A quantitative evaluation of the quality of informed consent in a developing country setting.

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This work is presented as partial fulfilment of the requirement for the Master of Public Health degree. The author developed the proposal and designed the measurement tool in consultation with his supervisors. Following departmental and ethical approval, the author selected, trained and supervised staff responsible for participant enrolment, data collection and capturing, conducted monitoring and performed analyses of the data.

Declaration

I, Deon Minnies, declare that the content of this document is the result of my original work, except where acknowledgements indicate otherwise. No part of this has been or is being submitted for a degree at this, or any other university.

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Acknowledgement

When the BCG study started in 2001, the researchers of the University of Cape Town set out to do a scientific trial and introduced randomization and blinding and informed consent to a largely research-naïve community. The researchers' involvement in thousands of peoples' lives triggered many unlikely (at the time) realizations, amongst others, the need to have a critical look at how bioethics theory is applied in community-based research projects.

I would like to thank the following people and organisations that made this study possible:

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Summary

Informed consent is an ethical and legal requirement for research involving human participants. However, there have been few studies that have evaluated the process, particularly in an African setting. In addition, standardized methods for assessing the quality of informed consent are not available in the literature.

Objective
The aim of the study was to evaluate the quality of consent in a large tuberculosis vaccine immunology study and to identify factors associated with the quality of consent.

Setting
Participants in an immunology case control study designed to identify correlates of immune protection against TB. This study was nested within a randomized clinical trial evaluating BCG vaccine efficacy amongst infants born in the Worcester area.

Methods
Caregivers of children participating in the immunology study were enrolled and interviewed by research nurses. A questionnaire dealing with the key requirements of informed process and content (i.e. voluntary participation, confidentiality, the main risks and benefits of the immunology study and understanding of the material) were completed by participants and the recall and understanding of consent items were measured.

Results & Conclusion
The majority of participants obtained high scores (> 75%) for both the *recall* and *understanding* sections. The median score for *recall* was 66 7% (IQR = 55.6%-77 8%) and for *understanding* 75% (IQR=50%-87.5%). Most (79 2%) were aware of the risks, but only 36.7% could recall that there were no direct personal benefits. A total of 65.1% knew that participation was voluntary. Education level of the participant and experience of research staff were predictive factors for good quality consent.

Conclusion
To the knowledge of the author, this is one of a very few studies of its kind in South Africa. The quality of informed consent for the immunology study can be considered as acceptable, in the context of public health research in a developing country. Although participants could recall most of the information of the consent document, there was some uncertainty in their perception of benefits. The study could also be useful in providing a method for informed consent assessments in future studies.

Chapter 1: Introduction

Although informed consent is an ethical and legal requirement for research involving human participants, standardized methods for assessing the quality of informed consent are not available (Joffe *et al*, 2001a) The tragic history of research on human subjects, e.g. the Nazi medical war crimes, the Tuskegee syphilis study of the 1930s, and the Willowbrook study [National Institutes of Health (NIH), 2002], have led Research Ethics Committees at academic centers to demand adherence to guidelines set by amongst others, the Declaration of Helsinki, the Nuremburg Code and the Belmont Report (Medical Research Council, 2000). These internationally accepted tools are contained in the International Convention for Harmonization's initiative on Good Clinical Practice (GCP). GCP guidelines have become the quality standards for the conduct of clinical trials in humans.

In 1982 the Council for International Organizations of Medical Sciences (CIOMS) issued guidelines for the application of bioethics to research. According to these guidelines, all research involving human subjects should be conducted in accordance with four basic ethical principles, namely respect for persons, beneficence, non-maleficence and justice. Researchers should be held accountable for addressing these principles in their research proposals and in the execution of their studies. Similarly, Research Ethics Review Boards are expected to use these guidelines when approving research proposals.

Despite these requirements, assessment of the quality of informed consent has seldom been high on the list of priorities of researchers. While some investigators have assessed the quality of informed consent in local clinical settings, very few have done this in large marginalized and impoverished communities, where participants are more vulnerable to unethical research practice.

Background

The BCG Study is a randomized controlled efficacy trial that compares two routes of administration of BCG vaccine in the prevention of severe forms of tuberculosis (TB) in infants and young children in a rural setting in South Africa. This trial (the BCG Study) has enrolled more than 12 000 pregnant women at antenatal clinics to have their babies receive Tokyo 172 BCG at birth, either by the percutaneous or intradermal route.

Enrollment of pregnant women at antenatal clinics in the northeastern part of the Boland region of the Western Cape Province of South Africa commenced in March 2001. Worcester, the biggest town of the study area[1], lies 100 km northeast of Cape Town, the capital city of the province.

Figure 1: Map of the Western Cape Province showing the study area (in box), the Breede River and the major national routes diverging from Cape Town to the interior.

[1] The study area is situated in the valley of the Breede River, which forms the backbone of its predominantly agriculture based economic activities. The data collected during the census conducted by Statistics SA in 2001 show that the region had a steady increase in population over the previous five years. The region is characterized by a median household income of under R20 000 per annum, an unemployment rate of 20%, with less than 10% of adults having finished school. The Hex River Valley, flanking a tributary of the Breede River, houses one of the richest wine producing districts of the country. Here, farmers produce export quality wine that can be sold for well over US$100 per case. Yet, farm workers earn as little as R180 (US$22-30) per week. This is frequently the only income available to support up to twelve household members, including young children.

Trained community health workers[2] counselled women who attended the antenatal clinics at public health facilities and enrolled them into the trial. The children of those women who were not reached or who did not consent to participate received the standard of care, which is the intradermal vaccination with Danish 1331 BCG (Staten Serum Instituut, Copenhagen). Study children received Japanese BCG by percutaneous or intradermal route. After vaccination, the babies are being followed up for another 2 to 5 years in order to identify, investigate and report protocol outcomes like Severe Adverse Events (including hospitalizations), TB and death.

Infants enrolled in the cohort of the BCG Study were eligible to participate in a nested Immunology Study. This study (a case control study) aims to identify immune correlates of protection against severe childhood TB, and involves the collection of blood from infants who are between 8 and 14 weeks of age. This blood is used to measure the amount of gamma-interferon[3] produced in response to BCG. It is expected that higher gamma-interferon levels would indicate better protection against severe TB than lower levels. Some of the blood is also used to separate, aliquot and store mononuclear cells for further immunological testing. Participants are asked to consent to the blood collection procedures of the Immunology Study on the day of the phlebotomy.

A week before the blood collection, prospective participants of the Immunology Study are contacted and requested to attend a phlebotomy clinic in their area. At this notification the parents or caregivers of the child would receive a note asking them to bring their child to the clinic on a given day, together with a pamphlet that gives a simple explanation of the purpose of the visit of the study team to their clinic. Members of the study team then arrive at the clinic on the scheduled day, complete with materials and equipment, and proceed to inform those parents / caregivers[4] present about the study. Afterwards all children's parents would seen individually by the research nurse[5], and the informed consent procedure would be completed. (See Appendix A, Standard operating procedure: Immunology Study enrollment and consent)

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[2] The community health workers possess a school-leaving certificate (Grade 12), and are trained by health professionals to provide lay counselling, health education and morbidity surveillance at public health facilities.

[3] Certain blood cells (T-lymphocytes) of individuals who had been in contact with an infectious tuberculosis agent produce gamma-inteferon when encountering mycobacterial antigens. A high level of gamma-inteferon production is presumed to be indicative of TB infection.

[4] Hereafter referred to as parents.

[5] The research nurses are Professional Nurses who have completed at least a 3 year diploma at a nursing college or a 4 year degree at a university.

All staff dealing with study participants had been trained in good clinical practice (GCP) and other research procedures Monitoring and evaluation are performed on a regular basis to assess the quality of procedures and documentation generated. High standards of research practice are expected from all research staff.

An earlier quality management exercise to assess the quality of consent in the Immunology Study was conducted in April 2002. A convenience sample of participants was interviewed after the consent and blood collection procedures, and asked to answer multiple-choice questions on certain aspects of the consent process The selected participants were chosen so that there was equal representation in respect of language and location. The procedures and practices of research workers were evaluated at the same time. Analysis of the first 60 completed questionnaires revealed that the quality of consent appeared to be reasonable, with 85% of the participants in the audit stating that the nurses explained "very well" (Hawkridge *et al*, 2002). Eighty three percent felt that they had understood "almost everything" of what was said to them. The audit was repeated six months later, with a different sample, giving similar results. These audits succeeded in identifying deficiencies in staff skill and techniques, and general areas of participant misunderstanding.

During another such audit, it was observed that the Immunology Study acceptance rate was extremely high (greater than 99%). This meant that only a small number of women approached for enrollment into the study refused to participate. Upon further investigation it was revealed that participants rarely asked exploratory questions, or contacted the study office when faced with a reportable[6] occurrence. This led the study team to question participants' perception of basic informed concepts and their understanding of topics explained during the consent procedure. In order to determine the level of recall and mental processing of the study concepts, it was considered necessary to conduct a formal quality of informed consent study. This is the subject of this dissertation.

Purpose & objectives

The purpose of the Consent Study was thus to determine the level of *recall* and understanding of the key aspects of informed consent as contained in the consent form of the Immunology Study.

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[6] According to the BCG Study protocol, participants are requested to report vaccine reactions, hospitalizations and the death of babies vaccinated with the study BCG. Suspicion of TB and contact with adults with active TB should also be reported. This would help to identify study outcomes in trial participants.

The Consent Study thus aimed to evaluate the quality of informed consent in the Immunology Study by using a specially designed questionnaire to be completed by mothers from whom informed consent was obtained.

The specific objectives of the Consent Study were:

a. To determine how well study participants understood the Immunology Study consent document contents by testing their recall of items discussed during the consent procedure;
b. To ascertain whether study participants made informed choices about their health and research options by testing how well participants understood the underlying principles of the consent topics;
c. To establish whether certain demographic predictors like age, level of education and language affected the quality of informed consent; and
d. To describe how the quality of informed consent is associated with the knowledge of health rights as contained in the South African Bill of Rights.

Preview of the dissertation

Chapter 2 deals with the results of a literature review. Health research ethical practices are viewed in the context of current standards and regulatory mechanisms recommended by the National Institutes of Health (NIH) in the USA and the Medical Research Council (MRC) in South Africa. This is followed by a discussion of the quality of informed consent in medical practice and research. A critical look at the methods and results of consent evaluation surveys is also included.

Chapter 3 describes the study design and the study population. A brief explanation of the sampling method is given, followed by the description of the questionnaire. The rest of the section contains details of the pilot study results, data capture and analysis techniques, and ethics of the consent study.

Chapter 4 is the results section. The response rate and the sample demographic information are given. The informed consent assessment results are tabled, as well as score graphs, stratified analysis, regression analysis, health rights, logistics and a cross-check section.

Chapter 5 contains a discussion of the findings. This starts with a summary of the main findings, and is followed by a review of the limitations of the study and the contextualization of the results. Conclusions are drawn and recommendations for improvement of the quality of informed consent and for conducting a consent evaluation study are offered

Important definitions

Informed consent refers to the collective procedures performed to give prospective research participants relevant information about the purpose and the procedures involved in a particular research project so that they can make competent decisions about their participation.

Percutaneous vaccination is the method of injecting a vaccine using a multiple puncture tool. The liquid vaccine preparation is spread on the skin of the upper arm and the nine needles of the multi-puncture tool puncture the skin so that a small amount of vaccine reaches the subdermal tissues.

Intradermal vaccination is the method of injecting a vaccine with a thin needle into the dermal layer of the skin, usually in the upper arm of the individual

The BCG Study is the randomized controlled trial, which aims to compare the efficacy of different types of BCG vaccination in the prevention of severe TB

The Immunology Study is the case control study that seeks to determine the immune correlates of protection against TB

The Consent Study is the Quality of Informed Consent Study, which is the subject of this dissertation

Phlebotomy refers to the collective procedures involved in preparing a study participant for blood collection, collecting blood from a suitable blood vessel, and the subsequent allocation and storage of blood specimens for analysis and processing.

Good Clinical practice (GCP) is the standard set of rules and principles that are based on the International Conference on Harmonization (ICH) guidelines for human subjects research.

Ethics is the "science of criteria, norms and values for human action and conduct" (*Guidelines on ethics for medical research, Medical Research Council, 2000*) Medical ethics can be described as the reflection on moral actions within the framework of health care. Ethics for health research utilize norms and values for regulation, application and scientific assessment of clinical experimentation or survey.

Chapter 2: Literature review

Very little appears to have been published about the quantitative assessment of the quality of informed consent in developing countries. However, informed consent policies, practices and problems are topics of an abundance of published materials, a number of which will be discussed here.

Standards for informed consent

The International Conference on Harmonization guidelines for Good Clinical Practice (ICH Guideline for Good Clinical Practice, 2001) are used as the reference for most accredited courses for investigators of clinical trials. These GCP courses contain large sections on informed consent. Medical doctors, professional nurses and other health professionals who perform research procedures, including informed consent, on behalf of the principal investigators, frequently do these courses as part of their training.

Other sources of reference include the National Institutes of Health (NIH) Office for Human Subjects Research (OHSR, 2004) and *Guidelines on ethics for medical research: general principles* of the South African Medical Research Council (MRC, 2000). The former provides extensive resources to equip researchers in the United States with skills to conduct research ethically. Its guidelines for writing informed consent documents (NIH, *Guidelines for writing informed consent documents*, 2004) contain suggestions that would ensure that all relevant information is disclosed, and that participants comprehend the information and agree to participate voluntarily.

The MRC's *Guidelines* is concerned with the medical ethics of research on human participants. It stipulates a number of basic ethics codes of behaviour, which should apply to any research programme in South Africa. These codes include the notions of autonomy, objectivity and fairness, respect for human rights and the ethic of justice. Researchers are also prompted to display competence, integrity, and sensitivity when dealing with human subjects. Confidentiality should be respected at all times, and there should be mutual understanding of the roles and responsibilities of research staff and research participants in any particular study

Development and implementation of international policy regarding informed consent in medical practice and research are largely guided by the Council for International Organizations of Medical Sciences directive released in 1982. A revised version of The *Proposed International Guidelines for Biomedical Research Involving Human Subjects*, adopted by the World

Medical Association, which contained guidelines for the application of the principles of the declaration of Helsinki, was issued in 1991 (CIOMS, 1991).

Statutory and institutional regulation of ethics

In the United States, specific conditions are imposed under which informed consent must be obtained from research participants (NIH, *Regulation and ethical guidelines*, 2004). These conditions involve proof that participants would have sufficient opportunity to consider whether or not to participate, that consent could be obtained with minimal possibility of coercion and undue influence, and that the information would be given in a language that is understandable to the participant or witness In addition, it is expected that the consent procedure would be conducted in a manner that informs the participants about their rights and the responsibilities of the investigator.

In South Africa, the 4th revision of the MRC *Guidelines (2000)* focuses particularly on South African needs, as entrenched in the *Bill of Rights* (SA Constitution, 1996). The same basic principles on which all ethical research involving human participants should be based are emphasized. Autonomy (respect for persons), beneficence (maximized benefits), non-maleficence (absence of harm) and justice (equal distribution of risks and benefits in a community) have heightened significance in South Africa owing to greater awareness of human rights, equality and democracy, following the sociopolitical transformation of the previous decade[7]. People who were previously regarded as third-class citizens, had no vote, and who were deprived of all the social benefits of a democracy, could now insist on and expect to enjoy human rights as supposed by these ethics principles. Others who were accustomed to the privileges of the previous regime had to recognize the changes and accept them as fair and to the greater benefit of all South Africans. The application of the first principle (respect for persons) is implicit in informed consent, affording participants the opportunity to choose what shall and what shall not happen to them. In post-apartheid South Africa, this requires that researchers as well as participants of research subscribe to the implications of these changes.

In addition, the government's Health Research Policy (Dept of Health, 2001) is broadly considered to provide an enabling framework for the conduct of research that improves human health and well being. As part of the strategy to develop a coordinated, coherent national research system, the government has appointed a statutory body, the National Health Research Ethics Council,

[7] In 1994, the African National Congress (ANC) came into power during the first democratic elections in South Africa, after decades of segregationist governance called Apartheid. Under the leadership of Nelson Mandela, who was imprisoned for 27 years by the Apartheid government, major changes occurred in almost all spheres of public life. These improvements of the lives of all South Africans were particularly welcomed by the previously disenfranchised majority black population.

to set standards for research ethics in South Africa. It is not known if any directives regarding Informed Consent have been forthcoming from that body to date.

Given the extent to which adherence to the bioethical principles is regulated by governments and statutory bodies, standard usage is expected from institutional review boards (IRBs), the bodies responsible for ethical review of research proposals Yet, the application of the ethical principles in reviewing research proposals varies considerably from country to country. This is illustrated by a study (Goodyear-Smith *et al*, 2002) done simultaneously in five different Westernised countries (New Zealand, the United Kingdom, Israel, Canada and the USA). The aim of the study was to test how believable reports of child sexual abuse were. The different IRBs had greatly differing ethical requirements, ranging from no special provisions in one country to substantial amendments in another.

IRBs have also been shown to fail their mandates of protecting participants. The United States Food and Drug Administration (FDA) inspected clinical trials done since 1977 and found that investigators tested drugs in more than a 1000 unsuspecting participants (Epstein & Sloat, 1997). In a large number of drug trials, men, women and children were tested without written evidence of informed consent. The same authors found that the Centers for Disease Control and Prevention (CDC) conducted a hepatitis vaccine experiment in a native-American community under the guise of an established immunization programme in 1991, and used a known unsafe measles vaccine in an efficacy trial in Los Angeles in 1990.

In addition to the above, IRBs appear to allow violations of ethics principles embedded in approved research protocols by failing to monitor consent practices. Researchers are rarely required to report on quality of consent. Epstein and Sloat's (1997) FDA analysis of 942 ethics review boards from 1990 to 1996 exposed a number of regulatory inadequacies in many of them. This included poor data safety monitoring, poor record keeping and reporting, and poor adherence to recommended consent practices. In 160 clinical trials approved by an IRB in Spain from 1995 to 1999, Gost *et al.* (2003) found that in 83% the informed consent document had shortcomings in legibility, and that in 43.4% the researcher did not sign the consent documents. This raises concern about the validity of the consent.

This same concern is expressed by Campbell, Boyd and Surry (1997), who found that 45% of 249 randomized controlled trials published in the *Archives of Diseases of Childhood* from 1982 to 1996 did not report on consent

practices, but of those that did, 81% quoted consent rates[8] of 100%. This high consent rate could imply that voluntariness was not present in the procedures, particularly in large trials and those that involved children. The authors argue that journals should require reporting on consent rates in order to raise awareness of inadequate consent practices.

The call for consent-sensitive publication is supported and emphasized by observers who realise that IRBs in developing countries are not always constituted to oversee proper review of informed consent practices. According to Squire *et al.* (1997), ethical review of a South African study about the effect of HIV on the clinical outcome of intensive care patients was done by a subcommittee of a postgraduate committee with "questionable judgement" This particular IRB was clearly not properly constituted. This poses a dilemma for research institutions from industrialized countries as their IRBs are considered to be adequately representative of the research community. When collaborating in projects in developing countries, however, researchers may be faced with a situation where independent review processes do not exist or are weak

International sponsors of research carried out in developing countries may also pressurize the IRBs in these countries to approve studies that have already been approved by IRBs in the sponsoring country (London, 2002). It can be hypothesized that the strict requirements for informed consent are mainly to protect the researchers, and not necessarily to protect the participant. In order to allay this and other concerns (for instance, that IRBs are more alert to procedural correctness than ethical reasoning, and that power and money exert undue influence in these IRBs), London (2002) proposed ways to improve the regulation of ethics practices in developing countries. These measures included proper ethical training to IRB members, lay representation and appropriate empowerment of such members in IRBs, transparency of IRB activities and decisions, and independent monitoring of research activities.

Some of these measures are endorsed by other leading bioethicists (Benatar, 2002), who share opinions that ethics is a dimension of quality that must be subject to evaluation. In a commentary about research ethics, Benatar *et al* (2001) have lauded efforts to evaluate clinical ethics progress, but considered these efforts inadequate to address the problems that perpetuate ethics violations in research in developing countries. Weaknesses in academic regulatory processes need to be identified and corrected Double standards in ethics requirements when dealing with developing country research projects need to be eradicated.

[8] Referred to here as the number of selected individuals from whom consent had actually been obtained, suggesting refusal rates of zero.

Funding institutions from industrialized countries also tend to turn a blind eye to "macro-ethics" (such as financial assistance to governmental and institutional programs without direct benefits to the community) while overemphasizing "micro-ethical" issues like confidentiality, coercion and payment for participation.

Informed consent in medical practice

The quality of informed consent in clinical medicine has been found to be generally very poor. In a study (O'Flynn & Rymer, 2003) involving 181women (90% response rate) aged 17-79 years who attended an inner London teaching hospital clinic, women's experiences of the consent procedures for involvement in medical education were examined. The majority (91%) of women did not object to the presence of medical students during their gynaecological examination, even though 58% of respondents did not recall being informed about this.

Poor quality of informed consent in this type of setting is further illustrated by the example (Fleischman & Garcia, 2003) of 85 consecutive patients who underwent micrographic surgery and were given verbal and written instructions and information about ten potential complications. These patients were asked to recall these complications at 20 minutes and at one week after the informed consent process. The overall group retention rate at 20 minutes and at one week was 26.5% and 24.4% respectively, a poor result.

In a clinical audit (done via postal questionnaires) of the practice of the members of the British Association of Otorhinolaryngologists, Head and Neck Surgeons, it was found that clinical staff used varying techniques to obtain informed consent (Saravanappa, Balfour & Bowdler, 2003). This resulted in widely differing reports given by respondents of potential complications in middle ear operations, aspects of the consent procedure (like the time taken to obtain consent), and the person conducting the consent interview.

Much debate followed the 1997 publication of the results of a study conducted at the King Edward Hospital in Durban, South Africa, in which patients in a surgical intensive care unit were tested for HIV without their consent. The comments that followed ranged from suggestions to improve the study design (Pfeffer & Alderson, 1997 and Malin & Lockwood, 1997) to the definition of criteria by which ethical review could be waived (Woodcock & Norman, 1997). Two South African doctors working in London (Mhlongo & Mdingi, 1997) suggested that true informed consent is "light years away for black South African patients". This amounts to an accusation that there is the perception amongst South African doctors that experiments can be done on black patients without their consent, and that no harm would result from such experimentation.

Patients' submissiveness to authority (albeit white-coated only) following decades of injustice could result in distorted perceptions of harms and benefits in South Africa. This means that their decision to agree to medical procedures or research may be due to coercion. Bratt (1997) argued that doctors, in the above case, were arrogant to think that they needed to debate whether or not informed consent from patients was required. Proper informed consent should be obtained from research participants ***and*** patients in any setting, developing countries included.

Informed consent in medical research

The fact that informed consent is the key requirement for participation in human subject research may imply that informed consent quality is better in research than in medical practice No direct comparison had been made, but available literature suggests similar shortcomings in consent quality in both research and medical practice.

In an assessment of the quality of informed consent in a cancer clinical trial conducted in Boston, USA, a response rate of 72% was obtained (Joffe *et al*, 2001b). Although 90% of the responders thought that they were "well informed", many had misconceptions about the key aspects of the informed consent documents such as risks, benefits and the treatment options available. Predictors of higher knowledge scores were associated with education, research nurse assistance and English as the home language.

Patients who participated in the 4th International Study of Infarct Survival (ISIS-4) in Israel replied to a postal questionnaire survey to determine the quality of informed consent (Yuval *et al*, 2000) A response rate of 56% was obtained. Of the responders, 31% claimed to have full understanding, 50% claimed to have partial understanding and 19% were not perceived to have any understanding. The proportion of participants who were satisfied with the consent process was 90%. Participants also had various reasons for giving consent, the majority (43%) being the hope of better treatment. These results show inadequacy of informed consent in at least 69% of participants, with poor adherence to GCP guidelines.

Lynoe, Sandlund, Dahlqvist and Jacobsson (1991) did a study in eight different centres in Sweden to determine the perception of information based on the Declaration of Helsinki. Although only 2% of participants had not been aware that they were taking part in a clinical trial, 40% did not know that participation was voluntary. Just over half of the participants thought that the quality of information given was good or very good.

Most participants in clinical trials understood the purpose and the aspect of voluntary participation in a Contraceptive Clinical Trial (Fortney, 1999)

conducted on three different continents, Africa, South America and North America. However, only 23% of women, when asked about the risks and benefits, recalled the pregnancy risk correctly, 40% underestimated and 19% overestimated the risk. According to the author, the findings of this study are in agreement with earlier studies that reported better recall rates among younger, healthier participants. The overall rate was still poor.

Researchers (Mason & Allmark, 2000) who investigated the quality of informed consent obtained from parents on behalf of their children in nine Western European countries found that many parents did not have an adequate understanding of the study they were being asked to enroll their infants into. The researchers assessed the validity of the informed consent processes, and found that only 29.5% of parents had given valid consent for neonatal trials. The criteria upon which this assessment was based were completeness of information given, parental competence, understanding and voluntariness of consent.

Contrary to this finding, Hayman *et al*, (2001) reported that all the parents who gave consent on behalf of their children felt they understood the purpose and procedures of a physiological research project on sudden infant death syndrome (SIDS), in Dunedin, New Zealand. Both consenting and declining parents were involved. Of the participants, 90% thought that the information about the study was good, and 27% were concerned about the safety of the tests. The authors conceded that the validity of the results may be affected by recall and selection bias.

Similarly, a study amongst parents of sick children in a neonatal unit in Scotland, found that most (79%) parents were happy to give consent (Stenson, Becher & McIntosh, 2004). The fact that 8% of parents felt unhappy about their decision to give consent, yet still gave consent, may imply that parents might not have assumed autonomy in this situation.

Informed consent in developing countries

The notion of diminished autonomy is illustrated by a study that described the quality of informed consent among pregnant women participating in an iron supplementation study in Bangladesh (Lynoe *et al*, 2001). Most women knew about the purpose of the study but many did not understand the concept of voluntariness and the right to withdraw. The vast majority (87%) said that they participated because of the perceived benefits such as treatment for themselves and their babies.

Women participating in a contraceptive trial in Santiago, Chile were found to understand the research as experimentation or "progress" (Sanchez *et al*, 2001). The information on the consent form was "occasionally

misunderstood". Their decisions to give consent were based on a number of factors such as the time provided for consideration and discussion with their partners or relatives, and the perceived risks and benefits. The degree of autonomy, as perceived by voluntary participation and right of withdrawal, is not clear from the information available.

Ramjee *et al.* (2000) conducted a randomised controlled trial to determine vaginal microbicide effectiveness against HIV infection amongst female sex workers at four sites in the developing world, including Durban in South Africa. At one of the sites, 30% of the women did not know the purpose of the study, and at another, the concept of *placebo* was misunderstood by 75% of the participants. Even after three months' participation, the majority of women did not fully understand the study. Researchers used role-playing and repeating the informed consent procedure at consecutive visits to improve understanding. At the Cotonou site in Benin, the poor understanding was attributable to the low level of schooling.

A qualitative consent evaluation done alongside a childhood malaria trial was helpful in identifying detractors from and predictors of good quality of informed consent, such as language, level of education and the recruitment environment (Molyneux, 2003). The trial is one of several funded by a British institution in Kilifi on the Kenyan coast. The researchers found that understanding of the details of the studies was low, and the participants agreed to participate because they wanted access to the benefits associated with the research. Factors that influenced the level of understanding included process barriers, fieldworker experience in consent procedures, and community relations. Process barriers refer to difficulties in explaining medical concepts to parents of sick children, for instance, and the various challenges posed by the language differences.

Doing research in developing countries pose several challenges, logistic as well as ethical. Participants frequently do not understand scientific concepts like *randomization* and *clinical trials* used in consent documentation. Others are given information at the discretion of the researcher, sometimes inaccurate or partial (Elbourne, Snowdon & Garcia, 1997).

Some informed consent concepts like *voluntary participation* and *benefits and risks* are difficult to understand by participants in the developing world (Upvall & Hashwani, 2001). Western-based concepts of informed consent cannot be easily applied to research communities in developing countries. Cultural differences between the West and developing countries can make the ethics principle of autonomy difficult to apply uniformly. It is commonly argued that the conceptions of autonomy in non-Western cultures are shaped by group-based community structures, and not by individualistic decision-making (Cullinan, 1997). For instance, in rural African societies women may

not believe that they can make important decisions on their own. Pressured to obtain consent from her for her own or her child's participation, she may agree to participate, which may satisfy the "legal" requirement, but violate the principle of autonomy. In the BCG Study, some pregnant women asked the fathers of their unborn children or their own mothers to decide whether to participate or not. This means that the resultant decision would not be based on proper informed consent of the participant.

Involving pregnant women or mothers breastfeeding a young child in research requires looking at the consent process differently (Mohanna, 1997). Mothers may be distracted, particularly when the child is in their company, as in the Immunology Study. Others may be tired, have a heightened awareness of the value of the services available to them, or may be too eager to co-operate with services staff.

Another problem experienced in the field is the unwillingness of participants to partake in spontaneous discussion about the studies they have been enrolled in. The research team overcame this by supplying participants with information pamphlets, which explained the research activities in simple form, in their language. Contact information was also available from posters set up on notice boards of district health facilities.

In South Africa racial segregation has left social and emotional scars on the population. This has resulted in differences in perception of social services such as health care. People from previously disadvantaged groups may feel suspicious about health services and medical research, in turn leading to differences in perceptions of voluntariness between groups. In a study done in South Africa (Barsdorf & Wassenaar, 2005), these differences were significant. Black participants, known to have suffered most from the injustices of the apartheid regime, showed poorer perception of voluntariness than their White and Indian counterparts. Education level was also predictive of perception of voluntariness. The study did not attempt to ascertain the adequacy of information disclosure and comprehension in the three racial groups studied.

Methods of informed consent evaluations

Joffe *et al* (2001b), in evaluating a questionnaire to measure the actual and perceived understanding of consent aspects of cancer clinical trials, used a system of subjective as well as objective questioning, and concluded that the questionnaire was a valid and reliable tool that could be used for consent evaluation of other studies as well. They found good test-retest reliability for both objective and subjective understanding.

In a study conducted by Colleti *et al.* (2003) in the United States, a prototype informed consent process was evaluated amongst 4892 persons at risk of HIV infection as part of an HIV vaccine preparedness study in eight metropolitan areas. Initial procedures consisted of an initial HIV trial education, repeated at six-monthly intervals. A random sample of people underwent the prototype informed consent procedures, which involved reading a booklet or listening to it on a recording, followed by a one-on-one educational session. At baseline the participants' recall of HIV vaccine trials was low, but those participants randomized to be subjected to the prototype format had consistent increases in their recall scores. Notably, level of education, race/ethnicity, and HIV risk status were not associated with these improvements.

Similar results were found in a Haitian study (Fitzgerald *et al*, 2002) in which resistance factors to HIV infection were to be identified. Researchers used a qualifying step to assess the understanding of research study details. Potential participants were expected to get at least 12 out of 15 questions correct. Only 20% of a sample of participants who were consented during a single interview obtained a pass mark. Better scores were obtained from those participants who attended information sessions over a period of longer than a week

Faced with low literacy in non-Western study participants, health workers have been found to overcome difficulties in participant understanding by using audiovisual aids and other means (Lam, Cheng & Chan, 2004, Sastry *et al.* 2004, and O'Connor *et al.*1999). Sastry *et al.* (1999) also found significant improvements in understanding of HIV-AIDS topics in an antenatal clinic in India after enhancement of the group education and counseling routine by means of audio-visual aids.

In a country such as Senegal, where consent was traditionally obtained by community elders on behalf of parents, Preziosi *et al.* (1997) observed that illiteracy did not necessarily present a barrier to understanding. The study which evaluated the change from consent obtained by community elders to that by parents, found that the parents understood the study sufficiently to make informed decisions, even though the literacy rates were 30% in men and 10% in women in that community

Approaches to evaluating consent quality have been diverse. Some researchers have used person-to person interviews (Lynoe *et al*, 2001, Sanchez *et al*, 2001, and Molyneux, 2003) and while others used postal questionnaires delivered to participants by post (Stenson *et al*, 2004, Upvall *et al*, 2001 and Lynoe *et al*, 1991). The validity of results obtained from postal surveys for quality of informed consent is limited. Respondents may

use help from any number of sources, thereby reducing the chances of measuring the participants' own understanding and recall of the study material.

Some researchers used questioning that requires participants to indicate how they felt and what they thought about aspects of informed consent. The subjective nature of this type of questioning also reduces the validity of the results. Other studies in which the effects of interventions were studied (e.g. Coletti *et al*, 2003, and Fitzgerald *et al*, 2002) used direct questioning, testing the participants' recall of the study concepts. This approach, or the one proposed by Joffe *et al* (2001a) – using the subjective and objective types of questioning in combination – has more potential for valid quality of informed consent assessment.

Obtaining consent from parents for research to be done on their children has implications for consent quality assessments Parents express their perceptions of voluntary participation, risks-benefits balance and confidentiality on behalf of their children, who are not competent to give consent or assent. The parents may not be directly affected by the risks of participating in such research. The results of studies that report parents to be "happy" and "satisfied" with the consent-obtaining procedures should therefore be interpreted with reserve. An objective assessment of parents' understanding is therefore likely to produce more reliable results.

Conclusion

In developing countries, vulnerability due to poverty, disease, low education, hardship, submissiveness, the effects of war, famine, pandemics, and social insecurity can lead to research exploitation. Many large scale research projects are launched in these settings. While participants in industrialised country projects are generally better educated, have more experience of decision-making regarding health, and make use of private health care, most developing country research involves participants who are dependent on under-resourced public health services when afflicted. Therefore, good quality of consent should be one of the key objectives of all research conducted in such settings.

Review of the literature reveals a number of recurring themes regarding quality of informed consent. The value of increased exposure to consent information in improving the quality of informed consent is emphasized. However, there are participants who wrongfully use perceived benefits and misunderstood risks as motives for deciding whether to participate in a study or not. However, owing to the shortage of research data, it is difficult to establish norms for acceptability in regard to informed consent surveys.

In general, there is a need to standardise the varying methodologies and interpretations of consent assessments. The literature available is sparse, indicating a reluctance to do scientific research on the topic or to publish research findings. More research needs to be done to explore the practices and outcomes of informed consent particularly in low literacy communities and in developing countries. The need for standardised methods to evaluate the quality of informed consent is therefore critical.

Assessment of consent quality in medical practice and research may produce results that reflect poorly on IRBs, whose role is to protect research participants against unethical conduct in research studies. Low acceptability (quality of informed consent) findings in industrialised countries suggest inadequate procedures and perceptions In addition, poor consent quality in developing countries perhaps raise more intense questions about human rights, equity and justice. However difficult these questions are, it is still necessary to invite critical discussion. Scientific literature should treat ethics topics as integral elements of scientific reporting. This can be done by requiring reporting on consent practices in papers, accepting more "ethics" papers in mainstream scientific journals, and publishing "ethics" debates periodically. In this way, a welcome increase in material will be generated in an area of shameful dearth.

A small number of selected clinics had no participants because the Immunology Study phlebotomy for those clinics had been postponed or cancelled. Two other clinics which were part of the sample were postponed owing to staffing problems on those days, but the clinics were included in the study at the end of the enrollment period.

On the day of the Consent Study, the study coordinator, a professional nurse, would arrive at the clinic where mothers were having consent taken for enrollment into the Immunology Study using the Immunology Study Consent form (Appendix B). The research nurse in charge of the phlebotomy would refer mothers to the Consent Study nurse. Mothers would be told about the purpose of the Consent study and asked to participate [see Appendix C: *Standard operating procedure: Consent Study enrollment and consent* and Appendices G, H & I: *Consent study consent form (*in three languages)]. Those who agreed would be taken to a private area and given a Consent Study questionnaire (Appendices D, E & F) in the appropriate language. The Consent Nurse would then explain to the mother how to complete the questionnaire, and then remain available for questions and assistance.

Measurement and data collection

The quality of informed consent was determined by using two measurements: (1) recall of consent document information and (2) understanding of the underlying principles of informed consent. A questionnaire (Appendix C), specifically designed for this study, was used and contained the following:

a) A demographics section for name, study number, date of birth, address, level of education, language, contact number and date;

b) Nine multiple choice questions[10] to test whether the mother:
   i. was aware that the baby was required to participate in a research study, and that the visit was not for routine primary health care;
   ii. knew the purpose of the research;
   iii. knew what research procedures were involved;
   iv. knew the duration of the study;
   v. knew what the main risks were;
   vi. knew what the main benefits were;
   vii. was aware that participation was voluntary;
   viii. was aware that information would be kept confidential; and
   ix. knew what would happen with the infant's stored blood.

[10] Hereafter referred to as "Recall" questions as they test how well participants could recall consent document contents (see Table 1a below).

Chapter 3: Methods

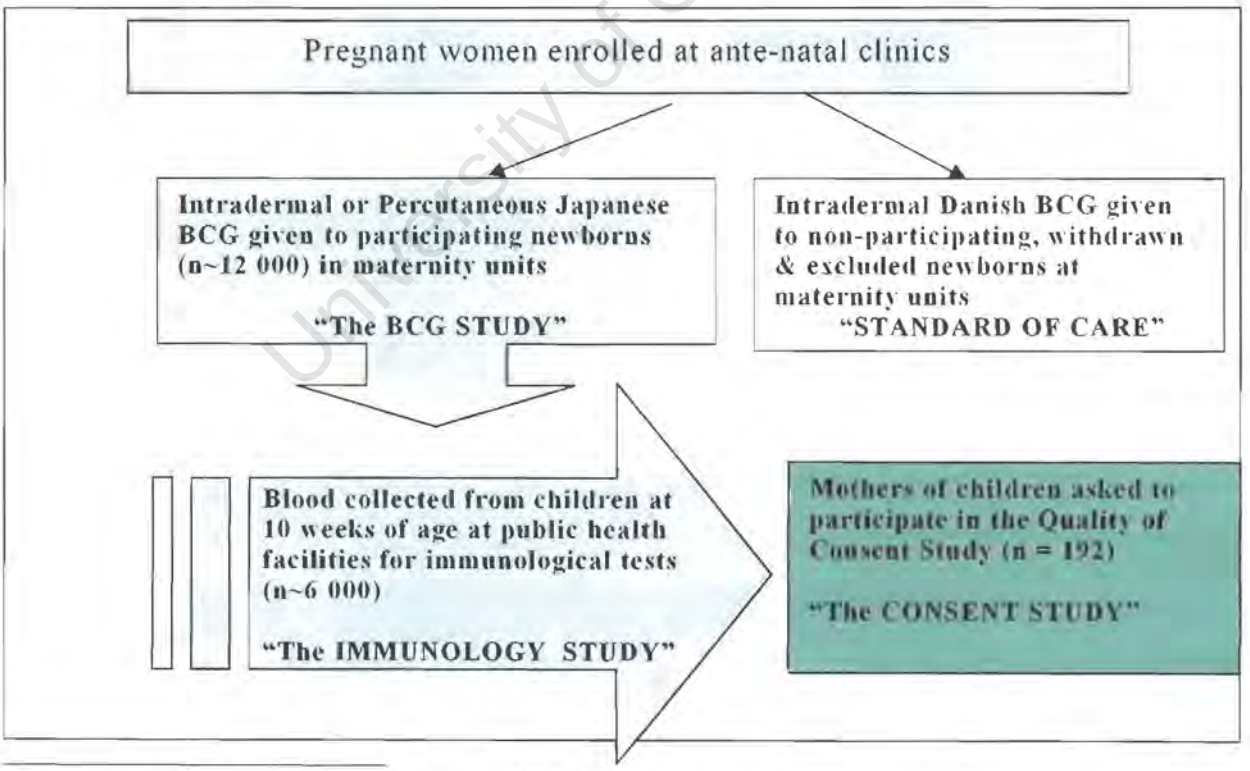
Study design

A cross-sectional study was conducted in the same cohort as the BCG Study and the Immunology Study described in Chapter 1.

Population and sampling

All participants visiting the clinics for the Immunology Study[9] phlebotomy were eligible for the Consent Study (see Figure 2: Schema of recruitment), and participating clinics were visited according to a two-monthly rotating schedule (Appendix J) which ranged from once weekly visits (biggest facility) to once every two months (smallest facility). Systematic random sampling of clinics was used in order to reduce the chance of selection bias. In order to ensure similar numbers of Afrikaans and Xhosa speaking participants, all clinics where the language of business is predominantly Xhosa and every fourth scheduled clinic where the language of business is predominantly Afrikaans were selected.

Figure 2: Schema of recruitment for the Consent Study



[9] Immunology Study participants were all BCG Study participants.

Table Ia: Recall questions of questionnaire

A. Select the ONE option that best completes the statement regarding the study you were asked to consent to earlier today (Correct answer underlined – for illustration only. For study all options will appear identical in print.)

1. I have been asked to attend the clinic today so that:
   1. *My baby can receive expert treatment.*
   2. *My baby can participate in a research study*
   3. *My baby can receive routine health care*

2. The purpose of the research study is to:
   1. *Test for protection against tuberculosis in my baby's blood*
   2. *Test for tuberculosis in my baby's blood*
   3. *Test for HIV in my baby's blood*

3. Research staff wants to enroll my baby into the research study so that:
   1. *They can test my baby for TB or HIV*
   2. *They can collect blood from my baby*
   3. *They can inject my baby with BCG*

4. The total amount of time my baby will be expected to participate in the study is:
   1. *2 to 3 years*
   2. *8 to 14 weeks*
   3. *1 day*

5. The most common risk involved when blood had been collected from my baby is:
   1. *My baby can become infected with TB or HIV*
   2. *My baby may suffer very slight scarring and some oozing*
   3. *My baby can loose too much blood*

6. The benefits available to me and my baby for participating in the study are:
   1. *There are no immediate benefits*
   2. *My baby will be protected against TB*
   3. *My baby and I will get better treatment at clinics*

7. If I didn't want to participate in this study, I could withdraw and
   1. *My baby and I would be denied access to health services at this clinic*
   2. *My baby and I will be treated differently by research and clinic staff*
   3. *My baby and I would suffer no loss at all*

8. My baby's personal details will never be linked with his / her blood because
   1. *Numbers with barcodes will be used to keep bloods anonymous*
   2. *Highly trained research staff will keep information secret*
   3. *Clinic staff will be sure not to give information to the research staff*

9. The blood of my baby that will be frozen and stored will be used
   1. *For all kinds of research in other countries*
   2. *For HIV testing*
   3. *For other tests concerning protection against TB*

c) Five differently phrased questions (Table Ib) to cross-check some answers in (b);

Table Ib: Cross-check questions of questionnaire

	Yes	No	Don't know
10. The procedures done on my baby in this study are:			
a. Safe and practically harmless	☐	☐	☐
b. Dangerous and harmful	☐	☐	☐
10. My baby's blood is going to be used to			
a. help develop a blood test for TB	☐	☐	☐
b. determine whether my baby has TB	☐	☐	☐
12. My baby's name is written on all the blood tubes	☐	☐	☐

d) Eight "yes/no" questions[11] that tested how participants understood the consent concepts Table Ic;

Table Ic: Understanding questions of questionnaire

	Yes	No	Don't know
13. I agreed to enroll my child in this study because:			
a. My child might get better treatment	☐	☐	☐
b. I want doctors to help learn more about TB	☐	☐	☐
14. I've decided to enroll my baby in the study			
a. even though my baby will receive no extra treatment	☐	☐	☐
b. because I knew I would receive a toiletries hamper	☐	☐	☐
15. If my baby gets a bruise from the blood test, I should			
a. Contact the police	☐	☐	☐
b. Speak to the nurse at the clinic	☐	☐	☐
c. Go to the doctor at his private surgery	☐	☐	☐
16. I was enrolled in the study in my home language	☐	☐	☐
17. If I was given the choice to participate again, I would	☐	☐	☐

f) One question that dealt with whether consent was obtained in the home language;

e) Five questions (Table Id) about health rights as defined in the South African Constitution[12];

[11] Hereafter referred to as "Understanding" questions, Table Ic.

[12] The Constitution contains a Bill of Rights which includes:
- the right to have access to health care services;
- the right to be free from bodily harm; and
- the right to freedom of association, religion, belief, opinion and political choices

Table Id: Health rights questions of questionnaire

	Yes	No	Don't know
18. Which of the following rights are protected in the South African constitution?			
(a) access to health care	☐	☐	☐
(b) concealment of private information	☐	☐	☐
(c) freedom from bodily harm	☐	☐	☐
(d) free health care to all	☐	☐	☐
(e) freedom of choice	☐	☐	☐

g) A question inviting comments from participants; and

h) Two questions about logistics that the study facilitator would answer to aid in assessing interview quality.

The participant completed item (a) to (g), and the research nurse completed item (h). The questionnaire was available in three languages, English, Afrikaans and Xhosa (Appendices D to F).

Information collected from the questionnaires included a number of variables considered to be influential in the quality of informed consent. Table IIa contains details of these "predictor" variables and Table IIb some of the "outcome" variables, generated from the data.

Table IIa: List of key predictor variables

Predictor variables	Comments
Age	Calculated from participant date of birth
Education	Given as highest standard completed at school. Standard 10 is equal to Grade 12 (equivalent to 12 years' schooling).
Socio-economic status (proxy)	Given as access or no access to a telephone, whether landline or mobile.
Language	Afrikaans or Xhosa
Research experience of nurses obtaining consent	Given as greater than or less than 2 years of work experience in the research field

Table IIb: List of key outcome variables

Outcome variables	Comments
Specific recall scores	Number or percentage of participants giving correct answers to specific recall questions
Participant recall score	Number or percentage of correctly answered recall questions for each participant
Participant understanding score	Number or percentage of correct[13] answers to understanding questions for each participant
Health rights questions	Number or percentage of participants giving correct answers to specific health rights questions.
Participant uncertainty score	Number or percentage of "Don't know" answers to yes / no questions for each participant

Pilot study results

For this study, the new questionnaire was piloted in two ways:

1. Six participants of the Immunology Study were approached to answer the questions. These were the first two recruitments from each of three clinics from the phlebotomy schedule. The purpose of this part of the pilot study was to determine the time taken to complete the questionnaire and the amount of assistance required to complete the questionnaire. It took volunteers approximately 20 minutes to complete the questionnaire, and most volunteers required minimal assistance (Table IIIa).

Table IIIa: Pilot study – time taken & assistance required

Participant	Language	Time taken	Assistance required
1	Afrikaans	18 minutes	Minimal
2	Afrikaans	12 minutes	Minimal
3	Afrikaans	16 minutes	Minimal
4	Afrikaans	23 minutes	Moderate
5	Xhosa	17 minutes	Moderate
6	Xhosa	25 minutes	Minimal

[13] Referred to here as the expected or preferred answers that best illustrate understanding and the correct interpretation of items in the informed consent document.

2. Four members of the research staff, two research nurses and two nurse assistants were asked to answer the questions. None of the volunteers thought that the questions were too difficult, and all thought that the language used was generally understandable (Table IIIb).

Table III(b): Pilot study – Difficulty of questions and language

Staff member	Language	Questions	Understanding
1	Afrikaans	Easy	Good
2	Afrikaans	Some difficult	Good
3	Xhosa	Some difficult	Slightly difficult
4	Xhosa	Easy	Good

The following additional measures were taken to enhance validity and repeatability:

- The questionnaire was translated from English into the two main regional languages (Afrikaans and Xhosa), and the translations verified by back-translation and piloting;
- All participants were interviewed in their home language;
- Written permission and consent for the Consent Study were obtained by a specially trained research nurse within an hour of enrollment into the Immunology Study;
- Appropriately trained research staff conducted the Consent Study interviews, and
- A separate research worker monitored the Consent Study procedure, including questionnaire checking and scoring.

All interviews were conducted in the following manner:

- The research nurse enrolled the participant into the Consent Study, obtaining informed consent;
- The research nurse handed the participant a questionnaire and explained how to complete it,
- The participants completed the questionnaire by themselves, without influence from others;
- The research nurse assisted with the explanation of the questions, but not with interpretation of the answers;
- The research nurse selected the appropriate answers for the two logistics questions;
- The research nurse did not lead answers through prompting; and
- The research nurse reviewed the completed questionnaire for obvious omissions and errors in the demographics section.

Data capture and analysis

Upon completion of the questionnaire, the research nurse transcribed the answers of the questionnaire onto the Data section of the questionnaire. This was verified by another member of the research staff. A second research nurse verified the transcription of the results. Double-checking of documentation and data was used to pick up errors. The results on the data form were captured, processed and analysed using Stata version 6[14] as illustrated in table IV.

Table IV: Stata-6 data processing and analysis

Procedure	Remarks
Data coding	• Answers to questions were coded "1" for correct (recall, health rights and cross check sections) or "expected" (understanding section) answers, and "0" otherwise. • Score variables were generated to summarize the recall and understanding answers for individual participants.
Data exploration	• Frequency tables were drawn up for categorical variables • Summary tables and graphs were drawn up for numeric variables.
Data analysis	• Stratified analysis was done to determine the effect of potential predictors of the quality of informed consent on the *recall* and *understanding* scores. • Measures of association were obtained between potential predictors of the quality of informed consent and binary derivatives of the *recall* and *understanding* scores; • Logistic regression analysis was carried out to model the relationships between the predictor variables and the *recall* and *understanding* scores. • The Kappa agreement test was done to test for agreement between questions which tested the same contents but were asked in different manners.

[14] Stata Corporation, 702 University Drive East, College Station, Texas, 77840, USA

In the absence of norms for acceptable quality of informed consent, the scores for the *recall* section were grouped in the following manner:

- 75% and more correct, was assigned the "High acceptability" classification,
- 50 – 75% was assigned "Above average acceptability",
- 25% - 50% was assigned "Below average acceptability", and
- less than 25% was assigned "Low acceptability".

The same classification was used for the understanding section.

Ethical considerations

The Research Ethics Committee of the University of Cape Town Health Sciences faculty approved the Consent Study.

After mothers had been enrolled into the Immunology Study, they were referred to the nurse of the Consent Study who was waiting in a separate room. An informed consent process was conducted. Participants received a simple letter explaining the study and requesting their participation. The research nurse explained the Consent Study to the participants, using the consent form as a template. If the participants agreed to participate, they were asked to sign the consent form. The research nurse also signed. The participants were given a signed and dated copy of the consent form to keep.

An amount of R50, considered to be adequate to reimburse additional transport and refreshment costs, were given to the mother at the end of the interview. (The Medicines Control Council has previously suggested that R150 be paid per participant in any research protocol approved in South Africa from that year onwards, however, this was applicable to clinical trials only)

Research staff also discussed wrong answers in the *recall* section with participants, thereby correcting misconceptions they may have Names and addresses were recorded, but only for bookkeeping purposes.

No personal details were directly linked to any data reporting.

No apparent harm or injury was anticipated from their participation in the Consent Study.

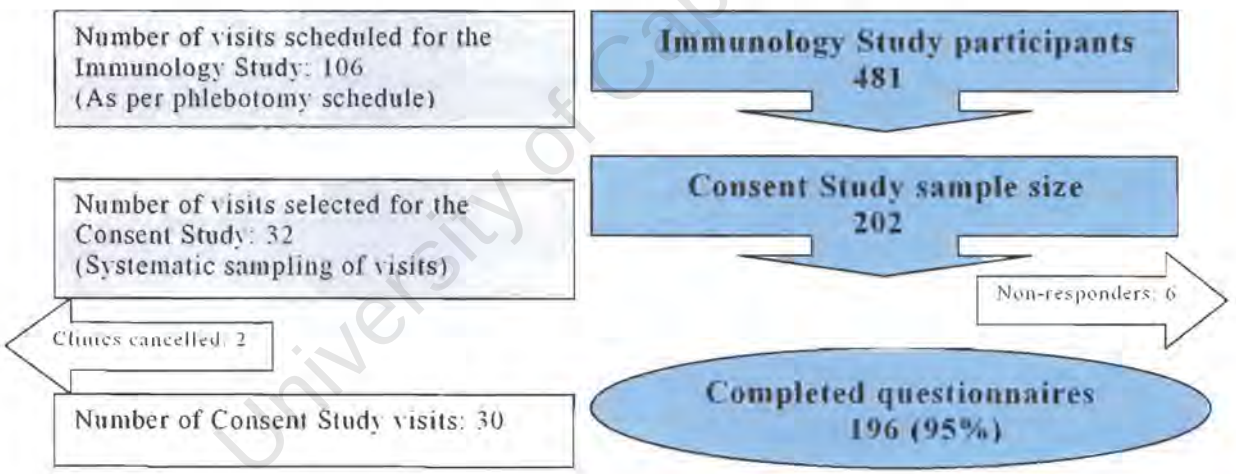
No benefit was available to participants other than the R50 paid for their time.

Chapter 4: Results

Response rates

From 23 March to 28 June 2004, the phlebotomy team visited the twenty-two primary health care facilities (clinics) in the study area. One hundred-and-six (106) clinic visits were made and 481 participants were enrolled into the Immunology Study. Of the 32 visits which were selected for the Consent Study, two visits were cancelled, and 202 Immunology Study participants were referred to the Consent Study staff. A total of 192 mothers completed the questionnaires for the Consent Study, resulting in a response rate of 95.0%. The non-responders were made up as follows: three left the clinic before the Consent Study team had started enrollments, four could not be enrolled because of an accidental language mismatch and a further three used a spoilt version of the questionnaire.

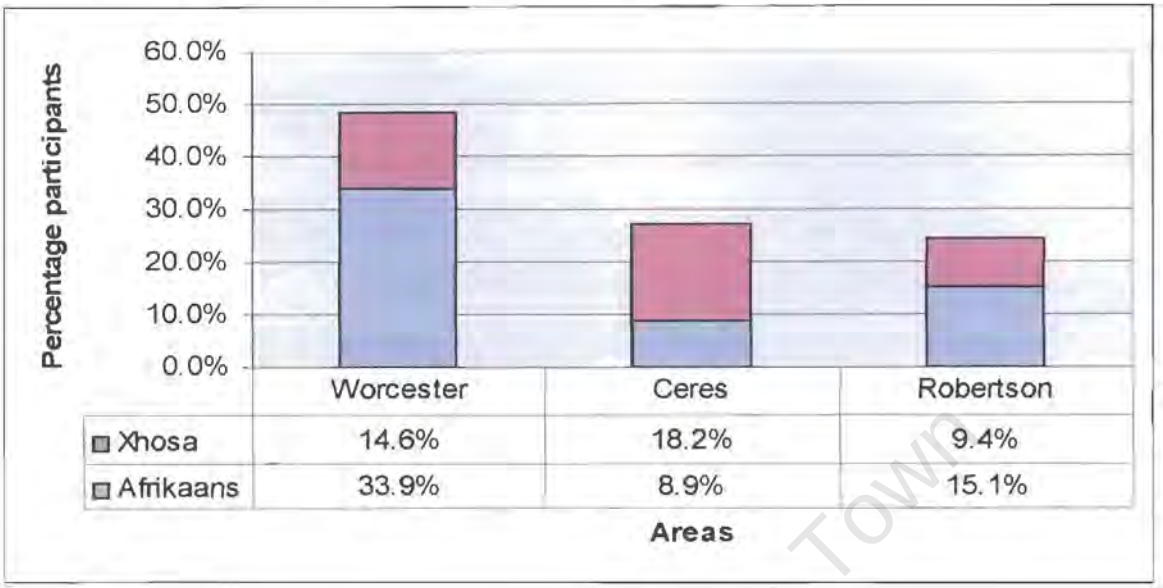
Figure 3: Schema to show how participants were selected for the Consent Study and relationship with parent studies



Demographic information

The study sample was selected out of a total of 481 caregivers of infants participating in the Immunology Study over a four-month period. Using the phlebotomy schedule of the Immunology Study, the study team visited clinics throughout the study area in Worcester, Ceres, Robertson and surrounding towns. From Figure 4 it can be seen that Worcester constituted the largest source area (48.4%). Of the 192 participants, 56.8% were consented in Afrikaans and 43.2% in Xhosa. More than 95% of participants of the Consent Study were enrolled into the Immunology Study in their home language.

Figure 4. Distribution of participants by area and language (n=192)



Between 1 and 15 participants attended the clinics on the study days. As Table V indicates, demographic factors of the Consent Study and the BCG[15] Study have comparable summary statistics. (The Immunology Study is nested within the BCG). The BCG Study figures come from data collected from the first two years' enrolments. It can be seen that the number of participants per clinic (a reflection of how busy the clinics were) for the Consent Study was similar to that of the Immunology Study participants.

Table V. Comparison of demographics between the Consent Study and BCG Study

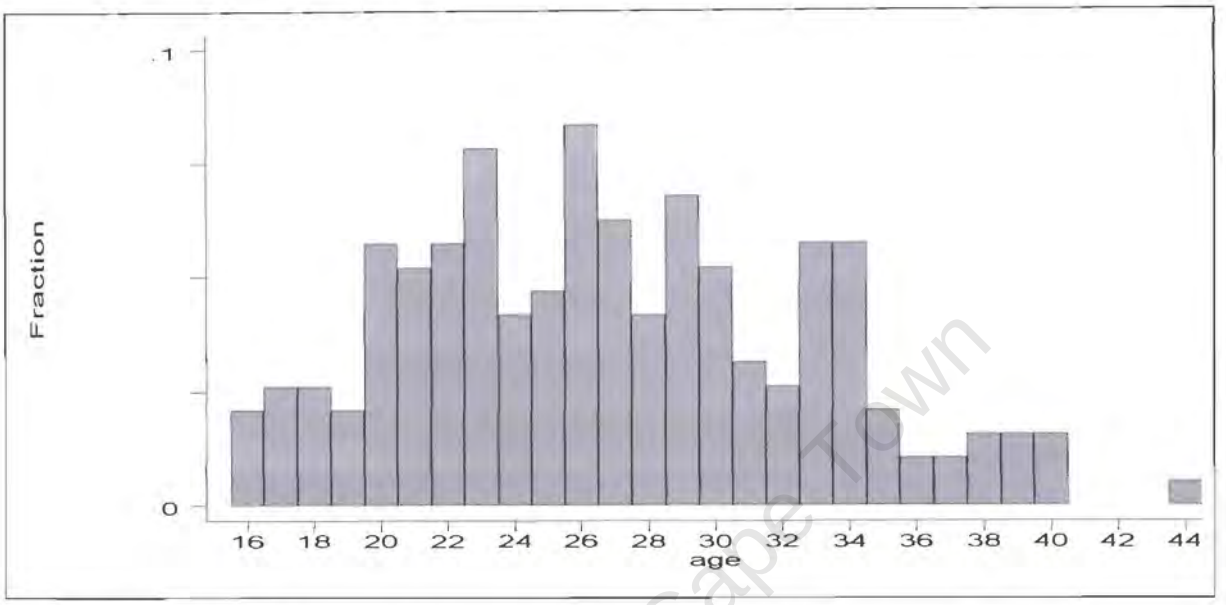
Aspect		Consent Study (n=192)	BCG Study (n=6140)
Language (%):	Afrikaans	56.8	59.7
	Xhosa	43.2	40.3
Participant age (years): median (range)		26 (16-44)	26 (14-45)
Area (%):	Ceres	27.1	25.1
	Robertson	24.5	24.1
	Worcester	48.5	50.8
Participants per clinic: median (range)*		8 (1-15)	7 (1-16)

** Note that the clinic figures given are for the Consent Study and the Immunology Study.*

[15] Data of BCG Study enrolments are used because of availability of appropriate data.

All participants were women, aged between 16 and 44 years with a median age of 26 years (Figure 5).

Figure 5. Age distribution of participants (n=192)



A total of 171 (89.1%) of participants had achieved the minimum recommended educational level for the Immunology Study (standard 5), and 65 (33.9%) had completed Standard 10 (or Grade 12), which is equivalent to 12 years' schooling. The education level distribution is illustrated graphically in Figure 6.

Figure 6. Distribution of educational level of participants (n=192)

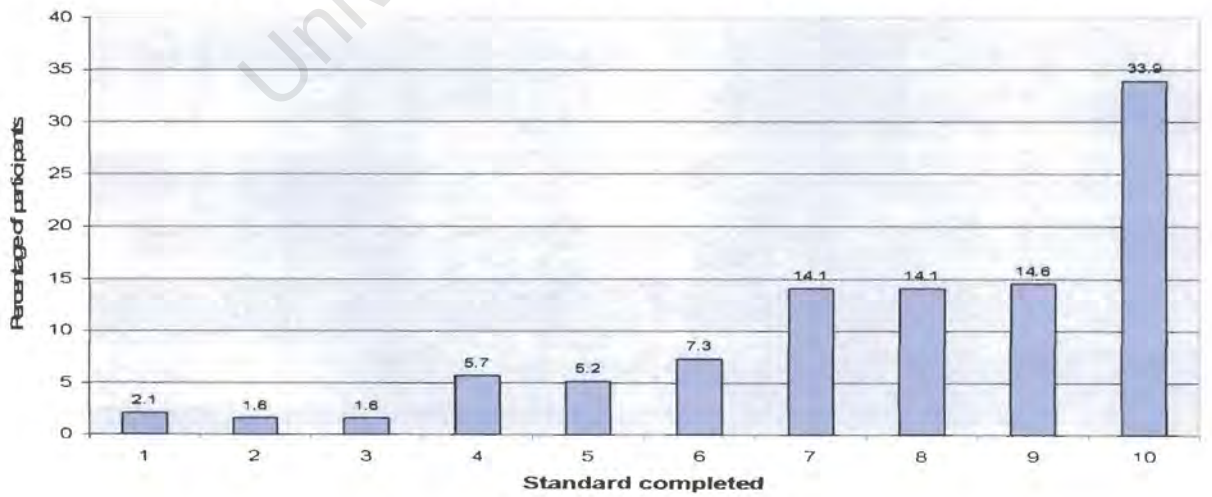


Table VI shows that the distribution of participants in relation to the educational requirement (Std 5) for informed consent was similar between the two language groups in the younger age group. However, in the older age group, 22% of participants in the Afrikaans-speaking group had not achieved a Std 5 or higher education, while the corresponding figure for the Xhosa-speaking group was almost half that (11.4%).

Table VI. Education level and age by language (n=192).

	Language = Afrikaans			Language = Xhosa		
	Std 5 & higher (%)	Lower than Std 5	Total	Std 5 & higher	Lower than Std 5	Total
Age =< 26	56 (94.9%)	3 (5.1%)	59	37 (94.9%)	2 (5.1%)	39
Age > 26	39 (78.0%)	11(22.0%)	50	39 (88.6%)	5 (11.4%)	44
Total	95 (87.2%)	14(12.8%)	109	76 (91.6%)	7 (8.4%)	83

Eleven (27.1%) of the participants had regular access to a cellular phone and a total of 30.8% had access to a land telephone line. More than 40% had no regular access to telephone or cellular phone services.

Informed consent assessment

The results of the consent assessment are shown in Tables VII (a) to (d), giving the number and percentage (in descending order) of participants' answers for each question. The correct answers for the first nine questions, which deal with the *recall* assessment, are in italics. Four out of nine questions had more than 75% correct answers, and another four had between 50% and 75% correct. The question dealing with the reason for the clinic visit received the most (85.4%) correct answers. Notably, only 36.5% of participants answered the question about the benefits correctly.

The next 4 questions (10, 11, 12 and 16) revealed that the majority of participants (88.5%) thought that the phlebotomy was safe and practically harmless, and almost 85% knew that their baby's blood would be used to develop a blood test for TB. However, more than half (55.2%) thought that the blood would be used to determine whether their baby had TB.

Questions 13, 14, 15 and 17 dealt with the *understanding* assessment. Most participants gave the expected answers for all questions. Although 87.5% of participants understood that the development of a bruise did not warrant a call to the police, a relatively low percentage (66.2%) knew that they could discuss the bruise with the nurse at the clinic.

The results of Question 18 are discussed under "Health rights assessment".

Table VIIa: Results of quality of informed consent assessment: Recall section[16]

1. I have been asked to attend the clinic today so that (n=192):	
My baby can participate in a research study	164 (85.4%)
My baby can receive expert treatment.	14 (7.3%)
My baby can receive routine health care	14 (7.3%)
2. The purpose of the research study is to (n=191):	
Test for protection against tuberculosis in my baby's blood.	154 (80.6%)
Test for tuberculosis in my baby's blood	35 (18.3%)
Test for HIV in my baby's blood	2 (1.1%)
3. Research staff wants to enroll my baby into the research study so that (n=189):	
They can collect blood from my baby	115 (60.9%)
They can inject my baby with BCG	40 (21.1%)
They can test my baby for TB or HIV	34 (18.0%)
4. The total amount of time my baby will be expected to participate in the study is (n=190):	
1 day	126 (66.3%)
2 to 3 years	45 (23.7%)
8 to 14 weeks	19 (10.0%)
5. The most common risk involved when blood had been collected from my baby is (n=192):	
My baby may suffer very slight scarring and some oozing	152 (79.2%)
My baby can become infected with TB or HIV	35 (18.2%)
My baby can loose too much blood	5 (2.6%)
6. The benefits available to me and my baby for participating in the study are (n=191):	
My baby will be protected against TB	98 (51.3%)
There are no immediate benefits	70 (36.7%)
My baby and I will get better treatment at clinics	23 (12.0%)
7. If I didn't want to participate in this study, I could withdraw and (n=189)	
My baby and I would suffer no loss at all	123 (65.1%)
My baby and I will be treated differently by research and clinic staff	47 (24.9%)
My baby and I would be denied access to health services at this clinic	19 (10.0%)
8. My baby's personal details will never be linked with her blood because (n=191)	
Numbers with barcodes will be used to keep bloods anonymous	140 (73.3%)
Highly trained research staff will keep information secret	40 (20.9%)
Clinic staff will be sure not to give information to the research staff	11 (11.8%)
9. The blood of my baby that will be frozen and stored will be used (n=187)	
For other tests concerning protection against TB	155 (82.9%)
For all kinds of research in other countries	29 (15.5%)
For HIV testing	3 (1.6%)

[16] The questions refer to the Immunology Study. See pages 25 to 28 for explanation.

Table VIIb: Results of quality of informed consent assessment: Cross-check section[17]

	Yes %	No %	Don't know %
10. The procedures done on my baby in this study are			
Safe and practically harmless	*88.5*	7.3	4.2
Dangerous and harmful	6.2	*84.4*	9.4
11. My baby's blood is going to be used to			
Help develop a blood test for TB	*82.3*	8.9	8.9
Determine whether my baby has TB	55.2	*38.5*	6.3
12. My baby's name is written on all the blood tubes	19.8	*73.4*	6.8
16. I was enrolled in the study in my home language*	*94.8*	3.6	1.6

* This question was not part of the agreement analysis

Table VIIc: Results of quality of informed consent assessment: Understanding section[18]

13. I agreed to enroll my child in this study because			
My child might get better treatment	44.8	*52.1*	3.1
I want doctors to help learn more about TB	*88.5*	4.7	6.8
14. I've decided to enroll my baby in the study			
Even though my baby will receive no extra treatment	*73.4*	19.3	7.3
Because I knew I would receive a toiletries hamper	13.0	*80.7*	6.3
15. If my baby gets a bruise from the blood test, I should			
Contact the police	5.7	*87.5*	6.8
Speak to the nurse at the clinic	*68.2*	30.7	1.1
Go to the doctor at his private surgery	22.4	*66.2*	11.4
17. If I was given the choice to participate again, I would	*90.6*	3.1	6.3

Table VIId: Results of quality of informed consent assessment: Health rights section

18. Which of the following rights are protected in the South African constitution?			
access to health care	*85.9*	5.7	8.3
concealment of private information[19]	67.7	*17.2*	15.1
freedom from bodily harm	*58.3*	20.8	20.8
Free health care to all	83.3	*11.5*	5.2
freedom of choice	*89.1*	4.2	6.7

[17] The questions refer to the Immunology Study. See pages 25 to 28 for explanation.
[18] The questions refer to the Immunology Study. See pages 25 to 28 for explanation.
[19] The actual wording in Afrikaans was "geheimhouding van privaat inligting". In Xhosa it was "imifihlelo yencukacha zako".

Figures 7 and 8 give graphical illustrations of the *recall* and *understanding* scores obtained by participants.

Figure 7. Recall of information (n=192)

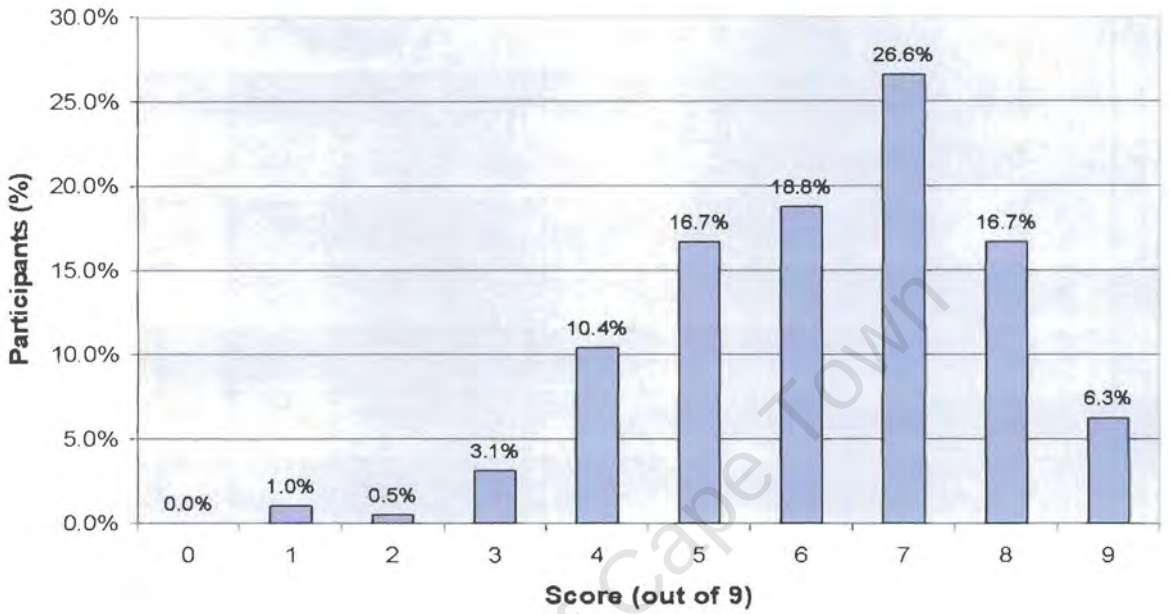
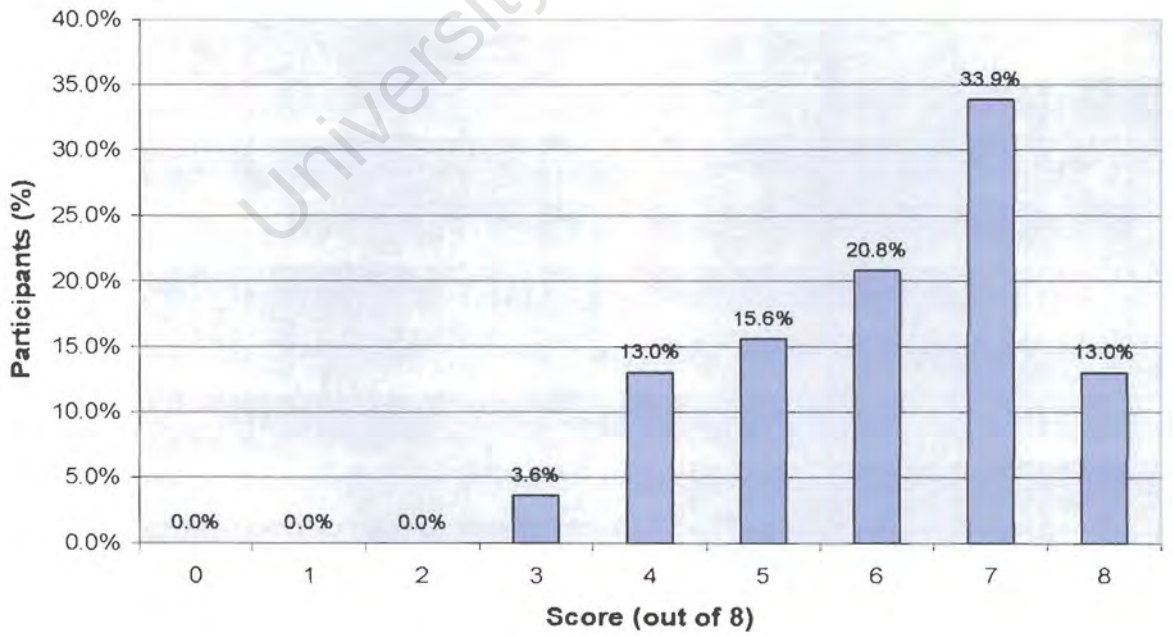


Figure 8. Understanding of information (n=192)



Participants obtained a median score of 66.7% (range 11.1% - 100.0%) in the *recall* and 75.0% (range 37.5% - 100%) in the *understanding* section. The *recall* and *understanding* scores follow the same general pattern: small numbers of participants with scores of less than 5 out of 9 (*recall*) or 4 out of 8 (*understanding*), and a sharp increase in participants with higher scores. Both scores were non-normally distributed with skewing towards the left.

Although only 12 (6%) and 25 (13%) of participants, respectively had all the answers to the *recall* and *understanding* questions correct, Table VIII shows that the majority of participants obtained scores in the 75% and greater category. Only 3 (1.6%) obtained a low score (less than 25% correct) for the *recall* test, and none had two or fewer correct of the eight *understanding* questions.

Table VIII: Summary of participants' scores for recall and understanding (n=192)

Score	High* n (%)	Above average* n (%)	Below average* n (%)	Low* n (%)
Recall (out of 9)	95 (49.5%)	68 (35.4%)	26 (13.5%)	3 (1.6%)
Understanding (out of 8)	130 (67.7%)	55 (28.7%)	7 (3.7%)	0 (0.0%)

Higher levels of *recall* scores were positively associated with higher levels of *understanding* levels scores (Pearson chi-squared = 14.73, p = 0.022). This can also be seen in Table IX, which presents the data in categories.

Table IX. Relationship between scores for recall and understanding (n=192)

		Understanding n (%)			
Recall n (%)	**Level**	**High***	**Above average***	**Below average***	**Low***
	High*	76 (80.0%)	17 (17.9%)	2 (2.1%)	0 (0.0%)
	Above average*	39 (57.3%)	25 (36.8%)	4 (5.9%)	0 (0.0%)
	Below average*	14 (53.9%)	11 (42.3%)	1 (3.9%)	0 (0.0%)
	Low*	1 (33.3%)	2 (66.7%)	0 (0.0%)	0 (0.0%)

* High: [≥ 75%]; Above average: [≥ 50% & < 75%]; Below average: [≥ 25% & < 50%]; Low: [< 25%]

Stratified analysis

The comparison of the *recall* levels (high, above average, below average and low) between the two language groups (Afrikaans or Xhosa), between age groups (26 years and younger or older than 26 years), and between those who had access to a telephone or cell phone and those who had not, showed no significant differences (Table X). However, an education level of Standard 5 and higher was significantly associated with higher *recall* scores (Fisher's exact p=0.000). Also, having research nurse experience of greater than two years was associated with higher *recall* scores (Fisher's exact p=0.000).

Table X: Stratified analysis results of recall scores (n=192)

Recall Score		High* n (%)	Above average* n (%)	Below average* n (%)	Low* n (%)
Language[20]	0	56 (51.4%)	33 (30.3%)	18 (16.5%)	2 (1.8%)
	1	39 (47.0%)	35 (42.2%)	8 (9.6%)	1 (1.2%)
			Fisher's exact, p = 0.276		
Education[21]	0	4 (19.1%)	8 (38.1%)	7 (33.3%)	2 (9.5%)
	1	91 (53.2%)	60 (35.1%)	19 (11.1%)	1 (1.6%)
			Fisher's exact p = 0.000		
Age[22]	0	48 (51.1%)	32 (34.0%)	13 (13.8%)	1(1.1%)
	1	47 (48.0%)	36 (36.7%)	13 (13.3%)	2 (2.0%)
			Fisher's exact p = 0.947		
Telephone[23]	0	38 (45.8%)	28 (33.7%)	16 (19.3%)	1 (1.2%)
	1	57 (52.3%)	40 (36.7%)	10 (9.2%)	2 (1.8%)
			Fisher's exact p = 0,236		
Experience of research nurse[24]	0	19 (33.3%)	20 (35.1%)	16 (28.1%)	2 (3.5%)
	1	76 (56.3%)	48 (35.5%)	10 (7.4%)	1 (0.7%)
			Fisher's exact p = 0.000		

* High: [≥ 75%]; Above average: [≥ 50% & < 75%]; Below average: [≥ 25% & < 50%]; Low: [< 25%]

[20] Language options were Afrikaans (0) & Xhosa (1)
[21] Education options were Lower than Std 5 (0) and Std 5 and higher (1)
[22] Age options were Older than 26 years (0) and Equal to and younger than 26 years (1)
[23] Telephone options were No access (0) and Access to telephone (1)
[24] Experience options less than 2 years (0) and 2 years and more (1)

The scores obtained for *understanding* levels had no significant association (Table XI) with any of the five predictors (language, age group, education level, access to telephone and research experience of the professional nurse) amongst the categories.

Table XI: Stratified analysis results of understanding scores (n=192)

Understanding Score		High* n (%)	Above average* n (%)	Below average* n (%)	Low* n (%)
Language[25]	0	75 (68.8%)	31 (28.4%)	3 (2.8%)	0 (0.0%)
	1	55 (66.3%)	24 (28.9%)	4 (4.8%)	0 (0.0%)
			Fisher's exact p = 0.767		
Education[26]	0	12 (57.1%)	9 (42.9%)	0 (0.0%)	0 (0.0%)
	1	118 (69.0%)	46 (26.9%)	7 (4.1%)	0 (0.0%)
			Fisher's exact p = 0.336		
Age[27]	0	71 (75.3%)	21 (22.3%)	2 (2.1%)	0 (0.0%)
	1	59 (60.2%)	34 (34.7%)	5 (5.1%)	0 (0.0%)
			Fisher's exact p = 0.060		
Telephone[28]	0	53 (63.8%)	27 (32.5%)	3 (3.6%)	0 (0.0%)
	1	77 (70.6%)	28 (25.7%)	4 (3.7%)	0 (0.0%)
			Fisher's exact p = 0.555		
Experience[29]	0	43 (75.4%)	12 (21.1%)	2 (3.5%)	0 (0.0%)
	1	87 (64.4%)	43 (31.9%)	5 (3.7%)	0 (0.0%)
			Fisher's exact p = 0.340		

* High: [≥ 75%]; Above average: [≥ 50% & < 75%]; Below average: [≥ 25% & < 50%]; Low: [< 25%]

[25] Language options were Afrikaans (0) & Xhosa (1)
[26] Education options were Lower than Std 5 (0) and Std 5 and higher (1)
[27] Age options were Older than 26 years (0) and Equal to and younger than 26 years (1)
[28] Telephone options were No access (0) and Access to telephone (1)
[29] Experience options were less than 2 years (0) and 2 years and more (1)

Logistic regression

Education level, age, language, access to telephones, and research experience of the nurse were included as binary variables in the initial model, together with the overall scores obtained for the health rights knowledge assessment. The final logistic regression model (Table XII) obtained for *recall* scores of 75% and greater included the same two significant predictors as found in the stratified analysis, namely experience of research nurse and education level. Participants who completed Std 5 and higher were almost 5 times more likely to obtain a minimum of 75% in the *recall* test compared to participants who did not progress that far in education. Also, consent obtained by nurses with more than two years research experience resulted in an almost three times odds of scoring at least 75% compared to nurses with less than 2 years experience.

Table XII: Logistic regression results for the recall assessment[30]

	Predictor	Odds ratio	95% Confidence Interval (CI)
High score obtained (≥ 75%)	Education level	4.94	1.57 -- 15.55
	Research experience	2.62	1.35 -- 5.07

The logistic regression model obtained for *understanding* scores of 75% and greater contained only the participant's age (Table XIII. Participants who were older than the median age were 2.17 times more likely to obtain high scores than those younger than 26 years. (The same independent variables were started with as for the logistic regression for *recall.)*

Table XIII: Logistic regression results for the understanding test[31]

	Predictor	Odds ratio	95% Confidence Interval (CI)
High score obtained (≥ 75%)	27 years and older	2.17	1.15 -- 4.07

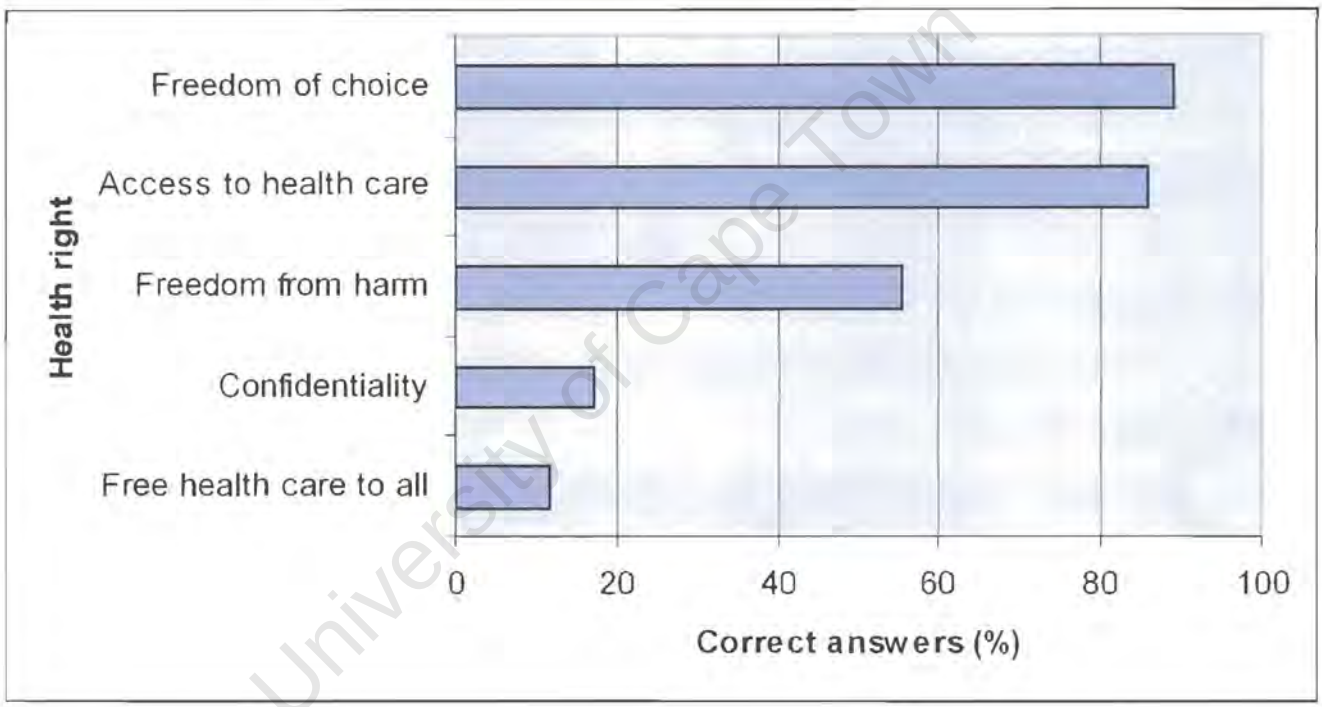
Model diagnostics picked up a number of outlying results, but none of them were influential. Removing some of the worst outliers did not result in any significant changes to the models.

[30] Log likelihood ratio, $\chi 2$ was 17.84 (p=0.0000).
[31] Log likelihood ratio, $\chi 2$ was 7.98 (p=0.0185).

Health rights assessment

The results of the five questions that were asked to assess the knowledge of health rights as contained in the South African Constitution are illustrated in Figure 8 below. Most participants knew about the constitutional right *access to health care* (86%) and *freedom of choice* (89%), and only some knew about *the right to be protected from bodily harm* (58%). Only 11% knew that health care was not free for all, and only 17% had the question about confidentiality of private information correct.

Figure 9. Illustration of knowledge of health rights as contained in the South African constitution (n=192)



The overall score for health rights was not linearly correlated with either the *recall* or the *understanding assessment* (Spearman's correlation coefficient not greater than |0.10| and p = 0.9605 and 0.4117, respectively). The individual scores for each of the health rights also had no association with the *recall* scores, and all but one of the *understanding* scores. The knowledge of right to freedom of choice was significantly associated with the *understanding* score (OR = 2.59, 95% CI = 1.06 – 6.34).

Other findings

- Table XIV contains the results of the logistics section. The majority of participants (74%) took between 10 and 20 minutes to complete the questionnaire. A small number (12%) took longer than 20 minutes. A total of 21 (11%) of participants required a substantial amount of assistance with the questionnaire. Eighteen (78%) of those who required excessive help took longer than 20 minutes as well.

Table XIV: Results of logistics section

The length of time it took to complete the questionnaire was (n=192):	
Under 10 minutes	27 (14.0%)
Between 10 and 20 minutes	142 (74.0%
Longer than 20 minutes	23 (12.0%)
The amount of assistance given by study staff to complete the questionnaire was (n=192):	
Minimal, only clarifications required here and there	73 (38.0%)
Moderate	98 (51.0%)
Substantial, the participant required much help	21 (11.0%)

- Participants obtaining a high score (75% and greater) for the *recall* section were 3.15 times (95% CI = 1.21 – 8.13) more likely than those obtaining a lower score to take less than 20 minutes to complete the questionnaire (Table XV). The association is even stronger between high *recall* scores and the amount of help required (Odds ratio = 4.83, 95% CI = 1.63 – 14.24). High scores for the *understanding* test showed no significant association with either of these factors.

Table XV: Quality of informed consent scores in relation to time taken and help required to complete the questionnaire

	High scores (75% and greater correct) for the recall test		**High scores (75% and greater correct)for understanding test**	
	OR	**95% CI**	**OR**	**95% CI**
Taking less than 20 minutes	3.15	1.21 – 8.13	2.12	0.89 – 5.03
No substantial help required	4.83	1.63 – 14.31	2.08	0.85 – 5.10

- The results of the agreement check between four questions in the *recall* section and corresponding questions in the "Yes/No" section are tabulated underneath. Table XVI shows moderately high total agreement, i.e. 60 – 73%. Kappa statistics were, however, low. The answers to the questions of the purpose of the Immunology Study had the least agreement (Kappa statistic = 0.009). The best agreement was found with the confidentiality questions (κ = 0.300).

Table XVI: Analysis of agreement between two types of questioning for 4 recall parameters

	Total Agreement %	Chance agreement	Agreement κ	95% Confidence Interval
Purpose	69 8	69.5	0 009	-0.132 – 0.150
Procedure	60.9	57.6	0.078	-0.026 – 0.182
Risks	72 9	70.1	0.096	-0.044 – 0.234
Confidentiality	72.4	60.7	0.297	0.155 – 0.438

Chapter 5: Discussion

Main findings

The aim of the study was to evaluate the quality of consent in a large tuberculosis vaccine Immunology Study and to identify factors that may influence quality of informed consent at the individual level. The setting was one of a low income, rural community in a developing country.

In the light of the strict guidelines set for bioethical principles in medical research, complete *recall* and *understanding* of research issues represents an ideal. However, the fact that most participants obtained high scores for both *recall* and for *understanding* indicates that the general quality of informed consent was acceptable. Almost all participants felt that they would participate again in a similar study if they were given the choice. In previous studies conducted in developing countries to assess the quality of informed consent, similar results were found (Lynoe *et al*, 2001, Sanchez *et al*, 2001, & Ramjee *et al*, 2000). However, it should be noted that some of those results were based on more subjective approaches to questioning.

The proportion of participants in whom the quality of informed consent was unacceptable was small. This proportion is even lower than that found in studies in industrialised countries (Yuval *et al*, 2000 & Fortney, 1999).

Most participants could recall the key aspects of the informed consent document, although there was some uncertainty about the procedures involved and the benefits available to participants. Yet judging from answers to other questions relating to the same items, it can be inferred that participants generally knew what the procedures were about. The question of benefits is interesting: while the consent form explicitly states that "there is no benefit for participating", participants saw their participation in the Immunology Study as personally beneficial in some way or another.

The level of education and research nurse experience were associated with the better scores obtained for the *recall* assessment[32]. No such association with the *understanding* score was demonstrated. In fact, none of the predictors (language, education, age, socio-economic status or nurse

[32] Even though the four research nurses who obtained the consent for the Immunology Study were aware that the Consent Study was taking place, they followed a standard operating procedure and were monitored regularly for quality control purposes. Also, obtaining consent was one of four study procedures that needed to be performed within tight time limits. These considerations make it less likely that their behaviour changed specifically under the influence of the Consent Study.

experience) showed any significant effect on the scores obtained for the *understanding*.

The only significant determinants of a high *understanding* score was the participant age, but with inverse effects. Older mothers were more likely to obtain high *understanding* scores. The *recall* and *understanding* scores were strongly positively correlated. These findings were confirmed in the logistic regression analysis.

The *understanding* assessment result supports earlier suggestions (Coletti *et al*, 2003) that low levels of education need not hinder participant's ability to understand consent concepts.

No significant association was observed between the overall score obtained for health rights and the two quality of consent scores. Knowledge of the right to freedom of choice, however, was strongly correlated with higher *understanding* scores.

It is reassuring that the two language groups had similar results, as there had been concerns that consent quality would be different between the language groups. Both training *and* quality monitoring for Xhosa consent taking in the Immunology Study was conducted in English with the help of an interpreter, whereas monitoring for Afrikaans consent taking was done in Afrikaans. The reason for this is that research workers whose first language is Afrikaans or English are not capable of using Xhosa as a third language. Those with Xhosa as first language are usually capable of communicating in all three languages. However, there is a general shortage of nursing staff in the area who have Xhosa as their first language. Also, the two languages broadly represent two different race groups. In the South African context this could imply differences in perceptions of research and result in differences in scores for *recall* and *understanding*. The differences in perceptions of the research between the race groups as reported by Barsdorf and Wassenaar (2005) were therefore not demonstrated in this study.

A few of the questions in the multiple choice section were checked for reliability. The cross-checking provided a mechanism by which the agreement of answers could be tested. Mothers tending young children may be distracted or tired and may answer questions without thinking, resulting in faulty *recall* or *understanding* answers. Although moderate total agreement was obtained for all four questions, significant agreement was only obtained only in the one dealing confidentiality.

Another way of reflecting on the reliability of the results was provided by the two questions that described logistical aspects of the Consent Study. The majority of participants completed their questionnaires well within the amount of time expected, and without excessive assistance from the study team.

These same participants tended to obtain higher scores for the *recall* and *understanding* assessment.

Limitations of the study

The study did not assess the ability of participants to hold information for longer periods of time (i.e. days, weeks or months) after their enrolment into the Immunology Study. Participants of health sciences research should be afforded the opportunity to have their research information repeated and rethought before they are expected to make a decision about participation. The consent obtaining procedures of the Immunology Study do not make provision for repeating information.

The amount of information made available to prospective participants is always a point of debate, as research workers may vary the level of interaction with the participants. The amount of technical information supplied also varies from study to study. Individuals have a limit on the amount of information that can be memorized in one session. Some complex scientific concepts are nearly impossible to transfer to people not trained in health sciences.

The questions posed to derive a score for *understanding* did not cover the full spectrum of emotional and intellectual processing involved when confronted with consent issues. The use of quantitative methods, and in particular questions that require "yes/no" answers, may not provide the best results under these circumstances. An alternative approach is to involve more open types of questioning as commonly used in qualitative research.

Access to a telephone or cell-phone may not be the best proxy for socioeconomic status as it may be too indirect and focuses only on the "economic" part. It might have been more useful if the expenditure on using of this commodity were known or at least verified. Marital status, dwelling type, household size and household income would have also been more appropriate, but this information was difficult to obtain owing to the brevity of the contact session with the respondents. Some of the measures (like household size) also have different meanings to different people, making them difficult to standardize.

Duration of employment in the research team was used as a proxy for research nurse experience. The research nurses working in the Immunology Study were involved in a number of different studies at the same time, performing various functions. However, as none of the staff employed in the Immunology Study had any previous research experience, it would be reasonable to equate the duration of employment with a staff member's experience.

This evaluation of the quality of informed consent was also limited in breadth. An evaluation of the consenting procedures, including regulatory intervention such as field monitoring of procedures, materials and documentation would be useful additions to a complete assessment of quality of informed consent.

Possible methods to improve the quality of informed consent

The findings of this study imply that methods to enhance informed consent quality in less educated participants need to be found, as well as adequate training of research staff involved in obtaining informed consent. In addition to system-wide monitoring and evaluation, competency assessment of staff would be useful.

Good quality informed consent requires a much greater focus on the consent process than just the way participants perform in a structured exit interview. Essential ingredients of good quality consent include the assurance that participants possess the required level of education (in South Africa Std 5 is considered minimum), that voluntary participation is encouraged, confidentiality is secured and that the whole process involves a level of interaction that promotes autonomy.

Rigid techniques of information transfer may be ineffective as some people may be more amenable to approaches shaped by their own intellectual and emotional abilities. Research (Lam, Cheng & Chan, 2004, Sastry *et al.* 2004, and O'Connor *et al.* 1999) had shown that visual aids like videos, pamphlets and other forms of multimedia get more information across than discussion only.

As an addendum to the consent process, an abridged form of self-assessment, such as the type described in this study, could improve the general understanding of research concepts. It proved very effective in strengthening understanding when participants were debriefed in a supportive manner about their wrong answers after the questionnaire was completed.

If the research process allows it, a second and even a third attempt at explaining some of the more difficult concepts would help to ensure better recall and understanding of information. This continuing consent would at the same time show the research team's commitment to ethical research practices, and reinforce participants' adherence to research protocol. The BCG Study involves person to person follow-ups over relatively long periods, and research staff takes every opportunity to talk about the participation and consent. This however, may not always be well-accepted as participants may become suspicious of the intentions of an over-servicing research team.

Greater adherence to accepted guidelines for informed consent should be pursued by regulatory bodies of funding organisations as well as academic institutions. Scrutiny of ethics practices of researchers in developing countries should be encouraged, regardless of the size or prominence of the collaborating organisations. Regular audits like those described (Epstein, 1997) will expose many consent violations.

The technique of conducting a preliminary assessment of understanding before obtaining consent, as described by Fitzgerald *et al* (2002), should also be considered, particularly in communities where illiteracy is a problem.

Recommendations to assess the quality of informed consent

Most research done to evaluate the quality of informed consent has focused on the procedures, and many researchers have used qualitative methods. The resultant findings are usually shaped by the particular setting (geography, time and size of the study). The Consent Study focused on objective testing of *recall* of consent topics and interpretative processing (understanding) of this information, as well as factors that might influence these results.

We proceeded on the assumption that a good way of evaluating the quality of informed consent is by objective, self-administered questionnaire, with or without a qualitative component. This method minimizes measurement bias and also confirms participant literacy and the language used at home.

In a once-off cross-sectional study or the enrollment phase of a prospective case control study such as the Immunology Study, it is probably adequate to conduct a once-off *recall / understanding* assessment as described in this study. The complexity of the material and the logistics of data collection will dictate at what stage of the study this assessment should take place. For determining the quality of informed consent in a randomized controlled trial, for instance, greater consideration to timing is required. Blinding, randomization and sampling may necessitate the progressive assessment of informed consent quality, as study details frequently differ between the different randomized groups and as the study progresses.

A combined *recall* and *understanding* strategy is recommended, as the former assesses short-term memory, while the latter gives a measure of how well participants process the information intellectually and emotionally. The two aspects should also be weighted equally.

Qualitative techniques in the grounded theory tradition could be used in conjunction with quantitative methods to assist with testing assumptions about the associations of education level, illiteracy and depth of information

transfer with the quality of informed consent. This type of data could best be collected through greater interaction with participants.

Cross-checking could be used with the objective of checking reliability of some of the key items of the study under scrutiny. No other studies were found to have attempted to measure agreement between different ways of questioning. However, the unsatisfactory agreement results found in this study suggest that special attention should be given to this aspect of the quality of informed consent assessment in future studies.

The quality of consent in the Consent Study can be considered as representative of the parent study (the Immunology Study) as the sample demographics (language, age and geographic distribution), the clinic schedules and the research nurses' workloads were roughly similar between the two studies.

The setting for the Consent Study is not unique. Many research studies are conducted in developing countries in similar settings, i.e. language difficulties and cultural differences, low education and socio-economic status and limited resources. Many academic researchers conduct their research in poor settlements like these, and are faced with similar challenges. There is therefore no reason not to expect that the quality of informed consent to be similar in other parts of Southern Africa and abroad.

Informed consent in this population

The Immunology Study was conducted in a rural district known for its low socio-economic status, high unemployment and high prevalence of diseases of poverty. Participants are generally research naive, and frequently confuse research activities with health service practice. Owing to the health system problems of staff shortage and scarce resources, participants welcome the attention of better resourced research initiatives.

Following from the above, the findings of the Consent Study can be considered acceptable, in particular because it seems as if most participants had made informed choices about their participation in the Immunology Study. Most participants had above average understanding of the Consent Study. The misunderstanding about perceived benefits is understandable, but it could also mean that participants made the decision to participate in the Immunology Study because of a belief that the benefits were more than they actually were.

The recent focus in this area on publicizing patients' rights by health authorities (notably the National patients' Rights Charter) may have had some impact as is suggested by the findings of the health rights questions (Department of Health, 1996). The high percentage of participants knowing

about "choice" and "access to health care" may indicate a sense of autonomy that is not easily detectable with other types of questioning. It can also be argued that the misconception about "free for all" health care is explicable by the fact that all participants had undergone or experienced free health care, i.e. for pregnancy, HIV testing, childbirth and immunizations, during the previous year or so. Participants might confuse the right to privacy with the undertaking of the health services to keep health information confidential. The mother-to-child-transmission HIV prevention program that is run by the health services contributed much to the increased sensitivity about confidentiality.

The ideal informed consent may require full recall of information and complete understanding, but given the uncertainties of human interaction, deviations from this ideal should be expected. Information will to some extent be misrepresented and / or misinterpreted during the consent process.

Conclusion

The quality of informed consent measured in this study is acceptable if compared to the poor *recall* of consent process and content as described in other studies. The fact that more than 90% felt that they would participate again in a study like the Immunology Study is also reassuring.

Studies to evaluate the quality of informed consent could be a requirement for the ethical basis of participant enrollment into research studies. Research ethics committees should insist on periodic reports on consent quality as part of their ongoing responsibility to fulfill their mandates of protecting the public against unethical research practices. Although *level of education* and *experience of the research staff* appeared to be predictors of good quality of consent in this study, researchers would need to identify the predictors of good quality consent in their studies. This would help them to develop the consent documentation and procedures that are most applicable for their populations in further studies.

Standardising methods for conducting these studies is also important. The Consent Study described in this report intended to achieve the objectivity and repeatability necessary for drawing valid conclusions regarding the quality of informed consent in a field study. The study aimed to develop a potentially standardisable questionnaire, containing appropriate, study-specific questions and more generic understanding questions. Norms of acceptability were suggested following analysis of binary risk factor and regression analysis. This study should add to the sparse literature dealing with the quantitative evaluation of informed consent in a developing country situation,

and potentially encourage commentary and further research in this important area of research ethics.

Differences in health priorities between developing and industrialised nations result in differences in allocation of resources for research. It is estimated that 90% of the global research budget is applied to 10% of the world's population, the inhabitants of industrialised countries. This means that insufficient funds are available to finance research studies in conditions of high-burden, usually preventable and treatable infectious disease. Participants in developing countries are frequently subjected to poorly regulated and monitored research procedures, including unethical consent practices. It is therefore important for researchers in developing countries to work towards improvement of the quality of consent.

Attention should also be given to methodological appropriateness of consent evaluations. The natural humility displayed by peoples from sub-Saharan Africa, parts of Asia and South America, may make the value of answers to subjective type of questioning questionable.

The factors that predict quality informed consent, e.g. education of participants and experience of research staff, should be determined for each study, then followed by parallel programmes of empowerment to the research community. Health promotion and rights education initiatives could also be launched in collaboration with the relevant local authorities in areas where community based research is being carried out.

While industrialised country-based sponsors are centrally concerned about the scientific question and research ethics committees concentrate on the ethical standards of proposed research, principal investigators in developing countries should consciously consider good quality informed consent as a key objective of all their research proposals. The harsh conditions of people living in these communities, i.e. wide-spread poverty, low level of education, insufficient access to resources, and limited access to information make the conduct of ethical research practice more challenging. This study has shown that if research staff was adequately trained (in policies, practices, and procedures of ethics), and an appropriately informed research community is involved, the ideal of good quality informed consent could be achieved, even in rural settings.

Given the limited data on consent and methods from other studies, much work is still to be done. The Consent Study, performed to assess the quality of informed consent in the Immunology Study in Worcester, South Africa, can be seen as an attempt to advance such work.

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STANDARD OPERATING PROCEDURE NUMBER 2

1 **Description**: Consent, Clinical evaluation, blood collection and transport

2 **Staff Involved**: Study Phlebotomy Team / Courier Drivers

3 **Principle**:

The University of Cape Town [UCT] and a group of overseas researchers, with the approval of the Boland Overberg Regional Health Department, are interested in studying the immune response to BCG vaccination in small infants. The aim of this immunology study is to determine whether we can measure with a blood test whether the vaccine has either protected, or has not protected, that infant against tuberculosis. Infants who have been enrolled into the larger randomised controlled trial comparing two routes of giving BCG vaccination (the "BCG Trial") may also be enrolled into this immunology study.

Blood will be collected from 8-14 week old infants that had been vaccinated with BCG at birth. This blood will be transported to the Groote Schuur Hospital BCG laboratory (Cell Bank) in Cape Town, where white blood cells will be isolated and stored in a freezer for immune tests at a later stage. Some blood will immediately be processed at the clinics to start measuring the immune responses caused by the vaccine while this blood is being transported to the Cell Bank.

This is a multidisciplinary trial and each member of staff will have specified tasks, either in the laboratory/cell bank or in the clinics. Careful co-ordination and team work will ensure smooth running of the study with minimal inconvenience to parents and infants and ensure that the blood samples get to the Cell bank for processing as soon as possible.

4 Contact/Telephone numbers:

Designation	Name	Office	Home	Cell
Field Manager				
Medical Officer				
Principal Investigator				
Driver				

5 **Preparation** - instructions for phlebotomy team

5.1 Ensure before leaving each day that you have:
5.1.1 The "bleed list" (list of infants due to present for blood taking for that day.)
5.1.2 Adequate supplies of the consumables listed below for that day's bleed.

6 **Venue**

6.1 Blood will be collected from infants at the fixed clinic nearest to their homes by members of the phlebotomy team. Phlebotomy *clinics will generally begin as soon as the clinic opens, usually at 08h00.*

7 **Reception**
Instructions to study nurses and nursing assistants
7.1 Check each infant's Road to Health Card (RTHC) to see that there is a Study label/number attached inside and an orange coloured study sticker on the outside. If the infant has a study sticker and number, go to 7.3 below.
7.2 If a infant arrives with no RTHC and no number:
7.2.1 Contact the study office to enquire whether the infant is on the database and if so what the infant's study number is.
7.3 Hand-write the study number onto 5 blank identification labels.
7.4 If the office has no record of the infant:
7.4.1 Take down the infant's details (surname, first name, date of birth) and give another date.

8 Consent

8.1 Consent is an ongoing process of informing participants about the study its aims, procedures, risks and benefits. All study staff are involved. Obtaining written informed consent is just one step in this process.
8.2 Study nurses will obtain written informed consent.
8.3 First counsel the infant's parents in a group about the study.
8.4 Then request consent for participation in the study from the parent(s) individually. This part of obtaining consent must be done in a private setting i.e. in a separate room, away from the rest of the infants' mothers/fathers. If such a room does not exist, then the individual counselling and signing of the consent must be done in the room used for the taking of the blood.
8.5 Allow sufficient time for the infant's mother/father to read the information brochure and consent form and to have any questions answered in full.
8.6 Obtain the signatures of either the mother or the father or both parents. All signatures to be dated in the spaces provided.
8.7 Get a third person (not the nurse taking the consent) to sign as witness.
8.8 Sign and date the "investigator's statement"
8.9 Give a copy of the consent to the parent(s) to keep. This should be taken home by the parents. not put into the infant's clinic records.

9 Assessing eligibility to take part in the study:

9.1 For each infant ask about:
9.1.1 Any contact with a healthcare giver
9.1.2 Any admission to hospital
9.1.3 Current or recent illnesses
9.1.4 Current or recent medications
9.1.5 Contact with a person suffering from tuberculosis or suspected to be suffering from tuberculosis
9.1.6 Signs and / or symptoms of tuberculosis in the infant. specifically:
9.1.6.1 Cough
9.1.6.2 Loss of weight
9.1.6.3 Night sweats
9.1.6.4 Fever
9.2 Make an assessment of the eligibility of the infant to participate in the study. Exclude the infant if:
9.2.1 Any acute or chronic disease that would make the infant ineligible for routine childhood vaccinations
9.2.2 Any contact with or signs and symptoms suggestive of tuberculosis. If unsure, contact the study medical officer or principal investigator.

10 Blood Taking

10.1 Leave the portable incubator plugged into the cigarette lighter of the car. Leave a digital minimum - maximum thermometer in the portable incubator. This will be reset just before the first specimen is placed in the incubator.
10.2 Plug the mini-incubator in at the wall in the consulting room of the clinic.
10.3 Wipe down all work surfaces with 100% EtOH. Keep the 2mL polypropylene Sarstedt tubes with the reagents in their cooler box until they are needed. When needed remove only 1 set of 3 at a time: leave the remainder in the cooler box. Wear gloves when handling the sarstedt tubes. Check the temperature in the cooler box periodically to make sure that it is not above 8 deg C.
10.4 Fill in the "Sample Identification List form" Form 3.0 in ballpoint pen. (Appendix 3). Attach a study identification label and write the patient's name down on the form.
10.5 Explain again to the infant's parent(s) that:
10.5.1 Blood will be taken from the best available vein, which will be either a peripheral vein or a neck vein. Wear gloves when drawing blood and use a fresh pair per donor.
10.5.2 A maximum of 10 ml of blood will be taken.
10.5.3 A maximum of three attempts in any one day will be made to obtain the blood. If it proves impossible to obtain a satisfactory specimen from an infant on a particular day, and the infant is aged less than 14 weeks. the infant's caregiver may be requested to bring the infant to the following phlebotomy session at that clinic if her/his age will be less than 14 weeks at that time.

10.6 Inform the parents that they may at any time ask the team to stop the procedure and withdraw the infant from the study.
10.7 Check that the temperature in the mini-incubator is more than 30°Celsius. If not, wait until it is. Reset the min./max. thermometer at this stage.
10.8 Two people will collect the blood; one will hold the infant and one will take the blood. A study nurse and phlebotomy assistant will perform this task together.
10.9 Do not ask the infant's parents to help with the procedure. Offer them the option of remaining with the infant whilst the blood is taken.
10.10 Both the study nurse and the assistant must put on gloves.
10.11 Write the first 3 letters of the infant's surname on 4 of the infant's study identification stickers, using the special black pens provided by the laboratory and taking care not to write over the pre-printed bar code area. If the infant's surname consists of more than one word e.g. "van der Merwe", "du Plessis", then write the first 3 letters of the main word e.g. "MER" or "PLE" in the example given above.
10.12 Clean the skin with an alcohol swab ("Webcol")
10.13 Draw 10ml of blood from the best vein e.g. in the antecubital fossa, using a 10ml heparinised syringe with a 23 gauge butterfly needle attached.
10.14 Gently invert the syringe 10 times. Remove the butterfly needle and discard in a sharps container
10.15 Filling and storing the 2 mL Sarstedt tubes
10.15.1 Unscrew the top of the sarstedt tube and place the top right side up on the working suface. Carefully inject the blood into the 2mL Sarstedt tubes. Avoid touching the inside of the tube with the syringe tip. Fill the red topped (BCG) tube up to the 1.0mL mark and the other two tubes (blue [medium] and white [SEB] topped) up to the 0.25mL marks.
10.15.2 Vortex each 2mL Sarstedt tube.
10.15.3 Study identification stickers:
Label the set of sarstedt tubes for the **WBA** with the **white study identification sticker.**
Label the set of sarstedt tubes for the **RNA isolation** with the **(single) red striped study identification sticker.**
10.15.4 Place the 2mL Sarstedt tubes in the mini-incubator.
10.16 Filling and storing the CPT tube:
10.16.1 Clean the rubber stopper in the CPT tube with an alcohol swab. Wait for it to dry.
10.16.2 Put a 19 gauge needle onto the syringe and allow the vacuum to draw the remaining blood into one 8mL heparinised vacutainer CPT tube as follows:
10.16.2.1 Place the tube on a table.
10.16.2.2 Remove the hand that places the tube there.
10.16.2.3 Place the tip of the 19G syringe needle on the rubber surface of the CPT PRIOR TO TOUCHING THE CPT AGAIN.
10.16.2.4 WHEN THE NEEDLE IS ON THE RUBBER SURFACE, STABILIZE THE CPT TUBE WITH THE OTHER HAND.
10.16.2.5 Inject the syringe contents into the tube. Allow the vacuum to draw the blood, do not put pressure on the syringe.
10.17 Put a study identification sticker on the CPT tube.
10.18 Reset the min-max thermometer in the CPT tube container (Coleman cooler box) before putting in the first CPT tube.
10.19 Place the CPT tube into the rack in the CPT transport container.
10.20 The temperature in the transport container must be maintained between 16 and 25°C. The packing of this box is therefore at the discretion of the phlebotomy team leader.
10.21 If less than 10mL of blood has been collected:
10.21.1 First fill the 2mL Sarstedt tubes in the following order: Red (BCG), White (SEB), Blue (MEDIUM).
10.21.2 Now allow the remainder of the blood to be drawn into an 8ml CPT tube.
10.22 After taking blood from each infant
10.22.1 Note the time of taking blood on Form 3.0.
10.22.2 Fill in the details requested on the "Daily temperature record sheet for clinic incubators" (appendix 2) i.e. time of taking blood, name of infant, study number, temperature in mini-incubator, temperature in CPT cooler box, temperature in Sarstedt-tube cooler box.

11 **Incentives**:

11.1 Distribute the incentives to the caregivers and their infants (details in SOP 1).
11.2 Fill in the incentive list (name, study number, clinic and date for each infant bled and given an incentive.) The infant's parent/guardian must sign for the incentive.

12 **Storage And Transport Of Tubes With Blood**:

12.1 Before leaving the clinic, check the specimens for number and integrity.
12.2 Transport all tubes upright, protected from sunlight.
12.3 They must all reach the laboratory within five hours from the time the first sample was taken.
12.3.1 Transport polypropylene tubes in the portable incubator at 37°C. Before transferring the specimens from the plug in mini incubator to the portable incubator, make sure that you reset the minimum maximum thermometer in the portable incubator.
12.3.2 Transport CPT tubes in a Coleman cooler box, packed to maintain the temperature between 16 and 25°C.
12.4 Transport the bloods back to the Worcester (Brewelskloof) project office.
12.5 At the project office:
12.5.1 Check the current temperatures of the incubator and cooler boxes.
12.5.2 DO NOT reset the minimum maximum thermometers at this stage.
12.5.3 If one or more of the temperatures is out of range, phone the laboratory for advice (021-406-6149) before proceeding any further. Any problems with equipment must be reported to the laboratory.
12.5.4 If the ambient temperature is more than 25°C, place the portable incubator in a large polystyrene cooler box surrounded by ice packs before giving it to the courier.
12.5.5 Unload the incubators and cooler boxes from your vehicle and load them into the courier vehicle intact / as is. Transfer them in their incubators / polystyrene containers to the courier's vehicle. Make sure that the portable incubator is plugged into the cigarette lighter socket in the courier vehicle and that the indicator light and temperature display show that it is working.
12.5.6 Note that all the details on Form 3.0 are completed before you or the courier driver sign the form.
12.5.7 The courier driver will sign for the forms and the bloods in the container.
12.5.8 Note the name of the driver and the time s/he leaves the project office.
12.5.9 Phone the laboratory (021-406-6149) and inform them that the specimens have left.
12.5.10 Give the completed "Daily temperature record sheet for clinic incubators" forms to the area manager for checking and subsequent filing at the Worcester project office. A 10% sample of these forms will be audited once a month by the study internal monitor and any violations reported to the medical officer and laboratory.
12.5.11 Cleaning of incubators:
At the end of each phlebotomy session, wipe down both the portable and mini-incubators with 100% EtOH.

13 **Safety Issues**:

13.1 Instructions To Nurses And Courier Handling The Specimens -

13.1.1 If you are injured by a contaminated or potentially contaminated object such as a bloody shard of glass from a broken test tube:
13.1.1.1 wash the affected part immediately with soap and water.
13.1.1.2 Study staff and Courier: contact the project medical officer, Dr. Tony Hawkridge, immediately and refer to the needlestick injury SOP.
You are welcome to contact Dr. Hawkridge for advice if necessary (*082 550 9002*)
13.1.2 In the event that a tube or tubes of blood are broken and blood is spilt:
13.1.2.1 Immediately pour sodium hypochlorite solution (Bleach) onto the broken tube and any leaked blood.
13.1.2.2 Note the details of the incident and the identification number(s) on the affected tube(s) on a "specimen incident" form (appendix 1). You should have a supply of these forms with you whenever you are dealing with study specimens. Submit the completed report to the Worcester Project office as soon as you can.
13.1.2.3 Inform the study area manager, Mr. Minnies, and the laboratory technologist in charge, Mr. Gelderblom, of the details by telephone as soon as is possible. Contact details are above under 2.

Appendix B: Immunology Study Consent form

THE UNIVERSITY OF CAPE TOWN

CONSENT FORM

Revised March 4,2002

Protocol title:
Immune correlates of vaccination-induced protection against tuberculosis. (Initial enrollment in case-control study.)

A. Doctors and nurses at the University of Cape Town and a group of overseas researchers are involved in research to determine how best to prevent tuberculosis in children, using BCG (the vaccine that prevents tuberculosis, especially severe tuberculosis). This study involves research In this specific study the doctors will measure in infants' blood how the immune system has responded to routine newborn BCG vaccination The researchers hope to identify a blood test that will inform them whether the BCG vaccination has protected, or has not protected, a specific child against future tuberculosis disease.

B. The expected duration of a child's participation in this research study is 1 day (only the enrollment day when my child will be evaluated and blood will be collected from him/her). However, as explained below, in the first 4 years of the child's life, if he/she develops tuberculosis disease, or is chosen as a healthy matched control subject for those children who develop tuberculosis, he/she may participate in the study for another day. At this time a separate written informed consent will be taken from t he parent/guardian.

C. The procedures to be followed are:

All children are immunized with the BCG vaccine soon after birth. At the 10 week routine childhood vaccination visit to a district clinic, 10mL (2 teaspoons) blood will be taken from the child, after a nurse has taken a brief history and has examined the child. This blood will be stored (processed and frozen), and may later be used to measure how that child has responded to the vaccine.
Blood will be taken from approximately 6,000 BCG vaccinated children to be enrolled in this study.
Many of the children enrolled in this study will be exposed to an adult who is spreading the tuberculosis bacterium through his/her own disease. Some of these children will become infected and develop tuberculosis disease The research team estimates that about 400 enrolled children will develop tuberculosis and will assume that the BCG vaccine has not protected these children.
However, not all children who are exposed to and infected with tuberculosis bacterium will develop disease. Their immune systems are somehow stronger and fight off disease. The research team will assume that because these children have not developed tuberculosis disease, the BCG vaccine has protected them. They will be called "matched control subjects" by the researchers.
Once children with tuberculosis, and matched controls, have been identified, the researchers will retrieve the blood stored taken from these children when they were 10 weeks old Immune responses in this blood will be compared between children who develop tuberculosis (not protected by the vaccine) and those who do not develop tuberculosis even though they have been infected by the tuberculosis bacterium (protected by the vaccine the "matched control subjects"). Two matched control subjects will be included in the study for each child with tuberculosis disease. In the event of a child developing tuberculosis, or if a child is selected as a matched control subject, the child will have an HIV blood test at that time.
At 10 weeks of age, doctors cannot predict who will develop tuberculosis and who will be infected with the tuberculosis bacterium without developing disease. Therefore, to later have blood samples available from all these children, blood must be collected at 10 weeks of age from all 6,000 children enrolled in the study.

Blood from each and every child enrolled in this study will therefore not be used for tests in this study, particularly if he/she does not develop tuberculosis, or is not chosen as a matched control. Nevertheless, blood will still have been stored from all children. The researchers may wish to use this blood for other infectious disease research studies. A code will be used to identify children's blood: his/her name will never be revealed. There will be an opportunity at the end of this document for parents/guardians to sign whether they wish to allow the researchers to use their child's blood for any infectious disease studies other than this study, if the stored blood is not used for this study. If a parent/guardian does not allow for the blood to be used for other studies, blood will still be collected from that child; however, it will be discarded after the study has been completed

D *The possible discomforts and risks attendant to this study are:*

The risks of taking blood from children are small, particularly as small amounts of blood will be taken. Slight pain or bruising can occur when blood is sampled; very rarely, the skin area from where the blood was taken may become infected or bleed a little. The research team will take precautions to prevent these complications.

E The benefits that a child might reasonably expect from participating in this study are:

There is no benefit for a child in participating in this study; rather, the information from this study may help doctors in future to predict whether the BCG vaccine given to a specific baby will protect him/her against tuberculosis disease, by doing a blood test measuring immune responses.

F. The alternative procedures, if any, that could be considered:

Not to participate in the study.

G. A copy of this consent will be handed to the parent/guardian to keep. Records connected with a child's participation in the clinical investigation will be kept strictly confidential. No parent/guardian or child's name will not be revealed in any publication that may arise from this study.

H. This study does not involve an investigational drug. BCG is a routine vaccine of childhood.

I. Opportunity will be provided for questions and discussion of the content of this document prior to signing of consent. If any questions concerning the research conducted remain, Professor Greg Hussey may be contacted at 021-685-4103 If any concerns arise about any child's rights as a research subject, the University of Cape Town Research Ethics Committee may be contacted at 021-406-6492. Any participant is free to withdraw consent at any time without penalty or loss of benefits to which a child may be otherwise entitled. The research team may also terminate the study, or any subject's participation, at any time.

J. In the event of a parent/guardian believing that participation in this research study has led to injury of a child, the parent/guardian may contact Professor Greg Hussey at 021-685-4103 to identify the medical resources which are available to the child and to assist the child in obtaining appropriate medical care.

I have read this document and understand its content. I have had the opportunity to discuss the study and its procedures, and questions that I may have, with the research staff. I hereby voluntarily consent to voluntary participation of my child, _____, in this study and to allow the treatment and procedures described above to be performed on my child.

Name of Parent /Guardian - please print	Signature or thumb print	Date

Name of witness (study personnel) - please print	Signature	Date

For use if a thumb print was used
I herewith confirm that the ink mark above is the right hand thumb print of the parent/guardian.

Name of independent third person please print	Signature	Date

I also understand that not all the blood that is stored will be used in this study.
I consent to the stored blood from my child, if not used for this specific study, to be used for other infectious disease research studies.

Name of Parent /Guardian - please print	Signature or thumb print	Date

I **do not** consent to the stored blood from my child, if not used for this specific study, to be used for other infectious disease research studies.

Name of Parent /Guardian - please print	Signature or thumb print	Date

Name of witness (study personnel) - please print	Signature	Date

For use if a thumb print was used
I herewith confirm that the ink mark above is the right hand thumb print of the parent/guardian.

Name of independent third person please print	Signature	Date

INVESTIGATOR'S STATEMENT
I have offered an opportunity for further explanation of this procedure to the individual whose signature appears above.

Name of Investigator - please print	*Signature*	*Date*

Note:
The subject must be given a copy of this consent form. A signed copy must be filed in the subject's medical record in the Medical Records Department.

Appendix C: Standard Operating Procedure: Consent Study

QUALITY OF INFORMED CONSENT: Standard operating procedure

Applied to: Professional Nurse (PN) conducting the Exit interview
Location: Clinic where Immunology Case control study enrolment takes place
Materials: Consent forms in appropriate language
Questionnaire in appropriate language
Closed envelopes containing R50 each, with participant's name
Environment: Chair & table / tablet to write on
Privacy
Help to hold baby
Guidance and assistance with questionnaire as required

Procedure:

1. Following initial enrolment into the ICCS, mother referred to QOIC
2. PN explains purpose of the survey
3. PN asks if willing / able to stay & participate
4. PN goes through consent letter
5. PN asks mother to sign consent
6. PN facilitates conduct of the interview:
   (a) Explains layout of questionnaire
   (b) Assists participant to complete demographics
   (c) Assists participant where necessary to interpret questions
   (d) Checks if all questions were answered at the end
   (e) Record duration & difficulty details
   (f) Checks participant answers against correct answers
   (g) Correct participant understanding where necessary
   (h) Signs and dates questionnaire
7. PN thanks mother then hands her the reimbursement after she signed a receipt
8. PN completes form and submit to office for capturing

Appendix D: Consent Study questionnaire (English)

Serial number

QUALITY OF CONSENT EVALUATION QUESTIONNAIRE

Study baby T-number		Participant name					
Participant date of birth		Participant address					
Date of interview		Language spoken at home eg A for Afrikaans		Education: Eg. G 8 for Grade 8 or St 8 for Standard 8		Tel	
						Cell	

A. Select the ONE option that best completes the statement regarding the study you were asked to consent to earlier today (Correct answer in red – for illustration only. For survey all options will appear identical in print.)

1. I have been asked to attend the clinic today so that:
   (a) My baby can receive expert treatment.
   (b) My baby can participate in a research study
   (c) My baby can receive routine health care

2. The purpose of the research study is to:
   (a) Test for protection against tuberculosis in my baby's blood.
   (b) Test for tuberculosis in my baby's blood
   (c) *Test for HIV in my baby's blood*

3. Research staff wants to enroll my baby into the research study so that:
   (a) They can test my baby for TB or HIV
   (b) They can collect blood from my baby
   (c) *They can inject my baby with BCG*

4. The total amount of time my baby will be expected to participate in the study is:
   (a) 2 to 3 years
   (b) 8 to 14 weeks
   (c) 1 day

5. The most common risk involved when blood had been collected from my baby is:
   (a) My baby can become infected with TB or HIV
   (b) My baby may suffer very slight scarring and some oozing
   (c) My baby can loose too much blood

6. The benefits available to me and my baby for participating in the study are:
   (a) There are no immediate benefits
   (b) My baby will be protected against TB
   (c) My baby and I will get better treatment at clinics

7. If I didn't want to participate in this study, I could withdraw and
   (a) My baby and I would be denied access to health services at this clinic
   (b) My baby and I will be treated differently by research and clinic staff
   (c) My baby and I would suffer no loss at all

8. My baby's personal details will never be linked with his / her blood because
   (a) Numbers with barcodes will be used to keep bloods anonymous
   (b) Highly trained research staff will keep information secret
   (c) Clinic staff will be sure not to give information to the research staff

9. The blood of my baby that will be frozen and stored will be used
   (a) For all kinds of research in other countries
   (b) For HIV testing
   (c) For other tests concerning protection against TB

B. State whether you agree with the statements below by ticking off the appropriate box next to each statement.

	Yes	No	Don't know
10. The procedures done on my baby in this study are:			
(a) Safe and practically harmless	☐	☐	☐
(b) Dangerous and harmful	☐	☐	☐
11. My baby's blood is going to be used to			
(a) help develop a blood test for TB	☐	☐	☐
(b) determine whether my baby has TB	☐	☐	☐
12. My baby's name is written on all the blood tubes	☐	☐	☐
13. I agreed to enroll my child in this study because			
(a) My child might get better treatment	☐	☐	☐
(b) I want doctors to help learn more about TB	☐	☐	☐
14. I've decided to enroll my baby in the study			
(a) even though my baby will receive no extra treatment	☐	☐	☐
(b) because I knew I would receive a toiletries hamper	☐	☐	☐
15. If my baby gets a bruise from the blood test, I should			
(a) Contact the police	☐	☐	☐
(b) Speak to the nurse at the clinic	☐	☐	☐
(c) Go to the doctor at his private surgery	☐	☐	☐
16. I was enrolled in the study in my home language	☐	☐	☐
17. If I was given the choice to participate again, I would	☐	☐	☐
18. Which of the following rights are protected in the South African constitution?			
(a) access to health care	☐	☐	☐
(b) concealment of private information	☐	☐	☐
(c) freedom from bodily harm	☐	☐	☐
(d) free health care to all	☐	☐	☐
(e) freedom of choice	☐	☐	☐

If contradictory or exploratory comments were made, please note the question number and record the details in the adjacent space. Also ask if there are any questions and record details.	

Question	Answer		Correct?	Question	Answer		Correct?
1		B		13b			
2		A		14a			
3		B		14b			
4		C		15a			
5		B		15b			
6		A		15c			
7		C		16		Yes	
8		A		17			
9		C		18a		Yes	
10a		Yes		18b		No	
10b		No		18c		Yes	
11a		Yes		18d		No	
11b		No		18e		Yes	
12		No					
13a				Total			

The length of time it took to complete the questionnaire was:

(a) Under 10 minutes
(b) Between 10 and 20 minutes
(c) Longer than 20 minutes

The amount of assistance given by study staff to complete the questionnaire was:

(a) Minimal, only clarifications required here and there
(b) Moderate
(c) Substantial, the participant required much help

Name of Consenter of Case Control Study	

_____ _____

(Signature of research nurse) (Date)

_____ _____

(Signature of data capturer) (Date)

Appendix E. Consent Study questionnaire (Afrikaans)

Serial number

"QUALITY OF CONSENT" EVALUASIE VRAAGBRIEF

Study baby T-number		Participant name					
Participant date of birth		Participant address					
Date of interview		Language spoken at home eg A for Afrikaans		Education I Eg. G 8 for Grade 8 or St 8 for Standard 8		Tel	
						Cell	

A.Kies die een opsie wat die beste pas by die vraag oor die studie , soos jy dit verstaan, uit die toestemming wat jy vroeër vandag gegee het.

1. Ek is gevra om die kliniek by te woon sodat:
   (a) My baba spesialis behandeling kan kry.
   (b) My baba kan deelneem in 'n navorsing studie.
   (c) My baba roetine gesondheidsorg kan kry.

2. Die doel van die studie is om te:
   (a) Toets vir beskerming teen TB in my baba se bloed
   (b) Toets vir TB in my baba se bloed .
   (c) Toets vir HIV in my baba se bloed.

3. Navorsing personeel wil my baba inskryf in navorsing studie sodat:
   (a) Hulle my baba kan toets vir TB of HIV
   (b) Hulle kan bloed trek by my baba.
   (c) Hulle my baba kan in ent met BCG

4. Die tyd wat my baba sal deelneem aan die studie is:
   (a) 2 tot 3 jaar
   (b) 8 tot 14 weke
   (c) 1 dag

5. Die mees algemene risiko by die trek van bloed by die baba is:
   (a) My baba kan besmet raak met TB of HIV.
   (b) Effe kneusing en bloeding mag voorkom.
   (c) My baba kan baie bloed verloor.

6. Die voordeel vir my en my baba om deel te neem aan die studie is:
   (a) Daar is geen onmiddelike voordele nie.
   (b) My baba sal beskerm wees teen TB.
   (c) My baba en ek sal beter behandeling kry by klinieke

7. As ek nie wil deelneem aan die studie nie, kan ek onttrek en:
   (a) My baba en ek sal toegang geweier word by hierdie kliniek.
   (b) My baba en ek sal anders behandel word deur personeel.
   (c) My baba en ek sal geen verlies lei nie.

8. My baba se persoonlike inligting sal nie gekoppel word met sy/haar bloed nie, want:
   (a) 'n Nommer met 'n strepieskode sal gebruik word om bloed naamloos te hou
   (b) Hoogs opgeleide navorsing personeel sal informasie geheim hou.
   (c) Kliniek personeel sal nie informasie gee aan navorsing personeel nie.

9. Die bloed van my baba wat gevries en gestoor word, sal gebruik word om:
   (a) Vir allerhande tipes navorsing in oorsese lande.
   (b) Vir HIV toetse.
   (c) Vir ander toetse oor beskerming teen TB wat nog nie bekend is nie.

B. Dui u antwoord aan deur die blokkie af te merk waarmee u saam stem.

	Ja	Nee	Weet nie
10. Die prosedures gedoen op my baba in hierdie studie is:			
(a) Veilig en eintlik skadeloos	☐	☐	☐
(b) Gevaarlik en skadelik	☐	☐	☐
11. My baba se bloed gaan gebruik word om:			
(a) 'n bloedtoets te ontwerp teen TB	☐	☐	☐
(b) vas te stel of my baba TB het	☐	☐	☐
12. My baba se naam is geskryf op al die bloed buisies	☐	☐	☐
13. Ek het ingestem om my baba in die studie in te skryf omdat			
(a) my baba dalk beter behandeling mag kry	☐	☐	☐
(b) ek graag dokters wil help om meer te leer van TB	☐	☐	☐
14. Ek het besluit om my baba in te skryf			
(a) al sal my baba geen ekstra behandeling kry nie	☐	☐	☐
(b) want ek het geweet ek sal 'n skoonheidspakkie ontvang	☐	☐	☐
15. Indien my baba 'n kneusplek kry van die bloed toetse, moet ek			
(a) Die polisie ontbied	☐	☐	☐
(b) Met 'n verpleegster by die kliniek praat daaroor	☐	☐	☐
(c) Na my huisdokter gaan by sy spreekkamers	☐	☐	☐
16. Ek is in my huistaal in hierdie studie ingeskryf	☐	☐	☐
17. Ek sal weer aan die studie deelneem as ek die keuse kry	☐	☐	☐
18. Watter van die volgende regte word gewaarborg deur die Suid-Afrikaanse grondwet?			
(a) toegang tot gesondheidsorg	☐	☐	☐
(b) geheimhouding van privaatinligting	☐	☐	☐
(c) vryheid van liggaamlike skade	☐	☐	☐
(d) gratis gesondheidssorg vir almal	☐	☐	☐
(e) vryheid van keuse	☐	☐	☐

Indien teenstrydige antwoorde gegee is en of sekere van die vrae meer navrae uitgelok het, skryf asseblief die vraagnommer neer en voeg toepaslike kommentaar in die spasie hieronder. Vra ook of daar enige verdere vrae is en noteer die besonderhede.	

Question	Answer		Correct?	Question	Answer		Correct?
1		B		13b			
2		A		14a			
3		B		14b			
4		C		15a			
5		B		15b			
6		A		15c			
7		C		16		Yes	
8		A		17			
9		C		18a		Yes	
10a		Yes		18b		No	
10b		No		18c		Yes	
11a		Yes		18d		No	
11b		No		18e		Yes	
12		No					
13a				Total			

The length of time it took to complete the questionnaire was:

(d) Under 10 minutes
(e) Between 10 and 20 minutes
(f) Longer than 20 minutes

The amount of assistance given by study staff to complete the questionnaire was:

(d) Minimal, only clarifications required here and there
(e) Moderate
(f) Substantial, the participant required much help

Name of Consenter of Case Control Study	

(Signature of research nurse) (Date)

(Signature of data capturer) (Date)

Appendix F Consent Study questionnaire (Xhosa)

Serial number

"QUALITY OF CONSENT" ENXULUMENE NALEMIBUZO

Study baby T-number		Participant name					
Participant date of birth		Participant address					
Date of interview		Language spoken at home eg A for Afrikaans		Education level Eg. G8 / St 8 for Grade 8 / Standard 8		Tel	
						Cell	

Ubuyibuzwe ukunika imvumelwano Impendulo elungileyo yile.

1. Ndicela ukuba ndize eKliniki namhlanje ukuze:
   a. Usana lwam luze kufumana unyango oluqatha
   b. Usana lwam luthabathe inxaxheba kuphando
   c. Usana lwam luzakufumana unyango lwesiqhelo
2. Injongo zoluphando kuku:
   a. Ukujonga ukuba usana lwam lukhuselekile na kwiT.B egazini lalo
   b. Ukukhangela ukuba lune T.B na egazini
   c. Ukujonga ukuba linentsholongwane ugawulayo egazini
3. Abophando bafuna ukubalisela usana lwam kuphando ukuze:
   a. Bavavanye ukuba usana lwam linayo iT.B okanye ugawulayo na
   b. Ukuze barsale igazi kusana lwam
   c. Ukuze bafake iBCG ngenaliti kusana lwam
4. Ixesha alilindelekileyo eliyakuthi usana lwam luthathe inxaxheba ngalo
   a. Yiminyaka emibini ukuya kwemithathu
   b. Ziveki azisibhozo ukuya kwezilishumi elinesine
   c. Lusuku olunye
5. Eyona ngxaki ibakho xa kutsalwe igazi kusana lwam yile:
   a. Usana lwam lungasuleleka kwiT.B okanye kwintsholongwane uGaulayo
   b. Usana lwam lungaba nendawana encinci ebonakalayo apho kutsalwe khona igazi nentwana yegazi ephumayo
   c. Usana lwam lungalahlekelwa ligazi elininzi
6. Umvuzo endithi ndiwufumane ngenxa yokuthabatha kosana lwam inxaxheba koluphando yile:
   a. Akukho malungelo angamanye endizakuwafumana
   b. Umntwana wam uyakukhuseleka kwiTB
   c. Umntwana wam uyakufumana unyango olungcono eKliniki
7. Ukuba andifuni kuthabatha nxaxheba koluphando ndinako ukurhoxa ngalonto:
   a. Mna nosana lwam asiyikuvumeleka kunyango eziKliniki
   b. Andiyikulahlekelwa nto, ngamalungelo okanye kunyango kumaziko empilo
   c. Akukho nanye into eyakuthi indiphose kumalungelo awo naluphi na uhlobo kumaziko empilo

8. Iincukacha ngokunxulumene nosana lwam azinakudityaniswa negazi lakhe
   a. Iinombolo nezazisi ezifihlakeleyo ziyakusetyenziswa ukugcina igazi lingaziwa
   b. Abezophando abaphezulu boyigcina iyimfihlelo yonke into malunga nosana lwakho
   c. Abasebenzi baseKliniki bakuqinisekisa ukuba banganikezi ngencukacha kubaphandi
9. Igazi losana lwam elifakwe kwisikhencezisi esiphezulu lagcinwa liyakusetyenziswa:
   a. Kwamanye amazwe nakwabanye abantwana bophando
   b. Liyakuvavanyelwa intsholongwane ugawulayo (HIV)
   c. Ukwenza olunye uxilono ukuthintela iTB

Chaza ukuba uyavumelana kusini na kwizihloko ezingazantsi ngokuthi ubonakalise uphawu kwibokisi nganye esecaleni kwesihloko:

	Ewe	Hayi	Andazi
10. Izinto ezenziwe kusana lwamkoluphando zezi:			
a. Zikhuselekile yaye azinangozi:	□	□	□
b. Ziyingozi	□	□	□
11. Igazi losana lwam liyakubalwalosetyenziswelwa:			
a. Ukucedisa uvavanyo kwiTB	□	□	□
b. Ukukhangela ukuba usana lwam lunayo iTB	□	□	□
12. Igama losana lwam libaliwe ezimbodleleni ezigalelwe igazi	□	□	□
13. Injongo zokuza kwam eKliniki namhlanje zezi:			
a. Usana lwam lufumane unyango olungcono	□	□	□
b. Ndifuna ukuncedisana noogqira ukuze bazi ngapezulu ngesifo seTB	□	□	□
14. Ndigqibe ukuba ndilubalise usana lwam koluphando noxa			
a. Usana lwam lungazukufumana nyango lugqithisileyo	□	□	□
b. Kuba bendisazi ndizakufumana ihamper yezinto zokuthambisa	□	□	□
15. Ukuba usana lwam luthe lwane khoko kulandawo belutsalwe kuyo igazi kumelwe ukuba ndi			
a. Ndiye emapoliseni	□	□	□
b. Mdithethe nomongikazi eKliniki	□	□	□
c. Ndiye kwagqira endaweni abonela kuyo izigulane	□	□	□
16. Ndaxelelwa ngoluphando ngolwimi lwam ndaza ndabaliswa	□	□	□
17. Xa bendinokucelwa ukuba ndibalise kwakhona bendiya kuthi	□	□	□
18. Ngawaphi kulamalungelo alandelayo akhuselweyo nguMthetho womZantsi Afrika ngawaphi amalungelo wakho?			
a. Ukuya nokufumaneka konyango	□	□	□
b. Imfihlelo yencukacha zako	□	□	□
c. Ukhuseleko emzimbeni wakho	□	□	□
d. Uncedo kwezempilo olungahlawulelwayo kumntu wonke	□	□	□
e. Ukuzikhetela ngokukhululekileyo?	□	□	□

Xa kuthe kwakho ukungangqinelani okanye kwakho ingcaciso ezithe zenziwa nceda qaphela inombolo yombuzo uze ubhale ecaleni kombuzo lowo. Buza ukuba ingaba ikhona na imibuzo kwaye uyibhale nayo.	

Question	Answer		Correct?	Question	Answer		Correct?
1		B		13b			
2		A		14a			
3		B		14b			
4		C		15a			
5		B		15b			
6		A		15c			
7		C		16		Yes	
8		A		17			
9		C		18a		Yes	
10a		Yes		18b		No	
10b		No		18c		Yes	
11a		Yes		18d		No	
11b		No		18e		Yes	
12		No					
13a				Total			

The length of time it took to complete the questionnaire was:

(g) Under 10 minutes
(h) Between 10 and 20 minutes
(i) Longer than 20 minutes

The amount of assistance given by study staff to complete the questionnaire was:

(g) Minimal, only clarifications required here and there
(h) Moderate
(i) Substantial, the participant required much help

Name of Consenter	

_____ _____

(Signature of research nurse) (Date)

_____ _____

(Signature of data capturer) (Date)

Appendix G: Consent Study Consent form (English)

"QUALITY OF CONSENT" EVALUATION CONSENT FORM

Serial number

Dear _____

Thank you for coming to the clinic with your baby today.

You just spoke to a nurse about enrolling your baby in a study, and you agreed by signing a consent form. As part of the ongoing process of ensuring that good quality informed consent is given by participants in research studies, the BCG study team wishes to ask you to answer a few questions after your baby had been seen by the phlebotomy team

Would you be willing to do this interview? If so, please listen carefully what the research nurse has to say. She will explain to you exactly what she wants you to do. Please be at ease and answer the questions as best as you can. If you need help with the questions, you can ask the research staff in attendance. If necessary, you can leave your child in the care of the research assistant who is available to look after your child during the 20 minutes or so of the interview.

At the end of the interview, your answers will be discussed with you.

You will receive R50 in lieu of the time you spent in order for us to collect valuable information to improve our quality of research.

Remember, you can also choose not to stay behind for the quality of consent evaluation exercise, and leave immediately after your baby had been seen by the phlebotomy nurse.

I agree to assist the BCG research team by participating in the quality of consent survey

_____ _____

(Signature of parent / caregiver) (Date)

I have received R50 in cash from the research nurse of the BCG study

_____ _____

(Signature of parent / caregiver) (Date)

_____ _____

(Signature of research nurse) (Date)

Appendix H: Consent Study Consent form (Afrikaans)

"QUALITY OF CONSENT" EVALUASIE TOESTEMMINGSBRIEFIE

Serial number

Geagte _____

Dankie dat u vandag u baba na die kliniek gebring het.

Jy het nou net met 'n verpleegster gepraat in verband met die deelname van u baba in 'n navorsingsprojek. Jy het aangedui dat jy instem deur op 'n toestemmingsbriefie te teken. Die BCG studie span wens hiermee om aan u 'n paar te stel nadat u baba ondersoek is deur "Phlebotomy " span om te verseker dat die proses van verkryging van inligte toestemming deurlopend korrek toegepas word.

Sal jy bereid wees om met ons 'n klein onderhoud te hou daaroor? Indien wel, vra ons u om asseblief noukeurig te luister na die verpleegster. Sy sal verduidelik hoe hierdie onderhoud gevoer moet word. Wees asseblief gemaklik en beantwoord die vrae so goed as wat jy kan. Indien jy hulp verlang met enige van die vrae, vra gerus enige van die studie-personeel. Indien nodig kan jy gerus jou baba by die assistant laat, aangesien die hele proses omtrent 20 minute sal neem.

Aan die einde van die onderhoud sal jou antwoorde met jou bespreek word.

Jy sal ook R50 ontvang vir die tyd wat jy spandeer het om ons te help om waardevolle inligting te versamel.

Onthou, indien jy verkies om nie in hierdie studie deel te neem nie, mag jy weier en die kliniek verlaat, sonder dat daar enige vrae gevra sal word.

Hiermee gee ek toestemming om deel te neem aan die BCG navorsing span se ondersoek oor die kwaliteit van die inligtingte toestemming.

_____ _____

(Handtekening van ouer / voog) (Datum)

Ek het R50 in kontant ontvang van die navorsingsverpleegkundige

_____ _____

(Handtekening van ouer / voog) (Datum)

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(Handtekening van novorsingsverpleegkundige) (Datum)

Appendix I: Consent Study Consent form (Xhosa)

IFOMU YOMGANGATHO OPHEZULU MALUNGA NEMVUMELELWANO

Mzali Othandekayo _____

Siyabulela ngokuzisa usana lwakho ekliniki namhlanje .

Uthethile nomongikazi malunga nokubalisa usana lwakho wasayina isivumelano. Nje ngenkqubo eqhubekekayo sinqwenela ukuba isivumelelwana esilungileyo sinikwe ngabathathi nxaxheba kuphando.abaphandi be-BCG banqwenela ukubuza imibuzo esinqwenela ukuba uyiphendule emva kokuba usana lwakho luboniwe ngabathathi begazi.

Uyavuma na ukuphendula le mbuzo? Uba uyavuma mamela ngononophelo lento izothethwa ngomongokazi wophando. Uzakukucacisela yonke into afuna ukuba uyenze. Umongikazi oqeqeshelwe oluphando ngokukodwa uzakwenza lemibuzo elula ukuqonda ukuba uvumelelwana lubenempumelelo kangakanani. Nceda ukhuleke ukuyiphendula kangangoko lemibuzo. Ukuba ufuna uncedo malunga nemibuzo ungabuza abophando abakhoyo ngeloxesha lemibuzo.

Emva koko iimpendulo zakho ziyakuxoxwa nawe.

Uyakufuma isipho esixabisa amashumi amahlanu eRandi (R50) ukukuxolisa ngexesha lakho ukuze sifumani inkcukacha eyakuthi isinike umgangatho ophezulu kuphando lwetu.

Ukuba kuyimfuneko, siyakuba nomntu oyakulujonga usana lwakho imizuzu engameshumi amabini elixesha ubuzwa

Khumbula unako ukwala xa ungafuni kuyiphendula lemibuzo uhambe emva kokutsalwa kwegazi.

Ukuba unqwenela ukuthatha inxaxheba kulemvumelwano nceda unike imvumelelwano ngokuthi utyikitye igama lakho nomhla kwisikhewu esilungele oko.

Ndiyavuma ukunceda abophando ngokuthi ndithathe inxaxheba.

_____ _____

(Utyikityo lomzali /umntu omele umzali) (Umhla)

Ndifumene amashumi amahlani eRandi (R50) kumongikazi wophando lweBCG.

_____ _____

(Utyikityo lomzali /umntu omele umzali) (Umhla)

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(Utyikityo lonesi wophando) (Umhla)

APPENDIX J: PHLEBOTOMY SCHEDULE FOR PERIOD 01 MARCH to 15 JULY 2004

Born after	Born before	Bleed Date	Day	Area	Clinic 1	Clinic 2	Comments
24-Nov-03	5-Jan-04	1-Mar-04	Monday	Worcester	Maria Pieterse	Rawsonville	
25-Nov-03	6-Jan-04	2-Mar-04	Tuesday	Ceres	Wolseley	Tulbagh	
26-Nov-03	7-Jan-04	3-Mar-04	Wednesday	Robertson	Cogmanskloof	Zolani	
27-Nov-03	8-Jan-04	4-Mar-04	Thursday	Worcester	De Dooms	Bonnievale	
1-Dec-03	12-Jan-04	8-Mar-04	Monday	Worcester	Maria Pieterse	Empilsweni	
2-Dec-03	13-Jan-04	9-Mar-04	Tuesday	Ceres	Annie Brown	Ndull	
3-Dec-03	14-Jan-04	10-Mar-04	Wednesday	Robertson	Victoria	Ashbury	
4-Dec-03	15-Jan-04	11-Mar-04	Thursday	Worcester	Villiersdorp	Breerivier	
8-Dec-03	19-Jan-04	15-Mar-04	Monday	Worcester	Maria Pieterse	Overhex	
9-Dec-03	20-Jan-04	16-Mar-04	Tuesday	Ceres	Bella	PA Hamlet	
10-Dec-03	21-Jan-04	17-Mar-04	Wednesday	Robertson	Nkqubela	McGregor	
11-Dec-03	22-Jan-04	18-Mar-04	Thursday	Worcester	De Dooms	Touwsrivier	
15-Dec-03	26-Jan-04	22-Mar-04	Monday	Worcester	HUMAN RIGHTS DAY - PUBLIC HOLIDAY		
16-Dec-03	27-Jan-04	23-Mar-04	Tuesday	Ceres	Bella Vista	De Wet	Started at De Wet clinic
17-Dec-03	28-Jan-04	24-Mar-04	Wednesday	Robertson	Cogmanskloof	Zolani	
18-Dec-03	29-Jan-04	25-Mar-04	Thursday	Worcester	Villiersdorp	Bonnievale	
22-Dec-03	2-Feb-04	29-Mar-04	Monday	Worcester	Maria Pieterse	Rawsonville	
23-Dec-03	3-Feb-04	30-Mar-04	Tuesday	Ceres	Annie Brown	Ndull	
24-Dec-03	4-Feb-04	31-Mar-04	Wednesday	Robertson	Strooidak	Nkqubela	
25-Dec-03	5-Feb-04	1-Apr-04	Thursday	Worcester	De Dooms	Sandhills	Clinic cancelled
29-Dec-03	9-Feb-04	5-Apr-04	Monday	Worcester	Maria Pieterse	Empilsweni	
30-Dec-03	10-Feb-04	6-Apr-04	Tuesday	Ceres	Bella Vista	PA Hamlet	
31-Dec-03	11-Feb-04	7-Apr-04	Wednesday	Robertson	Victoria	Ashbury	
1-Jan-04	12-Feb-04	8-Apr-04	Thursday	Worcester	Villiersdorp	Breerivier	
5-Jan-04	16-Feb-04	12-Apr-04	Monday	Worcester	PUBLIC HOLIDAY (FAMILY DAY)		
6-Jan-04	17-Feb-04	13-Apr-04	Tuesday	Ceres	NO PHLEBOTOMY CLINIC		
7-Jan-04	18-Feb-04	14-Apr-04	Wednesday	Robertson	PUBLIC HOLIDAY (ELECTIONS)		
8-Jan-04	19-Feb-04	15-Apr-04	Thursday	Worcester	NO PHLEBOTOMY CLINIC		
12-Jan-04	23-Feb-04	19-Apr-04	Monday	Worcester	Maria Pieterse	Empilsweni	
13-Jan-04	24-Feb-04	20-Apr-04	Tuesday	Ceres	Wolseley	Tulbagh	
14-Jan-04	25-Feb-04	21-Apr-04	Wednesday	Robertson	Cogmanskloof	Zolani	
15-Jan-04	26-Feb-04	22-Apr-04	Thursday	Worcester	Villiersdorp	Bonnievale	
19-Jan-04	1-Mar-04	26-Apr-04	Monday	Worcester	Maria Pieterse	Rawsonville	
20-Jan-04	2-Mar-04	27-Apr-04	Tuesday	Ceres	PUBLIC HOLIDAY (FREEDOM DAY)		
21-Jan-04	3-Mar-04	28-Apr-04	Wednesday	Robertson	Strooidak	Nkqubela	
22-Jan-04	4-Mar-04	29-Apr-04	Thursday	Worcester	De Dooms	Bonnievale	
26-Jan-04	8-Mar-04	3-May-04	Monday	Worcester	Maria Pieterse		
27-Jan-04	9-Mar-04	4-May-04	Tuesday	Ceres	Bella Vista	PA Hamlet	
28-Jan-04	10-Mar-04	5-May-04	Wednesday	Robertson	Victoria	Ashbury	
29-Jan-04	11-Mar-04	6-May-04	Thursday	Worcester	Villiersdorp	Breerivier	
2-Feb-04	15-Mar-04	10-May-04	Monday	Worcester	Maria Pieterse	Overhex	
3-Feb-04	16-Mar-04	11-May-04	Tuesday	Ceres	Wolseley	Tulbagh	
4-Feb-04	17-Mar-04	12-May-04	Wednesday	Robertson	Strooidak	McGregor	
5-Feb-04	18-Mar-04	13-May-04	Thursday	Worcester	De Dooms	Sandhills	
9-Feb-04	22-Mar-04	17-May-04	Monday	Worcester	Maria Pieterse	Empilsweni	
10-Feb-04	23-Mar-04	18-May-04	Tuesday	Ceres	Bella Vista	De Wet	
11-Feb-04	24-Mar-04	19-May-04	Wednesday	Robertson	Cogmanskloof	Zolani	
12-Feb-04	25-Mar-04	20-May-04	Thursday	Worcester	Villiersdorp	Bonnievale	
16-Feb-04	29-Mar-04	24-May-04	Monday	Worcester	Maria Pieterse	Rawsonville	
17-Feb-04	30-Mar-04	25-May-04	Tuesday	Ceres	Annie Brown	Ndull	
18-Feb-04	31-Mar-04	26-May-04	Wednesday	Robertson	Strooidak	Nkqubela	Clinic cancelled
19-Feb-04	1-Apr-04	27-May-04	Thursday	Worcester	De Dooms	Sandhills	

23-Feb-04	5-Apr-04	31-May-04	Monday	Worcester	Maria Pieterse	Empilisweni	
24-Feb-04	6-Apr-04	1-Jun-04	Tuesday	Ceres	Bella Vista	PA Hamlet	
25-Feb-04	7-Apr-04	2-Jun-04	Wednesday	Robertson	Victoria	Ashbury	
26-Feb-04	8-Apr-04	3-Jun-04	Thursday	Worcester	Villiersdorp	Breerivier	
1-Mar-04	12-Apr-04	7-Jun-04	Monday	Worcester	Maria Pieterse		
2-Mar-04	13-Apr-04	8-Jun-04	Tuesday	Ceres	Wolseley	Tulbagh	
3-Mar-04	14-Apr-04	9-Jun-04	Wednesday	Robertson	Strooidak	McGregor	
4-Mar-04	15-Apr-04	10-Jun-04	Thursday	Worcester	De Dooms	Sandhills	
8-Mar-04	19-Apr-04	14-Jun-04	Monday	Worcester	Maria Pieterse	Empilisweni	
9-Mar-04	20-Apr-04	15-Jun-04	Tuesday	Ceres	Bella Vista	De Wet	
10-Mar-04	21-Apr-04	16-Jun-04	Wednesday	Robertson	PUBLIC HOLIDAY (YOUTH DAY)		
11-Mar-04	22-Apr-04	17-Jun-04	Thursday	Worcester	Villiersdorp	Bonnievale	
15-Mar-04	26-Apr-04	21-Jun-04	Monday	Worcester	Maria Pieterse	Rawsonville	
16-Mar-04	27-Apr-04	22-Jun-04	Tuesday	Ceres	Annie Brown	Nduli	
17-Mar-04	28-Apr-04	23-Jun-04	Wednesday	Robertson	Strooidak	Nkqubela	
18-Mar-04	29-Apr-04	24-Jun-04	Thursday	Worcester	De Dooms	Sandhills	
22-Mar-04	3-May-04	28-Jun-04	Monday	Worcester	Maria Pieterse	Empilisweni	
23-Mar-04	4-May-04	29-Jun-04	Tuesday	Ceres	Bella Vista	PA Hamlet	
24-Mar-04	5-May-04	30-Jun-04	Wednesday	Robertson	Victoria	Ashbury	
25-Mar-04	6-May-04	1-Jul-04	Thursday	Worcester	Villiersdorp	Breerivier	
29-Mar-04	10-May-04	5-Jul-04	Monday	Worcester	Maria Pieterse	Overhex	
30-Mar-04	11-May-04	6-Jul-04	Tuesday	Ceres	Wolseley	Tulbagh	
31-Mar-04	12-May-04	7-Jul-04	Wednesday	Robertson	Strooidak	McGregor	
1-Apr-04	13-May-04	8-Jul-04	Thursday	Worcester	De Dooms	Sandhills	
5-Apr-04	17-May-04	12-Jul-04	Monday	Worcester	Maria Pieterse	Empilisweni	
6-Apr-04	18-May-04	13-Jul-04	Tuesday	Ceres	Bella Vista	De Wet	
7-Apr-04	19-May-04	14-Jul-04	Wednesday	Robertson	CogmansKloof	Zolani	
8-Apr-04	20-May-04	15-Jul-04	Thursday	Worcester	Villiersdorp	Bonnievale	