Conflicts of Interest

- I have no conflicts to declare

- I would like to thank the Conference organisers for allowing me to present this work

- I would like to thank ASTDA for covering my costs

Case Study of the Value of Historical Archives for Diagnostic Advancements

Shelley Facente, Michael Busch, Eduard Grebe, Christopher Pilcher, Alex Welte, Usha Sharma, Rachel Owen, **Gary Murphy**

We should be so proud

- Improved sensitivity and specificity of assays
- Reduced time to detect infection
- Increased range of markers
- Improved testing algorithms
- Developed techniques to better identify and predict resistance
- Supported automation and increased throughput
- Reduced costs
- Broadened our range of specimen types
- Taken testing into communities
- Improved estimates of when infection occurred
- Used data to support our findings

What is CEPHIA

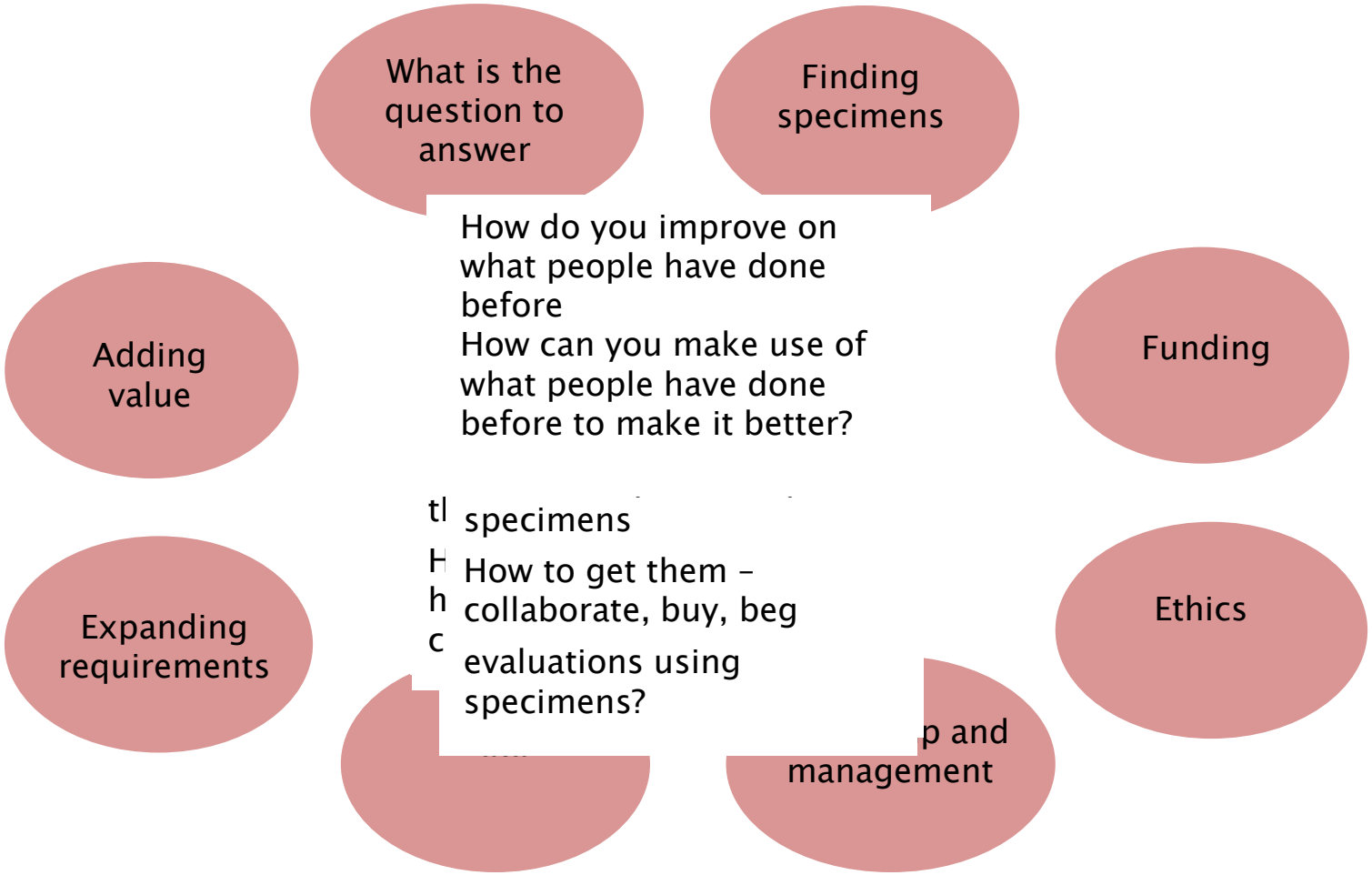
- **C**onsortium for the **E**valuation and **P**erformance of **HIV** **I**ncidence **A**ssays
- Formed to evaluate and support development of existing and new HIV Incidence assays, improve data analysis and help bring consensus to the field
- Independent evaluation of assays and formation of a repository of specimens to support the evaluations and enable new approaches
- Wide membership, an inclusive group, working with WHO Technical Working Group, UNAIDS, Funders, Researchers

What is in the CEPHIA repository

Specimen type	Number available (including aliquots)
Whole Blood	756
Urine / Unknown	44
Urine / Nothing	3620
Urine / Azide	2288
Stool / Unknown	26
Stool / RNAlater	1182
Stool / Nothing	2078
Serum	4190
Saliva / Pellets	51
Saliva	3128
Plasma	70773
PBMC	2019
Hair	0
DBS	3497
Buccal swab / Nothing	435
Buccal swab / Buffer	567

Nearly 95000 specimens of different sample types, collected from almost 3400 unique individuals with, almost 14000 different timepoints.

CEPHIA – Challenges we faced



CEPHIA Repository

- Since 2012, CEPHIA has distributed over 50 panels of well-characterized specimens to 19 investigators and groups.
- Supported the independent evaluation of 11 Incidence assays leading to improvements to understanding of use and improving accuracy of data outcomes
- Harmonised data from a number of different studies to support new categorisation of specimens
- Broadened repository from Plasma only to multiple sample types

A case study – CEPHIA supported projects

Study type	Examples
Focused hypothesis-driven studies	• How the gut inflammasome and specific HIV antibody subclasses change as HIV infection evolves • How timing of treatment initiation after HIV infection impacts kinetics of HIV reservoir seeding and opportunity for cure
Non-hypothesis-driven efforts to identify novel signatures of recent HIV infection	• Searches for antibodies reactive to peptoids in a large 'peptoid shape library' • Multiplexed assay utilizing viral and antibody markers identified and interpreted through a machine learning algorithm
CDC- and NIH-funded projects	• Examination of the factors in HIV resistance, including mutation, selection, recombination, and drift • Development of a single genomic assay for HIV incidence and transmitted drug resistance mutation screening • Independent evaluation of the Sedia Asanté™ HIV-1 Rapid Recency® Assay, currently in use by PEPFAR at international sites
Theoretical and toolkit innovations	• Development of a theoretical framework and web-based tool for consistent time of infection estimation based on subject-level diagnostic testing histories and the properties of diagnostic assays

Return on investment

- Specimens in a freezer are a drain on resources or a potential supply of invaluable material

- Difficult to quantify however:
  1. Poor performing assays identified
  2. Improved understanding and application of well preforming assays
  3. New research opportunities developed
  4. Value added to previous studies
  5. Supporting EQA Programmes

- Based on the value of projects supported directly or indirectly by the CEPHIA 1 Repository we estimate that:

  - **Each $1 invested in the repository generated $5 in return**

Current challenges

- Differentiating vaccine from natural infection
- Effect of PrEP on Immune responses and breakthrough infections
- Effect of early treatment
- Monitoring Cure approaches

Current challenges

- These challenges are different to that we have faced before for HIV Diagnosis
- They will need new approaches
- Potentially new tests and new algorithms
- As interventions change we need to be ready to adapt quickly

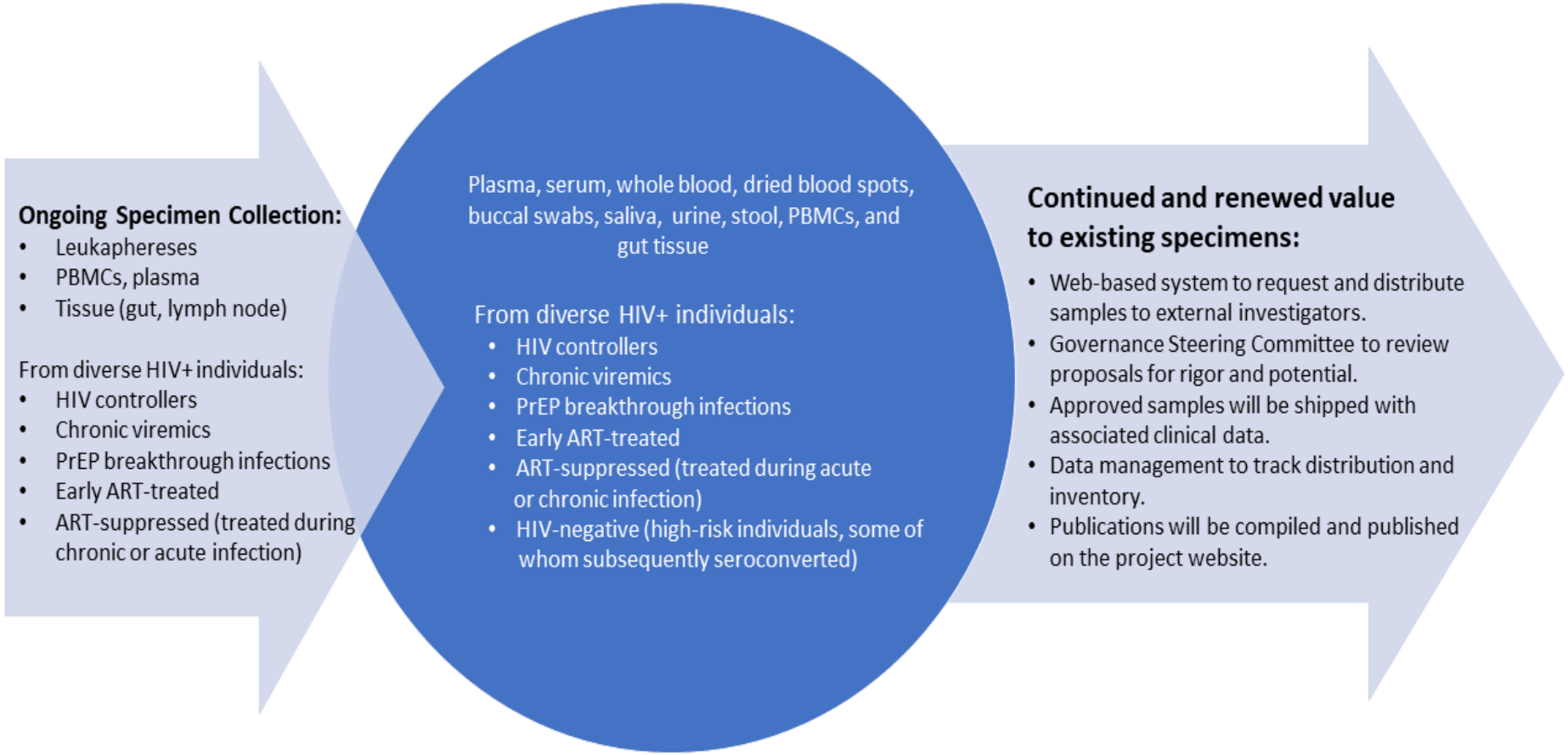
What is needed?

- 1) Large volume, extensively-characterized HIV+ samples, including serial specimens from seroconverters and treated subjects
- 2) Baseline samples from individual starting PrEP
- 3) Chronic Viremics and HIV Controllers
- 4) High-quality clinical background data on the patients to allow diagnostic, pathogenesis, cure, and co-morbidity studies

What is needed?

- 5) multiple collaborations facilitating ongoing specimen collection and replenishment
- 6) A managed system to ensure sustained records of high-level specimen turnover, with thousands of samples shared annually.
- 7) data management to track shipments, usage and outputs
- 8) High quality data analysis and sharing of information to support clinicians and researchers in understanding what results mean

Consolidated Repository Concept



Conclusion – A Call to Action

- Everyone in this room has something to offer
- To address new challenges for HIV Diagnostics:
  - Funding and development of a centrally-funded repository of appropriate specimens is crucial
  - Strong governance and leadership is needed.
  - Investigators and assay developers need easy access to diverse specimens
- Working together we can enable improvements to HIV diagnostic assays and ultimately the elimination of HIV

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