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Systematic Review

Informed consent comprehension in African research settings

Muhammed O. Afolabi[1,2], Joseph U. Okebe[1], Nuala McGrath[3], Heidi J. Larson[2], Kalifa Bojang[1] and Daniel Chandramohan[2]

1 *Medical Research Council Unit, Fajara, The Gambia*
2 *London School of Hygiene and Tropical Medicine, London, UK*
3 *University of Southampton, Southampton, UK*

Abstract

OBJECTIVE Previous reviews on participants' comprehension of informed consent information have focused on developed countries. Experience has shown that ethical standards developed on Western values may not be appropriate for African settings where research concepts are unfamiliar. We undertook this review to describe how informed consent comprehension is defined and measured in African research settings.

METHODS We conducted a comprehensive search involving five electronic databases: Medline, Embase, Global Health, EthxWeb and Bioethics Literature Database (BELIT). We also examined African Index Medicus and Google Scholar for relevant publications on informed consent comprehension in clinical studies conducted in sub-Saharan Africa. 29 studies satisfied the inclusion criteria; meta-analysis was possible in 21 studies. We further conducted a direct comparison of participants' comprehension on domains of informed consent in all eligible studies.

RESULTS Comprehension of key concepts of informed consent varies considerably from country to country and depends on the nature and complexity of the study. Meta-analysis showed that 47% of a total of 1633 participants across four studies demonstrated comprehension about randomisation (95% CI 13.9–80.9%). Similarly, 48% of 3946 participants in six studies had understanding about placebo (95% CI 19.0–77.5%), while only 30% of 753 participants in five studies understood the concept of therapeutic misconception (95% CI 4.6–66.7%). Measurement tools for informed consent comprehension were developed with little or no validation. Assessment of comprehension was carried out at variable times after disclosure of study information. No uniform definition of informed consent comprehension exists to form the basis for development of an appropriate tool to measure comprehension in African participants.

CONCLUSIONS Comprehension of key concepts of informed consent is poor among study participants across Africa. There is a vital need to develop a uniform definition for informed consent comprehension in low literacy research settings in Africa. This will be an essential step towards developing appropriate tools that can adequately measure informed consent comprehension. This may consequently suggest adequate measures to improve the informed consent procedure.

keywords informed consent, understanding, Africa, vulnerable population, systematic review

Introduction

Comprehension is one of the essential elements of a truly informed consent. International ethical guidelines stipulate that informed consent must be given in a comprehensible manner to a competent person who freely decides to participate after understanding the information (NBAC 2001; CIOMS 2002; Marshall 2006). However, the amount and quality of study information required to engender comprehension of a potential participant is unclear. There are also divergent opinions among researchers on the level of comprehension a potential participant should reach to be able to freely decide (Ijsselmuiden & Faden 1992; Hyder & Wali 2006). In most African settings, the majority of research participants have low literacy, but informed consent documents are designed and delivered in a complex, lengthy manner that makes comprehension very challenging for the participants (Priestley *et al.* 1992;

Jefford & Moore 2008; Falagas *et al.* 2009). In such settings, what constitutes 'satisfactory or adequate' comprehension of informed consent is vague (Sreenivasan 2003; Woodsong & Karim 2005). This phenomenon has raised concerns about the quality and ethics of data generated from the increasing number of clinical trials being conducted in these low literacy communities (Annas 2009).

A previous review of studies conducted in developed countries reported a lack of consensus definition of comprehension and an absence of a standardised tool to measure objectively the adequacy of participants' comprehension (Sand *et al.* 2010). The authors concluded that a contextual definition of comprehension and systematic design of an instrument could guarantee adequate measurement of participants' comprehension (Sand *et al.* 2010; Mandava *et al.* 2012). This underscores the need to contextualise the definition of comprehension of informed consent information for different research settings as this may inform the development of a locally acceptable, culturally sensitive measure of informed consent comprehension.

We undertook this review to examine how participants' comprehension of informed consent information has been defined and measured in clinical studies conducted in sub-Saharan Africa (SSA). This will be a major step towards reaching a consensus definition of informed consent comprehension in African research settings, which in turn will help to design improved informed consent procedures.

Methods

Literature search strategy

We searched five electronic databases for empirical studies on comprehension levels of different domains of informed consent among participants in SSA. The databases were Embase (1947–2010), Medline (1960–2010), Global Health (1960–2010), EthxWeb and Bioethics Literature Database (BELIT). To complement these databases, we also searched African Index Medicus (AIM) and Google Scholar for relevant bibliographies and grey literature. The last search was conducted on 11 October 2013. Studies were included if they satisfied the following three criteria:

- assessed or evaluated participants' comprehension of informed consent information;
- involved participants who were in clinical studies rather than hypothetical trials;
- were conducted in a SSA country.

The initial search was conducted on Ovid MEDLINE using a combination of medical subject headings (MeSH) and text words and then translated into the terms appropriate to Ovid Embase, Ovid Global Health, EthxWeb and BELIT. The AIM and Google scholar databases were also searched using text words. The search terms included (*informed consent* OR *consent* OR *informed decision*) AND (*understanding* OR *comprehension* OR *retention* OR *knowledge* OR *awareness* OR *recall*) AND (*clinical trials* OR *clinical research OR randomi ed clinical trials*). 'Sub-Saharan Africa' was searched using *Africa south of Sahara* OR *developing countries* OR *low-income countries* OR *vulnerable population* OR *underserved population*. To ensure all relevant countries were included in the review, sub-Saharan African countries listed in World RePORT database of global research (Collins *et al.* 2013) were used as a guide. Furthermore, to ensure the search was not limited to English language studies, specific Francophone and Lusophone country names such as Angola, Burkina Faso, Cape Verde, Cote d'Ivoire, Gabon, Guinea-Bissau, Mali, Mozambique, Sao Tome and Principe and Senegal were also included in the search terms. Specific search algorithms used in each database are presented in Table 1.

Duplicate results from the searches were removed, and thereafter, the abstracts of retrieved articles were reviewed for relevance prior to accessing the full paper. We excluded letters or responses to published articles, commentaries and editorials. Conference abstracts that had not been published as full papers were included where the abstracts could be retrieved, provided that the abstracts had sufficient information for either qualitative or quantitative analysis. In situations where a conference abstract had been published as a full paper, the paper was retrieved and the conference abstract excluded. We contacted authors of conference abstracts whose full-paper publications could not be accessed to ask whether the abstract had been published as a full paper and if not, to seek more information about the study. Of five authors contacted, only one responded by providing the full text paper of the conference abstract. However, the published article provided by the author (Ravinetto *et al.* 2010) did not meet the eligibility criteria and was not included in the final analysis.

Data extraction

We obtained 245 articles from the primary search and 64 articles from AIM and Google scholar. Two of the review authors (MOA and JUO) independently screened the searches and applied the eligibility criteria. Of these 309 articles, 192 were removed because they were duplicates. Another 88 articles were sequentially excluded for the reasons of ineligibility. 29 studies satisfied the three inclusion criteria and were reviewed in detail. Figure 1 illustrates the inclusion process. Twenty-three of the studies were

Table 1 Search strategy for the systematic review

Concept	Search terms	EMBASE via Ovid (1947–2013)	Global Health via Ovid (1910–2013)	Medline via Ovid (1946–2013)	EthxWeb	BELIT via DRZE (1850–2013)
Informed consent	#1: (informed consent OR consent OR informed decision). mp.	319882	10179	164307	22586	59923
Comprehension	#2: (understanding OR comprehension OR retention OR knowledge OR awareness OR recall). mp.	1318519	158692	662692	880	9630
Clinical research	#3: (biomedical research OR clinical research OR clinical trials OR randomi*ed controlled clinical trials OR random allocation trials OR intervention trials). mp.	275353	25182	363991	50885	117927
sub-Saharan Africa	#4: (Africa south of Sahara OR low-income countr* OR developing countr* OR vulnerable populations OR disadvantaged populations OR underserved populations).mp. exp Angola/ OR exp Burkina Faso/ OR exp Cape Verde/ OR exp Cote d'Ivoire/OR exp Gabon/ OR exp Guinea-Bissau/OR exp Mali Mozambique/ OR exp Sao Tome and Principe/ OR exp Senegal. mp.	107234	610100	103689	189847	373209
All	#1 AND #2 AND #3 AND #4	74	27	104	36	4

BELIT – Bioethics Literature Database: extensive bibliographic directory of literature in the area of bioethics, containing monographs, academic dissertations, collective works, reference works, books, journal articles, newspaper articles, legal documents, grey literature and electronic document. EthxWeb – Bioethics Research Library at Georgetown University, USA, Medline mp: [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier], Embase mp: [mp=title, subject headings, heading word, drug name, original title, device manufacturer, drug manufacturer, device trade name, keyword].

conducted in Anglophone countries (Abdool Karim *et al.* 1998; Leach *et al.* 1999; Joubert *et al.* 2003; Molyneux *et al.* 2004; Moodley *et al.* 2005; Pace *et al.* 2005; Marshall *et al.* 2006; Manafa *et al.* 2007; Hill *et al.* 2008; Minnies *et al.* 2008; Oduro *et al.* 2008; Taiwo & Kass 2009; Tekola *et al.* 2009; Vallely *et al.* 2010; Chaisson *et al.* 2011; Friedland *et al.*, 2011a,b; Hussein & Ahmed 2011; Kiguba *et al.* 2012; Ndebele *et al.* 2012; Vreeman *et al.* 2012; Oria *et al.* 2013; Saidu *et al.* 2013); five in Francophone countries (Préziosi *et al.* 1997; Coulibaly-Traore *et al.* 2003; Ekouevi *et al.* 2004; Krosin *et al.* 2006; Ellis *et al.* 2010) and one in a Lusophone country (Ciampa *et al.* 2012). Similarly, 12 of these studies were conducted in West Africa (Préziosi *et al.* 1997; Leach *et al.* 1999; Coulibaly-Traore *et al.* 2003; Ekouevi *et al.* 2004; Krosin *et al.* 2006; Marshall *et al.* 2006; Manafa *et al.* 2007; Hill *et al.* 2008; Oduro *et al.* 2008; Taiwo & Kass 2009; Ellis *et al.* 2010; Saidu *et al.* 2013), eight in East Africa (Molyneux *et al.* 2004; Pace *et al.* 2005; Tekola *et al.* 2009; Vallely *et al.* 2010; Hussein & Ahmed 2011; Kiguba *et al.* 2012; Vreeman *et al.* 2012; Oria *et al.* 2013) and nine in Southern Africa (Abdool Karim *et al.* 1998; Joubert *et al.* 2003; Moodley *et al.* 2005; Minnies *et al.* 2008; Chaisson *et al.* 2011; Friedland *et al.*, 2011a,b; Ciampa *et al.* 2012; Ndebele *et al.* 2012). Despite adoption of official languages of former colonial masters, countries in each subregion share similar socio-cultural factors that may influence informed consent comprehension (Angell 1997; Annas 2009). Therefore, this review focused on a regional comparison rather than the adopted official languages.

We extracted information on the type and sites of the studies, the sample size, definition of understanding/comprehension as provided by the authors, method and timing of evaluation of participants' comprehension. Also retrieved were data on participants' understanding/comprehension of study information including key concepts of informed consent: study nature and purpose, blinding, placebo, randomisation, voluntariness, rights of withdrawal, benefits/risks and adverse events. We performed

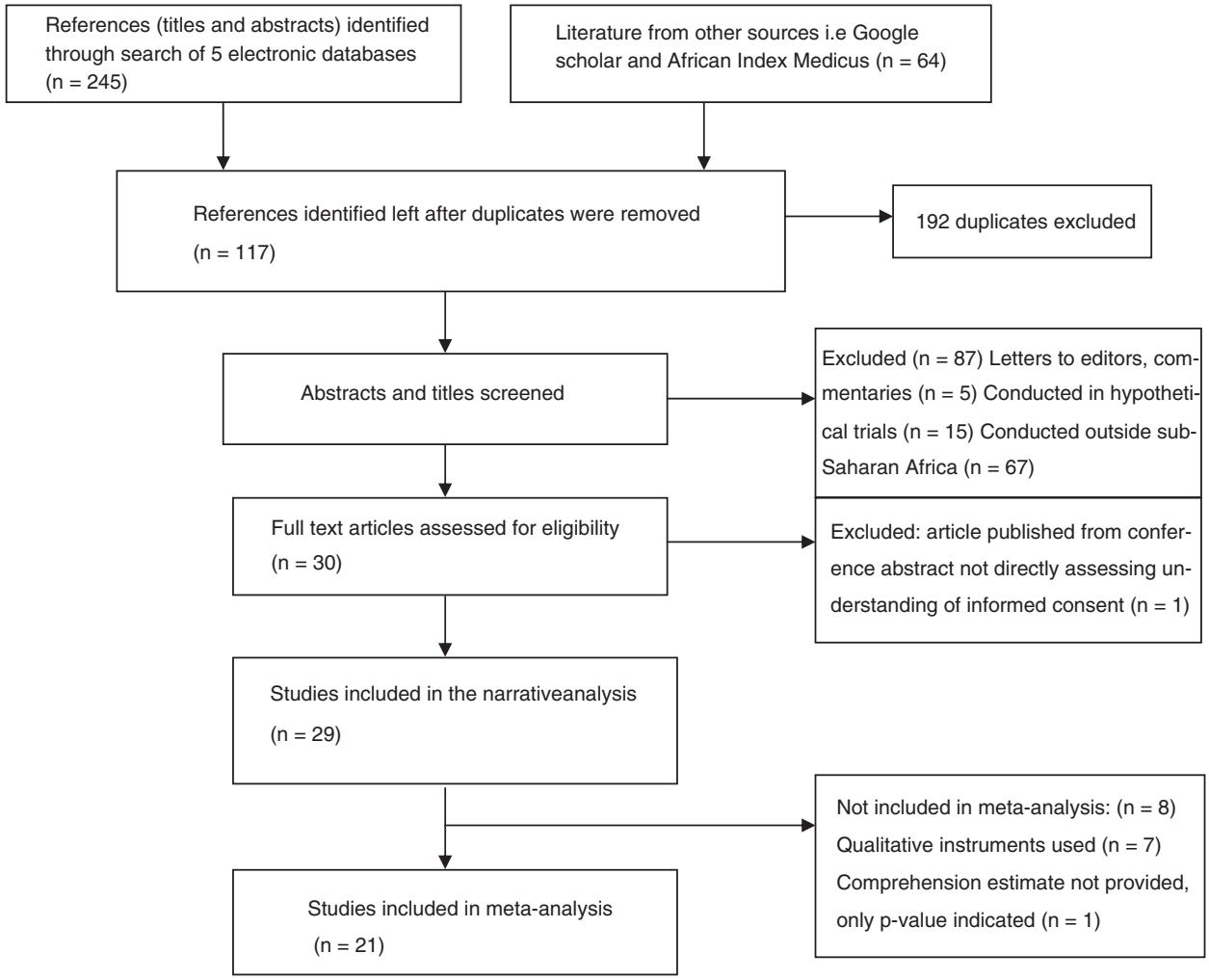

Figure 1 PRISMA flow chart showing inclusion process of papers for the review.

a detailed descriptive analysis and head-to-head comparison of study design, timing of informed consent, categories of participants recruited, instruments used for assessments and domains of informed consent assessed in each study (see Table 2).

Because only three authors provided a full questionnaire in their papers (Krosin *et al.* 2006; Minnies *et al.* 2008; Ellis *et al.* 2010), we did not analyse the few questionnaires for data extraction. We based our comparison on results provided in the papers included in this review.

Meta-analysis

We conducted meta-analyses of summary statistics from 21 studies (Abdool Karim *et al.* 1998; Joubert *et al.* 2003; Ekouevi *et al.* 2004; Moodley *et al.* 2005; Pace *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Manafa *et al.* 2007; Minnies *et al.* 2008; Oduro *et al.* 2008; Taiwo & Kass 2009; Ellis *et al.* 2010; Vallely *et al.* 2010; Chaisson *et al.* 2011; Friedland *et al.*, 2011a, b; Hussein & Ahmed 2011; Kiguba *et al.* 2012; Ndebele *et al.* 2012; Oria *et al.* 2013; Saidu *et al.* 2013) which provided comprehension or understanding levels of participants on different domains of informed consent. Studies which used qualitative methods for assessments of comprehension (n = 7; Préziosi *et al.* 1997; Leach *et al.* 1999; Coulibaly-Traore *et al.* 2003; Molyneux *et al.* 2004; Hill *et al.* 2008; Tekola *et al.* 2009; Vreeman *et al.* 2012) and one with insufficient information (Ciampa *et al.* 2012) were excluded from the meta-analysis.

Table 2 Summary of studies on comprehension of informed consent information among research participants in sub-Saharan Africa

Authors	Country	Type of clinical research	Sample size	Method of evaluation	Outcome measures	Domains of IC understanding targeted
Studies in Anglophone countries						
Saidu *et al.* (2013)	The Gambia	Pneumoprotein vaccine trial	1200 mothers of study infants	Closed-ended study quiz	Comprehension measured by percentage of study mothers who demonstrated understanding	Study purpose, study procedure, voluntary participation, confidentiality
Oria *et al.* (2013)	Kenya	Knowledge assessment to seasonal influenza vaccination	5284 parents for pre-assessment and 5755 parents for post-assessment	Pre- and post-assessment questionnaires; focus group discussions	Percentage of respondents who had knowledge of the vaccination	Reason for influenza vaccination
Vreeman *et al.* (2012)	Kenya	Community perspectives on informed consent and research participation	108 community members	Community group discussions	Proportions of respondents who demonstrated knowledge	Knowledge, attitude, community consent
Ndebele *et al.* (2012)	Malawi	Microbicide trial	36 women	Structured interviews with a questionnaire 8 months after completion of parent trial	Understanding measured by percentage of correct responses to the questionnaire	Randomisation, blinding, placebo
Kiguba *et al.* (2012)	Uganda	Eight clinical trials and seven observational studies	600 men and women	Semistructured interviewer-administered questionnaires	Satisfaction with informed consent process measured on a visual analogue scale (0–10 arbitrary scores)	Study purpose, study procedures, discomfort/risk, potential benefit, confidentiality, compensation, voluntary participation
Chaisson *et al.* (2011)	Botswana	Isoniazid prevention therapy trial	1995 men and women	20-item true/false quiz administered at enrolment, 2 years after enrolment and at subsequent 6 month visits	Passing scores of ≥16 correct responses of 20 questions	Study purpose, study procedures, randomisation, placebo, adverse events, blinding, compensation, voluntariness, risks
Friedland *et al.* (2011b)	Swaziland	Male circumcision scale-up	953 men	10-item questionnaire prior to surgery; qualitative interviews 1 week post-surgery	Comprehension about key informed consent measured by percentage of correct answers to true/false question items	Study procedure, motivating factor for undergoing the procedure, decision-making, post-operative care and complication

(continued)

Table 2 (*Continued*)

Authors	Country	Type of clinical research	Sample size	Method of evaluation	Outcome measures	Domains of IC understanding targeted
Friedland *et al.* (2011a)	Zambia	Male circumcision scale-up	290 men	10-item questionnaire prior to surgery; qualitative interviews 1 week post-surgery	Comprehension about key informed consent measured by percentage of correct answers to true/false question items	Study procedure, motivating factor for undergoing the procedure, decision-making, post-operative care and complication
Hussein and Ahmed (2011)	Ethiopia	HIV voluntary and counselling testing for PMTCT	422 pregnant women	Pre- and post-test questionnaire adapted from UNAID tool	Comprehension about VCT and PTMCT by percentage of participants who reported understanding	Comprehension and satisfaction about VCT and PTMCT
Vallely *et al.* (2010)	Tanzania	Placebo controlled microbicide trial	1146 women had comprehension assessment through checklist, while a subsample of 99 women completed in-depth interviews	Comprehension checklist administered at screening, enrolment, 12-, 24-, 40- and 50-week follow-up visits during the trial. In-depth interviews conducted immediately with a semistructured standardised interview guide after 4-, 24- and 52-week follow-up visits	Comprehension and retention of key messages evaluated through participants' internalisation of the messages and how understanding was incorporated into their beliefs, perceptions, risks and hopes of effectiveness of the gel	Understanding of three key messages was examined: (i) therapeutic misconception, that is, the microbicide gel may not protect against HIV acquisition, (ii) that consistent condom use would prevent HIV infection; (iii) discontinuation of microbicide gel in the event of pregnancy
Taiwo and Kass (2009)	Nigeria	Oral health research	113 men and women	Qualitative and quantitative instruments	Understanding of key informed consent concepts measured by proportion of participants who gave correct responses	Involvement in research, benefits, contacts, confidentiality and voluntariness
Tekola *et al.* (2009)	Ethiopia	Pilot study to develop appropriate informed consent procedure	27 men and 19 women	Qualitative instrument: in-depth interview and focus group discussion	Community understanding of participation in research	Therapeutic misconception

(continued)

Table 2 (*Continued*)

Authors	Country	Type of clinical research	Sample size	Method of evaluation	Outcome measures	Domains of IC understanding targeted
Oduro *et al.* (2008)	Ghana	Paediatric trials evaluating immune correlates of protection against malaria	270 mothers	Semistructured questionnaire administered at the end of the study	Comprehension measured by percentage of correct scores to the question items	Understanding about study procedure, selection criteria, study risks/ benefits, rights of withdrawal, confidentiality
Hill *et al.* (2008)	Ghana	Vitamin A supplementation trial	1971 men and women	60 semistructured interviews and 12 FGDs after consent. Survey carried out to explore knowledge of treatment allocation	Participants' perception and knowledge of the trial evaluated by correct description of study purpose and whether they received active medication or placebo	Knowledge about study purpose and placebo used in the trial
Minnies *et al.* (2008)	South Africa	Paediatric case–control trial of immune correlates of childhood TB	192 mothers	9-item questionnaire on 'recall' and 8-item questionnaire on 'understanding' administered within 1 h of consent	'Recall' measured by success in selecting the correct answers in the question items on voluntary participation, confidentiality, risks/ benefits. 'Understanding' evaluated as correctness of interpretation of statements presented in the question items	Question items covered voluntary participation, confidentiality, risks and benefits
Manafa *et al.* (2007)	Nigeria	Antiretroviral trial	88 men and women	Questionnaire with structured and unstructured items	Understanding assessed by selecting correct responses to the question items	Study purpose, participants' eligibility, risks/benefits, rights of refusal, right of withdrawal
Marshall *et al.* (2006)	Nigeria	Genetic studies of hypertension	307 men and women	3-item survey questionnaire and in-depth interviews at variable time after consent	Understanding of study purpose and voluntary participation measured by participants' responses to question items in the survey questionnaire and responses by participants at in-depth interviews	Question items covered study purpose and voluntary participation

(continued)

Table 2 (*Continued*)

Authors	Country	Type of clinical research	Sample size	Method of evaluation	Outcome measures	Domains of IC understanding targeted
Moodley *et al.* (2005)	South Africa	Influenza vaccine trial	334 men and women	6-item semistructured questionnaire administered. 4–12 months post-trial. Separate questionnaires for treatment and placebo group	Understanding and perception measured by participants' correct responses to the question items	Therapeutic misconception, study purpose, voluntary participation, right to withdraw, randomisation, placebo and compensation
Pace *et al.* (2005)	Uganda	Paediatric malaria treatment study	347 parents	In-person interview immediately after consent. 60-item questionnaire covering six key domains of IC	Comprehension of study information measured by correct responses to question items	Study purpose, study risks, number of clinic visits, ways treatment were assigned, option of quitting the study
Molyneux *et al.* (2004)	Kenya	One field-based and two hospital-based studies involving blood sampling	30 patients admitted to paediatric ward and 1600 adults and children in the field	Semistructured interviews, informal interviews and structured observation of the consent process	Perceptions and understanding explored through participant responses	Reasons for collecting blood samples, therapeutic misconception, risks/benefits
Joubert *et al.* (2003)	South Africa	Vitamin A trial for prevention; of mother-to-child HIV transmission	92 women	Interviewer-administered structured questionnaire at a median of 14 months after consent	Knowledge and perceptions regarding the trial measured by proportions of participants who gave correct responses at the interview	Medications used in the trial, reasons for administering medications, duration of follow-up visits, perceptions about HIV counselling and trial participation
Leach *et al.* (1999)	The Gambia	Paediatric trial of *Haemophilus influenza* type B conjugate vaccine	137 mothers who gave consent and 52 mothers who declined consent	Semistructured interview conducted in local languages within a week of consent. Interview about recall took place 1 week of joining the study	Knowledge/understanding and motive for joining the study were evaluated by participants' responses at the interview	Study purpose, risks/benefit, placebo, motives for participation, people involved in decision-making were explored at the interviews

(continued)

Table 2 (*Continued*)

Authors	Country	Type of clinical research	Sample size	Method of evaluation	Outcome measures	Domains of IC understanding targeted
Abdool Karim *et al.* (1998)	South Africa	Perinatal HIV transmission trial	Evaluation group: 56 women; control group: 56 women	Questionnaire administered before and after HIV counselling and consent	Knowledge and voluntariness of participation were measured by participant responses to the question items	Perception about study purpose, implications of positive HIV test result, voluntary participation, rights of withdrawal
Studies in Francophone countries						
Ellis *et al.* (2010)	Mali	Phase I malaria vaccine trial	89 men and women; 700 parents	9-item questionnaire administered before consent	Understanding measured by percentage of correct responses to the question items	The questionnaire focused on study design, study procedures, risk, benefit, right of withdrawal, randomisation
Krosin *et al.* (2006)	Mali	Paediatric malaria vaccine trial	163 parents	9-item questionnaire administered within 48 h after consent	Comprehension and recall of key messages were measured by correct responses to the question items	Question items covered study purpose, voluntary participation, compensation, rights of withdrawal, randomisation, risks/ benefits
Ekouevi *et al.* (2004)	Cote d'Ivoire	Prevention of mother-to-child transmission trial	55 men and women	Interviewer-administered questionnaire at a median of 136 days after consent	Perception and understanding measured by proportions of participants who gave correct responses to the questionnaire	Rights of withdrawal, knowledge of informed consent process, for example receiving, understanding consent information
Coulibaly-Traore *et al.* (2003)	Cote d'Ivoire	Prevention of mother-to-child transmission of HIV	57 women	In-depth interviews and structured interviews	Percentages of women who showed understanding	Study purpose, randomisation, placebo, motivation for participation
Préziosi *et al.* (1997)	Senegal	Pertussis vaccine trial	2071 mothers	Group consensus meetings	Refusal rates before and after introduction of individual informed consent	Study rationale, blinding, adverse events
Study in a Lusophone country						
Ciampa *et al.* (2012)	Mozambique	Association of HIV knowledge with literacy and numeracy levels of rural women	3557 women	Validated measure of literacy and numeracy	Participants' scores assessed by correct responses to the validated test	Knowledge of HIV testing, prenatal care, PTMCT

Owing to differences in methods of outcome assessments (understanding scores or percentages of participants who demonstrated understanding), we generated the proportions of participants who had 'understanding' and 95% confidence intervals (95% CI) for each domain of informed consent. Random effects meta-analysis was used to pool the estimates of proportions across the studies because heterogeneity of study participants, study designs and assessment tools was envisaged. We estimated heterogeneity statistically using I squared statistics, which is the proportion of true heterogeneity that could be explained by chance (Higgins *et al.* 2003). Expectedly, I squared statistics revealed a substantial heterogeneity in all domains of informed consent assessed (I^2 = 98–99%, $P < 0.0001$). Tables 3 and 4 summarise the meta-analytic results. The meta-analysis was conducted using MedCalc statistical software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org, 2013).

Table 3 Meta-analytic results of studies examining comprehension of 'generic' domains of informed consent

Domain	Studies	Total sample size	Proportion (%)	95% CI
Compensation (n = 3)	Chaisson *et al.* (2011) Oduro *et al.* (2008) Krosin *et al.* (2006)	2428	76.2	39.0–98.5
Voluntariness (n = 8)	Chaisson *et al.* (2011) Oduro *et al.* (2008) Krosin *et al.* (2006) Taiwo *et al.* (2009) Kiguba *et al.* (2012) Moodley *et al.* (2005) Joubert *et al.* (2003) Abdool Karim *et al.* (1998)	3679	78.6	63.1–90.8
Right of withdrawal (n = 13)	Ekhuoevi *et al.* (2004) Oduro *et al.* (2008) Saidu *et al.* (2013) Krosin *et al.* (2006) Ellis *et al.* (2010) Abdool Karim *et al.* (1998) Manafa *et al.* (2007) Marshall *et al.* (2006) Minnies *et al.* (2008) Pace *et al.* (2005) Joubert *et al.* (2003) Friedland *et al.* (2011) Moodley *et al.* (2005)	4183	56.7	33.3–78.6
Right of refusal (n = 6)	Ekhuoevi *et al.* (2004) Manafa *et al.* (2007) Kiguba *et al.* (2012) Moodley *et al.* (2005) Minnies *et al.* (2008) Taiwo *et al.* (2009)	1382	48.6	25.6–71.9
Therapeutic misconception (n = 5)	Ekhuoevi *et al.* (2004) Krosin *et al.* (2006) Taiwo *et al.* (2009) Moodley *et al.* (2005) Manafa *et al.* (2007)	753	30.1	4.6–66.7
Confidentiality (n = 4)	Oduro *et al.* (2008) Minnies *et al.* (2008) Saidu *et al.* (2013) Taiwo *et al.* (2009)	1775	55.4	11.1–94.7

Table shows that about 80% of study participants across the studies understood compensation and voluntariness, while only 30% understood therapeutic misconception, 55% understood confidentiality and <60% understood right to withdraw.

Table 4 Meta-analytic results of studies examining comprehension of 'trial-specific' domains of informed consent

Domains	Studies	Total sample size	Proportion (%)	95% CI
Risks (n = 10)	Minnies *et al.* (2008) Abdool Karim *et al.* (1998) Oduro *et al.* (2008) Pace *et al.* (2005) Krosin *et al.* (2006) Vallely *et al.* (2010) Ellis *et al.* (2010) Taiwo and Kass (2009) Marshall *et al.* (2006) Ndebele *et al.* (2012)	3419	51.3	32.1–70.2
Benefits (n = 5)	Oduro *et al.* (2008) Taiwo and Kass (2009) Pace *et al.* (2005) Vallely *et al.* (2010) Friedland *et al.* (2011a,b)	2829	72.1	42.0–94.0
Placebo (n = 6)	Moodley *et al.* (2005) Vallely *et al.* (2010) Chaisson *et al.* (2011) Pace *et al.* (2005) Ndebele *et al.* (2012) Manafa *et al.* (2007)	3946	47.9	19.0–77.5
Blinding (n = 4)	Chaisson *et al.* (2011) Ndebele *et al.* (2012) Pace *et al.* (2005) Vallely *et al.* (2010)	3524	68.8	55.7–80.6
Randomisation (n = 4)	Ellis *et al.* (2010) Krosin *et al.* (2006) Moodley *et al.* (2005) Pace *et al.* (2005)	1633	46.6	13.9–80.9
Study purpose (n = 17)	Saidu *et al.* (2013) Minnies *et al.* (2008) Abdool Karim *et al.* (1998) Pace *et al.* (2005) Marshall *et al.* (2006) Taiwo and Kass (2009) Krosin *et al.* (2006) Joubert *et al.* (2003) Ekouevi *et al.* (2004) Ndebele *et al.* (2012) Friedland *et al.* (2011a) Friedland *et al.* (2011b) Ellis *et al.* (2010) Manafa *et al.* (2007) Chaisson *et al.* (2011) Hussein and Ahmed (2011) Oria *et al.* (2013)	12 382	64.8	34.9–89.4

(continued)

Table 4 (*Continued*)

Domains	Studies	Total sample size	Proportion (%)	95% CI
Study procedure (n = 13)	Chaisson *et al.* (2011) Saidu *et al.* (2013) Oduro *et al.* (2008) Ellis *et al.* (2010) Manafa *et al.* (2007) Taiwo and Kass (2009) Kiguba *et al.* (2012) Pace *et al.* (2005) Friedland *et al.* (2011a) Friedland *et al.* (2011b) Abdool Karim *et al.* (1998) Minnies *et al.* (2008) Joubert *et al.* (2003)	6985	72.9	55.2–87.4

Table shows that about 50% of participants across various studies understood placebo, randomisation and risks, while higher proportions (about 70%) understood benefits, blinding and study procedure.

Results

Study characteristics and design

Twenty-nine studies conducted in 20 countries from SSA examined participants' comprehension of informed consent information in clinical research on vaccines, tuberculosis treatment in HIV-infected patients, HIV prevention trials, male circumcision scale-up, oral health, vitamin A supplementation, immune correlates in paediatric age group and genetic studies of hypertension (Table 2). The number of study participants in the studies ranged from 36 to 5755. Of the studies, 17 interviewed participants close to the time of consent (Abdool Karim *et al.* 1998; Leach *et al.* 1999; Coulibaly-Traore *et al.* 2003; Pace *et al.* 2005; Fairhead *et al.*, 2006a,b; Krosin *et al.* 2006; Hill *et al.* 2008; Minnies *et al.* 2008; Taiwo & Kass 2009; Tekola *et al.* 2009; Ellis *et al.* 2010; Hussein & Ahmed 2011; Ciampa *et al.* 2012; Kiguba *et al.* 2012; Vreeman *et al.* 2012; Saidu *et al.* 2013); interviews were conducted 1–14 months after participants gave consent in six studies (Joubert *et al.* 2003; Ekouevi *et al.* 2004; Moodley *et al.* 2005; Hill *et al.* 2008; Vallely *et al.* 2010; Ndebele *et al.* 2012) and longer than 14 months in two studies (Oduro *et al.* 2008; Chaisson *et al.* 2011); pre- and post-assessments were carried out in two studies (Préziosi *et al.* 1997; Oria *et al.* 2013), while baseline and repeated assessments of understanding were carried out in another two studies (Vallely *et al.* 2007; Chaisson *et al.* 2011). Six studies interviewed the mothers of study children (Préziosi *et al.* 1997; Leach *et al.* 1999; Minnies *et al.* 2008; Oduro *et al.* 2008; Oria *et al.* 2013; Saidu *et al.* 2013); nine studies interviewed adult male and female participants (Joubert *et al.* 2003; Ekouevi *et al.* 2004; Moodley *et al.* 2005; Marshall *et al.* 2006; Hill *et al.* 2008; Tekola *et al.* 2009; Vallely *et al.* 2010; Friedland *et al.*, 2011a,b), seven interviewed only female participants (Abdool Karim *et al.* 1998; Coulibaly-Traore *et al.* 2003; Joubert *et al.* 2003; Vallely *et al.* 2010; Hussein & Ahmed 2011; Ciampa *et al.* 2012; Ndebele *et al.* 2012), two interviewed only male participants (Friedland *et al.*, 2011a,b) and five studies interviewed both parents and adult participants (Molyneux *et al.* 2004; Pace *et al.* 2005; Krosin *et al.* 2006; Ellis *et al.* 2010; Vreeman *et al.* 2012).

Measurement tools

Sixteen studies used questionnaires to assess participants' comprehension (Abdool Karim *et al.* 1998; Joubert *et al.* 2003; Ekouevi *et al.* 2004; Moodley *et al.* 2005; Krosin *et al.* 2006; Manafa *et al.* 2007; Minnies *et al.* 2008; Oduro *et al.* 2008; Ellis *et al.* 2010; Chaisson *et al.* 2011; Hussein & Ahmed 2011; Ciampa *et al.* 2012; Kiguba *et al.* 2012; Ndebele *et al.* 2012; Oria *et al.* 2013; Saidu *et al.* 2013); six employed in-depth qualitative interviews (Leach *et al.* 1999; Coulibaly-Traore *et al.* 2003; Molyneux *et al.* 2004; Pace *et al.* 2005; Hill *et al.* 2008; Tekola *et al.* 2009) and five used both qualitative and quantitative methods (Marshall *et al.* 2006; Taiwo & Kass 2009; Vallely *et al.* 2010; Friedland *et al.*, 2011a,b) and two used community group discussions

(Préziosi *et al.* 1997; Vreeman *et al.* 2012). The majority of the questionnaires used closed-ended response formats. The questionnaires varied significantly in the number of items, and the domains addressed by these items. The authors indicated the number of question items in eight studies (Moodley *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Minnies *et al.* 2008; Ellis *et al.* 2010; Chaisson *et al.* 2011; Friedland *et al.*, 2011a,b); the number ranged from 3- to 20-item quiz. The items in the questionnaire could be classified into two broad domains: generic and trial-specific questions (Joffe *et al.* 2001). The generic questions focused on general aspects of research such as confidentiality, compensation, rights of withdrawal or refusal (Table 3), while the trial-specific questions focused on individual research-related domains such as study purpose, study rationale, study procedures, medications, risks and adverse events (Table 4). A complete questionnaire was included in the appendix in three papers (Krosin *et al.* 2006; Minnies *et al.* 2008; Ellis *et al.* 2010). Participants were assessed on several domains of informed consent, while two studies (Tekola *et al.* 2009; Vallely *et al.* 2010) focused only on participants' understanding of therapeutic misconception. The format adopted in the semistructured or in-depth interviews was not clearly discussed in most of the papers except one study (Vallely *et al.* 2010) which used a standardised interview guide.

Development of measurement tools

Only four manuscripts (Krosin *et al.* 2006; Vallely *et al.* 2010; Ciampa *et al.* 2012; Ndebele *et al.* 2012) provided an account of how the measurement instrument was developed. One study (Taiwo & Kass 2009) mentioned that the questionnaire was adapted from previously developed questionnaires such as the Quality Questionnaire of Informed Consent and the Deaconess Informed Consent Questionnaire. Another study (Ciampa *et al.* 2012) adapted and validated its questionnaire from the Wide Range Achievement Test. Ten reported that they translated and back-translated the questionnaires from foreign languages to participants' local languages (Joubert *et al.* 2003; Moodley *et al.* 2005; Pace *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Oduro *et al.* 2008; Chaisson *et al.* 2011; Ciampa *et al.* 2012; Kiguba *et al.* 2012; Ndebele *et al.* 2012). Significant linguistic diversity made it costly and logistically challenging to translate informed consent documents from English, French or Portuguese into effective written versions of several local languages of participants in each country (Préziosi *et al.* 1997; Tekola *et al.* 2009; Chaisson *et al.* 2011; Ciampa *et al.* 2012; Ndebele *et al.* 2012).

In three studies, participants' comprehension was measured by the proportion of correct responses to the question items (Krosin *et al.* 2006; Oduro *et al.* 2008; Ellis *et al.* 2010), while other studies assessed proportions of participants who gave correct responses to questionnaires and interviews (Joubert *et al.* 2003; Ekouevi *et al.* 2004; Moodley *et al.* 2005; Marshall *et al.* 2006). Additionally, terms such as 'understanding', 'comprehension', 'knowledge', 'remembering', 'retention', 'recall, 'awareness' or 'recognition' were used interchangeably without clear definitions. Only one study (Minnies *et al.* 2008) defined the outcome variables: recall as 'success in selecting the correct answers in the question items' and understanding as 'correctness of interpretation of statements presented in the question items'. There was also no consensus on the time points to measure comprehension as participants (Pace *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Sand *et al.* 2010; Friedland *et al.*, 2011a,b) were evaluated at different times.

Comprehension of informed consent information

This section focuses on the meta-analytic results on 21 studies (Abdool Karim *et al.* 1998; Joubert *et al.* 2003; Ekouevi *et al.* 2004; Moodley *et al.* 2005; Pace *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Manafa *et al.* 2007; Minnies *et al.* 2008; Oduro *et al.* 2008; fTaiwo & Kass 2009; Ellis *et al.* 2010; Vallely *et al.* 2010; Chaisson *et al.* 2011; Friedland *et al.*, 2011a,b; Hussein & Ahmed 2011; Kiguba *et al.* 2012; Ndebele *et al.* 2012; Oria *et al.* 2013; Saidu *et al.* 2013) and complementary narrative comparison of all eligible studies.

Study purpose. Meta-analytic results showed that 65% of a total of 12 382 participants in 17 studies (Abdool Karim *et al.* 1998; Joubert *et al.* 2003; Ekouevi *et al.* 2004; Pace *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Manafa *et al.* 2007; Minnies *et al.* 2008; Taiwo & Kass 2009; Ellis *et al.* 2010; Chaisson *et al.* 2011; Friedland *et al.*, 2011a,b; Hussein & Ahmed 2011; Ndebele *et al.* 2012; Oria *et al.* 2013; Saidu *et al.* 2013) understood the purpose of the studies they were involved in (95% CI 34.9–89.4%). Furthermore, on descriptive comparison, comprehension of study purpose assessed in 18 studies (Préziosi *et al.* 1997; Abdool Karim *et al.* 1998; Leach *et al.* 1999; Coulibaly-Traore *et al.* 2003; Joubert *et al.* 2003; Ekouevi *et al.* 2004; Molyneux *et al.* 2004; Moodley *et al.* 2005; Pace *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Manafa *et al.* 2007; Hill *et al.* 2008; Taiwo & Kass 2009; Chaisson *et al.* 2011; Ciampa *et al.* 2012; Kiguba *et al.* 2012; Saidu *et al.* 2013) was markedly high among participants in southern Africa (Minnies *et al.* 2008;

Chaisson *et al.* 2011; Friedland *et al.*, 2011a,b). This ranged from 88% to 98.7%, while East and West African participants had comprehension rates between 8% and 47% (Joubert *et al.* 2003; Molyneux *et al.* 2004; Taiwo & Kass 2009; Kiguba *et al.* 2012). Most participants in countries with poorer comprehension had a low level of education. Endemicity of the conditions studies also explained the disparities in the observed responses. For instance, there were marked differences in comprehension of the causes, routes of transmission and prevention of HIV by pregnant women in Cote d'Ivoire and South Africa, with most participants in Cote d'Ivoire demonstrating poor understanding of the study rationale (Coulibaly-Traore *et al.* 2003; Ekouevi *et al.* 2004). Similarly, poor comprehension was observed in participants enrolled in an oral health study in Nigeria (Taiwo & Kass 2009).

Voluntary participation. About 80% of 3679 participants across eight studies (Abdool Karim *et al.* 1998; Joubert *et al.* 2003; Moodley *et al.* 2005; Krosin *et al.* 2006; Oduro *et al.* 2008; Taiwo & Kass 2009; Chaisson *et al.* 2011; Kiguba *et al.* 2012) demonstrated comprehension about voluntariness towards participation (95% CI 39.0–98.5%), with perceived medical benefit cited as a main determinant (Leach *et al.* 1999; Pace *et al.* 2005; Oduro *et al.* 2008). Inadequate access to health care and other poor socio-economic factors in developing countries were reported as strong motives for joining clinical trials (Préziosi *et al.* 1997; Leach *et al.* 1999). Severity of diseases also contributes to the sense of compulsion to participate. In a Kenyan study, only 4% of mothers of seriously ill children agreed that participation was voluntary, while most participants believed that they would have been chased away if they refused to join the study (Molyneux *et al.* 2004). In contrast, 97% of mothers whose children were less seriously sick in the same study reported voluntary participation during admission; 14% spontaneously reported this on discharge and 59% after prompting (Molyneux *et al.* 2004).

Right of withdrawal. Of 4183 participants across 13 studies (Abdool Karim *et al.* 1998; Joubert *et al.* 2003; Ekouevi *et al.* 2004; Moodley *et al.* 2005; Pace *et al.* 2005; Krosin *et al.* 2006; Marshall *et al.* 2006; Manafa *et al.* 2007; Minnies *et al.* 2008; Oduro *et al.* 2008; Ellis *et al.* 2010; Friedland *et al.*, 2011a; Saidu *et al.* 2013), 57% understood right of withdrawal (95% CI 33.3–78.6%). Further descriptive comparison of findings in seven studies (Abdool Karim *et al.* 1998; Ekouevi *et al.* 2004; Pace *et al.* 2005; Krosin *et al.* 2006; Manafa *et al.* 2007; Oduro *et al.* 2008; Ellis *et al.* 2010) showed that understanding of the right to withdraw from a study was low among most study participants across West African subregion. In a Malian trial (Krosin *et al.* 2006), participants believed that leaving before the end of the study would be disrespectful to the investigators who might consequently deny them medical benefits associated with participation. Their counterparts from a South African (Abdool Karim *et al.* 1998) study showed better comprehension of their rights to stop participation. Similar trends were observed for rights of refusal to participate. Taiwo and Kass (2009) reported that social status in the study community might positively influence a participant to enrol in a study. One example was cited of a highly educated community officer who enrolled in a trial so as not to discourage other community members from joining the trial. Participants in a Gambian study (Leach *et al.* 1999) also expressed the fear of serious, unknown side effects of an experimental vaccine as a major reason for declining to enrol in the study.

Confidentiality. Meta-analytic results showed that 55% of a total of 1775 participants in four studies (Minnies *et al.* 2008; Oduro *et al.* 2008; Taiwo & Kass 2009; Saidu *et al.* 2013) did not understand the concept of confidentiality. However, descriptive comparison showed a high level of comprehension in two studies (Minnies *et al.* 2008; Saidu *et al.* 2013), but in other two studies (Taiwo & Kass 2009; Kiguba *et al.* 2012), participants were not aware of how their research records would be kept.

Compensation. Across three studies (Krosin *et al.* 2006; Oduro *et al.* 2008; Chaisson *et al.* 2011) involving 2428 participants, 76% understood compensation (95% CI 39.0–98.5%). Understanding of compensation associated with participation was largely dependent on how the questions were framed and presented to the participants, who generally considered personal benefit a high priority. Participants in two studies (Oduro *et al.* 2008; Chaisson *et al.* 2011) misunderstood reimbursement of transport fares as payment for study participation.

Risks. About 51% of 3419 participants understood risks involved in study participation (95% CI = 32.1–70.2%) in 10 studies (Leach *et al.* 1999; Molyneux *et al.* 2004; Pace *et al.* 2005; Krosin *et al.* 2006; Manafa *et al.* 2007; Minnies *et al.* 2008; Taiwo & Kass 2009; Ellis *et al.* 2010; Chaisson *et al.* 2011; Kiguba *et al.* 2012). This was found to be better among participants from southern Africa (Minnies *et al.* 2008; Chaisson *et al.* 2011) than among participants in West African studies (Krosin *et al.* 2006; Taiwo & Kass 2009).

Therapeutic misconception. Only 30% of 753 participants across five studies (Ekouevi *et al.* 2004; Moodley *et al.* 2005; Krosin *et al.* 2006; Manafa *et al.* 2007; Tai-

wo & Kass 2009) understood the concept of therapeutic misconception. This occurs when participants believe that the study is solely aimed at providing health care rather than generating research data. It featured prominently among West African participants (Ekouevi *et al.* 2004; Krosin *et al.* 2006; Manafa *et al.* 2007; Taiwo & Kass 2009), while a South African study (Moodley *et al.* 2005) reported that a significant proportion of participants recognised they were participating in a research as opposed to seeking medical care.

Randomisation and placebo. Of 1633 participants in four studies (Moodley *et al.* 2005; Pace *et al.* 2005; Krosin *et al.* 2006; Ellis *et al.* 2010), 47% demonstrated understanding about randomisation (95% CI = 13.9–80.9%). Similarly, 48% of 3946 participants in six studies (Moodley *et al.* 2005; Pace *et al.* 2005; Manafa *et al.* 2007; Vallely *et al.* 2010; Chaisson *et al.* 2011; Ndebele *et al.* 2012) had understanding of placebo (95% CI 0.19.0–77.5%). Descriptive comparison showed that methods employed in explaining the concepts of randomisation and use of placebo during informed consent process influenced participants' understanding. Malawian participants (Ndebele *et al.* 2012) demonstrated good understanding of randomisation when a locally designed narrative was used to illustrate the research terms. About 75–78% of these participants comprehended randomisation and placebo, while 10–19% of East and West African participants demonstrated good understanding of the concepts (Leach *et al.* 1999; Pace *et al.* 2005; Hill *et al.* 2008).

Autonomy/decision-making. Seven studies (Leach *et al.* 1999; Coulibaly-Traore *et al.* 2003; Ekouevi *et al.* 2004; Molyneux *et al.* 2004; Krosin *et al.* 2006; Friedland *et al.*, 2011a,b) assessed this concept. Ninety-nine percentage of Gambian participants (Leach *et al.* 1999) submitted that parents and village leaders were involved in decision-making. Similar patterns were reported in East and other West African studies (Ekouevi *et al.* 2004; Molyneux *et al.* 2004; Krosin *et al.* 2006), while individual decision-making was common in southern African countries (Friedland *et al.*, 2011a,b).

Predictors of comprehension. In most studies reviewed (Oduro *et al.* 2008; Taiwo & Kass 2009; Chaisson *et al.* 2011; Kiguba *et al.* 2012; Ndebele *et al.* 2012), demographic variables like age and literacy did not show statistical significance, but male sex was reported as the only independent predictor of higher comprehension scores in one study (Ellis *et al.* 2010). Conversely, primary education and residence in urban areas were predictors of understanding among women (Hill *et al.* 2008). Similarly, another study (Krosin *et al.* 2006) reported higher comprehension scores in most urban participants than their rural counterparts. Among Mozambican participants, numeracy level was significantly associated with comprehension of study purpose and this was independent of respondent's age, income, distance from the hospital and the language of survey administration (Ciampa *et al.* 2012). Moodley *et al.* (2005) also reported a positive linear correlation between participants' comprehension scores and their mini-mental state examination scores.

Discussion

To our knowledge, this is the first comparison of participants' comprehension of informed consent information in studies conducted across SSA. Previous reviews have either concentrated on informed consent comprehension in developed countries (Sand *et al.* 2010) or compared the quality of informed consent between Western and developing countries in Africa and Asia (Mandava *et al.* 2012).

Our review reveals that the methods used for assessing participants' comprehension differed significantly. Such variations in methodology limited comparison of findings and raise challenges about how to measure comprehension of informed consent information. Very few studies (Ciampa *et al.* 2012; Ndebele *et al.* 2012) described the format and justifications for deciding to use a set of question items. A sizeable proportion of the tools were developed ad hoc for each study without following standard guidelines of instrument development and validation.

We also identified a lack of a uniform definition of comprehension as studies in the review used the term 'comprehension' to mean 'understanding' or 'recall' or 'retention' or 'knowledge'. It is important to establish a distinction between these terms as it would help in developing a uniform definition for the concept. This effort is capable of providing an acceptable method for determining how an instrument can be constructed, implemented, interpreted and applied to measure the concept (Spreitzer & Sonenshein 2004).

The domains of informed consent assessed by the studies also vary considerably with little regard to the crucial information that could engender comprehension. There is a need to develop guidelines that define the most crucial information relevant for comprehension of informed consent in African research settings as well as the best way this information should be communicated.

Most study participants in this review did not understand the distinction between research participation and seeking medical care. This concept of therapeutic misconception has been documented among participants in resource poor settings where inadequate access to health

care exists (Appelbaum *et al.* 1982; Préziosi *et al.* 1997). This is due to a mix of heavy burden of disease, poor access to health care, poor education, low literacy levels and the overriding impact of illness, suffering and poverty on decision-making. A National Bioethics Advisory Commission reported that therapeutic misconception does not imply that participants will most likely get adequate clinical care during research, but subsists when participants believe that the sole aim of clinical trials is to provide treatment rather than collect data (NBAC 2001). Consequently, African researchers should strive to harmonise the research of essential medicines with the ethical requirements of making them accessible. Improved access to such care could reduce vulnerability and ultimately improve comprehension of African participants.

The time interval between informed consent process and assessment of comprehension in most of the studies was long, some more than 14 months after the trials have ended. Given the background of low literacy among participants, and not being familiar with research terms, it is very unlikely that reliable inferences can be drawn from assessments carried out after such long periods. There are no existing guidelines on the timing of such assessments as these are likely to be study or context specific.

Availability of the questionnaires in local languages was reported to aid participants' understanding in few countries (Chaisson *et al.* 2011; Ndebele *et al.* 2012). However, this is not always possible as some African languages are spoken and do not have standardised writing formats. Translations and back-translation of informed consent documents are practically challenging in the Gambia for this reason.

A major strength of this review is the combination of meta-analytic results with the narrative comparison of the findings. This provided a robust summary of the findings on informed consent comprehension despite significant disparities in methodologies and heterogeneity of the data. Further contributing to this, we excluded participants in hypothetical studies so that our findings could reflect true clinical research situations as much as possible. We also included studies where participants were legally and cognitively competent, to remove factors which might confound our findings.

Limitations

Very few of the studies included in this review provided adequate information on the instruments employed to assess comprehension of informed consent. This did not permit analysis of wordings of the questionnaires to establish what the authors actually explored in their studies. Such analysis could have provided useful insights that might have contributed to appropriate interpretations of findings of the studies.

Also, findings of this review need to be cautiously interpreted because majority of the quantitative instruments used in this review contained closed-ended questionnaires, which are known to be an imperfect method of assessing comprehension, because respondents could guess answers correctly or provide socially desirable responses. This could have over-estimated the comprehension levels, thereby leading to inaccuracies in our findings. Studies (OnvomahaTindana *et al.* 2006; Ndebele *et al.* 2012) have shown that requesting participants to explain, using their own words, their comprehension of study information may truly manifest what participants understand.

It could also be inferred that studies in this review examined the 'performance' of participants, but apparently did not evaluate the communication skills of the researchers administering the consent; and this plays a key role for comprehension. This may represent an asymmetry, where researchers ask 'why participants do not comprehend' but we do not ask ourselves 'why are we not good at explaining crucial information to our participants?'

Nevertheless, the representativeness of studies in this review provides a comprehensive knowledge base for setting research agenda and plans.

Conclusions

Our review confirmed the findings of previous reviews that comprehension of informed consent in Africa settings varies from country to country with relatively better comprehension among participants in southern Africa. Tools for measuring participants' comprehension are neither validated nor standardised. To overcome potential pitfalls in effectiveness of conventional informed consent procedures in African research settings, it is crucial to engage a body of knowledge on the development of clear guidelines to design adequate tools for improving informed consent comprehension and maximise the voluntariness of the choice to participate in clinical trials. Such tools should translate the respect for fundamental ethical principles, by taking into considerations local cultural values and constraints.

Furthermore, due to wide linguistic variability that made effective translations of informed consent documents to local languages challenging, appropriately developed tools using orally interpreted procedure with non-verbal support like video and animations may improve the comprehensibility of unfamiliar research concepts among African participants. Experts who are familiar with the local context and influence of communication and

demographic factors on informed consent process need to be involved in the design. This multidisciplinary approach should harmonise local contextual and behavioural factors, including the expectations of the community, in developing comprehensible consent tools.

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Corresponding Author **Muhammed O. Afolabi**, Medical Research Council Unit, Fajara, PO Box 273, Banjul, The Gambia.
E-mail: mafolabi@mrc.gm