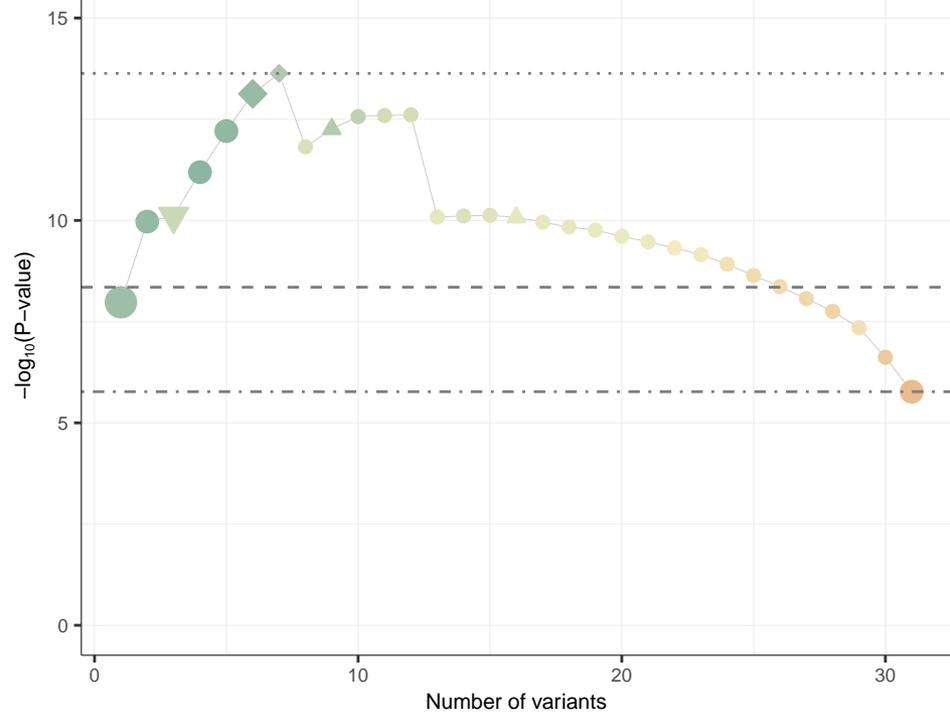
Thresholds

- Significance Threshold
- · - Total P-value
- · · · · Lowest P-value

N-acetylhomocitrulline in urine at SLC7A9 (LoF_mis)

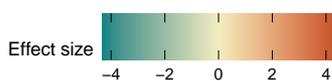


N-acetylhomocitrulline in urine at SLC7A9 (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- ▽ splicing
- △ stop gained



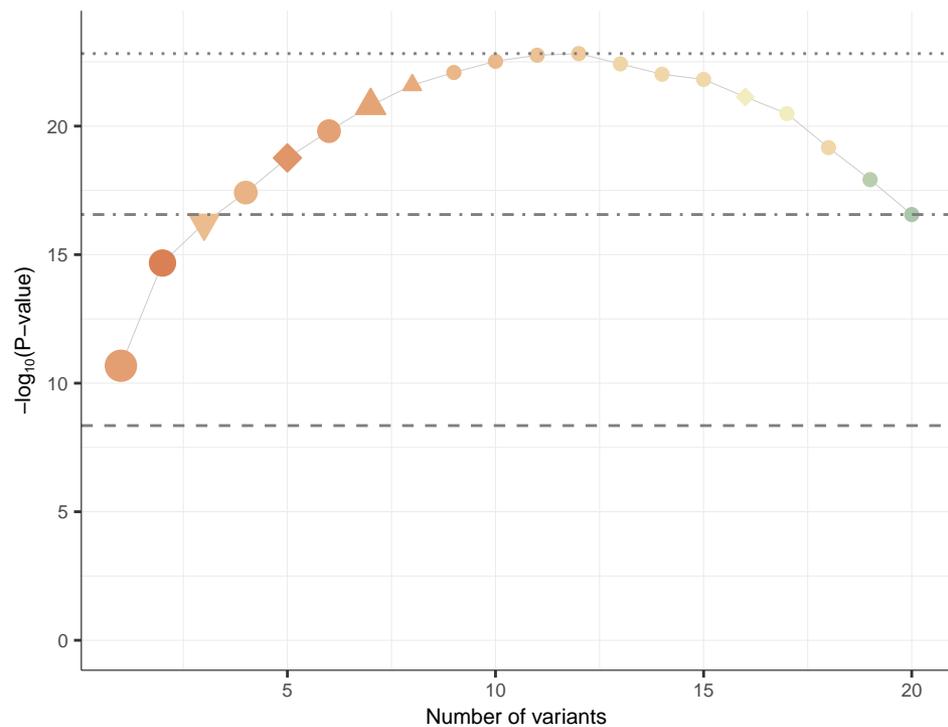
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8

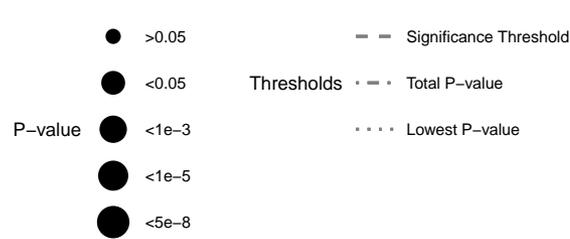
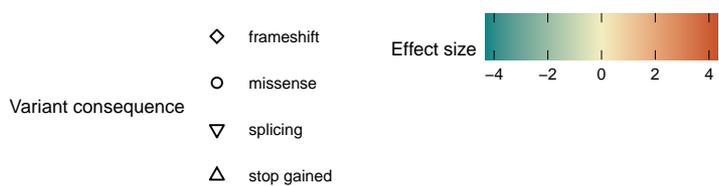
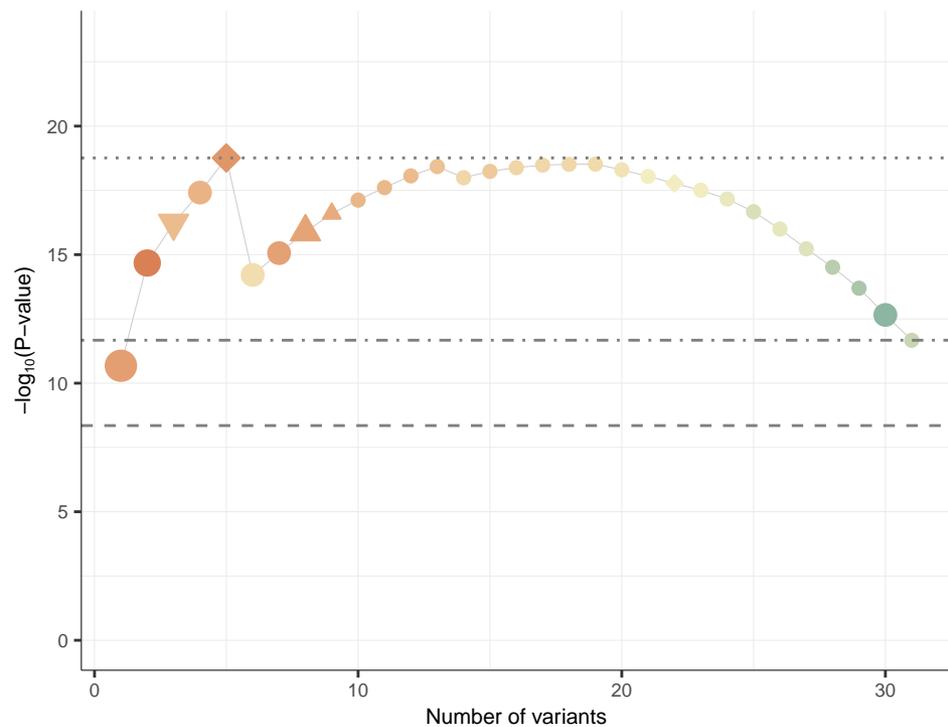
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

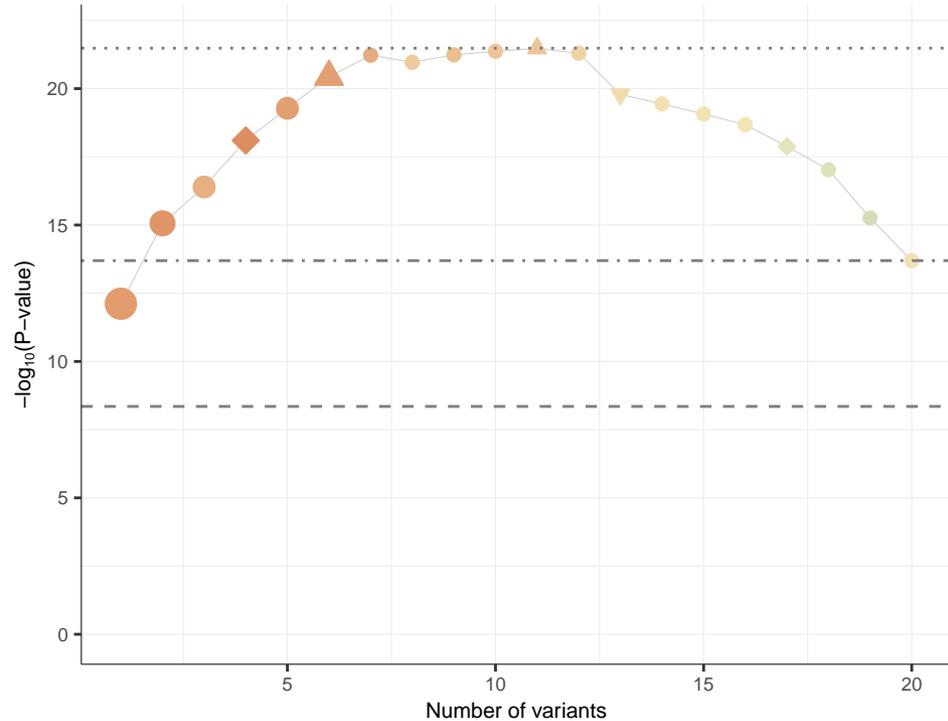
N6-methyllysine in urine at *SLC7A9* (LoF_mis)



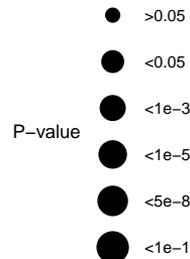
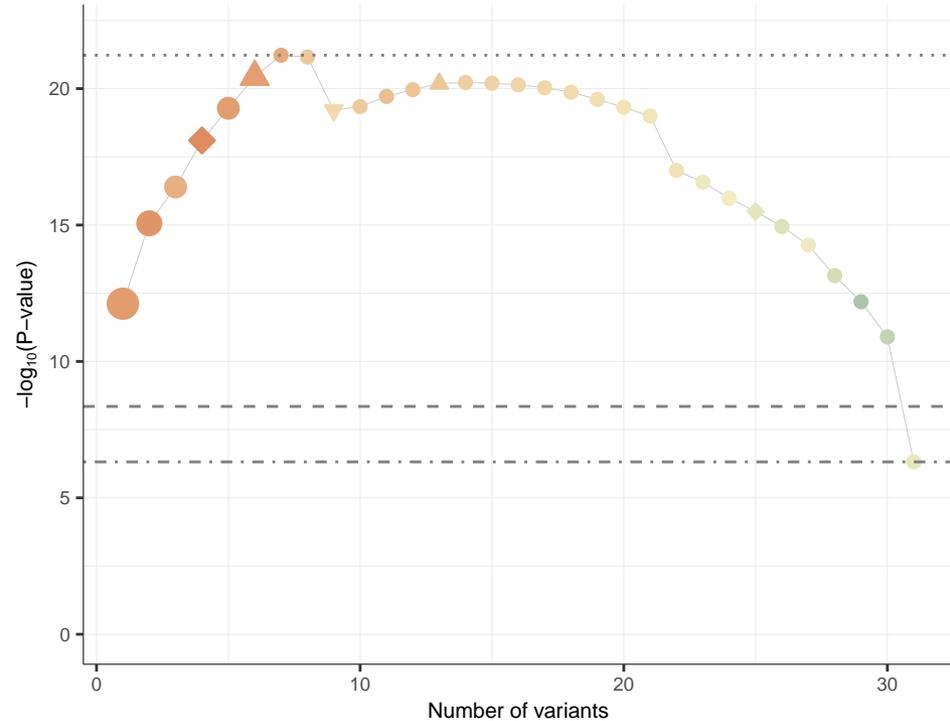
N6-methyllysine in urine at *SLC7A9* (HI_mis)



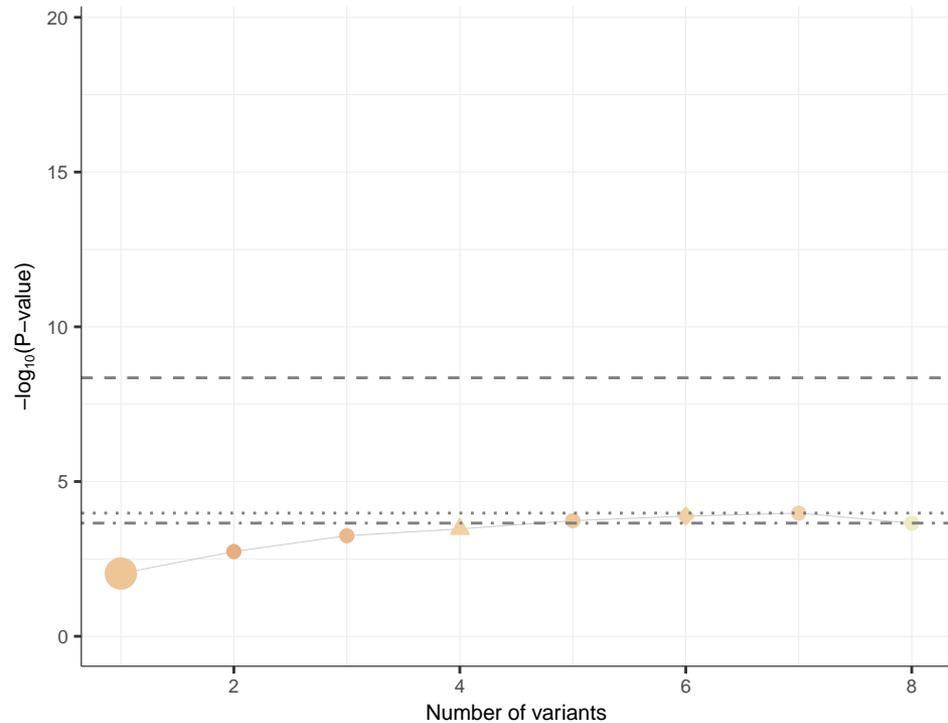
ornithine in urine at SLC7A9 (LoF_mis)



ornithine in urine at SLC7A9 (HI_mis)

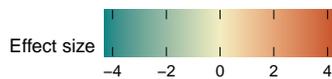


adipate (C6-DC) in urine at *SUGCT* (LoF_mis)

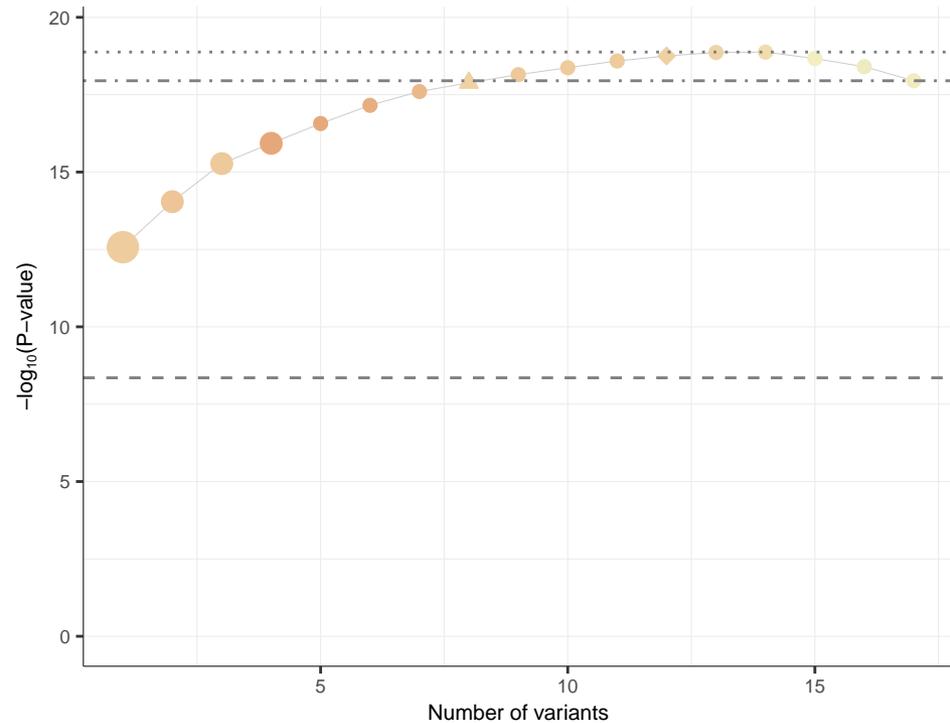


Variant consequence

- ◇ frameshift
- missense
- △ stop gained



adipate (C6-DC) in urine at *SUGCT* (HI_mis)



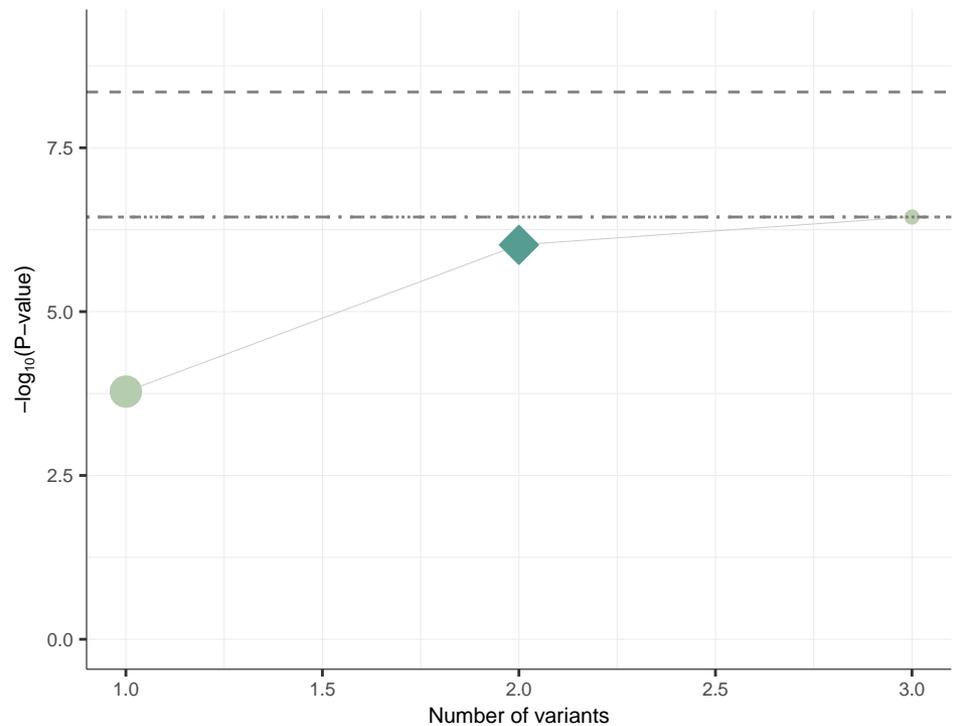
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

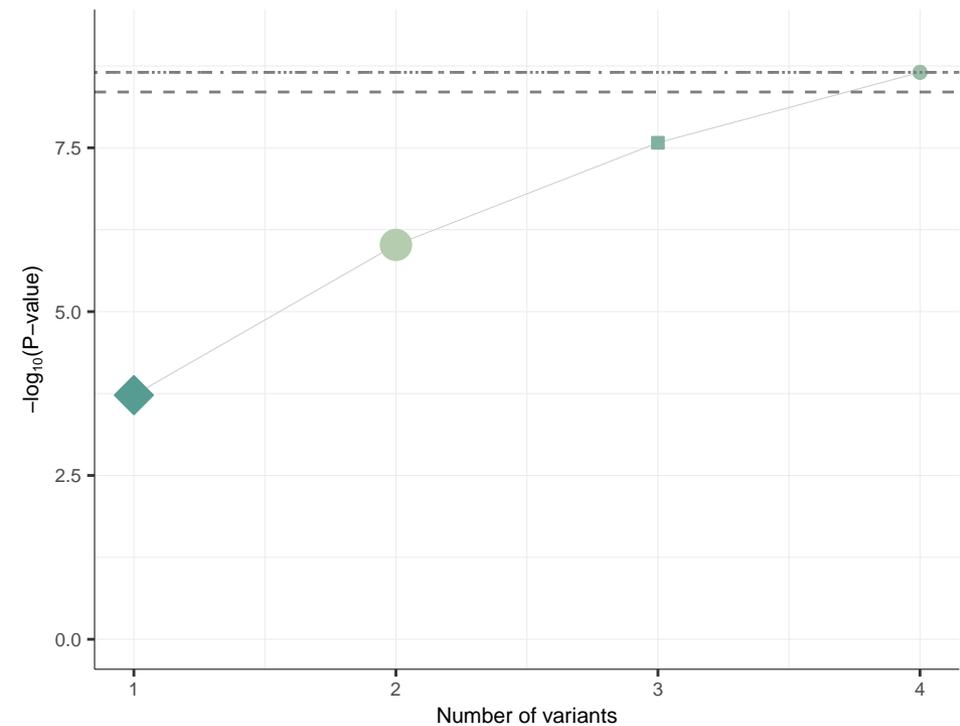
Thresholds

- - - Significance Threshold
- · - · Total P-value
- · · · · Lowest P-value

androstenediol (3beta,17beta) disulfate (1) in urine at *SULT2A1* (LoF_mis)

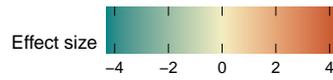


androstenediol (3beta,17beta) disulfate (1) in urine at *SULT2A1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- start/stop lost



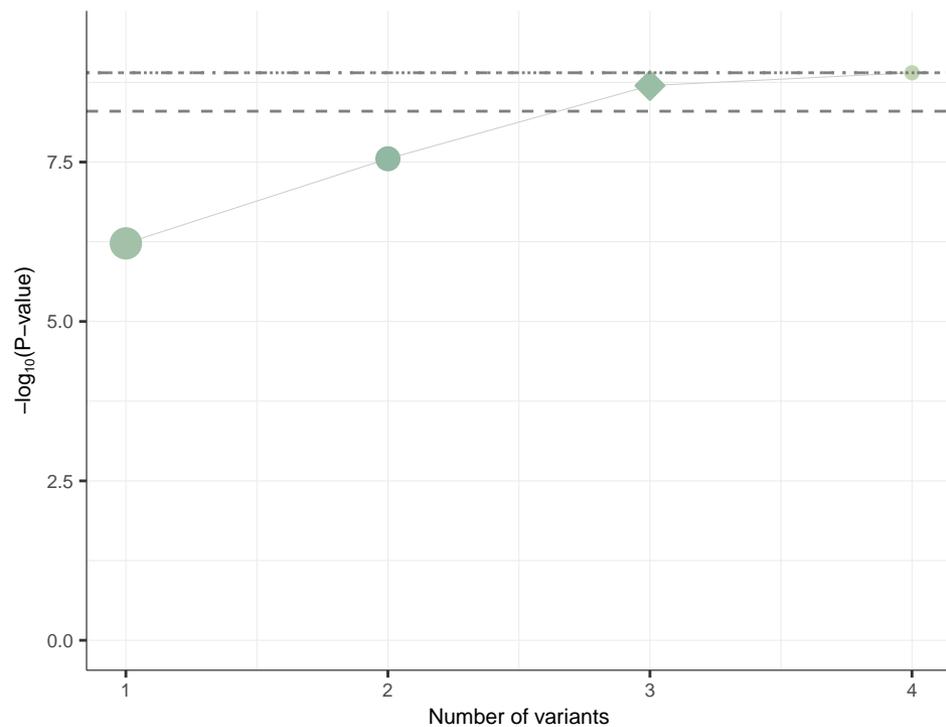
P-value

- <0.05
- <1e-3

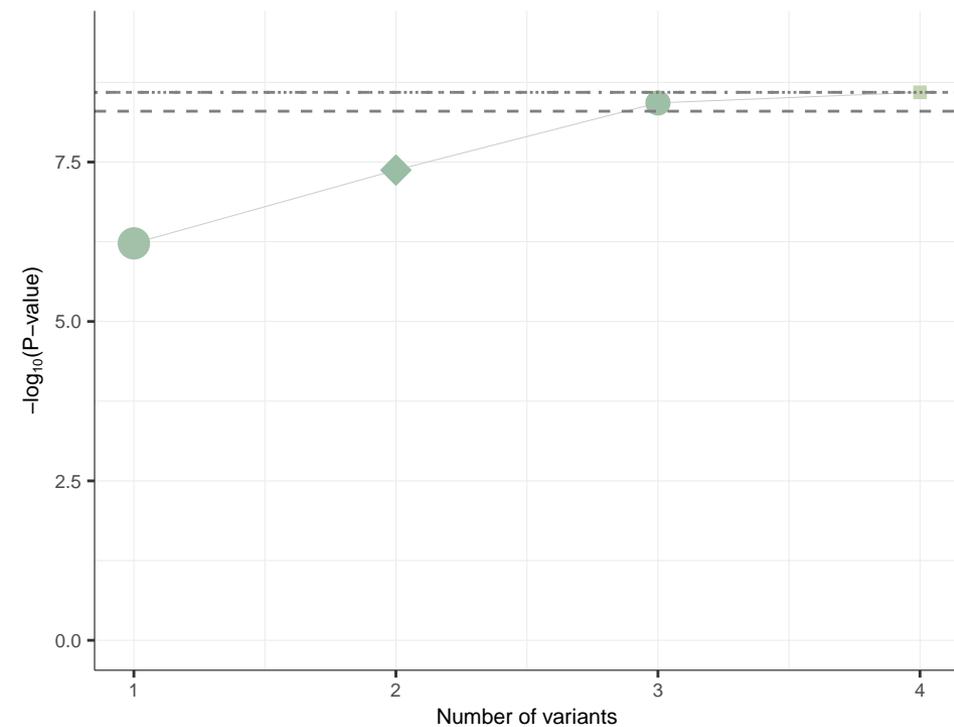
Thresholds

- Significance Threshold
- · - · Total P-value
- · · · Lowest P-value

pregnenediol disulfate (C21H34O8S2)* in plasma at *SULT2A1* (LoF_mis)

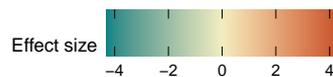


pregnenediol disulfate (C21H34O8S2)* in plasma at *SULT2A1* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- start/stop lost



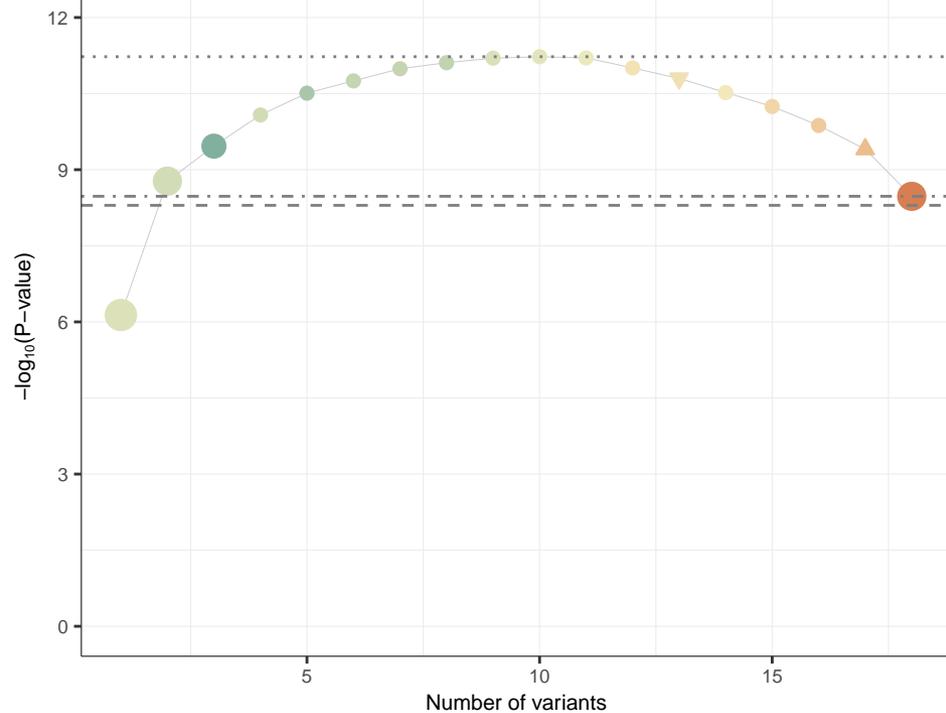
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

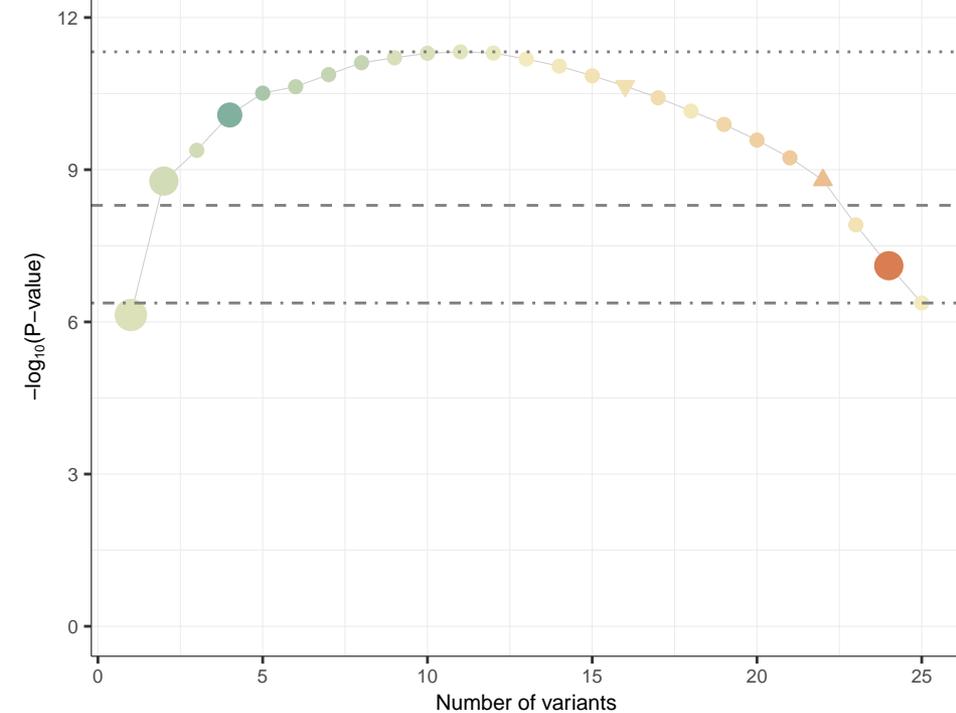
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯⋯ Lowest P-value

X - 11470 in plasma at *TAP2* (LoF_mis)

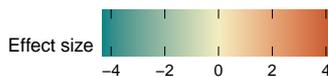


X - 11470 in plasma at *TAP2* (HI_mis)



Variant consequence

- missense
- ▽ splicing
- △ stop gained



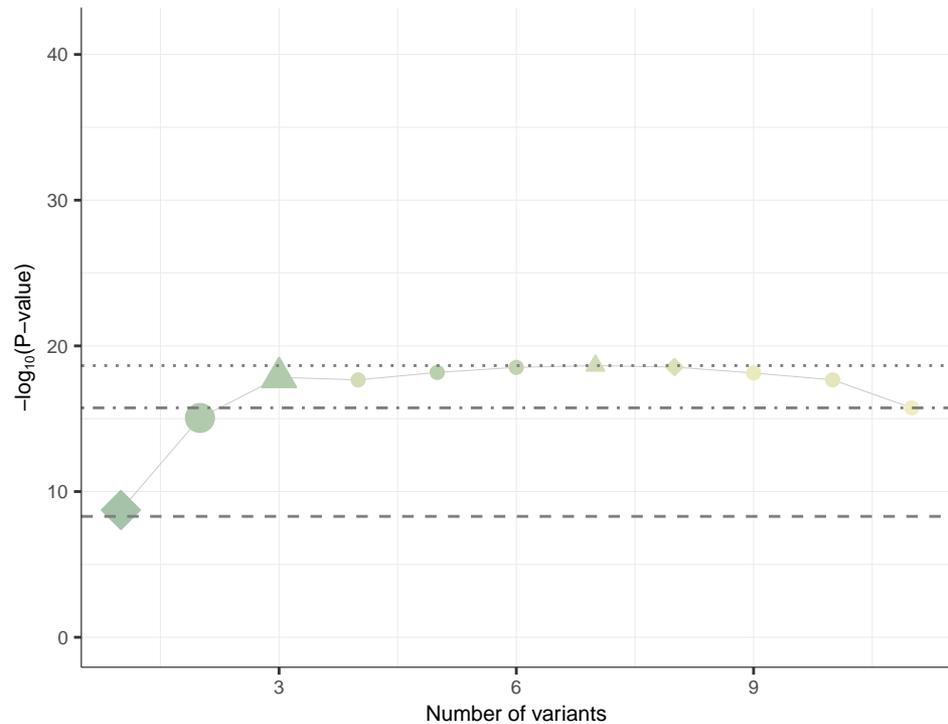
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5

Thresholds

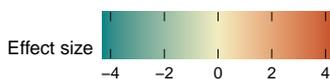
- - - Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

deoxycarnitine in plasma at *TMLHE* (LoF_mis)

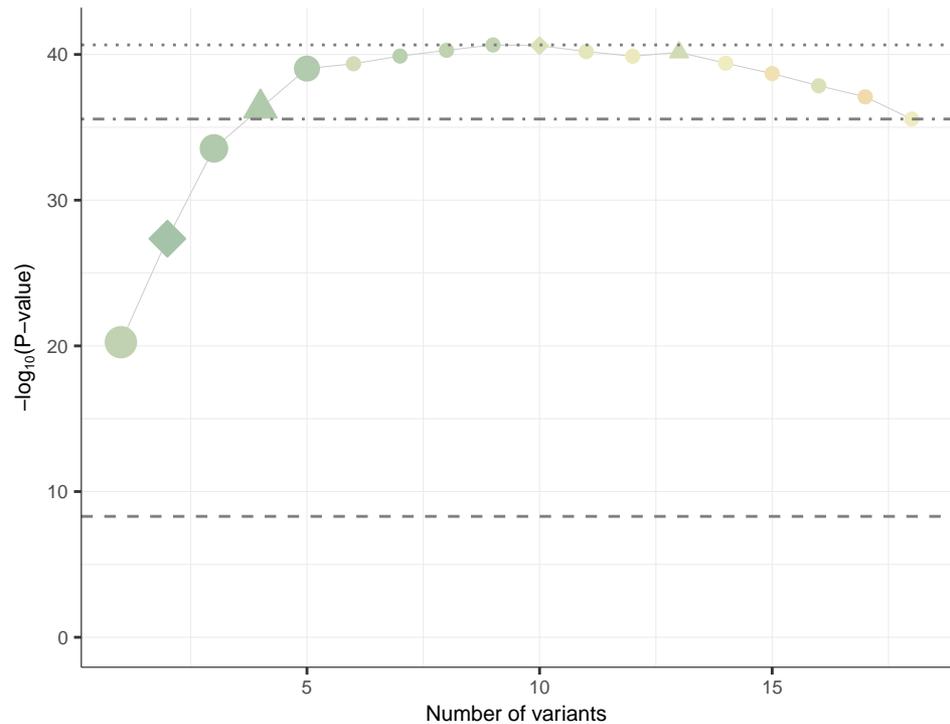


Variant consequence

- ◇ frameshift
- missense
- △ stop gained



deoxycarnitine in plasma at *TMLHE* (HI_mis)



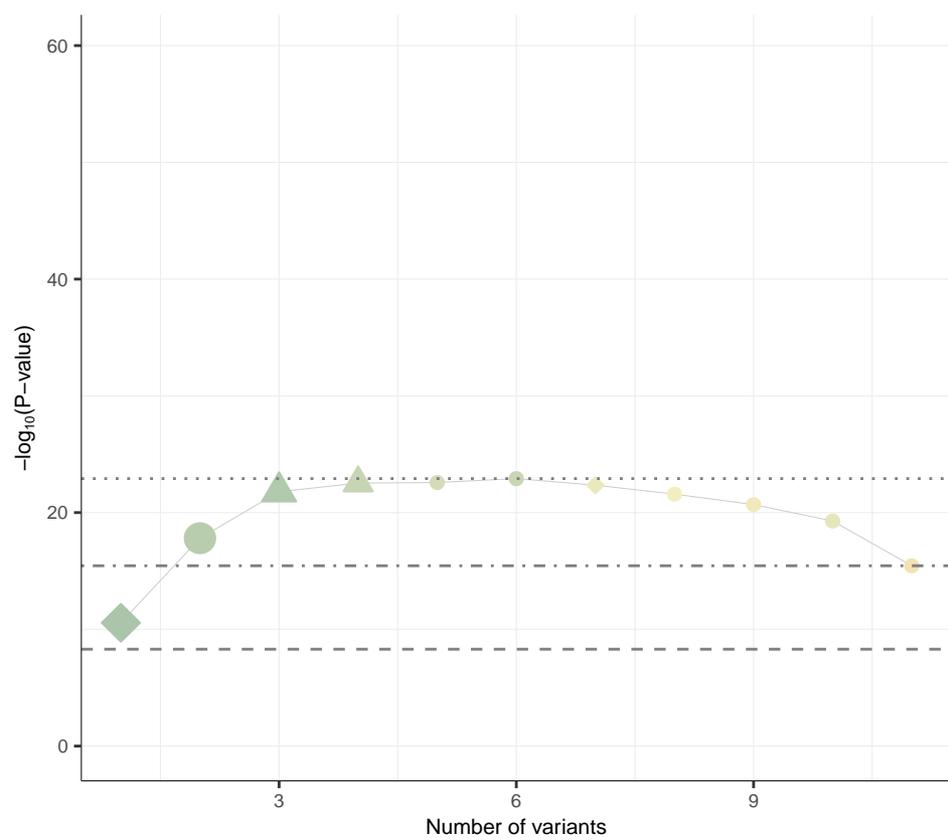
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

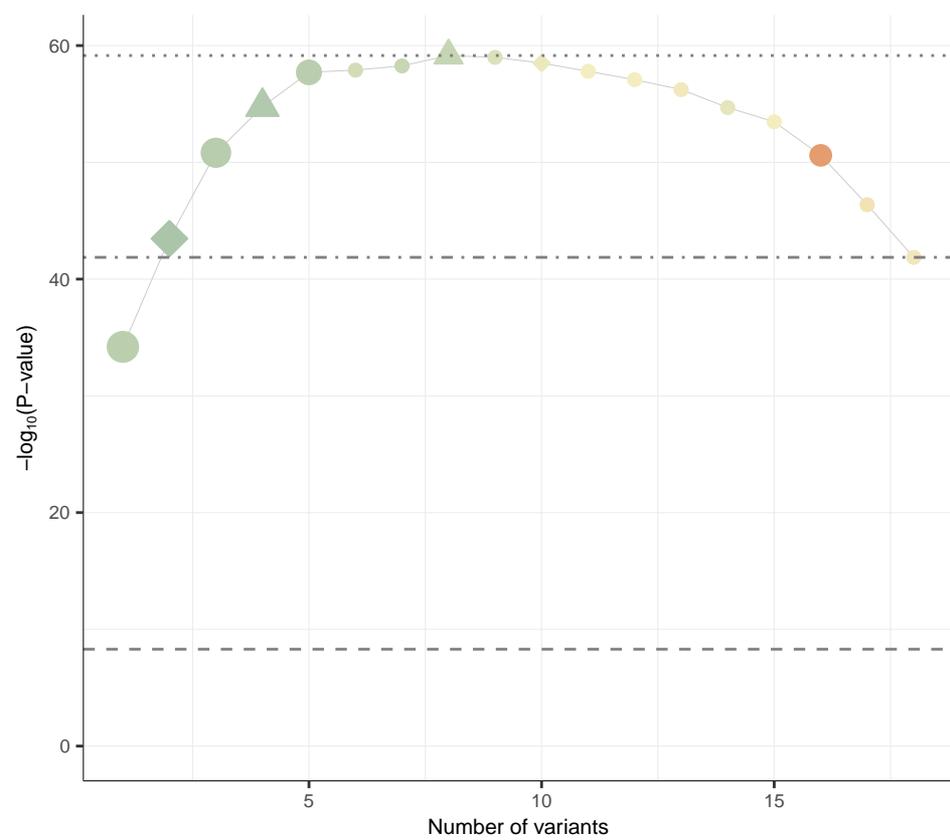
Thresholds

- Significance Threshold
- · - Total P-value
- · · · · Lowest P-value

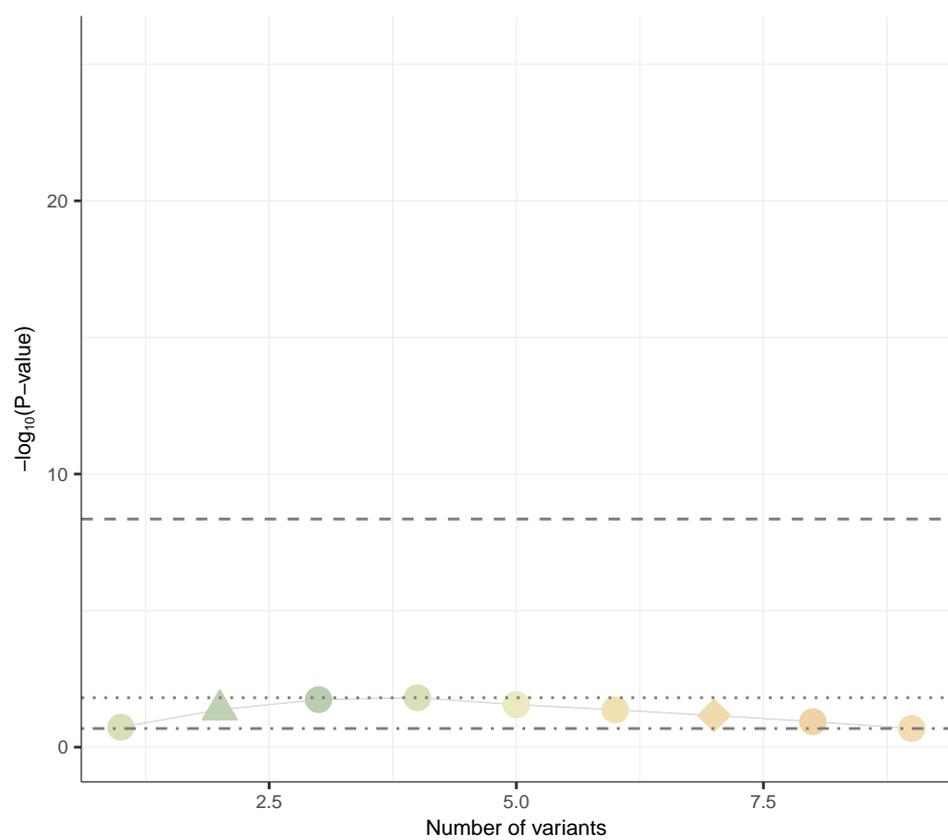
hydroxy-N6,N6,N6-trimethyllysine* in plasma at *TMLHE* (LoF_mis)



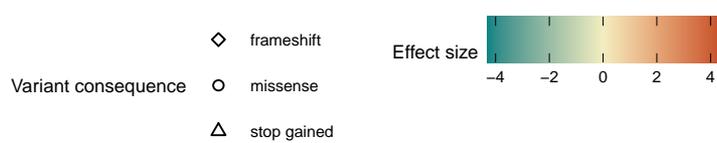
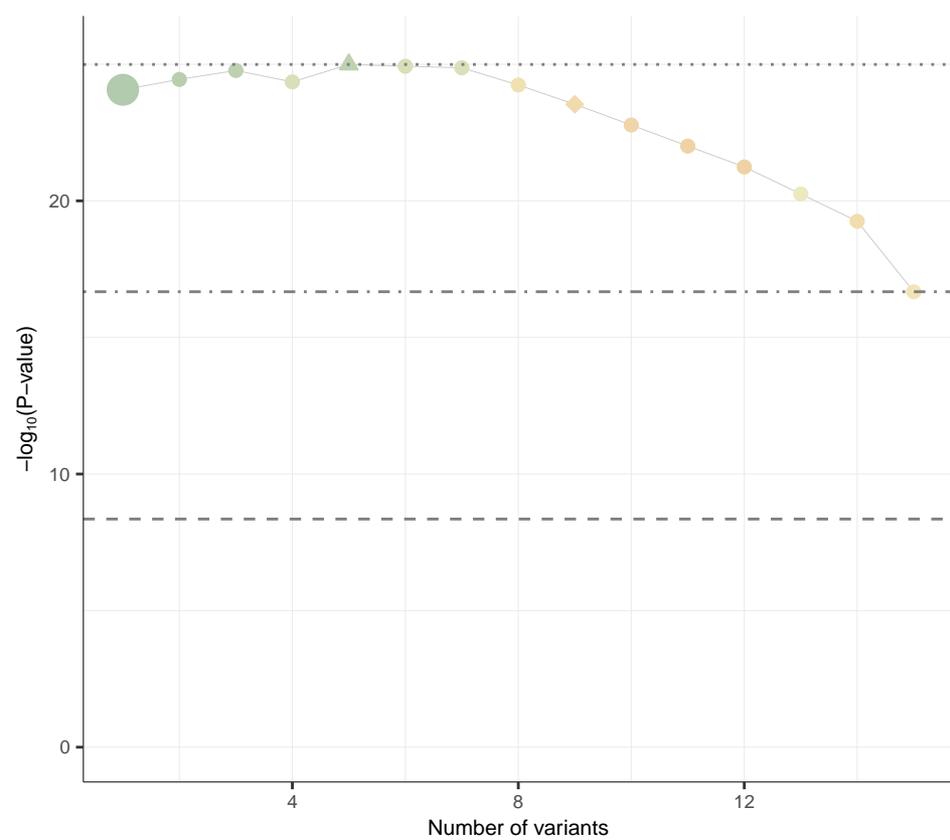
hydroxy-N6,N6,N6-trimethyllysine* in plasma at *TMLHE* (HI_mis)



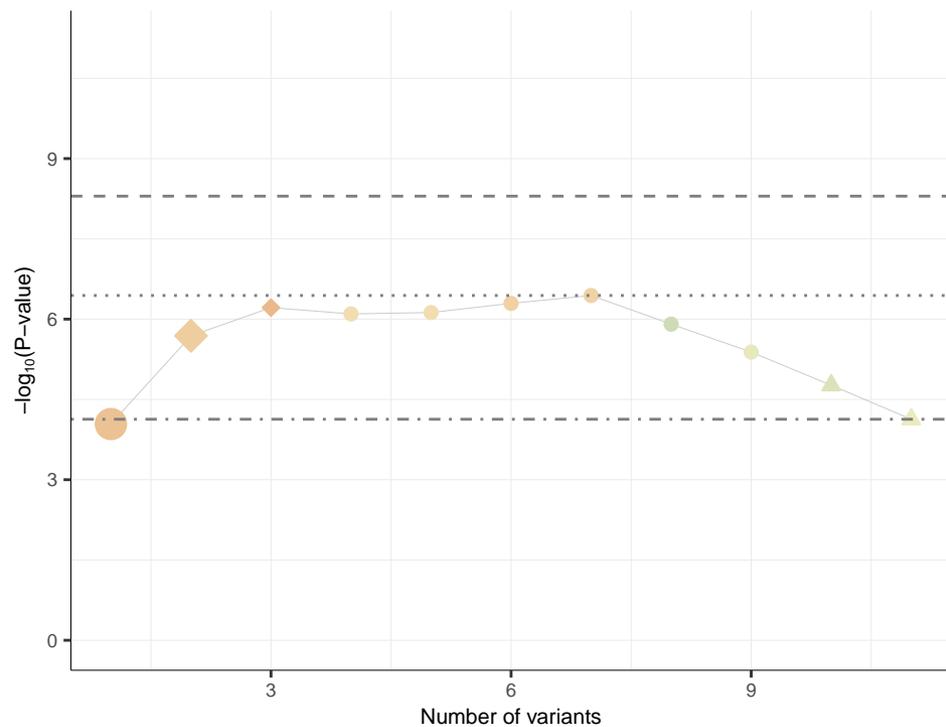
hydroxy-N6,N6,N6-trimethyllysine* in urine at *TMLHE* (LoF_mis)



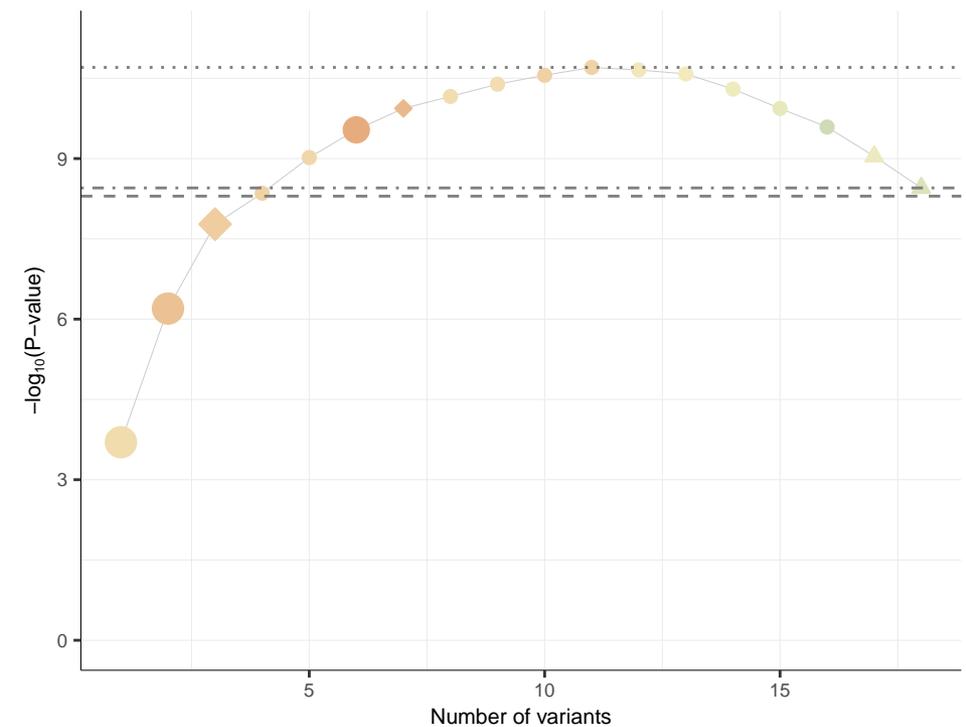
hydroxy-N6,N6,N6-trimethyllysine* in urine at *TMLHE* (HI_mis)



N,N,N-trimethyl-5-aminovalerate in plasma at *TMLHE* (LoF_mis)

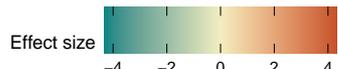


N,N,N-trimethyl-5-aminovalerate in plasma at *TMLHE* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



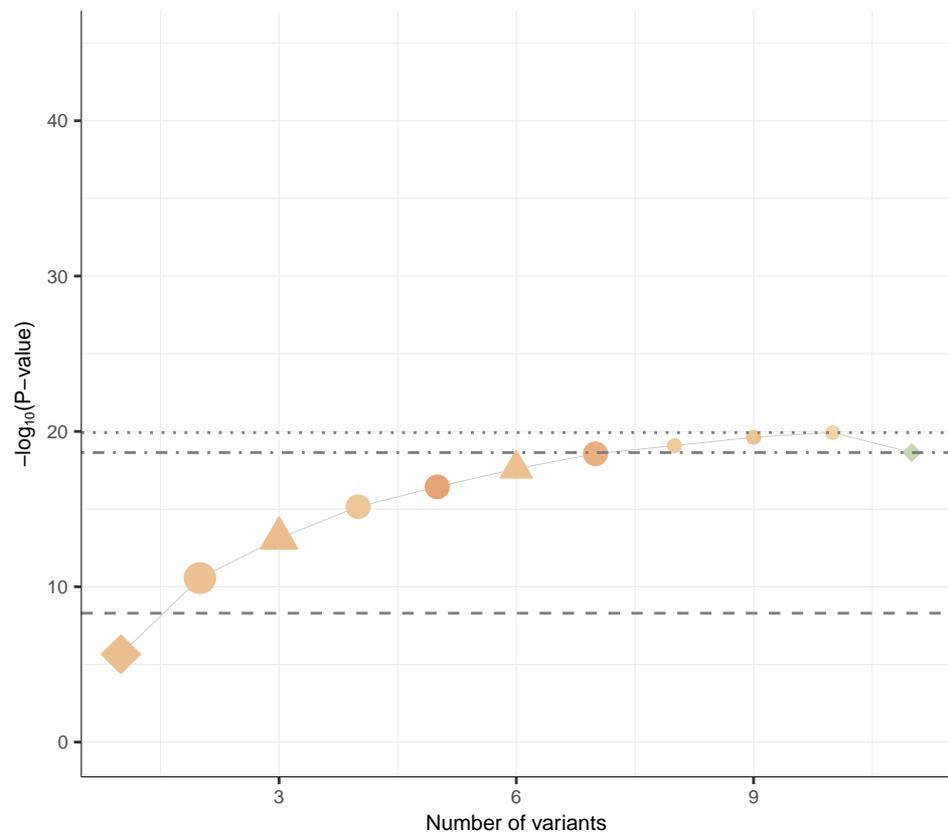
P-value

- >0.05
- <0.05
- <1e-3

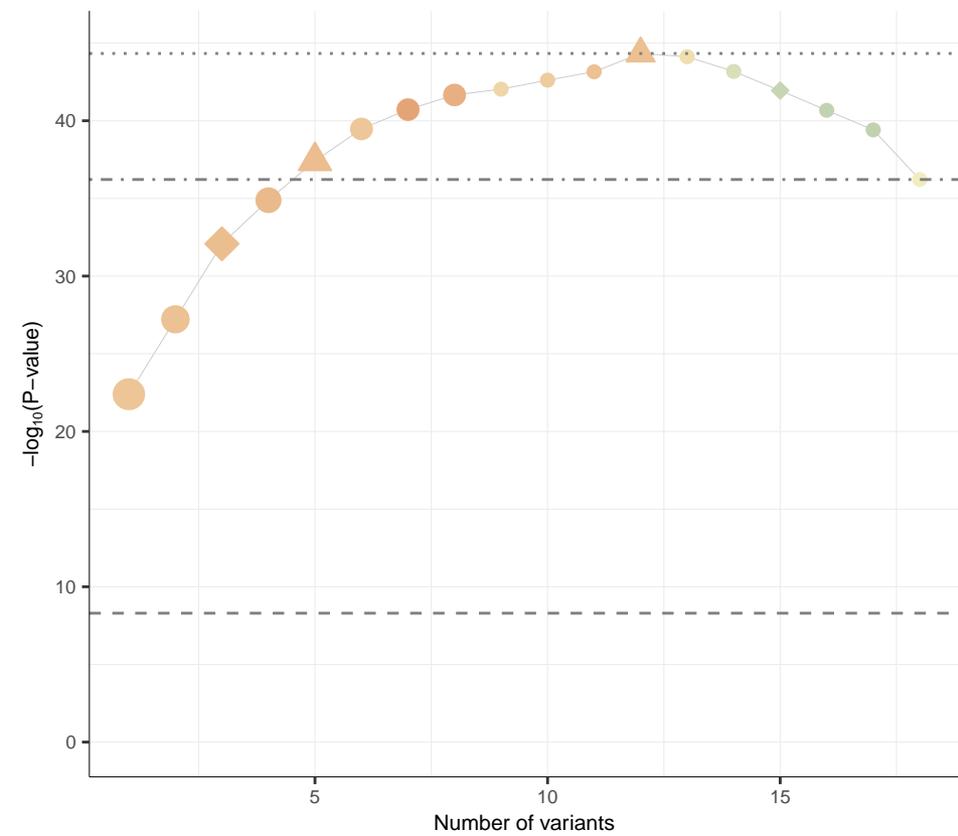
Thresholds

- - - Significance Threshold
- · - Total P-value
- · · Lowest P-value

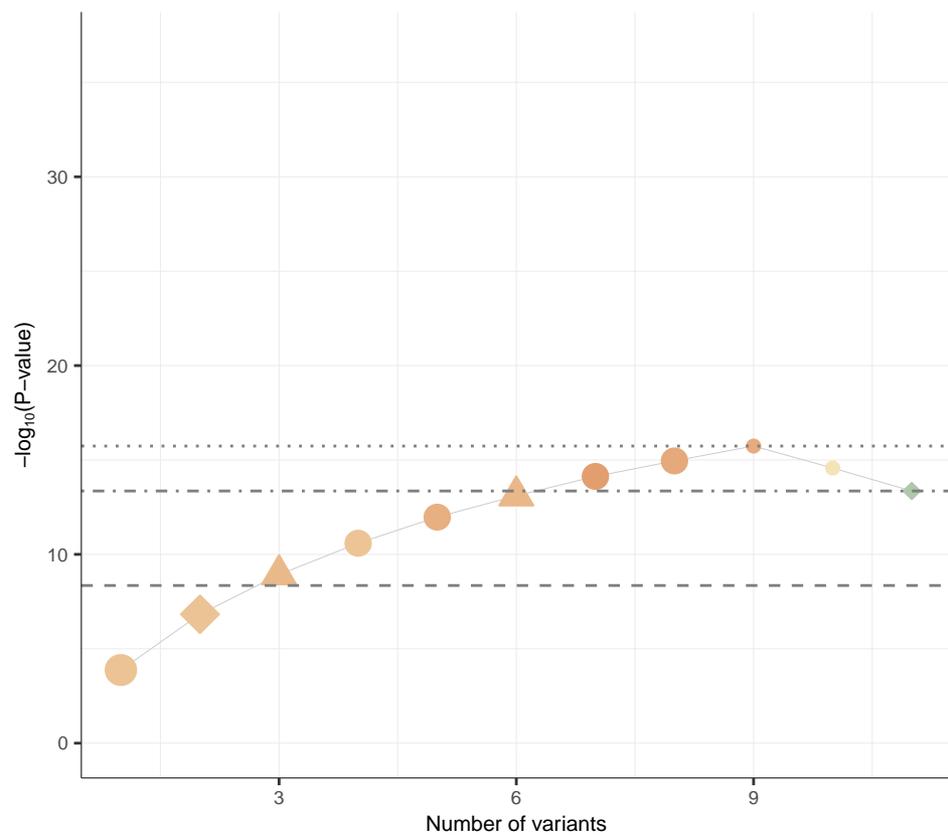
N6,N6,N6-trimethyllysine in plasma at *TMLHE* (LoF_mis)



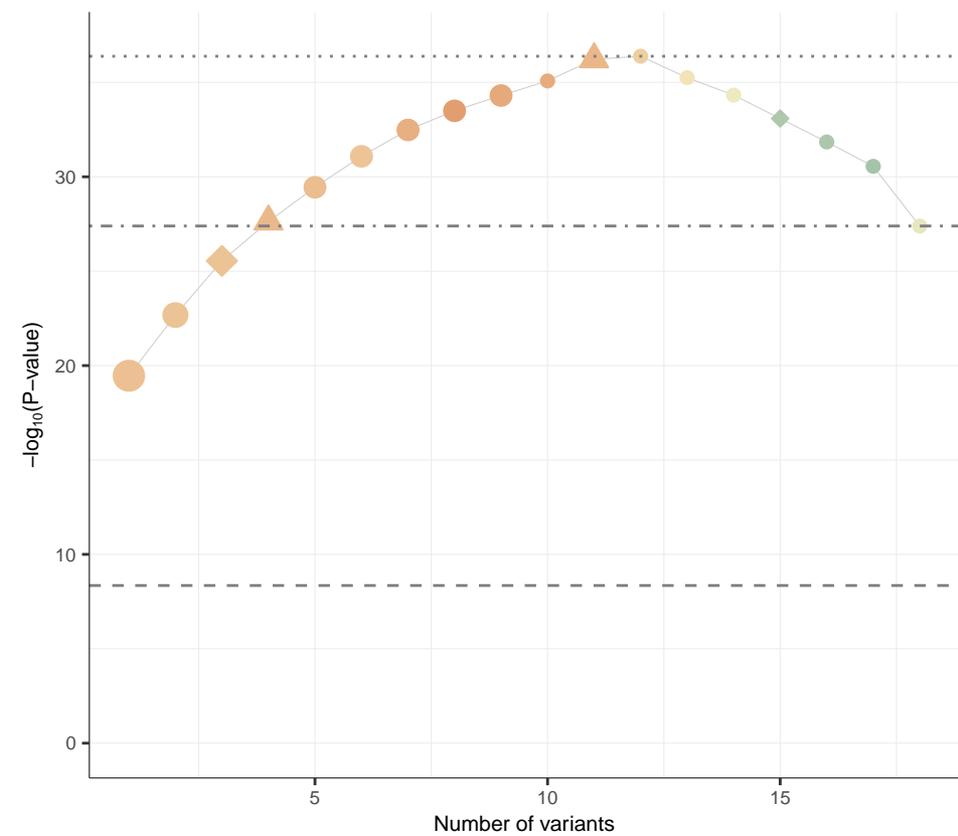
N6,N6,N6-trimethyllysine in plasma at *TMLHE* (HI_mis)



N6,N6,N6-trimethyllysine in urine at *TMLHE* (LoF_mis)

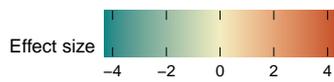


N6,N6,N6-trimethyllysine in urine at *TMLHE* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



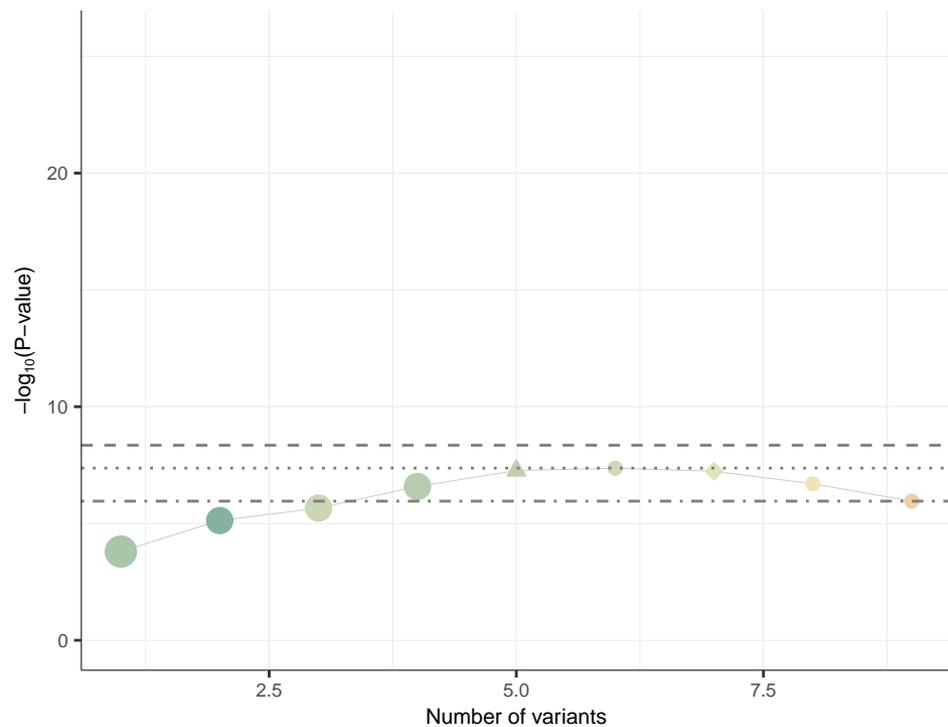
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

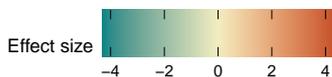
Thresholds

- Significance Threshold
- - - Total P-value
- Lowest P-value

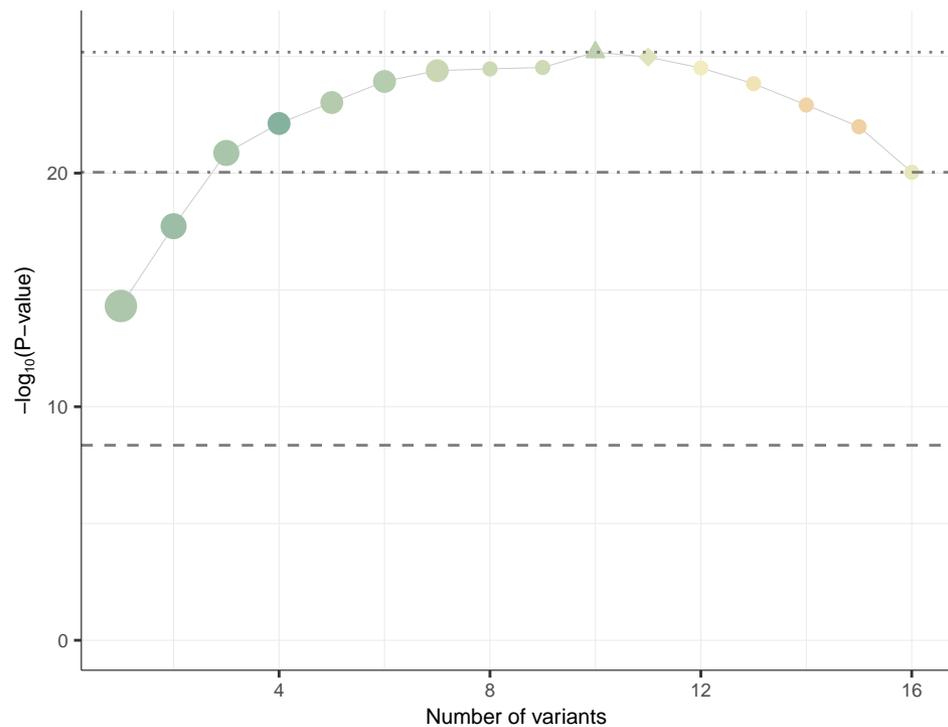
X - 23666 in urine at *TMLHE* (LoF_mis)



- Variant consequence
- ◇ frameshift
 - missense
 - △ stop gained



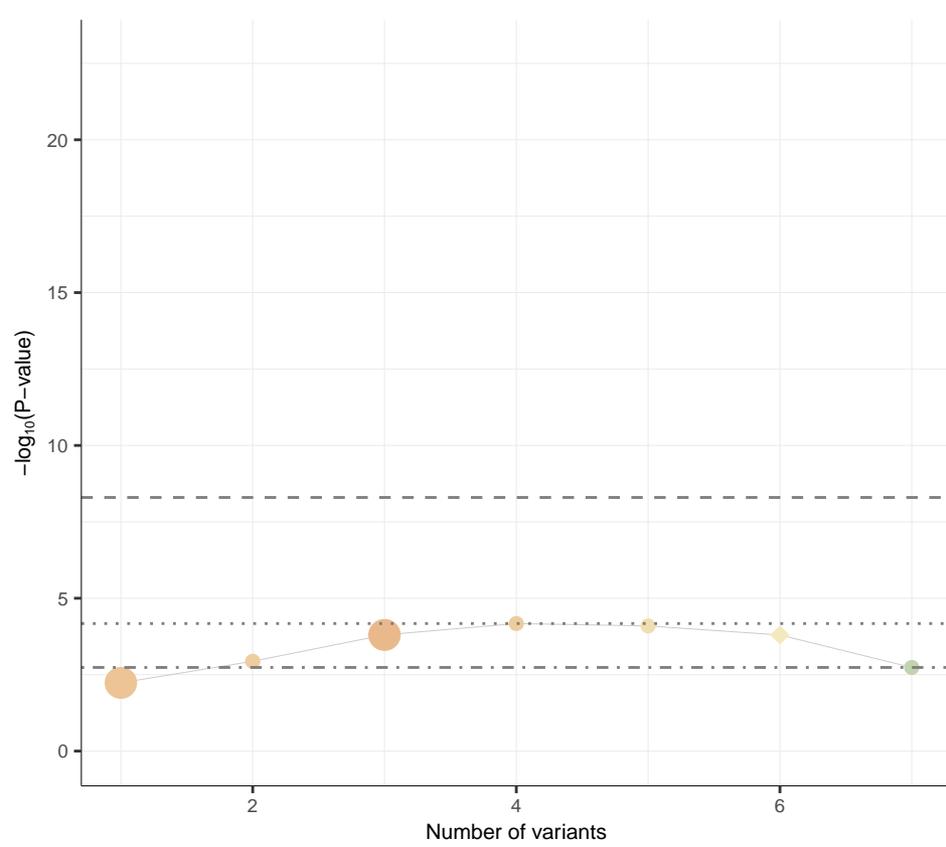
X - 23666 in urine at *TMLHE* (HI_mis)



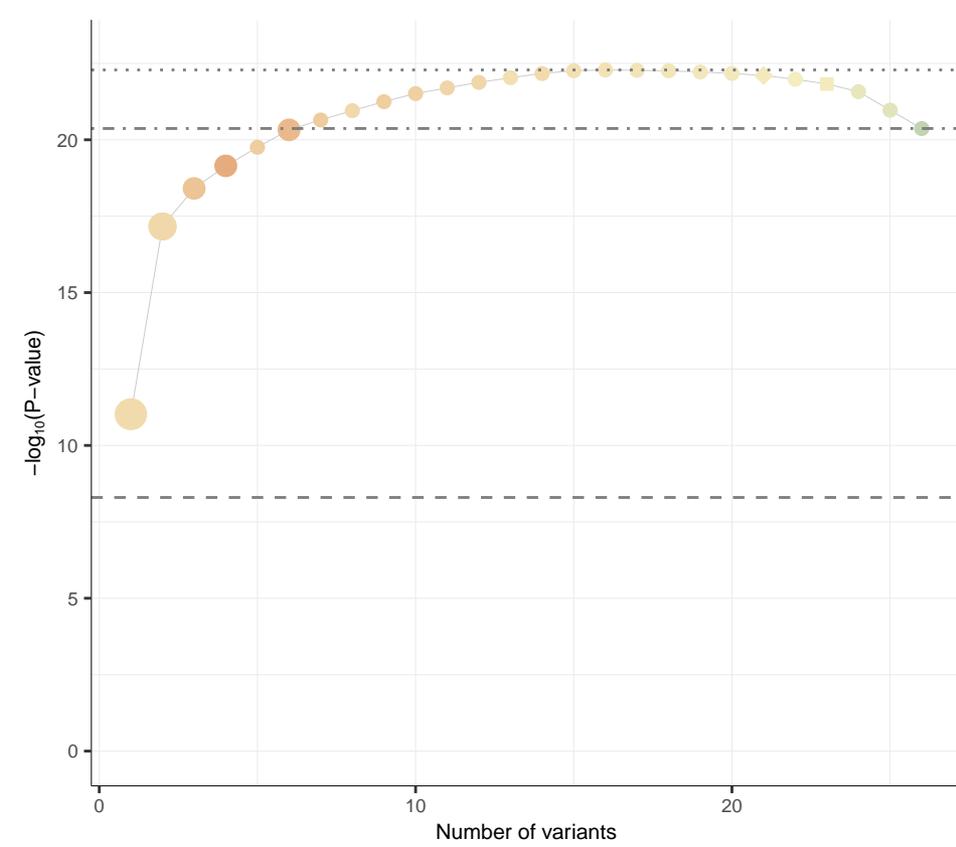
- P-value
- >0.05
 - <0.05
 - <1e-3
 - <1e-5
 - <5e-8
 - <1e-11

- Thresholds
- - - Significance Threshold
 - · - Total P-value
 - · · · · Lowest P-value

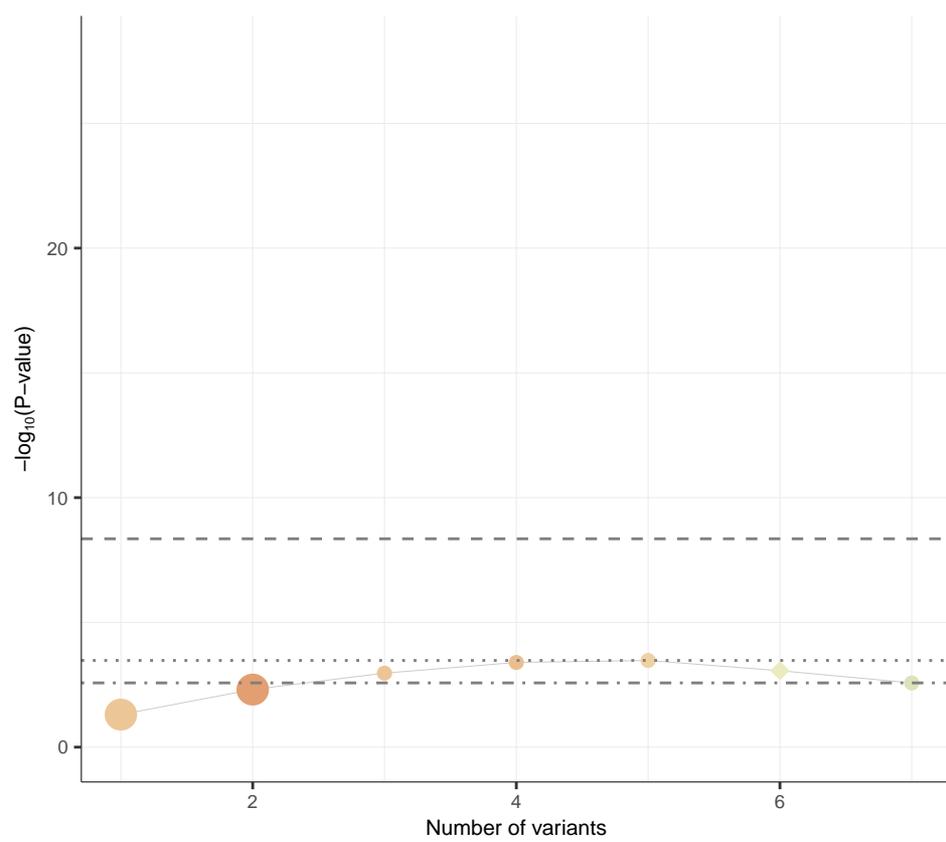
X - 22162 in plasma at *TTC38* (LoF_mis)



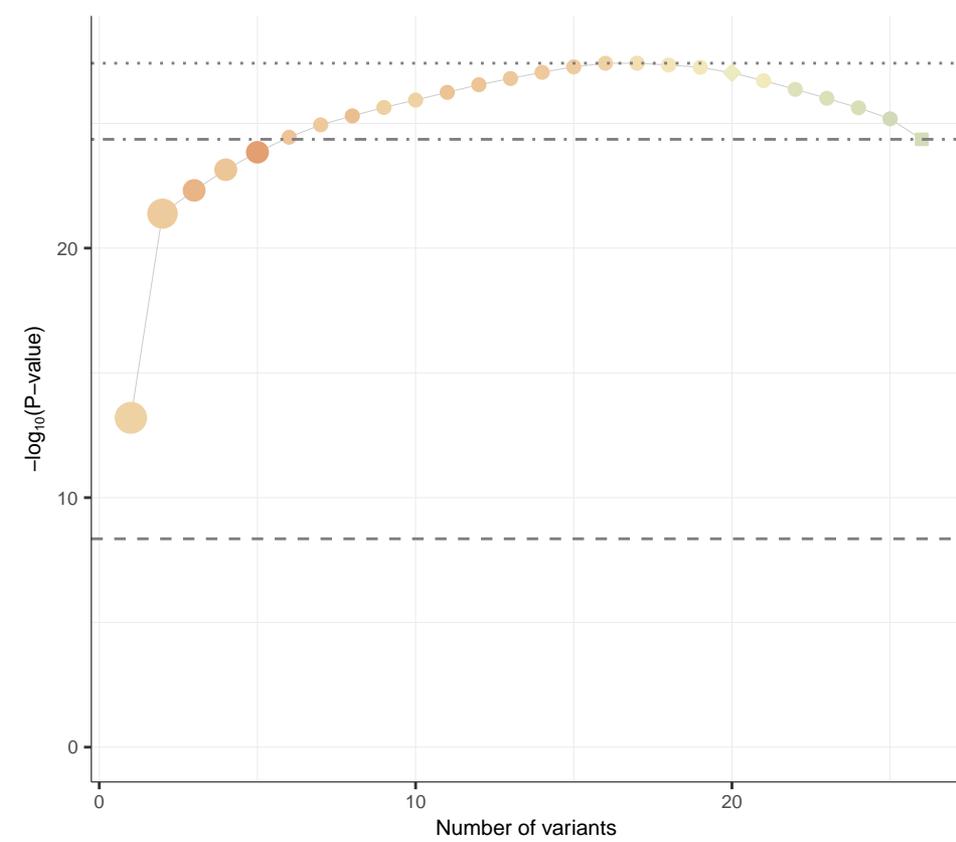
X - 22162 in plasma at *TTC38* (HI_mis)



X - 22162 in urine at *TTC38* (LoF_mis)

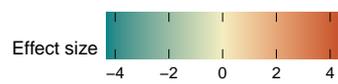


X - 22162 in urine at *TTC38* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- start/stop lost



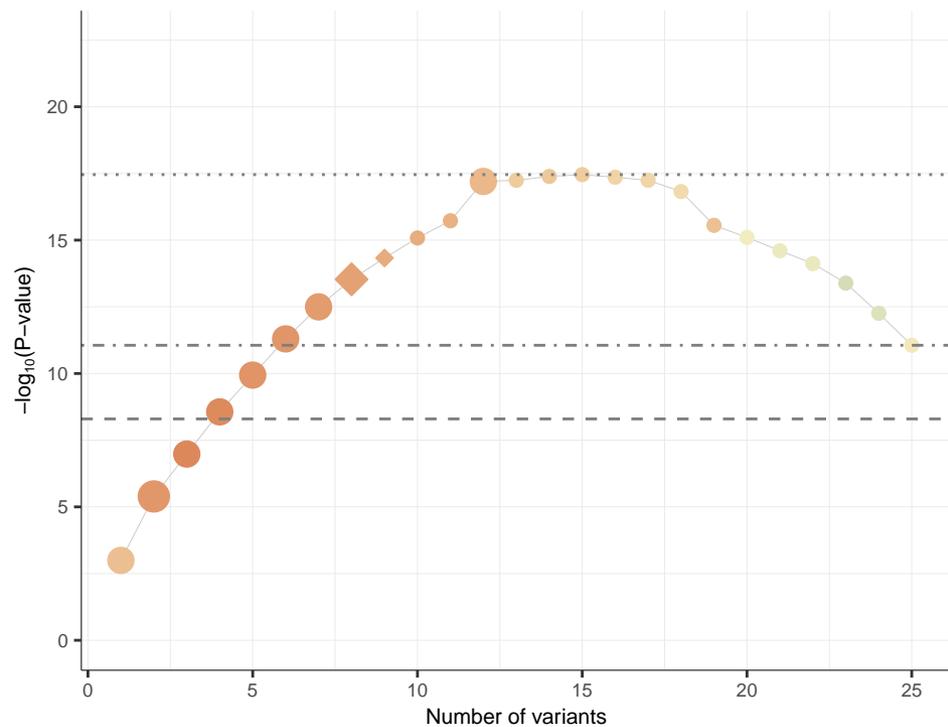
P-value

- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

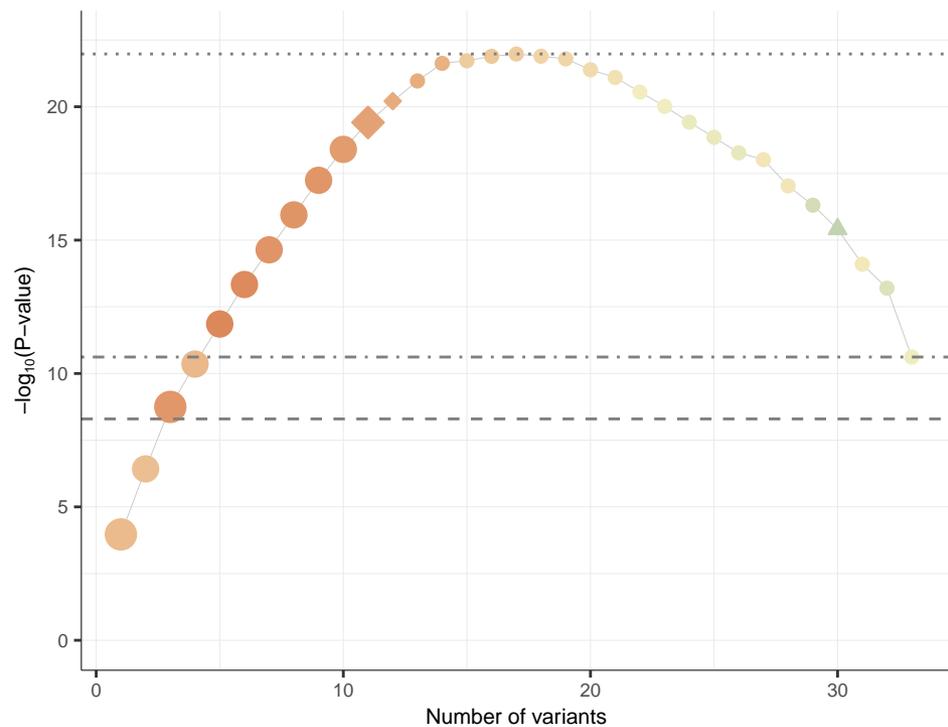
Thresholds

- - - Significance Threshold
- · - · Total P-value
- · · · · Lowest P-value

5-methyluridine (ribothymidine) in plasma at *TYMP* (LoF_mis)



5-methyluridine (ribothymidine) in plasma at *TYMP* (HI_mis)



Variant consequence

- ◇ frameshift
- missense
- △ stop gained



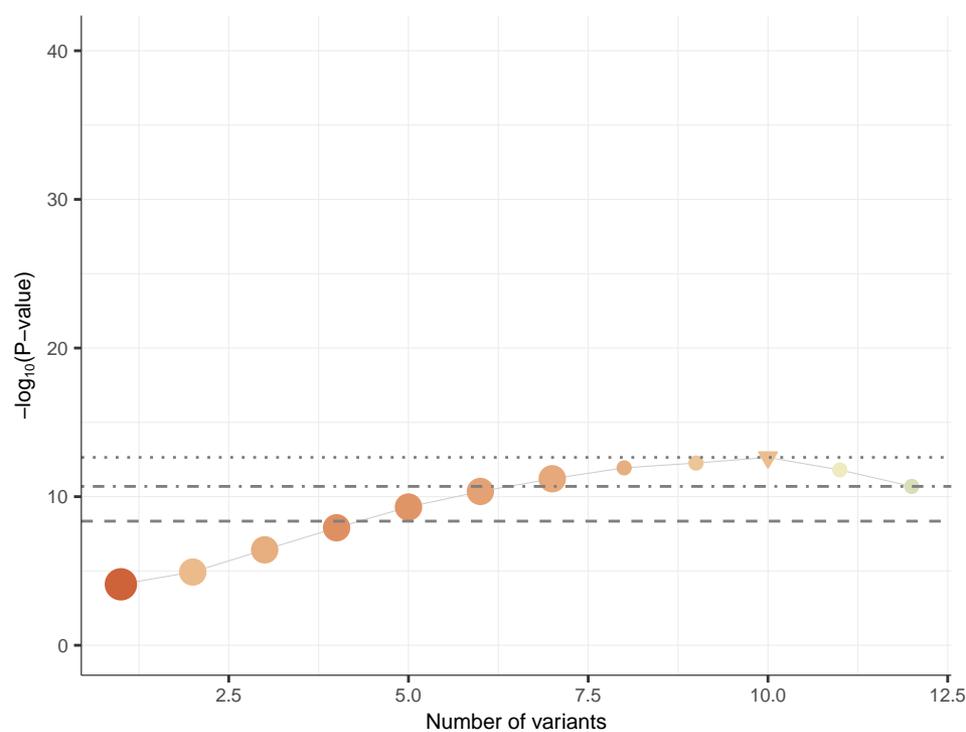
P-value

- >0.05
- <0.05
- <1e-3

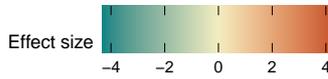
Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

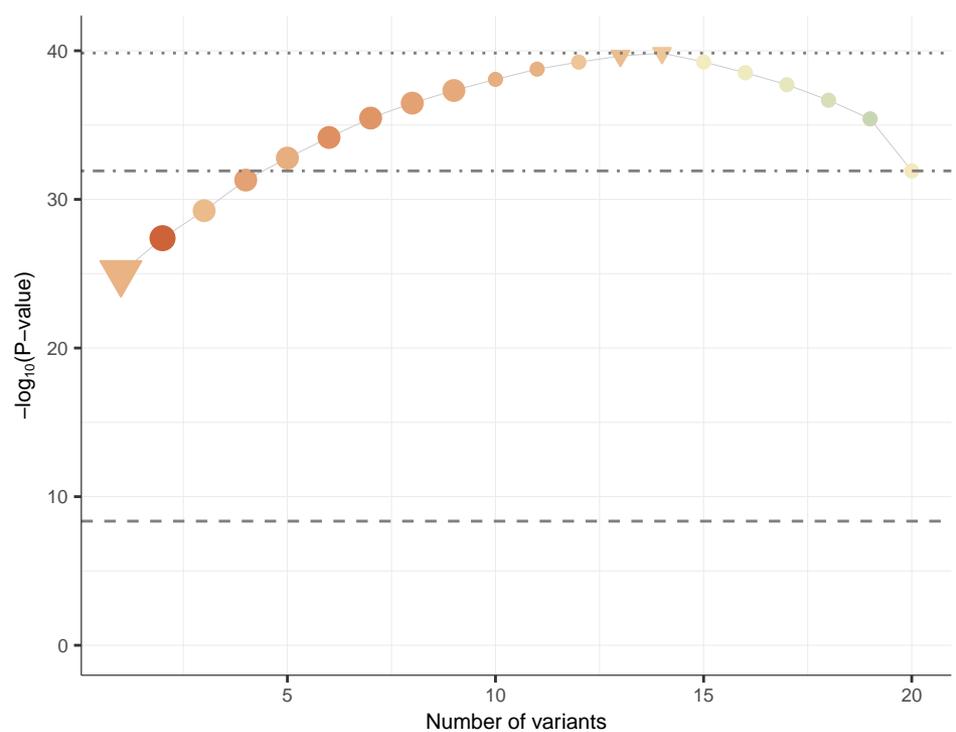
3-ureidoisobutyrate in urine at *UPB1* (LoF_mis)



Variant consequence
 ○ missense
 ▽ splicing



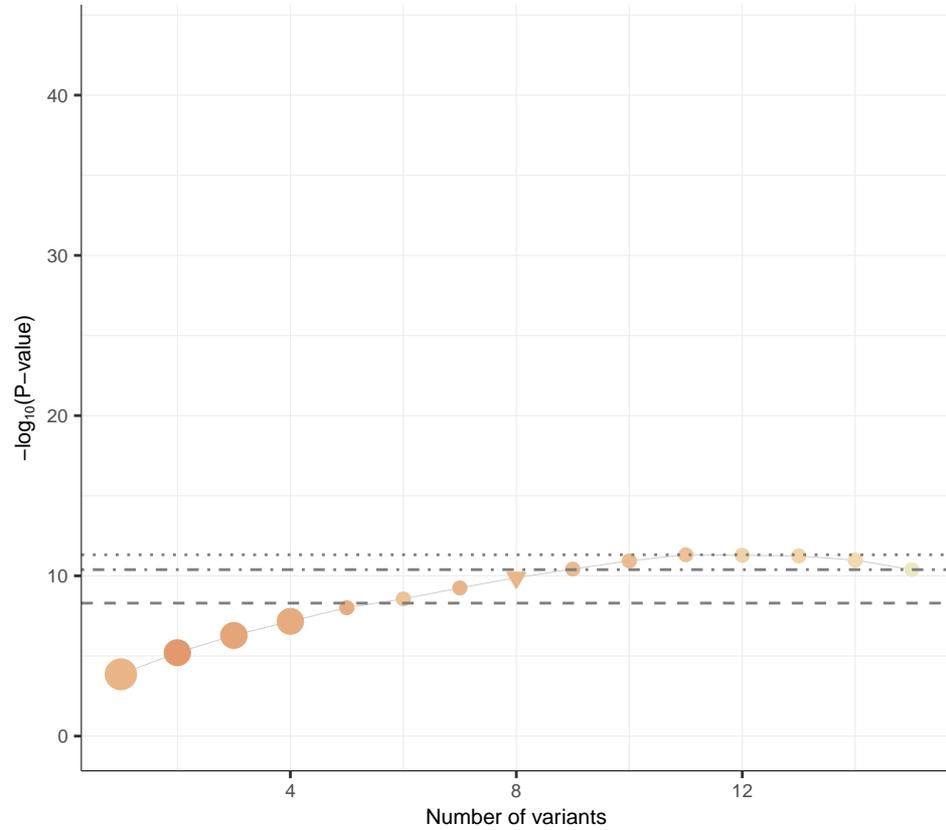
3-ureidoisobutyrate in urine at *UPB1* (HI_mis)



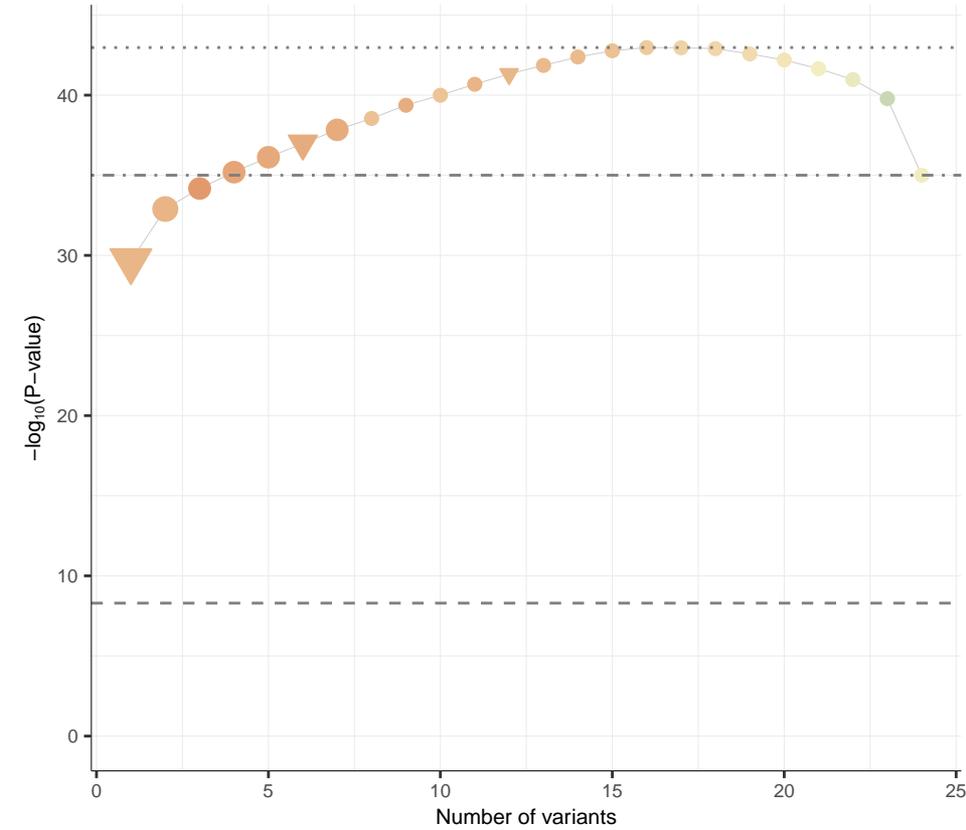
P-value
 ● >0.05
 ● <0.05
 ● <1e-3
 ● <1e-5
 ● <5e-8
 ● <1e-11

Thresholds
 - - Significance Threshold
 - · - Total P-value
 · · · Lowest P-value

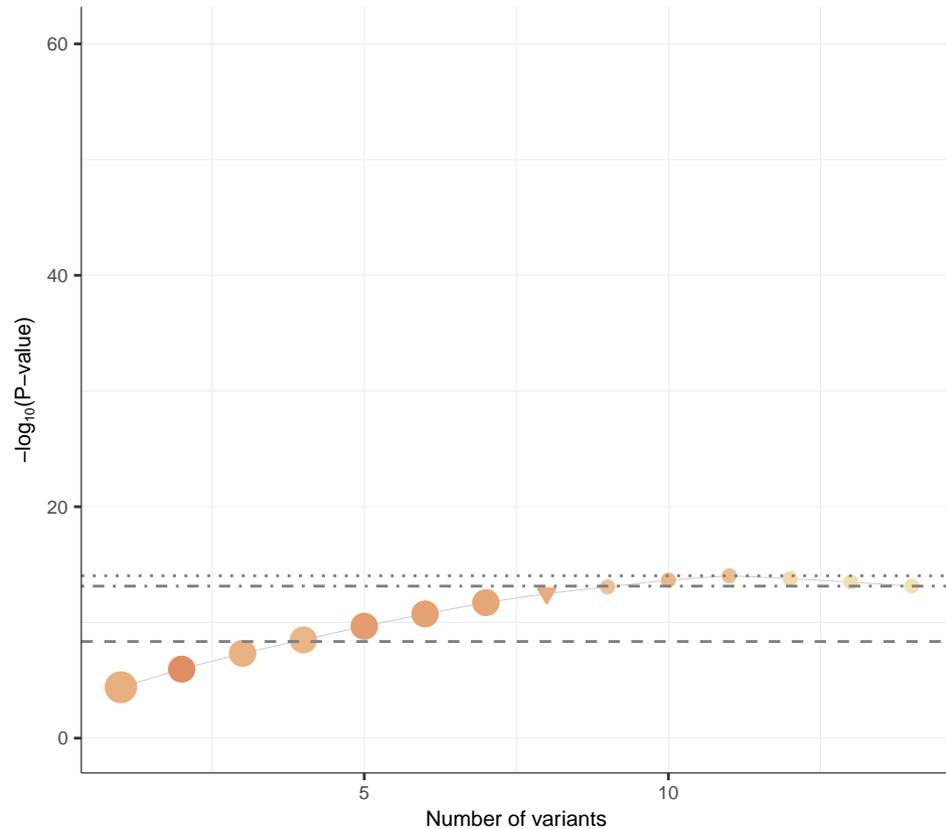
3-ureidopropionate in plasma at *UPB1* (LoF_mis)



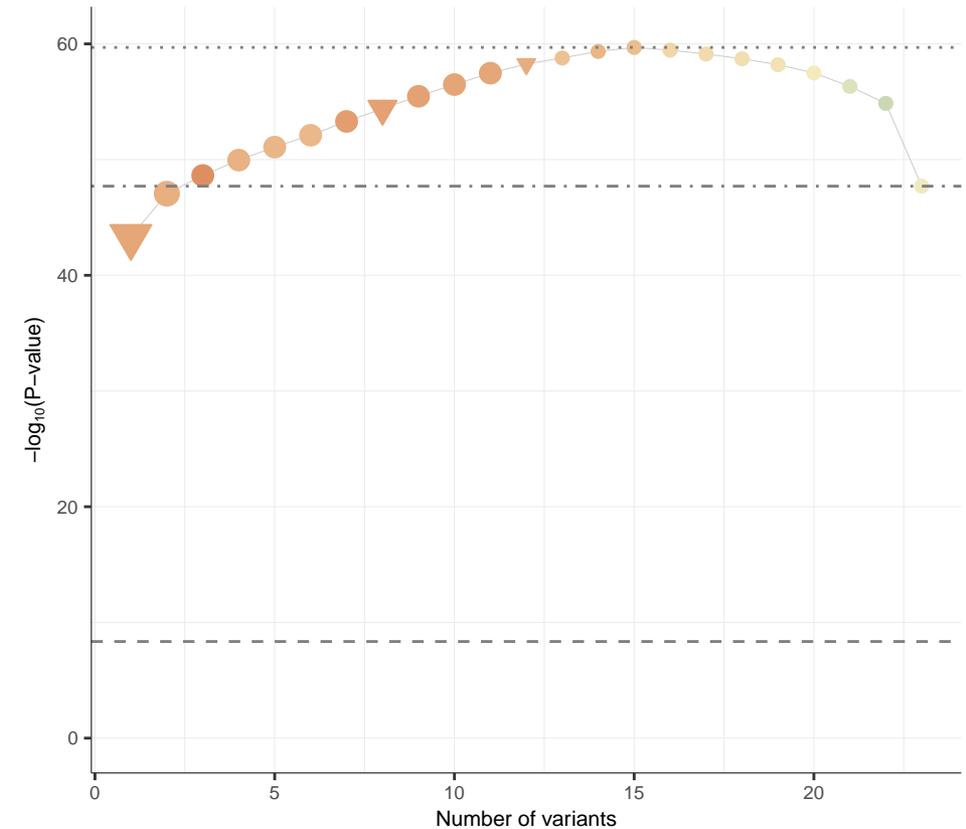
3-ureidopropionate in plasma at *UPB1* (HI_mis)



3-ureidopropionate in urine at *UPB1* (LoF_mis)

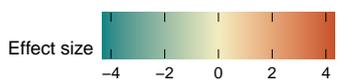


3-ureidopropionate in urine at *UPB1* (HI_mis)



Variant consequence

- missense
- ▽ splicing



P-value

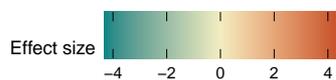
- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

Thresholds

- Significance Threshold
- - - Total P-value
- ⋯ Lowest P-value

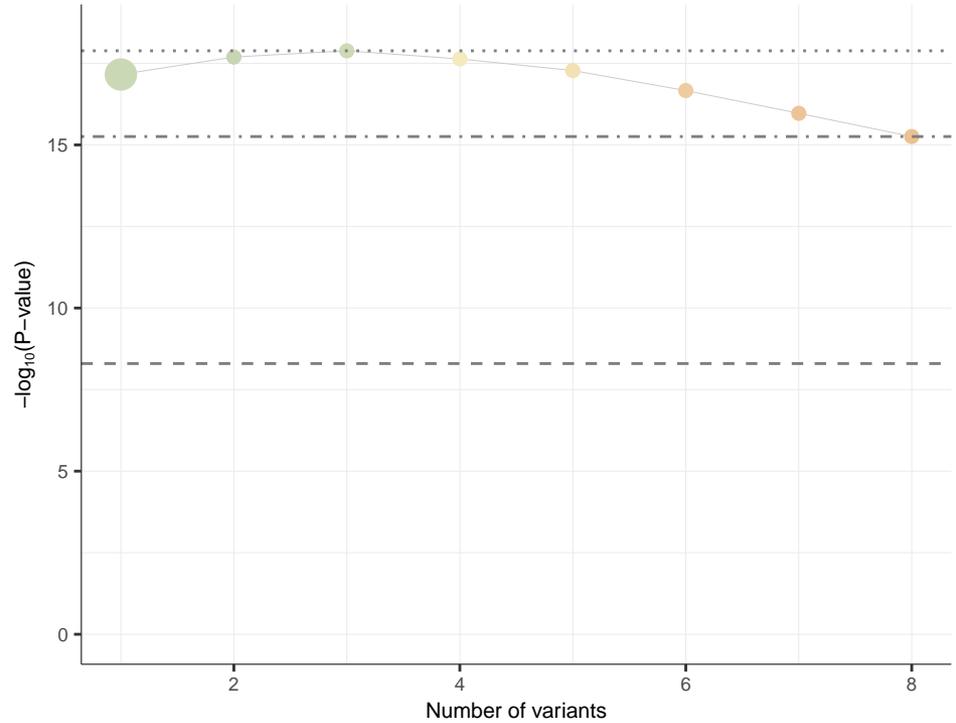
androsterone sulfate in plasma at ZNF655 (HI_mis)

Variants consequence ○ missense

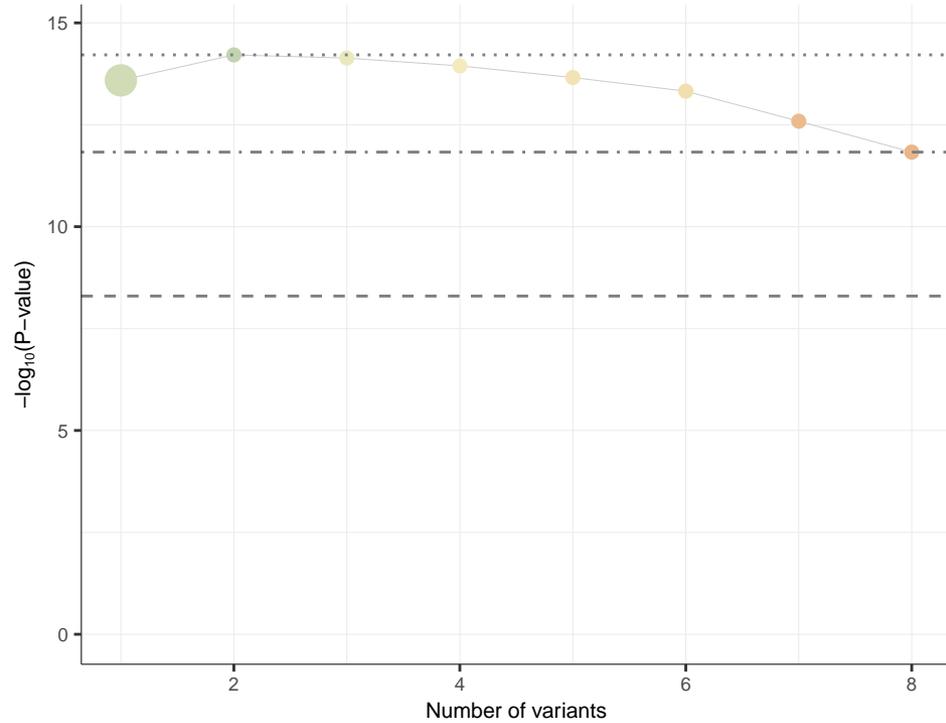


- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

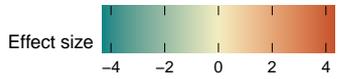
- Thresholds
- - - Significance Threshold
 - - · Total P-value
 - · · Lowest P-value



epiandrosterone sulfate in plasma at ZNF655 (HI_mis)



Variants consequence ○ missense



- >0.05
- <0.05
- <1e-3
- <1e-5
- <5e-8
- <1e-11

- Significance Threshold
- Thresholds
- - - Total P-value
- · · Lowest P-value