

**ESTIMATION OF THE PREVALENCE AND INCIDENCE OF ANTIBODIES AGAINST THE -COVID-19 VIRUS
IN SOUTH AFRICA**

A two-wave cross-sectional population-based household sero-prevalence survey of COVID-19

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Background:	Since the beginning of 2020, the majority of countries in the world have been facing the global public health pandemic of coronavirus disease (COVID-19) which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). To date, very little is known internationally and nationally about the magnitude and determinants of the epidemic as prevalence is estimated mainly from confirmed cases based on polymerase chain reaction (PCR) testing for patients who have mild to serious symptoms. The proportion of asymptomatic cases in the general population is unknown and marks an important goal of the present study. In South Africa, both the incidence rate and actual prevalence of COVID-19 remain unknown. Given the large variation in the estimated proportion of SARS-CoV-2 cases that remain asymptomatic, it is important to estimate both the incidence rate and the actual prevalence of the SARS-CoV-2 virus in the South African population. Furthermore, it is also important to understand the immune responses and correlates of protection in the South African to inform herd immunity and other estimations
Purpose:	The purpose of this study is three-fold <ol style="list-style-type: none"> 1) To estimate the actual number of infected persons at a community level both nationally and in all the nine provinces in South Africa. 2) To estimate the incidence rate using an embedded cohort sub-study in the four metros with the highest reported cases of COVID-19 infections in the country 3) To investigate immune responses to COVID-19 infection in a sub-sample of the respondents.
Study Site:	Nationally representative study across randomly selected SAL's in all 9 provinces of South Africa.
Study Design:	The proposed study is a two-wave repeated cross-sectional population-based household seroprevalence survey of SARS-CoV-2 with an embedded cohort. The survey will purposefully be implemented in all nine provinces. In South Africa, provinces and districts are divided into small geographical areas called Small Area Layers (SALs) that consists of approximately 150 to 250 households in each SAL. Each of the selected provinces will be used as the primary sampling

	units. Four hundred and thirty-six SALs will be purposely targeted across all nine provinces.
Study population:	Household population – individuals aged 12 years and older
Study size:	<p>Wave 1:</p> <p>A random sample of 6,540 households from 436 SALs will realise an estimated eligible sample of 19,620 respondents, based on the assumption of an average of three people per household. Based on a 70% response rate, it is estimated that 13,734 sero-tests will be completed nationally.</p> <p>Furthermore, a random subsample of 10% of households in the 4 metros will be selected to participate in additional antibody testing.</p> <p>Wave 2:</p> <p>The same 436 SALs will be revisited nationally, but different households will be selected to participate.</p> <p>However, in the 4 metros, namely, the City of Cape Town, eThekweni, City of Johannesburg and Nelson Mandela Bay, we will have an embedded cohort. Thus the same households will be revisited.</p>
Study Duration:	All fieldwork for each of the two waves of the study will be conducted across the respective provincial SALs over a total of 16 weeks.
Study Hypothesis:	The study outcomes will inform both the incidence rate and actual prevalence of COVID-19 in South Africa and will include information on the proportion of asymptomatic cases. It will also provide information to further understand the immune responses and correlates of protection in the South African population to inform herd immunity amongst other estimations.
Primary Objective:	<p>The primary objectives are threefold:</p> <ol style="list-style-type: none"> 1) To determine the extent of SARS Cov-2 virus infection in the general population with age-specific prevalence, as determined by seropositivity; 2) To determine the proportion of asymptomatic or subclinical COVID-19 infections; 3) To determine the incidence rate of COVID-19 infections as determined by change from negative to positive serostatus in an embedded cohort of respondents in four metropolitan municipalities with the highest reported cases of COVID-19 infections in the country (viz., City of Cape Town, Nelson Mandela Bay, eThekweni, and City of Johannesburg) .
Secondary Objectives:	<ol style="list-style-type: none"> 1) To determine risk factors for COVID-19 virus infection 2) To estimate the prevalence of Covid-19 antibodies in age and sex sub-groups

	<ol style="list-style-type: none"> 3) To assess antibody levels quantitatively and neutralising antibody concentrations for future comparisons with correlates of protection for herd immunity estimations 4) To assess cytotoxic T-cell responses in a sub-group of respondents who have and do not have antibody responses, in order to identify what proportion of individuals may have been infected with SARS-CoV-2 but do not have detectable antibodies
<p>Statistical considerations:</p>	<p>The sample size of 19,620 eligible individuals to be tested from 6,540 households in 436SALs across 9 provinces and stratified by the three geographic localities (urban areas, rural formal and rural informal areas) was estimated based on the following assumptions:</p> <ol style="list-style-type: none"> 1) an expected 2% prevalence (coverage) of positive seroprevalence nationally; 2) to be measured within a minimum desired precision of 2%; 3) with 95% confidence levels and 5% level significance; 4) assuming a design effect of 4; 5) an average household size of 3 people aged 12 years and older. <p>This sample size is therefore adequately powered to also provide an estimate in the provinces, localities and areas also in the four metros. The study design and sample size calculation were adapted from the 2005 WHO EPI Vaccination Coverage Cluster Survey</p>