EB_2020_4_Cherif

Ebola Data Platform - Data Access Application Form

Please review the Data Access Guidelines and the Data Transfer Agreement[1] before completing this form. Note that the details of all approved applications will be made publicly available on the Ebola Data Platform website.

Please complete all sections of this form *fully* and return to ebolaDAC@iddo.org with the following attachments:

- Academic CV of the Lead Requestor (any format)
- Conflict of Interest Forms completed by the Lead Requestor and each of the Co-applicants listed

SECTION A: RESEARCHER / RESEARCH TEAM INFORMATION	
Lead Requestor Details *(please attach an academic CV)*	
Title	**Dr**
First name (given name)	**Mahamoud Sama**
Surname (family name)	**CHERIF**
Gender	**Male**
Position at employing organisation/ institution	**Research assistant / Gamal Abdel Nasser University of Conakry**
ORCID ID https://orcid.org/	
Email	[redacted]
Telephone/Skype/WhatsApp	[redacted]
Employing Organisation/Institution *Institution with a remit including health, research or academic pursuit, and with legal status which includes the scope to sign the **Data Transfer Agreement***[1]	
Institution name	**Gamal Abdel Nasser University of Conakry, Guinea**
Address	**Commune de Dixin, BP : 1147, Conakry.**
Department (if applicable)	**Faculty of Sciences and Heath Technics**
Please acknowledge that your institution agrees to execute the Data Transfer Agreement (in the case of your application being approved)	YES (delete as appropriate)

[1] The ***Data Transfer Agreement*** *is a contract between the University of Oxford (on behalf of IDDO) and the recipient institution that governs the legal obligations and restrictions, as well as compliance with applicable laws and regulations, related to the **transfer** of such **data** between the parties. The named Institution will be required to sign the data transfer agreement before the release of any data by IDDO.*

Co-applicants (ALL individuals accessing the data must be listed. Any additions must be notified to the Ebola DAC) *Add rows as necessary.* *Please attach copies of the Conflict of Interest Form, completed by each of the individuals above.*	
1. Name	Prabin Dahl
1. Title	Statistician
1. Organisation/Institution	IDDO Oxford.
2. Name	Trokon Yeabah
2. Title	Researcher
2. Organisation/Institution	National Public health Institute of Liberia
3. Name	Kwame O'oneil
3. Title	Reseacher
3. Organisation/Institution	Ministry of Health and Sanitation, Sierra Leone (MoH&S,SL)

SECTION B: RESEARCH PLAN

Title of Proposed Research	Characterising evolution of clinical signs and symptoms in patients with Ebola Virus Diseases (EVD) in west Africa at baseline and during hospitalisation period: An individual participant data meta-analysis
Is this a re-submission of a previous application that has been reviewed by the Ebola DAC? If so, please provide the surname of the Lead Requestor and submission date of the previous application.	No

Summary of Research in Lay Language *(suggested ~ 100 words)*

Sparse data available from extremely challenging conditions during the 2014-2016 epidemic has shown several factors are predictive of mortality. These include: high viral load, age of the patients (infants, young children <5 years age and elderly > 60 years), haemorrhagic fever, interval between onset of symptom and admission (delayed admission), pregnancy, symptom of confusion, chest pain, coma, and co-infection with malaria.

In an emergency outbreak situation, it is important to have a reliable indicator for medical screening of the patients and monitoring the evolution of the signs and symptoms associated with the disease to identify those at substantially increased risk of death. This can ensure optimisation of palliative and curative care delivery.

Scientific Summary of Research *(suggested maximum 300 words)*

This application seeks to characterise the evolution of the signs and symptoms of EVD using the individual patient data hosted by the IDDO Ebola data platform. Individual participant data meta-analysis (IPD-MA) is currently considered to be the gold-standard approach for synthesis of results across several studies and provides a unique opportunity to characterise the evolution of the disease symptoms.

Outcome will be each of the following symptoms or signs: fever, bleeding, confusion, conjunctivitis, intense fatigue, hiccups, vomiting, diarrhoea, anorexia, hypovolemic shock, anaemia, temperature, blood pressure; and clinical biomarkers: white blood cell count, haemoglobin, platelet, C-reactive protein, electrolytes, creatinine, liver transaminases, CPK, lactic acid, base excess, PTT; viral load, PCR cycle threshold antibody titres.

Summary of Research Objectives *(suggested maximum 200 words)*

Primary objective

- To describe clinical signs and symptoms at baseline and during hospitalisation period in ETC in patients with confirmed EVD

Secondary objectives

- To carry out longitudinal mixed effects modelling to characterise the population averaged trajectory of the clinical signs and symptoms

- To carry out competing risk survival analysis to estimate the cumulative incidence of fever cleareance, hemataological recovery, and viral clearance (If data permitting)

Primary and Secondary Outcome Measures *(suggested maximum 200 words)*

The primary outcomes are the clinical signs and symptomas at baseline and during follow-up hospitalisation period in ETC

Proposed Methodology and Statistical Analysis Plan *(suggested maximum 400 words)*

Primary objective:

In patients with a laboratory-confirmed EVD diagnosis, the frequency, relationships at baseline and temporal trends of clinical signs, symptoms, biomarkers, and the dynamics of viral load will be explored. Descriptive statistics (mean and standard deviation, geometric mean or median and range, and frequencies as appropriate), scatter plots, box plots and spghetti plots over time will be presented overall, within each country and at different time in the epidemic.

The evolution of the presence of different clinical signs and symptoms will be measured from the time of patient admission until death or discharge. The proportion of patients with given signs and symptoms will be presented at given time point during hospitalisation period (e.g: days 1, 2, 3 etc.).

The proportions will be presented by groups of interests, some of which (but not restricted to) are: age categories, gender, pregnancy, high viral load, country, different timepoints in the epidemics, duration of symptoms before admisison, intervention regimens.

Secondary objectives:

Longitudinal mixed effects modelling

Longitudinal mixed effects modelling with random slopes for patients will be considered to characterize the population averaged trajectory of the parameters of interest over time and variability between patients. Host factors will be used to explain this variability and group-based trajectories for geographic locations will be studied.

Competing risk survival analysis for symptomatic resolution

Data permitting, the time to symptomatic resolution of fever, anaemia and viral load (or any other symptoms) will be generated using competing risk survival analysis using cumulative incidence function (CIFs). In generation of CIFs, death or discharge will be considered as a competing risk endpoint. Differences in CIFs estimates between groups of interest will be tested using the Gray's *k*-sample test.

However, identification of putative factors associated with the symptomatic resolution will be carried out using Cox's regression analysis.

Ethics *(suggested maximum 300 words)*
Provide details of any ethical considerations relating to the research proposal. Additionally, list any approvals required by your institution to undertake this work, list reference numbers of any approved proposals, or explain why no approvals are required.

This project involves accessing and re-using patient data collected in the context of a public health emergency for research. To ensure the ethical integrity of the project, the lead requestor's key responsibility is to protect the privacy and interests of the individuals and communities of data origin. This application will be using retrospective anonymised random data. This would ensure that the confidentiality of patients is maintained.

The ethical clearance for this study has been obtained from the Guinean National Ethics Committee (CNERS).This approval includes the project's detailed approach to data access, informed consent, vulnerable participants, protection of privacy, community engagement and benefits sharing, and will be renewed annually throughout the project. The project for which this application is made, adopts the data security measures put in place by the Ebola Data Platform. This is in compliance with general data protection regulation.

Publication and Dissemination Plan *(suggested maximum 300 words)*
Provide details of plans for authorship/acknowledgement of data contributors. Provide details of timelines for publication and dissemination of research findings.

The analytic results from the study will be presented in the forms of graph for easy understanding. Dissemination of the findings from the study will be published in Medical and review journals as well as posted on website of the Ministry of Health and sanitation Sierra Leone, other websites as appropriate and also on social media streams.

The essence of this application is to promote access to data and make available information on Ebola that would enable a robust response to any future outbreak. There will be local and international conferences wherein results and outputs will be shared. The first meeting is expected to happen in 2021 in Freetown sierra Leone and 2023 in Conakry Guinea. As a follow up to the meetings, the results will also be published in medical journals and gazette. However, this will limit access to the information emerging from the project. To improve on access, many avenues will be explored including but not limited to electronic, print and social media platforms. Within the tropics especially in districts that have no connectivity to the internet or even SMS using telephone technology, the aforementioned means of communication would not be effective. To salvage this situation focus discussion at district level especially with the Survivor communities will be held facilitated by district Medical officers .This structured means of communication is specific to Sierra Leone for this particular application, however other players within the research community are also encouraged to use this for communication of the results of the project for which this application is made.

Addressing Knowledge Gaps (*suggested maximum 300 words)*
Provide details of how this research will address knowledge gaps of importance to those affected by or at risk of emerging and poverty-related diseases.

The Ebola outbreak of 2013-2016 reinforced the need for collaboration and an integrated approach to the response to an outbreak of such magnitude. Since Ebola appeared in 1976 data and information has been scanty and not well coordinated. This project seeks to address that need by cross referencing different data sets and put forward a meaningful case definition for EVD that will influence policy and decision making.

There is currently a paucity of Information regarding best treatment options. The current analysis will help in characterisation of the signs and symptoms of the patient

This will go a long way in reducing case fatality rates and mortalities associated with EVD. Due to this paucity of information , the WHO Ebola/Marburg Research and Development Road map has called for the establishment of an interoperable system to enhance capabilities for collecting ,reporting, analysing and sharing data. The EDP is a forum wherein several entities including the national health agencies and Ministries of health of Sierra Leone Guinea and Liberia and other institution like West Africa Health Organisation World health organization and Oxford University to name but a few are collaborating to pool resources in coming up with research questions of priority which the project for which this application is been made seeks to answer in an attempt to address the need identified by WHO.

Ebola-affected countries and its experts will guide the process in coming up with priority questions and the capacity needs that have to be addressed to ensure that a robust health system is created to respond to any future outbreaks. The results from this application would form the bedrock on which these recommendations to the various Government, institutions and Non- Government organizations will be made.

To the survivor cohort an explanation would be put forward for the improved case fatality and also triangulate the most prevalent complication as a sequela to their infection. Of concern to the survivors is their potential risk to their loved ones. Information on the prevalence of the virus or viral fragment of Ebola has now improved but still not yet optimal. Due to the large quantum of data from the EDP, an attempt will be made to help reform sexual and reproductive health guidelines for survivors.

The prognostic indicators as determined from this study will inform the management of viral haemorrhagic fever in Guinea. It will place emphasis on which biomarkers that should be looked for to show progress of the disease and delineate specific interventions that would affect the health outcome. Hence it will trigger the evaluation of laboratory test and diagnostic required for Viral Haemorrhagic fever patients .This will then inform policy and guidelines on laboratory test done for Ebola patients.

Equity and Capacity Building *(suggested maximum 300 words)*
Provide details of how this research will support health equity and/or capacity building in endemic regions affected by or at risk of emerging and poverty-related diseases.
Please refer to the Ebola Data Platform Approaches to Capacity Building for guidance.

The project for which this application is made seeks to improve on the preparedness response and treatment of future outbreaks of Ebola Virus Disease.it is a collaborative effort between Ministry of Health Sierra Leone, the National public health institute of Liberia the National Health Security Agency of Guinea and Oxford University. Importantly, the approach to evidence generation taken by this project maximises benefits to the communities affected by Ebola. As part of its responsibility for ensuring capacity building the researcher has been awarded a TDR clinical fellowship for one year located in Oxford to do statistical and Data management. The skills acquired during his training will be used in the Analysis of the Data stored in repository of the EDP that would go a long way in influencing policy making in the Ministry of Health and Sanitation in Sierra Leone. As part of his training he is expected to do reviews and publish results and recommendation from his work which could be leveraged on by local researches within Sierra Leone. The bond signed between the researcher and the Ministry of Health and Sanitation, obligates the researcher to do a cascade of his training in Data Management and Statistical analysis to Monitoring and evaluation officers and researchers within the directorate of planning policy and information in the form of training of trainers for onward training of researchers in the districts.

The strength of the Ebola case definition has also been questioned due to low sensitivity and specificity demonstrated in a number of settings. The project partners have prioritised the need to better understand how to balance the strength of the definition with the utility of the definition in different contexts for future outbreaks. By leveraging the pooling of the largest individual patient data repository assembled under the EDP, the most conclusive evidence on these research questions can now be generated by this project. This will be used to influence policy on future management of Ebola.
The equitable and sustainable partnership between the various partners is built on collaboration and data sharing to enhance capacity building and training opportunities for a more robust national health security system.

Funding *(suggested maximum 100 words)*
Provide details of how this research will be funded/resourced.

The UK MRC grant will support the remuneration of the researcher, Co-investigators and principal investigator and logistics for software traveling cost and review meetings in Conakry, Monrovia and Freetown. MOHS Sierra Leone will pay for the cascade of training and result dissemination in the districts.

Scientific Review *(suggested maximum 200 words)*
Provide details of how the details of the project outlined above have been scientifically reviewed. This could be by your institution, a funder/donor or review committee.

The research priority as outlined in this application is part of the research questions in the Ebola data Platform research agenda. This application was reviewed by Ben cooper a renowned statistician.

SECTION C: DATA

Data Variables
*Provide a list of the **data variables and data sources** required to achieve the research objectives.*
Note: Data sources can be listed as populations (e.g. all EVD-positive pregnant women, or all children under 16 years of age from Liberia) or as datasets from a source listed on the Accessing Data web page (these should be named by 'Contributing organisation, Country, City' as listed in the table). Get in touch if you have any questions about this ebolaDAC@iddo.org

Based on the case definition given by WHO which was applied in the outbreak of 2013 - 2016 which reads: 1) any person, alive or dead, who has (or had) sudden onset of high fever and contact with a suspected, probable, or confirmed EVD case-patient, or a dead or sick animal; or 2) any person with sudden onset of high fever and ≥3 signs/symptoms (headache, generalized or articular pain, intense fatigue, nausea/vomiting, loss of appetite, diarrhoea, abdominal pain, difficulty swallowing, difficulty breathing, hiccups, miscarriage); 3) unexplained bleeding; or 4) sudden unexplained death.

The data variables are:

Patient demographics

- Age
- Gender
- Weight
- Country of residence
- location of Ebola Treatment Centre
- Profession

Clinical signs and symptoms

- Abdominal pain
- Fever
- Diarrhea
- Vomitting
- Bleeding
- Confusion
- Unconsciouness
- Hypovolemic shock (dizzy)
- Anaemia

- Co-morbidity with malaria
- Body temperature
- Blood pressure

Disease diagnosis

- Laboratory test to confirm haemorrhagic fever diseases
- Laboratory test to confirm other diseases (HIV, malaria, tuberculosis)
- Date of sample collection
- Date of laboratory test

Disease exposure factors

- History of traveling to known hotspot area
- Direct contact with EVD suspected or confirmed case
- Participating in the funeral of an EVD suspected or confirmed case
- Touching the body of an EVD suspected or confirmed case
- Time between symptomatic onset to admission at ETC
- Time between admission at ETC and death/discharge

Disease specific characteristics

- Viral load (or cycle threshold value)
- Date of admission
- Date of onset of symptom
- Symptoms present at the time of admission (self-reported)
- Clinical signs (observed by a clinician)

Treatment (Debatable whether to include or not in a prognostic models)

- Antiviral/antibacterial/rehydratation (infusion or oral) therapy
- Duration and dosage of treatment administered
- Route of administration
- Date of treatment start
- Date of treatment completion

Laboratory parameters

- White blood cell count
- Haemoglobin
- Platelet
- C-reactive protein
- Electrolytes
- Creatinine
- Liver transaminases
- CPK
- Lactic acid
- Base excess
- PTT
- Antibody titers

Epidemiological demographics

- Time since Ebola outbreak per country
- The number of cases at that week per country

Formulaire de demande d'accès aux données Ebola

Veuillez consulter les directives d'accès aux données et l'accord de transfert de données[†] avant de remplir ce formulaire.

Veillez à remplir toutes les sections de ce formulaire *entièrement* et retourner à ebolaDAC@iddo.org avec les documents suivants joints:

- CV académique du demandeur principal
- Formulaires relatifs aux conflits d'intérêts remplis par le demandeur principal et chacun des codemandeurs

SECTION A: INFORMATION SUR LE CHERCHEUR / L'ÉQUIPE DE RECHERCHE	
Détails du demandeur principal *(veuillez joindre un CV académique)*	
Titre	
Préom	
Nom (nom de famille)	
Sexe	
Poste au sein de l'organisation / institution d'emploi	
ID ORCID https://orcid.org/	
Email	
Téléphone/Skype/WhatsApp	
Organisation / Institution d'emploi *Institution avec un mandat incluant la santé, les poursuites de recherche ou d'étude, et disposant d'un statut juridique ayant la capacité de signer* ***l'accord de transfert de données***	
Nom de l'institution	
Adresse	
Département (si applicable)	
Votre institution accepte-t-elle de signer **l'accord de transfert de données**? (dans le cas où votre demande est approuvée)	OUI / NON

[†] ***L'accord de transfert de données*** *est un contrat entre l'Université d'Oxford (pour le compte d'IDDO) et l'institution destinataire, qui régit les obligations et restrictions juridiques, ainsi que le respect des lois et réglementations applicables, en ce qui concerne le* ***transfert*** *de ces* ***données*** *entre les parties. L'établissement désigné devra signer l'accord de transfert de données avant la publication des données par IDDO.*

Codemandeurs (TOUTES les personnes accédant aux données doivent être répertoriées. Tous les changements doivent être notifiés au CAD Ebola) *Ajouter des lignes si nécessaire.* *Veuillez joindre une copie du formulaire de conflit d'intérêts rempli par chacune des personnes susmentionnées.*	
1. Nom	
1. Titre	
1. Organisation / Institution	
2. Nom	
2. Titre	
2. Organisation / Institution	
3. Nom	
3. Titre	
3. Organisation / Institution	
SECTION B: PLAN DE RECHERCHE	
Titre de la recherche proposée	
S'agit-il d'une nouvelle soumission d'une demande antérieure qui a été examinée par le CAD Ebola ? Si oui, veuillez indiquer le nom de famille du demandeur principal et la date de soumission de la demande antécédante.	
Résumé de la recherche en langage non scientifique *(suggéré ~ 100 mots)*	
Résumé scientifique de la recherche *(maximum de 300 mots suggéré)*	
Résumé des objectifs de recherche *(200 mots maximum suggérés)*	
Mesures des résultats primaires et secondaires *(200 mots maximum suggérés)*	
Méthodologie proposée et plan d'analyse statistique *(maximum de 400 mots suggéré)*	
Ethique *(maximum de 300 mots suggéré)* *Fournissez des détails sur toutes les considérations éthiques relatives à la proposition de recherche. En outre, indiquez toutes les approbations requises par votre institution pour effectuer ce travail ou expliquez pourquoi aucune approbation n'est requise.*	

Plan de publication et de diffusion *(maximum de 300 mots suggéré)*
Fournir des détails sur les délais de publication et de diffusion des résultats de recherche. Fournir des détails sur les plans pour la paternité / reconnaissance des contributeurs de données.

Combler les lacunes dans les connaissances (*maximum de 300 mots suggéré)*
Indiquez en détail comment cette recherche permettra de combler les lacunes de connaissances d'importance pour les personnes touchées par les maladies émergentes ou liées à la pauvreté ou à risque de le devenir.

Équité et renforcement de capacités *(maximum de 300 mots suggéré)*
Indiquez en détail comment cette recherche contribuera à l'équité en santé et/ou au renforcement de capacités dans les régions d'endémie touchées par les maladies émergentes ou liées à la pauvreté ou à risque de le devenir. Veuillez vous référer aux approches de la plateforme de données Ebola pour le renforcement des capacités.

Financement *(maximum suggéré 100 mots)*
Fournissez des détails sur la manière dont cette recherche sera financée.

Examen scientifique *(maximum suggéré 200 mots)*
Fournir des détails sur la façon dont les détails du projet décrit ci-dessus ont eu une évaluation scientifique. Cela pourrait être par votre institution, un donateur ou un comité de révision.

SECTION C: DONNÉES

Variables de données

*Fournissez une liste des **variables de données et des volumes** nécessaires pour atteindre les objectifs de recherche. Note : Les sources de données peuvent être des populations (par exemple, toutes les femmes enceintes séropositives ou tous les enfants en Liberia qui à moins de 16 ans) ou des ensembles de données provenant d'une source figurant sur la page web Accès aux données (ces sources doivent être nommées par "Organisation contributrice, pays, ville" comme indiqué dans le tableau). Contactez-nous si vous avez des questions à ce sujet eboladac@iddo.org*