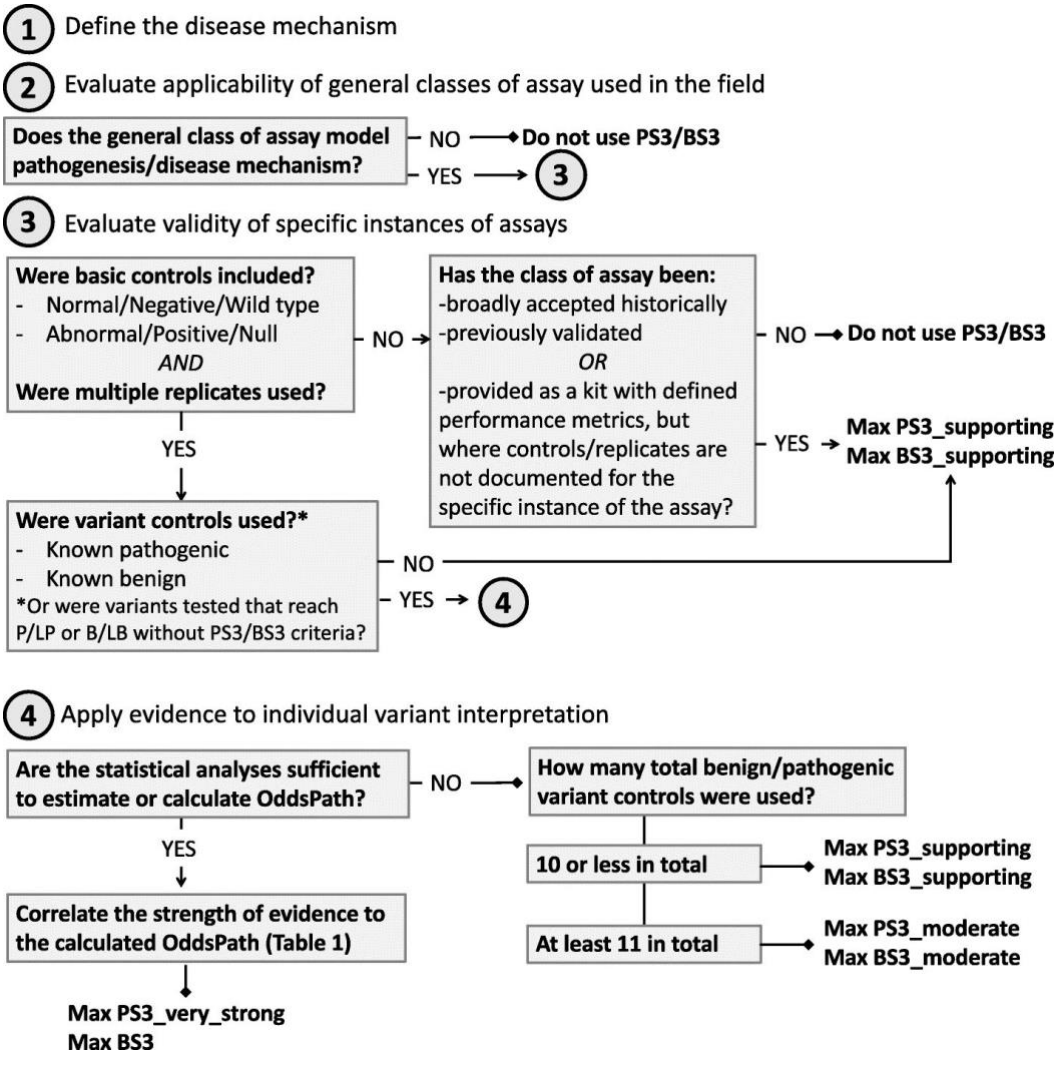
1
Define the disease mechanism
2
Evaluate applicability of general classes of assay used in the field
Does the general class of assay model pathogenesis/disease mechanism?
NO
Do not use PS3/BS3
YES
3
3
Evaluate validity of specific instances of assays
Were basic controls included?
- Normal/Negative/Wild type
- Abnormal/Positive/Null
AND
Were multiple replicates used?
NO
Has the class of assay been:
-broadly accepted historically
-previously validated
OR
-provided as a kit with defined performance metrics, but where controls/replicates are not documented for the specific instance of the assay?
NO
Do not use PS3/BS3
YES
Max PS3_supporting
Max BS3_supporting
YES
Were variant controls used?*
- Known pathogenic
- Known benign
*Or were variants tested that reach P/LP or B/LB without PS3/BS3 criteria?
NO
YES
4
4
Apply evidence to individual variant interpretation
Are the statistical analyses sufficient to estimate or calculate OddsPath?
NO
How many total benign/pathogenic variant controls were used?
YES
10 or less in total
Max PS3_supporting
Max BS3_supporting
At least 11 in total
Max PS3_moderate
Max BS3_moderate
Correlate the strength of evidence to the calculated OddsPath (Table 1)
Max PS3_very_strong
Max BS3