AMoCo Study

Abortion-related **Mo**rbidity and **Mo**rtality in **Co**nflict-affected and fragile settings **Study**

Study protocol version 3.9
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Epicentre – MSF
Guttmacher Institute
Ipas

Title: AMoCo Study

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Study partners:

- Ipas: international organization solely focused on expanding access to safe abortion and contraceptive care (USA-based).
- Epicentre – Médecins Sans Frontières (MSF): Epicentre conducts research and training activities in the range of MSF interventions. MSF is an international independent medical humanitarian organization, providing medical assistance to people affected by conflict, epidemics, disasters, or exclusion from healthcare. Inside the MSF movement, Epicentre, MSF-Bureau International, MSF-Operation Centre Paris (OCP) and MSF-Operation Centre Brussels (OCB) are involved in the study.
- Guttmacher Institute: leading research and policy organization committed to advancing sexual and reproductive health and rights in the United States and globally.
- Ministries of Health of Central African Republic, Jigawa State – Nigeria, Democratic Republic of Congo.

Coordinating Institution: Ipas

Implementing Institutions: Epicentre – MSF-OCP – MSF-OCB

Funders: Elrha - R2HC: 70% – Médecins Sans Frontières: 30%

Study International Coordinating committee:

- Tamara Fetters, MPH (Ipas)
- Estelle Pasquier, MD, Msc PH (Epicentre/MSF)
- Bill Powel, FNP, PhD (Ipas)
- Caroline Marquer, MPsych, PhD (Epicentre)
- Ann Moore, PhD (Guttmacher Institute)
- Onikepe Owolabi, MD, MBBS, PhD (Guttmacher Institute)
- Catrin Schulte-Hillen, MMid, Msc PH (MSF – Bureau International)
- Claire Fotheringham, MD, Msc PH (MSF-OCP)
- Daphne Lagrou, MMid (MSF-OCB)

Study sites: North Kivu (Democratic Republic of Congo – MSF-OCB); Bangui (Central Africa – MSF-OCB); Jigawa State (Nigeria – MSF-OCP)

Coordinator Principal Investigators:

Name - Contact	Institution	Roles
Estelle Pasquier, MD, MPH Medical epidemiologist researcher	Epicentre (MSF)	Study oversight Leader in study design and protocol development, medical data collection tools, study implementation as well as database design and data management. Substantial input into other data collection and training tools development, quantitative data analysis, report writing and publications.
Tamara Fetters, MPH Senior Researcher	Ipas	Study oversight Leader in coordination of all partners, the coordinating agency and the main funder. Leader in quantitative interview data collection and training tools development.

		Substantial inputs into study design and protocol development, central data management supervision, data analysis, report writing and publications.

International Co-investigators:

Name - Contact	Institution	Roles
Caroline Marquer, PhD Qualitative researcher	Epicentre	Responsible of the qualitative part of the study: design, protocol writing, data collection and training tool development, data collection supervision, data analysis, report and publication writing
Ann Moore, PhD Qualitative researcher	Guttmacher Institute	Co-Responsible of the qualitative part of the study: substantial input into study design, protocol writing, data collection and training tool development, data collection supervision, qualitative data analysis, report and publication writing
Onikepe Owolabi, MD, MBBS, PhD Medical Epidemiologist researcher	Guttmacher Institute	Substantial Input into protocol development, data collection supervision, data analysis plan, report writing and publications
Bill Powel, FNP, PhD Sexual and Reproductive Health senior clinical advisor	Ipas	Substantial input into study design and protocol development, data collection and training tools development, data analysis plan, report writing and publications
Catrin Schulte, MMid, MPH Responsible of the Intersectional MSF Reproductive health and sexual violence care working group	MSF Bureau International	Substantial input into study design ad protocol development, data collection and training tools development, data analysis plan, report writing and publications
Claire Fotheringham, MD, MPH Gynecology-Obstetric clinical advisor	MSF-OCP	Substantial input into study design and protocol development, data collection and training tools development, data collection supervision, data analysis plan, report writing and publications
Daphne Lagrou, MMid Woman health clinical advisor	MSF-OCB	

Study sites Investigators:

Lucien Ngabo Mulamira, MD	Ministry of Health (MoH)- DRC	Link between the site MoH, Epicentre study team and site MSF team Ensure involvement of MoH in the study. MoH input into the study protocol, results interpretation and diffusion. Link with local authorities and communities (Ethical Committee, Administrative authorization, communities' leaders, etc.)
Marietta Claudia Adame, MD	MoH - CAR	
NGBALE Norbert Richard, MD PhD	MoH - CAR	
Dodane, Aimé Théodore, MD, MPH	MoH - CAR	
Sulaiman Ado, MD Replaced by Abdullahi A. Habib, MD (Dec 2020)	MoH - Nigeria	
Nadine Neema Mitutso, MD	MSF-DRC (OCB)	Link between the site MSF clinicians and the Epicentre study team Input in the study protocol, study implementation (support the study staff in data collection), data analysis plan and result interpretation. Site study completion and archiving activities.
Laurentine Nguengo, BMid	MSF-CAR (OCB)	
Samuel Audu, MD	MSF-Nigeria (OCP)	

Mahmoud BADAWI, PH, MPH then Huiwu CHEN, MD, MPH	Epicentre - MSF	Coordination of the implementation of the study in CAR and DRC sites Support to standardization of processes and procedures in all study sites
Timothy WILLIAMS, MD, MPH,	Epicentre - MSF	Nigeria site study coordinator

Other contributors:

Name - Contact	**Institution**	**Roles**
Jamie Manzel,	Ipas	Support to data analysis Administrative support
Marielle Kirstein,	Guttmacher Institute	Administrative support
Klaudia Porten	Epicentre	Epicentre representation Protocol development and review Input into report writing, publication, communication and dissemination Epidemiology expertise
Elisabeth Baudin	Epicentre	Support to data management and data analysis
Julita Gil,	MSF- OCB	Technical advisor: advice on protocol development, study implementation and data collection for OCB
Clair Mills,	MSF - OCP	MSF movement representation (final validation) Protocol development and review Input into report writing, publication, communication and dissemination Medical and public health expertise
Isabelle Mouniaman, Christopher Mambula, MSF Medical Coordinators (and deputy medical coordinators) of Nigeria mission	MSF - OCP	Protocol review and input into report writing. Support on operationalisation of the study
Annick Antierens, Emmanuel Lampaert, Ahmed Abd-Elhraman, MSF Medical Coordinators (and deputy medical coordinators) of DRC and RCA missions	MSF - OCB	Protocol review and input into report writing. Support on operationalisation of the study

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Study

Version n°3.9.En

SIGNATURE PAGE

Coordinating Institution

Ipas
P.O. box 9990
Chapel Hill, NC 27515 - USA
Representative : Tamara Fetters
In Atlanta
Date : 20/02/19

Fetters Tamara
Senior Research Advisor
Signature :

Coordinator Principal Investigators

Dr PASQUIER Estelle, MD, Msc PH
Epicentre – Médecins sans Frontières
11 rue Saint Sabin
75011 Paris - France
In Paris
Date : 20/02/19

Dr Pasquier Estelle
Signature :

FETTERS Tamara, MPH
Ipas
P.O. box 9990
Chapel Hill, NC 27515 - USA
In Atlanta
Date : 20/02/19

Fetters Tamara
Signature :

Investigateurs sites (to be fulfilled on-site and put in the study site file):

XXXXXXXXXXXXXXX
- hospital
In
Date :

XXXXXXXXXXXXXXXX
Signature :

XXXXXXXXXX
Médecins sans Frontières -
In
Date :

XXXXXXXXXXXXXXXX
Signature :

Table of Content

Protocol versions:

Version n°	Date	Amendment n°	Principal modifications
1	**30/06/2018**		**First draft**
2	**14/10/2018**		- Feedback of all members of international coordinating committee included - Definitions and classifications clarified - South Sudan site removed
2.2	**27/10/18**		- Threshold of 22 weeks of gestation removed (for comparability with WHO study) - Classification of severity according to WHO multi-country study
3	**20/11/18**		- No age neither gestational age limit in inclusion criteria as per WHO protocol - Feedback of all members of international coordinating committee + MSF medical and operational directions+ MSF field teams - Verbal consent rather than written consent for interview (safer for protecting included women)
3.1	**27/11/18**		- Qualitative part changed to include all feedbacks
3.2	**29/11/18**		- Emancipated minor: need agreement of health care provider and study coordinator to be considered as emancipated - Confidentiality information for qualitative component
3.3	**05/12/18**		- Division of the component 3 into component 3 (health facility assessment) and 4 (KAPB survey)
3.4 and 3.4_TC=3.5	**11/12/18 And 14/01/19**	**MSF-ERB approval 18110 05/03/19 (v3.5)**	- Reformulation and editing

		Central Africa Republic ethical committee **Favorable opinion** **8/UB/FACSS/CSCVPER/19** **09/04/2019 (v3.5)** **Nigeria (Jigawa State) ethical committee approval** **MOH/Sec.3/S/548/I** **02/05/2019 (v3.5)** **DRC ethical committee approval** **120/CNES/BN/PMMF/2019** **13/06/2019 (v3.5)**	
3.6	**15/06/19**	**Guttmacher Institute IRB approval** **24/04/2019** **(received 27/06/19) (v3.6)** **Central African Republic ethical committee approval** **18/UB/FACSS/CSCVPER/19** **23/07/19** **(v3.6)**	- Clarification about the presence of psychosocial counselors in the health facilities + addition of the informed consent process figure + addition of the possibility to give in kind gift or transport to participants for compensation of time according to site feasibility and relevance + inclusion of intermediary analysis to be done to check if the original hypothesis of inclusion in all study components are going to be reached (request from Guttmacher partner and IRB) - Modifications of the CAR site investigators (CAR ERB request) - Clarifications on definitions (hospitalized/admitted >24h, gestational age,)
3.7	**11/05/2020**	**Information letter to Jigawa State ERB dated 20/04/20** **Information letter and request for time extension of ethical approval sent to DRC ethical committee => approval received**	- Adaptation of the witnessing system in the consent process for illiterate women. Even if the witness was not mandatory, we added new options of witnessing to give the woman as much chance as possible to get an unbiased informed

		15/06/20 (until 31/12/2021) **Request for expedited review sent to Guttmacher Institute ethical committee the 07/05/20** **Information letter sent to MSF-ERB the 11/05/20 => request of ERB to send an Amendment request with explanations included in the protocol.**	consent.
3.8	**27/06/2020**	**Answer to the questions of MSF-ERB regarding the amendment on illiterates => Approval received 03/07/20** **Request for expedited review sent to Guttmacher Institute ethical committee again (to take into consideration MSF-ERB request)** **Information letter to Jigawa State ethical committee**	- Changes in the adaptation of the witnessing process for illiterates at the request of MSF-ERB: removal of the possibility to use one research team member + audio-record the process - Adaptation of the medical record review process into a retrospective way to collect the data during the first months of Covid-19 pandemic until a prospective process is feasible again
3.9	**15/12/2020**	**Adaptation made to overcome challenges due to multiple events in conflict-affected and fragile settings like North-Kivu in DRC (increased conflict-related events, volcanoes eruption, Ebola, Covid-19)**	- Adding the option of off-site retrospective medical record review in case of irresistible reasons on site (additionally to Covid-19) - Request for exemption from individual information (opt-out process) for retrospective medical review in case of no other solutions - Adding options to use the scans of de-identified medical records to collect the data off-site - Change of MoH site investigator in Jigawa State site - Adding secondary analysis: Covid-19-AMoCo sub-study (appendix 15)

Protocol Synopsis

AMoCo Study

Abortion-related **Mo**rbidity and **Mo**rtality in **Co**nflict-affected and fragile settings **study**

Study Partners:

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- **Guttmacher Institute:** leading research and policy organization committed to advancing sexual and reproductive health and rights in the United States and globally.
- **Ministries of Health** of Central African Republic, Jigawa State – Nigeria, Democratic Republic of Congo.

Coordinator Principal Investigator(s)

- Tamara Fetters, Ipas
- Estelle Pasquier, Epicentre

Participating countries:

- Democratic Republic of Congo (North-Kivu)
- Republic of Central Africa (Bangui)
- Nigeria (Jigawa State)

Aim and Objectives

Overall Aim

To describe and estimate the burden of abortion-related complications, particularly near-miss complications and deaths, and their associated factors among women presenting for abortion-related complications in health facilities supported by Médecins Sans Frontières (MSF) in African fragile and/or conflict-affected settings.

Objectives

Primary objective:

- To describe the frequency of near-miss events and deaths among women presenting for abortion-related complications.

Secondary objective:

- To describe the frequency of abortion-related complications overall and by types (hemorrhage, infection, perforation, etc.)
- To describe the severity of abortion-related complications overall and by types (hemorrhage, infection, perforation, etc.)
- To identify risk factors quantitatively associated with abortion-related near-miss events;
- To describe the quality of the clinical management of abortion-related complications (including near-miss cases) and the heath facilities capacity to manage these complications
- To describe the experiences of women who present as near-miss cases, including their decision-making processes, access, pathways to care as well as conditions and factors that could contribute to the life-threatening conditions and near-miss event.
- To describe the knowledge, attitudes, practices, and behaviors of health care workers in relation to abortion;
- To describe the characteristics, management, outcomes of ectopic and molar pregnancies

Design

Multi-sites mixed-methods study with 4 components:

1- *A Quantitative observational descriptive study* among women presenting for abortion-related complications to determine the frequency and severity of abortion-related complications including near-miss cases and death. Data will be collected through a *medical records review* and a *quantitative survey* among women presenting for abortion-related complications to determine the sociodemographic and clinical characteristics of the women with abortion-related complications, the type of abortion, the type and severity (near-miss) of complications (using the WHO criteria) and the clinical management received. It will also give insight into the characteristics of near-miss events following unsafe abortion.

2- *A qualitative study* about women's experiences associated with a near-miss event (and life-threatening conditions): their pathway of access to care including their decision-making process, their own perceptions and opinions and other factors or conditions that might contribute to the near-miss event (in-depth face to face interviews).

3- *A rapid health facility assessment with the health professional* in charge of Post-Abortion Care will complement the assessment of the quality of management of complications

4- *A Knowledge Attitudes, Practice and Behavior quantitative survey* among health care providers involved in the management of abortion-related complications will identify provider-associated factors that may contribute to near-miss events.

Endpoints

Primary Endpoint

From the Quantitative observational descriptive study: Proportion of near-miss cases among all women presenting for abortion-related complications.

Secondary Endpoints

1- *Quantitative observational descriptive study (medical record review + quantitative interviews):*

   a. Facility-based ratio of abortion-related complications per annum, overall and by type of complication (hemorrhage, infection, perforation, etc.) will be calculated for the following denominators: all admissions, live births, and deliveries in each health facility.
   b. Facility-based ratio of each of the 4 levels of complication severity (Appendix 5) especially the severe complications: Severe Maternal Outcome (near-miss events and deaths) and life-threatening complications, per annum, overall and by type of complication will be calculated for the following denominators: all women admitted for abortion-related complications, live births, and deliveries in each health facility.
   c. Facility-based abortion-related near-miss ratio per annum for the following denominators: live births, abortion-related admissions, all admissions and deliveries
   d. Facility-based abortion-related mortality ratio per annum for the following denominators: live births, abortion-related admissions, all admissions and deliveries
   e. Facility-based abortion-related near-miss mortality ratio: ratio between abortion-related near- miss cases and abortion-related deaths
   f. Facility-based abortion-related mortality index: number of abortion-related maternal deaths divided by the number of women with abortion-related severe maternal outcome expressed as a percentage
   g. Proportional morbidity (proportion of each type of complications) among all abortion-related complications and among all near-miss cases
   h. Frequencies of the exit outcomes (discharged, dead, referred, leave against medical advice) after abortion-related complications by severity level and by type of complication.

i. Proportion of women with abortion-related complications disclosing or presenting signs of an induced abortion attempt.
j. Frequencies of each induced abortion method used, type of provider who performed it and setting where it was performed.
k. Frequencies of each clinical intervention used to manage the abortion-related complications.
l. Frequencies of each key quality of care indicator for the treatment of abortion-related complications (cf. Appendix 8).
m. Risk factors associated with near-miss complications among the participants' characteristics (socio-demographic characteristics, obstetrical history, displacement, exposure to conflict, and exposure to sexual violence), the characteristic of the abortion (type, method used if induced), complications type, the 3 delays in receiving care and the medical management received.
n. Frequencies of characteristics and outcomes (discharged, dead, referred, leave against medical advice) of ectopic and molar pregnancies.

2- Qualitative study (qualitative in-depth interviews):
a. Description of the woman pathways to care (women's experiences and decision-making processes to abortion, seeking care),
b. A description of perceptions and opinions about their own experience
c. A description of conditions and factors that could contribute to the life-threatening conditions and near-miss event.

3- Rapid facility assessment:
a. Facility-level description of the infrastructure, readiness, and capacity to deliver quality PAC.
b. Frequency of Safe Abortion Care (SAC)/PAC signal functions : indicators of SAC/PAC service quality and availability as described in Healy et al. model(1) improved by Campbell et al.(2)[a] (cf. Appendix 13)

4- *Knowledge Attitude Practice and Behavior (KAPB) survey:*
a. Description of knowledge, attitudes, exposure, and capacity of health facility staff related to PAC and SAC.
b. Description of attitudes related to PAC and SAC associated with socio-demographic characteristics of health facility staff
c. Frequencies of each reported KAPB factor among health facility staff that can be barriers for access to quality PAC and SAC services including contraception.

Eligibility and Estimated enrolment

1- *Quantitative observational descriptive study* among women with abortion-related complications:
a. *Medical Record Review:* 430 women per site presenting for abortion-related complications will allow a precision of 3.5% of the primary endpoint, the proportion of near-miss among abortion-related complications, if it is at 12% (5% type 1 error and 20% of attrition rate).
b. *Quantitative survey*: all women included in the medical record review sub-component and hospitalized (who stayed overnight or more)[b] will be eligible (estimated at 300 per site)

[a] SAC/PAC model according to Healy et al. is comprised of three elements that contribute to reductions in maternal mortality: 1) Safe induced abortion for all legal indications, 2) treatment of abortion complications, 3) Provision of Post-abortion Contraception

[b] In different MSF hospitals, hospitalized women, i.e. who stayed overnight or more, are often classified as « women admitted >24h » even if the women stayed overnight but didn't effectively stayed more than 24h.

2- *Qualitative study* among women included in the medical record review sub-component, hospitalized and who experienced a near-miss event (or a life-threatening condition) will be eligible. A purposive sample will be chosen until reaching the principle of saturation (estimated at around 30 women per site).
3- *Rapid health facility assessment*: the health professional in charge of Post-Abortion Care ward in each study site will be eligible
4- *Knowledge Attitudes, Practice and Behavior quantitative survey*: all health care providers involved in the management of abortion-related complications will be eligible (between 60 and 100 according to site).

Expected Impact

The evidence collected by the study will quantify abortion-related complications, making these more visible inside and outside MSF, in particular among stakeholders working in fragile and/or conflict-affected settings. The understanding of the factors that explain the abortion-related near-miss events will help in proposing adapted operational strategies to address the issues around unwanted pregnancy and unsafe abortion.
Additionally, the understanding of the magnitude and management of the different complications related to abortion will

- help in improving the quality of care of such complications in health facilities of fragile and/or conflict-affected settings
- give arguments to advocate for better access to post abortion, safe abortion care including contraception.

Acronyms:

BEmONC: Basic Emergency Obstetric and Neonatal Care
CAR: Central African Republic
CEmONC: Comprehensive Emergency Obstetric and Neonatal Care
CIOMS: Council for International Organizations of Medical Sciences
CoC: Certificate of Confidentiality
CRF: Case Report Form
DRC: Democratic Republic of Congo
DSA: Data Sharing Agreement
EVA: Exploration of Values and Attitudes
ICU: Intensive Care Unit
IDI: In-depth Interview
IDP: Internally Displaced Person
IAWG: Inter-Agency Working Group
KAPB: Knowledge Attitude Practice Behavior
LGA: Local Government Area
LMP: Last Menstrual Periods
MoH: Ministry of Health
MoU: Memorandum of Understanding
MSF: Médecins Sans Frontières
OCB: Operation Centre Brussels
OCP: Operation Centre Paris
OECD: Organization for Economic Co-operation and Development
OPD: OutPatient Department
PAC: Post-Abortion Care
PMM: Prospective Morbidity Methodology
R2HC: Research for Health in Humanitarian Crisis (funding instrument of Elrha)
SAC: Safe-Abortion Care
SOP: Standard Operating Procedures
SRH: Sexual and Reproductive Health
UN: United Nations
VCAT: Value Clarification and Attitude Transformation
WHO: World Health Organization

Definitions and Classifications:

Fragile and/or Conflict-affected settings: Settings (context, country or region) in which a singular event or a series of events are threatening in terms of health, safety or well-being for a community or large group of people and/or where the deficient response capacity results in increasing levels of morbidity and mortality. (World Bank(3))

Abortion: is a loss of pregnancy (process leading to the expulsion of the products of conception from the uterus) before fetal viability, i.e. before a foetus becomes capable of independent extra-uterine life, either spontaneously (***miscarriage***) or as a result of a deliberate intervention (***induced abortion***). Foetus viability age is variable according to settings.(4)
Note: The term "abortion" is sometimes used to only refer to "termination of pregnancy on request" also called "induced abortion" but in the study, the term "abortion" includes both miscarriage (= spontaneous abortion) and induced abortion.

Miscarriage or Spontaneous abortion: is an abortion which is not induced, even if an external cause is involved such as accidental trauma or communicable disease.(4,5)

Induced Abortion: also called sometimes "Termination of Pregnancy on Request" or simply "Termination of Pregnancy", is an abortion initiated by deliberate action undertaken with the intent of terminating the pregnancy either for medical reasons (health of the mother, foetal malformations, etc.) or any other reasons. (4,5)
Note: The Figa-Talamanca criteria allow to classify induced abortions into certainly induced, probably induced, possibly induced (6) *(cf. appendix 2)*

Different terms describe the progressive stages of abortion (spontaneous or induced):

- **Threatened abortion (pregnancy may continue):** is a threat of abortion of an intrauterine pregnancy but the embryo/fœtus is still viable (cardiac activity is present if ultrasound is available) and the pregnancy may continue(4,7).
- **Inevitable abortion:** means that it is impossible for the intrauterine pregnancy to continue and it will proceed to incomplete/complete abortion even though there has not yet been expulsion of products(4,7)
- **Incomplete abortion:** is an abortion of an intrauterine pregnancy where products of conception are partially expelled.(4,7)
- **Complete abortion:** an abortion of an intrauterine pregnancy where all the products of conception - embryo/fetus, placenta and membranes – have been expelled.(4,7)
- **Missed abortion:** is an abortion of an intrauterine pregnancy where the products of conception have not been expelled but fetal cardiac activity is absent(7).

Case-definitions are in appendix 3.

Abortion-related complications: there is no standards definition and understanding of what differentiates an abortion with complications from an abortion without complications. Therefore, for ensuring comparability of our results with the results of a similar multi-country study led by the World Health Organization (WHO) in 30 stable limited-resource settings, the present study uses the same definition(8). It considers that **any abortion-related signs or conditions except the ones related to a threatened abortion constitute** an abortion-related complication. In other words, abortion-related complications are **any signs or conditions** resulting from inevitable, incomplete, complete or missed abortion whatever the abortion origin (induced or spontaneous) and the severity (up to near-miss and death). For example, these "complications" include (but are not limited to),

isolated non severe symptoms like vaginal bleeding, abdominal/genital pain, vaginal discharge as well as more severe conditions like organ perforation, fistula, hemorrhage, septic abortion (including lower genital tract infection, chorioamnionitis, endometritis, peritonitis, septic shock) up to organ failure at near-miss stage and death. This definition takes also into consideration the woman' perspective: the fact that the woman comes to the health facility might reflect that she considers that she has a complication.

Ectopic and molar pregnancy are not abortion-related complications. Nevertheless, at presentation, it is difficult to differentiate ectopic and molar pregnancies from abortion-related complications in contexts without access to Beta-HCG and ultra-sound. Therefore, at presentation, they are often classified as abortion-related complications. Exit diagnosis allow to differentiate most of them from abortion-related complications (when the uterus has been evacuated and/or the surgery performed).

Septic abortion: is one of the abortion-related complication types. It is defined as abortion of an intrauterine pregnancy complicated by infection. An infection may occurs if organisms rise from the lower genital tract following either spontaneous or induced abortion. An infection is more likely to occur if there are retained products of conception and evacuation has been delayed.(4,7) Its case-definition is in appendix 3.

Maternal near-miss: A woman who nearly died, but survived a complication that occurred during pregnancy, childbirth or within 42 days of the end of the pregnancy. (9)

Abortion-related near-miss: A maternal near-miss case that occurs due to abortion. It is a woman who nearly died but survived a life-threatening complication that occurred during any type of abortion (i.e. miscarriage or induced abortion) or within 42 days of the end of the pregnancy.(10) WHO near-miss criteria adapted to abortion are described in Appendix 5.

Ectopic pregnancy: An ectopic pregnancy is one in which implantation occurs outside the uterine cavity. The fallopian tube is the most common site of ectopic implantation (greater than 90%) more rarely, it can be in other locations such as the abdominal cavity or the cervix.(4,7) Its case-definition is in appendix 3.

Molar pregnancy: Molar pregnancy is characterized by an abnormal proliferation of chorionic villi with an absence of embryo/fœtus or an abnormal embryo/fœtus.(4) Its case-definition is in appendix 3.

Safe abortion (or safe induced abortion): induced abortion done by persons with the necessary skills to perform it and done according to current medical standards (in the study, current WHO or MSF guidelines).(11)
*Note: In the study, we will classify an induced abortion as **safe** as per WHO classification described by Ganatra et al.*(12) *in appendix 4.*

Unsafe Abortion (or unsafe induced abortion): induced abortion done by persons lacking the necessary skills to perform it and/or not done according to current medical standards. (11)
Note: In the study, we will classify further the unsafe abortion in less-safe and least-safe abortions as per WHO classification described by Ganatra et al.(12) *in appendix 4.*

Safe Abortion Care (SAC): care provided to induce abortion by persons with the necessary skills to perform it and done according to current medical standards (in the study, according to WHO or MSF current guidelines).(11)

Post Abortion Care (PAC): Care provided to treat symptoms and complications resulting from miscarriage/spontaneous or induced abortion.(13) Post abortion care is an integral component of comprehensive abortion care and includes the treatment of abortion-related complications (either induced or spontaneous), the counselling, the offer of contraceptives (family planning) to help women prevent future unwanted pregnancies and abortions and the link with comprehensive sexual and reproductive health services.(13–15)

As at presentation, it is difficult to clearly differentiate ectopic and molar pregnancy from abortion, women with ectopic or molar pregnancies are often managed in PAC services but are not per se women receiving post-abortion care.

1. Background and Rationale

Abortion-related complications are one of the five main causes of maternal mortality worldwide(16); almost all would be related to unsafe abortion and nearly all (97%) occur in developing countries(17). Although unsafe abortion is the only cause of maternal mortality that is entirely preventable, it is also the most neglected cause of maternal mortality, showing the smallest decline in cause-specific maternal mortality between 1990 and 2013(16). Complications of abortion increased as a proportion of maternal deaths from 13% to 18% during the same time period(16).

Abortion is defined as the loss of pregnancy before fetal viability, either spontaneous or induced. Spontaneous abortion occurs in 20% of all clinically confirmed pregnancies(18). All types of abortion can result in complications with different degrees of severity, from minimal to life-threatening "near-miss events" and death. So far, there is no standards definition and understanding of what differentiates an abortion with complications from an abortion without complications. Therefore, the present study uses the definition currently implemented in a similar multi-country study led by the World Health Organization (WHO) in 30 stable limited-resource settings(8). It considers that **any abortion-related signs or conditions except the ones related to a threatened abortion constitute** an abortion-related complication. In other words, abortion-related complications are **any signs or conditions** resulting from inevitable, incomplete, complete or missed abortion whatever the abortion origin (induced or spontaneous) and the severity (up to near-miss and death). For example, these "complications" include (but are not limited to), isolated non severe symptoms like vaginal bleeding, abdominal/genital pain, vaginal discharge as well as more severe conditions like organ perforation, fistula, hemorrhage, septic abortion (including lower genital tract infection, chorioamnionitis, endometritis, peritonitis, septic shock) up to organ failure at near-miss stage and death.
An abortion-related near-miss event is defined as "a woman who nearly died but survived a life-threatening complication that occurred during any type of abortion or within 42 days of the end of the pregnancy."(10) The World Health Organization (WHO) has developed a uniform set of criteria to identify maternal near-miss events, to facilitate the review of these cases for monitoring and improving quality of obstetric care(9). These criteria have been adapted to abortion-related near-miss events(10) and are presented in appendix 5. From a clinical point of view, making the distinction with absolute certainty between complications resulting from a miscarriage and those resulting from an induced abortion, safe or unsafe, is difficult(19). However, there is some evidence that the most severe complications resulted from unsafe procedures(20).

Addressing the topic of induced abortion is a challenge in part because of the stigma which results in under-reporting that contributes in turn, to a lack of accurate data. In stable, limited-resource countries, evidence on the burden of abortion complications is increasingly available. In these settings, systematic literature reviews found that 6% to 9% of women with abortion-related complications arriving at facilities (either presenting or hospitalized) could be classified as near-miss events (range [0.5%-56.5%]), and 0.3% to 1.5% of these women with abortion-related complications died (range [0%-3.3%]) (21–23). Induction (versus spontaneous)(24,25), delays in seeking care(24), being single (versus in couple)(26), low level of education(25–27), female genital mutilation(28), nulliparity(26), gestational age> 12 weeks(24) and infections (compared to other types of complications)(29,30) have been shown to be associated with near-miss events and/or death. Nevertheless, results need to be interpreted with caution as the quality of the studies is very heterogeneous and inclusion criteria, abortion-related complications and near-miss definitions as well as denominators used in these studies were not standardized; and most of them didn't adjust for confounders in their analysis(22,23).

Fragile and conflict-affected settings increase the vulnerability of affected population to sexual violence. Increased sexual violence has been reported while women are separated from their partners and family; while collecting water, fuel or animal fodder; and during armed attacks, abduction and detention.(31) Disruption and dislocation from health and contraceptive services also increase the risk of unwanted pregnancy and pregnancy complicated by co-existing conditions, such as malnutrition or severe anemia(31). These factors may result in more abortion-seeking behavior and early pregnancy complications, including abortion-related complications(32).

Nevertheless, to our knowledge, exposure to conflict, displacement, insecurity and violence contexts has never been explored as potential risk factors for adverse abortion-related outcome(22). And research about abortion, abortion-related complications, and abortion care in fragile and conflict-affected settings is very limited(32,33). To our knowledge, only three studies have attempted to assess components of this care in such settings (compared to 70 studies assessing abortion-related complications in stable limited-resource contexts according to the last literature review(22)). Two studies identified big gaps in availability of safe abortion and post-abortion care services compared to other sexual and reproductive health services (34,35). One study showed that community-based distribution of misoprostol can be a safe and effective strategy for increasing access to safe abortion in a legally restricted, low-resource fragile setting like Bangladeshi refugee camps(36). None of the studies assessed the magnitude of severe abortion-related complications and near-miss events in these contexts. Additionally, knowledge about risk factors associated with severe/near-miss abortion-related complications and death in fragile/conflict-affected areas of limited-resource countries is very limited or non-existent. And qualitative research identifying facilitators and barriers in the pathway of care of women seeking abortion care, specifically in this context has not been published.

This lack of evidence results in a lack of attention to preventable abortion-related complications in these settings. Knowledge about abortion in fragile and conflict-affected settings has been identified by the research community(37,38) and the 45 organizations in the Safe Abortion Care Inter-Agency Working Group (IAWG)(39), as the most important sexual and reproductive health research gap in these settings. Additionally, an MSF response to the 2016 Lancet report on maternal mortality trends (40) urged caution in applying the authors recommendations calling policymakers, funding bodies, and health actors to give greater importance to indirect rather than direct causes of maternal mortality (abortion, hemorrhage, infection, dystocia and eclampsia). MSF specifically alerted on the inadequacy of these recommendations to fragile and conflict-affected settings where maternal mortality is the highest and where abortion and other direct causes remain predominant (41,42)

Within MSF, safe abortion care is a political and operational priority, but in missions and projects, abortion-related complications have only recently started to come to attention. Post-Abortion Care (PAC) specific data collection has only started 5 years ago. In 2016, only 65 of 111 projects (60%) providing maternity care reported annual figures on PAC(43). In 2017, the proportion of projects with maternity care, reporting on PAC, has increased to close to 90%. Almost 22,900 women coming for PAC were reported in 2017, corresponding to one woman seeking PAC for every 13 deliveries(44).
Nevertheless, the definition of Post-Abortion Care and abortion-related complications are not standardized across MSF missions and only aggregated data are available for 2 to 3 indicators according to the sites (usually number of PAC with or without “complications” and their outcomes). To date, MSF has no data on the types, severity, associated factors and outcomes of abortion-related complications, nor on the quality of clinical management of abortion. While recognizing abortion care as a priority, MSF has highlighted that a lack of data as well as a lack of awareness and non-supportive staff attitudes represent important barriers to the provision of abortion care in MSF projects(41).

To address these important knowledge gaps in the MSF movement as well as at international level, this study proposes to describe the magnitude and severity of abortion-related complications and to identify factors associated with abortion-related near-miss events in three facilities providing PAC and supported by MSF in the North Kivu of the Democratic Republic of Congo (DRC), in the Jigawa State of Nigeria and in Bangui in Central African Republic (CAR). These three sites are in countries classified fifth to fourteen (over 178 states) on the 2018 Fragile States Index(45) and have a significant PAC caseload to achieve the necessary sample size in a limited period of time.

2. Expected Impact

The research is expected to generate evidence highlighting the magnitude and severity of abortion-related complications. In addition, it will provide information on women's trajectories to experiencing near-miss complications and identify the challenges and barriers to health care experienced by women seeking PAC in African fragile and/or conflict-affected settings. The evidence provided by this research will help MSF missions and ministries of health (MoH) to develop strategies to overcome the barriers to contraception and abortion care and to improve quality of this care in these facilities and all MSF-supported facilities.
More generally, previous work on abortion-related complications has excluded fragile and/or conflict affected contexts because of security concerns and other challenges associated with collecting data in fragile areas. Therefore, the collection of these data will provide previously undocumented evidence of the consequences of this lack of access to abortion services. Further, the evidence gathered in these different African settings will provide a base for advocacy, highlighting the abortion care needs in fragile and/or conflict-affected settings generally, and the factors that need to be considered to reduce abortion-related morbidity and death. We expect that the collected evidence will be used to prioritize and improve access to abortion care (PAC and SAC) including contraception, for all women and girls who need it in fragile and/or conflict affected settings, adapting them to their needs. In the long-term, the uptake of these recommendations may result in improved technical and clinical policies and guidelines that are useful for policymakers, humanitarian service providers and stakeholders, ministries of health, and health professionals.

In summary, the evidence generated from the study will inform efforts aimed at:

- Improving knowledge and awareness of women and their partners for preventing unwanted pregnancy and on the availability of safe abortion care;
- Improving training for providers and building capacity in health facilities;
- Orienting national and international guidelines on access to safe abortion care and quality post abortion care including provision of contraceptives in fragile and conflict-affected settings;
- Informing efforts to reduce abortion stigma;
- Informing advocacy efforts to improve the legal context surrounding abortion;

3. Objectives

The overall aim of this study is to describe and estimate the burden of abortion-related complications, particularly near-miss complications and deaths, and their associated factors among women presenting for abortion-related complications in health facilities supported by MSF in African fragile and/or conflict-affected settings.

3.1. Primary objective

- To describe the frequency of near-miss events among women presenting for abortion-related complications.

3.2. Secondary objectives

- To describe the frequency of abortion-related complications overall and by types (hemorrhage, infection, perforation, etc.)
- To describe the severity of abortion-related complications overall and by types (hemorrhage, infection, perforation, etc.)
- To identify risk factors quantitatively associated with abortion-related near-miss events;
- To describe the quality of the clinical management of abortion-related complications (including near-miss cases) and the heath facilities capacity to manage these complications
- To describe the experiences of women who present as near-miss cases, including their decision-making processes, access, pathways to care as well as conditions and factors that could contribute to the life-threatening conditions and near-miss event.
- To describe the knowledge, attitudes, practices, and behaviors of health care workers in relation to abortion;
- To describe the characteristics, management and outcomes of ectopic and molar pregnancies

4. Methods

4.1. Study design

This mixed-methods study will include 4 main components:

1- **Component 1:** *A quantitative observational descriptive study* among women presenting with abortion-related complications including:

   a. *A prospective*[c] *medical record review* of all women presenting with abortion-related complications in the study facilities.
   b. *A cross-sectional quantitative survey* among women included in the medical record review and hospitalized (who stayed overnight or more)[b] h thanks to a *quantitative interview*.

   This component will provide estimates of the frequency of different abortion-related complications, their severity (including near-miss and death) and outcomes and will identify the risk factors associated quantitatively with near-miss cases. It will also describe the clinical management of abortion-related complications.

[c] The participant medical record is reviewed prospectively on a daily basis.

This component will adapt the existing "prospective morbidity methodology" (PMM) developed over the last 3 decades by a task force of the World Health Organization (WHO) that includes the Ipas and Guttmacher Institute researchers involved in this study(46). The PMM uses a cross-sectional approach to collect data among women presenting for post-abortion care in health facilities. It includes a prospective[c] medical record review to identify and classify the morbidities experienced by the woman as well as a quantitative survey among the women to identify the factors quantitatively associated with the morbidities and their severity. This methodology has already been widely applied in different limited-resources stable contexts like Kenya(24), Cambodia(47), Ethiopia(48,49) and Zambia(10) with the development of a set of data collection instruments. The most up-to-date methodology is currently being used by a Multi-country Survey on Abortion Morbidity and Mortality led by the World Health Organization in 30 stable limited-resource settings(8). It has proposed to classify the severity of abortion-related complications in 5 categories described in Appendix 5 (least severe, less severe, life-threatening, near-miss and death). Therefore, we will use this most updated methodology and tools to provide a certain degree of comparability between the results of our study in fragile/conflict-affected settings and the ones of WHO study in stable settings.

To adapt the process to the Covid-19 pandemic, if the medical record review can't be achieved prospectively to ensure Covid-19 prevention measures, a retrospective process can be implemented in order to prevent any interruption in the data collection among all cases presenting for abortion-related complications. Indeed, this retrospective process allows more easily the application of the Covid-19 prevention measures while allowing to reach the primary objective of the study.

The retrospective medical record review may also be implemented in case of the research activities is strictly limited by irresistible reasons like field security context or instability in the conflict affected study area. If the data collection is not possible prospectively, the retrospective data collection will nevertheless allow to obtain information to permit the estimation of the primary end point on a study site currently under conflict and instability. It will also permit to describe an important part of the secondary endpoints aiming for care quality improvement. This retrospective medical record review may be implemented off-site (i.e. data collection and entry would be done at distance) in case the security conditions don't allow an on-site data collection. In collaboration with the study site facility, the data collection process will comply with the confidentiality and data security protocol of routine medical records (cf. below § 8.2 and § 8.3).

2- **Component 2:** *A qualitative study* with a subset of women who experienced potentially life-threatening conditions and near-miss complications (cf. case-definitions in Appendix 5), using *in-depth interviews* (IDIs) will capture women's experiences of their decision-making processes, pathways to care, and other potential conditions and factors that contributed to the near-miss event.

3- **Component 3:** A *rapid facility assessment* of each of the study sites health facilities.
This component will inform the assessment of health facilities capacity to manage abortion-related complications and identify infrastructure factors that may contribute to near-miss events.

4- **Component 4:** A *Knowledge, Attitudes, Practice, and Behavior (KAPB) survey* among all PAC health providers of each of the study sites
This component will assess the knowledges, attitudes and practices of health professionals regarding abortion care and identify provider-associated factors that may contribute to near-miss events.

An interdisciplinary approach will be used to triangulate[d] quantitative and qualitative data from the different study components to enrich understanding and contextualization, and to improve reliability of the conclusions (cf. §7. Analysis).

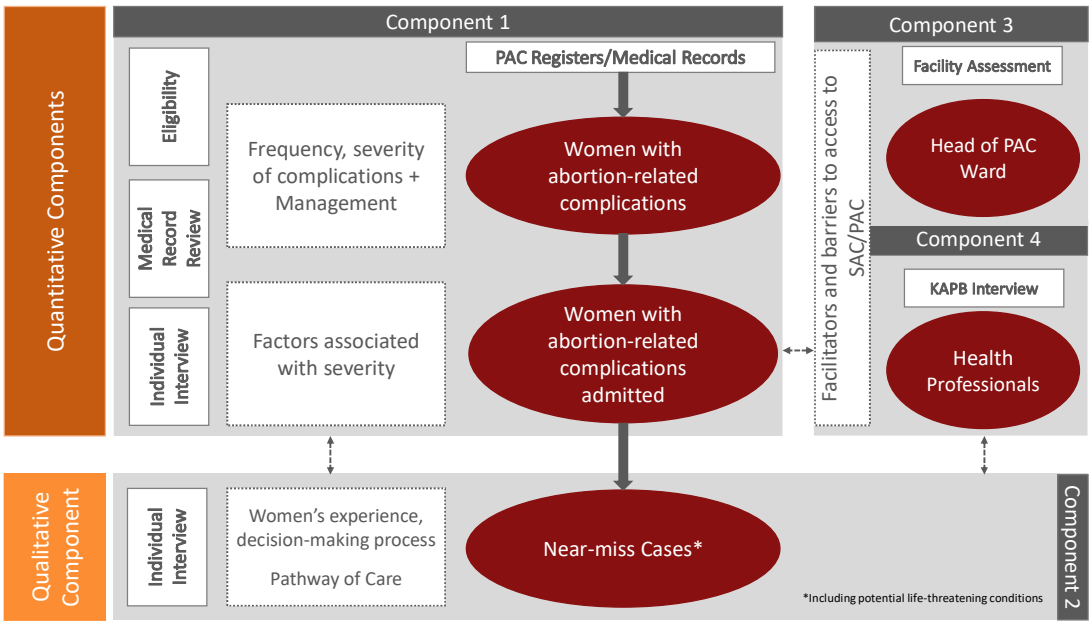

Figure 1: Articulation of the 4 components of the study design

4.2. Study Endpoints

4.2.1. Primary Endpoint

From the Quantitative observational descriptive study: Proportion of near-miss cases among all women presenting for abortion-related complications.

4.2.2. Secondary Endpoints

1- *Quantitative observational descriptive study (medical record review + quantitative interviews):*
   a. Facility-based ratio of abortion-related complications per annum, overall and by type of complication (hemorrhage, infection, perforation, etc.) will be calculated for the following denominators: all admissions, live births, and deliveries in each health facility.
   b. Facility-based ratio of each of the 4 levels of complication severity (Appendix 5) especially the severe complications: Severe Maternal Outcome (near-miss events and deaths) and life-threatening complications, per annum, overall and by type of

[d] in the sense of generating complementarity between components(63)

complication will be calculated for the following denominators: all women admitted for abortion-related complications, live births, and deliveries in each health facility.

c. Facility-based abortion-related near-miss ratio per annum for the following denominators: live births, abortion-related admissions, all admissions and deliveries
d. Facility-based abortion-related mortality ratio per annum for the following denominators: live births, abortion-related admissions, all admissions and deliveries
e. Facility-based abortion-related near-miss mortality ratio: ratio between abortion-related near- miss cases and abortion-related deaths
f. Facility-based abortion-related mortality index: number of abortion-related maternal deaths divided by the number of women with abortion-related severe maternal outcome expressed as a percentage
g. Proportional morbidity (proportion of each type of complications) among all abortion-related complications and among all near-miss cases
h. Frequencies of the exit outcomes (discharged, dead, referred, leave against medical advice) after abortion-related complications by severity level and by type of complication.
i. Proportion of women with abortion-related complications disclosing or presenting signs of an induced abortion attempt.
j. Frequencies of each induced abortion method used, type of provider who performed it and setting where it was performed.
k. Frequencies of each clinical intervention used to manage the abortion-related complications.
l. Frequencies of each key quality of care indicator for the treatment of abortion-related complications (cf. Appendix 8).
m. Risk factors associated with near-miss complications among the participants' characteristics (socio-demographic characteristics, obstetrical history, displacement, exposure to conflict, and exposure to sexual violence), the characteristic of the abortion (type, method used if induced), complications type, the 3 delays in receiving care and the medical management received.
n. Frequencies of characteristics and outcomes (discharged, dead, referred, leave against medical advice) of ectopic and molar pregnancies.

2- *Qualitative study (qualitative in-depth interviews):*

a. A description of the women's pathways to care (women's experiences and decision-making processes to abortion, seeking care).
b. A description of perceptions and opinions about their own experience
c. A description of conditions and factors that could contribute to the life-threatening conditions and near-miss event.

3- *Rapid facility assessment:*

a. Facility-level description of the infrastructure, readiness, and capacity to deliver quality PAC.
b. Frequency of Safe Abortion Care (SAC)/PAC signal functions : indicators of SAC/PAC service quality and availability as described in Healy et al. model(1) improved by Campbell et al.(2)[e] (cf. Appendix 13)

[e] SAC/PAC model according to Healy et al. is comprised of three elements that contribute to reductions in maternal mortality : 1) Safe induced abortion for all legal indications, 2) treatment of abortion complications, 3) Provision of Post-abortion Contraception

4- *Knowledge Attitude Practice and Behavior (KAPB) survey:*
   a. Description of knowledge, attitudes, exposure, and capacity of health facility staff related to PAC and SAC.
   b. Description of attitudes related to PAC and SAC associated with socio-demographic characteristics of health facility staff
   c. Frequencies of each reported KAPB factor among health facility staff that can be barriers for access to quality PAC and SAC services including contraception.

4.3. Setting

The study will be conducted in three MSF-supported maternity care centers located in a range of fragile and/or conflict-affected contexts in Africa. Each center has a significant enough PAC caseload (≥ 500/year) to achieve the necessary sample size in a limited data collection period. The hospitals are in areas where the security of participants and researchers can be ensured. They have catchment areas with ≥ 500 000 inhabitants; conduct >1,000 deliveries per year; and are capable of providing all CEmOC signal functions, including capacity for removal of retained products and surgical capability(8). The proposed sites are Bangui in CAR, North Kivu in DRC, and Jigawa State in Northern Nigeria.

The selected sites can be characterized as fragile and conflict- affected settings as they rank from fifth to fourteen over 178 states on the 2018 Fragile States Index, all in "Alert" situation(45). They are classified as extremely fragile (DRC and CAR) or fragile (Nigeria) States and within the top 10 countries hosting refugees by the Organization for Economic Co-operation and Development (OECD)(50). All study sites contexts are affected by repeated armed conflicts and/or population displacement with fragile health care systems. The research will take place in maternity centers in both urban and rural settings surrounded by chronically and/or recently displaced populations.

Contextual changes in any of these settings is possible prior to study initiation, possibly leading to a need to reconsider final study locations.

4.3.1. Referral maternity center, Bangui, Central Africa

With an estimated population at 4.6 million inhabitants, the Central African Republic (CAR) has a maternal mortality ratio at 880/100,000 live birth(51). The study is planned to be conducted in a referral maternity center in Bangui supported by MSF. This CEmONC (Comprehensive Emergency Obstetric and Newborn Care) health facility had an urban catchment population of about 345 000 people and a number of internally displaced people that fluctuated between 100 000 and 160 000 in 2017. The conflict situation in CAR has resulted in internally displaced persons (IDPs) residing in the city, for a short time or several years.

MSF is supporting the maternity (60 beds) including an IPD gynecological ward (11 beds) where the women with abortion-related complications are admitted. In 2017, the maternity provided skilled birth attendance to 8400 women (among which 34% were complicated deliveries) and managed almost 3200 women seeking PAC. In the last year, abortion-related complications caused over half of maternal deaths in the facility.

In CAR, safe induced abortion is authorized by the law before 8 weeks of pregnancy for "therapeutic termination of pregnancy" (if the mother's health – general sense - is in danger), fetal impairment (if health/viability of the foetus is in danger) as well as in case of incest, rape (providing there is evidence) or when a minor is in a "serious distress state". It must be provided by a medical doctor. CAR hasn't yet ratified the Maputo protocol but discussions are ongoing at official level to integrate notions of the protocol into an expanded access to safe abortion care. Legal guidance in CAR stipulates parental/guardian consent for care to minors (per se, safe induced abortion) but according to central Africa's law, the medical team has the duty to act at the best interest of the patient and superior interest of the child.(52)

4.3.2. Referral Maternity center in North Kivu, Democratic Republic of Congo

With an estimated population at 67 million inhabitants, DRC has a maternal mortality ratio at 730/100,000 live birth(53). The maternity center is in a small urban setting in North-Kivu. Since 1996,

two regional wars have taken place in the province of DRC's North Kivu. These were followed by a period of continued insecurity and multiple displacements of population. Today, the conflict is considered to be chronic with periods of more or less intense confrontations between different armed opposition groups active in the region and the government army. Till mid-2017, different UN peace keeping forces have also been based in the region.

The referral hospital of this area delivers CeMoNC and provides care to more than 520,000 inhabitants[f] and fluctuating numbers of internally displaced people, estimated being at more than 175,000 in August 2017[g].

In 2017, almost 3200 women received skilled birth attendance in the general hospital and 550 patients were admitted for post-abortion care[h]. The maternity has 25 beds, 13 beds are reserved for "gynecology" and 6 beds for "continuous care" (low level of intensive care). Abortion-related complications are admitted in the "gynecology" beds and "continuous care" beds.

Until recently in DRC, safe induced abortion was authorized by the penal code in exceptional cases stipulated in the medical deontology code[i] for "therapeutic termination of pregnancy" before fetal viability (28 weeks of gestation) and when the mother's life was seriously threatened and that the "therapeutic termination of pregnancy" was the only mean to save her. In April 2018, the ratification of the Maputo protocol by DRC State was published in the official journal. Then, following a "circulaire" of the superior Magistrate council[j], it took immediate precedent over DRC national law, thus expanding the scope of legal permission for safe abortion care to a variety of cases including threat to the woman's health and life as well as in case of rape (no need for evidence) and incest.

Legal guidance in DRC stipulates parental/guardian consent for care to minors (per se, safe induced abortion) but according to DRC's law, the medical team has the duty to act at the best interest of the patient and superior interest of the child.(52)

4.3.3. Referral maternity center in Jigawa State, Nigeria

With an estimated population at 170 million inhabitants, Nigeria has a maternal mortality ratio at 560/100,000 live birth(54). The study is planned to be conducted in a referral hospital of the Jigawa State, which has been supported by MSF since 2008. This CEmONC tertiary hospital has a rural catchment population of about 507 000 situated in a rural remote area of Northern Nigeria. Additionally, 60% of patients admitted come from outside the catchment area(55). It serves both general and displaced people from the current conflict involving Boko Haram in the Borno State (Northern Nigeria). MSF is supporting the maternity (63 beds) and the women intensive care unit (7 beds), where abortion-related complications are admitted. In 2017, this maternity admitted 12 600 women and assisted 8300 deliveries (among which 67% were complicated deliveries) and managed almost 1100 women seeking PAC.

According to Nigerian law[k], safe induced abortion is legal when performed by qualified practionners and when the procedure aims to preserve the life a pregnant woman[l]. Nigeria (South and North)

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[f] Source : Ministère de la Santé, dénombrement janvier 2017

[g] Source: Commission Mouvements de Population

[h] Source : Medical activity report, SRH OCB 2017.

[i] Source; Ordonnance n° n°70-158 du 30/04/70 in the « code de deontology médical » de RDC.

[j] Circulaire n° 04/SPCSM/CFLS/EER/2018 du 06 avril 2018 relative à la mise en execution des dispositions de l'article 14 du protocole à la charte Africaine des Droits de l'Homme et des Peuples relative aux Droits de la Femme en Afrique (Protocole de Maputo)

[k] South Nigerian laws include Federal laws, Criminal Code Act and Criminal Code only applicable to the Southern Sates of Nigeria. Northern Nigerian laws include federal laws, Penal Code and Penal Code Act.

[l] Section 297 of the Criminal Act: "*A person is not criminally responsible for performing in good faith and with reasonable care and skill a surgical operation upon any person for his benefit, or upon an unborn child for the preservation of the mother's life […]".*

court cases explicitly confirm that health of the women includes mental health grounds[m]. Safe induced abortion in case of rape or incest is not permitted *as such* by the law but is allowed by law and Nigerian courts on the basis of mental health. Additionally, Nigeria has ratified the Maputo protocol. Minors in Nigeria can consent to receive safe induced abortion and be offered medical confidentiality from their parents or guardians provided that the medical practitioner believes the minor has sufficient understanding and intelligence to enable her to understand fully the medical treatment/ procedure.(52)

4.4. Study population and sampling

4.4.1. Women with abortion-related complications

4.4.1.1. Medical Record review of women with abortion-related complications

4.4.1.1.1. Inclusion criteria

All women presenting to the wards of the study sites which see women presenting for PAC (emergency unit, gyn/obs units, ICU unit, PAC unit, etc. according to site)

- with any signs or symptoms of abortion-related complications, i.e. any signs or symptoms of complications of spontaneous or induced abortion, whatever the abortion stage: inevitable, missed, incomplete, complete abortion (definitions in appendix 3).
- Or with a presentation primary diagnosis of ectopic pregnancy or molar pregnancy (definitions in appendix 3)

Medical records of women who died from abortion-related complications will also be reviewed. If the woman had opted out before she died, her records will be excluded from review.

Even though ectopic and molar pregnancy are not per se, abortion-related complications, the present study will include them for three main reasons: 1) as explained in the definitions paragraph, at presentation, it is difficult to differentiate them from abortion-related complications in contexts without access to Beta-HCG and ultra-sounds. Therefore, it is not possible to exclude all of them at inclusion; a late exclusion criteria at discharge would be necessary and some ectopic and molar pregnancies will still be misclassified as abortion 2) the present study is seeking to collect data the most comparable possible to the WHO Multi-Country study in stable limited resource setting; this WHO study include also ectopic and molar pregnancies; 3) molar pregnancy, and especially ectopic pregnancy might also lead to near-miss events; the data that will be anyway collected on these cases up to discharge, can be of interest for orienting strategies and management of these 2 less studied conditions.

[m]As per the provision of the English case *Rex vs. Bourne* which is applied and followed in ALL Nigerian Courts (South and North)

4.4.1.1.2. Exclusion criteria

- Threatened abortion (defined as vaginal bleeding with a closed cervix after having excluded the diagnosis of ectopic pregnancy or molar pregnancy) (definition in appendix 3)
- History of abortion-related complications and presenting for an unrelated issue
- Opt-out to participate

4.4.1.1.3. Sample size

The sample size was computed to estimate with precision the primary endpoint of the study: the proportion of abortion-related near-miss events among all women seeking care for abortion-related complications. Using the normal approximation to the binomial calculation(56) and based on our hypothesis that the proportion of near-miss events among these women will be approximately 12% (twice the expected proportion in stable contexts(22,23)), a sample of 344 women presenting with abortion-related complications per site will allow estimation with 3.5% of precision and a type I error of 5% (95% confidence intervals). Estimating an attrition rate of 20%, we would need to include and review the medical record of **430 women presenting for abortion-related complications per site**.

The table 1 presents the different width of the 95% confidence interval of the primary endpoint if the proportion of near-miss event varies from 6% to 30% and we include 430 women. This sample size will provide estimates with a precision included between 2.5% and 5% at a 5% type 1 error. These precisions seem reasonable.

Table 1: Precision of the confidence interval according to different hypothesis of the proportion of near-miss events among women presenting with abortion-related complications according to different scenario of sample sizes (normal approximation method).

Proportion of near-miss	2%	4%	6%	9%	12%	20%	30%
Sample size (normal approx)	344	344	344	344	344	344	344
Precision (Width of the confidence interval)	1,5% (0,5%-3,5%)	2,1% (1,9%-6,1%)	2,5% (3.5%-8.5%)	3% (6%-12%)	3,4% (8.6%-15.4%)	4,2% (15,8%-24,2%)	4,8% (25,2%-34,8%)
Sample size with 20% attrition rate	430	430	430	430	430	430	430

Each identified site has a potential recruitment of at least 430 women for PAC during the data collection period of approximately six to nine months according to sites.

4.4.1.2. Quantitative survey among women with abortion-related complications

All women with abortion-related complications included in the medical record review, who are hospitalized (i.e who stayed overnight or more)[n] and who consent to participate (cf. §12.2) will be administered an in-person quantitative interview. According to the 2017 monitoring data of the hospital in CAR, we can assume that approximately 70% of the abortion-related complications will be hospitalized (i.e who stayed overnight or more), leading to an expected sample size of 300 women eligible for the quantitative survey in each site (240 minimum if 80% of response rate). This will

[n] In different MSF hospitals, hospitalized women, i.e. who stayed overnight or more, are often classified as « women admitted >24h » even if the women stayed overnight but didn't effectively stayed more than 24h.

provide reasonable power to describe the characteristics and to identify risk factors of severe complications.

If a woman was referred or died before the quantitative survey, she will not be included in this component of the study. This might be a source of selection bias. Nevertheless, all women eligible who will receive care at presentation (before an eventual referral or before dying) will be recorded in the medical record review to decrease this bias.

4.4.1.3. Qualitative interviews among women with potentially life-threatening/near-miss abortion-related complications

4.4.1.3.1. Inclusion criteria

Women eligible for the quantitative interview and who experienced at least 1 criterion of near-miss event or life-threatening conditions will be eligible for the qualitative in-depth interview. Criteria to identify near-miss events or life-threatening conditions are the ones used by the WHO multi-country survey in stable contexts(8) and are derived from the WHO near-miss approach for maternal health(57). They are described in Appendix 5.

4.4.1.3.2. Exclusion criteria

- Refusal to participate
- Participation to the interview identified as potentially harmful to the woman according to her health care provider (based on criteria adapted to each site that will be developed during the training by the psychologist, qualitative researcher responsible of this component).

4.4.1.3.3. Sample Size

We will attempt to identify and recruit a purposive sample of approximately 30 women per site. If our recruitment strategy that we intend to pursue does not yield a sample of 30 women, we will explore other recruitment strategies to reach our desired sample size.

4.4.1.4. Intermediary analysis for checking hypothesis

Regarding the sample sizes of the 3 components with women (file review, quantitative survey and qualitative survey):

Since the assumptions on which our sample size estimates are based are very uncertain (in particular the proportion of women hospitalized, the proportion of near-miss and the inclusion rates), intermediate analyzes will be carried out on each site after including 25% of the planned sample size. This will assess whether our initial assumptions are confirmed or whether it will be necessary to increase the sample size to achieve the objectives of the study.

4.4.2. Health professionals

4.4.2.1. Rapid Facility assessment

In each of the study sites, the provider in charge of the service providing post-abortion care will be the key-informant who will answer the rapid facility assessment questionnaire. If the head of the PAC ward is not willing to answer the questionnaire, we will propose to another staff manager who is over heading PAC activity (for e.g., deputy responsible of the PAC ward, head of the gynecological/obstetric ward, MSF medical team leader/medical referent).

4.4.2.2. KAPB survey among Health professionals

All health professionals (i.e. doctors, midwives, clinical officers, medical officers, nurses, aid-midwives, aid-nurses) involved in PAC and SAC services and literate will be proposed to participate in

the KAPB survey. A census of these professionals will take place prior to the beginning of the data collection. It is estimated that a 60 to 100 professionals per site will be eligible.

4.5. Procedures and study activities

4.5.1. Overall flow of the study

The overall organization and flow of the study procedure is given in the figure 2:

The data collection of the study will be collected sequentially and organized in 2 phases:

- Phase 1: data collection among health professionals
- Phase 2: data collection among women with abortion-related complications

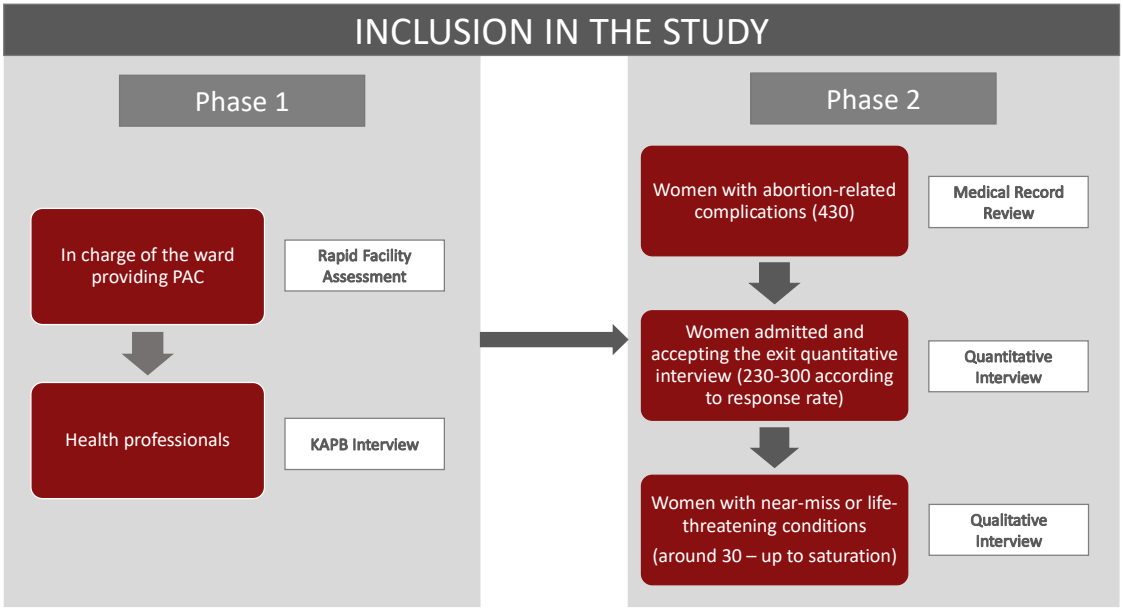


Figure 2: Flow chart of the study organization

4.5.2. First phase: data collection among health professionals

4.5.2.1. Rapid Facility assessment (head of PAC service)

First of all, prior to beginning field training, after informed consent has been given, the provider in charge of post-abortion care service will be interviewed by the study coordinator on the abortion care preparedness, capability and services provided at each of the sites including:

- Description of the abortion services available in the facility
  - Patient flow
  - PAC/SAC services availability thanks to the criteria of the model of "signal functions" developed by Healy et al.(1) and improved by Campbell et al.(2)
  - Supplies/Key drugs and Equipment for SAC/PAC/Contraception including frequencies of stock-out
- Description of services available in the facility to ensure pain management, infection prevention and control and privacy.

The rapid facility assessment questionnaire is in appendix 6. This interview should take 30 to 60 minutes.

To verify the information given, the study coordinator will build quick checks for some components of the assessment such as verifying caseload numbers from patient registers of the hospitals Health and Medical Information System.

4.5.2.2. KAPB survey (among health professionals providing PAC)

Then, also prior to beginning field training, a quantitative survey will take place to collect information on the Knowledge Attitude Practice and Behavior (KAPB) of eligible health professionals regarding abortion care. It will identify potential factors among health professionals that may contribute to severe complications and near-miss, i.e. that can be barriers to quality PAC and SAC.

At the beginning of the study orientation workshops, each provider who will consent to participate in the KAPB survey will answer a self-administered questionnaire including:

- Sociodemographic characteristics
- Description of their experience in abortion complications care, safe abortion care and contraception within and outside MSF-supported facilities.
- Description of the time length of their experience working with MSF +/- MoH
- Education/Training/exposure (including workshop, conferences) and supervision received about these topics
- Knowledge about the local law, regulation, policies on abortion in the country and in the organization
- Knowledge about existing practices on induced abortion in the region (these practices will be classified as safe, less and least safe according to WHO(12) (cf. appendix 4))
- Opinion about safe abortion care and post-abortion care in the community.
    - Where would women go?
    - What should be authorized?
    - How to improve existing services (PAC/SAC/Contraception) in the catchment area?
    - How to improve existing services (PAC/SAC/Contraception) in the MSF facility

  The KABP questionnaire is in Appendix 6. This interview should take between 15 to 30 minutes. No causation between provider attitudes and quality of care will be made in any papers.

4.5.3. Second phase: data collection among women with abortion-related complications

Then, after the study site training and the pilot phase (cf. §6), the data collection among women with abortion-related complications will be implemented.

4.5.3.1. Medical Record Review

Registers and medical records screening:

The first step involves the daily screening of registers and medical records of the wards receiving women presenting with abortion-related complications (Emergency ward, Maternity, Gynecology/Obstetric ward, Intensive Care Unit). The study coordinator and the study clinicians will be trained to identify all women who come for abortion-related complications. The study clinicians and/or the study coordinator will screen daily the registers of each ward and will participate in the clinical staff morning meeting to ensure that all women potentially eligible for the study are identified. Then s/he will ask the corresponding medical record from the health care provider and will check for eligibility according to inclusion and exclusion criteria thanks to a standardized screening form (cf. Appendix 6).

Medical record review:

With the help of the health care provider, the study coordinator or the study clinicians, specifically trained for the study, will extract data from medical records of eligible women into a standardized case report form (CRF) designed for the study (adapted from WHO PPM forms(8) - cf. Appendix 6). Data from the medical record of study participants who died will also be extracted. Data collected will include:

- Sociodemographic characteristic present in the medical record: age, residential area, marital status (no direct identifier, cf. §8.3)
- Mode of admission (coming directly from home, referred from another health facility)
- Any abortion care received in the previous days/weeks,
- Medical history (general and obstetric including gravida, parity, previous abortion/miscarriage, previous C-section, etc.)
- History of this pregnancy with estimated gestational age
- Symptoms at presentation/admission
- Clinical examination (Presence of Female Genital Mutilation at examination)
- Type of abortion
- Induced abortion or not (as written in the medical record)
- Clinical signs of induction
- Laboratory findings
- Management (method used/clinical intervention to treat the complication)
- Initial and Exit diagnosis
- Severity criteria (adapted WHO near-miss approach criteria in appendix 5)
- Outcome (death <24h, death >24h, referred, leave against medical advice, discharged)
- Length of stay
- Contraception prescribed or given

If for irresistible reasons, on-site data collection will not be possible, an off-site retrospective data collection process will be set-up. Medical records of women eligible during the retrospective period will be fully de-identified and then scanned by a trained study staff on site. The digital version of the de-identified medical record will be put on a secured sharepoint only accessible by the study staff in charge of the data collection and data entry. Data collection, data entry and data monitoring will be done at distance (off-site) using the routine information available in the scanned de-identified medical records (more details on confidentiality in § 8.4)

For this component of the study, no individual informed consent will be sought as only routine clinical information will be collected. The woman will nevertheless have the opportunity to opt-out if she wants and if it is possible (prospective). Further information is provided in the §8, Ethical considerations.

Additionally, every week, the study coordinator will collect in a standardized data collection form, the aggregated monitoring data necessary for calculating the denominators of our endpoints: total number of deliveries, live births, admissions in each of the ward where women with abortion-related complications are identified (emergency ward, maternity, gynecology/obstetric ward, ICU), pregnancy-related admissions. (Cf. Appendix 6)

4.5.3.2. Quantitative interview

Eligible women for the *quantitative interviews* will be identified by the study clinicians and/or the study coordinator with the help of her health care provider during the medical record review. The study coordinator or the study clinicians will inform the interviewer of her eligibility if the woman grants her/him permission to do so. Interviews procedures will be explained, and verbal documented informed consent obtained (cf. §12.2) when the woman is medically stabilized, i.e. physically and psychologically stable as well as able to consent. An interview of about 1 hour will be conducted through semi-directed face-to-face interviews in a dedicated and confidential room by the interviewer, during her hospitalization. A standardized quantitative questionnaire (cf. Appendix 6) will be administered by the study interviewer specifically trained for this study's component. It will include:

- Sociodemographic characteristics not included in the medical record, including
  - Socio-demographic characteristics including socio-economic level, education level and religion (religion might influence values and attitudes around access to safe abortion care and contribute indirectly to the severity of abortion-related complications)
  - Displacement/migration status
  - Living in areas exposed to conflicts/violence
- Personal exposure to violence (conflict/war related, sexual violence including intimate partner and or domestic violence, other types of violence)
- Access to and use of Contraception before the event and unintended status of the pregnancy
- Delays in receiving care according to the 3 delays model[o](58)
- Induced or spontaneous abortion, if induced, method used (provider, setting)
- Satisfaction with the quality of care delivered (experience of care relative to effective communication, respect, dignity and emotional support) to measure the "patient-centered care" component of the MSF quality of care framework (adapted from WHO standards on quality of care in maternal health(59))
- Contraception proposed/given at discharge
- Costs engaged by the woman/her family for this event before and upon arriving in the health facility supported by MSF
- Knowledge about existing regulations and practices on induced abortion in the region

To ensure comparability, the questionnaire has been designed on the current WHO multi-country study(8) with additional questions from existing questionnaires already widely used in similar studies(10,24). It includes a specific flow of well-designed questions regarding sensitive issues like induction of abortion or violence that have been tested in different African contexts. Our questionnaire has been designed in English and will be translated into French and local languages. It will then be back-translated into English or French to ensure the quality of the translation. The study interviewers will manage the questions in a language understandable to the woman. To facilitate a good interviewer-interviewee relationship, interviewers will be female. As far as possible, interviewers speaking the local language will be hired. If not, translators will be used as fully part of the study team, with the same confidentiality requirements and engagements.

To ensure a respectful and confidential implementation of the sensitive questions, a specific training on ethics principle, confidentiality, empathy as well as attitudes to adopt in case of emotional reactions will be provided to the interviewers, the study coordinators and the study clinicians. They

[o] The 3 delays model in maternal health includes (1) the delay in decision to seek adequate care, (2) the delay in reaching health facility, (3) the delay in receiving adequate health care at health facility.

will also sign certificate of confidentiality. The study coordinator (or the study clinicians) will provide regular supervision and continuing training to the interviewers. A psychological support set-up is planned for both the women and the study staff in case of need. More information is provided in §5 (Training), §8.3 (Confidentiality) and 8.4 (Risks and Benefits).

4.5.3.3. Qualitative in-depth interview

As explained above, eligible women for the *qualitative interviews* will be identified by the study clinicians and/or study coordinator with the help of her health care provider during the medical record review. The study coordinator or the study clinicians will inform the interviewer of her eligibility if the woman grants her/him permission to do so. Qualitative interview procedures will be explained, and verbal documented informed consent will be sought (cf. §4.5.3.2 and 12.2). The woman will be free to participate to one, both (quantitative and qualitative) or no interviews without any consequences on her current or future care. If the eligible woman consents to participate in the qualitative interview (§12.2), the study interviewer(s), who will have been trained for this qualitative study component, will propose a face-to-face *qualitative in-depth interview* in the same confidential location. If the woman accepts to participate in both interviews (quantitative and qualitative), the qualitative interview will be conducted after the quantitative interview at a different time. It will last around 1 hour and will be proposed to the women at a convenient time for her, during the hospitalization or the latest just after discharge. Eligible women will be asked open-ended questions focused on different themes related to the previously described objectives. Interviews will be conducted in the local language of preference and audio-recorded. In case the woman doesn't consent to the audio recording, written notes will be taken by the interviewer. Trained counselors or psychologists will be on-site during these interviews, and participants will be given their contact information should they need it. All counselors and psychologists will be sensitized about the study, and the study team will work with them to make sure they are able to accept referrals during the study period. Furthermore, interviewers will specify to women that counselors are on-site during the interviews and will only hold interviews when the counselor is on site.

The content of the interview will include

Theme 1: Pathway to care

- Describe her pathway to care, including all steps linked to her abortion-related medical condition
    - From knowing the woman is pregnant to her arrival to MSF facility
        - Decision-making process to seek care
        - Any traditional practices which the respondent used
        - The role of family, social environment
- Direct and Indirect Costs involved in the pathway to care (impact on the woman)

Theme 2: Perceptions, opinions

- Perceived barriers related to accessing abortion care which led to her choice of where to obtain the care (fears)
- Perceived difficulties, challenges faced, perceived response, help from the man involved in the pregnancy:
    - If she declares that she terminated the pregnancy,
        - Whether she told her partner/husband about her desire to terminate the pregnancy

        - How she perceived his position towards her decision
    - Presence of violence

Theme 3: Factors influencing where she got care

- What factors influenced the woman to get care where she did
- How she felt about the care she received (experiences with the care including satisfaction)
- Factors that could contribute to the life-threatening conditions and near-miss event (like 3 Delays)

A semi-structured in-depth interview guide will be developed to guarantee all the themes are included during the discussion (cf. appendix 6).

5. Training and Pilot

Central training:
An in-person meeting will be centrally organized to orient and train study coordinators on ethical principles, opt-out process, informed consent, confidentiality, the protocol, the procedures (SOPs), data collection instruments, supervisory/monitoring plans and data management.

Study site training:
At each study site level, the study coordinators will organize local training.
After the facility assessment and the KAPB survey (phase 1), a study orientation session for all the health care providers involved in PAC, including introduction to the study protocol, data collection process, opt-out process, informed consent, confidentiality, MSF code of conducts and processes of alert in case of abuse.
Then, the study staff (site investigators, study clinicians, key health care providers, and interviewers, translators and data clerks) and the health care providers involved in PAC will participate in an Exploring Values and Attitudes (EVA) workshop. The EVA workshop is an MSF adaptation of the Abortion Value Clarification and Attitude Transformation (VCAT) workshop developed by Ipas(60). VCAT workshops are grounded within existing cultural and social structures and ideologies. Cultural and social norms are extremely influential in shaping people's attitudes and values. This framework places the process of values clarification within a larger context of abortion attitudes, behavioral intention, and action. Whereas the goal of a traditional values clarification workshop is for participants to unpack and understand their values in a neutral setting, this framework and toolkit are designed to advance an agenda: to move participants along a progressive continuum of support for abortion care and sexual and reproductive rights, to the extent allowed by law. Therefore, it will improve awareness about the abortion topic as well as ensure adhesion of the study team to the study. Even though some of the health professionals have already benefited from an EVA workshop few months or years ago in the framework of their employment in MSF, they will be invited to participate again.

A specific training for the study staff will be organized. It will include training on the study protocol, CRF, questionnaires, qualitative interview guide, databases, procedures and manuals. All study staff will also be trained on ethical principles such as the Belmont Report ethical codes(61) adapted to this study including informed consent and confidentiality processes (cf. below §8.3). MSF code of conducts and processes of alert in case of abuse will also be part of the training program. All training will include theoretical and practical training phases. Refresher training will be conducted by study coordinators according to needs during the data collection and entry.

Pre-test and Pilot phase:

All data collection tools and the developed databases will be pre-tested by the study coordinator and the site investigators before the site training. After the study site training, the study processes of the data collection among women with abortion related complications will be piloted. It will include the test of the full study flow from register screening for identification of eligible woman, opt-out process, medical record review, informed verbal documented consent for quantitative and qualitative interviews to the interviews themselves to the data entry/processing. Minor modifications may be made to the protocol, data collection tools, informed consent forms and procedures based on what is learned during this pilot phase and tools pre-test. Additionally, this pilot phase, implemented prior to the collection of data, will also reinforce the capacities of the study staff thanks to on-the-job training.

The pilot phase will begin after having obtained approvals of the international ERBs and of the ethical committee of the site's country. The consent process will be the same during the pre-test and pilot phase as during the main data collection phase. Same information notice and consent forms will be used and tested. If necessary, after the pre-test, the used language will be adapted to ensure a full understanding of their content by the women. In this case, all ethical committees will be informed. The duration of interviews specified in the information notices will be tested and modified if necessary. We do not anticipate that the risks to participants in the pre-tests and pilot phase will differ from those in the study and will implement similar procedures to ensure confidentiality and de-identification of the data collected as in the main data collection phase. Pilot data will not be published or included in the final analyses.

6. Data management and monitoring

6.1. Quantitative data

Data from the medical record review and quantitative survey among women with abortion-related complications as well as from the rapid facility assessment and the KAPB survey among health professionals will be collected using standardized case report form (CRF) and questionnaires with binary or multiple choices. Procedure (SOP) manuals (including CRF fulfilling, interviews, data entry, and monitoring procedures) will be developed and provided to the study team. Each participant will receive a unique study code and all CRF and questionnaires will be completed with this unique identification code. Data will be monitored for accuracy, completeness, and consistency before being entered twice in databases specifically designed for this study. The databases will therefore contain only de-identified data and will be stored on password-secured computers in an encrypted folder only accessible to authorized study personnel. Back-up of the databases will be organized at regular intervals on external hardware. Original and back-up databases will be stored in 2 different safe locked locations (locked study rooms located on the study sites and at the level of MSF office). Access to databases will be protected with specific login and password. Data will be checked and cleaned by data entry staff supervised by study coordinator. Data cleaning will involve validation and checking for outliers, missing data, inconsistencies, etc. The study teams will transfer the de-identified databases files at regular intervals at the central system managed by Epicentre, through safe channels for ensuring confidentiality. Then, the Epicentre central study team will share the de-identified data files with the members of the international coordination committee through encrypted and safe channels for ensuring confidentiality. Access to transferred de-identified data files will also be protected with a login and password only assigned to the authorized international study team (i.e., Ipas, Guttmacher Institute, MSF/Epicentre central study team).

6.2. Qualitative data

Interviews will be transcribed directly into French or English by the interviewer. All sensitive materials (audio files, transcripts) will be stored in locked locations (locked study rooms located on the study sites and at the level of MSF office). The study teams will transfer the de-identified transcript files at regular intervals to the central system managed by Epicentre, through safe channels for ensuring confidentiality.

6.3. Data Sharing Agreement

The Memorandum of Understanding includes a chapter on data sharing agreement (DSA) between each of the partners (MSF-Epicentre/Ipas/Guttmacher) (cf. §8).

7. Data analysis

7.1. Quantitative data

A detailed statistical analysis plan will be commonly developed by the study international coordinating committee (cf. §9). Interpretation of the results will be done with the study site steering committees (cf. §9) and MSF-MoH staff of the sites.

Analysis of the data of women with abortion-related complications:

Data collected during the medical record review (CRF) and during the quantitative interview will be linked and analyzed jointly.

Primary analysis:

Data will be first analyzed separately for each site at the end of the corresponding site data collection. The objective of these primary analyses is to interpret results of each facility supported by MSF in order to formulate recommendations to improve operations of each site. Participants' characteristics (age, education level, socio-economic level, marital status, displacement, and exposure to conflict, exposure to violence, obstetrical history, etc.) will be summarized using counts and proportions for categorical data, and median with interquartile ranges for continuous data. The primary endpoint (proportion of near-miss event among all abortion-related complications) will be estimated by dividing the number of women who presented a near-miss event from presentation to discharge by the total number of women presenting to the facility with an abortion-related complications. It will be reported with its 95% confidence interval computed using the normal approximation method. Methods to compute secondary endpoints described in the § 5.2 will be detailed in the statistical analysis plan. Definitions of abortion-related complications, induced abortion, severity levels of the complications (including near-miss events) and the safety level of induced abortion that will be used for the analysis are described in Appendixes 2, 3, 4 and 5.

Secondary analysis:

A pooled analysis of the data of all sites will be conducted to estimate the same endpoints once the data collection of all study sites will be completed. By conducting pooled analysis, we are aiming at pooling results of the fragile and conflict-affected study sites in order to be able to compare them with existing literature in stable context. Nevertheless, we will keep in mind the limits of this comparison because our sample will not be representative of an homogenous full conflict-affected population (it is impossible to get a representative sample in conflict-affected areas because of movement restrictions) and because the heterogeneity of the methods and definitions used in the literature will limit this interpretation(21,22). Nevertheless, the comparability of our design and tools with the ones used in the WHO multi-country study currently implemented in stable contexts will allow some comparison(8).
Pooled data will also be used to conduct an exploratory analysis of the association between different characteristics of the study population and the occurrence of near-miss events using univariate and

multivariate analysis adapted to the type of variables. The correlation of within-sites data (heterogeneity) will be accounted using GEE or random effect models.
The between-sites heterogeneity will be explored and if the heterogeneity is too important, pooled analyses might not be performed.

The limitation of the retrospective data compared to prospective data of the medical record review will be clearly acknowledged during discussion, interpretation, and diffusion of the results. These limitations include mainly information bias with additional incompleteness and/or inaccuracies as the information available in the medical record will not be completed by daily clarification given by the clinician. To help assessing the impact of these additional limitations, the proportion of missing data will be compared between the prospective and retrospective dataset in the same study site.

Analysis of the data of the rapid facility assessment and KAPB survey among health professionals:

Proportion of responses to the facility assessment and KAPB questions will be presented separately for each site and tabulated.

For all multivariate analysis, missing data will be imputed after examining if underlying hypothesis are verified. Statistical analysis software like STATA 13 (College Station, Texas) or R will be used.

7.2. Qualitative data

During analysis, criteria to identify women with life-threatening conditions vs. with near-miss abortion-related complications will be derived from the WHO ones described in Appendix 5. The coding will be performed using NVIVO 12 according to major themes of interest. Coding will remain alert to emerging themes and the node structure will be flexible enough to accommodate unexpected results. Thematic content analysis will be conducted to analyze the data systematically so as to be able to draw conclusions which can be illustrated through respondents' quotes.

7.3. Triangulation of the 4 components

While the data will be collected sequentially (as detailed in the § 4.5), this mixed method study will use a concurrent (simultaneous) triangulated approach (62), in the sense that qualitative and quantitative data will be collected and analyzed separately and then combined to generate complementarity between them. The findings will complement one another at the data interpretation stage.(63)
In other words, first, all components will be analyzed in parallels. Then, results of the 4 components will be compared and put into perspective. The results from one component will help in/complement the interpretation of those from another. For example, the results of the qualitative component might help interpreting the quantitative findings regarding the 3 delays in accessing care for the woman. If the first delay is the most quantitatively associated with near-miss events, the results of the qualitative interviews might help understanding the roots of the barriers in the identification of the danger signs by the woman. Another example is the complementarity between the barriers to access care identified in the quantitative and qualitative components among women, and the barriers to access care identified in the KAPB survey among health professionals or in the health facility assessment.

8. Ethical Considerations

8.1. Ethics regulation and authorizations

The study will be conducted in accordance to the revised Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects, http://www.wma.net/en/30publications/10policies/b3/index.html)

Before study initiation, the protocol, the opt-out process documents, the information sheets, the consent forms (Appendix 7) and any other relevant documents will be submitted for approval to the National Ethics Committees and regulatory authorities as well as the international MSF Ethical Committee and the Guttmacher Institute Ethical Committee. The written National Ethic Committee /International Ethical Review Boards approval must be made available to the international coordinating committee before the study can start.

8.2. Informed consent

Informed consent procedures for health professionals: For the *rapid facility assessment* (component 3) and the *KAPB survey* (component 4), the responsible of the service providing PAC and the health professionals providing PAC will be informed by the study coordinator of the purpose and objectives of these components of the study. The study coordinator will explain to them that participation is fully voluntary, that refusing it will not affect their employment status with MSF and that they have the right to skip some questions and/or stop their participation at any time. Written informed consent will be obtained by the study coordinator prior to beginning the questionnaires. Because of the sensitive subject, the names of the health professionals will not appear in the consent forms (nor in the questionnaire). Only their study identification numbers will appear.

Opt-out process and informed consent procedures for women with abortion-related complications:

Figure 3 summarizes the consent procedure for women and who will administer consent for each phase of the study.

Medical Record Review of women presenting for abortion-related complications for who the opt-out process is feasible:

In this component, individual consent will not be necessary because as per the Council for International Organizations of Medical Sciences (CIOMS) guidelines(64) (1) the data collected in this component is only clinical data that is routinely registered in the medical records; no identifying information will be entered in the dataset, the data will be coded in alpha-numeric format and confidentiality clauses will be explicitly specified for those conducting the data extraction (the study coordinator, the study clinicians and health care providers will be thoroughly trained about this principle and will sign a certificate of confidentiality); (2) the research would not be practicable to carry out with an informed consent process: some of these women coming for PAC will stay only a few hours in a busy medical ward where a formal informed consent would take a substantial amount of time in a context of emergency care and would probably lead to a low response rate.(3) the research has important social value: not collecting data on all women with abortion-related complications, including the less severe ones that would stay only few hours in the facility would induce a selection bias in the study preventing a valid estimation of the primary endpoint (proportion of near-miss events among all abortion-related complications) and the identification of risk factors associated with severity; as highlighted in § 2), these data can have a high impact in informing access to better Post-Abortion Care and Safe Abortion Care in fragile and conflict-affected areas.

Nevertheless, although we are not seeking individual informed consent for the medical record review, we will use an informed opt-out procedure that will be carried out for women presenting for Post-Abortion Care. Indeed, as highlighted in the (CIOMS) ethical guidelines for Health-related Research Involving Humans(64), « when used data are collected in the context of routine clinical care, an informed opt-out procedure must be used ».

Posters and information material explaining the involvement of the facility in the study with medical record review will be available in areas visible to the women in each of the study sites, especially in each ward where women with abortion-related complications can be identified (emergency ward, maternity, gynecology/obstetric ward, ICU according to sites). The information material, developed in local languages, will clearly state the confidentiality engagement and the de-identification of the data extracted as well as that data are collected to improve the care provided. The information material will include a note stating that the woman can inform a study staff or their health care provider if they want to "opt-out" of the medical record review. Health providers will be trained to convey women about the opt-out option at the start of the clinical visit so that they can brief the women (including illiterate ones) and answer any questions. They will be also trained to check if the illiterate woman understood the opt-out process. If needed, a study staff will be called to explain the process to her. In case of opt-out, health providers will clearly write it in the medical record and will fulfill a specific verbal documented opt-out form (cf. Appendix 7). For illiterate women, a witness may be present during the opt-out process. In this case, data of the women who opt-out will not be extracted from their medical review. Thanks to this process, all CIOMS conditions for the informed opt-out procedure will be full filled: (1) women will be aware of its existence and 2) sufficient information will be provided thanks to the posters and information material that will be available in visible areas 3) women will be informed that they can withdraw their data and that 4) they have a genuine possibility to object. The opt-out process of the women who are not able to opt-out because of the severity of their condition will be done once she is medically stabilized and able to opt-out if she wishes. She is likely to be hospitalized and will therefore be eligible for the quantitative interview.

In any case, all women hospitalized will be given again the opportunity to opt-out from the medical record review component during the process of individual verbal documented informed consent for the quantitative interviews (cf. below).

The opt-out process of the women who died will be done with the women's family.

The same informed opt-out process is currently implemented in the 30 stable countries participating to the WHO Multi-country Survey on Abortion-related morbidity and mortality(8).

Retrospective Medical Record Review of women presenting for abortion-related complications for who the opt-out process is not feasible:

If for irresistible reasons, the medical record review can be done only on a retrospective way and no opt-out system was implemented during the routine data collection in the medical records, a request for exemption from individual information is made to the ethical committees for those patients who were already discharged.
This is possible because as per CIOMS guidelines (64), "when researchers seek to use stored data collected for past research, clinical or other purposes without having obtained informed consent for their future use for research, the research ethics committee may consider to waive the requirement of individual informed consent." To do so, the following conditions have to be fulfilled
1) "the research would not be feasible or practicable to carry out without the waiver". The opt-out system was not in place during their hospitalization (the study didn't start on this site) and it is not possible in this context, to attempt to retrospectively obtain informed consent from discharged patients. Several factors contribute to this impossibility: security context, the tracing may increase

the risk of stigmatization to the contacted women and the cost to trace these women for consent will be un-proportionally expensive.
2) "the research has important social value." The objective of the study is to assess the magnitude and severity of abortion-related complications in conflict-affected setting. Giving-up on collecting these data in the site where the exposure to conflict is the highest would be an important loss of information as such data would never be possible to collect otherwise, excluding some of the most vulnerable populations from research. Even though the level of evidence will be lower, this retrospective design will allow to obtain information to estimate the primary end point on a study site currently under high conflict and instability. It will also permit to describe an important part of the secondary endpoints aiming for care quality improvement
3) "the research poses no more than minimal risks to participants or to the group to which the participant belongs." Risks for participants and the community will not be different from the ones described in § 8.4. Additional processes will be set-up to reinforce the confidentiality in the context of off-site data collection, including an early full anonymization of the dataset (cf. § 8.3 below).
As for the prospective design, the data collection will be done in collaboration with local health authorities and results will be shared with the local stakeholders as described in § 8.6

Interviews with women hospitalized for abortion-related complications (quantitative and qualitative):

Verbal documented informed consents will be obtained for both women participating in the quantitative interview and women participating in the qualitative interview.
Verbal documented informed consent has been used in previous abortion incidence studies in Malawi(65), Kinshasa(66), Ethiopia(67), Zimbabwe(68) and Uganda(69). Verbal consent is superior to written consent in this context because it minimizes the risk of revealing a study participant 's identity and compromising her confidentiality, in the unlikely event that informed consent documents with study participants' names and signatures are misplaced or requisitioned in the course of fieldwork.
Women eligible for quantitative and/or qualitative interviews will be identified by the study coordinator and/or the study clinicians with the help of the clinician in charge of her medical management. Each eligible woman will be proposed to participate in the interview(s) once she is physically and psychologically stable. Physical and psychological stability[p] will be determined by the study coordinator, study clinicians or her care provider who, as medical professionals, are capable of making this judgment. Proposing the interviews when she is medically and psychologically stable will help to preclude any fear that not consenting to the study might cause them to be denied appropriate treatment. The study coordinator, the study clinicians or her health care provider will inform her, discreetly about the existence of this study and seek verbal permission to introduce her to the interviewer in charge of doing the informed consent process. If the woman provides permission, she will be invited in a confidential room, where the interviewer (who is not the woman health provider) will propose her to participate in the quantitative interview and obtain verbal documented informed consent. Then, if she is also eligible to participate in the qualitative interview, a complementary verbal documented informed consent will be obtained.
Interviewers will be trained to seek consent in a way that does not disclose the woman's reason for seeking care or her eligibility for a study of post-abortion care to any other patients or providers in

[p] This protocol will follow the American Hospital's Association's definition of stability: "Vital signs are stable and within normal limits. Patient is conscious, but may be uncomfortable. Indicators are favorable."

the facility. It will be explained to the woman that study participation is voluntary and that refusing participation will not affect the woman's current or future access to health care.
For each interview, the verbal documented informed consent process will be implemented as follow. The paper-based information notices (appendix 7) for the interviews will be available in either English or French or local languages. It will be given to the woman and explained verbally in-person by the trained interviewer in the language of the respondent's choice. If necessary, a translator will assist the interviewer. The woman will also be informed that the information collected from her will be fully confidential and will be used only for research purposes. Sufficient time will be given for questions and clarifications. Then, if the woman accepts to participate, the consent form will be signed only by the interviewer (in English or French). If the woman is illiterate, she may identify an independent witness who will participate to the informed consent process to check her understanding and willingness to participate. The presence of the witness is proposed to be optional because for such a sensitive subject, involving an external independent person can be felt risky (of breach of confidentiality) by the woman. The woman can have the willingness to go through the information process refusing any person external to the study to be involved as the information notice mention the topic of the subject. So, if the presence of an independent witness is not accepted or not possible, an adapting witnessing process will be proposed to the woman. She will be proposed to listen to an audio-recorded information notice in local language that will be pre-validated by an external independent witness. An example of detailed process for the Jigawa state's site is presented in Appendix 14.
It will be explained to each woman eligible to the qualitative interview additionally to the quantitative interview that she can choose to participate in one, both or no interviews. If she accepts to participate in the qualitative interview, it will be explained to the woman that this interview will be recorded to ensure the quality of the research methodology, that all recording will be kept strictly confidential, but that she is free to accept or refuse this recording.

Every respondent has the right to end her participation at any time. If a woman wants to withdraw and if she gives the reason for her withdrawal, her permission to put this information in the questionnaire will be sought. Then, the woman will be thanked for her time and the conversation will be ended.
All consent forms are subject to review by all Ethical Review Boards.

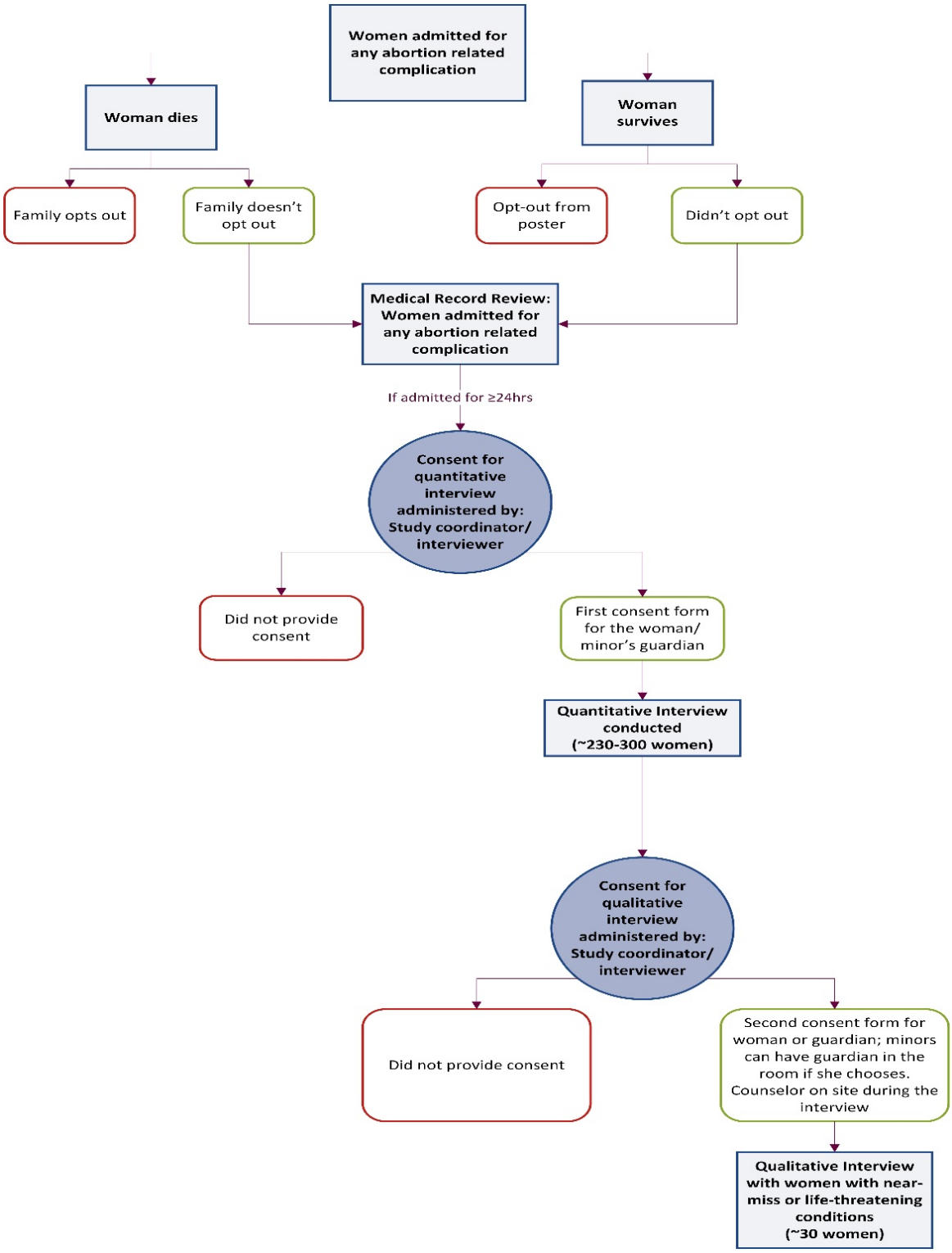
Interviews (quantitative and qualitative) with minors presenting for abortion-related complications:

For minors, the verbal documented informed consent process for interviews will follow the country and local regulation where available and CIOMS guidelines when absent. As highlighted in the CIOMS(64), giving sensitive information to a third party (such as information related to abortion) may expose the minor to social and legal risks : "In these cases, parental knowledge of the topic of the research may place the children or adolescents at risk of questioning, intimidation, or even physical harm by their parents/guardian."(64) Therefore, if there are no country regulations and CIOMS is adhered to, minor women will be considered as "emancipated" or "mature" minors if their health care provider and the study coordinator believe they have sufficient understanding and intelligence to enable them to understand fully the study information and decide for herself. And, in this case, with their confidentiality as our main concern, we propose to waiver parental/guardian consent and rely on the documented verbal informed consent of the minor. And, as advised by CIOMS, to ensure the protection of her best interests, the minor will be proposed to identify an independent adult witness (i.e. child advocate) who will participate in the informed consent process, and help the minor understanding the information.
Overall, if the minor is treated as emancipated and therefore, authorized to consent for herself and if she chooses to participate, she will be included after a verbal documented informed consent process (by the interviewer) with the help of an independent child advocate according to her choice. Then,

for each country, we will include country-adapted information about the local regulation. For example the 2016 Nigerian Policy Statement Regarding Enrollment of Children in Research in Nigeria(70), waiver of parental consent can be granted when the proposed study a) poses no more than minimal risk: as highlighted in the identified risks section (Section B.6) of this non-therapeutic study will be mitigated by all the measures described and the risks following a breach of confidentiality might be higher for the minor if her parents/guardian consent is sought; b) holds out potential to benefit the children being involved in the study; and c) the study objectives could not otherwise be achieved where parents have to be consented: we foresee that most of the minor will be an important group to include in the research as their age is probably a risk factor for more severe abortion-related complications. The Federal MoH guidelines for young person's participation in research and SRH services in Nigeria mentioned that "In such situations, consent from another adult who can ensure the young person's safety, security, and wellbeing might be more appropriate." (71)

If the other country regulations requires the team to collect the informed consent of the guardian/parent or if the country regulation requires the team to collect the informed consent of the guardian/parent, or if her health care provider or the study coordinator considers that she is unable to understand fully the study information, the agreement of the minor to involve her parents/guardians will be sought. Additionally, a formal verbal documented agreement (assent) of the minor will be sought. Thereafter, if the minor is willing for the study staff to contact her guardian/parent and if she gives her assent to participate into the study, we will proceed with the enrolment process after a verbal documented informed consent of the guardian/parent additionally to the minor's formal assent. However, if the country regulation, the health care provider or study coordinator require to collect the informed consent of the parent/guardian and the minor does not agree to inform this parent/guardian, she will not be invited to participate.

Figure 3: Flow chart outlining the recruitment and consent process for women.



8.3. Confidentiality

The survey data provided by respondents will be used for analytical purposes only and we will not present results that will permit identification of the respondents.

For the women presenting with abortion-related complications, data extracted from medical records and interviews will be de-identified in the data collection tools. The study data collection tools will only include the following identifying information: the study individual identification number, the date of presentation to the facility or the date of the interview, her area of residence (no address) and the age of the participant (no birth date).
The screening and inclusion logbooks will include the name, birth date, residence (neighborhood), medical record number and study identification number. This screening and inclusion log connecting the participant study identification number and her personal information will be kept only on a paper form in a locked cabinet in the locked study room and will be accessible only by the authorized study staff
If for irresistible reasons, the medical record review is done retrospectively and off-site, medical records will be scanned and put on a secure MSF-validated sharepoint after full de-identification. The data extraction will be done at distance (off-site) by the trained study staff with the same process as described in the prospective medical record review. The digital format of de-identified data will be kept only in password protected USB, password protected research computer or password protected secured MSF-validated sharepoints, accessible only to authorized research staff. No paper-based research documents will be kept onsite except the logbooks connecting the participant study identification number and her personal information for a limited period of time. These logbooks will be kept only on a paper form in a locked cabinet only accessible by the study staff in charge of scanning medical records. These logbooks will be destroyed immediately after data collection and monitoring is completed, in order to fully anonymize the final retrospective database.
All these additional measures set-up may better limit risks of breach of confidentiality in case of important security incidents on the study site. Indeed, when secure processing of paper based original medical records and research documents might be hampered by field security context (quick destruction of paper could not be possible), using digital format such as de-identified scan and password protected coded spread sheets can be safer to secure the data and to mitigate the risk of breach of confidentiality.

The transcripts of the audio records will only include the study individual identification number of the participant. The audio records will be destroyed once the electronic databases are frozen.

Data extracted from KAPB interviews with health professionals involved in PAC and from the rapid facility assessment will be de-identified in the data collection tools. The questionnaire will only include the following identifying information: the study individual identification number, the date of the questionnaire fulfillment, the age and sex of the participant (no birth date), and the professional category (doctor, midwives, nurses, midwife/nurse assistant). The list connecting the health professional study identification number and his/er personal information (name) will be kept only on a paper form in a locked cabinet in the locked study room and will be accessible only by the authorized study staff.

All study documents will be kept confidential by the study team (study coordinator, study clinicians, interviewers, translators, data clerks) and will be stored in a locked cabinet in the locked study room of each site, when not used by authorized staff. Each member of the study team as well as the health care providers, will sign a certificate of confidentiality (CoC). This CoC commits them to following the confidentiality principles and intends to prevent them from disclosinging data that can identify a research participant in legal proceedings**.** The paper-based screening and inclusion logbook with names and the informed consent with study staff's signatures will be stored separately, and will be

accessible only by the research team. All transcript data or data entered into the electronic databases will be de-identified. The transcripts, audio records and databases will be stored on password-secured computers in an encrypted folder only accessible to authorized study personnel. All consent files, the logbooks, CRFs, filled questionnaires and transcripts will be destroyed 10 years after the databases freeze.

8.4. Expected risks and benefits

Risks:

For women presenting for abortion-related complications, the study poses no direct physical risk to women as there is no intervention provided.
There is some risk of psychological distress induced by some of the questions in the interviews. Abortion is a sensitive subject; some fieldworkers may have differing attitudes towards abortion. To minimize these risks, different mitigation strategies will be set-up. The EVA workshop will help the study team in developing an empathetic behavior, preventing negative attitudes as well as preventing information biases in the collection of data. After values exploration, any potential staff of the study team who is unable to understand and provide tolerant and empathetic non-biased counsel will be dismissed. Additionally, interviewers will be trained to always remain neutral and empathic. They will be asked to remind respondents that they may skip any question or stop the interview at any point. To inform respondents about options to deal with any distress associated with the study, the interviewer will provide women with a list of counsellors and/or psychologist she can visit for her needs. Each study location has on-site counselling services that will be identified before the beginning of the data collection (at least MSF intersectional psychologist in CAR or DRC, local psychologist in Nigeria). Counselling services specific to children and adolescents will also be listed and clearly identified if they exist on-site.
There is also a risk of social stigma and legal prosecution for the participants if a breach of confidentiality happens. This risk will be carefully mitigated by all the confidentiality measures set-up (cf. previous §). In addition, all interviews will be conducted at the health facility where the woman received treatment for PAC when she is medically, physically and psychologically stable. Conducting interviews when the woman is stable ensures that enrolment in the study will not affect the woman's care in any way and that she is feeling well enough to participate in the interview. Additionally, conducting the interview while she is still in hospital avoids further stigmatizing the respondent and may instead give the appearance that the interview is a routine part of her post-abortion care, a lifesaving treatment recognized in each of these countries as an integral component of maternal health care.
We don't expect specific additional risks for minor women.

The KAPB survey among health professionals might identify some negative attitudes that may have negative psychological and social consequences on their patients (not only the study participants). While this risk is not inherent to the study (but to the care provided by MSF-MoH), the study may allow to highlight such an existing issue. The EVA workshop that will take place after the KAPB survey has also the objective to mitigate it, creating a group dynamic that help moving participants along a progressive continuum of support for abortion care. And, while reporting of individual self-reported negative attitudes will not be possible (KAPB survey information will be fully confidential and the study engage itself to prevent any consequences on study participants' work), the study coordinator will briefly analyse the results of the KAPB survey before the EVA workshop. And if the KAPB survey identify some specific negative attitude, the EVA workshop will be adapted accordingly to focus more specifically on these identified issues and all health professionals providing PAC will be invited to participate even if they have already participated to a former one few months or year ago in the context of their employment. Additionally, the study being in an MSF context, MSF code of conducts and processes for abuse alert will automatically applied to the study. It will be part of the health

professionals and study team training.

For health professionals, there is also some risk of breach of confidentiality. This risk will be mitigated by the fact that all consent forms and questionnaires will be de-identified and self-administered during the first part of the study training sessions, as well as by all confidentiality measures set-up (cf. previous §). The risk that health professionals interpret the KAPB survey as an evaluation of their work will be alleviated by the study coordinator in explaining in detail the subjects of the study and in which way it will benefit the study. Furthermore, the study coordinator will reassure that everything they say is kept confidential and that their participation is not linked to the performance of their work.

The study team and in particular the interviewers may face some risks of psychological distress induced by some difficult stories of the interviewed women with abortion-related complications. Therefore, to mitigate this risk, the study staff will also be proposed to benefit from psychological support in case of need. The system set-up will be adapted to each site. It can include: proposition to participate in group discussion led by a counsellor/psychologist external to the study and/or individual support with pre-identified psychologists or counsellors (MSF intersectional psychologist in CAR or DRC, local psychologist in Nigeria).
Other risks to the study team (including national or international study staff posted or making a study visit) associated with the study are risks associated with the context (nearby conflict areas). Research staff is not at increased risk of harm compared to other MSF and MoH staff working at the facilities. This risk is mitigated by the fact that the study staff (MSF, Epicentre or any external visitor to the study) are under MSF security rules, guidelines and protocols as for any MSF staff.

Even though the study is focused on abortion-related complications, and the study team will not provide safe abortion care to the participants, the latter may face some social and legal risks because they are linked to a study on this subject of “abortion”. To mitigate those risks, they will be clearly informed about the topic of the study during the recruitment process, the training and pilot phase. They will be free to withdraw at any time if they face any issues. And in case a social or legal issue happens, MSF will use all possible strategies to protect them.

To finish, a special care will be taken to ensure that external communication will not put participants, communities, health professionals, health facilities and involved partners at social or legal risk. All external communication will be first validated by each study partner (MSF, Ipas, Guttmacher Institute) before diffusion. Information on potential induced abortion performed in the health facility is only collected for the understanding of the context but will not be subject to external communication.

Benefits:

No direct benefit for the women participating to the study is expected. Nevertheless, it is expected that the study will bring longer-term indirect benefit for the local communities (cf. §8.5 below) as well as for the general community of women living in fragile and conflict-affected settings. Despite documentation showing risks to women’s sexual and reproductive health in fragile and/or conflict affected settings, there is almost no data on abortion, its ensuing complications, or women’s access to abortion care. This persistent lack of evidence results in reduced attention to the need for safe abortion care and the burden of morbidity and mortality due to unsafe abortion. The study will generate evidence on abortion-related complications and factors associated with near-miss events for women presenting with abortion-related complications in fragile and/or conflict affected settings, where the challenges women face managing their reproductive health are different from those in stable settings. As explained in the Impact §, we expect that the collected evidence will provide

arguments to prioritize access to safe abortion care for all women and girls who need it in fragile and/or conflict affected settings, and to improve access to contraception and abortion services adapted to the needs of the women and girls.

As far as possible the interviews will be done while women are still hospitalized and all care provided at the health facility (including food for those who cannot afford to feed themselves during their admission) is free. Some water, biscuits, or other in-kind provision will be offered to the women during interviews to ensure her comfort. According to each context, we also intend, if appropriate, to offer respondents to the qualitative component a small in-kind gift to take home to acknowledge the time spent in participation. This will depend on each context and be decided by the local team who know what could be appropriate and supportive for the participant (e.g. washing soap).
To finish, health professional participants will benefit from the sensitization and training implemented by the study.

8.5. Disclosing obligation

Obligatory disclosure is a traversal concern in MSF action (certain diseases, sexual violence, incidences involving minors, etc.) and addressed by the legal department as follows. The below is equally applicable to the question of legal reporting requirement in care or research context. In the context of his clinical practice or in the context of an investigation or judicial/criminal proceedings, an MSF medical practitioner or MSF as a legal entity can be obliged to declare to authorities or can receive a request of declaration for: 1. the medical examination of a person; or 2. the communication of documents/ information/ name(s) of patient; or 3. testimony before a tribunal or a court of justice. The above requisitions are legally valid but do not exempt the medical practitioner or MSF from complying with its legal and ethical medical obligations including: (1) the strict respect of medical confidentiality: which protects the health status of the patient but also their name: MSF must not communicate the names of the individuals who benefit/have benefited from MSF medical services to any third party; (2) the obligation to act in the best interest of the patient. Respect with these rules must always prevail over any request received, including any rule that may be contrary to these principles because the declaration or disclosure of this information may put the patient at risk. Thus, in case a woman (minor or adult) mentioned during the interview(s) that she has been victim of violence, the interviewer (who is not a health professional) will not make any declaration even if an authority requests it and even if there is a legal obligation to do so, since strict respect for medical confidentiality and the obligation to act in the best interests of the participant prevail (same rule as for any health care provider working in structures supported by MSF). Nevertheless, the woman or girl will be informed that she has the possibility to report it to the competent authorities and will be encouraged to do so if she wishes and if it is in her interest.

Thus, if the interview reveals that a minor or a woman has been victim of any form of violence, the interviewer will refer the woman or the girl to the MSF/MoH healthcare professional in charge of the care for violence, reassuring her about the total confidentiality of the process. If the woman / girl wishes, the interviewer will help her to explain the situation to the health professional. Then, it will be the MSF/MoH health professional who will take over. He will be responsible for offering all available services including medical and psychological care as well as social and legal support (providing a forensic certificate where appropriate, reference and accompaniment to competent organizations that provide shelter if necessary, legal support, including support to inform the competent authorities).

8.6. Local community participation and benefits

First, the study will contribute to improving quality of care relevant to this important health need for the communities using participating facilities.
Second, communities using the participating facilities will be informed about the study through the posters and leaflets that will be available in the study sites. Additionally main local authorities will be informed about the study and its importance through the site steering committee, written communication or other means of communication according to local feasibility. It will allow an initial attention of local authorities and communities regarding the potential harmful complications of abortion. It will be emphasized that the study is carried out in collaboration with the Ministry of Health. As far as possible, the local authorities and local civil society will be represented in the site steering committee of the study. At the end of the study, a local and national dissemination of the results will be conducted in each of the research site countries to engage communities, stakeholders and policymakers through different modes of diffusion adapted to the context (reports, leaflets, medias, or workshops).
While men in the communities are excluded from being respondents in the data collection regarding abortion-related complications, we will target women and men in the dissemination of results, as we believe this will increase overall understanding of gender inequality for the broader communities. Additionally, the results of the study will be available at facilities supported by MSF at the end of the study through posters, leaflets or other adapted communication means. All participants of the study will be informed during their interviews that they will have access to the results of the study at their facility at the end of the study. All this information will benefit the communities in raising their awareness regarding the issues of abortion-related complications. Particular care will be taken while developing these communications to ensure that the wording is at an acceptable reading level.
Finally, unsafe abortion causes harm to women worldwide, yet little is known about the abortion experiences of women living in fragile and conflict-affected areas including the consequences and the kinds of complications they experience. Bringing attention to this neglected health problem in the participating communities will result in recommendations to improve the quality of abortion-related care in the study locations. Drawing attention to the persistence of unsafe abortion in these communities has the potential to facilitate policies that minimize needless morbidity and mortality due to unsafe abortion and can highlight the role safe abortion can play in reducing these health sequelae.

9. Research oversight and Partnership management

The study will be led by a partnership of 3 different organizations with complementary areas of expertise:

- Ipas has a multi-faceted approach to improving women's access and rights to safe, high-quality abortion, post-abortion, and contraceptive services. Their approach focuses on: improving Ipas's global, regional, and country programs through training and technical assistance for service-delivery improvement; increased community support and access to care; as well as research and policy support to increase women's access to lifesaving care. Ipas aims to eliminate unsafe abortions around the world by working in collaboration with a wide range of partners such as MSF-Epicentre and the Guttmacher Institute. Ipas has already led 4 abortion-related morbidity studies in limited resource countries. Ipas co-leads (research design, protocol, tools, analysis, and dissemination) the study development and coordinates the partnership.
- Médecins Sans Frontières (MSF) is an international, independent, medical, humanitarian organization that delivers emergency aid to people affected by armed conflict, epidemics, natural disasters, and exclusion from healthcare. MSF offers assistance to people based on need and irrespective of race, religion, gender, or political affiliation. The organization's core work is providing emergency medical assistance in situations of armed conflict. Over the years MSF's involvement in reproductive health and sexual violence care has increased significantly;

emergency obstetrics and newborn care, post-partum care and safe abortion care are at the forefront of the activities for their direct contribution to the reduction of maternal mortality and suffering. Epicentre is an association created in 1986 by MSF to provide epidemiological expertise and develop research in support of MSF operations. Nowadays, Epicentre conducts research and training activities in the range of MSF interventions. A partner with international medical research teams, its work is anchored in modern scientific knowledge, in particular in the field of epidemiology. Epicentre co-leads the study development (research design, protocol, tools, analysis, and dissemination) and leads the field data collection and data management.

- The Guttmacher Institute is in its fifth decade as a leading research and policy organization committed to advancing sexual and reproductive health and rights in the United States and globally. The Guttmacher Institute is guided by its values of: commitment to rigor, prioritizing the needs of disadvantaged groups, addressing emerging questions, and collaborating with others. The Institute relies on these collaborative relationships to stimulate innovation, ground their work in the proper context, and amplify the research findings and recommendations. The Guttmacher institute has already led a dozen of abortion-related morbidities studies in different limited-resource countries and will provide its expertise in research methodology and tools on abortion-related topics.

A Memorandum of Understanding (MOU) between the partner organizations is in the process of being signed. This document details the exact role of each partner and guides communication, planning and design, problem-solving, decision-making as well as data sharing principles including data confidentiality principles.
We envision a partnership based on our commitment to a shared vision and objectives; commitment to upholding the integrity of scientific research and its outcomes; full participation of all partners; trust, mutual respect, and cooperation; joint decision-making; management of differences of opinion in the spirit of dialogue, flexibility, and compromise; recognition of individual contributions; and celebration our joint achievements.

The partnership will be represented by the **international coordinating committee of the study** that will be in charge of overseeing the study. It is composed of members of the 3 partners that are listed in the front pages of the document. Its role is to ensure that the study is carried out appropriately, (i.e. scientifically and ethically), including

- A guarantee that the research remains scientifically relevant by ensuring the relevancy of the research questions and that the methods used are valid and appropriate ;
- Making all decisions regarding study protocols and study tools development and modifications, including actions needed to facilitate participants' recruitment or decisions to open/close study sites.
- Ensuring that the study personnel carry out the research properly, adhere to the protocol and procedures and maintain participants safety; review the data collection practices and procedures
- Monitoring recruitment of study participants in each of the study component
- Enforcing the rules pertaining to access to the study data as well as reports and publications of the results;
- Reviewing the allocation of resources (as appropriate)

At each site, a **study site steering committee** will be set-up involving the site investigators (MoH and MSF), the study coordinator, the ministry of health, other ministries (if relevant), key local leaders, local MSF-mission, Ipas and Guttmacher representatives (if presents in the country), local researcher(s) and local association(s) of woman if possible. Its role is to ensure the implementation of the study locally including

- Ensuring that the views of the local stakeholders and communities are taken into account
- Ensuring the respect of local regulations and processes in the implementation of the

study
- Providing inputs in the study strategy and interpretation
- Follow-up of the implementation of the study locally, addressing study implementation challenges
- Ensuring the local diffusion of results

10. Study management:

10.1. Human resources set-up

The organizational chart of the study is presented in Appendix 11.

Each study site will have a full-time study coordinator with a medical/paramedical and a research background. The study coordinator and the site investigators will identify local clinicians (medical doctors, midwives, and clinical officers) currently involved in the management of abortion-related complications. According to the expected workload (estimated from the admission capacity of each site), one to three study clinician(s) may be hired and one to four local interviewers (+/- translators), and 2 data clerks (double entry) per site will be hired.
The study coordinator will oversee coordination of the data collection and management of the field study team. During the first phase of the study, the study coordinator will be in charge of the collection of the quantitative data from the rapid facility assessment and the KAPB survey. Then, during the second phase of the study, the study coordinator with the study clinicians in some of the sites will be in charge of the medical data collection of the medical record review. Additionally, the study coordinator will supervise the data collection performed by the interviewers (quantitative and qualitative surveys among women with abortion-related complications) and the study clinicians, as well as the data entry performed by the data clerks to ensure quality. H/she will make the link with the central data manager and central study team (study international coordinating committee). He will also be in charge of the coordination of the study with all local stakeholders and partners (site investigators, Ministry of Health, local MSF-mission, ERBs, local authorities, associations, site steering committee, etc.).
The interviewers (+/- translators) will perform the quantitative and qualitative interviews among eligible women with abortion-related complications as well as the transcription of qualitative interviews.
And the data clerks will ensure the double data entry of the quantitative data in the databases.

10.2. Site monitoring/Supervision

To ensure the respect of procedures and the quality of the data collection, each study coordinator will be in charge of the study internal monitoring according to a pre-defined monitoring plan that can be adapted alongside the study if necessary. H/she will provide regular activity and monitoring/supervision reports to the study international coordinating committee through the Epicentre Co-PI of the study.
Additionally, if the security conditions allow it, each study site will host at least one in-person supervisory visit of a team member from the collaborating organizations (i.e. from the study international coordinating committee) during the data collection period according to a predefined standardized monitoring plan.

11. Protocol Deviation

A protocol deviation is defined as any change, deviation, or departure from the study design or study procedures that is not approved by the Ethics committees prior to its initiation or implementation, or deviation from standard operating procedures, ethical or local regulations. These protocol violations may be major or minor deviations.

A major deviation is a protocol deviation that adversely affects the rights and welfare of participants, or places participants at increased risk of harm, or significantly damages the completeness, accuracy and reliability of the data collected for the study
Examples of major protocol deviation include but are not limited to:

- Any failure to obtain informed consent or follow the opt-out process.
- Violation of inclusion/exclusion criteria
- A breach of confidentiality

All protocol major deviations will be recorded in standardized form and the study coordinator or the site investigators will notify them to the Co-PIs of the study, the site steering committee and the international coordinating committee in order to undertake the necessary action. In addition, the ethical committees of the countries where the research is conducted will be notified of all changes in and/or deviations from the protocol that may increase risk to the subject, and/or that may adversely affect the rights of the subject or validity of the investigation.

Each investigator and study staff must adhere to the protocol as described in this document and agree that deviations to the protocol, with the exception of medical emergencies, must be discussed and approved by the site steering committee and the international coordinating committee prior to seeking approval from the ethical committees.

12. Duration of the study and timeline

Key milestone, achievement or result	Activity	Completion date
Protocol and study tools ready	Research protocol writing + case report forms, questionnaires, in-depth interview guide, interviewer manual, standard operating procedure manuals (SOPs), training material development	July-December 2018
MOU, DSA and agreement	Development and signature of collaboration documents between the 3 partners	May-November 2018
Study inception meeting for all partners	Consortium meeting in Paris (tools, protocol)	June 2018
Submission and approval of study protocols	Submission of study protocols to Guttmacher, Epicentre, and national IRBs + administrative authorisations	November 2018-July 2019
Central training Site training Pilot phases	Preparation of training tools Centralized orientation and training meeting for investigators and study coordinators on data collection and SOPs	April-August 2019
Quantitative and qualitative data collection completed	3 to 10 months of quantitative and qualitative data collection in all sites + 2 month of preparation and data collection tools piloting	September 2019-February 2021
Data entry and transcription completed	Concurrent data entry, supervision of data collection and quality control measures (9 months including pilot and end of data cleaning)	October 2019- March 2021
Meeting held to discuss analysis, results, and dissemination of findings	Paris meeting to discuss analysis, results, and dissemination of findings internally in our organizations (MSF, Ipas and Guttmacher) and externally for a broader impact	July 2020 – March 2021
Data analysis and full study report completed	Data analysis at MSF, Ipas, & Guttmacher + full study report and paper writing	June 2020-July 2021
Local dissemination of findings completed	Dissemination of findings to MSF national staff, local leaders, communities, women associations, etc. in study locations through study report, conferences, and posters	January 2021-December 2021
International	Dissemination of findings internationally via scientific	July 2021-December

dissemination of findings	meetings, MSF scientific panels and organizational meetings, and peer review journals	2021

13. Study completion and archiving

At the end of the data collection and before close-out, the following activities will be completed by the study coordinator and the site MSF investigator with the support of the coordinating principal investigators and the MSF medical coordinator of the mission:

- Completion of all data forms and resolution of all data queries
- Review of all study documents ensuring safety of their storage
- Long-term archiving of study documents and databases:
    - Because of the sensitive topic of the study and the fragility of the contexts, all study documents will be sent to Paris and archived in Epicentre archiving system under the responsibility of the Epicentre Coordinating Principal Investigator following applicable regulations. The paper-based screening and inclusion logbook as well as the informed consent will be stored in sealed envelopes before transferring to Paris.
    - Study records will be securely stored in boxes labeled with information describing the content for 10 years;
    - Locked electronic databases will be stored on the Epicentre secure server in Paris.

If a security incident happens in one study site, based on MSF mission management analysis and decision, a temporary or definitive stop of the data collection might happen. If the stop is definitive, the study team will do their best to inform the participants of the study through the most feasible communication mean (local authorities, leaders, etc.). Ethical committees and the ministries of health will be informed too. As far as possible, the process of long-term archiving of study documents and databases described above will be implemented.
Depending on the stage of the study, data might be analyzed and diffused as described in § 7 and 13, taking into consideration the limitations of the results as well as explaining the reasons for premature stop of the study.
Additional potential sites have been explored so that they could be approached as alternative sites. (cf. Research Implementation risk analysis in Appendix 9)

14. Dissemination of findings

The three partner organizations represent a wide variety of stakeholders. The organizations comprise researchers, clinicians, practitioners, and policy experts. Our collective work with all levels of stakeholders within communities, as well as local Ministries and international organizations, provides entrée to a vast array of individuals and organizations at a variety of levels.

This research is designed to closely link with quality improvements in service delivery as well as practice and policies first in the 3 MSF sites, then in all MSF sites providing PAC in fragile settings and finally among global fragile and/or conflict affected actors. This research is responsive to the programmatic needs of our country-based partners, the global reproductive health and fragile and/or conflict affected communities, and other stakeholders around the world.

Communication and advocacy related to the study and its results will range from very concrete, localized field-level outreach, sensitization, and advocacy efforts, to strategies that contribute to the global understanding of safe abortion as a medical necessity and operational priority within fragile and/or conflict affected settings.

Efforts will include:

- At field level: as described in § 8.5, 1) communication of the main study results to the participants through the development of posters, leaflets or other adapted communication

means that will be available at the study sites facilities; 2) a local and national dissemination of the results in each of the research site countries to engage communities, stakeholders and policymakers through different modes of diffusion adapted to the context (reports, leaflets, medias, or workshops); 3) In each of the study countries, the results of the study will be used to open a dialogue with different stakeholders and authorities at various levels (health professionals, decision makers, ministry of health official, local leaders, associations) in order to inform and support improvement in maternal health strategies in the study sites as well as in the country.

- At the MSF internal level: internal advocacy for improved access to safe abortion care and a better understanding of abortion-related burdens on MSF operations and patients
- At international level: 1) Articles presenting study results in relevant scientific publications; 2) Presentation of findings at relevant conferences; 3) External communication through the three organizations and their respective channels, networks, websites, and other relevant outlets.

Research impact will be maximized by the ability to use communications expertise for press and social media from all three international organizations.
A combined report and if possible, a national dissemination workshop will be conducted in each of the research site countries to engage stakeholders and policymakers.

As written in the ethical paragraph, a special care will be taken to ensure that external communication will not put participants, communities, health professionals, health facilities and involved partners at social or legal risk. All external communication will be first validated by each partner (MSF, IPAS, Guttmacher Institute) before diffusion. Information on potential induced abortion performed in the health facility is only collected for the understanding of the context but will not be subject to external communication.

To conclude, all efforts will be done in order to use the study's results to improve the access and the quality of abortion care.

- In the 3 MSF sites, the study results will be used to orient operational strategies to improve the access and the quality of post-abortion care and prevent as far as possible the most severe conditions (near—miss). To do so, the MSF/Epicentre members of the international coordinating committee (medical departments) and the intersectional task force on abortion at HQ levels as well as the site investigators at field level will engage in discussions with the MSF mission coordination and cells during the yearly planning of their projects.
- The intersectional task force on abortion will also use the study results to inform other MSF missions acting in fragile and conflict affected settings in improving access and quality of post-abortion care and safe abortion care.
- At international level, the communication plans described above led by Ipas, Guttmacher institute and MSF might have the potential to contribute to orient international policies and guidelines for a better access to PAC and SAC in fragile and conflict-affected settings.

15. Forecast budget and funding (cf. appendix 12)

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17. Appendices.

Appendix 1: Protocol versions

Protocol versions (cf. front pages)

Appendix 2: Figa-Talamanca et al. classification of abortion induction(6)

Table 2-2 WHO Figa-Talamanca criteria used for reclassification of abortion cases

	Criteria	Certainly induced abortion	Probably induced abortion	Possibly induced abortion	Spontaneous
1	**Woman's statement that she had an induced abortion**	Classify in this category if (1) OR (2) OR (3) is present	Not present	Not present	Not present
2	**Health worker or relative's statement if woman died due to abortion**		Not present	Not present	Not present
3	**Evidence of genital trauma or foreign body**		Not present	Not present	Not present
4	**Sepsis or peritonitis or admission thereafter**	This criterion may be present or not present	Classify in this category if criteria (4) AND (5) are present	Classify in this category if criteria (4) OR (5) is present	Not present
5	**Pregnancy unplanned (use of contraception during the cycle of conception)**	This criterion may be present or not present		Classify in this category if criteria (4) OR (5) is present	Not present

Source Figà-Talamanca et al. (1986)(25).

Appendix 3: Ectopic, molar pregnancies and abortion related diagnosis case-definitions

Threatened abortion:

Definition: is a threat of abortion of an intrauterine pregnancy but the embryo/fœtus is still viable and the pregnancy may continue(4,7).

Case-definition: light bleeding and/or abdominal pain with a closed cervix and embryo/foetal cardiac activity in a pregnant woman prior to fœtal viability[q].

It is diagnosed when there is vaginal bleeding in a pregnant woman prior to fœtal viability[q] but there is no expulsion of products, membranes remain intact and fetal cardiac activity (after 5 weeks) is present. Pain is usually absent but if present is mild. If a pelvic examination is done (speculum and bimanual examination), the cervical os is seen to be closed. (4,13)

Inevitable abortion:

Definition**:** means that it is impossible for the intrauterine pregnancy to continue and it will proceed to incomplete/complete abortion even though there has not yet been expulsion of products(4,7)

Case-definition: bleeding +/- abdominal pain in with an open cervix, product of conception still inside the cavity (with or without embryo/foetal cardiac activity at ultra-sound if done) in a pregnant woman prior to fœtal viability[q].

The key difference between inevitable abortion and threatened abortion is that in inevitable abortion, the cervix is open. Bleeding and pain are usually more severe than a threatened abortion. Regardless of any intervention, an abortion has started and subsequently part or all of the products of conception will be expelled (incomplete or complete abortion)(13)

Incomplete abortion:

Definition: is an abortion of an intrauterine pregnancy where products of conception are partially expelled.(4,7)

Case-definition: bleeding + expulsion of some product of conception +/- abdominal pain with an open cervix and retention of product of conception in the uterus cavity (with no embryo/foetal cardiac activity at ultra-sound if done) in a pregnant woman prior to fœtal viability[q].

There is usually severe bleeding, although the pain may have stopped. The cervix is open and products may be viewed on speculum examination. This is more likely to occur in the second trimester of pregnancy.(13)

[q] i.e. before a fœtus becomes able of an extra-uterine independant life. In MSF guidelines, faetal viability is defined before 22 weeks of gestation. Nevertheless, in the study, no gestational age has been defined for 2 reasons : 1) the fœtal viability varied according to contexts (according to neonatal intensive care units capacity, according to law) ; 2) to capture women who would come with complications of induced abortion that happened after 22 weeks of gestation.

Complete abortion:

Definition: an abortion of an intrauterine pregnancy where all the products of conception - embryo/fetus, placenta and membranes – have been expelled.(4,7)

Case-definition: bleeding + expulsion of all product of conception +/- abdominal pain in a pregnant women with a closed + an empty uterus cavity (no gestational sac & endometrial thickness <8mm(72)*) at ultra-sound in a woman who was pregnant at a gestational age prior to fœtal viability*[q]*.*

This is more likely to occur in the first eight weeks of pregnancy.(13) Products may be viewed or the woman may give a history of expulsion of products. Vaginal bleeding and pain have settled after the expulsion of products and the cervix is closed. If the clinician is unsure whether the abortion is complete or not then ultrasound may be used (but is not required for diagnosis). Presence of a gestational sac or fetus on ultrasound excludes complete abortion. Blood clot may be seen on ultrasound and complicate the diagnosis, in general, if endometrial thickness less than 8mm then a complete abortion can be diagnosed (provided all the clinical criteria for a complete abortion are met)(72). If, after this diagnosis, the woman needs further treatment for suspected retained products of conception (e.g. ongoing bleeding, signs of infection) then the diagnosis should be changed to incomplete abortion.

Missed abortion:

Definition: is an abortion of an intrauterine pregnancy where the products of conception have not been expelled but fetal cardiac activity is absent(7).

Case-definition: embryo/foetal demise with product of conception still inside the uterus cavity confirmed by ultrasound (gestational sac ≥ 25mm with no yolk sac or embryo; OR a fetus with a crown-rump length (CRL) of ≥7mm with no cardiac activity) with a closed cervix and no vaginal bleeding in a pregnant woman prior to foetal viability[q]*.*

It describes a pregnancy where the embryo/fetus has died but the fetal tissue and placenta are retained in the uterus. Any pain or bleeding (usually brown rather than red) should be minimal and does not need to be present for the diagnosis. Signs of pregnancy (e.g. nausea and vomiting, breast tenderness), if previously present, disappear due to falling bHCG(13). This diagnosis is more common in settings where early ultrasound is frequently performed. In order to make this diagnosis, an intrauterine pregnancy with one of the following must be present: a. gestational sac ≥ 25mm with no yolk sac or embryo; OR b. a fetus with a crown-rump length (CRL) of ≥7mm with no cardiac activity [r].

Septic abortion:

Definition: is defined as abortion of an intrauterine pregnancy complicated by infection. Sepsis may result from infection if organisms rise from the lower genital tract following either spontaneous or induced abortion. Sepsis is more likely to occur if there are retained products of conception and evacuation has been delayed.(4,7)

Case-definition: fever with foul smelling vaginal discharge associated with an abortion or within 42 days after an abortion.

[r] According to Royal College of Obstetricians and Gynecology and American College of Radiology guidelines

It may occur following any kind of abortion but is more common following induced unsafe abortion (following the use of mechanical methods to force the cervix open, the introduction of objects, leaves, potions into the vagina) and missed or incomplete spontaneous abortion. Infection will first occur in the uterus but will rapidly spread to the fallopian tubes, pelvic organs and peritoneum and will cause septicemia if not promptly treated. Main symptoms include fever, rapid pulse, headache, lower abdominal pain, and profuse and offensive smelling lochia.(13)

Ectopic pregnancy:

Definition: an ectopic pregnancy is one in which implantation occurs outside the uterine cavity. The fallopian tube is the most common site of ectopic implantation (greater than 90%) more rarely, it can be in other locations such as the abdominal cavity or the cervix.(4,7)

Case-definition:

- *Ectopic pregnancy found during the laparotomy (surgery)*
- *OR, if laparotomy is not done,*
    - *low abdominal pain/cramp or bleeding or scapular pain or faint or hypovolemic shock in a pregnant woman <12 weeks of gestation with exquisite pain in the pouch of Douglas and/or culdocentesis showing blood*
      Or
    - *implantation of the pregnancy outside the uterus cavity at ultrasound*

As medical management is not available in MSF fields and expectant management is not recommended, almost all should be diagnosed on laparotomy. Due to the difficulties in diagnosis, in the very rare case of suspicion of a cervical ectopic, it should be classed as an intrauterine pregnancy per the criteria given (incomplete/complete abortion).

Molar pregnancy:

Definition: Molar pregnancy is characterized by an abnormal proliferation of chorionic villi with an absence of embryo/fœtus or an abnormal embryo/fœtus.(4)

Case-definition:

- *vaginal bleeding with a uterus larger or softer than expected for gestational age and/or BHCG higher than expected for gestational age and passage of abnormal vesicular tissue during abortion in a pregnant woman* prior to foetal viability[q]
- *or heterogeneous vesicular placenta filling the entire uterine cavity with an abnormal embryo/fœtus at ultra-sound.*
- *Or Evacuation of abnormal hydropic vesicles at manual vacuum aspiration during treatment of abortion.*

This will primarily apply to complete molar pregnancies as partial molar pregnancies are frequently only diagnosed with histology which is not available in MSF fields. If the diagnosis is uncertain, it should be considered an intrauterine pregnancy and classed per the abortion diagnoses given above (complete/incomplete abortion)

Table: Differential diagnosis of vaginal bleeding in early pregnancy from WHO, "Pocket Book for Hospital Care for Mothers" (7)**:**

Table 1.3: Differential diagnosis of vaginal bleeding in early pregnancy

Probable Diagnosis	Symptoms	Signs	Ultrasound Findings
Threatened abortion	• Cramping/lower abdominal pain • Light bleeding	• Closed cervix • Uterus softer than normal and corresponds to dates	• Live embryo • Rarely subchorionic bleed
Inevitable abortion	• Cramping/lower abdominal pain • Heavy bleeding • No expulsion of products of conception	• Dilated cervix • Uterus corresponds to dates • Uterus tender	• Dilated cervical os • Sac seen partially extruding into vagina
Incomplete abortion	• Cramping/lower abdominal pain • Heavy bleeding	• Dilated cervix • Uterus smaller than dates	• Retained products of conception seen

	• Partial expulsion of products of conception		
Complete abortion	• Light cramping/ lower abdominal pain • Light bleeding • History of expulsion of products of conception	• Closed cervix • Uterus smaller than dates • Uterus softer than normal	• Empty uterus, thin endometrium
Missed abortion	• Bleeding may or may not be present	• Closed cervix • Uterus smaller than dates	• Discrepancy between sonographic dating and period of gestation • Absent fetal cardiac pulsations
Molar pregnancy	• Cramping/lower abdominal pain • Heavy bleeding • Nausea, vomiting • Partial expulsion of products of conception which resemble grapes • Spontaneous abortion	• Dilated cervix • Uterus larger than dates • Uterus softer than normal • Ovarian cysts (easily ruptured) • Early onset pre-eclampsia • No evidence of a fetus	• Complete molar pregnancy shows fine vesicular or honeycomb or snowstorm appearance along with large theca lutein cysts • Partial mole is seen as scattered cystic spaces in the placenta along with fetus
Ectopic pregnancy	• Amenorrhoea • Abdominal pain • Light bleeding • Fainting	• Closed cervix • Uterus softer and slightly larger than normal • Tender adnexal mass • Cervical motion tenderness	• Empty uterine cavity • Adnexal mass • Free fluid in pelvis

Heavy bleeding: it takes less than 5 minutes for a clean pad or cloth to be soaked.

Appendix 4: Safe and Unsafe abortion classification

According to WHO classification described by Ganatra et al.(12):

Safe abortion: induced abortion

- done with a method recommended by WHO or MSF (medical abortion, vacuum aspiration, or dilatation and curettage) that was appropriate to the pregnancy age
- **AND** if the person providing the abortion was trained

Unsafe abortion:

- **Less safe abortion:** induced abortion with one of the two criteria met—ie,
  - **either** the abortion is done by a trained provider but with a method not recommended by WHO or MSF for the gestational age (medical abortion, vacuum aspiration, or dilatation and curettage)
  - **either** a recommended method of abortion appropriate for the gestational age was used but provided by untrained individual.

- **Least safe abortion:** induced abortion
  - provided by untrained individuals
  - **AND** without using a recommended method by WHO or MSF, appropriate for the gestational age

Appendix 5: Abortion-related severity classification adapted from the WHO multi-country study on abortion related morbidity(8)

Moderate (Less Severe) complications

Vaginal Bleeding: At least one of the 3 following items is present:

- *Heavy bright red vaginal bleeding (with or without clots),*
- *Pads, towels, or clothing blood-soaked within five minutes*
- *Pallor*

Abdominal syndrome (intra-abdominal injury suspicion): At least one of the 4 following items is present: -

- Abdominal pain/cramping and nausea/vomiting
- Distended/tense/hard abdomen (defense/contracture)
- Shoulder pain
- Decreased bowel sounds, rebound, tenderness.

Infection (endometritis or chorioamnionitis): At least one of the 2 following items is present:

- *Chills, fevers, sweats*
- *Foul smelling vagina discharge*

+/- an History of intervention on the pregnancy

Potentially life-threatening complications

Severe hemorrhage: *Perceived abnormal blood loss greater than 1000mL, and/or any bleeding with hypotension (systPA<100mm Hg), and/or any bleeding requiring blood transfusion (<2 units), and/or Hemoglobin <4g/dL*

Generalized peritonitis: *T°C>38°C + abdominal guarding (contracture = hard abdomen like roc) or rebound +/- ileus (decreased/no bowels sound, tenderness)*

Severe systemic infection

- ☐ *Presence of fever (body temperature>38 degrees Celsius) + confirmed or suspected infection (for eg. septic abortion, endometritis, chorioamnionitis, generalized peritonitis) + at least one of the following signs: 1) new/worsened altered mentation, 2) respiratory rate ≥ 22, 3) systolic blood pressure ≤ 100mm Hg*

OR

- ☐ *Tetanus infection signs*

Uterine perforation: *Perforation of uterus confirmed by laparotomy*

Other Intra-abdominal perforation: *Evidence of bladder, rectum, bowels mechanical perforation confirmed by laparotomy or examinations*

Near miss complications (Severe organ dysfunction)

Cardiovascular dysfunction

- ☐ *Shock : SystPA<90mmHg for >60min with pulse rate>120/min despite aggressive fluid replacement (>2L)*
- ☐ *Cardiac arrest: loss of consciousness and absence of pulse/heart beat*
- ☐ *Severe hypoperfusion: lactate>5mmol/L or 45mg/dl*
- ☐ *Severe acidosis : PH<7,1*

- ☐ *Use of continuous vasoactive drugs (for eg: dopamine, epinephrine, dobutamine, norepinephrine, adrenaline)*
- ☐ *Cardiopulmonary resuscitation*

Respiratory dysfunction
- ☐ *Acute cyanosis,*
- ☐ *Gasping (terminal respiratory pattern where the breath is convulsively and audibly caught)*
- ☐ *Severe tachypnea (respiratory rate>40 breaths/min)*
- ☐ *Severe bradypnea (respiratory rate<6 breaths/min*)
- ☐ *Severe hypoxemia (O2 saturation <90% or PAO2/FiO2<200 for >60 min)*
- ☐ *Intubation/ventilation >60min not related to anaesthesia*

Renal dysfunction
- ☐ *Oliguria non responsive to fluids or diuretics: urine <30mL/h for 4h or <400mL/24h*
- ☐ *Severe acute azotemia (creatinine > 300mcmol/ml or >3.5 mg/dL)*
- ☐ *Dialysis for acute renal failure*

Coagulation dysfunction
- ☐ *Failure to form clots*
- ☐ *Severe acute thrombocytopenia (<50,000 platelets/mm3)*
- ☐ *Massive transfusion of blood or red cells (≥ 2 units)*

Hepatic dysfunction
- ☐ *Jaundice in the presence of pre-eclampsia*
- ☐ *Severe acute hyperbilirbuinemia (bilirubin>100mcmol/L or > 6.0 mg/dL)*

Neurologic dysfunction
- ☐ *Prolonged unconsciousness or coma (Glc <8 lasting>12hrs.)*
- ☐ *Stroke*
- ☐ *Uncontrollable fit/status epilepticus*
- ☐ *Global paralysis*

Uterine dysfunction*: Hysterectomy due to*
- ☐ *uterine infection,*
- ☐ *rupture of uterus or*
- ☐ *haemorrhage*

Death

Mild (Least severe) complications:
any other signs linked to an abortion that are not classified as less severe, life-threatening, near-miss complications or death.

Appendix 6: Study data collection tools

- **Rapid facility assessment questionnaire**
- **KABP for health professional's questionnaire**
- **Women with abortion-related complications screening form**
- **Women with abortion-related complications case report form (CRF)**
- **Denominator data collection tool.**
- **Quantitative interview questionnaire for hospitalized women with abortion-related complications**
- **Qualitative in-depth interview guide for women with life-threatening conditions and near-miss events**

Appendix 7: Information notices and consent forms

- **Rapid facility assessment information notice and consent form**
- **KABP for health professionals information notice and consent form**
- **Women with abortion-related complications information documents for opt-out process from the medical record review**
- **Quantitative interview questionnaire information notices and consent forms for Women hospitalized with abortion-related complications**
- **Qualitative in-depth interview guide information notices and consent forms Women with life-threatening or near-miss abortion-related complications.**

Appendix 8: Examples of key process indicators of good quality post-abortion care

Based on MSF framework adapted from the model of WHO standards on quality of care in maternal health(59)

- %age of tetanus status assessed among all patients with abortion-related complications
- %age of septic abortion receiving antibiotics as per MSF guidelines
- %age of patients with bleeding having an MVA
- %age of patients benefiting MVA who received para-cervical block
- %age of patients who receive pain management
- %age of perforation of uterus receiving antibiotics
- %age of patients who have been prescribed iron and folic acid
- %age of patients who has been proposed with contraception.

Appendix 9: Research implementation risk analysis:

During the time prior to data collection, any of the selected sites could experience a change in the activity volume or security, or new emergencies or other changes in priorities could impact the capacity to host the study. However, MSF manages over 100 projects in obstetric care (including PAC); systems are already in place to ensure replacement study locations in the event of a change.

Delays in ethics approvals could occur due to the topic's sensitivity or other factors; however, mitigating strategies for this have already been proposed and are already taking place. Additionally, the partner organizations and individual researchers selected for the study team are all experienced in research around sensitive topics such as abortion and sexual violence.

Once the sites have been definitively determined, early discussions with ministries of health to increase local knowledge and ownership will increase the likelihood of widespread dissemination and utilization of the study findings. Each organization has experience and expertise working with national organizations to increase local ownership of research findings. The project partners have already established relationships with government stakeholders in the project countries.

Collecting data in fragile and conflict settings always carries some risk. But working with an experienced partner in fragile and/or conflict affected settings and globally-respected such as MSF provides increased safety and security in volatile field settings. However, certain risks are unique to fragile and/or conflict affected settings and this research collaboration. These include the following:

- A change in operational priorities and security concerns may affect the study sites, activities, and capacity to post staff during the proposed study period.
- A health epidemic or outbreak in these fragile and/or conflict affected settings would result in a delay in data collection until safety and security of the study team can be assured.

If one of these conditions were to occur, a list of potential sites that meet selection criteria has already been prepared for review and consideration.

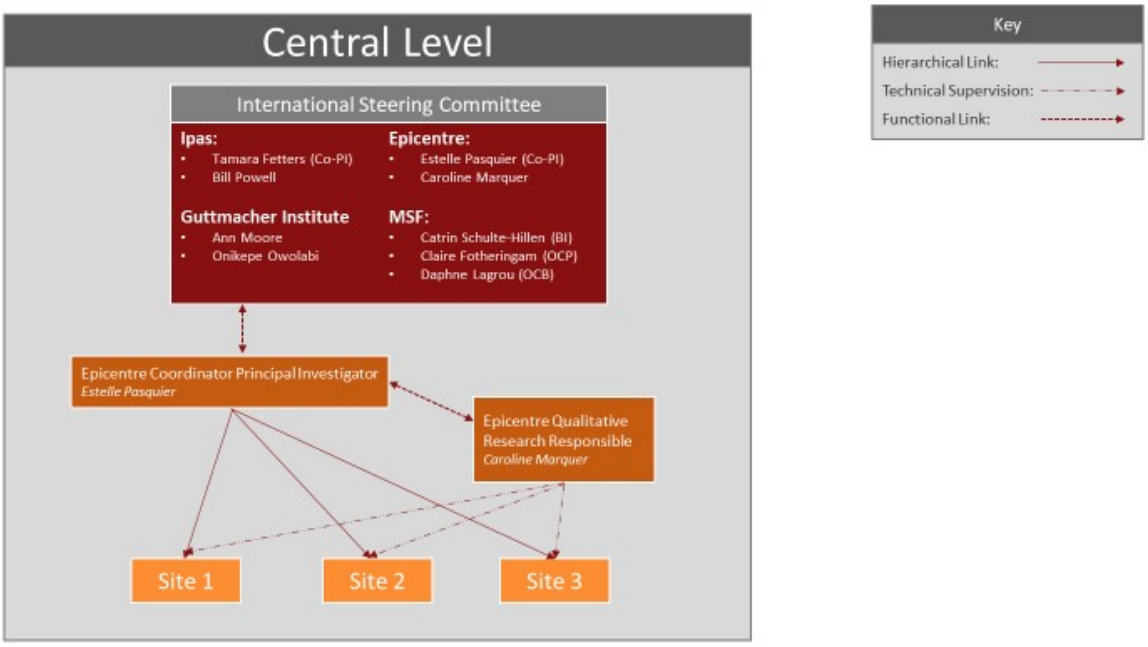
Additionally, there is risk that any one of the persons in charge of the various selected sites may not be supportive of conducting the research. However, MSF research team members have already secured buy-in from the respective MSF Operational Centers. Orientation to the project objectives, tangible benefits expected for the sites, and values clarification on abortion care will be conducted prior to implementation at each site.

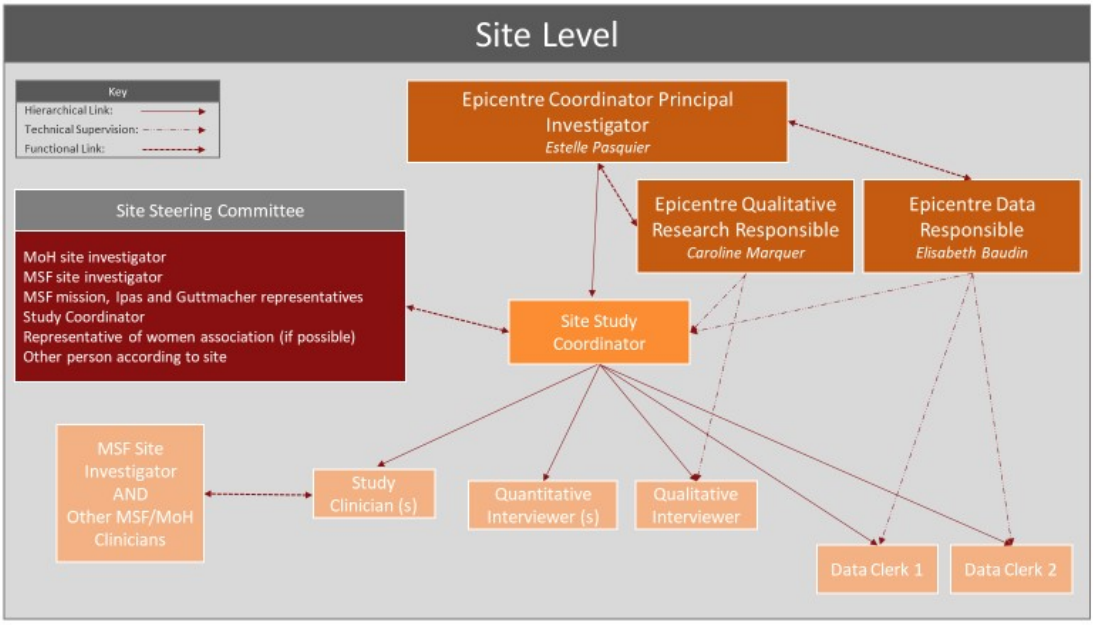
Appendix 10: Context analysis

A context analysis will be done to put the results of the study into the perspective of general context of the country and area. Guttmacher institute will lead a literature review of existing published or non-published documents, reports, law, policies, articles, etc. will allow to describe:

- The legal context regarding abortion
- The social belief about abortion
- The availability of services in the health facilities of the area (not supported by MSF):
    - PAC services available in the catchment area
    - Signal functions of the SAC model (Healy et al 2006(1) improved by Campbell et al 2016(2))
- The existing access to misoprostol

Appendix 11: Organizational Chart of the study





Appendix 12: Forecast budget and funding

The study is funded by ELRHA on the funding instrument called R2HC (http://www.elrha.org/r2hc/home/) and co-funded by MSF, Guttmacher Institute and Ipas.

Coordination budget:

Sites budget:

Bangui (RCA)

Jigawa state (Nigeria)

North Kivu (DRC)

[Available on request]

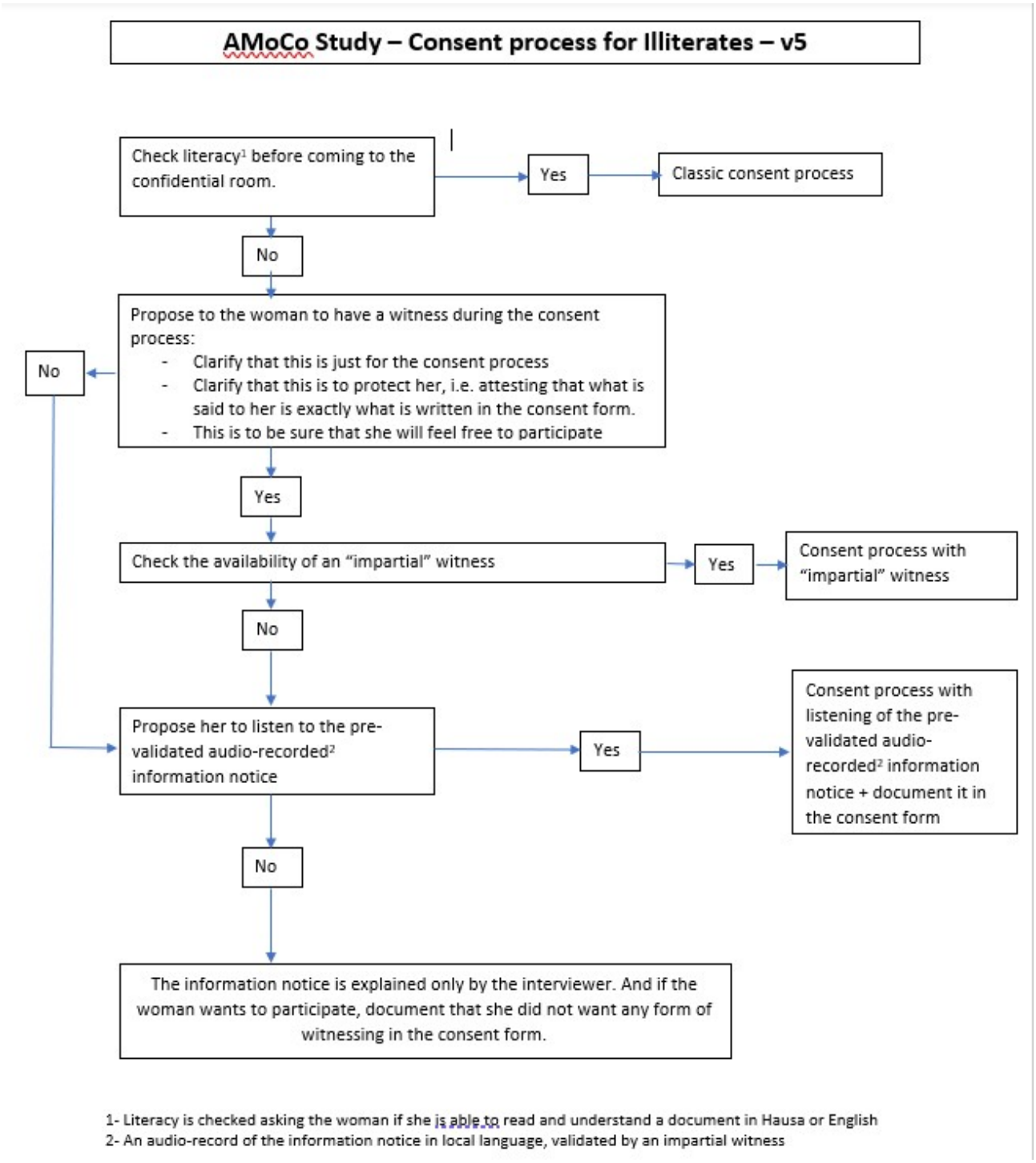
Appendix 13: Campbell et al. 2016(2) classification of signal functions of Safe Abortion Care and Post Abortion Care in comparison with the ones of Healy et al. 2006(1)

Table 1 Signal function classification system: criteria for termination of pregnancy (TOP) and post-abortion care (PAC) in comparison to previously suggested SAC criteria

	TOP capability		PAC capability		SAC capability[a]	
	Basic	Comp	Basic	Comp	Basic (≤12 weeks)	Comp (>12 weeks)
Vacuum aspiration	X	X			X	X
Medication abortion	X	X			X	X
Dilation & Curettage (D&C)						X
Dilation & Evacuation (D&E)		X				
Removal of retained products			X	X	X	X
Parenteral antibiotics			X	X	X	X
Uterotonics			X	X	X	X
Intravenous fluids			X	X	X	X
Blood transfusion				X		X
Surgical/laparotomy capability				X		X
Contraceptives (condoms + pills + injectables)	X	X	X	X		
Long-acting reversible contraceptives (LARCs): implants or IUDs		X		X		
Family planning at least once per week	X	X				
Family planning 7 days a week			X	X	X	X
Facility open 24 h per day, 7 days a week (24/7)			X	X	X	X
1+ health professionals on duty	X	X	X		[a]	[a]
3+ health professionals registered (needed for 24/7 PAC service)			X		[a]	[a]
1+ medical doctors on duty				X		[a]
3+ medical doctors registered (needed for 24/7 PAC service)				X		[a]
Communication means or referral capacity (for facilities without comprehensive PAC)	X	X	X			

comp comprehensive, *iv* intravenous, *IUD* intrauterine device
[a]Criteria for safe abortion care (SAC) as defined by Healy and colleagues [8] are shown for comparison. In their classification system, staffing is implied by having service provision 24/7 but not stated explicitly

Appendix 14: **Consent process for Illiterates – example of Jigawa state site**



1- Literacy is checked asking the woman if she is able to read and understand a document in Hausa or English
2- An audio-record of the information notice in local language, validated by an impartial witness

Appendix 15: AMoCo-COVID-19 sub-study: the impact of the COVID-19 pandemic on patients access to SRH services in the study sites of the AMoCo study

Background :

Ensuring access to sexual and reproductive healthcare is essential to reduce maternal and neonatal mortality and morbidity. In humanitarian contexts, women may be exposed to greater Sexual and Reproductive Health (SRH) challenges compared with those in stable settings, including a greater risk of sexual violence and disrupted or reduced access to SRH healthcare. Global events like the COVID-19 pandemic are likely to impose a significant strain on health systems ability to deliver essential services such as SRH and people's willingness and ability to seek reproductive healthcare. Studies conducting expert interviews have documented disruptions in availability of and access to essential SRH health services have been reported in contexts where health systems are poorly funded and have comparatively low capacity to provide resuscitative (Endler et al 2020). However, there is very little data exploring the impact of COVID-19 from humanitarian contexts where women may face more hurdles to obtaining SRH care. Evaluating the impact of this unanticipated epidemic on access to SRH care using facility level data has been a little challenging in many contexts as it is hard to ethically field and collect data under the circumstances and routine data is not readily available.
We have identified a timely opportunity to evaluate the impact of COVID-19 on access to essential SRH care, especially post-abortion care in a conflict-affected setting by performing secondary analyses of data collected within the ongoing study on abortion-related morbidity and mortality in conflict-affected and fragile settings (AMOCO) led by Ipas, Médecins Sans Frontières/Doctors Without Borders (MSF)and Guttmacher Institute. The overall goal of this analysis is to compare trends in the number and ratio (compared with the other reproductive health indicators) of admissions for abortion-related complications before and during the COVID-19 period

Objectives :

1- To examine trends in the absolute number of admissions for abortion-related complications before, during, and after the period of first wave of COVID-19 transmission[s].
2- To examine trends in the rates and ratios of abortion-related admissions using other reproductive health indicators as denominators e.g., abortion-related admissions per 1000 live births, abortion-related admissions per 1000 deliveries, abortion admissions as a proportion of gynecological admissions before, during, and after the period of first wave of COVID-19 transmission.
3- To examine trends in the proportion of abortion-related severe maternal outcome (near-miss events and deaths) among all abortion-related admissions during and after the period of first wave of COVID-19 transmission
4- To examine trends in the absolute numbers of women accessing other reproductive health services before (e.g. deliveries/births) during, and after the period of first wave of COVID-19 transmission.

[s] The period of the first wave COVID-19 transmission is linked to potential changes in the hospital services access and provision as consequences of the measures taken to mitigate Covid-19 pandemics that will be described in each study site.

Methods:

Description of the data that will be used:

The AMoCo study includes a medical record review of the files of patients admitted for abortion-related issues (prospectively or retrospectively when the prospective design is not feasible). These data allow to classify the severity level of abortion-related complications of women admitted in the study sites hospitals as well as to describe the medical management of these women.
Additionally, the AMoCo study collects routine aggregated data from the MSF/MoH Health and Medical Information System (HMIS) for the whole period of the medical record review as well as the 3 years preceding the start of the medical record review (thanks to the data collection tool named "secondary denominators"). These data include reproductive health indicators like the number of total admissions, abortion-related admissions, live births, deliveries, maternal deaths.

The secondary data analysis will concern study sites for which the data collection covers a period that includes pre/per and post COVID-19 first wave transmission periods.
In the Jigawa state study site (Nigeria), the study data collection started just before the start of the Covid-19 pandemic and included individual data (medical record review) and aggregated data (HMIS) of women admitted during and after the first wave of COVID-19 transmission. The aggregated data (HMIS) of the 3 years before the start of the data collection are pre-COVID baseline data.
In the North Kivu study site (DRC), data collection should start early 2021 and at least the aggregated data (HMIS) of the 3 years before the start of the data collection should cover pre/per and post COVID-19 first wave transmission periods.

We will use monthly routine program monitoring aggregated data (HMIS) from 3 years before the start of the data collection until the end of the data collection period including reproductive health indicators like monthly absolute number of all admissions, abortion-related admissions, births, deliveries and maternal deaths to examine changes in access to reproductive health services related to the COVID-19 pandemic.
From the medical record review data, we will estimate monthly proportion of abortion-related severe maternal outcome among all abortion-related admissions as well as other indicators to examine changes in the severity and management of complications in relation to the COVID-19 pandemic.

Inclusion criteria:

The inclusion criteria for abortion related admissions will be the same as within AMoCo but will exclude ectopic or molar pregnancies: "All women presenting to the wards of the study sites which see women presenting for PAC (emergency unit, gyn/obs units, ICU unit, PAC unit, etc. according to site) with any signs or symptoms of abortion-related complications, i.e. any signs or symptoms of complications of spontaneous or induced abortion, whatever the abortion stage: inevitable, missed, incomplete, complete abortion".

Description of method of data analysis:

The unit of observation will be monthly observation points divided in 3 periods of time: 1 before (from maximum January 2017 to the date of the first Covid-19 case notification in the study site area), 1 during (from the date of the first Covid-19 case notification in the area to the end of the first Covid-19 wave) and 1 after the first wave of COVID-19 transmission. The Covid-19 transmission period will be deducted from the epicurve provided by the countries' ministries of health (for eg., the Jigawa State epicurve of the Nigerian Control Disease Center: https://covid19.ncdc.gov.ng/state/).

The outcome of interest will be:

- The primary outcome will be the number of abortion-related admissions.
- Secondary outcome may include
    - the number of abortion-related admissions per 1000 deliveries or live births
    - the proportion of abortion-related severe maternal outcome (near-miss and death) among all women admitted for abortion-related complications
- Other general maternal health outcomes explored will be the number of deliveries, number of gynecological and obstetric admissions, maternal mortality ratio.

Descriptive statistics will be used to summarize the monthly estimate of for each outcome over the period of data collection. Data will be explored for outliers and the general shape of the trend.

Trends in monthly hospitalizations/admissions/number of cases/proportion of severe maternal outcome will be assessed using interrupted time series analyses. We will describe changes in trends during three periods: pre COVID-19 first wave, during COVID-19 first wave, and post COVID first wave (cf. above). The time series model will be fitted adjusting for secular trends and controlling for autocorrelation as appropriate. To estimate the sustainability or delayed effect of the intervention, changes in the slope and change in level between pre and post COVID-19 will be examined.

Ethical considerations :

Data used has already been collected as part of AMoCo and for this analysis we will be using data on the absolute number of cases admitted for abortion-related diagnoses and routinely collected data on other admissions as described above. We will not be using any identifying information and this study poses no additional risks to women,providers, communities or partners than the ones described in AMoCo study protocol for which mitigation measures have been taken (cf. §8 in the main protocol).

Expected impact :

We expect this study to provide information on the possible changes in access to different services women experienced during COVID-19 and help them understand how events like this may affect access to maternal health by the communities they serve as well as severity of complications.

Diffusion of results :

We propose to produce a short (two-page) brief summarizing trends in gaps in hospitalizations and severity of admissions before and during the COVID-19 period, along with accompanying data tables to present to colleagues at the MSF mission and ministries of health. We hope these preliminary results can provide useful information to MSF operations and the larger health system in each country regarding COVID-19's impact on essential health care provision.
Thereafter, if the results of the study allow it, we would like to work with colleagues within MSF to write up an in-depth analysis and article on a case study of the impact of COVID-19 on access to reproductive health services in the context for submission to a peer-reviewed journal.