# United Kingdom
# Community Advisory Board (UKCAB)
## HIV treatments advocates network

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## Meeting Report
## CAB 34 – DHICE Community Training Day
### 18 June 2010

**Contents:**



Presentations are all available to download for the June 2010 meeting at:

http://www.ukcab.net/jun10/index.html

## Members attending

| | Name | Organisation | Destination |
|---|---|---|---|
| 1 | Abena Sarimu | Waverley Care | Edinburgh |
| 2 | Adela Mugabo | George House Trust | Manchester |
| 3 | Alastair Hudson | IPPF/The People Living with Stigma Index | Edinburgh |
| 4 | Anthony Smea | UCL CHIME Project | London |
| 5 | Ben Cromaty | North Yorkshire AIDS Action | Yorkshire |
| 6 | Caroline Sabin | Royal Free and University College Medical School | London |
| 7 | David Baird | Personal | London |
| 8 | David Dunn | UK HIV Resistance Database, CTU, MRC | London |
| 9 | Eunice Sinyemu | HIV Scotland | Edinburgh |
| 10 | Fabiola Bayavuge | Black Health Agency | Manchester |
| 11 | Gertrude Anyango-Wafula | Black Health Agency | Manchester |
| 12 | Hauwa Abbas | Silver Lining Initiative | London |
| 13 | Kama Hajiyeva | AVERT | Horsham |
| 14 | Kapunu Simonde | Waverley Care | Edinburgh |
| 15 | Katie Walker | Personal | London |
| 16 | Kingsley Oturu | Inst for Int. Health & Development | Edinburgh |
| 17 | Lillian Herbert | Black Health Agency | Manchester |
| 18 | Memory Sachikonye | UKCAB | London |
| 19 | Michael Marr | UKCAB | Edinburgh |
| 20 | Nakamba N'gambi | Zambia Leeds Community Assoc | Leeds |
| 21 | Paul Clift | King's College Hospital | London |
| 22 | Paul Elfick | Buckinghamshire County Council | Amersham |
| 23 | Rachel King | AVERT | Horsham |
| 24 | Sam Lattimore | Health Protection Agency | London |
| 25 | Silvia Petretti | Positively Women | London |
| 26 | Simon Collins | HIV i-Base | London |
| 27 | Tsepo Young | NHS Dumfries and Galloway | Stranraer |

## Programme

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| **Chair:** Paul Clift | **Timekeeper**: Michael Marr |
| 09:30 - 10:00 | Registration, refreshments and expenses |
| 10:00 - 10:15 | Welcome, introductions and UKCAB Updates |
| 10:15 – 10.45 | Introduction: What are observational studies, and how do they differ from clinical trials?<br>Caroline Sabin - Professor of Medical Statistics and Epidemiology, Royal Free & University College Medical School |
| **Summaries of the key studies in the UK** | |
| 10:45 - 11:05 | The UK Collaborative HIV Cohort Study (UK CHIC)<br>Caroline Sabin/Loveleen Bansi |
| 11:05 – 11:25 | The UK HIV Drug Resistance Database<br>David Dunn, Clinical Trials Unit, MRC |
| 11:25 - 11:40 | **Break** |
| 11.40 – 12.00 | National Study of HIV in Pregnancy and Childhood (NSHPC)<br>Pat Tookey - Senior Lecturer, MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health |
| 12.00 – 12.20 | The Collaborative HIV Paediatric Study(CHIPS)<br>Pat Tookey |
| 12:20 – 12:40 | HPA Surveillance databases<br>Dr Sam Lattimore |
| 12:40-14:00 | **Lunch** |
| 14:00-15:00 | Community Discussion - Simon Collins |
| 15.00 – 15.15 | **Break** |
| 15:15 – 15.45 | New IT methods to protect data and how are they being used?<br>Nathan Lea – Research Fellow, UCL Centre For Health Informatics & Multiprofessional Education (CHIME) |
| 15.45 - 16:15 | How do we analyse observational databases and what biases do we have to be aware of?<br>Caroline Sabin or David Dunn |
| 16.15 | Close |

**Introduction to the DHICE project (Databases for HIV: Integration, Collaboration, Engagement)**

Memory introduced the DHICE project and explained that it is a new project at i-Base to encourage collaborative working practice between different HIV cohort projects in the UK. DHICE have produced some of the most important and exciting research and they are looking for community involvement and advice. This training was an exciting opportunity for CAB members to have specialist training.

Memory's role is working with database coordinators and community organisations to:

- Identify and document patient concerns relating to database research, including the use of personal information, and to work to resolve any issues if they arise.
- Increase the involvement of community members in study design and management (e.g. through steering committee membership etc).
- Raise the profile of HIV research in the community; especially cohort studies that are database projects.

Research groups and cohorts involved in the DHICE project have produced research that includes:

- Recent/early infection - giving us data on how fast or slow HIV progresses. Data shows that 25% people need treatment within 2 years. (CASCADE)
- Mother-to-child transmission - why the UK has some of the best result. (NSHPC)
- Children's database – follows children's health, both those who are HIV-positive and any child whose mother used HIV treatment during pregnancy. (CHIPS)
- Treatment responses - all the combined data about how and when people start treatment and how long it works for. (UKCHIC)
- Resistance - tracking drug resistance in new infections and generally in US patients - is this is growing problem? (UKHIVRD)
- Surveillance and safety databases - for reporting side effects, including from patients (Health Protection Agency – HPA)

Expectations from the meeting:

- To increase community awareness of this important area of research
- To use this opportunity to try to get CAB members to raise any concerns or issues that we might have about the databases

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**What are observational studies and how do they differ from clinical trials?**
Caroline Sabin, Dept of Infection and Population Health

Caroline Sabin is a Professor of Medical Statistics and Epidemiology in the Research Department of Infection NS Population Health at UCL campus at the Royal Free Hospital in London. The department's aim is to reduce the population impacts of infection, and to promote individual health by means of the prevention and treatment of communicable and non-communicable disease. She is also the chair of UKCHIC Steering Committee and the DHICE project.

**Experimental study** – investigator (researcher) intervenes in the care of the patient in a pre-planned way and records the outcome, also known as randomised controlled trials or laboratory studies.

**Observational study** - investigators observe patients and measure variables of interest without assigning treatments. The treatment that each patient receives is determined beyond the control of the investigator.

**Randomised Control Trials** (RCTs) are experimental studies where treatments are allocated randomly to patients. This ensures that characteristics of those in each treatment arm are broadly similar with any differences being due to chance. Any differences in outcome are unlikelyto be explained by baseline differences between the groups. RCTs are a comparison of two or more treatment strategies and the control group enables the investigator to estimate additional gain from the new drug over and above that which would have occurred anyway.

Limitations of RCTs with 2 or 3 comparisons groups

- Cannot be done if there are no people willing to be randomised.
- Patients maybe unrepresentative of clinic population, outcome may differ due to different management from what would be expected.
- Short periods (48 weeks) and focus on two or three main treatment components.
- May focus on short-term surrogate marker changes rather than long-term clinical endpoints (occurrence of a disease, symptom, sign or laboratory abnormality that constitutes one of the target outcomes of the trial).

**Cohort studies**

A cohort is a group of people who share a common characteristic or experience within a defined period. Cohort studies follow individuals over time to assess the incidence of a disease (or some other outcome) and used to describe the effect of exposure to one or more factors of interest. They can be prospective or retrospective/historical.

Cohort designs:

Fixed or closed; new patients are unable to join the study

- Dynamic or open; new patients may be recruited as the cohort follow-up progresses combination. In some instances at the beginning of a cohort all patients are almost never recruited on the same day and recruiting may be a lengthy process.
- Combination of fixed and dynamic.
- Patients attend study visits at centre on regular occasions (e.g. 6-monthly) and may complete questionnaire since last visit, lab tests performed a pre-defined time intervals and patients must give consent to participate.

In observational databases, cohort are designed to:

- Collect data that are already routinely collected as part of patient's medical care.
- Patient does not attend study visits or complete any questionnaires.
- Lab tests are performed according to clinical need and will be more frequent if patient is ill or needs further investigation and are intermittent from centre to centre.
- May not require patient consent, in the UK data routinely collected as part of patient's medical care (virtual cohort), no need to pt to attend a study visit.
- Challenge: some data items may be difficult to collect if not part of patient's routine care.

Case-control studies are retrospective; where people with a disease (often, a specific diagnosis) are matched with people who do not have the disease (the 'controls'). Further data is then collected on those individuals and the groups are compared to find out if other characteristics are also different between the two groups.

Recall bias - systematic error due to differences in accuracy or completeness of recall to memory of past events or experiences, e.g. association of cigarette smoking to lung cancer.

In nested case-control studies, cases of a disease that occur in a defined cohort are identified and, for each, a specified number of matched controls is selected from among those in the cohort who have not developed the disease by the time of disease occurrence in the case. Useful if additional data collection is required which cannot be performed through standard data collection.

**Discussion:**

*Q: Are patients informed of experimental studies?*

***A: All patients are informed and sign a form, lab tests – anonymised and patients asked if they want their blood stored for research purposes.***

*Q: Do patients get the results?*

***A: No, data is for the investigator. It is not the clinicians' role to interpret the data.***

***Comment: MACS – only recruited MSM from 1984, till 2001 when they included ethnic minorities and women.***

*Q: Did they have CD4 counts for HIV negative people back then?*
***A: They probably did, someone has done a study to look at progression from seroconversion.***

*Q: What happens when people drop out from fixed studies, do you continue?*
***A: Yes, people die and sometimes investigators will re-open the study.***

*Q: If different people from different hospital develop a similar side effect e.g. gall stones, how do they research on that?*
***A: This is how cohorts capture case series/case note review and document any side effects on different clinics. Written up as a case report and a study will be done.***

*Q: Do you need a certain number of people to do a study?*
***A: If you have about 3, difficult to know, no fixed number.***

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**UK Collaborative HIV Cohort Study (UK CHIC)**
Caroline Sabin, UCL Medical School

UK CHIC, an observational study, was initiated in 2001 to collate routinely collected data from HIV-positive individuals attending some of the largest treatment centres since 1st January 1996. Its specific aims are:

- To describe the characteristics of patients with HIV under care
- To provide information on exposure to combination antiretroviral therapy (cART) and changes to the immunological and virological status of patients over time
- To monitor the frequency of AIDS and survival over time

UK CHIC collects information from 12 clinical centres, MRC, Dept of Infections and Population Health (UCL) and the Health Protection Agency Centre for Infections. Information on HIV infection in the UK comes from a variety of sources; these are often limited in scope. Many clinical centres routinely collect information about patients with HIV infection when they attend. This provides an ideal opportunity to study HIV-infected individuals in their clinical setting can use existing infrastructure for data collection. UK CHIC can include patients from a wide variety of clinics so that the cohort becomes more representative of individuals with HIV infection in the UK.

A recent study presented at BHIVA showed that 10-15% of patients with a CD4 of 200-350 initiated ART in the next six months. 9.5% with a CD4 of <350 had not started cART. It concluded that whilst there is a small cohort of patients who remain untreated despite having had a low CD4 count, these patients probably have CD4 counts that are hovering around 350. The long-term trends for people on treatment show CD4 continues going up on uptake of treatment and most have an undetectable viral loaf after taking treatment for six months.

How does UK CHIC protect your data?

- UK CHIC adheres to extensive confidentiality and has a UK CHIC data protection policy
- Data encrypted before it comes to UK CHIC
- Data checks performed at MRC
- No use of personal information, taken out before data is distributed
- Only minimum dataset required is sent out
- Data to external sources is blinded

Routinely collected clinical data offers opportunities for conducting clinical research at a fraction of the cost of equivalently sized epidemiological studies. UK CHIC is able to monitor adherence to guidelines and identify areas where clinical management could be improved. Study findings cited in (BHIVA) and international treatment guidelines, and frequently discussed in community literature and findings from studies have contributed directly to improvements in patient care.

**UK HIV DRUG RESISTANCE DBASE (UKHIVRD)**
David Dunn, MRC Clinical Trials Unit

David Dunn is a member of the UKCHIC Steering group and works on the UK HIV Resistance Database.

The UKHIVRD was established in 2001 and is a central repository for resistance tests performed as part of routine clinical care throughout the UK. A key feature of the UKHIVRD is extensive patient-level linkage with several clinical cohorts and surveillance databases in the UK. This has allowed analyses that have given important insights into the epidemiology and clinical aspects of HIV drug resistance.

Resistance-conferring mutations are classified according to the class of antiretroviral drug to which they confer a reduced sensitivity. The classes of antiretroviral drugs currently include: NRTIs; NNRTIs; PIs entry/fusion inhibitors and integrase inhibitors.

The systematic collation of HIV drug resistance data from drug-naïve individuals is vital to understanding the epidemiology of transmitted drug resistance (TDR), whilst data from those already receiving antiretroviral drugs provides indirect evidence of the contribution drug resistance makes to virological failure. These data are therefore extremely important for healthcare providers.

The number of resistance tests being carried out has increased as a result of the British HIV Association guidelines recommending routine pre-therapy testing. Testing became available in UK in late 1990s and was given boost by BHIVA guidelines. UKHIVRD links to various studies, UK CHIC being most important. The findings of the UKHIVRD of significant levels of TDR in the UK were instrumental in this recommendation being adopted.

- The database has over 61,000 tests made up of a mixture of tests on naïve, experienced and unknown.
- Number of tests on experienced is constant (~1800)
- There is a real rise in number of naives testing
- 20% of tests are unclassified

**Transmitted Drug Resistance (TDR)**
Tests on treatment-naïve patients tell us about transmitted drug resistance i.e. when patient is infected with strain of virus already carrying resistance mutations. There is concern that an epidemic of primary drug resistance could negate major clinical benefits achieved from anti-HIV drugs. Defining TDR is challenging so the key objective is surveillance of TDR.

From 2001 resistance was around 14% with a steady decline to 2006, steady rise in 2008 to 8%. There is less PI resistance.

**Why the decline in TDR?**

- True reduction in transmitted drug resistance with more effective antiretroviral regimens?
- Testing of treatment-naive patients becoming less selective?
- Some treatment-experienced patients may have been misclassified as treatment-naïve?
- Greater proportion of imported infections from countries where access to ART is limited; UK has many epidemics – MSM and sub-Saharan Africa have limited treatment options

Surveillance of ART-experienced patients provide information on:

- The relative contribution of drug resistance as the cause of virological failure, overall decline in resistance down to 40%
- The need for new non-cross-resistant drugs
- The pool of viruses which is potentially transmissible.

*Q: How often do you have to be tested for resistance?*
***A: Tests are only on experienced patients when there is blip in viral load. A resistance test is done when viral load is above 1000 copies.***

**Criminalisation** - Use of virological or scientific evidence in criminalisation
It is evident from number of the cases examined that investigating officers had effectively been misled into believing that they could obtain scientific proof that A had infected B beyond reasonable doubt. While virological evidence will form part of any prosecution case of this kind, it is important that officers understand its limitations and the possibility of other sources of infection where a complainant has had multiple partners without regular testing.

Data protection – UKHIVRD use same fundamental procedures as UK CHIC.

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**National Study of HIV in Pregnancy and Childhood (NSHPC)**
**and Collaborative HIV Paediatric Study (CHIPS)**
Pat Tookey, UCL Institute of Child Health

NSHPC is the national surveillance of, and research on, obstetric and paediatric HIV in UK and Ireland. NSHPC reports comprehensively on:
- All women diagnosed HIV positive in pregnancy in the UK or Ireland
- All infants born to diagnosed women (exposed infants)
- All children diagnosed in the UK or Ireland with HIV infection (infected children), regardless of country of birth.

Antenatal HIV testing was recommended since 2000 with an uptake of over 90%; ¾ of the women were born in sub-Saharan Africa. 60% of women are aware of their HIV status before current pregnancy and most diagnosed women accept intervention resulting in UK having the lowest rates in the world of mother to child transmission. There has been a rise in the number of women diagnosed before pregnancy to date.

Children born to HIV positive women are followed up to establish infection status. CHIPS collect information on follow up on treatment and health of infected children. For uninfected children; information is available for the first year of life. There is minimal follow up at present, detailed follow up not possible (too many children). NSHPC flags with the Office of National Statistics for death/cancer reports.

NSHPC has no direct contact with patients, does no enrolment, no interventions and has no patient names or addresses. It links mothers and babies by date, place and other details. Information collected about patients is on demographics, timing of women's diagnosis, treatment and outcome of pregnancy, infection status of infants, and diagnosis in children and regular standard surveillance datasets are sent to HPA to combine with adult HIV surveillance data.

Perinatal transmissions still occur mostly due to:
- Women not diagnosed before delivery.
- Had long-standing infection, not offered or declined the offer for testing.
- Women who tested negative at antenatal testing and seroconverted during pregnancy (hence debate on screening more than once in pregnancy, rather than the one time).
- Women who seroconvert while breastfeeding having tested negative during pregnancy.

CHIPS is a collaboration of 70 clinics in the UK and Ireland caring for HIV positive children, NSHPC and the MRC. It currently holds 1645 records. NSHPC sends data for each child to CHIPS who then sends a baseline questionnaire to clinic of care for annual data on:
- Current health and growth
- Treatment details (including any reasons for change)
- Clinical results – viral load, CD4, etc
- Hospital admissions

*Discussion*
*Q: Are those women in your cohort on ARVs?*

***A: Data is for all women diagnosed HIV positive and become pregnant, some may have been on ARVs.***

*Q: Do you know how many women declined testing?*
***A: There is data from surveillance; a woman should be told she could change her mind at any time about testing. Antenatal testing is not mandatory, but is recommended. Clinicians can have a court order to test the child when a child is born.***

*Q: Do you think pregnant women are more at risk of getting HIV during pregnancy?*
***A: Catching HIV during pregnancy is the highest risk for transmitting, as the concentration of HIV in blood is high during the few weeks between infection and seroconversion.***

*Q: How does perinatal transmission occur?*
***A: It occurs mostly among women who lack prenatal care or who are not offered voluntary HIV counselling and testing during pregnancy. Many of the perinatal HIV infections can be attributed to the lack of timely HIV testing.***

*Q: What are the recommendations on women who refuse HIV testing e.g. fear of domestic violence?*
***A: Guidelines recommend voluntary HIV testing to preserve a woman's right to participate in decisions regarding testing to ensure a provider-patient relationship conducive to optimal care for mother and child and to support a woman's right to refuse testing if she does not think it is in her best interest.***

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**HIV in the UK**
Dr Sam Lattimore, Health Protection Agency (HPA)

Dr. Sam Lattimore is a Senior Scientist in the department of HIV and STI, HIV and AIDS Reporting Section for HPA Centre for Infections.

**Monitoring the epidemic at the national level**
Surveillance is the collation of data, and its analysis, to detect trends and events such that action maybe taken to protect and promote public health for the HPA to visualise how the epidemic has evolved in the UK by looking at how the data they have collected has impacted on a few of these mass media campaigns dating from the late 1980's to now. Number of people accessing HIV care has tripled from 2000.

HIV epidemic in the UK is tracked through:
- Case reports of new diagnoses
- Surveillance of people in HIV care through SOPHID
- CD4 surveillance
- Unlinked anonymous programmes to track undiagnosed cases
- Prevalence estimates
- HIV and sexual health screens

**Data protection**
HPA works closely with NGOs, all data is reviewed by PIAG. They closely adhere to the data protection legislation and are there to protect patients health and identity, they do not collect any names and de-duplicate records to link reports.

**New diagnoses and deaths**
These are monitored to determine the number and epidemiological characteristics of newly diagnosed HIV infections and AIDS cases over time. This is done through voluntary and confidential reports from laboratories and clinicians. The advantage of this surveillance is to capture information gathered routinely in the clinical process, allows follow-up of transmission routes.

The disadvantage however is this will not necessarily reflect current HIV transmission, and reporting may be delayed and incomplete. HIV deaths are declining since the introduction of ART in 1996 with approximately 800 AIDS deaths per year. There were 570 deaths in 2008.

Factors that drive new diagnoses include testing, migration and travel, changes in population size (eg MSM), improved reporting and transmission incidents.

Survey of Prevalent HIV Infections Diagnosed (SOPHID) began in 1995 and is a cross-sectional survey of all individuals with diagnosed HIV infection who attend for HIV-related care within the NHS in England, Wales, and Northern Ireland within a calendar year. There is currently around 83 000 HIV diagnosis and almost 23 000 are undiagnosed. People may be infected for many years before they have symptoms. AIDS symptoms develop on average 9-10 years after infection.

BHIVA treatment guidelines recommend starting treatment when CD4 falls between 200-350, one-third of persons diagnoses in the UK have a CD4 of below 200 and is higher among black Africans and Caribbeans.

Unlinked anonymous (blinded) surveys are used to estimate HIV prevalence and associated risk factors, done by using sera residues from blood specimens collected from routine laboratory tests or saliva samples are tested for HIV. Patient identifiable information is irreversibly removed from samples before testing, some information e.g. sex, age group retained. No explicit consent is sought from the patient.

Testing in healthcare settings:
- 93% GUM attendees tested
- 25% of HIV infections remain undiagnosed
- 93% testing uptake in antenatal
- 95% of HIV positive mothers diagnosed before giving birth

**Serological Testing Algorithm for Recent HIV Seroconversion testing (STARHS)**
The standard HIV antibody test tells whether or not a person is infected with HIV, not *when* they were infected. STARHS has been developed to determine whether people with HIV may have been infected recently (within four to six months).

Standard testing strategies are unable to determine how much of this increase has been due to ongoing HIV transmission or to increasing testing among high-risk individuals. STARHS has made it possible to distinguish whether or not an infection is likely to have been acquired recently. STARHS tests have been part of the Unlinked Anonymous Serosurveillance of HIV in MSM for over ten years, and have shown an annual incidence of HIV of around 3% per year.

*Q: Do newly diagnosed queries form people who think they have been newly diagnosed? Are the numbers high?*
***A: The numbers come from voluntary case reporting.***

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**Community Discussion** led by Simon Collins

DHICE - This was a discussion to engage attendees to discuss what they had learnt in the morning. Simon asked how many of the studies the attendees had been aware of. Response was they had been aware of some of the studies and some had heard of the NSCPH for the first time. He asked how many of the studies attendees thought they were part of and most responded that they are part of HPA, SOPHID, UKHIVRD and UK CHIC.

**Resistance – comments and discussion**

Resistance tests are done on all treatment naïve patients on diagnosis. Questions raised to David Dunn were:

- How many samples are stored for later?
- How many samples are re-tested before treatment – in cases of re-infection?
- Are there resistance tests for pregnant women taking MTCP?
- How can we capture data on why people switch treatment?

***A: On HIV diagnosis, sample should be saved. UKHIVRD have information on the date the sample was taken and when the test was done, usually within a week, there is no information on stored samples. There are low resistance rates from stored samples.***
*Q: Information from studies is fed back clinicians. How best can improve to feedback to the community?*
***A: Suggest a simplified summary on CAB forum about each database, HPA brochures are already in readable format, have posters in waiting rooms.***

*Q: Lots of patients change medication without knowing why?*
***A: Possibly resistance.***

**Ethical issues**: - A discussion on ethical issues raised the question on how anonymised the data is – children is birthdates, race, etc. What guidelines govern the kind of data that is published? Collected data is given to commissioners to help plan services.

**Testing:** - Testing in high-risk groups should be properly targeted. 8000 pregnancy women are offered HIV tests antenatally, should we look at testing them more than once during pregnancy?

Meeting recommended that pregnant women should be tested through various trimesters as women get infected while pregnant. Testing of their partners should be standard. This would link to a recent study on achieving an undetectable viral load at delivery. Treatment guidelines reflect practice and what needs to be done.

Discussion concluded that as advocates we should have a contribution to the databases as patients and to bring advocacy skills to members to be able to ask questions.

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**New IT methods to protect data and how they are being used?**
Nathan Lea, Research Fellow, UCL Centre For Health Informatics & Multiprofessional Education (CHIME)

CHIME works with the UKCHIC clinic data managers who collect and send data in order to suggest solutions or improvements to the data processes and ways in which the different databases can be linked. As most patients have concerns around data security and confidentiality he explained how the data is "de-identified" and the techniques used to do that.

De-identification is a process by which an identifying record is rendered "un-identifying" – anonymous – where the association between an individual and their data has been severed so they cannot be identified from it.

Psuedonymisation is where the associations remain, but are represented in an unrecognised fashion (alias).

**Discussion**

*Q: Does the use of d.o.b in Julian date prevent going to identify the patient?*
***A: Pseudonymous i.d. generation links data to the i.d. of the record that has been de-identified.***

*Q: When you de-indentify, is the original data still stored elsewhere or is it destroyed?*
***A: It is not destroyed until the study is complete, depends on the ethics on that study.***

*Q: If original data is not destroyed; you keep the bits you have used; do you go back after say 10years to refer to it?*
***A: UCL retains data for 21 years. You apply to the ethics committee to retain some data.***

*Q: Is there any policy on people who do want de-identified?*
***A: Not aware of any but it could be a way of signing off your privacy and human rights. Risk is that data may not end up where that information will end up and this could compromise a study. Ethics committee would not approve recording such detail, normally cut it out. If we get data we are not supposed to, we have an obligation to get rid of it.***

*Q: Have you had scenarios where you used data the way you want, have shared it and have re-called data back after some time?*
***A: Haven't come across any data withdrawal. There have been incidents in some studies and compromises the relevance of the study. UKCHIC only release data needed by researchers; not the full data from source. CHIPS uses year of birth and age; test x at 3 days, drug y at 8 days, etc.***

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**Bias and how it can affect outcomes from research?**
Caroline Sabin

Bias occurs when there is a systematic difference between the results from a study and the true state of affairs. It is often introduced when a study is being designed, but can be introduced at any stage. Appropriate statistical methods can reduce the effect of bias, but may not eliminate it totally. Increasing the sample size does not reduce bias; it is preferable to design the study in order to avoid bias in the first place. Bias can be categorised in the form of selection bias and information bias.

**Selection bias** - in which there is an error in choosing the individuals or groups to take part in a study. It often refers to the distortion of a statistical analysis, resulting from the method of collecting samples. If the selection bias is not taken into account then any conclusions drawn may be wrong. If the population studied is not representative of the population we want to draw conclusions about, then the study has a selection bias.

**Information bias** - If the way in which we measure an outcome or an exposure within a study is flawed, then there is an information bias.

**Bias due to confounding** - bias involves error in the measurement of a variable; confounding involves error in the interpretation of what may be an accurate measurement. Confounding is a function of the complex interrelationships between various exposures and disease. Confounding can be controlled in the design and in the analysis. The best that can be done about unknown confounders is to use a randomized design. Randomization ensures that potential confounding factors, known or unknown, are evenly distributed among the study groups.

The consequence of confounding is that the estimated association is not the same as true effect. In contrast to other forms of bias, in confounding bias the actual data collected may be correct but the subsequent effect attributed to the exposure of interest is actually caused by something else. An example of confounding is the initial association between alcohol consumption and lung cancer (confounded by smoking, which is associated with alcohol use and an independent risk factor for lung cancer).

**Survivorship bias** occurs when survival is compared in patients who do/do not receive an intervention, when this becomes available sometime in the future. To receive the intervention, patients must survive until its introduction; anyone dying prior to this time will not receive it. It will appear that those who receive the intervention have particularly good survival compared to those who do not receive it.

**Lead-time bias** is used where clinical outcomes are generally better in those who start HAART at higher CD4. This has been used as a justification for recommending starting treatment with a higher CD4. Those starting treatment with a low CD4 have remained well enough for their CD4 to fall to this level and patients who died would be excluded.

Appropriate statistical methods maybe used to minimise the impact of bias, but are unlikely to remove it fully.

***Q: Even after an adjustment, do funders (pharmas) influence these studies?***
*A: All papers are supposed to be reviewed independently by peer reviewers. The D.A.D study is the only study funded by all drug companies with approved drugs in Europe. 10% of people have died in the 10 years of the study.*

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**UK CAB AOB**

Date of next meeting: 9 July 2010
Topic: Primary HIV Infection