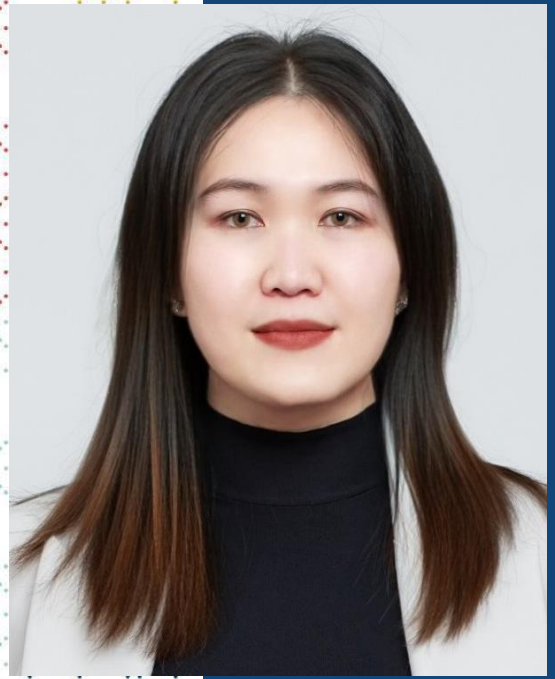

# Enhancing Meta-Analysis Through TMF Methodologies

Presented by Yen Phan, Sr Clinical Data Scientist, CodLad/University of Oxford



# Meet the Speaker

## Yen Phan

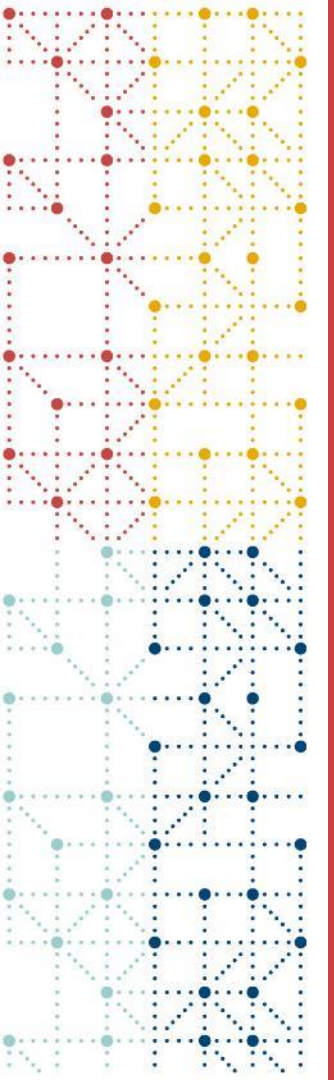
Title: Founder and Sr Clinical Data Scientist

Organization: CodLad/University of Oxford

Yen Phan is a founder of CodLad and a Senior Data Scientist with over 10 years of experience in the industry. She has also been lecturing at Technological University Dublin, Ireland for 8 years on Pharma Science and Evidence based healthcare. At the same time, she is finalizing her dissertation at University of Oxford with a focus of a meta-analysis.

# Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*
- *This presentation is intended for informational purposes only. While every attempt has been made to ensure the accuracy and reliability of the information provided, the author does not make any representations or warranties of any kind, express or implied, about the completeness, accuracy, reliability, suitability, or availability of the information contained in this presentation.*
- *The presenter declares no conflicts of interest in relation to this presentation. Any views or opinions presented are solely those of the presenter and do not necessarily represent those of the respective organizations mentioned within the presentation. Any examples of companies, studies, or technologies mentioned are for illustrative purposes only and do not constitute endorsements or recommendations.*



# Agenda

1. Introduction and Background
2. Implementation of TMF Principles
3. Expected Outcomes and Potential Impact
4. Challenges, Limitations, and Future Directions
5. Q&A Session

# Introduction and Background

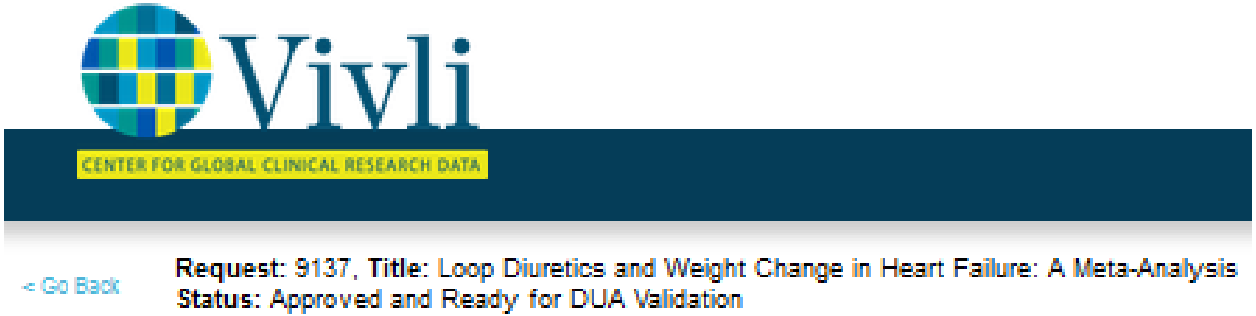
# Meta-Analysis in Academic Research

- Meta-analysis is a statistical technique that combines the results of multiple studies to come up with a more comprehensive and reliable understanding of a research topic.
- It is a powerful tool for synthesizing research findings and drawing stronger conclusions than would be possible from any single study.

## Steps in a Meta-analysis


cdisc

# The study




- **Title**: Loop Diuretics and Weight Change in Heart Failure: A Meta-Analysis
- Includes 5 trials:
  - 2 from Boehringer Ingelheim (collaborates with Eli Lilly)
  - 2 from Bayer
  - 1 from GlaxoSmithKline
- Through **Vivli** platform

# Records

- aCRF
- Analysis Datasets Plan
- Statistical Analysis Plan
- Protocol
- Raw data/SDTM/ADaM
- Define.xml
- Programs
- etc.

# Implementation of TMF Principles

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| 1.0 Trial Management | | |
| | 1.1 Trial Oversight | |
| | 1.2 Trial Team | |
| | 1.3 Trial Committee | |
| | 1.4 Meetings (Trial Mgmt) | |
| | 1.5 General (Trial Mgmt) | |
| 2.0 Central Trial Documents | | |
| | 2.1 Prod & Trial Docs | |
| | | 2.1.1 Investigat Brochure |
| | | 2.1.2 Protocol |
| | | 2.1.7 Sample CRF |
| | 2.2 Subject Documentation | |
| | | 2.2.1 Subject Diary |
| | | 2.2.2 Subj Questionnaire |
| | 2.3 Reports (Cent Trial) | |
| | | 2.3.1 Clin Stud Rpt (CSR) |
| | | 2.3.2 Bioanalytical Rpt |
| | 2.4 General (Cent Trial) | |
| 3.0 Regulatory | | |
| | 3.1 Trial Approval | |
| | 3.2 Invest Med Product | |
| | 3.3 Trial Status Report | |
| | 3.4 General (Regulatory) | |
| 4.0 IRB/IEC & Other Approval | | |
| | 4.1 IRB/IEC Trial Approv | |
| | 4.2 Other Committees | |
| | 4.3 Trial Status Rep | |
| | 4.4 General (IRB/IEC) | |
| 5.0 Site Management | | |
| | 5.1 Site Selection | |
| | 5.2 Site Set-up | |
| | 5.3 Site Initiation | |
| | 5.4 Site Mgmt | |
| | | 5.4.6 Protocol Deviation |
| | | 5.4.11 Source Data |
| | | 5.4.13 Subj Eligibility |
| | 5.5 General (Site Mgmt) | |

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| 6.0 IP and Trial Supplies | | |
| | 6.1 IP Documentation | |
| | 6.2 IP Release Process | |
| | 6.3 IP Allocation Docs | |
| | | 6.3.1 IP Treat Allocation |
| | | 6.3.2 IP Unblinding Plan |
| | | 6.3.3 IP Treat Decoding |
| | 6.4 Storage (IP) | |
| | 6.5 Non-IP Documentation | |
| | 6.6 Interactive Resp Tech | |
| | 6.7 General (IP Supply) | |
| 7.0 Safety Reporting | | |
| | 7.1 Safety Documentation | |
| | | 7.1.1 Safety Mgmt Plan |
| | | 7.1.2 PV Database Line |
| | 7.2 Trial Status Rpting | |
| | | 7.2.1 Expedited Sfty Rpt |
| | | 7.2.2 SAE Report |
| | | 7.2.3 Pregnancy Rpt |
| | | 7.2.4 Special Events |
| | 7.3 General (Safety Rpt) | |
| 8.0 Centralized Testing | | |
| | 8.1 Facility Documents | |
| | | 8.1.3 Lab Results Docs |
| | | 8.1.4 Normal Ranges |
| | | 8.1.8 Standard Methods |
| | 8.2 Sample Documentation | |
| | 8.3 General (Testing) | |
| 9.0 Third Parties | | |
| | 9.1 Third Party Oversight | |
| | 9.2 Third Party Setup | |
| | 9.3 Third Party General | |

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| 10.0 Data Management | | |
| | 10.1 Data Mgmt Oversight | |
| | 10.2 Data Capture | |
| | | 10.2.2 Annotated CRF |
| | | 10.2.4 Doc of Corrections |
| | | 10.2.5 Final Subject Data |
| | 10.3 Database | |
| | | 10.3.1 Database Specs |
| | | 10.3.8 SAE Reconciliation |
| | | 10.3.9 Dictionary Coding |
| | | 10.3.11 DB Lock/Unlock |
| | | 10.3.12 DB Change Control |
| | 10.4 EDC Management | |
| | 10.5 General (Data Mgmt) | |
| 11.0 Statistics | | |
| | 11.1 Statistics Oversight | |
| | | 11.1.1 Stat Analysis Plan |
| | | 11.1.2 Sample Size Calc |
| | 11.2 Randomization | |
| | | 11.2.1 Randomization Plan |
| | | 11.2.2 Randomization Proc |
| | | 11.2.3 Master Random List |
| | | 11.2.4 Randomization Prog |
| | | 11.2.5 Randomiz Sign Off |
| | | 11.2.6 End/Interm Unblind |
| | 11.3 Analysis | |
| | | 11.3.1 Data Def Datasets |
| | | 11.3.2 Analysis QC Docs |
| | | 11.3.3 Interim Raw Data |
| | | 11.3.4 Interim Programs |
| | | 11.3.5 Interim Datasets |
| | | 11.3.6 Interim Output |
| | | 11.3.7 Final Raw Datasets |
| | | 11.3.8 Final Programs |
| | | 11.3.9 Final Datasets |
| | | 11.3.10 Final Output |
| | | 11.3.11 Subj Eval Criteri |
| | 11.4 Report (Statistical) | |
| | | 11.4.1 Interim Stat Rpts |
| | | 11.4.2 Statistical Report |
| | 11.5 General (Statist) | |

# Data Integrity and Quality Control

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| 10.0 Data Management | | |
| | 10.1 Data Mgmt Oversight | |
| | 10.2 Data Capture | |
| | | 10.2.2 Annotated CRF |
| | | 10.2.4 Doc of Corrections |
| | | 10.2.5 Final Subject Data |

➔Accurate and Verifiable Data Collection

Standardized data capture methods, including the use of annotated CRFs and documentation of corrections, ensure that data is accurately recorded and verifiable, reducing the likelihood of errors.

# Data Integrity and Quality Control

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| **10.0 Data Management** | | |
| | 10.3 Database | |
| | | 10.3.1 Database Specs |
| | | 10.3.8 SAE Reconciliation |
| | | 10.3.9 Dictionary Coding |
| | | 10.3.11 DB Lock/Unlock |
| | | 10.3.12 DB Change Control |

➔Rigorous and Transparent Data Handling

Detailed database specifications and a controlled process for any changes in the database provide a transparent record of how data is managed, bolstering the robustness of your analysis.

# Data Integrity and Quality Control

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| **10.0 Data Management** | | |
| | 10.3 Database | |
| | | 10.3.1 Database Specs |
| | | 10.3.8 SAE Reconciliation |
| | | 10.3.9 Dictionary Coding |
| | | 10.3.11 DB Lock/Unlock |
| | | 10.3.12 DB Change Control |

➔Comprehensive Data Verification

Processes such as Serious Adverse Event (SAE) reconciliation and dictionary coding ensure that data is verified and classified correctly, enhancing the overall quality of the dataset.

# Data Integrity and Quality Control

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| **11.0 Statistics** | | |
| | 11.1 Statistics Oversight | |
| | | 11.1.1 Stat Analysis Plan |
| | | 11.1.2 Sample Size Calc |
| | 11.2 Randomization | |
| | | 11.2.1 Randomization Plan |
| | | 11.2.2 Randomization Proc |
| | | 11.2.3 Master Random List |
| | | 11.2.4 Randomization Prog |
| | | 11.2.5 Randomiz Sign Off |
| | | 11.2.6 End/Interm Unblind |

➔Standardized Statistical Processes and Methodologies

Understand the variability of methods used for randomization in each trial to identify potential bias. A predefined statistical analysis plan and structured reporting practices ensure consistency in how results are analyzed and presented, facilitating peer review and comparison of the studies.

# Data Integrity and Quality Control

| TMF Zone | TMF Section | TMF Artifact |
|---|---|---|
| 11.0 Statistics | | |
| | 11.3 Analysis | |
| | | 11.3.1 Data Def Datasets |
| | | 11.3.2 Analysis QC Docs |
| | | 11.3.3 Interim Raw Data |
| | | 11.3.4 Interim Programs |
| | | 11.3.5 Interim Datasets |
| | | 11.3.6 Interim Output |
| | | 11.3.7 Final Raw Datasets |
| | | 11.3.8 Final Programs |
| | | 11.3.9 Final Datasets |
| | | 11.3.10 Final Output |
| | | 11.3.11 Subj Eval Criteri |
| | 11.4 Report (Statistical) | |
| | | 11.4.1 Interim Stat Rpts |
| | | 11.4.2 Statistical Report |

➔Ensured Quality of Analysis

The detailed planning and execution of data analysis through established programs and procedures ensure that the analysis is carried out to the highest standards, bias is minimized and the integrity of the data is preserved.

# Expected Outcomes and Potential Impact

# Expected Outcomes

1

**Improved data quality**:

- With TMF's rigorous documentation and data management protocols, the data used in meta-analyses are likely to be of higher quality, leading to more reliable and valid results.

2

**Increased transparency**:

- TMF principles require thorough documentation of all processes and changes, which can significantly enhance the transparency of the research, allowing for better scrutiny

3

**Enhanced research integrity**:

- Adopting TMF standards can help in aligning the meta-analysis processes with regulatory and ethical requirements, thereby enhancing the overall integrity of the research.

# Expected Outcomes

4

**Greater efficiency**:

- The standardization of documentation and data management can streamline research processes, leading to greater efficiency in the conduct of meta-analyses.

5

**Reduced risk of errors**:

- Through TMF's comprehensive data management and quality control checks, the risk of errors in data collection, storage, and analysis is minimized.

6

**Consistency across studies**:

- Implementing TMF can lead to greater consistency in the way data is collected and reported across different studies, making it easier to compare and synthesize findings.

# Potential Impact

**Elevated standards for meta-analysis research**

- The integration of TMF could raise the bar for quality and reliability in meta-analysis research, setting new standards for academic and clinical research studies.

**Improved patient outcomes**

- High-quality meta-analyses can inform clinical guidelines and policies, potentially leading to improved patient care and outcomes.

**Informed decision-making**

- Better data quality and transparency can provide clinicians and policymakers with more reliable information, aiding in informed decision-making.

# Potential Impact

**Strengthened trust in findings**

- As TMF principles lead to more rigorous research, the trust in the findings of meta-analyses by the scientific community and the public is likely to increase.

**Broader adoption in research practices**

- Success in implementing TMF in meta-analysis could encourage its broader adoption across various domains of research, beyond clinical trials.

**Facilitation of regulatory approval**

- For meta-analyses that inform clinical trial design or drug approval processes, adherence to TMF standards can facilitate smoother regulatory review and approval processes.

# Challenges, Limitations, and Future Directions

# Challenges

| | |
|---|---|
| **Adaptation to Meta-Analysis Context** | • TMF is primarily designed for clinical trials, so adapting its principles to the meta-analysis setting requires innovative approaches and may encounter resistance or difficulty in fitting into established meta-analysis protocols. |
| **Training and Familiarity** | • Ensuring that all researchers and analysts are adequately trained in TMF standards and understand their application in meta-analysis could be resource-intensive. |
| **Data Harmonization** | • Meta-analyses often involve combining data from diverse sources with varying quality and formats, which can be challenging to standardize according to TMF principles. |
| **Technological Infrastructure** | • Implementing TMF requires a robust technological infrastructure, which can be a significant hurdle, especially in terms of funding and maintenance. |

# Limitations

| | |
|---|---|
| **Scope of TMF** | • TMF is not specifically tailored for meta-analyses, which might limit its applicability to certain aspects of meta-analytic research, potentially requiring further customization. |
| **Resource Intensiveness** | • The thorough documentation and quality checks demanded by TMF can be resource-intensive, necessitating more time and financial investment. |
| **Data Privacy and Ethics** | • When dealing with patient data from multiple trials, TMF's strict compliance standards may conflict with varying ethical and legal data privacy regulations across countries. |
| **Technological Limitations** | • There may be technological limitations in integrating TMF systems with existing meta-analysis software or databases. |

# Future Directions

| | |
|---|---|
| **Custom TMF Guidelines for Meta-Analyses** | • Development of TMF guidelines tailored specifically for meta-analysis research could be a significant advancement. |
| **Cross-disciplinary Collaboration** | • Working with data scientists, ethicists, and regulatory experts to refine TMF applications and address privacy concerns could lead to more robust frameworks. |
| **Global Standardization Efforts** | • Encouraging global cooperation to standardize TMF applications across borders, aligning with international data protection laws, could facilitate broader acceptance and utility. |
| **Continuous Improvement and Updating** | • As with any methodology, continuously revising and updating TMF principles based on feedback and evolving research needs will be crucial for maintaining relevance and effectiveness. |

# Thank You!

# QUESTION?