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## **Cohort Profile: Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord**

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**Cohort Profile: Collaboration of Observational HIV  
Epidemiological Research Europe (COHERE) in EuroCoord**

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**Title:** Cohort Profile: Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord

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For Review Only

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**Abstract**

Many questions about the long-term effects of combination antiretroviral therapy (cART) on clinical outcomes in people living with HIV (PLWH) and their impact on health systems remain unanswered. The Collaboration of Observational HIV Epidemiological Research Europe (COHERE) was formed in 2005 to pool and harmonize existing longitudinal data on people living with HIV in Europe, to answer key research questions that could not be addressed adequately by individual cohorts. Key research questions include long-term prognosis, rare outcomes, and variations across patient groups, settings and health systems. COHERE uses the HIV Cohorts Data Exchange Protocol, a standardized and validated method of data structure and transfer, to compile data from over 40 cohorts of PLWH residing in Europe, representing 331 481 individuals, including 2808 children (<13), representing 2 135 896 person-years of follow-up. COHERE compiles data on clinical characteristics, antiretroviral therapy and other medications, estimated date of HIV seroconversion, opportunistic infections, laboratory results and socio demographic data. External collaborators interested in conducting a project in COHERE should submit a project proposal to the Regional Coordinating Centres in Bordeaux and Copenhagen for review by COHERE's governing bodies (see [www.cohere.org](http://www.cohere.org) for further information).

**Key Messages:**

- COHERE adds value by focusing on questions that cannot be addressed by single cohorts because of sample size requirements, ensuring the sustainability of individual cohorts.
- Recent and exemplary reports by COHERE suggest that earlier and more widespread testing for HIV with linkage to care was required to reduce the incidence of late presentation.

- Non-injection drug users living with HIV with CD4 cell counts above 500/mm<sup>3</sup> after starting cART had mortality patterns similar to those in the general population.
- COHERE has informed models of HIV progression and the effect of therapy which have been used to characterize HIV-infected populations, inform public health policy and serve as a basis for cost-effectiveness analysis.

For Review Only

### Why was COHERE set up?

Widespread access to effective combination antiretroviral therapy (cART), beginning in 1996, dramatically reduced the number of AIDS-related events and deaths in people living with HIV (PLWH) in high-income settings.<sup>1</sup> The study of prognosis and specific clinical outcomes therefore requires larger populations. The Collaboration of Observational HIV Epidemiological Research Europe (COHERE) was founded in 2005 to continue to advance epidemiological research on the prognosis of PLWH in Europe. COHERE has expanded and strengthened collaborative efforts in Europe and facilitated those with other regions by ensuring that longitudinal data, the product of early investments in clinic-based databases and observational studies, were compiled and harmonized. In 2011, COHERE joined three other European HIV collaborations, PENTA, EuroSIDA, and CASCADE to form “EuroCoord”, a Network of Excellence funded by the European Commission Seventh Framework Programme.<sup>2</sup> COHERE also collaborates with the ART Cohort Collaboration (ART-CC) and the International Epidemiologic Databases to Evaluate AIDS (IeDEA) global network.<sup>3,4</sup>

### How does COHERE operate?

COHERE operates according to the principles set out in Box 1. Projects in COHERE provide added value by only addressing scientific questions that cannot be answered by participating cohorts.

Two Regional Coordinating Centres (RCCs), based at the University of Bordeaux’s Institut de Santé Publique, d’Épidémiologie et de Développement (ISPED) in Bordeaux, France and the Center for Health and Infectious Diseases Research (CHIP), Department of Infectious Diseases and Rheumatology, Rigshospitalet, in Copenhagen, Denmark, maintain COHERE’s infrastructure. The COHERE Steering Committee (SC) -- composed of representatives from the participating cohorts -- oversees the COHERE Collaboration, ensuring compliance with its principles; it also elects the Chair and the “Regional Representatives” to the COHERE

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3 Executive Committee (EC). The EC -- composed of three representatives from each of the  
4 two regions, and the two RCC Heads -- acts as the functional link between the RCCs and the  
5 SC.  
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10 COHERE projects are organized by “themes” (Prognosis and the effect of antiretroviral  
11 therapy (ART), Hepatitis, Opportunistic Infections, Malignancies, Late Presentation, and  
12 Socio-economic Inequalities) to encourage collaboration and streamline the project proposal  
13 process. Theme Leads stimulate scientific enquiry within their theme and develop projects. A  
14 detailed account of how COHERE operates is described in the Manual of Operations  
15 (www.cohere.org).  
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### 22 **Who participates in COHERE?**

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25 COHERE has grown from 33 cohorts in 2005 to 40 in 2015. COHERE initially approached  
26 cohorts because of their proven ability to address scientific questions and collect good quality  
27 data at clinical sites. As COHERE is a project-based collaboration, the data pooled in annual  
28 mergers depend on the projects included. Western European countries with longstanding  
29 national cohorts contribute a large proportion of person-years of follow-up, but there is an  
30 increasing number of individuals in care in Eastern Europe, primarily via the EuroSIDA  
31 network.<sup>5</sup> Figure 1 presents the number of people living with HIV (excluding deaths) included  
32 in COHERE as of 31/12/2011 as a percentage of UNAIDS 2011 estimates of people living  
33 with HIV by country.  
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45 COHERE includes both clinic/hospital-based cohorts of HIV-infected individuals, where data  
46 are extracted primarily from medical records in the context of routine care, and interval  
47 cohorts of specific populations of HIV-infected people, where data are collected at regular  
48 intervals that are unrelated to participants ongoing health care. Since people with HIV are  
49 seen regularly over a long period of time at a clinic/hospital, and are not just attending at  
50 times when they are symptomatic, the group of people seen at a given hospital naturally  
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3 forms a cohort. Table 1a and 1b present a complete list of the cohorts, their characteristics  
4 and funding sources. All COHERE cohorts follow local ethical standards.  
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8 The 2014 merger included data from 331 481, including 2,808 children (<13), representing  
9 2 135 896 person-years of follow-up. Table 2a highlights the demographic characteristics  
10 and prognostic markers of HIV in those aged 13 and older enrolled in adult cohorts.  
11  
12 Approximately a quarter of the COHERE sample is female (27%). The median age at  
13 inclusion is 35 [IQR: 30, 43]. The primary mode of HIV transmission is sexual contact  
14 [homosexual/bisexual contact (38.7%), heterosexual contact (37%)], followed by injection  
15 drug use (IDU) (13.5%). Overall, 71.6% of the sample has never had a clinical AIDS  
16 diagnosis before or during enrolment. The median CD4 cell count at enrolment, defined as  
17 the period six months prior to and one month after enrolment date, was 340 cells/mm<sup>3</sup> [IQR:  
18 170, 530] in adults (Table 2a). Of those with an available CD4 cell counts at enrolment, 29%  
19 had <200 cells/mm<sup>3</sup>, 22% had between 200 and 350 cells/mm<sup>3</sup>, and 49% had >350  
20 cells/mm<sup>3</sup>. Of those younger than age 13 (N=2808, representing 23 458), 93.7% were  
21 infected via vertical transmission and 73.4% had never had an AIDS diagnosis (Table 2b).  
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### 35 **How often have they been followed up?**

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38 As a consortium of cohorts comprising clinic and interval cohorts, patient follow-up varies.  
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40 For clinic or hospital-based cohorts, average patient follow-up reflects current standards of  
41 care in those countries.  
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46 A derived measure of lost to follow-up (LTFU) was constructed by estimating the median last  
47 clinical encounter (defined as either visit and/or the date of last laboratory test) per active  
48 cohort. Those individuals who had not had a clinical encounter in the 18-months prior to this  
49 date were considered to be LTFU. Those who died during the same period were excluded.  
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51 On average, 25% of the COHERE 2014 sample met this definition of LTFU, with variation  
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53 between cohorts. LTFU in paediatric cohorts was estimated among those under age 17 as  
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3 many cohorts discontinue follow-up at age 18. LTFU among paediatric patients aged <17 (N  
4 = 1,960) was 20% overall and ranged from 1.8-22% across cohorts.  
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### 7 8 **What data are collected and how?** 9

10 COHERE has benefited from dynamic data management processes, which have evolved to  
11 accommodate new projects and scientific questions. COHERE's Data Managers (DMs) work  
12 with Project Leads and Statisticians to conduct preliminary surveys, feasibility studies and,  
13 occasionally, collect additional data. COHERE collects data on basic clinical information  
14 including: date of first HIV positive test, estimated date of seroconversion, cART and other  
15 medications, opportunistic infections, and laboratory results (CD4, CD8, plasma viral load  
16 values, hepatitis B and C serological tests, and HIV drug resistance tests), as well as socio-  
17 demographic data (see [www.hicdep.org](http://www.hicdep.org) for more information about the definition of different  
18 variables). COHERE, via EuroCoord, conducts an inventory of data items and biological  
19 samples collected by participating cohorts. The submission of data to COHERE is facilitated  
20 by the use of the HIV Cohorts Data Exchange Protocol (HICDEP), a flexible data structure,  
21 developed in 2004, to guide the mapping of individual cohort data into a standard format to  
22 facilitate data merging.<sup>6</sup>  
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37 For approved projects, COHERE DMs organize data collection by developing a standardized  
38 operating procedure (SOP) for individual cohort DMs. Data are submitted in two stages via  
39 the HIV-Distributed Data Management (HIV-DDM) Tool.<sup>7</sup> This implies that data submissions  
40 must therefore pass all format and edit checks, defined in HICDEP, before the submission  
41 can be completed. Additional inconsistencies are identified centrally. Cohorts are given an 8-  
42 week window to address said data inconsistencies before completing the second and final  
43 submission. Once data are merged, likely duplicate patient records between and within  
44 cohorts are identified using probability linkage. Data items used are gender, year of birth,  
45 treatment history, viral load measurements and CD4 cell counts. Duplicate records are  
46 reconciled based on prior agreements between participating cohorts. DMs identified and  
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3 resolved 20,953 duplicate records in 2014. Cohorts resolve issues identified over time,  
4 ultimately improving data quality with each merger. To ensure transparency, the content of  
5 each merger together with cohort's QA check feedback is summarized in a report. DMs  
6 extract data for projects based on specified and agreed eligibility criteria. After signing a data  
7 protection agreement, project leads are sent data extractions in a secure format.  
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### 13 14 **What has been found?** 15

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17 Projects within the COHERE collaboration have led to the publication of 28 articles in peer-  
18 reviewed journals as of April, 2016, contributing high-quality evidence that has informed  
19 clinical and public health decision-making.  
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### 23 24 **Prognosis and the effect of ART** 25

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27 The "Prognosis and the effect of ART" group focuses on clinical outcomes in patients treated  
28 with cART. The effect of age on the response to cART was studied in around 50,000  
29 antiretroviral-naive individuals. Older individuals were characterized by low pre-ART CD4 cell  
30 counts, and experienced poorer immunological responses but better virologic responses,  
31 indicating those who are diagnosed or treated late are at increased risk of clinical events.<sup>8</sup>  
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38 Non-IDU HIV-infected individuals who achieved high CD4 cell counts after starting cART  
39 were found to have mortality patterns similar to those in the general population. Mortality was  
40 found to be persistently higher in individuals with a prior AIDS diagnosis<sup>9</sup>, while the  
41 incidence of AIDS events continued to decline until CD4 cell counts were greater than 750  
42 cells/mm<sup>3</sup>.<sup>10</sup> In patients with viral suppression, the risk of a new AIDS events or death  
43 followed a CD4 cell count gradient, even benefiting those with a CD4 cell count  $\geq 500$   
44 cells/mm<sup>3</sup>.<sup>11</sup> Individuals who were virally suppressed on cART for more than three years but  
45 had incomplete CD4 cell recovery experienced substantially higher rates of mortality from  
46 both AIDS and non-AIDS causes, suggesting that these individuals should be monitored for  
47 diseases not conventionally considered HIV-related, especially non-AIDS defining cancers  
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3 and liver diseases.<sup>12</sup> Future research will focus on new markers of the risk of morbidity and  
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5 cause-specific mortality, outcomes in individuals treated for many years, and outcomes in  
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7 people aging with HIV, particularly in the context of multi-morbidity and polypharmacy.  
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10 The COHERE's Pursuing Later Treatment Options (PLATO) II project looked at the rate of  
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12 development of virologic failure in adults, adolescents and children. When virologic failure  
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14 has occurred with at least two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs),  
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16 a non-nucleoside reverse transcriptase inhibitor (NNRTI) and a ritonavir-boosted protease  
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18 inhibitor (PI), patients are said to have experienced triple class virologic failure (TCVF).  
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20 Fewer than 9% of adult patients had experienced TCVF at year nine after starting cART.<sup>13</sup>  
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22 The risk of TCVF was somewhat higher in children and particularly higher in adolescents.<sup>14</sup>  
23  
24 Virologic suppression after TCVF was found to have increased from 20% in 2000 to 58% in  
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26 2009. Rates of AIDS and death also declined over time in people with TCVF.<sup>15</sup> The incidence  
27  
28 of TCVF in people on cART declined after 2008, and prevalence stabilized at around 2.5%.<sup>16</sup>  
29  
30 An approximately linear inverse relationship between  $\log_{10}$  viral load and CD4 cell count in  
31  
32 people with TCVF points to likely immunologic benefits of reducing viral load, even by  
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34 modest amounts, without necessarily resulting in an undetectable viral load.<sup>17</sup>  
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### 37 **Late Presentation**

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40 Late presentation is defined as an HIV-diagnosis with a CD4 cell count  $<350/\text{mm}^3$  or an AIDS  
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42 diagnosis, regardless of CD4 cell count, within six months of HIV-diagnosis. This definition  
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44 was applied to 84,524 PLWH presenting for care between January 1<sup>st</sup>, 2000 and June 30<sup>th</sup>  
45  
46 2011 in Europe. Late presentation was present in over half (53.8%) of the sample. It  
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48 decreased over time in both Central and Northern Europe among homosexual men and  
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50 heterosexuals, but, in contrast, increased over time in Southern Europe among female  
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52 heterosexuals and male IDUs and in Eastern Europe among IDUs. Late presentation was  
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54 associated with increased mortality, especially in the first year after diagnosis, with significant  
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56 variation across Europe.<sup>18</sup> Further analyses study changes in late presentation within  
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3 different regions and demographic groups since 2010.<sup>19</sup> These findings have provided  
4 comprehensive evidence of patterns in late presentation in Europe and have informed  
5 discussions around earlier and more widespread testing for HIV and linkage to HIV care.<sup>20</sup>  
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### 10 **Opportunistic Infections**

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13 Thirty per cent of HIV infected people either present late with an OI or are at significant risk  
14 of an OI.<sup>18</sup> The COHERE OI group has described both the spectrum and incidence of OIs in  
15 patients on cART with high CD4 cell counts.<sup>10, 11</sup> By including viral suppression as a cofactor,  
16 it was found that *Pneumocystis jirovecii* prophylaxis could safely be stopped in an additional  
17 40% of patients when compared with guidelines based exclusively on CD4 cell counts,<sup>21</sup>  
18 findings which informed both the American and European treatment guidelines<sup>22, 23</sup>. The  
19 group is conducting similar analyses for toxoplasmosis and other OIs and intends to  
20 reassess the guidelines on the timing for discontinuing secondary prophylaxes against  
21 specific OIs.  
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32 While the early start of cART in the course of cryptococcal meningitis has been shown to be  
33 harmful in some clinical trials performed in resource-limited settings<sup>24, 25</sup>, in Western settings  
34 with advanced clinical monitoring this may not be the case.<sup>26</sup> Current COHERE projects are  
35 examining the effect on mortality of the time of cART initiation after a diagnosis of  
36 cryptococcal meningitis or *Toxoplasma gondii* encephalitis. Preliminary results from a  
37 COHERE, NA-ACCORD and CNICS collaboration have shown that early cART did not  
38 increase mortality in AIDS patients with cryptococcal meningitis in high-income countries and  
39 overall mortality was lower than that reported by the clinical trials conducted in Africa.<sup>27</sup>  
40 Current analyses explore how specific OIs influence long-term immune reconstitution,  
41 morbidity and mortality in the most recent cART era.  
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### 53 **Malignancy**

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3 The COHERE malignancy group has focused on defining the incidence, risk factors and  
4 prognosis of HIV-associated cancers in the cART era, with a focus on systemic non-Hodgkin  
5 lymphoma (NHL) and primary brain lymphoma (PBL), Hodgkin's lymphoma and, more  
6 recently, Kaposi's sarcoma.<sup>28-30</sup> The incidence of non-Hodgkin's lymphoma, primary brain  
7 lymphoma and Kaposi's sarcoma were substantially reduced in patients on cART, and timely  
8 initiation of therapy at high CD4 cell counts is important for preventing these malignancies.<sup>28,</sup>  
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<sup>30</sup> In contrast, the incidence of Hodgkin's lymphoma was not reduced by cART. Patients whose CD4 cell counts declined despite suppression of HIV-1 replication on cART were at increased risk of Hodgkin's lymphoma.<sup>29</sup> Comparative analyses are planned in collaboration with the African regions of IeDEA.<sup>4</sup>

### **Hepatitis**

The immunological changes over the course of HCV treatment and their effect on mortality were estimated in 6,433 HIV-HCV-co-infected adults ( $\geq 16$ ), 12% of whom had initiated HCV treatment (n=692 interferon and ribavirin; n=88 interferon alone).<sup>31</sup> CD4 cell counts decreased over the first 12 weeks but stabilized from week 24 onwards with no negative impact on mortality. The group is poised to monitor the effect of the introduction of direct-acting antiviral agents in co-infected patients.

### **Socio-economic inequalities**

The Socio-economic inequalities group studies differences in key outcomes by sex, race/ethnicity, migrant status and educational level as a proxy for socioeconomic position. Even in European countries with universal health care systems, it has been documented that individuals with lower educational level do not benefit equally from timely cART initiation and have a poorer response to cART.<sup>32</sup>

Mortality in migrants has been found to be lower compared to native populations, which has been attributed to the "healthy migrant effect". COHERE's larger sample size has allowed

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3 this group to study mortality in men and women from multiple geographical origins  
4 separately, highlighting heterogeneity among migrant groups and revealing how certain  
5 groups are at an increased risk of mortality<sup>33</sup>, work which was featured in the first issue of  
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7 UNAIDS Science Now. The group plans to examine differences in cause-specific mortality by  
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9 country of origin.  
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### 12 13 14 **What are the main strengths and weaknesses?**

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16 COHERE in EuroCoord's infrastructure is a unique research platform which has prompted  
17 collaborations both within and beyond Europe. EuroCoord's cross-network work packages on  
18 data capture, HIV tuberculosis, migrant health and modelling and its interdisciplinary working  
19 groups (clinicians, virologists, epidemiologists, biostatisticians) have formalized this cross  
20 network collaboration and fostered intra-European capacity building. COHERE's further  
21 investment in data harmonization (HICDEP) has benefitted other regional collaborations.  
22 Efforts to streamline data submission with the CASCADE and ART-CC cohort collaborations  
23 improved efficiency and reduced the workload of DMs. Finally, COHERE has provided  
24 excellent training opportunities for junior researchers (PhDs and Fellowships).  
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28 COHERE's greatest strength is its size, enabling stratification of subgroups of interest<sup>8</sup> (e.g.  
29 across 10 age groups and sex-stratification) and the study of uncommon outcomes.<sup>28</sup> The  
30 robustness of COHERE's findings transcends Europe, benefiting the global HIV-patient  
31 community. COHERE data are highly representative of those in care in countries with large  
32 regional and national cohorts. Such cohorts enable COHERE to monitor trends across  
33 countries. However, adequate representation of marginalized groups such as migrant  
34 populations has become a challenge as a consequence of informed consent requirements in  
35 some countries as well as barriers to accessing care.<sup>34</sup>  
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39 Although COHERE uses HICDEP, the heterogeneity in data quality remains an ongoing  
40 challenge. In collaboration with ART-CC<sup>3</sup>, COHERE has been an ideal platform for  
41 harmonizing the collection and validation of causes of deaths in HIV-1 infected individuals.  
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3 With a growing proportion of deaths now caused by non-AIDS events, accurately monitoring  
4 causes of death is critical to identify trends and evaluate risk factors. The progressive  
5 implementation of the “Coding Causes of Death in HIV” Protocol (CoDe), a uniform  
6 classification system for collecting and validating (via a centralized review process) data on  
7 causes of death and contributing factors in HIV-1 infected patients, developed by the D:A:D  
8 collaboration, has become a priority.<sup>35</sup>

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16 Despite COHERE’s demonstrated ability to evolve and adapt to respond to new research  
17 questions, it is now facing the challenge of expanding cohort and clinic-based databases to  
18 include clinical outcomes that were not initially of interest. As the cohort of PLWH in Europe  
19 ages, comorbidities, such as cardiovascular, metabolic, neurocognitive, and bone diseases,  
20 have become increasingly relevant to the study of prognosis in the era of cART. If COHERE  
21 and its contributing cohorts were formed today, more emphasis would be placed on linking  
22 HIV databases with other health databases (e.g. cancer registries, hospital or other  
23 administrative databases, etc.).

### 32 33 **COHERE from a patient’s perspective**

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36 COHERE has maintained close ties with the patient community via its patient representative  
37 on the COHERE SC. Data from COHERE helped to demonstrate the value of high quality  
38 treatment strategies and enabled people living with HIV understand the evolving nature of  
39 the epidemic as well as face the ongoing challenges of growing older with HIV. Findings from  
40 COHERE have informed and guided the patient community’s discussions with governments  
41 and authorities about treatment guidelines and standards of care.

### 47 48 49 **Can I get hold of the data? Where can I find out more?**

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52 COHERE welcomes applications from Principal Investigators (PIs) of European cohorts  
53 interested in joining the COHERE collaboration. Interested cohorts must be willing to  
54 transform their data to fit HICDEP codes and adhere to the data submission timeline laid out  
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3 in the COHERE Data Management SOP. COHERE DMs hold several explanatory webinars  
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5 covering the data submission process to facilitate data transfer.  
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8 Those interested in using COHERE data to conduct a project can download a COHERE  
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10 Project Proposal Form and a Data Specification Form from our website ([www.cohere.org](http://www.cohere.org)).  
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12 Proposals from external investigators will undergo the same rigorous scrutiny as those from  
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14 investigators within the study group (details outlined in the COHERE Manual of Operations,  
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16 available at [www.cohere.org](http://www.cohere.org)).  
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## 18 19 **Conclusion**

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21 COHERE is now a mature collaboration, which is unique in its size and coverage. It  
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23 continues to produce new evidence on clinical outcomes, particularly AIDS-defining  
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25 complications, late presentation and socio-economic inequalities, which inform clinical  
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27 guidelines and public health policy recommendations. As PLWH live longer with a chronic  
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29 infection, comparisons between them and cohorts of uninfected individuals are needed to  
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31 disentangle the role of HIV infection from its long-term treatment and comorbidities,  
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33 especially those linked to ageing.  
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## 36 37 **Profile in a nutshell**

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39 • The Collaboration of Observational HIV Epidemiological Research Europe (COHERE)  
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41 is a project-driven cohort consortium that was set-up to address scientific questions  
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43 that could not be addressed by single cohorts because of sample size requirements.  
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- 45  
46 • COHERE has grown from 33 cohorts in 2005 to 40 in 2015. The 2014 merger,  
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48 representing 14 projects, compiled data from 331 481 individuals from 34 European  
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50 countries, including 2808 children (<13), representing 2 135 896 person-years of  
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52 follow-up.  
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- As a consortium of cohorts comprising clinic/hospital-based and interval cohorts, the frequency of patient follow-up varies. For clinic or hospital-based cohorts, average patient follow-up reflects current standards of care in those countries.
- COHERE compiles data on clinical characteristics, antiretroviral therapy and other medications, estimated date of HIV seroconversion, opportunistic infections, laboratory results and socio demographic data according to the requirements of projects.
- External collaborators interested in conducting a project in COHERE should submit a project proposal to the Regional Coordinating Centres in Bordeaux and Copenhagen for review by COHERE's governing bodies (see [www.cohere.org](http://www.cohere.org) for further information).

## Conflicts of Interest

DC was a member of the French Gilead HIV board up until 2015 and gave lectures for Janssen-Cilag, Merck-Sharp & Dohme-Chibret, ViiV and received travel/accommodations/meeting expenses from Gilead, ViiV, Janssen-Cilag. DC also conducted post-marketing studies for Janssen-Cilag, Merck-Sharp & Dohme-Chibret and ViiV. DC is currently a consultant at Innavirvax. HF has received grants from the Swiss National Science Foundation. His institution has received grants from ViiV, Abbvie, MSD, Janssen, Roche, BMS, and Gilead. The other co-authors have no conflicts of interest to declare.

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**References:**

1. Mocroft A, Ledergerber B, Katlama C, et al. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. *The Lancet* 2003; **362**: 22-9.
2. *EuroCoord : Enhancing clinical and epidemiological HIV research in Europe through cohort collaborations*. 2014 [cited 2014 5 February ]; Available from: <http://www.eurocoord.net/>
3. May MT, Ingle SM, Costagliola D, et al. Cohort profile: Antiretroviral Therapy Cohort Collaboration (ART-CC). *Int J Epidemiol* 2013.
4. Egger M, Ekouevi DK, Williams C, et al. Cohort Profile: the international epidemiological databases to evaluate AIDS (IeDEA) in sub-Saharan Africa. *Int J Epidemiol* 2012; **41**: 1256-64.
5. *EuroSida*. 2015 [cited 6 July, 2015]; Available from: <http://www.cphiv.dk/Ongoing-Studies/EuroSIDA/About>
6. Kjaer J, Ledergerber B. HIV cohort collaborations: proposal for harmonization of data exchange. *Antivir Ther* 2004; **9**: 631-3.
7. *HIV-Distributed Data Management*. 2016 [cited 2016 8 April]; Available from: <http://www.hiv-ddm.net/>
8. Sabin CA, Smith CJ, d'Arminio Monforte A, et al. Response to combination antiretroviral therapy: variation by age. *AIDS (London, England)* 2008; **22**: 1463-73.
9. Lewden C, Bouteloup V, De Wit S, et al. All-cause mortality in treated HIV-infected adults with CD4  $\geq$ 500/mm<sup>3</sup> compared with the general population: evidence from a large European observational cohort collaboration. *Int J Epidemiol* 2012; **41**: 433-45.
10. Mocroft A, Furrer HJ, Miro JM, et al. The incidence of AIDS-defining illnesses at a current CD4 count  $\geq$  200 cells/ $\mu$ L in the post-combination antiretroviral therapy era. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2013; **57**: 1038-47.
11. The Opportunistic Infections Project Team of the Collaboration of Observational HIVeRIE. CD4 Cell Count and the Risk of AIDS or Death in HIV-Infected Adults on Combination Antiretroviral Therapy with a Suppressed Viral Load: A Longitudinal Cohort Study from COHERE. *PLoS Med* 2012; **9**: e1001194.
12. Engsig FN, Zangerle R, Katsarou O, et al. Long-term mortality in HIV-positive individuals virally suppressed for  $>$ 3 years with incomplete CD4 recovery. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2014; **58**: 1312-21.
13. Lodwick R, Costagliola D, Reiss P, et al. Triple-class virologic failure in HIV-infected patients undergoing antiretroviral therapy for up to 10 years. *Arch Intern Med* 2010; **170**: 410-9.
14. Castro H, Judd A, Gibb DM, et al. Risk of triple-class virological failure in children with HIV: a retrospective cohort study. *Lancet* 2011; **377**: 1580-7.
15. Castagliola D, Ledergerber B, Torti C, et al. Trends in virological and clinical outcomes in individuals with HIV-1 infection and virological failure of drugs from three antiretroviral drug classes: a cohort study. *Lancet Infect Dis* 2012; **12**: 119-27.

16. Nakagawa F, Lodwick R, Costagliola D, et al. Calendar time trends in the incidence and prevalence of triple-class virologic failure in antiretroviral drug-experienced people with HIV in Europe. *J Acquir Immune Defic Syndr* 2012; **59**: 294-9.
17. PLATO II COHERE in EuroCoord. Predictors of CD4+ T-Cell Counts of HIV Type 1–Infected Persons After Virologic Failure of All 3 Original Antiretroviral Drug Classes. *Journal of Infectious Diseases* 2013; **207**: 759-67.
18. Mocroft A, Lundgren JD, Sabin ML, et al. Risk factors and outcomes for late presentation for HIV-positive persons in Europe: results from the Collaboration of Observational HIV Epidemiological Research Europe Study (COHERE). *PLoS Med* 2013; **10**: e1001510.
19. Mocroft A LJ, Kirk O for the Late Presentation Working Group of COHERE. Continued late presentation for HIV care across Europe. *HepHIV Barcelona*; 2014.
20. Pharris A, Spiteri G, Noori T, Amato-Gauci AJ. Ten years after Dublin: principal trends in HIV surveillance in the EU/EEA, 2004 to 2013. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin* 2014; **19**: 20968.
21. Mocroft A, Reiss P, Kirk O, et al. Is it safe to discontinue primary *Pneumocystis jiroveci* pneumonia prophylaxis in patients with virologically suppressed HIV infection and a CD4 cell count <200 cells/microL? *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2010; **51**: 611-9.
22. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. 2015: 19.
23. European AIDS Clinical Society (EACS). Guidelines Version 8.0. 2015.
24. Bisson GP, Molefi M, Bellamy S, et al. Early versus delayed antiretroviral therapy and cerebrospinal fluid fungal clearance in adults with HIV and cryptococcal meningitis. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2013; **56**: 1165-73.
25. Boulware DR MD, Muzoora C, Rolfes MA, Huppler Hullsiek K, Musubire A, Taseera K, Nabeta HW, Schutz C, Williams DA, Rajasingham R, Rhein J, Thienemann F, Lo MW, Nielsen K, Bergemann KL, Kambugu A, Manabe YC, Janoff EN, Bohjanen PR, Meintjes G, COAT Team. Timing of antiretroviral therapy after cryptococcal meningitis. *N Engl J Med* 2014.
26. Lortholary O, Nicolas M, Soreda S, et al. Fluconazole, with or without dexamethasone for experimental cryptococcosis: impact of treatment timing. *The Journal of antimicrobial chemotherapy* 1999; **43**: 817-24.
27. Ingle S, Miro J, Furrer H, et al. Impact of ART on Mortality in Cryptococcal Meningitis Patients: High-Income Settings. *CROI*. Seattle; 2015.
28. Bohlius J, Schmidlin K, Costagliola D, et al. Prognosis of HIV-associated non-Hodgkin lymphoma in patients starting combination antiretroviral therapy. *AIDS (London, England)* 2009; **23**: 2029-37.
29. Bohlius J, Schmidlin K, Boue F, et al. HIV-1-related Hodgkin lymphoma in the era of combination antiretroviral therapy: incidence and evolution of CD4(+) T-cell lymphocytes. *Blood* 2011; **117**: 6100-8.

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30. Wyss N EM, Bohlius J. *Kaposi Sarcoma in the Era of Combination Antiretroviral Therapy*. Conference on Retroviruses and Opportunistic Infections (CROI); 2014 March 3-6, 2014; Boston; 2014.

31. Effect of hepatitis C treatment on CD4+ T-cell counts and the risk of death in HIV-HCV-coinfected patients: the COHERE collaboration. *Antivir Ther* 2012; **17**: 1541-50.

32. Lodi S, Dray-Spira R, Touloumi G, et al. Delayed HIV diagnosis and initiation of antiretroviral therapy: inequalities by educational level, COHERE in EuroCoord. *AIDS (London, England)* 2014; **28**: 2297-306.

33. Mortality in migrants living with HIV in western Europe (1997-2013): a collaborative cohort study. *The lancet HIV* 2015; **2**: e540-9.

34. ECDC. *Improving HIV data comparability in migrant populations and ethnic minorities in EU/EEA/EFTA countries: findings from a literature review and expert panel.*: European Centre for Disease Control; 2011.

35. Kowalska JD, Friis-Moller N, Kirk O, et al. The Coding Causes of Death in HIV (CoDe) Project: initial results and evaluation of methodology. *Epidemiology* 2011; **22**: 516-23.

Review Only

## Box 1: COHERE's Principles

- COHERE should neither threaten nor compete with the scientific agendas of participating cohorts/cohort collaborations.
- The individual contributing cohorts must express their interest in participating in COHERE.
- The scientific questions addressed by COHERE are determined by consensus according to both their scientific relevance and originality (not being addressed elsewhere).
- Individual cohorts may veto the use of their data in any new project.

For Review Only

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Persons Living with HIV (PLHIV) in COHERE as of 31/12/2011 as a proportion of 2011 UNAIDS estimates of PLHIV per country

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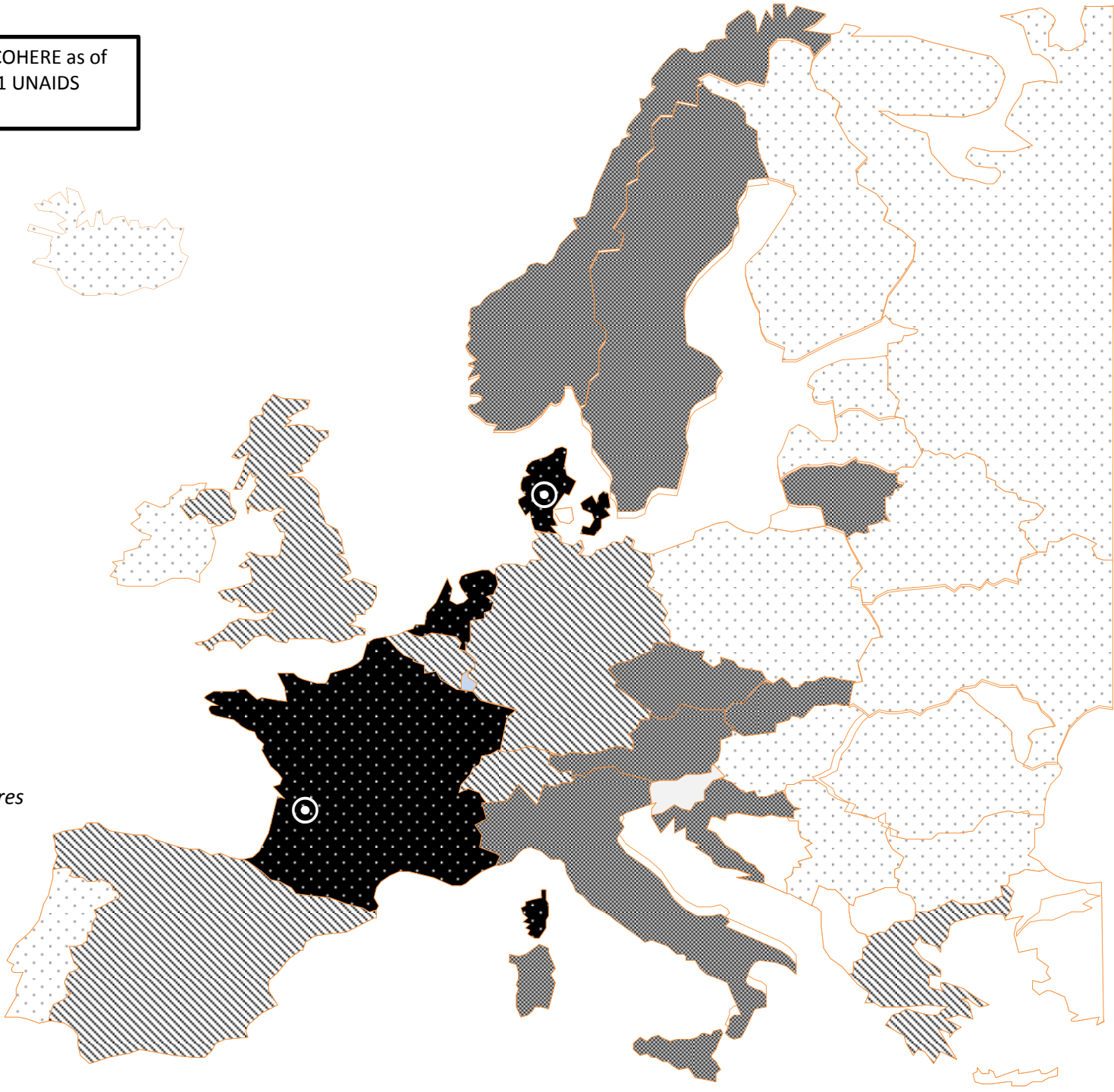
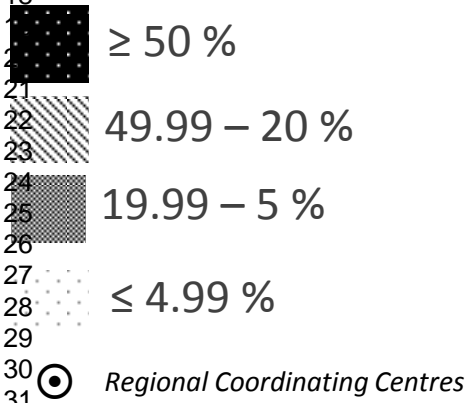


Table 1a: Description of the cohort type, eligibility criteria, period of enrolment, and location of data collection of the adult or mixed (adult/paediatric) cohorts participating in COHERE (circa 2015)

Cohort	Cohort Type	Eligibility criteria	Beginning of Enrolment	End of Enrolment	Data Collection	N Sites/ Countries	Location of sites
AHVCO5	Hospital-based, Surveillance System	All HIV+ persons in care at 6/7 national centres	1/1/1996		Prospectively	6	Austria (National)
AMACS	Clinic-based, Hospital-based	All HIV+ persons in care at affiliated sites for at least 1 year, alive on 1/1/1996	1/1/1996		Both prospectively and retrospectively	13	Greece (Regions : Attiki, Pelopon, Alexandroupolis)
ANRS CO2 SEROCO	Interval cohort	HIV diagnosis <1 year before enrolment or a known date of infection identified by incomplete Western blot or an interval of less than 2 years between a negative and a positive ELISA	1/1/1988	12/31/2009	Prospectively	25	France (Paris area, Marseille, Nice)
ANRS CO3 AQUITAINE	Hospital-based	HIV+ >= age 13, seen at least once at a site & signed informed consent	1/1/1987		Prospectively	13	France (Region : Aquitaine)
ANRS CO4 FHDH	Hospital-based	HIV-1 or HIV-2- individuals who have provided written informed consent	1/1/1989	12/31/2005	Prospectively	70	France (National, except Aquitaine)
ANRS CO6 PRIMO	Interval cohort	HIV+ patients presenting during primary infection in sites	1/1/1996		Prospectively	80	France (National)
ANRS CO8 APROCCO-COPILOTE	Hospital-based	HIV-infected patients >= 18 years old, naive for protease inhibitors	14/1997	6/6/1999	Prospectively	49	France (National)
ANRS CO13 HEPAVIH	Hospital-based	Phase I : [12/2005, 12/2008] HIV-1/HCV chronically infected >= age 18. Phase II : [9/2011, 3/2016] HIV-1/HCV chronically infected >= age 18, beginning anti-HCV treatment comprising Telaprevir or Boceprevir, or having cleared HCV spontaneously in the absence of anti-HCV treatment. Phase III : [Q1/2014, Q1/2016]. Individuals who have received, are receiving, or will receive within the next 6 months combination therapy with new anti-HCV drugs, with or without peginterferon and/or ribavirin (temporary authorization, full marketing authorization, or within clinical trials) & individuals previously included in ANRS clinical trials evaluating new anti-HCV drugs	11/10/2005		Prospectively generally, and Prospective & Retrospective for Phase II	27	France (National)
ATHENA	Clinic-based	Any HIV+ person entering care in one of the 27 adult (28 including Curacao) or 4 pediatric HIV treatment centers in the Netherlands and who does not object to standardized collection of data obtained as part of routine care	1/1/1998		Both prospectively and retrospectively	31	The Netherlands, Curacao (National)
Bonn Cologne Cohort	Clinic-based, Hospital-based	HIV+	1/5/1988		Both prospectively and retrospectively	2	Germany (Bonn, Cologne)
CASCADE	Clinic-based, Hospital-based	HIV+ with well estimated dates of HIV seroconversion	1/1/1979		Both prospectively and retrospectively	-	11 countries*
Cinsev	Clinic-based, Hospital-based	All patients HIV+ presenting at the clinical sites after 0/0/1999	1/1/1999		Both prospectively and retrospectively	18	Germany
CORIS	Clinic-based	Confirmed HIV+, cART-naive, attending participating sites aged >16 & signed informed consent	1/1/2004		Prospectively	37	Spain (Multi-region)
CORIS-MD	Clinic-based	HIV+	1/1/1997	12/31/2003	Retrospectively	10	Spain (Multi-region)
DHK	Hospital-based	HIV+ & in care in HIV treatment centres	1/1/1995		Prospectively	8	Denmark (National)
ECS	Clinic-based, Hospital-based	Pregnant HIV+ women, diagnosed before or during pregnancy or as a result of HIV leading intrapartum, delivering liveborn infant.	7/15/1985		Prospectively	10 countries	10 countries*
EuroSIDA	Clinic-based, Hospital-based, Interval cohort	Aged > 16 & booked hospital appointment	1/6/1994		Both prospectively and retrospectively	109 sites, 34 countries	34 countries**
Frankfurt	Clinic-based	HIV+ > age 16 in care at affiliated sites	1/1/1987		Prospectively	5	Germany (Frankfurt)
Genes Haemo	Clinic-based, Surveillance System	HIV+ haemophiles infected in early 1980s	5/26/1999	4/26/1999	Both prospectively and retrospectively	2	Spain (Madrid, Barcelona)
Georgian National HIV Cohort	Clinic-based, Hospital-based, Surveillance System	HIV+ adults	1/1/2007		Both prospectively and retrospectively	1	Georgia
ICC (IMI Clinical Cohort)	Clinic-based, Hospital-based	HIV+ individuals in care at site	1/1/1995		Prospectively	1	Italy (Rome)
ICONA	Hospital-based	HIV+, ART-naive, >= age 18 & signed informed consent	1/1/1997		Prospectively	42	Italy
Infectious Disease Database (IDD) San Raffaele	Hospital-based	All HIV+ patients in care at site	1/1/1991		Prospectively	1	Italy (Milan)
Italian MASTER Cohort	Clinic-based	HIV-1 or HIV-2- (antibody test or positive HIV RNA) in care in participating sites	1/1/1997		Both prospectively and retrospectively	8	Italy (multi-city)
Modena	Clinic-based	All new HIV diagnosis in adult patients (>= 18 year) since 1985, inhabitant in Province of Modena and referred to Regional Surveillance System. Data were retrospectively collected from 1992.	1/1/1992	12/31/2014	Retrospectively	1	Italy (Modena)
PISCIS	Clinic-based, Hospital-based	HIV+ >= age 16 in care at one of the sites after January 1st 1998, irrespective of the stage of disease or degree of immunosuppression.	1/1/1998		Both prospectively and retrospectively	11	Spain (Region : Catalonia)
SHCS	Clinic-based, Hospital-based	Any HIV+ persons >= age 18	1/1/1988		Prospectively	7	Switzerland (National)
St Pierre	Clinic-based, Hospital-based	HIV+ & at least one visit at affiliated sites	1/25/1980		Prospectively	1	Belgium (Brussels)
Swedish InCare HIV cohort	Clinic-based, Hospital-based, Surveillance System	All HIV+ persons in care in Sweden, opt out system	1/1/1983		Both prospectively and retrospectively	29	Sweden (National)
UK Collaborative HIV Cohort Study (UK CHIC)	Clinic-based	HIV+ persons > age 16 & <= 1 visit at affiliated site after 1/1/1995	1/1/2001		Both prospectively and retrospectively	19	United Kingdom (National)
VAZH	Hospital-based	HIV+ persons > age 16 & 1st visit at affiliated site.	1/1/1997		Prospectively	23	Spain

\* Austria, France, Germany, Greece, Italy, Netherlands, Norway, Spain (Barcelona, Madrid, Valencia), Sweden, Switzerland, United Kingdom

\*\* Belgium, Denmark, Germany, Netherlands, Poland, Italy, Spain, Sweden, Ukraine, United Kingdom

\*\* Argentina, Austria, Belarus, Belgium, Bosnia-Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Georgia, Greece, Hungary, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg/Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine, United Kingdom)

Table 1b: Description of the cohort type, eligibility criteria, period of enrolment, and location of data collection of paediatric or adolescent cohorts participating in COHERE (circa 2015)

Name of Cohort	Cohort Type	Eligibility Criteria	Enrolment period	Data Collection	N Sites/ Countries	Location of sites
AALPHI	Clinic & community-based, Interval cohort	HIV+ age 13-21 and in paediatric care in UK, HIV-uninfected age 13-23, sibling of HIV-infected or has HIV+ parent	06/01/2012 - 12/31/2014	Prospectively	-	United Kingdom (Region : England)
ANRS CO10 EPF	Interval cohort	HIV+ children included at birth (born to HIV-pregnant women enrolled in the CO1-EPF cohort), or, since 2005, at time of first HIV care management in the clinical participating sites	09/07/1985 -	Prospectively	24	France
CHIPS	Clinic-based, Hospital-based, Surveillance System	All HIV+ children living in the UK/Ireland	04/01/2000-	Prospectively	-	United Kingdom (National), Ireland (National)
CoRISPE-cat	Hospital-based	HIV+ <18 years at diagnosis	01/01/2008 -	Both prospectively and retrospectively	13	Spain (regions : Catalonia, Balearic Islands)
CoRISpeS-Madrid	Hospital-based	HIV+, infected before age 18	01/01/2002 -	Both prospectively and retrospectively	59	Spain (national)
KOMPNET Children Cohort	Clinic-based	HIV+, < 18 age	06/01/2005 -	Both prospectively and retrospectively	7	Germany (National)
Madrid PMTCT Cohort	Hospital-based	HIV-1+ women during pregnancy and their HIV-exposed infants	1/2/0200	Prospectively	7	Spain (Madrid)
NENEXP	Hospital-based	HIV+ pregnant women & HIV-exposed children, HAART-exposed children until 18 month-old age.	01/01/2000 -	Prospectively	12	Spain (region: Catalonia)
NSHPC	Surveillance System	All pregnancies in HIV+ women living in the UK or Ireland, their exposed infants, and all children with HIV infection	01/01/1990 -	Prospectively	230	United Kingdom & Ireland (National)
St Pierre Paediatric	Hospital-based	All HIV+ children/adolescents in care at site	01/01/2000 -	Both prospectively and retrospectively	1	Belgium (Brussels)

Table 2a : Number of individuals, person-years of follow-up, patient demographics, prior AIDS status, mode of infection, median CD4 cell count and logarithm viral load in individuals older than 13 years old, (COHERE, 2014 merger)

Cohort	N	Person-years	Female [N (%)]	Median Age (IQR)	No AIDS [N, (%)] prior to/during follow-up	Mode of infection [N (%)]						HIV RNA(log10 cp/ml) assessment at enrolment*, N (%)	Median HIV RNA (log10 cp/ml) at enrolment* (IQR)	CD4 cell count assessment at enrolment*, N (%)	Median CD4 cell count at enrolment* (IQR)	
						MSM**	Hetrosexual contact	IDU	Blood Products	Perinatal infected	Unknown					
AHIVCOS	4676	30505	1247 (27)	34 (28; 42)	3232 (69.1)	1727 (36.9)	1673 (35.8)	1008 (21.6)	88 (1.9)	5 (0.1)	175 (3.7)	3296 (70.5)	4.7 (3.8; 5.3)	3865 (82.7)	354 (175; 552)	
AMACS	5359	35101	870 (16)	34 (27; 42)	4377 (81.7)	2707 (50.5)	1399 (26.1)	351 (6.5)	101 (1.9)	9 (0.2)	792 (14.8)	3821 (71.3)	4.5 (3.7; 5.1)	4244 (79.2)	348 (169; 548)	
ANRS CO2 SEROCO	1543	15766	452 (29)	30 (26; 36)	824 (53.4)	711 (46.1)	494 (32.0)	143 (9.3)	92 (6.0)		103 (6.7)	911 (59.0)	4.1 (3.6; 4.7)	1526 (98.9)	480 (326; 669)	
ANRS CO3 AQUITAINE	8457	63667	2202 (26)	35 (29; 43)	5354 (63.3)	3268 (38.6)	2398 (28.4)	1969 (23.3)	390 (4.6)	29 (0.3)	403 (4.8)	2640 (31.2)	4.3 (3.0; 5.0)	6205 (73.4)	330 (155; 516)	
ANRS CO4 FHDH	87925	637178	28899 (33)	35 (30; 43)	65261 (74.2)	28609 (32.5)	41088 (46.7)	9090 (10.3)	1560 (1.8)	298 (0.3)	7280 (8.3)	52143 (59.3)	4.4 (3.5; 5.1)	75154 (85.5)	337 (175; 520)	
ANRS CO6 PRIMO	1563	7997	219 (14)	35 (29; 43)	1522 (97.4)	1101 (70.4)	366 (23.4)	4 (0.3)	1 (0.1)		91 (5.8)	1558 (99.8)	5.2 (4.5; 5.8)	1558 (99.7)	514 (370; 666)	
ANRS CO8 COPILOTE	1184	8761	280 (24)	36 (32; 43)	873 (73.3)	464 (39.2)	405 (34.2)	194 (16.4)	30 (2.5)		91 (7.7)	1176 (99.3)	4.5 (3.7; 5.2)	1173 (99.1)	273 (126; 424)	
ANRS CO13 HEPAVIH	1146	4431	325 (28)	46 (42; 49)	805 (70.2)	155 (13.5)	184 (16.1)	688 (60.0)	71 (6.2)	1 (0.1)	47 (4.1)	1076 (93.9)	1.6 (1.6; 1.9)	1071 (93.5)	450 (312; 647)	
ATHENA	21177	136563	4190 (20)	39 (32; 46)	15667 (74.0)	12323 (58.2)	6434 (30.4)	749 (3.5)	233 (1.1)	32 (0.2)	1406 (6.6)	19806 (93.5)	4.4 (2.6; 4.9)	19736 (93.2)	360 (190; 550)	
Bonn***	1978	13125	377 (19)	36 (30; 44)	1512 (76.4)	937 (47.4)	502 (25.4)	200 (10.1)	189 (9.6)	5 (0.3)	145 (7.3)	1270 (64.2)	4.1 (2.6; 4.9)	1653 (83.6)	365 (191; 563)	
Cologne***	1742	1951	221 (13)	37 (30; 45)	926 (53.2)	1010 (58.0)	230 (13.2)	142 (8.2)	37 (2.1)		323 (18.5)	573 (32.9)	4.3 (3.1; 5.0)	946 (54.3)	250 (50; 490)	
CASCADE	9037	66196	1387 (15)	31 (26; 38)	7288 (80.6)	5565 (61.6)	1467 (16.2)	1735 (19.2)			270 (3.0)	2655 (29.4)	4.9 (4.2; 5.6)	4223 (46.7)	514 (368; 711)	
ClinSurv	17599	98130	3467 (20)	38 (32; 46)		9055 (51.5)	2581 (14.7)	1622 (9.2)	125 (0.7)	38 (0.2)	4178 (23.7)	13904 (79.0)	4.6 (3.8; 5.2)	14201 (80.7)	330 (160; 520)	
CoRIS***	6466	19589	1070 (17)	35 (29; 43)	5432 (84.0)	3728 (57.7)	1893 (29.3)	621 (9.6)			224 (3.5)	5504 (85.1)	4.7 (4.0; 5.2)	5553 (85.9)	375 (194; 538)	
CoRIS-MD***	3493	14953	990 (28)	35 (31; 39)	2334 (66.8)	492 (14.1)	755 (21.6)	1975 (56.5)	94 (2.7)		177 (5.1)	854 (24.4)	4.5 (3.0; 5.2)	1448 (41.5)	310 (140; 527)	
DHK	6367	49416	1573 (25)	38 (31; 46)	4776 (75.0)	2894 (45.5)	2409 (37.8)	586 (9.2)	84 (1.3)	8 (0.1)	386 (6.1)	3704 (58.2)	4.6 (3.7; 5.1)	4772 (74.9)	300 (120; 500)	
ECS	5295	5453	5295 (100)	27 (24; 31)	5074 (95.8)		4736 (89.4)	320 (6.0)	16 (0.3)		223 (4.2)	895 (16.9)	3.9 (2.8; 4.6)	1528 (28.9)	439 (301; 604)	
EuroSIDA	13384	85203	3854 (29)	36 (30; 43)	8168 (61.0)	4645 (34.7)	4218 (31.5)	3665 (27.4)	169 (1.3)		687 (5.1)	7782 (58.1)	4.0 (2.8; 4.8)	12477 (93.2)	316 (165; 486)	
GEMES Haemo	94	2210	5 (5)	21 (17; 24)	72 (76.6)				94 (100.0)					3 (3.2)	130 (111; 748)	
Infectious Disease Database (IDD) San Raffaele	2870	21618	485 (17)	36 (31; 43)	2397 (83.5)	1257 (43.8)	620 (21.6)	274 (9.5)	8 (0.3)	4 (0.1)	707 (24.6)	2817 (98.15)	4.3 (3.3; 5.0)	2698 (94.0)	420 (228; 620)	
ICC (INMI Clinical Cohort)	2947	24752	823 (28)	37 (31; 43)	2043 (69.3)	595 (20.2)	911 (30.9)	752 (25.5)	31 (1.1)	8 (0.3)	650 (22.1)	1795 (60.9)	4.5 (3.1; 5.2)	2696 (91.5)	315 (135; 525)	
ICONA	9894	50626	2586 (26)	36 (31; 43)	8882 (89.8)	2913 (29.4)	3933 (39.8)	2436 (24.6)	44 (0.4)		568 (5.7)	8772 (88.7)	4.5 (3.8; 5.1)	9104 (92.0)	401 (208; 593)	
Italian MASTER Cohort	12728	74753	3458 (27)	37 (31; 44)	9558 (75.1)	2250 (17.7)	5074 (39.9)	2583 (20.3)	62 (0.5)	5	2754 (21.6)	9723 (76.2)	4.6 (3.9; 5.2)	9927 (78.0)	304 (122; 511)	
Modena	1730	18239	560 (32)	33 (27; 41)	1252 (72.4)	334 (19.3)	732 (42.3)	545 (31.5)	11 (0.6)	1 (0.1)	107 (6.2)	718 (41.5)	4.6 (3.8; 5.3)	907 (52.4)	321 (133; 555)	
PISCIS	14202	75297	3164 (22)	36 (31; 43)	11054 (77.8)	5105 (35.9)	5340 (37.6)	2481 (17.5)	47 (0.3)	60 (0.4)	1169 (8.2)	9878 (69.6)	4.5 (3.4; 5.2)	10184 (71.7)	312 (136; 516)	
SHCS	10193	70179	2961 (29)	37 (31; 44)	7957 (78.1)	4106 (40.3)	4197 (41.2)	1000 (9.8)	80 (0.8)	9 (0.1)	801 (7.9)	8028 (78.8)	4.4 (3.3; 5.1)	10147 (99.5)	349 (179; 533)	
St Pierre	6925	40047	2613 (38)	35 (28; 42)	4909 (70.9)	2158 (31.2)	3834 (55.4)	429 (6.2)	128 (1.8)	53 (0.8)	323 (4.7)	3238 (46.8)	4.5 (3.4; 5.0)	4396 (63.5)	334 (169; 528)	
UK Collaborative HIV Cohort Study (UK CHIC)	47117	291082	12923 (27)	34 (29; 40)	37616 (79.8)	23208 (49.3)	17178 (36.5)	1690 (3.6)			296 (0.6)	4745 (10.1)	21366 (45.3)	4.4 (3.1; 5.1)	25873 (54.9)	307 (140; 488)
VACH	21582	149654	5020 (23)	35 (30; 41)	16205 (75.1)	5914 (27.4)	6504 (30.1)	7089 (32.8)	76 (0.4)	14 (0.1)	1985 (9.2)	9344 (43.3)	4.8 (4.1; 5.3)	10000 (46.3)	308 (129; 504)	
<b>TOTAL</b>	<b>328,673</b>	<b>2112438</b>	<b>91,516 (28)</b>	<b>35 (30; 43)</b>	<b>235,370 (71.6)</b>	<b>127,231 (38.7)</b>	<b>121,555 (37.0)</b>	<b>44341 (13.5)</b>	<b>3861 (1.2)</b>	<b>875 (0.3)</b>	<b>30,810 (9.4)</b>	<b>199,247 (60.6)</b>	<b>4.5 (3.5; 5.1)</b>	<b>247,268 75</b>	<b>340 (170; 530)</b>	

\* Enrolment : measurements taken in the period six months prior to and one month after the variable "enrolment date"

\*\* Includes a small proportion of MSM+IDU

\*\*\* Cohorts who have merged administratively but which represent 'one cohort' insofar as COHERE governance

Table 2b : Number of individuals, person-years of follow-up, patient demographics, prior AIDS status, mode of infection, median CD4 cell count and logarithm viral load in individuals enrolled in paediatric cohorts or enrolled in mixed cohorts and younger than 13 years old, (COHERE, 2014 merger)

Cohort	N	Person-Years	Female [N (%)]	Median Age (IQR)	No AIDS [N (%)]		Mode of infection				HIV RNA (log10 cp/ml) assessment at enrolment*, N (%)		Median HIV RNA values (log10 cp/ml) at enrolment* (IQR)		CD4 cell count assessment at enrolment*, N (%)		Median CD4 values (cells/µl) at enrolment* (IQR)	
							Sexual Contact	Blood products	Perinatal infected	Unknown								
ANRS CO10 EPF	193	1583	112 (58.0)	0 (0; 3)	176 (91.2)		1 (0.5)	188 (97.4)	4 (2.1)	0	-	-	-	130 (67)	1535 (708;2349)			
ATHENA**	254	1605	126 (49.6)	5 (3; 8)	204 (80.3)		5 (2.0)	235 (92.5)	14 (5.5)	241 (95)	2.5 (1.7; 4.8)	241 (95)	1000 (620; 1550)					
CHIPS	1765	14793	914 (51.8)	4 (0.7; 8)	1281 (72.6)		33 (1.9)	1662 (94.2)	70 (4.0)	546 (30)	4.7 (4.0; 5.4)	618 (35)	553 (254; 1000)					
CORISPE-cat	219	2834	129 (58.9)	1 (0.3; 3)	121 (55.3)		3 (1.4)	200 (91.3)	8 (3.7)	70 (32)	5.4 (4.9; 5.9)	79 (36)	1206 (464; 2185)					
CoRISpeS-Madrid	318	2514	159 (50.0)	2 (0.3; 5)	237 (74.5)	3	0.9	5 (1.6)	294 (92.5)	16 (5.0)	235 (73)	5 (4.3; 5.6)	100 (31)	927 (358; 1977)				
KOMPNET Children Cohort	59	129	28 (47.5)	8 (4;11)	49 (83.1)			53 (89.8)	6 (10.2)	44 (75)	1.7 (1.7; 2.5)	0	-	-				
<b>Total</b>	<b>2808</b>	<b>23,458</b>	<b>1468 (52.3)</b>	<b>3 (0.5; 8)</b>	<b>1953 (73.4)</b>	<b>11</b>	<b>0.4</b>	<b>47 (1.7)</b>	<b>2632 (93.7)</b>	<b>118 (4.2)</b>	<b>1136 (40)</b>	<b>4.6 (3.3; 5.4)</b>	<b>1168 (42)</b>	<b>762 (366;1425)</b>				

\* Enrolment : measurements taken in the period six months prior to and one month after the variable "enrolment date"

\*\* Mixed (adult/paediatric) cohorts

## Pocket Profile

**Title:** Cohort Profile: Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord

**Authors:** COHERE in EuroCoord (A complete list of the members of the writing committee is available in the full version of the profile)

**Keywords:** HIV, AIDS, cohort collaboration, prognosis, observational epidemiology

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**Cite this as:** The full version of this profile is available at IJE online and should be used when citing this profile.

**Cohort purpose:** The Collaboration of Observational HIV Epidemiological Research Europe (COHERE) was formed to pool and harmonize existing longitudinal data on people living with HIV (PLWH) collected across Europe to answer key research questions that, in the era of potent combination antiretroviral therapy (cART), could not be addressed adequately by individual cohorts.

**Cohort Basics:** COHERE has grown from 33 cohorts in 2005 to 40 cohorts as of 2015. As COHERE is a project-based collaboration, the nature of annual mergers depends on the projects included. The 2014 merger compiled data from 331 481 individuals from 34 European countries, including 2808 children (<13), representing 2 135 896 person-years of follow-up. Approximately a quarter of the COHERE sample is female (27%). The median age at inclusion is 35 [IQR: 30, 43]. The primary mode of HIV transmission is sexual contact [homosexual/bisexual contact (38.7%), heterosexual contact (37%)], followed by injection drug use (13.5%). Overall, 71.6% of the sample had never had a clinical AIDS diagnosis before or during enrolment.

**Follow-up and attrition:** As a consortium of cohorts comprising clinic and interval cohorts, patient follow-up varies. For clinic or hospital-based cohorts, average patient follow-up reflects current standards of care in those countries.

**Design and Measures:** COHERE is a cohort consortium that compiles data from 40 diverse cohorts of PLWH in Europe annually. The specific data merged is dictated by the eligibility criteria for included projects. Data categories commonly include clinical characteristics, antiretroviral therapy and other medications, estimated date of HIV seroconversion, opportunistic infections, laboratory results and socio demographic data.

**Unique features :** The submission of data to COHERE is facilitated by the use of the HIV Cohorts Data Exchange Protocol (HICDEP), a flexible data structure, developed in 2004, to guide the mapping of individual cohort data into a standard format to facilitate data merging, and the HIV Distributed Data Management Tool (<http://www.hiv-ddm.net/>). A series of quality assurance checks are conducted centrally and cohorts address data inconsistencies before data are merged. Likely duplicate patient records between and within cohorts are identified using probability linkage and reconciled.

**Reasons to be cautious :** Although COHERE uses HICDEP, the heterogeneity in data quality remains a challenge. With a growing proportion of deaths in PLWH are caused by non-AIDS events, accurately monitoring these causes is key to identifying trends and evaluating risk factors. The “Coding Causes of Death in HIV” Protocol (CoDe), a uniform classification system for collecting and validating data on causes of death and contributing factors in HIV-1 infected patients is being implemented.

**Collaboration and data access :** External collaborators interested in conducting a project in COHERE should submit a proposal to the Regional Coordinating Centres for review by COHERE’s governing bodies (see [www.cohere.org](http://www.cohere.org)).

**Funding and competing interests :** The COHERE has received unrestricted funding from: Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (ANRS), France; HIV Monitoring Foundation, The Netherlands; and the Augustinus Foundation, Denmark. The research leading to these results has received funding from the

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Participating cohort funders are listed at [www.COHERE.org](http://www.COHERE.org).

For Review Only