Bridging Knowledge Gaps in PBPK through Open Science

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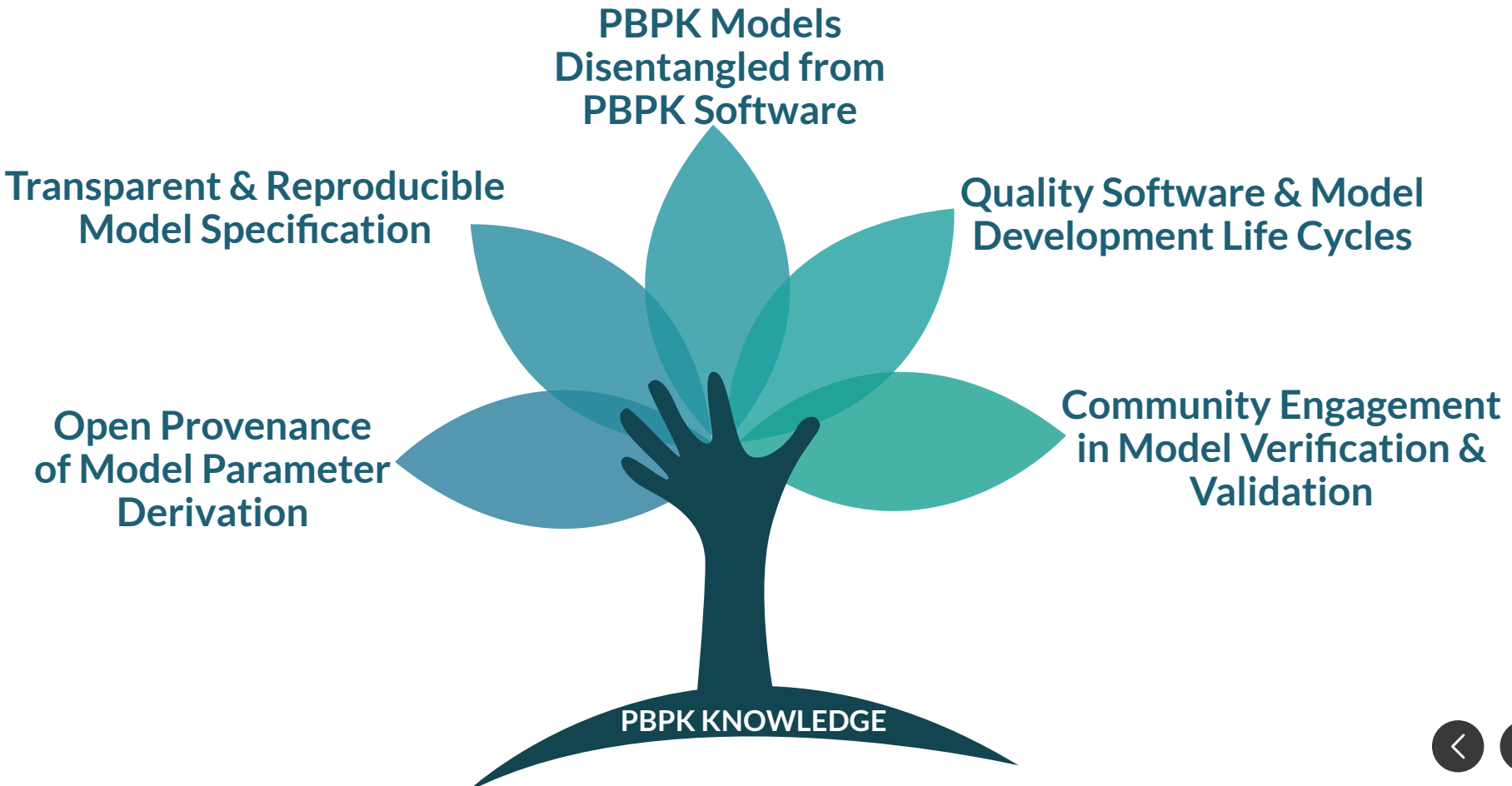
Contributors to Knowledge Gaps in PBPK

1. **Growth of Science (Global Knowledge Gaps)**
   - Emerging information on quantitative physiology: e.g. ontogeny, expression levels
   - New therapeutic modalities and targets

2. **Closed Science (Local Knowledge Gaps / Silos)**
   - Currently, most published PBPK modeling results are not reproducible
   - Missed opportunity to share precompetitive learnings

PBPK Knowledge Growth with Open Science



PBPK Knowledge Growth with Open Science

PBPK Models Disentangled from PBPK Software

Separate Software from Science

- Goals are not always aligned

Evaluate Models Independent of Software

- Performance of each is important but should be independently verified and validated

Let Physiology be Free and Open

- Allows for interoperability, accessibility, shared learning

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Transparent and Reproducible Model Specification

Structural Model Transparency

- Provide complete mathematical specification for the model structure

Statistical Model Transparency

- Provide complete specification of parameters, distributions, and related hierarchical structure

Specific Software Implementation

- Provide complete model specification code set and code for generation of derived tables and figures for the tool or tools used to conduct the work.

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Open Provenance of Model Parameter Derivation

Define for Each Parameter

- Source, species, units, sample size, precision, disease state, functional relationships, optimized or experimentally derived

Explore Alternative Parameters/Sources

- If available, other cited values or the plausible range of values used in global and local sensitivity analyses

Interoperability Standards

- Develop parameter specification standards for content and format (e.g. XML)
- Allows for automated connectivity with various software tools.

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Quality Software & Model Development Life Cycle Management

Software Development Life Cycle

- Professional software development standards and best practices
- Peer reviewed
- Iterative or pre-specified requirements, implementation, tests, acceptance, and documentation
- Commercial or open-source

Model Development Life Cycle

- Similar principles and processes applied to model development

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Community Engagement in Model Verification & Validation

Quality

- "Given enough eyeballs, all bugs are shallow." -E.S. Raymond

Scientific Relevance

- Allows varied scientific expertise to impact the model

Credibility

- Widespread, documented, qualified testing and use leads to credibility = understanding and documentation of how (and where) the models work (or don't).

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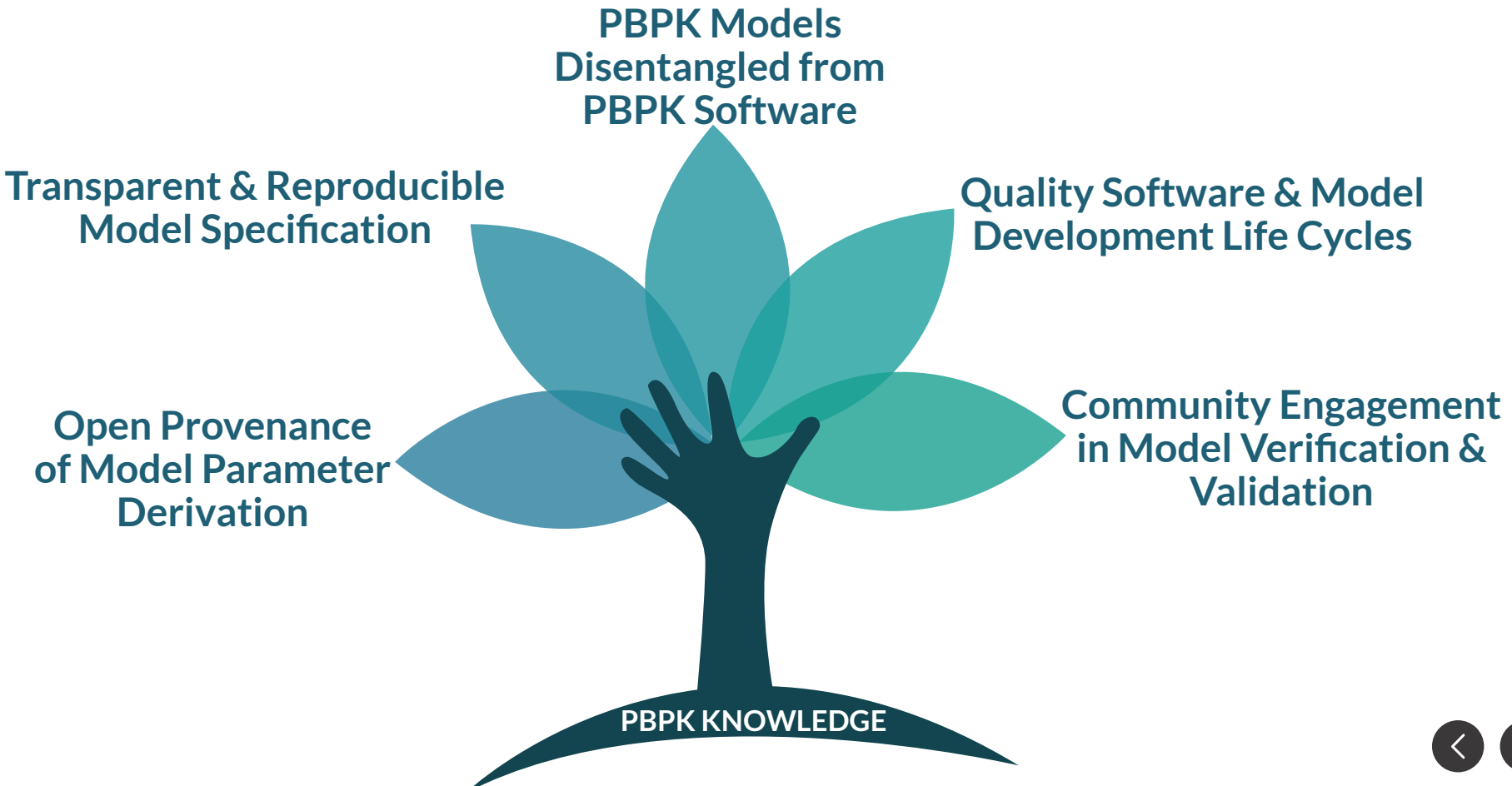

Thank You

Presentation available: https://metrumrg.com/publications/

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