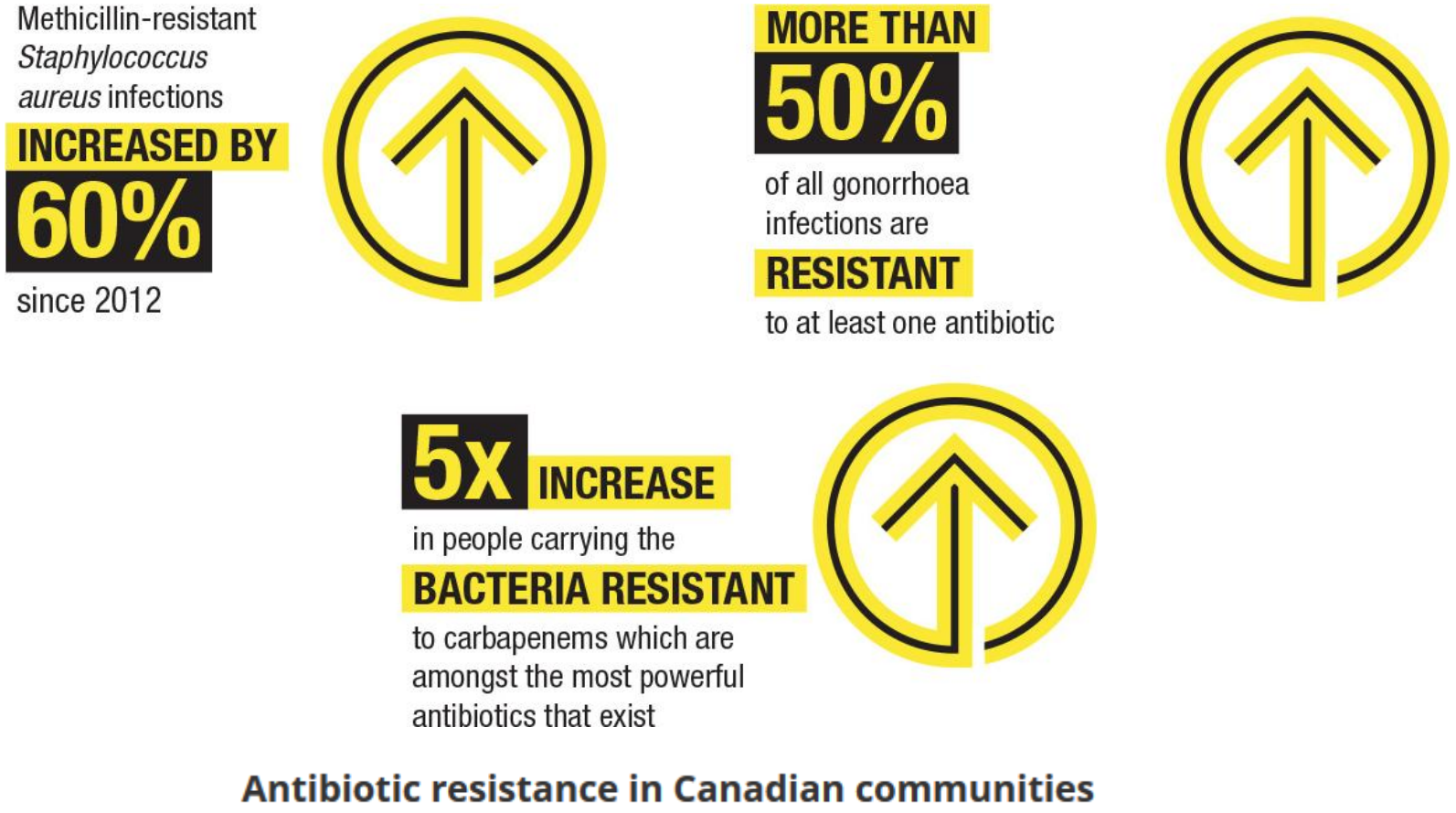
Identification of Pathogen Associated Antimicrobial Resistance Genes

APRIL 14, 2023

BRINKMAN LAB MEETING

Antimicrobial Resistance (AMR) is a Problem on the Rise



(Canadian Antimicrobial Resistance Surveillance System Report 2019, 2021)

Pathogen-associated genes (PAGs)

Genes with homologs only in bacterial pathogens and not in non-pathogens

Ho Sui et al. (2009). PloS one.

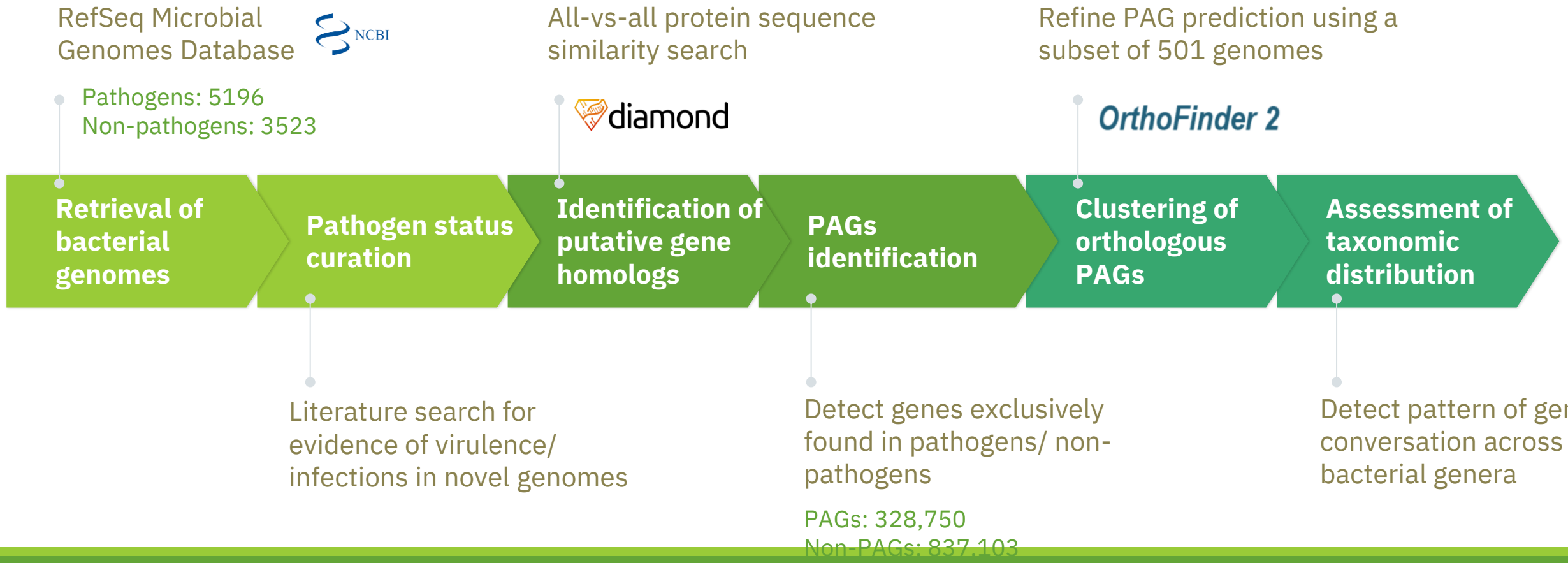
- Likely more pathogen-specific
- Likely associated with virulence
- Likely non-essential for bacterial growth and survival

Identification of 3 PAGs in P.aeruginosa PA14 that may encode novel virulence factors.

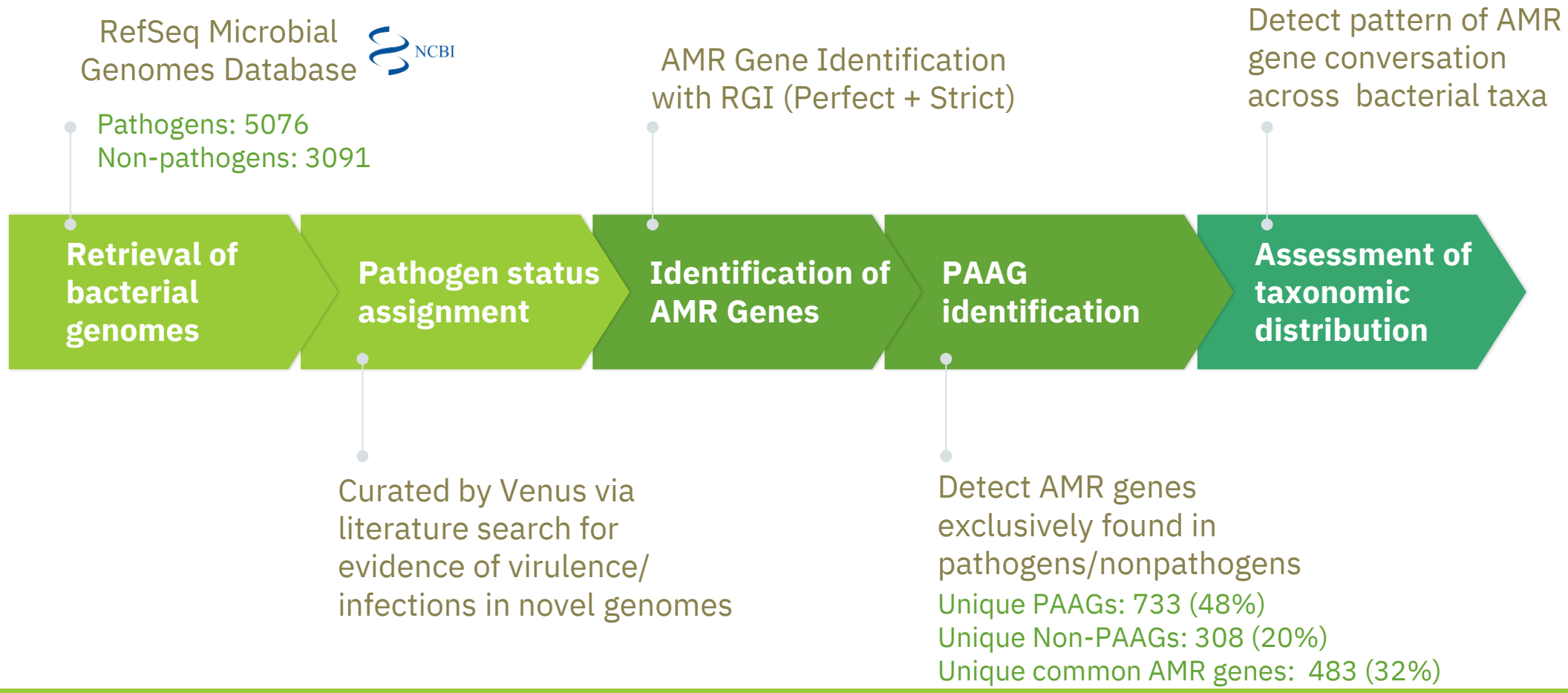
Lau. (2022).

Are there any pathogen associated AMR genes?

Pathogen-associated genes (PAGs) analysis



Pathogen-associated AMR genes (PAAGs) analysis



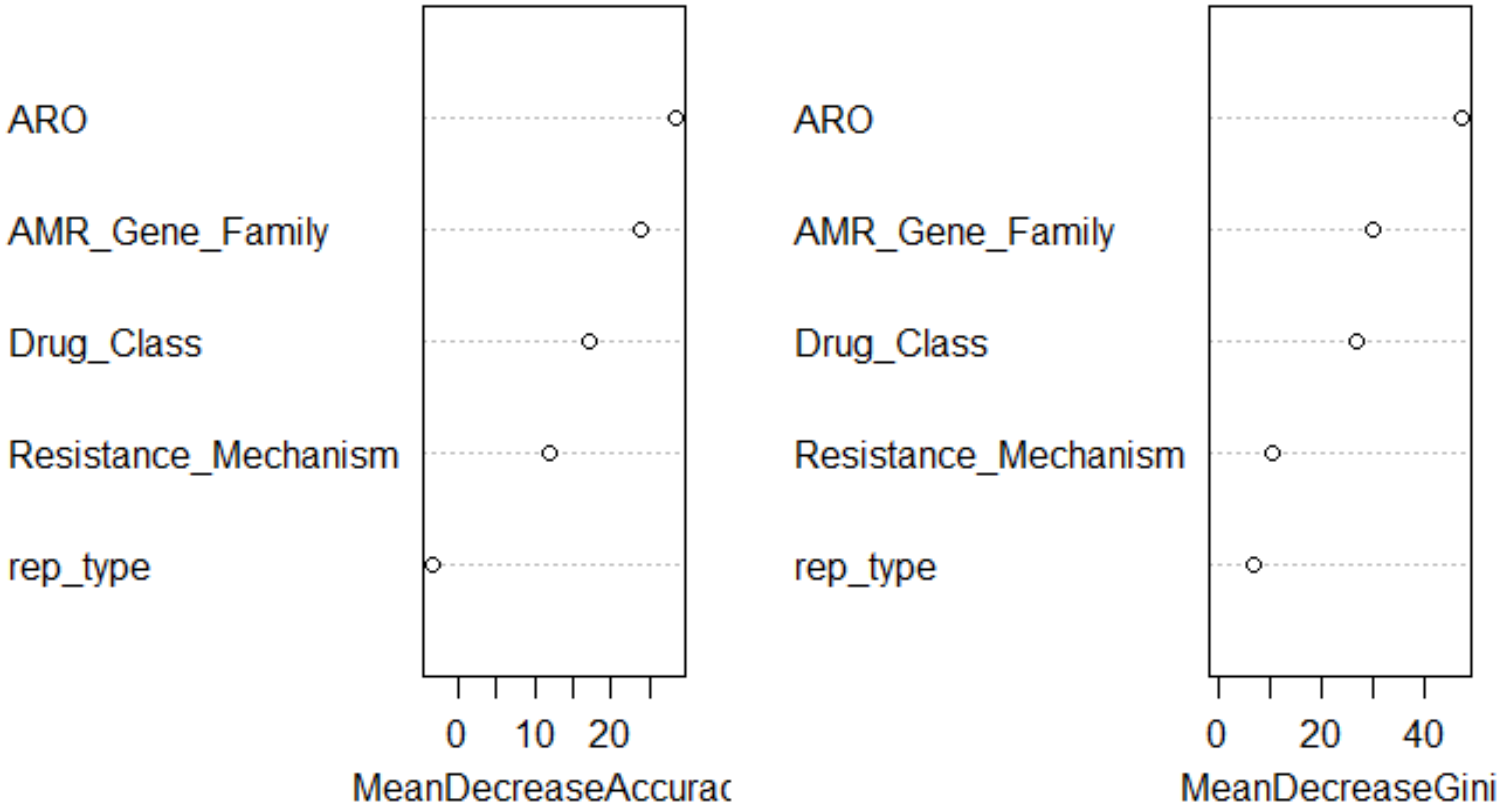
AMR Metadata Categories

Using the Comprehensive Antimicrobial Resistance Database

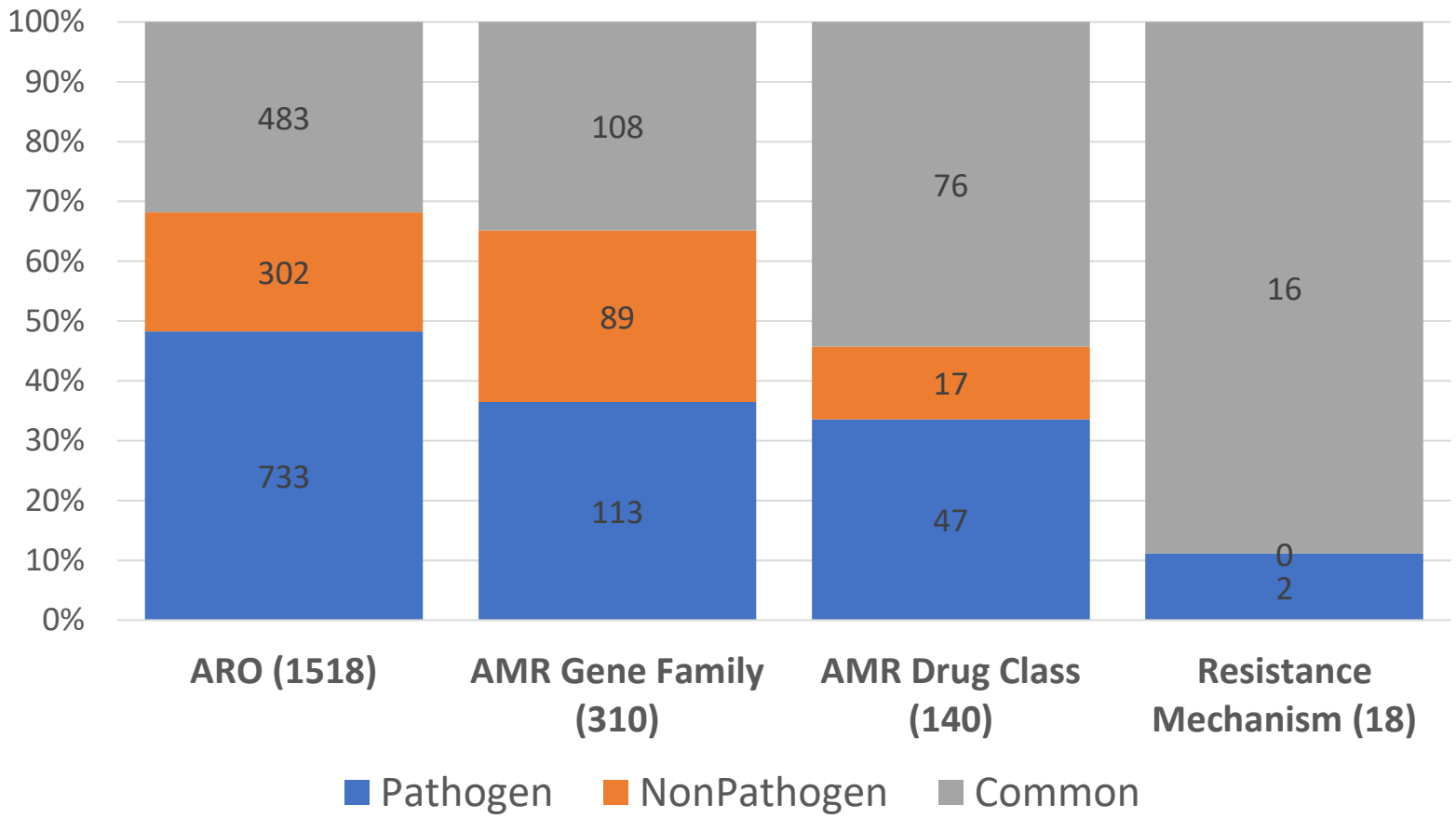
- AMR Gene Family
- Resistance Drug Class
- Resistance Mechanism
- Gene Length
- Model Type
- Etc… (11 total)

Categories that are important for classifying pathogen and non-pathogen

Top 5 categories with the highest importance in a random forest model:



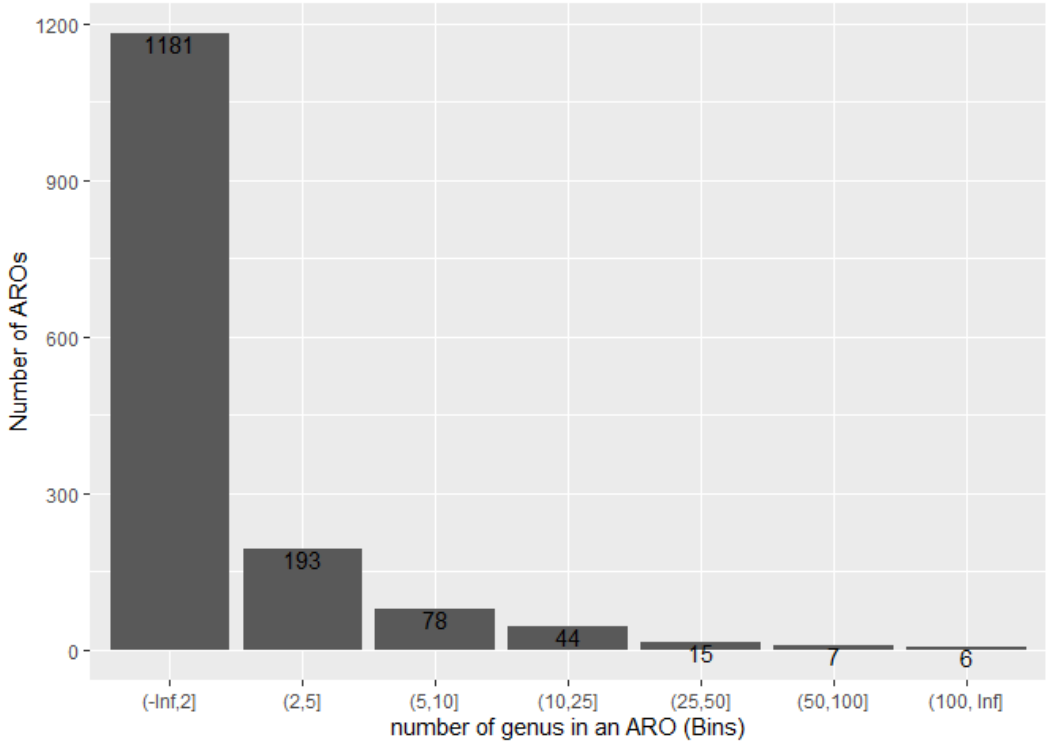
Within each category, there are pathogen and non-pathogen associated members



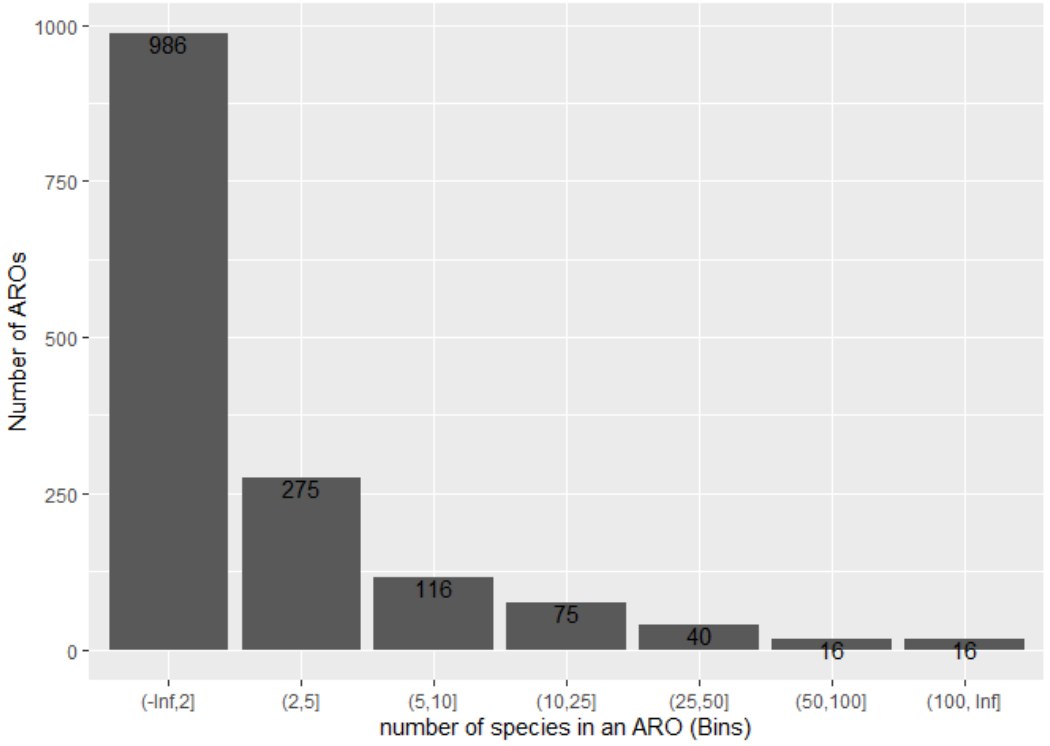
Are there any PAAGs that are across bacterial taxa?

Large portion of AMR genes are only found in 1-2 taxa

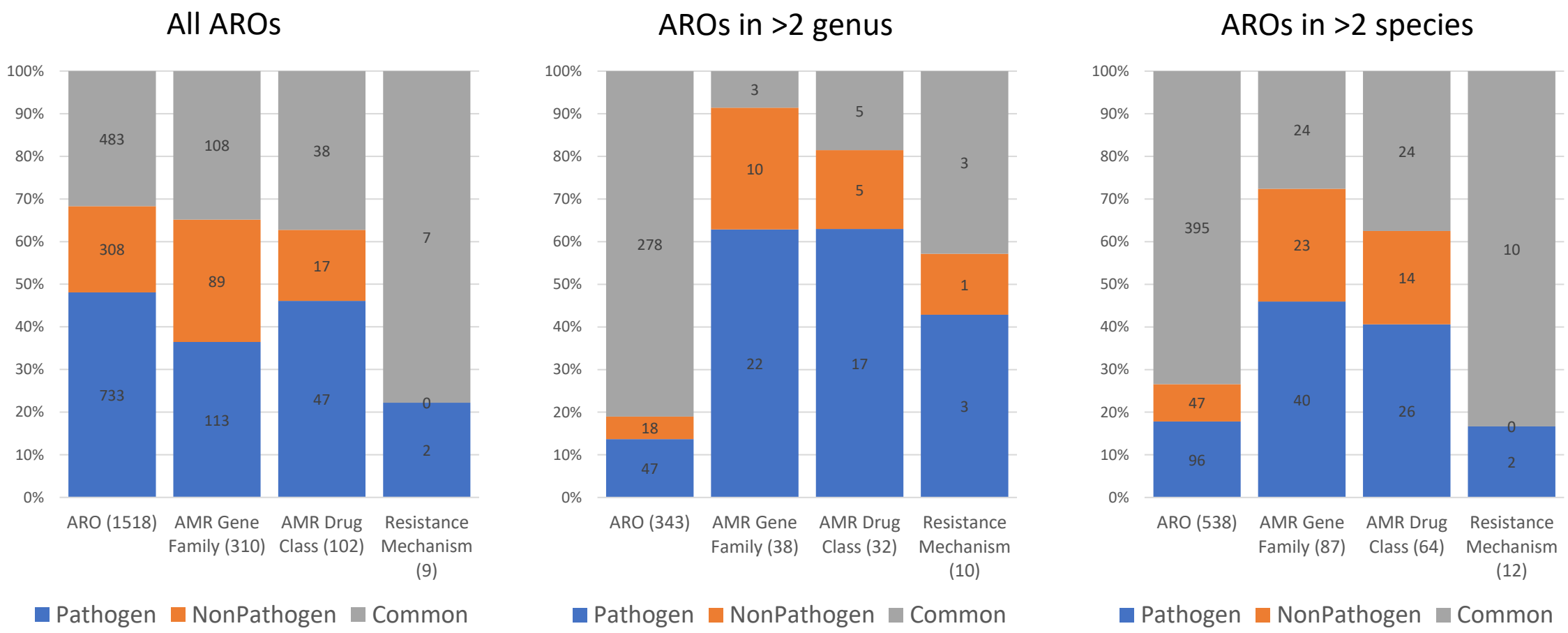
343 (23%) AROs are in >2 genus



538 (35%) AROs are in >2 species



While proportion of PAAGs decreased with filtering, the proportion of categories didn't



AMR Gene Families

- 22 Pathogen associated families:
  - Beta-lactamases (9)
  - RDS Efflux (3)
  - ANT (2)
  - Other (12)
- 10 Non Pathogen associated families:
  - Glycopeptide resistance clusters (Van families) (4)
  - Beta-lactamase (1)
  - Other (5)
- 3 Common:
  - AAC
  - MDS Efflux
  - Erm 23S ribosomal RNA methyltransferase

AMR Drug Class

- 17 Pathogen associated drug classes:
  - Fluoroquinolone
  - monobactam
  - Carbapenem
  - rifamycin
  - phosphonic acid
  - diaminopyrimidine
- 5 Non Pathogen associated drug classes:
  - Nucleoside
  - Glycopeptide
  - Elfamycin
- 5 common:
  - Aminoglycoside
  - Cephalosporin
  - Peptide
  - Macrolide
  - phenicol

Resistance Mechanisms

- 3 Pathogen associated mechanisms:
  - Antibiotic target replacement (Mobile)
  - Antibiotic target protection (Mobile)
- 1 Non Pathogen associated drug classes:
  - Reduced permeability to antibiotic (non-mobile)
- 3 common
  - Target alteration (non-mobile)
  - Inactivation (mobile)
  - Efflux (non-mobile)