EB_2020_2_Oneill

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)	**Kwame**
Surname (family name)	**Oneill**
Gender	**Male**
Position at employing organisation/ institution	**District Medical officer**
ORCID ID https://orcid.org/	**0000/-0003-0711-4177**
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	Ministry of Health and Sanitation Sierra Leone
Address	4th floor Youyi building Brookfields, Freetown ,Sierra Leone
Department (if applicable)	Primary Health care
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	Sama Cherif
3. Title	Reseacher
3. Organisation/Institution	National Health Security agency Guinea

SECTION B: RESEARCH PLAN

Title of Proposed Research	Inform and risk stratify the EVD case definition through analysis of clinical data at presentation
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.	Yes Oneill 13/03/2020

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

The Ebola virus one of the Viral haemorrhagic fever is a highly infectious disease that can be transferred from one person to another or from an animal e.g. Bat to a human. The previous case definitions for EVD were not sufficient to identify all cases with signs and symptoms of Ebola, which may be similar to other diseases like Malaria and Typhoid Fever.
This application seeks to improve on the case definition of Ebola by looking at the huge amount of data emanating from the 2014-2016 Ebola outbreak in west Africa .The identification of the EVD positive patient will help in providing specialist care for that patient , whiles ensuring the non EVD patient continue with routine outpatient consultation. This would go a long way in breaking the transmission of the disease and provide the surveillance team with adequate information on contact tracing and line listing.

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

The Ebola virus disease of 2014-2016 showed how inadequate the case definition of EVD is .This is in part attributed to its low sensitivity and specificity demonstrated in known settings[1,2]
This application seeks to improve on the case definition by looking at the huge amount of patient data contained in the Ebola data platform. This data will be analysed to risk stratify the case definition of Ebola.
The study will look at key variables like the all signs and symptoms at presentation at the Ebola treatment unit , history of exposure to EVD patient be it a live or dead contact, Laboratory results on admission and follow up and pregnancy status .A common denominator in the laboratory test will be Reverse transcriptase polymerase chain reaction as the confirmatory test for EVD positive or negative.
This project will put forward a more definitive case definition that would capture as many EVD patient whilst excluding non EVD with similar signs and Symptoms. This would inform policy

making and ensure leveraging on the the data to predict transmission trends and how transmission can be halted from EVD patient to Health personnel and the general population.
A mixed logistics regression model will be fitted to capture the interaction of risk factors with geographical location and time of infection and admission in correlation to morbidity and mortality rates. The statistical analysis will be done using the PRISMA guideline for IPD meta-analysis.
To ensure feed back and leveraging on this application for future referencing on a more appropriate case definition , dissemination will use reviews, electronic print and social media as a platform.

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

Broadly this application aims at improving management of future outbreaks of Ebola Virus Disease. The key specific objectives are:

1) To cross reference several data sets to put forward a more definitive case definition that identifies all Ebola patients within a population be it a community, District or County
2) To put forward evidence based criteria to separate non EVD patients from EVD patients for routine care.
3) To prevent/break transmission of EVD during future outbreaks by leveraging on the definitive case definition.
4) Create a regional network that will reinforce the depth and availability of capacity for improved health security
5) Confirmed EVD cases by reverse transcriptase polymerase chain reaction

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

The primary outcome is the confirmed case of EVD defined by positive result of real-time reverse transcription polymerase chain reaction (RT-PCR) with at least one sign and symptom of Ebola.

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

A mixed effects logistic regression model (or Cox model) will be fitted. Random intercepts for EVD treatment centres will be included in all models (as frailty terms in Cox regression); and for patients will be included in longitudinal models. Interactions of main risk factors with geographical locations and time during the outbreak will be examined. Variable selection process will follow recommendations in Heinze et al (2018)[3].
Statistical analysis will follow PRISMA guidelines for IPD meta-analysis and TRIPOD statement for the development of prediction models. The risk of bias for individual studies will be evaluated at the outcome level assessing: missing data and methodology to evaluate outcomes (if applicable). Internal validation of prediction model will be performed using bootstrapping and cross-validation, estimating overfitting of the developed models and optimism in their predictive performance. Missing data is anticipated and statistically principled approaches of multiple imputation or inverse probability weighting under Missing At Random (MAR) mechanism will be used; sensitivity analysis considering departures from this mechanism will be conducted. All the codes and the details of the fitted models will be made publicly available to facilitate an individual external validation and incorporation into existing diagnostic applications.

Patients with no RT-PCR results will be excluded from analysis. The study/analysis will delineate the Ebola case definition. The model will be based on clinical presentations that includes signs and symptoms, laboratory values, PCR negative or positives test results. Looking at various data sets, the analysis will attempt to contrast the sensitivity and specificity of test thereby informing the development of accurate diagnostic tools.
The ethical clearance for this study has been obtained from the Ethics committee of the Ministry of Health and Sanitation in Sierra Leone.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.

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 Sierra Leone Ethics Committee has given its clearance for this project. 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 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 projects 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 was a paucity of Information about best treatment options .The prognostic indicators will help guide treatment protocols for EVD and other viral haemorrhagic fevers. 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.[4] 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 exposure factors and how they affect the patient will help in strengthening the response in terms of Surveillance with specific reference to contact tracing and active case search. This would inform protocols or guidelines on infection prevention and control within the health facilities and community. These exposure factors will be taken into consideration in defining a comprehensive case definition that would capture all suspected and probable cases of Ebola.

Once this case definition is been defined the Electronic Integrated Disease Surveillance and Reporting (eIDSR) tools will be updated to capture information on Ebola as one of the reported Diseases of importance in Sierra Leone. The tools will then be widely distributed to all Health Facilities.

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 funding landscape for the project for which this application is made involves two main donors and the Ministry of Health and Sanitation counter- part funding. For six months the salary of the Researcher will be paid by TDR/WHO to do the analysis of the data . Whiles going forward the UK MRC grant will support the remuneration of the researcher, Co-investigators and principal investigator and logistics for soft ware 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. In the Spirit of collaboration as one of the tenets of the Ebola Data Platform, this application and project is been supervised by Dr Alie Wurie ,Director of Primary Health Ministry of Health and Sanitation Sierra Leone.

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 belong to the following broad categories:
1) All patients with signs and symptoms of Ebola reporting at the Ebola treatment unit
2) All contact with a suspected, probable or confirmed EVD patient
3) Pregnancy status
4) All patients with positive Reverse Transcriptase polymerase chain reaction including asymptomatic patients
5) All unexplained death

Therefore, the data variables under consideration are:
Demographics
Age
Sex
Date illness started
Date of Admission
Signs and symptoms
Fever
Headache
Vomiting
Red eyes
Bleeding
Joint pain
Abdominal pain
Musculoskeletal pain
Difficulty in breathing
Sore throat
Insomnia
Pain behind Eye
Exposure factor
Lived with someone ill in the family
Someone recently died in the family
Visited an ill person
Visited a quarantine home
Been to a funeral recently
Touched body fluid of confirmed Ebola patient
Had sex with a confirmed Ebola patient
Handled clothes or personal item of confirmed Ebola patient

Contact with confirmed Ebola corpse
Diagnosis
Final status (confirmed by RT-PCR)
Pregnancy Status

Data Source : Ebola Data Platform data on Ebola virus disease.
This study seeks to delineate a more specific and comprehensive case definition of Ebola Virus Disease, hence all variables captured are based on real time symptoms as exhibited by patients that would qualify them as suspected of having Ebola. However the signs and symptoms of Ebola are not specific to Ebola but could be attributed to a number of Diseases hence to reduce the burden of testing all individuals with non-specific signs and symptoms, the history of contact comes into play .Once you are a suspected case your final status will be determined by a laboratory test.
The most reliable test available in Sierra Leone to confirm Ebola is the RT-PCR. This is the test widely used to confirm the status of a suspected case. Hence the use of RT-PCR as one variable in the Study.
Limited studies exist on Ebola in pregnancy. This application will attempt to look at data sets that include pregnant women who were positive for Ebola.

[1]Desclaux A, Malan MS, Egrot M, Group KS for ES, Group FA for E-CS. Surveillance in the field: Over-identification of Ebola suspect cases and its contributing factors in West African at-risk contexts. Glob Public Health. 2019 May 4;14(5):709–21.
[2] Hsu CH, Champaloux SW, Keïta S, Martel L, Bilivogui P, Knust B, et al. Sensitivity and Specificity of Suspected Case Definition Used during West Africa Ebola Epidemic - Volume 24, Number 1—January 2018 - Emerging Infectious Diseases journal - CDC. [cited 2020 Jan 3]; Available from: https://wwwnc.cdc.gov/eid/article/24/1/16-1678_article
[3]Heinze G, Wallisch C, Dunkler D. Variable selection - A review and recommendations for the practicing statistician. Biom J. 2018 May;60(3):431-449. [4]CIDRAP. Ebola/Marburg Research and Development (R&D) Roadmap. WHO Research and Development Blueprint. May 2018. Available from: https://www.who.int/blueprint/priority-diseases/key-action/ebola

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*