

The Importance of the Temporal Dimension in Identifying Relevant Genomic Variants: a Case Study

Conceptual Modeling for Life Science (CMLS) @ER2020

Nov 4, 2020

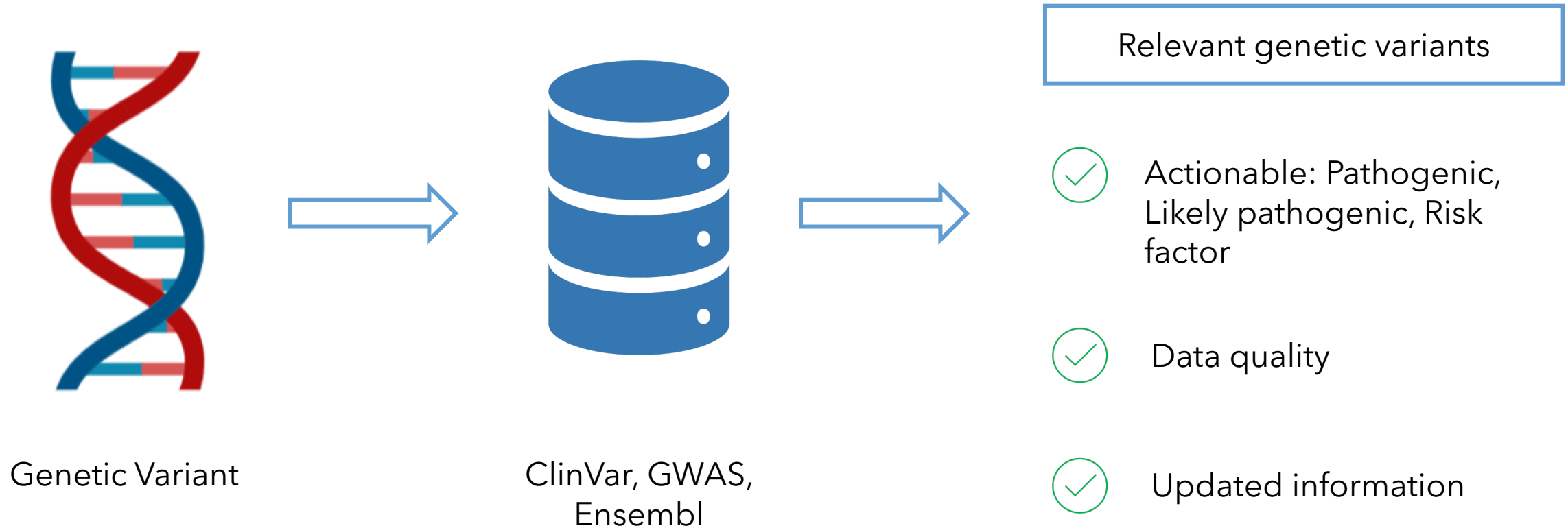
Mireia Costa
Ana León
Óscar Pastor

micossan@etsii.upv.es
aleon@pros.upv.es
opastor@pros.upv.es

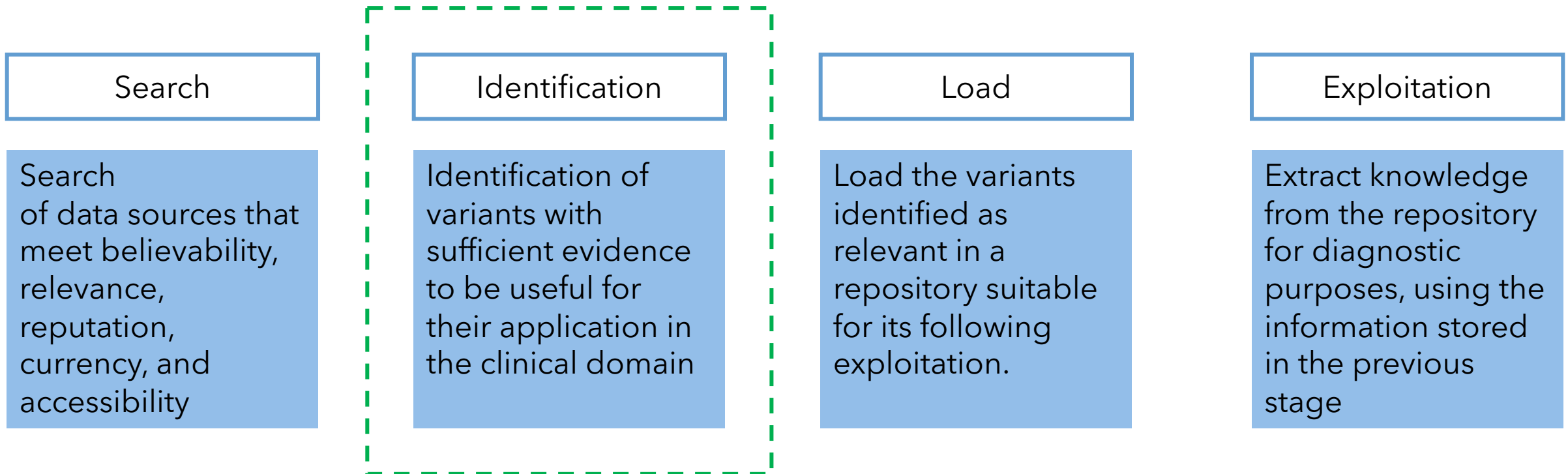
Index

1. Introduction
2. Methodology: SILE method
3. Case Study: Variant Identification in Early Onset Alzheimer's Disease
4. Conclusions and Future Work

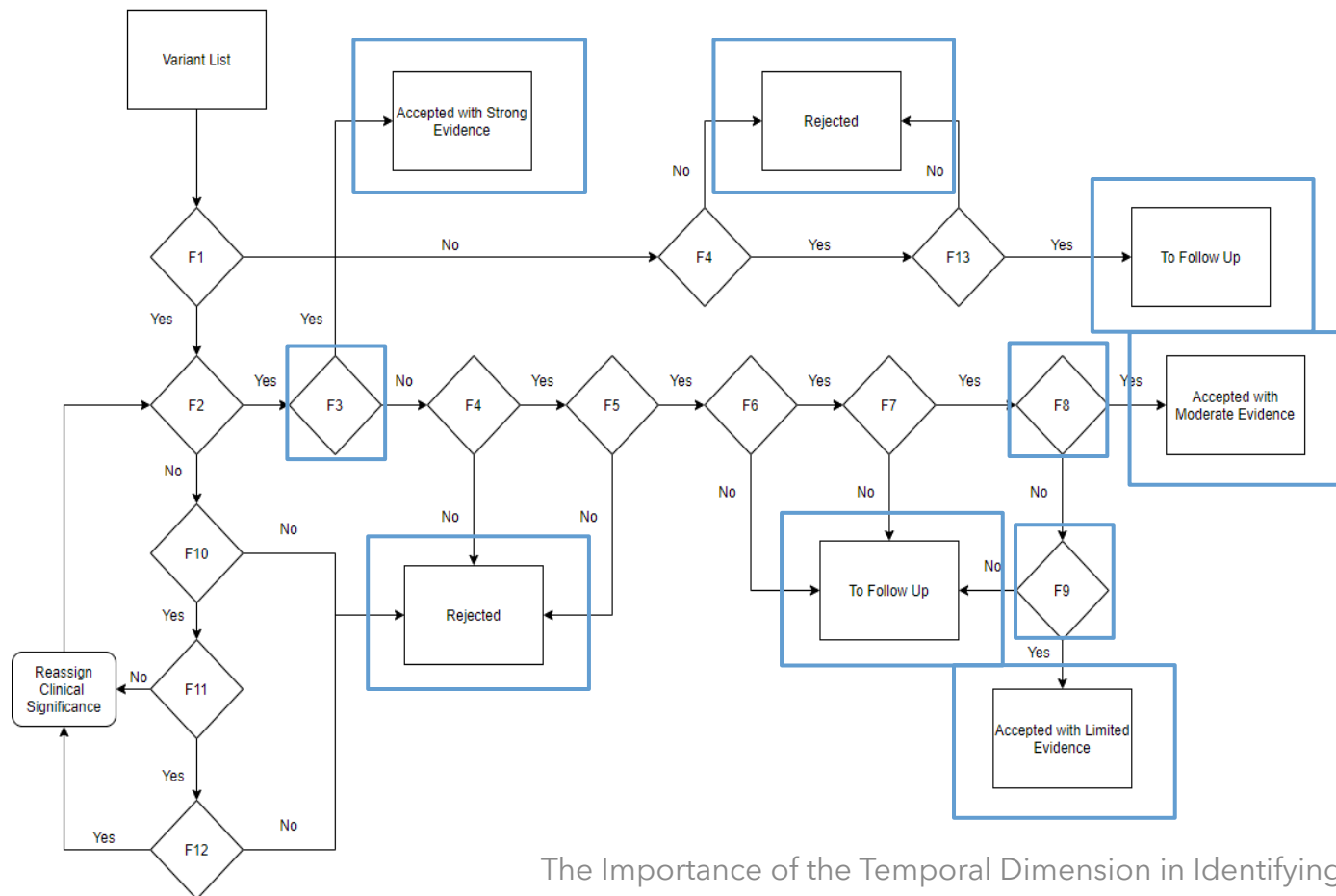
Introduction



Methodology: SILE method



SILE method: Identification

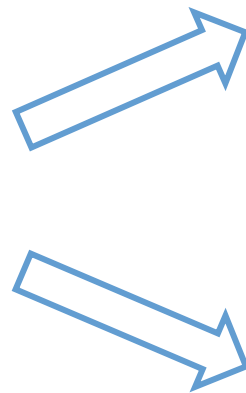


- ❑ Evaluation of clinical relevance (F1 and F2).
- ❑ Clinical practice guide or expert panel submitters (F3).
- ❑ The gene is related to the disease (F4).
- ❑ Type of method clinical trial (F5).
- ❑ The assertion criteria used for the interpretation of the variation is provided (F6).
- ❑ Submitters with at least 200 submissions (F7).
- ❑ Assertion criteria are the ACMG/AMP guidelines (F8).
- ❑ Variant revised less than three years ago (F9).
- ❑ Treatment of variations with clinical significance and conflict of interpretation (F10 to F12).
- ❑ Variants not interpreted (F4 and F13).

Case Study: Variant Identification in Early Onset Alzheimer's Disease



ClinVar



May 18, 2020

July 9, 2020

Query

```
((alzheimer[Disease/Phenotype]
AND "early
onset"[Disease/Phenotype])) OR
((alzheimer[Disease/Phenotype]
AND ("type 1"[Disease/Phenotype]
OR "type 3"[Dis-ease/Phenotype]
OR "type 4"[Disease/Phenotype]))
```

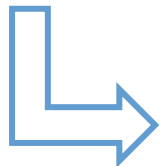
Case Study: Variant Identification in Early Onset Alzheimer's Disease

MAY

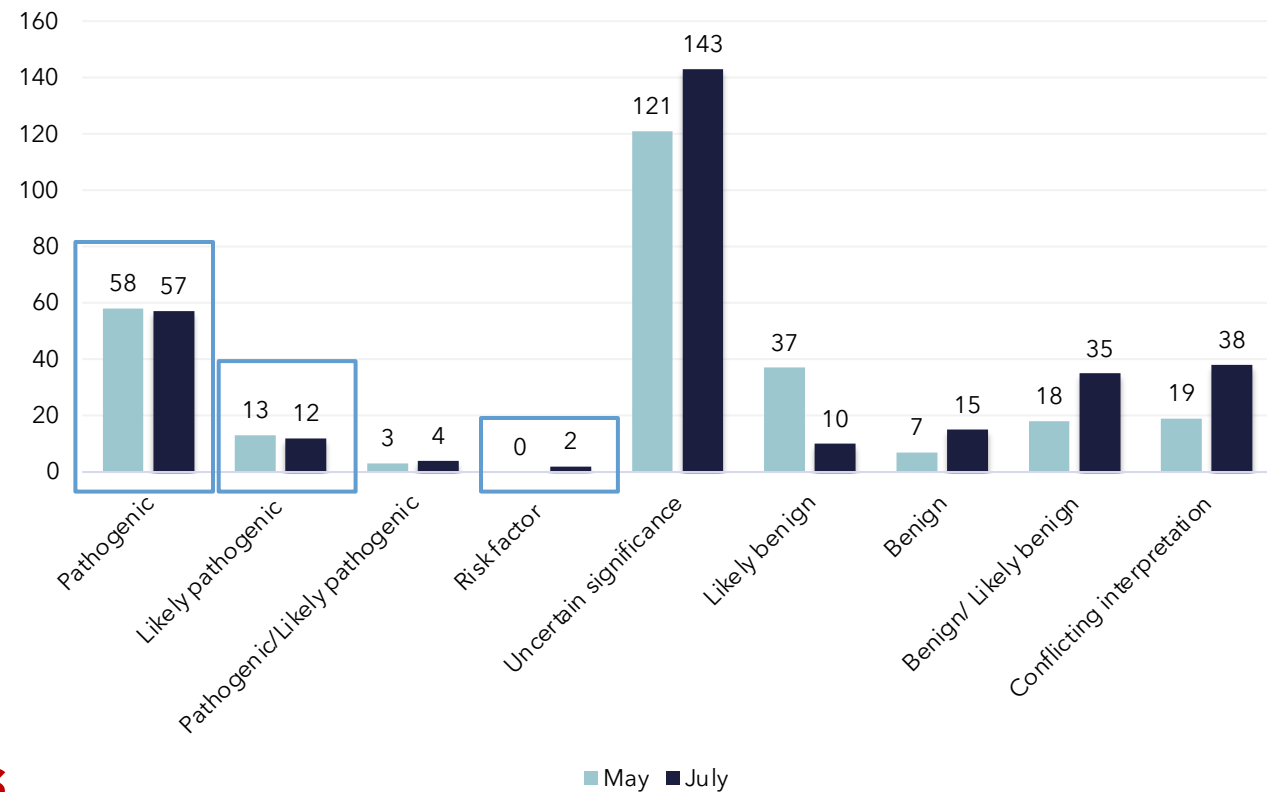
276 variants

JULY

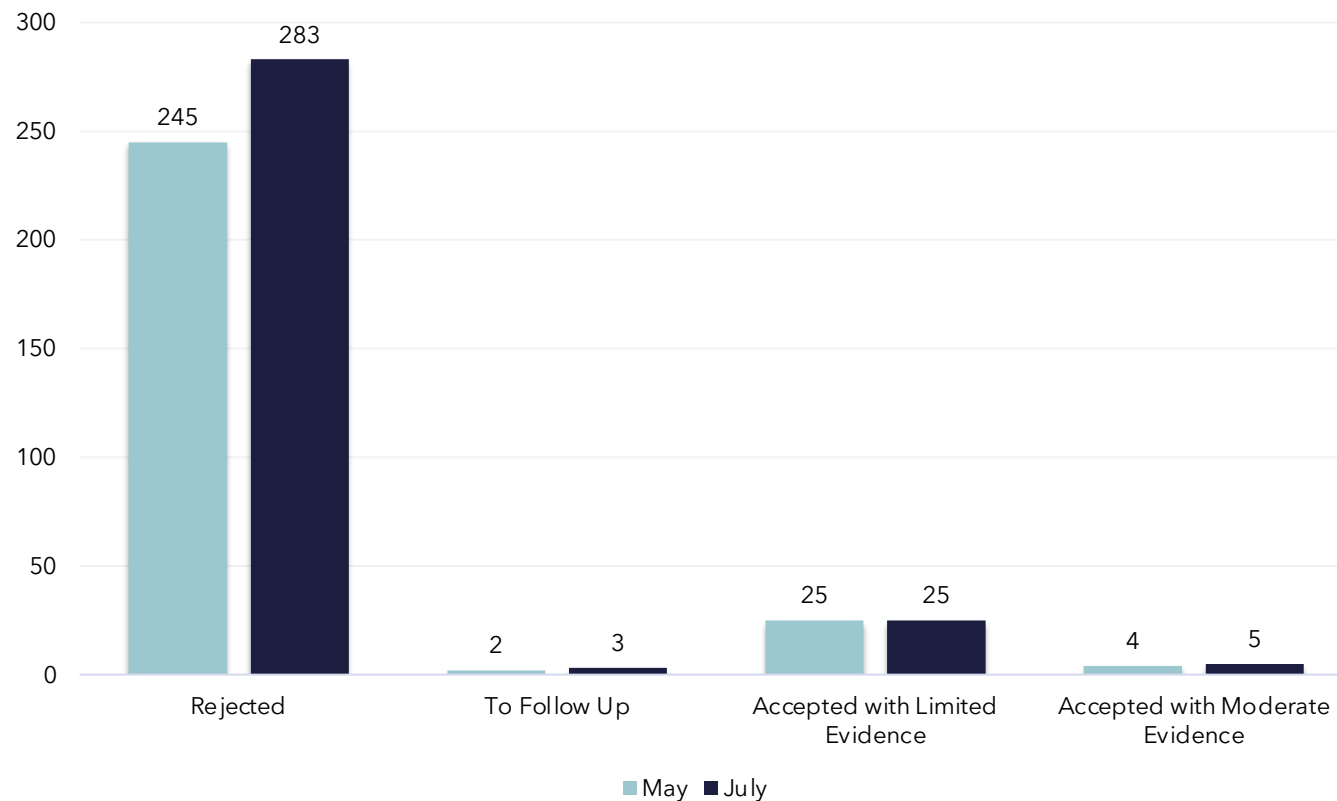
316 variants



There are differences



Case Study: Variant Identification in Early Onset Alzheimer's Disease



- More Rejected variants
- New To Follow Up variant
- New Accepted with Moderate Evidence



The number of relevant variants to be considered in a genomic diagnosis had changed in a short period

Conclusions and Future Work

- ❑ The temporal dimension of the genomic data should be considered when using this information for clinical diagnosis
- ❑ SILE method provides a clear explanation for whether or not a variant should be considered for genomic diagnosis, so the results and their evolution over time can be easily compared
- ❑ Further work associated with the SILE method must study new features related to the temporal evolution of genomic data
- ❑ We plan to apply the method at different time points to other diseases in order to gain a more accurate perspective of how information evolves in different contexts



Centro de Investigación en Métodos
de Producción de Software



UNIVERSITAT
POLITÈCNICA
DE VALÈNCIA

Thank you



Mireia Costa



micossan@etsii.upv.es