Executive Summary

Four years since its inception, CIPHER Cohort Collaboration has yielded significant results. For determining the next steps, the group met in San Servolo, Venice on 24 and 25 April 2017. The key objective of the meeting was to determine the collective vision for cohort research over the next 5 to 10 years, identifying potential public health impact and utility of this data to improve care and outcomes for infants, children and adolescents as well as discussing ways of operationalizing these next steps. The key roles identified for the CIPHER Cohort Collaboration over the next few years are as follows:

- *Informing programme planning:* Overall it was agreed that the Collaboration should continue to move forward with the UNAIDS estimates and forecasting work. Opportunities would be explored with WHO and UNAIDS for support and timelines for future work.

- *Informing policy:* Overall it was agreed that pharmacovigilance is an area where the Collaboration could bring added value. A sentinel site approach was identified as potentially the most effective way forward. Potential funding opportunities would be identified and explored for this work with support from CIPHER.

- *Deep data research and HEU agenda:* It was agreed that CIPHER is a unique platform that could be leveraged to launch deep data collaborations. Further research questions would be explored with the help of a young investigator and oversight of the CIPHER Steering Committee. CIPHER could also potentially fund a young investigator to map current HEU work and support harmonization work to push the HEU agenda forward.

For next steps, more discussion will be needed to refine the future priorities identified, especially with regard to the feasibility of new data merge and what the most effective and efficient way to approach would be. CIPHER will provide support to strengthen and formalize the future course of action with consultation and input from the Steering Committee.
Introduction

Background
In May 2013, CIPHER convened a Paediatric HIV Cohort Investigator Consultation with researchers from major paediatric HIV cohorts worldwide. This meeting defined a research agenda of priority knowledge gaps in paediatric HIV that can be effectively addressed by cohort collaboration, and resulted in agreement by the investigators present to collaborate on major data-sharing projects addressing two of those gaps:

- The durability of first-line antiretroviral treatment (ART) in children in resource-limited settings;
- The global epidemiology of adolescents living with HIV since birth.

These two projects aimed to fill research gaps and support evidence-informed clinical, policy and programmatic decision making to optimize care and treatment of children and adolescents. Also, these projects were chosen as the ‘low hanging fruit’, recognizing that this was a first attempt to explore if a multi-cohort collaboration of such diverse cohorts was indeed possible. To support this endeavor, CIPHER provided an initial grant of US$500,000.

Key outputs
Four years since inception, this collaboration has yielded significant results. Following is a brief summary of the key outputs so far.

<table>
<thead>
<tr>
<th>Data SOP finalised</th>
<th>Deadline for first data transfer from cohort groups</th>
<th>Data queries returned to cohorts</th>
<th>Adolescent data finalized</th>
<th>First line data finalized</th>
</tr>
</thead>
</table>

First-line:
2016: Abstracts at Paeds Wkshp, AIDS 2016, data presented at UNAIDS modelling mtg
2017: Predictors of switch to 2nd-line poster at CROI
Additional concepts in pipeline: Duration of 2nd-line, UNAIDS/forecasting

Adolescent:
2016: abstracts at IWHOD, Paeds Wkshp, AIDS 2016
2017: Additional sub-Saharan Africa analysis abstract at IWHOD, Paeds Wkshp, IAS 2017
sub-Saharan Africa manuscript submitted to JIAS
Main adolescent epidemiology manuscript submitted to PLOS Med
Additional concepts in pipeline: sub-Saharan Africa analysis, Growth and Immunology concept.

Figure 1: Summary of timeline and key outputs of the CIPHER Cohort Collaboration
Adapted from presentation by Mary Ann Davies, IeDEA, Annual CIPHER Cohort Collaboration Meeting, April 2017.

Objective of the annual meeting
With this backdrop, the key objectives of the present meeting were to explore the following questions:

- As a community of experts in paediatric and adolescent HIV, what is our collective vision for cohort research over the next 5 to 10 years? What do we
want to happen in 5-10 years’ time with regard to making good use of the huge amount of data that has been collected and will continue to be collected.

- **How do we see that being managed in the most useful way possible** to inform policy and implementation programming, to improve care and outcomes for infants, children and adolescents?
- **Once we have that vision, we will work backwards to see how we can get there,** what do we need, what does it look like, what is the role of IAS/CIPHER and how does our collaboration within CIPHER need to change so we can get to that point.

Over two days the members and supporters of the CIPHER Cohort Collaboration discussed these questions keeping the following principles in mind:

a. Blue sky thinking towards what is ideally needed;

b. What is the best use of observational data;

c. What CIPHER Cohort Collaboration should do vs what it can do;

d. How to get there most efficiently;

e. What is the role of the Collaboration and its added value;

f. How can IAS/CIPHER support the plans.

### Future Vision for the CIPHER Cohort Collaboration

**Key Summary Points**

- There is agreement on the spectrum of cohorts idea and the placement of the individual cohorts along the spectrum (IeDEA was moved more to the left);
- This implies that a different approach would be needed for different types of questions, not necessarily requiring participation of all cohorts for all questions. This underlines the value of having different kinds of cohorts in the collaboration;
- The diversity of CIPHER cohorts is important for questions related to programme planning and policy development, as this provides generalizability at the global level;
- “One stop shop” concept is critical from policy perspective because it brings together data and expertise.

### Spectrum of cohorts

The concept of a “spectrum of cohorts” was introduced at the meeting. The various kinds of data being collected by cohorts could be mapped on a spectrum with lower quality but more generalizable programmatic data on the left side of the spectrum and the higher quality but less generalizable research cohort data on the right side of the spectrum. To get a more real world picture as well as a magnified public health impact, the full spectrum is useful. Looking at the spectrum, this means that a different approach is needed to answer different kinds of questions. For example, questions at the global, programme planning level benefit from input from all cohorts, while pharmacovigilance would require identifying specific sites in certain cohorts. Deeper data questions would more likely require a collaboration towards the right hand side of the spectrum. This implies an evolution of the way CIPHER Cohort Collaboration has been working as it moves to being a platform, from all partners contributing to the first two questions, to addressing different questions with the most appropriate approach. This spectrum of data as well as the expertise within the CIPHER Cohort Collaboration has
immense value for programme planners and policy makers such as UNAIDS and WHO. **This would be a key value driver for continuing the cohort collaboration.**

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**Potential Roles for the CIPHER Cohort Collaboration**

The key potential opportunity for the CIPHER Cohort Collaboration is evolution into a platform which would serve as a one-stop observational resource for pediatric cohort data. The key roles this could serve to fulfill are the following:

a. Programme planning: working with UNAIDS and providing data to support the global estimates of disease burden and working with WHO to support development and provide data for of a paediatric ART model;

b. Policy making: providing information needed by global policy makers such as WHO by answering questions such as the first two the collaboration has addressed, and pharmacovigilance and enhanced monitoring;

c. Deeper data research: collaboration between cohorts for deeper analysis on topics of interest;

d. Opportunity to advance collaborative research on HIV-exposed uninfected (HEU) children.

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**Informing Programme Planning**

**Key Summary Points**

- There is a role for CIPHER in informing UNAIDS Spectrum estimates as well as WHO forecasting work and thereby amplifying the public health impact of the data; funding would be available from the respective organizations for work on this;

- The volume of non-IeDEA data in the current CIPHER dataset is around 44%, and there are differences in the CIPHER data compared to the IeDEA data, pointing to an added value in collaboration;

- For informing Spectrum estimates and forecasting, there is a need for as real-time data as possible;

- There is a potential role for IAS/CIPHER in advocacy at country level for disaggregated data for children and adolescents.
**Informing UNAIDS global estimates**

**Validated data is needed to improve estimates for programme planning**

Accurate programme planning depends on the best possible estimates of the disease burden and ART and related services coverage. Many countries still do not have accurate detailed data on service coverage to accurately estimate at what age children are starting on treatment. UNAIDS Spectrum estimates are used to inform countries where national programme data is weak. Pooled cohort data to complement country level data would greatly enhance the accuracy of the current models. This, in turn, would help enhance efficiency of the programmatic response including availability of ART - a growing area of concern for programme planners.

The CIPHER Cohort Collaboration brings together some of the top expertise and data from a wide variety of geographical contexts. Mindful of the principle of non-competition and that the Collaboration should only be doing what no one network cannot do on its own, due diligence with respect to this point was done throughout the meeting, especially with regard to the largest CIPHER partner, the IeDEA network. Table 1 (below) shows that 44% of the children included in the time on first line ART CIPHER dataset were from non-IeDEA networks, contributing a large proportion of children in the rest of sub-Saharan Africa and Asia Pacific regions.

![Table 1: Contribution of IeDEA and Non-IeDEA Cohorts to the CIPHER Data (restricted analyses focused on data from Africa, Asia Pacific and Caribbean, Central and South America)](image)


Additionally, the CIPHER data on the proportion of children starting ART aged < 3 years old helped adjust estimates for UNAIDS Spectrum model which were previously based on data from the IeDEA Network alone. When compared the UNAIDS Spectrum distribution of age at start of ART to the CIPHER data, including data from both IeDEA and non-IeDEA networks, there were significant variations in the age distribution at ART start, Figure 2 (below). The CIPHER data has since been used as the data source for the UNAIDS updated Spectrum model at end of 2016. This reflects the benefits of the larger sample size of the CIPHER dataset and the impact of inclusion of data from a broader range of networks including large cohorts from low-income countries and non-research settings.
Ideal needs for UNAIDS estimates and SPECTRUM

It was highlighted that the following are ideally needed by UNAIDS to help improve estimates and thereby fast-track the response to the HIV epidemic:

**Data Needed by UNAIDS to improve estimates**
- Maternal (prenatal and postnatal) disengagement from care – within the PMTCT setting(?
- Mother-to-child transmission probabilities;
- Disengagement from care among children living with HIV;
- ART initiation distribution by age (continuous);
- Survival among those not on ART (?);
- Differential survival of vertical vs horizontal infected young people;
- Sexual debut and fertility of adolescents on ART.

**Advocacy and capacity building:** A key gap in current data needs for programme planning is also availability of disaggregated data to help targeted programme planning. Through regular Global AIDS Monitoring (GAM) reporting, only 76 out of 147 countries provided ART data disaggregated by age for adolescents 10-14 years old in 2016. Dr. Mary Mahy (UNAIDS) highlighted that there is also a potential advocacy role for CIPHER to encourage national governments to report age-disaggregated data through GAM. Additionally, investigators could potentially provide technical support at country level, thus contributing significantly to capacity building of national level data systems influencing the quality of data.

**Distinct value of CIPHER**

This is a great opportunity for the CIPHER Cohort Collaboration to play a rather critical role in supporting the response to the epidemic. The Collaboration has already contributed to UNAIDS’ Spectrum estimates with UNAIDS clearly demonstrating interest in future data as well as willingness to financially support the work.
Paediatric ART demand forecasting

Need to improve forecasting to ensure sufficient supply of ART
Forecasting ART demand helps industry, donors, country programmes, and other key stakeholders at global and national levels to ensure sufficient supply and production capacity of ART. There are nuanced needs for country-level, pediatric HIV data for forecasting including weight/age band distribution, number of formulations, as well as changing pediatric trends with development of new drugs, diagnostics and strategies.

Ideal needs for improving forecasting
Ideally, a forecasting model should be able to answer and address the below issues and be as real time as possible:

- a. New paediatric infections;
- b. Age at diagnosis;
- c. Paediatric treatment coverage;
- d. New regimen/formulation introduction;
- e. Survival and retention (transition to adult cohorts);
- f. New diagnostics (VL, DRT);
- g. Future demand (need ≠ demand);
- h. Estimate the paediatric ARV market which is generally small, rapidly evolving and complicated by multiple age/weight bands.

Distinct Value of CIPHER
CIPHER data could be a critical data source in a rapidly changing landscape by providing the below data. However, new data merge would be needed for this, as the previous merge went up to 2014:

Data needed for improving forecasts
- DOB;
- All ART drugs and start/stop dates;
- Age at start of ART (derived from above two points);
- First line regimens (alignment with guidelines);
- Estimates of retention and deaths;
- 2nd line use (by age/weight);
- Weight/age band distribution (all drugs);
- Treatment combinations used over time (NRTIs used) : include treatment modifications;
- Formulations (when go to adult formulations);
- All weights (~80%? available in last merger);
- Follow up status and date of death/LTFU/transfer out;
- Reason for drug change.

There is particularly interest in informing regarding the following:
a. Option B+, scale up of early infant diagnosis;
b. 90-90-90 survival and retention in cascade of care;
c. Scale up of VL monitoring;
d. Adoption of WHO guidelines on preferred drugs;
e. New paediatric formulations: DTG;
f. Ageing: moving up to adult formulations.

The WHO/UNITAID work-stream on development of paediatric model is expected to start soon with CIPHER/CEPAC/AVENIR. This is a potential for funding support opportunity for CIPHER Cohort Collaboration.

**Key considerations for informing UNAIDS estimates and forecasting**

There is value in supporting the UNAIDS estimates and forecasting and some of this work is underway using current CIPHER data. UNAIDS is keenly interested in the CIPHER data and would potentially support the effort through funding. As a next step the cohorts could identify the data points they could supply from the UNAIDS data request. A data new merger would be needed for continuing to support the UNAIDS estimates and forecasting.

For building in-country data capacity, the junior investigators trained through CIPHER represent a great resource, and CIPHER was encouraged to continue this approach. With rigorous training through CIPHER, junior investigators can increase in-country capacity to work with national data.

The key challenge for the CIPHER Cohort Collaboration would be weighing the heavy lift required for a new data merger against the need for “real-time” data. The merging and analysis of data takes time and represents a lot of work. However, while it won’t be real time, the processes can be made more efficient the second time.

**Informing Policy**

### Key Summary Points
- There is an established need for a ‘one stop shop’ (place to go for query) to inform policy;
- CIPHER Cohort Collaboration brings together varied cohorts as well as the expertise in pediatrics in one place, offering a great opportunity for WHO;
- Pharmacovigilance and enhanced monitoring is a concrete current need.

### Informing normative guidance

**Need for data to strengthen evidence for policy making**

WHO needs validated evidence to develop accurate guidelines to address pediatric HIV issues. The schematic below broadly describes the data needed for development of global guidelines. So far, WHO has been collaborating with IeDEA, among others, for observational data to inform policy making but there is scope to improve this by triangulating data from different cohorts.
Ideal data needed for supporting policy
WHO would ideally need the following data for informing its global guidelines and policy.

Ideal data needed to inform policy

Research Gaps for Newborns

Neonatal Prophylaxis
- PMTCT risk on maternal DTG – transmission risk and risk of transmission of DR virus
- PMTCT in low risk infants: No ART vs standard of care
- Duration of infant prophylaxis in unsuppressed BF mother
- AZT prophylaxis dose older than 6 week

Newborn Treatment
- Long acting agents in neonates – PK and safety, muscle bulk issues
- Monoclonal antibodies – long acting formulations
- Novel delivery systems
- ABC down to <3M
- Safety in HIV exposed uninfected

Remission research
- IMPAACT P1115, EPIICAL (novel agents, vaccines)

Research Gaps for Sequencing

Dosing and formulations
- TB-HIV trials: nest PK studies in all ongoing trials to gather data in children that acquire TB while on studies
- Taste masking and bioequivalence of crushed tablets
- LATs -injectables/patches: 1mo vs 2 mo
- Collection of more toxicity data (i.e. in children < 3 years and bone/renal effect of TAF)

Alternative agents
- INSTIs vs bPIs (i.e. DTG vs bPIs) in NNRTI resistance
• Future third line: DTG/Ril and DTG/DRV
Innovative strategies
• Dual therapy: DTG/3TC, DRV/r/3TC, DRV/r/DTG in a non-inferiority trial including naïve and experienced children
• Weekend off with DTG/EFV (?)

Distinct Value of CIPHER
The CIPHER Cohort Collaboration brings together varied cohorts as well as the expertise in pediatrics in one place, offering a great opportunity for WHO. There is definite interest and support within WHO towards these activities. WHO has identified the following areas where CIPHER Cohort Collaboration could play a significant role in informing policy.

• Inform optimal use of drugs where RCT data is not available and adult data cannot be extrapolated;
  o Efficacy (ie RAL in young children)
  o Safety (ie ABC < 3 months)
  o PK
• Inform the development of paediatrics formulations;
• Inform quantification, forecasting and future demand of ARVs;
• Support accelerated introduction of new ARVs with pharmacovigilance;
• Implementation science? (i.e. introduction of new formulations)

Key considerations for supporting and guiding policy
With new guidelines not planned for the immediate future, it is hard to predict what questions will be most relevant. However, WHO and CIPHER have just developed global research agendas for children and adolescents living with HIV, which are aimed at guiding research and funding and can serve as a guide to the Cohort Collaboration.

Pharmacovigilance and enhanced monitoring

Need for more validated data to assess long-term safety of ART
To assess the long-term safety of current treatment regimens, pharmacovigilance was identified as an important theme that the CIPHER Cohort Collaboration could help address. There is a need for enhanced safety monitoring of generic drugs since this is not covered by statutory requirements as in the case of branded drugs. Following are some of the current challenges faced with respect to pharmacovigilance of generic drugs:

• Studies have focused on single drugs
  o Some drugs of less interest / small n (FPV, ETR);
  o Some drugs of interest have EMA PASS waiver (eg TAF);
  o Some studies have been EU only;
  o Individual studies, lack of comparative data.
  o Some cohorts have not participated
  o Do not collect right variables;
  o Cannot meet timelines/ ethics/ regulatory demands;
  o Do not have any patients on drug.

Ideal needs to improve pharmacovigilance for generic drugs
The following data would ideally be needed from cohorts for effective pharmacovigilance of generic drugs.

**Ideal data needs for pharmacovigilance**
- Reasons for stopping drug;
- Clinical adverse events;
- Laboratory adverse events;
- Dose and weight – essential for regulatory pharmacovigilance.

**Distinct role of CIPHER**
A few cohorts are already collecting some of the needed data; pooled together this data could provide insights into the safety of drugs across geographies. Identifying sentinel sites within CIPHER partners was discussed as a way forward here.

The key pharmacovigilance priorities for the group could be:
- Improve evidence base for long-term safety;
- Focus on pregnancy, HEU and HIV+;
- Focus on drugs with likely rapid scale-up in SSA eg DTG, TAF, FDC;
- Compare different drugs or regimens
  - Not just regulatory studies – CIPHER studies too?
- Deeper data for some questions (eg TDF - TAF)
  - May require prospective data collection)

**Key considerations in supporting pharmacovigilance**
Availability of data among cohorts to support this activity would be the key driver for supporting pharmacovigilance. Funding would need to be obtained for this activity; current CIPHER industry funders have shown interest in funding the Collaboration to provide this type of information, and other potential funding sources such as DAD sponsors were discussed.

**Informing Deeper Research and the HEU Agenda**

**Key Summary Points**
- CIPHER is a unique platform, offering opportunity to cohorts to collaborate to answer some deeper data research questions;
- CIPHER Cohort Collaboration is in a critical position to support harmonization of approaches for agenda of HIV Exposed Uninfected (HEU) children.

**Collaborating for deeper data research**

Need for deeper research to improve understanding and preparedness for the epidemic and distinct role for CIPHER
There is a significant amount of valuable and deep research data being collected by cohorts; combined, this data has the potential to greatly improve understanding of the HIV epidemic. CIPHER offers a unique platform for potentially launching collaborations on deeper data questions among the participating cohorts. Through years of working together the participating cohorts have developed better working mechanisms and this could fuel further collaboration for additional studies.
**Potential topics for deeper research**

Some of the topics that can be addressed have been summarized in the following schematic shared by Dr. Annette Sohn.

![Schematic diagram](image)

*Figure 4: Potential Topics for Deeper Research for cohort or sites with deeper routine monitoring data and specialized data
Annette Sohn, IeDEA, Annual CIPHER Cohort Collaboration meeting, April 2017.*

**Key considerations for supporting deeper research**

To move forward on this, the CIPHER Steering Committee should identify which questions the group can focus on. Potentially, a young investigator funded by CIPHER could help develop a concept. Furthermore, a pilot study within CIPHER (pending funding) could be conducted to test the feasibility of the model with collaborating cohorts bridging out of CIPHER. Given the need for specific expertise depending on the field of study, it is expected that these collaborations would be further developed outside of CIPHER.

**Potential for collaboration to harmonize data and approaches for the HEU agenda**

HIV exposed-uninfected children is a group which receives very little attention due to “perceived” absence of any pressing medical and associated complications. With the move to treat all and ART scale-up, the population of HEU children is rapidly increasing; there is a need for further analysis on this group to develop greater understanding on the potential effects of HIV and ART exposure on HEU children. The CIPHER Cohort Collaboration could function as platform to highlight the need for greater attention on this group and bring cohorts together to standardize and harmonize data and approaches for studies on HEU.

**Key considerations around HEU**

CIPHER, in collaboration with WHO and PHACS is already supporting the HEU Workshop this year at IAS 2017, where this discussion can continue. Going forward, as a first step, CIPHER could fund a young investigator to map current work and support harmonization work to push this agenda forward. This young investigator could build on the current work and proposals with Dr. Mary-Ann Davies and Dr. Amy Slogrove.
The CIPHER Dataset: Past Lessons and Way Forward

Overall data quality and variability across cohorts
The first CIPHER data merge has taken over four years, and much has been learned. Delays were experienced due to technical issues with the datasets, lack of familiarity with datasets from different networks, ethical approvals, and overall data quality and variability issues. It is important to note that the initial phase of any such data merge takes time as there are several processes that need to be established. Going forward, if the future concepts do not have significantly different data merge demands, it would be relatively faster. One of the key advantages of the Cohort Collaboration has been the increasing partnership among the participating cohorts and this has led to better working across different cohorts. This would significantly reduce the amount of time and effort needed for future work.

One of the main challenges of the Collaboration is with regard to quality and availability of data across the different cohorts. An analysis of the overall quality of data within the CIPHER dataset across domains is provided in Figure 5 below.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Assessment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics basic</td>
<td>😊</td>
<td>birth date, sex</td>
</tr>
<tr>
<td>Demographics detail</td>
<td>😞</td>
<td>Born abroad, Transmission mode</td>
</tr>
<tr>
<td>Basic HIV info</td>
<td>😊</td>
<td>Receipt of ART, ART start date, AIDS diagnosis</td>
</tr>
<tr>
<td>Outcome data</td>
<td>😞</td>
<td>LTFU, Death date, Death reason</td>
</tr>
<tr>
<td>PMTCT</td>
<td>😞</td>
<td>Unknown for &gt;80% of children except entry through PMTCT program</td>
</tr>
<tr>
<td>ART history</td>
<td>😊</td>
<td>Lots (and lots) of queries 1 network 28% missing drug data</td>
</tr>
<tr>
<td>Anthropometry</td>
<td>😊</td>
<td>Weight, Height (≥2 measures)</td>
</tr>
<tr>
<td>CD4</td>
<td>😋</td>
<td>Mostly good but some cohorts with 100% missing</td>
</tr>
<tr>
<td>Viral load</td>
<td>😋</td>
<td>PHACS, IMPAACT, EPPICC, eDEA-AP</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>😞 😊</td>
<td>Unclear if missing info or no disease (78%) Type of TB and start date patchy No info on diagnosis or treatment</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>😊</td>
<td>Unclear if missing info or no CTX (34%) CTX start date</td>
</tr>
</tbody>
</table>

- 😊 Great: >80-90% complete for all cohorts
- 😋 Not too bad/patchy: 50-80% complete or some cohorts with 80-90% complete
- 😞 Unusable: almost all cohorts <50% complete

Figure 5: Diversity of Data among CIPHER Cohorts
Adapted from presentation by Mary Ann Davies, iDEA, Annual CIPHER Cohort Collaboration meeting, April 2017.

It is also important to note that data quality varies significantly within networks, with some cohorts within networks providing better data than others. This is something that should be explored when planning future projects.

Lessons for future data merges
For future data merges the following should be kept in mind:
a. The process would be easier and quicker the second time if there are same/similar data and networks;
b. The inclusion criteria should be broader;
c. Ethical issues should be identified and addressed early on;
d. Data quality can vary within and across networks, with pockets of good data;
e. Additional concepts should be developed early on.

The IeDEA Network has been developing a set of best practices and data standardization protocols to allow for cross-network data merges. This could be used as an example to strengthen CIPHER Cohort Collaboration processes.

In summary, the past progress of CIPHER Cohort Collaboration has paved the way for future collaboration. Though processes and working modalities would continually need to be refined, the effort is worth the final outcome and its potential public health impact.

**Prospective challenges**
Though future data merges offer a great opportunity, there are some significant challenges which the CIPHER Cohort Collaboration would need to watch out for:

a. Some of the cohorts may have stopped collecting data on their subjects because they progressed out of the programme due to various reasons including aging;
b. Addition of new cohorts and programmatic data could be challenging if the new cohorts have not been publishing their data since that helps refine, standardize and clean up the data and make it more usable;
c. Though there is a use for sentinel site data, data ages quickly and therefore there is a need to make sure that the systems being set up for data merges and analysis offer efficient timelines.
Overall Summary of Vision for CIPHER 2.0

The following table provides an idea of what the group could aim at achieving, going forward. It clearly represents the possible future direction vis-à-vis its public health impact, added value of CIPHER Cohort Collaboration as well as availability of funding.

<table>
<thead>
<tr>
<th>Programme Planning</th>
<th>Public Health Impact</th>
<th>Added Value for CIPHER</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNAIDS paediatric/adolescent estimates</td>
<td>😊</td>
<td>😊</td>
<td>😊</td>
</tr>
<tr>
<td>Forecasting</td>
<td>😐</td>
<td>😊</td>
<td>😊</td>
</tr>
<tr>
<td>Informing Policy</td>
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<tr>
<td>Informing guidelines</td>
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<td>😊</td>
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<tr>
<td>Pharmacovigilance</td>
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<td>🎈🎈</td>
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<tr>
<td>Deeper Data Research</td>
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<tr>
<td>Deeper data</td>
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<td>😊</td>
<td>🎈🎈</td>
</tr>
<tr>
<td>HEU Agenda</td>
<td></td>
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<tr>
<td>HEU</td>
<td>😐</td>
<td>😊</td>
<td>🎈🎈</td>
</tr>
<tr>
<td>Over-arching roles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capacity building role</td>
<td>😐</td>
<td>😊</td>
<td>😊</td>
</tr>
<tr>
<td>Advocacy</td>
<td>😐</td>
<td>😊</td>
<td>😊</td>
</tr>
</tbody>
</table>

😊 Clear high public health impact/Definite added value of CIPHER Cohort Collaboration/Available.
😊 Public health impact not discussed, evaluated or un-determined by the group/Moderate added value of CIPHER Cohort Collaboration/Potential to explore options within current funding (through a funded student or preliminary analysis).
😊 Limited public health impact/little added value of CIPHER Cohort Collaboration/Funding would need to be sought for project implementation.

Roadmap and next steps

The overall way forward was mapped out for the work streams discussed above, taking into consideration where there is added value in collaboration:

Informing programme planning

- Overall it was agreed that the Collaboration should continue to move forward with the UNAIDS estimates and forecasting work.
- This work stream is currently underway and approved by the SC as an additional analysis in 2017 with the current dataset, with Jeannie Collins and Mary-Ann Davies as co-chairs.
- Funding from CIPHER is available for an additional concept/analysis in 2017 regarding the current dataset.
- Further discussion is needed with UNAIDS and WHO, regarding timeline and funding for future work. A new data merge would be needed for future work; network representatives would need to go back and see if they did indeed have the data and agreement from their networks needed for this.
Informing policy
- Overall it was agreed that pharmacovigilance is an area where the Collaboration could bring added value. A sentinel site approach was identified as potentially the most effective way forward.
- Ali Judd identified as co-chair, second co-chair needed. Concept to be developed.
- Funding potentially available from CIPHER in 2017 to support concept development. Potential to leverage any future data merge to inform this.

Deep data research and HEU agenda
- It was agreed that CIPHER is a unique platform that could be leveraged to launch deep data collaborations.
- To move forward on this, the CIPHER Steering Committee would need to identify which questions the group can focus on.
- A young investigator could potentially be funded by CIPHER to help develop a concept.
- Pending funding, a pilot study within CIPHER could be conducted to test the feasibility of the model with collaborating cohorts bridging out of CIPHER.
- HEU: As a first step, CIPHER could potentially fund a young investigator to map current work and support harmonization work to push this agenda forward.

Over-arching next steps
1. More discussion is needed to refine the above roadmap, especially with regard to the feasibility of a new data merge, and best approach.
2. Way forward will require endorsement of all CIPHER networks. An MoU would be developed by CIPHER to formalize this.
3. Some of the above (as indicated) can be funded through CIPHER in 2017 and potentially 2018. Funding will need to be sought for further activities.
# Annex 1: List of Participants

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First name</th>
<th>Affiliation</th>
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<tbody>
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