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Obtaining informed consent for genomics research in Africa: analysis of H3Africa consent documents

Munung NS, Marshall P, Campbell M, Littler K, Masiye F, Ouwe-Missi-Oukem-Boyer O, Seeley J, Stein DJ, Tindana P, de Vries J.

BACKGROUND:
The rise in genomic and biobanking research worldwide has led to the development of different informed consent models for use in such research. This study analyses consent documents used by investigators in the H3Africa (Human Heredity and Health in Africa) Consortium.

METHODS:
A qualitative method for text analysis was used to analyse consent documents used in the collection of samples and data in H3Africaprojects. Thematic domains included type of consent model, explanations of genetics/genomics, data sharing and feedback of test results.

RESULTS:
Informed consent documents for 13 of the 19 H3Africa projects were analysed. Seven projects used broad consent, five projects used tiered consent and one used specific consent. Genetics was mostly explained in terms of inherited characteristics, heredity and health, genes and disease causation, or disease susceptibility. Only one project made provisions for the feedback of individual genetic results.

CONCLUSION:
H3Africa research makes use of three consent models-specific, tiered and broad consent. We outlined different strategies used byH3Africa investigators to explain concepts in genomics to potential research participants. To further ensure that the decision to participate in genomic research is informed and meaningful, we recommend that innovative approaches to the informed consent process be developed, preferably in consultation with research participants, research ethics committees and researchers in Africa.

Factors associated with dropout in a long term observational cohort of fishing communities around Lake Victoria, Uganda

Andrew Abaasa, Gershim Asiki, Juliet Mpendo, Jonathan Levin, Janet Seeley, Leslie Nielsen, Ali Ssetaala, Annet Nanvubya, Jan De Bont, Pontiano Kaleebu and Anatoli Kamali.

Background

Fishing communities are potentially suitable for Human immunodeficiency virus (HIV) efficacy trials due to their high risk profile. However, high mobility and attrition could decrease statistical power to detect

the impact of a given intervention. We report dropout and associated factors in a fisher-folk observational cohort in Uganda.

Methods

Human immunodeficiency virus-uninfected high-risk volunteers aged 13–49 years living in five fishing communities around Lake Victoria were enrolled and followed every 6 months for 18 months at clinics located within each community. Volunteers from two of the five communities had their follow-up periods extended to 30 months and were invited to attend clinics 10–40 km (km) away from their communities. Human immunodeficiency virus counseling and testing was provided, and data on sexual behaviour collected at all study visits. Study completion was defined as completion of 18 or 30 months or visits up to the date of sero-conversion and dropout as missing one or more visits. Discrete time survival models were fitted to find factors independently associated with dropout.

Results

A total of 1000 volunteers (55 % men) were enrolled. Of these, 91.9 % completed 6 months, 85.2 % completed 12 months and 76.0 % completed 18 months of follow-up. In the two communities with additional follow-up, 76.9 % completed 30 months. In total 299 (29.9 %) volunteers missed at least one visit (dropped out). Dropout was independently associated with age (volunteers aged 13–24 being most likely to dropout), gender [men being more likely to dropout than women [adjusted hazard ratio (aHR) 1.4; 95 % confidence interval (CI) 1.1–1.8)], time spent in the fishing community (those who stayed <1 year being most likely to dropout), History of marijuana use (users being more likely to dropout than non-users [1.7; (1.2–2.5)], ethnicity (non-Baganda being more likely to dropout than Baganda [1.5; (1.2–1.9)], dropout varied between the five fishing communities, having a new sexual partner in the previous 3 months [1.3 (1.0–1.7)] and being away from home for ≥2 nights in the month preceding the interview [1.4 (1.1–1.8)].

Conclusion

Despite a substantial proportion dropping out, retention was sufficient to suggest that by incorporating retention strategies it will be possible to conduct HIV prevention efficacy trials in this community.

Virological Response and Antiretroviral Drug Resistance Emerging during Anti retroviral Therapy at ThreeTreatment Centers in Uganda

Kaleebu P, Kirungi W, Watera C, Asio J, Lyagoba F, Lutalo T, Kapaata AA, Nanyonga F, Parry CM, Magambo B, Nazziwa J, Nannyonjo M, Hughes P, Hladik W, Ruberantwari A, Namuwenge N, Musinguzi J, Downing R, Katongole-Mbidde E; HIV Drug Resistance Working group.

BACKGROUND; with the scale-up of antiretroviral therapy (ART), monitoring programme performance is needed to maximize ART efficacy and limit HIV drug resistance (HIVDR).

METHODS; we implemented a WHO HIVDR prospective survey protocol at three treatment centers between 2012 and 2013. Data were abstracted from patient records at ART start (T1) and after 12 months (T2). Genotyping was performed in the HIV pol region at the two time points.

RESULTS; Of the 425 patients enrolled, at T2, 20 (4.7%) had died, 66 (15.5%) were lost to follow-up, 313 (73.6%) were still on first-line, 8 (1.9%) had switched to second-line, 17 (4.0%) had transferred out and 1 (0.2%) had stopped treatment. At T2, 272 out of 321 on first and second line (84.7%) suppressed below 1000 copies/ml and the HIV DR prevention rate was 70.1%, just within the WHO threshold of ≥70%. The proportion of participants with potential HIVDR was 20.9%, which is higher than the 18.8% based on pooled analyses from African studies. Of the 35 patients with mutations at T2, 80% had M184V/I, 65.7% Y181C, and 48.6% (54.8% excluding those not on Tenofovir) had K65R mutations.

22.9% had Thymidine Analogue Mutations (TAMs). Factors significantly associated with HIVDR prevention at T2 were: baseline viral load (VL) <100,000 copies/ml [Adjusted odds ratio (AOR) 3.13, 95% confidence interval (CI): 1.36-7.19] and facility. Independent baseline predictors for HIVDR mutations at T2 were: CD4 count <250 cells/µl (AOR 2.80, 95% CI: 1.08-7.29) and viral load ≥100,000 copies/ml (AOR 2.48, 95% CI: 1.00-6.14).

CONCLUSION; Strengthening defaulter tracing, intensified follow-up for patients with low CD4 counts and/or high VL at ART initiation together with early treatment initiation above 250 CD4 cells/ul and adequate patient counselling would improve ART efficacy and HIVDR prevention. The high rate of K65R and TAMs could compromise second line regimens including NRTIs.

The social context of gender-based violence, alcohol use and HIV risk among women involved in high-risk sexual behaviour and their intimate partners in Kampala, Uganda

Schulkind J, Mbonye M, Watts C, Seeley J.

This paper explores the interaction between gender-based violence and alcohol use and their links to vulnerability to HIV-infection in a population of women and their regular male partners in Kampala, Uganda. Data derive from 20 life history interviews (10 women and 10 men). Participants were drawn from a cohort of women at high risk of sexually transmitted infection (including HIV). Six of the women were current or former sex workers. Findings reveal that life histories are characterised by recurrent patterns of gender inequity related to violence, limited livelihood options and socioeconomic disadvantage. Overall, findings suggest women are able to negotiate safer sex and protect themselves better against abuse and violence from clients than from their intimate partners, although the status of men as 'client' or 'partner' is transitory and fluid. Among male respondents, alcohol led to intimate partner violence and high levels of sexual-risk taking, such as engagement with sex workers and reduced condom use. However, male partners are a heterogeneous group, with distinct and contrasting attitudes towards alcohol, condom use and violence. Actions to address gender-based violence need to be multi-pronged in order to respond to different needs and circumstances, of both women and men.

Prediction of Peak Expiratory Flow Rate in a Ugandan population

Nakubulwa S; Baisley K; Levin J; Nakiyingi-Miiro J; Kamali A

Background; Peak expiratory flow rate (PEFR) measurement is one of the commonly used methods for assessing lung function in general practice consultations. The reference values for use by this method are mainly from Caucasian populations; data for African populations are limited. The existence of ethnic and racial differences in lung function necessitates further generation of PEFR reference values for use in African populations.

Objective; to generate equations for predicting PEFR in a Ugandan population.

Methods; the PEFR study was cross-sectional and based in rural south-western Uganda. Participants were aged 15 years or more, without respiratory symptoms and were residents of the study area. Multiple regression equations for predicting PEFR were fitted separately for males and females. The model used for PEFR prediction was: logePEFR = intercept + a(age, y) + b(logeage) + c(1/height in cm), where a, b and c are the regression coefficients.

Results; the eligible study population consisted of 774 males and 781 females. Median height was 164 cm (males) and 155 cm (females). The majority of participants had never smoked (males 76.7%; females 98.3%). The equation which gave the best fit for males was logePEFR = 6.188 – 0.019age + 0.557logeage – 199.945/height and for females: logePEFR = 5.948 – 0.014 age + 0.317logeage – 85.147/height.

Conclusion; The curvilinear model obtained takes into consideration the changing trends of PEFR with increasing age from adolescence to old age. It provides PEFR prediction equations that can be applied in East African populations.

Macrophage inflammatory protein-1 beta and interferon gamma responses in Ugandans with HIV-1 acute/early infections

Obuku AE, Bugembe DL, Musinguzi K, Watera C, Serwanga J, Ndembi N, Levin J, Kaleebu P, Pala P.

Control of HIV replication through CD4+ and CD8+ T cells might be possible, but the functional and phenotypic characteristics of such cells are not defined. Among cytokines produced by T cells, CCR5 ligands, including macrophage inflammatory protein-1 beta (MIP-1β), compete for the CCR5 coreceptor with HIV, promoting CCR5 internalization and decreasing its availability for virus binding. Interferon (IFN)-γ also has some antiviral activity and has been used as a read-out for T cell immunogenicity. We used cultured ELISpot assays to compare the relative contribution of MIP-1β and IFN-γ to HIV-specific responses. The magnitude of responses was 1.36 times higher for MIP-1β compared to IFN-γ. The breadth of the MIP-1β response (45.41%) was significantly higher than IFN-γ (36.88%), with considerable overlap between the peptide pools that stimulated both MIP-1β and IFN-γ production. Subtype A and D cross-reactive responses were observed both at stimulation and test level, but MIP-1β and IFN-γ responses displayed different effect patterns. We conclude that the MIP-1β ELISpot would be a useful complement to the evaluation of the immunogenicity of HIV vaccines and the activity of adjuvants.

Psychological correlates of suicidality in HIV/AIDS in semi-urban south-western Uganda.

Rukundo GZ, Mishara B, Kinyanda E.

Abstract

There is a paucity of data on the prevalence of suicidality in HIV/AIDS, and associated psychological factors in sub-Saharan Africa, shown to be high in Uganda. Yet, the region accounts for over 70% of the world HIV burden. Our study used a cross-sectional survey of 226 HIV-positive (HIV+) adults and adolescents (aged 15-17 years) in Mbarara, Uganda. The relationship between suicidality and depressed mood, anxiety symptoms, state anger, self-esteem, trait anger and hopelessness was examined; anger was the predominant factor in suicidality, suggesting that anger management could potentially lower the prevalence of suicidality.
