Social and cultural features of vaccine acceptance and cost-effectiveness of an oral cholera mass vaccination campaign in Zanzibar

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Basel, den 13. Dezember 2011

Prof. Dr. Martin Spiess
Dekan

Not everything that counts can be counted; not everything that can be counted counts.

Attributed to Albert Einstein

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SUMMARY

Worldwide, cholera was responsible for 317,534 cases and 7,543 deaths in 2010, mainly reported from Africa, South Asia and the Caribbean. The true burden of cholera is likely to be more than ten times higher since underreporting due to technical issues and political motivations is suspected.

Cholera is caused by the bacterium *Vibrio cholerae* serogroup O1 and O139, which spreads mainly through fecal contamination of water and food by infected persons. Patients develop acute watery diarrhea and vomiting. Large volumes of rice-water-like stool and concurrent loss of electrolytes can lead to severe dehydration and eventually death if patients are not rapidly treated. Treatment includes rehydration with intravenous fluids for severe cases and administration of oral rehydration solution for moderate cases. Without treatment the case-fatality rate may reach 50%.

Classical cholera control is based on prevention—safe water, sanitation and education of people on the importance of hygiene and diarrheal diseases (WASH)—health system preparedness and a timely response to provide appropriate treatment in the event of an outbreak. The World Health Organization (WHO) recommends vaccination with an oral cholera vaccine (OCV) as a supplement to WASH for prevention and control of epidemic and endemic cholera. Two killed whole-cell OCVs are currently available for public use in low- and middle income countries.

Consideration of local cultural concepts of illness among potential vaccine recipients and how these may affect vaccine acceptance is crucial. To date, no published studies have examined the influence of social and cultural features of cholera on vaccine acceptance in African settings.

Cholera is endemic on the archipelago of Zanzibar, East Africa. A collaborative research project between the WHO, the International Vaccine Institute, the Swiss Tropical and Public Health Institute, and the Ministry of Health and Social Welfare of Zanzibar (MoHSW) was launched in 2008. The project's overall goal was to reduce the burden of cholera on Zanzibar by vaccinating a target population of 50,000 residents living in cholera hotspots and by conducting studies to address key research questions that remained unanswered from an earlier OCV mass campaign in Mozambique.

The overall aims of the research presented here were to study social and cultural features of OCV acceptance and to assess the cost-effectiveness of the 2009 OCV mass campaign in Zanzibar. Findings should inform governments and ministries, in particular the MoHSW, regarding the introduction of an OCV as part of a sustainable and financially viable strategy to improve prevention and control of endemic cholera on this archipelago.

To address the first aim, the integrated-methods approach of cultural epidemiology was used to study local views of cholera-like illness and to examine their influence on OCV acceptance in endemic communities in Zanzibar before and after the mass vaccination campaign. The second aim was addressed by estimating public and private costs of illness due to cholera and costs of the OCV mass campaign to assess the cost-effectiveness of using OCVs from a health care provider and a societal perspective.

A prevaccination survey was conducted with a locally adapted semi-structured interview based on the Explanatory Model Interview Catalogue (EMIC). Vignette-based EMIC interviews assessed sociocultural features of illness, operationalized as categories of distress, perceived causes, self treatment and help seeking outside the household. A random sample of 356 unaffected adults from a periurban and a rural community was interviewed. This descriptive study showed that cholera was more often recognized as serious illness that may be fatal without appropriate treatment than shigellosis. Features of distress were primarily related to the negative social and financial impact cholera can have on a patient's life. Interference with work- or income-related activities was the most prominent category of distress. The most prominent somatic symptoms were related to dehydration and to general gastrointestinal features. Cholera was mainly attributed to a dirty environment and microbiological contamination while causes unrelated to the biomedical basis were also identified, but with less prominence. Even though rehydration of the patient (primarily in the periurban community) and use of herbal treatment and antibiotics (rural community) were the preferred self-treatment options, professional health facilities were universally recommended at both sites. This survey showed that cholera represented a significant perceived illness burden in periurban and rural Zanzibar.

Subsequent analysis showed that community willingness for a free OCV was almost universal (94%), but declined with increasing price to 61% if the OCV was offered at a low price (~USD 0.9), to 19% if offered at a medium price (~USD 4.5) and to 15% if offered at a high price (~USD 9). Logistic regression models including somatic symptoms (low and high price), social impact (low and medium price) and perceived causes (medium and high price) explained anticipated OCV acceptance better than models containing only sociodemographic characteristics. This showed that prevaccination assessments of community demand for OCV should not only

consider the social epidemiology, but also examine local sociocultural features of cholera-like illness.

Since only 50% of the interviewed respondents had drunk two doses of the free OCV—with higher priority in the rural (59%) than in the periurban (41%) community ($p<0.01$)—study of social and cultural determinants of OCV uptake was deemed necessary. Similar to the previous study of determinants of anticipated OCV acceptance, this study showed that consideration of sociocultural features of illness explained uptake better than a purely social epidemiological analysis. Loss of appetite and nausea, both nonspecific features of cholera were negative determinants. Recognition of unconsciousness as a sign of serious dehydration and concern that cholera outbreaks could negatively impact the local health care system in the rural area were positive determinants of acceptance. Female gender, rural residence and older age were also positive determinants of OCV uptake.

A sample of 367 vaccinated and unvaccinated adults from the same two communities was studied in a postvaccination survey with a revised EMIC interview. Factors associated with uptake indicated a positive impact of the vaccination campaign and of sensitization activities on vaccine acceptance behaviour. Analysis of barriers among unvaccinated people identified logistical issues as main reasons for the low community coverage, with people's own busy daily schedules as the most prominent feature. Unlike communities opposed to cholera control or in settings where public confidence in vaccines is lacking, this study indicated a good campaign implementation and trust in the health system.

The incremental cost-effectiveness ratio (ICER) of USD 119,339 per disability-adjusted life-year averted exceeded three times the Tanzanian per capita gross domestic product; thus, use of OCVs was not considered a cost-effective strategy in comparison to the current practice based on decentralized cholera treatment centers in Zanzibar. This was probably due to the expensive OCV (Dukoral® was purchased at a price of USD 10.28 per course) and use of it in a relatively low incidence setting (mean annual incidence was 0.65 per 1,000 population).

In conclusion, the research presented here suggests little community opposition to vaccination and good prospects to use OCVs for endemic cholera control in Zanzibar. Future campaigns should offer OCVs at no cost, be announced a few months before vaccination posts open, extend hours and days for improved access and concentrate efforts among young adults, periurban areas, and men. Information material for community sensitization and mobilization for a campaign should emphasize that cholera causes severe dehydration and highlight the value of vaccination for prevention rather than antibiotics for treatment. The usually mild side effects of

OCVs should also be better explained to maintain or improve community coverage. From an economic perspective, prospects to use OCV mass campaigns under current conditions seem to be limited. However, at a subsidized purchase price and subsidized delivery costs of ~USD 1 each per immunized individual, OCV mass campaigns may become economically and financially feasible for cholera control in high-incidence areas of Zanzibar.

ZUSAMMENFASSUNG

Im Jahr 2010 wurden weltweit 317'534 Krankheits- und 7'543 Todesfälle wegen Cholera gemeldet, wobei vor allem Länder in Afrika, Südasien und der Karibik betroffen waren. Dies ist jedoch nur die offizielle Statistik. Aufgrund von technischen Unzulänglichkeiten und politischen Motiven muss von einer mehr als zehnfach erhöhten Fall- und Todeszahl ausgegangen werden.

Cholera wird durch das Bakterium *Vibrio cholerae* (Serogruppen O1 und O139) verursacht. Die Übertragung geschieht hauptsächlich durch fäkale Kontamination von Wasser und Esswaren durch infizierte Personen. Cholera verursacht beim Patienten akuten, wässrigen Durchfall und Erbrechen. Grosse Mengen an Stuhl, der Reiswasser ähnlich sieht, mit gleichzeitigem Verlust von Elektrolyten, können zu schwerer Dehydratation und schliesslich zum Tod führen, wenn die Patienten nicht schnell behandelt werden. Die Behandlung besteht aus intravenöser Rehydratation bei schweren Fällen; bei milderen Fällen genügt oft die Gabe von oralen Rehydratations-Lösungen. Ohne Behandlung kann die Letalität 50% erreichen.

Die herkömmliche Cholerabekämpfung beruht auf Prävention – Bereitstellung von sauberem Wasser, einer sanitären Infrastruktur und Aufklärung über Hygiene und Durchfallkrankheiten – und einem Gesundheitssystem, das bereit ist, im Falle eines Ausbruchs rechtzeitig mit einer adäquaten Behandlungsstrategie zu reagieren. Die Weltgesundheitsorganisation (WHO) empfiehlt deshalb Schluckimpfungen gegen Cholera (*Oral Cholera Vaccines*, OCVs) als Ergänzung zur herkömmlichen Prävention bei der Bekämpfung von epidemischer und endemischer Cholera. Zurzeit sind zwei auf inaktivierten Bakterien beruhende OCVs erhältlich, die für den Gebrauch in Ländern mit niedrigen und mittleren Einkommen zugelassen sind.

Lokale kulturelle Sichtweisen zum Kranksein können sich bei potentiellen Impfempfängern auf die Impfakzeptanz auswirken. Bislang wurden aber noch keine Artikel über Studien publiziert, die den Einfluss sozialer und kultureller Merkmale hinsichtlich der Impfakzeptanz im afrikanischen Kontext studiert haben.

Cholera ist endemisch auf dem ostafrikanischen Archipel Sansibar. Im Jahr 2008 wurde ein Forschungsprojekt zwischen der WHO, dem Internationalen Impfinstitut, dem Schweizerischen Tropen- und Public Health-Institut und dem Ministerium für Gesundheit und Wohlfahrt von Sansibar (MoHSW) gestartet. Ziel dieses Projekts war die Reduktion der Cholerafälle mittels

einer Impfkampagne; es war geplant, 50'000 Bewohner in Gegenden, die als Cholera-Hotspots bekannt sind, zu impfen. Dazu wurden Studien durchgeführt, um wichtige Fragen zur Forschung, die nach einer früheren Massen-Impfkampagne in Mosambik offen geblieben waren, weiter zu bearbeiten.

Die Hauptziele der hier präsentierten Arbeit bestanden darin, soziale und kulturelle Merkmale zur Akzeptanz von OCVs in der lokalen Bevölkerung zu untersuchen und die Kosten-Effektivität der 2009 in Sansibar durchgeführten Massen-Impfkampagne zu beurteilen. Die Ergebnisse sollen dazu dienen, Regierungen und Ministerien, insbesondere aber das MoHSW, über die Einführung von OCVs als Teil einer nachhaltigen und finanziell tragfähigen Strategie zur Prävention und Bekämpfung von endemischer Cholera auf dem Archipel zu informieren.

Zur Bearbeitung des ersten Ziels wurden lokale Sichtweisen zu Cholera-ähnlichen Erkrankungen in endemischen Gemeinden in Sansibar vor und nach der Massen-Impfkampagne untersucht, um deren Einfluss auf die Akzeptanz von OCVs abzuschätzen. Dazu wurde der auf integrativen Methoden beruhende Forschungsansatz der Kulturellen Epidemiologie verwendet. Als zweites Ziel wurde die Kosten-Effektivität von OCVs aus Sicht des öffentlichen Gesundheitswesens und aus gesellschaftlicher Perspektive abgeschätzt. Dazu wurden durch Cholera verursachte Behandlungskosten für die öffentliche Hand und die Betroffenen und die Kosten der Massen-Impfkampagne erhoben.

Zuerst wurde eine Umfrage mit einem auf die lokalen Verhältnisse angepassten halbstrukturierten Interview, basierend auf dem *Explanantory Model Interview Catalogue* (EMIC), durchgeführt. Mit Vignetten eingeführte EMIC-Interviews wurden für die Erhebung der lokal relevanten soziokulturellen Merkmale von Cholera eingesetzt. EMIC-Interviews untersuchten Kategorien im Bezug auf Krankheitserfahrungen, deren wahrgenommenen Ursachen, und Behandlungsoptionen inner- und ausserhalb des Haushalts. Es wurde eine Zufalls-Stichprobe von 356 nicht von Cholera betroffenen Erwachsenen aus einer periurbanen und einer ländlichen Gemeinde interviewt. Diese deskriptive Studie zeigte, dass Cholera häufiger als Shigellose als schwere Krankheit, die ohne angemessene Behandlung tödlich sein kann, eingeschätzt wurde. Die negativen sozialen und finanziellen Auswirkungen einer Choleraepisode auf das Leben eines Menschen wurden als Hauptmerkmale dieser Erkrankung identifiziert. Darunter wurde die Beeinträchtigung von Arbeits- oder Einkommens-relevanten Tätigkeiten als grösstes Problem angesehen. Als prominenteste somatische Symptome wurden solche, die auf Dehydratation und allgemeine Magen-Darm-Infektionen hinwiesen, genannt. Cholera wurde vor allem im Zusammenhang mit einer schmutzigen Umgebung und mit mikrobiologischer Kontamination gesehen; Ursachen ohne schulmedizinischen Hintergrund

wurden auch genannt, jedoch mit weniger Priorität. Obwohl Rehydratation (vor allem in der periurbanen Gemeinde) und pflanzenmedizinische Behandlungen und der Gebrauch von Antibiotika (ländliche Gemeinde) bevorzugte Optionen für die Behandlung zu Hause waren, wurden öffentlichen Gesundheitseinrichtungen von jeder interviewten Person empfohlen. Die Umfrage ergab, dass Cholera im periurbanen und ländlichen Sansibar als eine signifikante Krankheitsbelastung wahrgenommen wird.

Eine an diese Untersuchung anschliessende Analyse zeigte eine fast universelle Bereitschaft der lokalen Bevölkerung zum Empfang einer kostenlosen Schluckimpfung gegen Cholera (94%). Diese Rate sank jedoch auf 61% ab, wenn der OCV zu einem niedrigen Preis von ~USD 0.9 angeboten wurde. Bei einem mittlerem Preis von ~USD 4.5 waren noch 19% und bei einem hohen Preis von ~USD 9 noch 15% der Befragten bereit für die Impfung. Logistische Regressionsmodelle, die somatische Symptome (bei niedrigem und hohem Preis), soziale Auswirkungen (niedriger und mittlerer Preis) und lokal wahrgenommene Ursachen (mittlerer und hoher Preis) untersuchten, erklärten die Impfabsicht besser als Modelle, die nur soziodemographische Merkmale beinhalteten. Diese Ergebnisse zeigten, dass sich Nachfrageabschätzungen bezüglich OCV in der lokalen Bevölkerung nicht nur auf die Sozialepidemiologie abstützen sollten, sondern auch lokal relevante soziokulturelle Merkmale von Cholera-ähnlicher Erkrankung in Betracht gezogen werden müssen.

Da nur 50% der befragten Personen die benötigten zwei Dosen des gratis angebotenen OCVs – mit höherem Anteil in der ländlichen (59%) verglichen mit der periurbanen (41%) Gemeinde ($p<0.01$) – getrunken hatten, wurde eine Untersuchung der sozialen und kulturellen Determinanten der Impfakzeptanz als notwendig erachtet. Ähnlich wie bei der vorangegangenen Studie wurde hier aufgezeigt, dass eine Berücksichtigung soziokultureller Krankheitsmerkmale die Impfakzeptanz besser erklären kann, als eine rein sozialepidemiologische Analyse. Appetitlosigkeit und Übelkeit, beides nicht Cholera-spezifische Merkmale, wurden als negative Determinanten identifiziert. Die Wahrnehmung, dass Bewusstlosigkeit als ein ernstes Zeichen von Dehydratation gilt, und die Sorge, dass sich Choleraausbrüche negativ auf die lokale Gesundheitsversorgung in den ländlichen Gegenden auswirken könnten, waren positive Determinanten der Impfakzeptanz. Weibliches Geschlecht, ländliches Umfeld und zunehmendes Alter waren auch positive Determinanten der Impfakzeptanz.

Nach der Impfkampagne wurde eine zweite Zufalls-Stichprobe aus den gleichen zwei Gemeinden der ersten Umfrage gezogen. Es wurden 367 geimpfte und nicht geimpfte Erwachsene mit einem überarbeiteten EMIC-Interview befragt. Faktoren, die mit

Impfakzeptanz assoziiert waren, zeigten eine positive Auswirkung der Impfkampagne und der Sensibilisierungsaktivitäten auf das Impfverhalten. Logistische Probleme, vor allem im Zusammenhang mit täglichen Aktivitäten, wurden als Haupthürden für die tiefe Durchimpfungsrate identifiziert. Im Gegensatz zu Bevölkerungsgruppen, die in Opposition zur staatlichen Cholerabekämpfung stehen, oder wo das Vertrauen der Öffentlichkeit in Impfstoffe fehlt, zeigte diese Studie eine gute Umsetzung der Massen-Impfkampagne und Vertrauen der lokalen Bevölkerung in das Gesundheitssystem.

Das inkrementelle Kosten-Effektivitäts-Verhältnis (ICER) von USD 119'339 pro abgewendetes behinderungsbereinigtes Lebensjahr betrug mehr als dreimal so viel wie das tansanische Pro-Kopf-Bruttoinlandprodukt; somit kann die Verwendung von OCVs in Sansibar nicht als wirtschaftliche Strategie angesehen werden im Vergleich zur derzeitigen Praxis, welche auf dezentralen Cholera-Behandlungszentren beruht. Als Hauptgründe sind wahrscheinlich der hohe Einkaufskaufpreis (Dukoral® wurde zu einem Preis von USD 10.28 pro Person beschafft) und die relativ niedrige Cholerainzidenz (die mittlere jährliche Inzidenz betrug 0.65 pro 1'000 Personen) zu nennen.

Fazit: die hier vorgestellte Forschung hat gezeigt, dass in der Bevölkerung wenig Opposition gegen Impfungen besteht und dass die Aussichten für den Einsatz von OCVs zur Bekämpfung von endemischer Cholera in Sansibar gut sind. Zukünftige Kampagnen sollten OCVs kostenlos anbieten. Dazu sollten sie mindesten einige Monate im Voraus, bevor die Impfposten öffnen, angekündigt werden. Für einen verbesserten Zugang sollte die Anzahl Tage und Stunden, an denen die Impfposten offen sind, verlängert werden. Besonders im Fokus der Anstrengungen sollten junge Erwachsene, periurbanen Gebiete, und Männer sein. Informationsmaterial zur Sensibilisierung und Mobilisierung der Bevölkerung vor einer Impfkampagne sollte insbesondere das Dehydratations-Potenzial von Cholera betonen und den Wert von Impfungen für die Prävention, anstelle von Antibiotika für die Behandlung, unterstreichen. Die hauptsächlich milden Nebenwirkungen von OCVs sollten noch besser erklärt werden, um die Durchimpfungsrate der Bevölkerung aufrechtzuerhalten oder weiter anzuheben. Aus wirtschaftlicher Sicht scheinen die Aussichten auf Massen-Impfkampagnen unter den gegenwärtigen Bedingungen noch begrenzt zu sein. Jedoch könnten ein subventionierter Impfstoffeinkaufspreis und Verimpfungskosten von je ~USD 1 pro Impfling dazu beitragen, dass die Cholerabekämpfung mittels Massen-Impfkampagnen in Sansibar in Gebieten mit hoher Inzidenz wirtschaftlich und finanziell machbar wird.

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Kipindupindu kilikuwa chanzo cha matukio 317,534 na vifo 7, 543 kwa mwaka 2010 duniani, matukio haya yaliripotiwa hasa katika nchi za Afrika, kusini mwa bara la Asia na Caribbean. Ugonjwa huu unakadiriwa kuwa mara kumi zaidi kuliko unavyotazamiwa na hii ni kutokana na kwamba matukio haya yamekuwa yanatolewa taarifa kwa kiwango cha chini kutokana na sababu zinazodhaniwa kuwa ni za kiufundi na motisha za kisiasa.

Kipindipindu kinasababishwa na bakteria aitwae *Vibrio cholerae* serogroup O1 na O139, na kinaenezwa hasa na mtu aliyeathirika kupitia chakula na maji vilivyochanganyika na kinyesi. Wagonjwa hutokewa na tatizo sugu la kuharisha maji maji na kutapika. Choo kinachoshabihiana na maji ya mchele kwa wingi pamoja na upungufu wa elekroliti vinaweza kusababisha upungufu mkubwa wa maji mwili na hatimaye kifo iwapo wagonjwa hawatapata tiba ya haraka. Matibabu yake ni pamoja na kuongezewa maji mwilini hasa kwa wagonjwa walio kwenye hali mbaya zaidi na wagonjwa walio katika hali ya kawaida hupatiwa maji au dawa ya kunywa maalum kwa tatizo hilo. Bila matibabu, kiwango cha matukio ya vifo kinaweza kufikia asilimia 50.

Mikakati ya kisasa ya kudhibiti kipindupindu imelenga katika uzuiaji- maji salama, usafi wa mazingira na kuelimisha watu juu ya umuhimu wa usafi na magonjwa ya kuharisha (hii inajulikana zaidi kwa Kingeraza kawa WASH ikimaanisha, Water, Sanitation and Hygiene na Kiswahili kama Maji, Usafi wa mazingira na Usafi), Utayari wa mfumo wa afya na uwajibikaji wa kutoa matibabu kwa wakati muafaka katika tukio la mlipuko. Shirika la Afya duniani (WHO) linapendekeza chanjo ya kipindupindu kwa njia ya matone ijulikanayo kwa Kingereza kama *Oral Cholera Vaccine* (OCV) kama mbadala wa mkakati wa kisasa ujulikano kama WASH unaolenga katika uzuiaji na udhibiti wa maradhi na usugu wa magonjwa ya kipindupindu. Chanjo ya kipindupindu ijulikanayo kama *Two killed whole-cell OCVs* inapatikana kwa ajili ya matumizi ya umma katika nchi zenye kipato cha chini na kati.

Uzingatiaji wa dhana za magonjwa za kiutamaduni ndani ya sehemu husika na hasa kwa wapokeaji wa chanjo na jinsi gani zinaweza kuathiri ukubalikaji wa chanjo kwa jamii ni suala muhimu. Hadi sasa, hakuna matokeo ya utafiti yaliyochapishwa katika majarida ya kisayansi yanayoelezea ushawishi wa vipengele vya kijamii na kiutamaduni vya kipindupindu juu ya ukubalikaji wa chanjo ya kipindupindu katika mazingira ya Afrika.

Kipindupindu kimeenea zaidi katika kisiwa cha Zanzibar, Afrika Mashariki. Ushirikiano kati ya mradi wa utafiti wa Shirika la Afya Duniani (WHO), Taasisi ya Kimataifa ya Chanjo na Wizara ya Afya na Ustawi wa Jamii ya Zanzibar (MoHSW) ulizinduliwa mwaka 2008. Lengo kuu la mradi ilikuwa ni kupunguza tatizo la kipindupindu Zanzibar, kwa kutoa chanjo kwa wakazi 50,000 wanaoishi maeneo yenye kipindupindu na kwa kufanya utafiti ili kujibu maswali muhimu ya utafiti ambayo yalikaa bila kuwa na majibu tokea kampeni umma za mwanzo za chanjo ya kipindupindu ya matone (OCV) zilizofanyika nchini Msumbiji.

Malengo ya jumla ya utafiti huu ilikuwa ni kutafiti vipengele vya kijamii na kiutamaduni vinavyohusiana na ukubalikaji wa chanjo ya kipindupindu ya matone na kutathmini gharama fanisi za kampeni ya umma ya chanjo ya matone ya mwaka 2009 kisiwani Zanzibar. Matokeo ya utafiti huu yanalenga kuipa taarifa serikali na wizara, hususani Wizara ya Afya na Ustawi wa Jamii (MoHSW), kuhusu kuanzishwa kwa chanjo ya kipindupindu ya matone kama sehemu ya mkakati endelevu na wa kifedha, juu ya faida ya kuboresha kinga na udhibiti wa kipindipindu katika kisiwa hiki kilichoenea tatizo hilo.

Kuelezea lengo la kwanza, mfumo wa njia za pamoja unaochanganua vipengele vya kitamaduni vya matukio ya magonjwa ulitumika kujifunza maoni ya jamii juu ya magonjwa yanayoendana na kipindupindu na kuchunguza ushawishi wake juu ya ukubalikaji wa chanjo ya matone ya kipindipindu katika jamii zilizoenea na tatizo hili kisiwani Zanzibar, kabla na baada ya kampeni umma ya chanjo. Lengo la pili lilielezewa kwa kukadiria gharama za umma na gharama binafsi za ugonjwa zinazotokana na kipindupindu, gharama za kampeni ya umma ya chanjo ya matone ya kipindupindu pamoja na gharama fanisi ya kutumia chanjo ya matone ya kipindupindu kutoka kwa mtoa huduma wa afya na mtazamo wa jamii kwa ujumla.

Utafiti kabla ya chanzo ulifanyika kwa kutumia zana ya utafiti iliyorakabishiwa kutokana na mazingira halisi, zana hii ilitokana na mahojiano yanayolenga kupata maelezo ya kina ya mgoinjwa kuhusu ugonjwa wake inayojulikana kwa Kingereza kama *Explanatory Model Interview Catalogue*. Pia mahojiano kwa kutumia njia ya kulezea tatizo la mtu na kusubiri wahojiwa wajibu wangefanya nini ilitumika kutathmini vipengele jamii-tamaduni vya ugonjwa, vinavyotumika na kuelezewa kama dalili, chanzo, tiba binafsi na utafutaji wa matibabu nje ya kaya. Jumla ya watu 356 wasioathirika na kipindupindu walihojiwa, watu hawa walichaguliwa bila utaratibu maalum kutoka jamii za miji midogo na vijijini. Utafiti huu ulionyesha kuwa kipindupindu kilichukuliwa na jamii kama ugonjwa hatari unaoweza kusababisha kifo pasipokuwa na tiba sahihi kuliko magonjwa mengine ya tumbo na kuhara. Vipengele vya dhiki vilihusiana zaidi na madhara hasi ya kijamii na kifedha ambayo kipindupindu kinaweza

kusababisa kwa maisha ya mgonjwa. Muingiliano wa shughuli za kikazi au kipato ilionekana kuwa tatizo kubwa wakati wa ugonjwa. Dalili kuu zilihusiana zaidi na kuishiwa maji mwilini na matatizo yanayohusiana na tumbo. Kipindipindu kilihusishwa zaidi ya uchafu wa mazingira na maambukizo ya mikorobiojia wakati sababu za msingi zisizohusiana na kitabibu pia zilitajwa ingawa zilipewa umuhimu kidogo zaidi. Pamoja na kwamba uongezewaji wa maji mwilini (hasa kwa jamii za miji midogo) na utumiaji wa tiba za kiasili na dawa za vijiua sumu (kwa jamii za vijijini) zilipendelewa zaidi kama tiba binafsi, vituo vya afya vilipendekezwa zaidi katika maeneo yote mawili. Utafiti huu ulionyesha kuwa kipindupindu kinasimama kama ugonjwa muhimu na tatizo katika jamii za miji midogo na Zanzibar vijijini.

Uchambuzi wa utafiti ulionyesha ukubalikaji kwa asilimia 94 wa chanjo ya kipindupindu ya matone inayotolewa bure, lakini asilimia hii ilipungua kufikia 61 iwapo bei ya chanjo ingeongezeka, kama chanjo hii ingetolewa kwa bei ndogo (dola ya kimarekani 0.9), mpaka asilimia 19 iwapo itatolewa kwa bei ya kati (dola za kimarekani 4.5) na mpaka asilimia 15 kama itatolewa kwa bei ya juu (dola za kimarekani 9). Mahesabu ya uwezekano wa kutokea matokeo fulani ikiwemo dalili (bei ya chini na juu), madhara ya kijamii (bei ya chini na ya kati) na sababu zinazofikiriwa (bei ya kati na juu) yalielezea matarajio ya ukubalikaji wa chanjo ya matone ya kipindupindu vizuri zaidi kuliko mahesabu yaliyohusisha sifa ya kijamii kuhusiana na idadi ya watu. Hii ilionyesha kuwa tathmini ya mahitaji ya jamii kabla ya chanjo haipaswi kuzingatia tu matukio ya afya jamii lakini pia kuchunguza vipengele vya jamii na tamaduni vya magonjwa yanayoshabihiana na kipindupindu.

Kwa vile ni asilimia 50 tu ya watu waliohojiwa walishakunywa dozi mbili ya chanjo ya matone ya kipindupindu iliyotolewa bure, iliyopata kipaumbele hasa katika maeneo ya vijijini (asilimia 59) kuliko miji midogo (asilimia 41) ($p<0.01$), ilkuwa ni muhimu kufanya utafiti unaoangalia ni kwa jinsi gani vigezo vya kijamii na kitamaduni vinavyoweza kuchangia upokelewaji wa chanjo hii. Kama ilivyokuwa kwa utafiti wa awali ulioangalia mchango wa vigezo vilivyopelekea ukubalikaji wa chanjo hii, utafiti huu umeonyesha kwamba mchango wa vigezo vya kijamii na kitamaduni kuhusu magonjwa, vilielezea vizuri upoekelewaji wa chanjo kuliko uchambuzi wa kijamii wa matukio ya magonjwa. Kupoteza hamu ya kula na kichefuchefu vilikuwa vigezo hasi ambavyo havikuambatana na ukubalikaji wa chanjo. Kupoteza fahamu kama ishara hatari ya kuishiwa maji mwilini na wasiwasi kuwa kipindupindi kinaweza kuathiri vibaya mfumo wa huduma za afya katika maeneo ya vijijini vilikuwa ni vigezo chanya vilivyopelekea ukubalikaji wa chanjo katika jamii. Jinsia ya kike, kuishi vijijini na umri mkubwa vilikuwa pia ni vigezo chanya vilivyopelekea ukubalikaji wa chanjo ya matone ya kipindupindu.

Idadi ya watu wazima 367 waliochanjwa na wasiochanjwa kutoka katika jamii mbili zinazoshabihiana, walifanyiwa utafiti katika zoezi lililofanyika baada ya shughuli ya chanjo kuisha, watu hawa walifanyiwa mahojiano kwa kutumia hojaji iliyorakabishiwa kutokana na mazingira halisi, ijulikanayo kwa Kingereza kama *Explanatory Model Interview Catalogue*. Mambo yanayohusiana na upokelewaji wa chanjo yalionyesha matokeo mazuri ya kampeni ya chanjo na shughuli za uhamasishaji wa chanjo sababu zilizopelekea ukubalikaji wa chanjo kwa jamii. Uchambuzi wa vikwazo kwa wale ambao hawakupata chanjo ulionyesha shughuli rasilimali kama sababu ya watu wengi kutokupata chanjo, hasa shughuli za binadamu ya kila siku. Tofauti na jamii ambazo zilikuwa kinyume na udhibiti wa kipindipindu au maeneo amabapo wanajamii walishindwa kujiamini kuhusu chanjo, utafiti huu ulionyesha utekelezaji mzuri wa kampeni ya chanjo na imani katika mfumo mzima wa afya.

Kwa sababu gharama fanisi zilizoongezeka kwa uwiano wa dola za kimarekani 119,339 kwa makadirio ya janga la magonjwa, hii ilikuwa zaidi ya mara tatu kwa mtanzania kulingana na pato la ndani, matumizi ya chanjo ya matone ya kipindupindu hayakuchukuliwa kama mkakati wa gharama nafuu kulinganisha na shughuli za kawaida za tiba katika vituo vya tiba za kipindupindu. Pengine hii ilitokana na matumizi ghali ya chanjo ya matone ya kipindupindu (Dukoral® ilinunuliwa kwa dola za kimarekani 10.28 kwa dozi) katika mazingira yaliyokuwa na matukio machache ya ugonjwa (wastani wa matukio kwa mwaka ilikuwa 0.65 kwa kila watu 1,000)

Kwa kuhitimisha, utafiti huu unaonyesha kuwa jamii ilipinga chanjo ya kipindipindu kwa kiasi kidogo, wakati huo huo unaonyesha matarajio mazuri ya kutumika kwa chanjo hii kudhibiti kipindupindu katika maeneo yenye tatizo hili kisiwani Zanzibar. Kampeni za baadae zinapaswa kutoa chanjo ya matone ya kipindupindu bila gharama yoyote, itangazwe miezi michache kabla ya kufunguliwa vituo vya chanjo, masaa na siku za chanjo ziongezwe kuboresha upatikanaji wa chanjo na nguvu ziongezwe hasa kwa vijana, watu wazima, wanaume na pia katika maeneo ya miji midogo. Elimu inatakiwa kusisitiza kuwa kipindupindu kinasababisha upungufu hatari wa maji mwilini na kuongeza mkazo juu ya umuhimu wa chanjo kwa ajili ya kujikinga na maambukizi kuliko utumiaji wa dawa za viua sumu kama tiba. Madhara ya kawaida ya chanjo ya matone ya kipindupindu yanatakiwa yaelezwe kwa kina kwa wanajamii ili kuboresha ukubalikaji wa chanjo. Kwa mtazamo wa kiuchumi na kulingana na hali halisi, matarajio ya matumizi ya kampeni za chanjo ya matone ya kipindupindu yanaonekana kuwa madogo. Hata hivyo kwa bei ya ruzuku na gharama za utoaji ruzuku ya dola ya kimarekani moja, kwa kila chanjo, kampeni za chanjo ya matone ya kipindupindu zinaweza kuwa yakinifu kiuchumi na kifedha kwa ajili ya kudhibiti kipindupindu kwenye maeneo yenye matukio zaidi ya kipindupindu kisiwani Zanzibar.

ABBREVIATIONS

AICc	Akaike Information Criterion, corrected for finite sample size
BCE	Before Common Era
CE	Cost-Effectiveness
CEA	Cost-Effectiveness Analysis
CFR	Case-Fatality Rate
CI	Confidence Interval
COI	Costs of Illness
CT A (or B)	Cholera Toxin A (or B) subunit
CTC	Cholera Treatment Center
DALY	Disability-Adjusted Life-Year
DANIDA	Danish International Development Agency
DHMT	District Health Management Team
DOMI	Disease of the Most Impoverished Program
DRC	Democratic Republic of Congo
EKBB	Ethics Committee of Basel, Switzerland
EMIC	Explanatory Model Interview Catalogue
EPI	Expanded Program on Immunization
EU	European Union
GDP	Gross Domestic Product
ICDDR,B	International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh
ICER	Incremental Cost-Effectiveness Ratio
IQR	Interquartile Range
IV	Intravenous
IVI	International Vaccine Institute, Seoul, Korea
MoHSW	Ministry of Health and Social Welfare, Zanzibar, United Republic of Tanzania
NGO	Non-Governmental Organization
OCV(s)	Oral Cholera Vaccine(s)
ORS/T	Oral Rehydration Solution/Therapy
OTC	Over-The-Counter (Drugs)
PAHO	Pan American Health Organization
PE	Protective Efficacy
PHCC	Primary Health Care Center

PHCU	Primary Health Care Unit
PHL	Public Health Laboratory, Chake-Chake, Pemba, United Republic of Tanzania
SAGE	Strategic Advisory Group of Experts on Immunization to the WHO
SEB	Socioeconomic and Behavioral study
Swiss TPH	Swiss Tropical and Public Health Institute, Basel, Switzerland
TZS	Tanzania Shilling (Tanzanian Currency)
UK	United Kingdom
UN	United Nations
UNICEF	United Nations Children's Fund
USA	United States of America
USD	United States of America Dollar (U.S. Currency)
V. cholerae O1	*Vibrio cholerae* serogroup O1
V. cholerae O139	*Vibrio cholerae* serogroup O139
WASH	Provision of Safe Water, Sanitation and Hygiene Education
WC-rCT B	Whole-Cell killed OCV with recombinant CT B
WHO	World Health Organization, Geneva, Switzerland
YLD	Years of Life Lived with Disability
YLL	Years of Life Lost
ZMO	Zonal Medical Officer

LIST OF FIGURES, TABLES AND TEXT BOXES

1

INTRODUCTION

1.1 Cholera: an old scourge still raging today

Cholera is a disease that has affected humans since antiquity. Although its origins are not known, Sanskrit texts describe the presence of an acute form of diarrhea with cholera-like symptoms in South Asia, especially in the Ganges Delta, since at least the fifth century BCE [1]. The disease was first documented in 1817 in what was later to be defined as the first pandemic, affecting not only the Indian subcontinent but also other parts of Asia, eastern Africa, the Indian Ocean islands and even present-day Armenia. The reasons why cholera became an international menace after being rather geographically confined for many centuries remains unclear until today. According to Echenberg [1], extreme climate change following the eruption of the volcano Mount Tambora in Indonesia in 1815 might have been a factor together with political change as "the first modern cholera pandemic coincided with the beginning of a new era in world history: the economic transformation of the world system [...] after Britain led a European alliance to defeat France in 1815 [and] people's lives everywhere were changed by the economic reordering of their societies." (p. 15) Cholera's spread throughout the modern world was greatly increased by global trade driven by colonial powers (e.g., the British East India Company in South Asia) as well as accompanying warfare. Five pandemics followed after 1817[1] up to the seventh pandemic, which began in 1961 in Indonesia and then spread to India in 1964, Africa and Southern Europe in 1970 and South America in 1991 [2]. Cholera now affects populations across the entire globe.

In 1884 the German scientist Robert Koch identified the bacterium *Vibrio cholerae* as the cause of the disease [3,4]; however, risk factors for cholera had been identified more than 30 years earlier by John Snow in his seminal epidemiological study on London's Broad Street pump cholera outbreak [5]. Snow referred to a "cholera poison" in water contaminated by effluents from a nearby sewer and vigorously advocated for boiling water as a means of protection against

[1]First pandemic: 1817-1826, second: 1828-1836, third: 1839-1861, fourth: 1863-1879, fifth: 1881-1896, sixth: 1899-1947 [1]

the illness [6]. Since the first pandemic, cholera has become widely feared, mainly due to the speed with which it can spread and escalate mortality in vulnerable populations.

In response to the second and third pandemics, which affected many countries across the globe including in Europe, several countries convened in 1851 in Paris for the first *International Sanitary Conference* to reach an international agreement on the standardization of quarantine regulations to prevent the importation of cholera (in addition to plague and yellow fever) [7]. A series of conferences followed thereafter aimed at limiting the epidemic, eventually leading to the establishment of the World Health Organization (WHO) in 1948. Although it was removed from the International Health Regulations in 1973 [8], cholera remains *politically stigmatized* today. Cases are systematically underreported to the WHO or are termed as *acute watery diarrhea* by certain authorities that wish to keep a low profile on cholera [9].

Zanzibar was likely the first region in sub-Saharan Africa to be affected by cholera in the modern age [1]. This East African archipelago was an easy target for cholera due to its links with Oman[2] and the Indian Ocean trade system. It is believed that cholera reached Zanzibar as early as 1821; but this assumption is not verified by historical documentation. However, it is known that pilgrims returning in 1836 from Mecca brought cholera to Somalia, from where dhows, engaged in the East African coastal trade, transported cholera to Zanzibar and further down the coast to Mozambique [1]. The impact of the epidemics in Europe was indeed considerable[3] but in Africa, they were catastrophic. During the fourth pandemic, for example, an outbreak affected not just poor people or slaves, but also French elites, and reportedly took the lives of 10% of the population of Zanzibar island (Text box 1-1).

CHOLERA EPIDEMIC IN ZANZIBAR.

TOWARDS the end of last November, the cholera which had been prevailing in the central parts of Africa was carried down to the eastern coast, and was thence conveyed to the island of Zanzibar, and prevailed for about five or six weeks in a very fatal form, as in that time, in the town and suburbs alone, it is estimated to have caused ten thousand deaths, being about a tenth part of the population. It then ceased in the town, but continued its ravages in other parts of the island and amongst the shipping. Last March it broke out again, and from that time to the end of April it continued to prevail with more or less severity. In the beginning of May, it had nearly ceased in the island, there occurring only one or two isolated cases amongst the slaves, though it was stated to be prevailing in some of the neighbouring French settlements.

Text box 1-1: Description of a cholera outbreak in Zanzibar that literally decimated the population in 1869/1870

[2]Zanzibar was ruled by the sultans of Oman between 1698 and 1890 and was an important hub in the slave trade between the interior of Africa and the Arabian Peninsula and the Persian Gulf.

[3]A detailed overview of cholera outbreaks and related morbidity and mortality before systematic collection of data began with the seventh pandemic is given by Echenberg [1] (p. 13-85).

Despite the emergence of modern medicine and improvements in infrastructure and health education, the disease continues to wreak havoc around the world, especially in populations affected by humanitarian crisis situations. Examples abound of cholera outbreaks following natural or man-made disasters in the 20th and the 21st century [9,11]. The large outbreak that happened in a refugee camp near Goma in northeastern Democratic Republic of Congo (then Zaïre), after ~700,000 Rwandans had fled the genocide in their country in July 1994, was another stark reminder of cholera's potential for inflicting massive devastation and suffering. During this three-week period, an estimated 35,000 cases were treated for cholera-like diarrhea from July 20 to August 12, 1994, which roughly equaled the number of presumed unreported cases. This epidemic caused the loss of ~23,800 lives; the maximum case-fatality rate (CFR) for cases seen in facilities reached 22% [12].

1.2 Global cholera-related morbidity and mortality

In 2010, a total of 317,534 cases and 7,543 deaths (CFR: 2.4%) were reported by 48 countries to the WHO (Figure 1-1) [9].

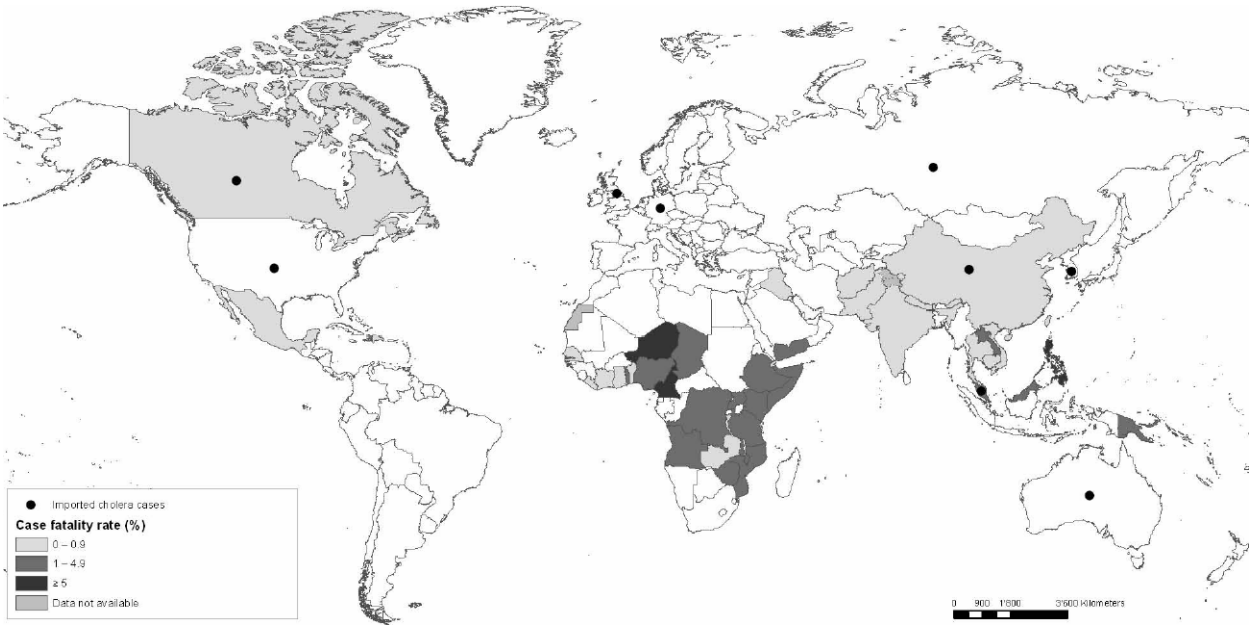

Figure 1-1: Countries reporting cholera in 2010
Source: Adapted from WHO [9]

Twenty-three of these countries are located in Africa, but the majority of cases were reported from the Caribbean island of Hispaniola. This peak was mainly due to a large outbreak that started in October 2010 in Haiti in the aftermath of the devastating earthquake that had shaken the island on January 12, 2010. Even though an increase in diarrhea-related morbidity and mortality had been anticipated following this natural disaster in Haiti, the authorities were not

prepared for a cholera outbreak as the island had been considered cholera-free for over 100 years [13].[4] As of July 10, 2011, a total of 388,958 cases and 5,899 deaths (CFR: 1.5%) have been reported from Haiti and the Dominican Republic—and the epidemic is still raging [16].

Despite this huge outbreak and an exception in the early 1990s—after *V. cholerae* O1 had hit Peru in 1991 and subsequently affected all but three Latin American countries [17]—the majority of the ~50,000 to 600,000 cases of cholera that were reported every year to the WHO over the past two decades had come from Africa (Figure 1-2) [9].

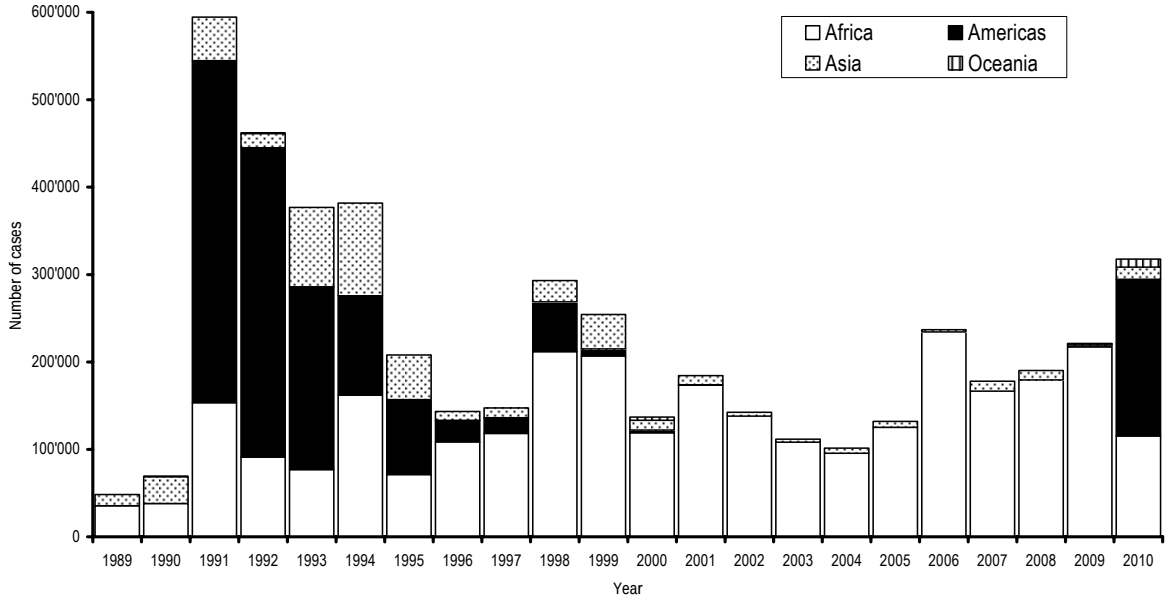

Figure 1-2: Global annual number of cholera cases reported to the WHO, by continent, 1989-2010
Source: Adapted from WHO [9]

The number of cases from Africa increased considerably from 20% in the 1970s to 94% in the years from 2000 to 2005; with Asian rates dropping from 80% to 5.2% over the same three decades [18]. A similar trend is found with regard to reported deaths: Africa's share increased from 22% to 97% and Asia's share showed a steep decline from 77% to 2.4%. Among the 32 countries that reported deaths due to cholera in 2010, 20 of them are in the Africa continent (Figure 1-1).

[4]A cholera strain originating from South Asia was later identified as the causal agent; it had inadvertently been introduced by UN peacekeepers [14]. The official UN report stated that "the evidence overwhelmingly supports the conclusion that the source of the Haiti cholera outbreak was due to contamination of the Meye Tributary of the Artibonite River with a pathogenic strain of current South Asian type *Vibrio cholerae* as a result of human activity." [15] (p. 29)

As noted above, these official figures do not reflect the true burden of cholera since serious underreporting due to technical issues (i.e., surveillance system limitations, problems with case definition and lack of standard vocabulary) and political motivations (i.e., fear of travel or trade sanctions) is suspected [9]. Zuckerman *et al.* [19] identified mainly underreporting from the Indian subcontinent and Southeast Asia in a review carried out in 2004. The WHO estimates that annual morbidity and mortality may exceed three million cases and 100,000 deaths [20].

1.3 Economic burden due to cholera

The public health importance of cholera and its micro- and macroeconomic impacts are widely recognized. However, systematic data on costs due to cholera outbreaks are still relatively scarce in the published literature.

Detailed local data about public and private costs of illness (COI) due to cholera are needed for economic evaluations to improve planning of cholera control. The first systematic study on COI was published very recently only [21]; it compared public costs of treatment and private, i.e., direct and indirect, costs borne by patients between four different cholera-endemic sites in Asia and Africa in a standardized manner. Total COI per episode of hospitalized cases amounted to 2005 USD 31.5 in Matlab, Bangladesh, USD 205.7 in North Jakarta, Indonesia,[5] USD 35.4 in Kolkata, India, and USD 47.2 in Beira, Mozambique.

For the WHO African Region,[6] Kirigia *et al.* [22] estimated that public and private COI amounted to 2002 USD 53 million in 2005, USD 128 million in 2006 and USD 60 million in 2007. At a first glance, these figures do not seem to be very substantial, but since they are based on the annual number of documented cholera cases, they are also likely to be underestimated and thus only represent the tip of the iceberg of the economic burden due to cholera. Mozambique alone, for example, reported annual costs of USD 145 million to respond to cholera outbreaks [23].

In addition to costs borne by the health system and by families in response to outbreaks, cholera can also negatively affect national economies. Even though trade sanctions are not believed to limit the spread of cholera effectively, losses due to restricted or even interrupted trade have had a significant negative impact on African economies. Based on a EU embargo to export fresh fish from Lake Victoria imposed in 1998 on Uganda, Kenya, Tanzania and Mozambique, Kimball *et*

[5]Costs were highest in Jakarta due to higher fees than in the other sites and inclusion of private treatment facilities in the study.

[6]Consisting of 46 countries, excluding Morocco, Tunis, Libya, Egypt, Sudan, South Sudan, Djibouti and Somalia (http://www.afro.who.int/en/countries.html).

al. [24] modeled the loss in trade as a percentage of total gross domestic product (GDP) and total export. They showed that the combined GDP of these four countries dropped by 1% and total export volumes by over 10%, totaling a loss in trade of ~USD 1 billion over the five-year period from 1998 to 2002. They concluded that such losses represent a significant macroeconomic burden for poor countries where fishery products are important export commodities and called "for additional resources to prevent or curtail epidemic threats in a timely way." [24] (p. 829)

1.4 Etiology and clinical features of cholera

Cholera is an intestinal disease caused by the rod-shaped gram-negative bacterium *V. cholerae* that spreads mainly through fecal contamination of water and food by infected individuals [2]. Eating raw or undercooked seafood can also cause infection since *V. cholerae* was found on phyto- and zooplankton in marine, estuarine and riverine environments independent of infected human beings [25,26]. Two out of ~240 serogroups of *V. cholerae*—O1 and O139—have shown the potential to cause outbreaks and pandemics [2]. The O1 serogroup can be divided into two biotypes, classical and El Tor, both of which can further be subdivided into two major serotypes, Ogawa and Inaba. *V. cholerae* colonizes the upper small intestine and releases an enterotoxin that is the direct cause of cholera diarrhea. The B subunit of the cholera toxin binds to the small intestine mucosa while the active A subunit interferes with the sodium and chloride transport leading to massive outpouring of water and electrolytes. Contrary to other enteropathogens like *Salmonella* spp. or *Shigella* spp. that cause diarrhea with blood or mucus and pus in stool, cholera is a non-inflammatory diarrhea since the cholera toxin only stimulates secretory processes without invading the mucosa.

After an incubation period of 18 hours to five days, infected individuals develop acute watery diarrhea. Large volumes of rice-water-like stool and concurrent loss of electrolytes can lead to severe dehydration and eventually death if patients are not rapidly treated. Most of the infected individuals, however, are asymptomatic or suffer only from mild diarrhea. An inoculum of ~10^8 bacteria is needed in healthy individuals to cause severe acute watery diarrhea while a 1,000-fold lower dose is sufficient to cause the disease when gastric acid production is reduced. Other clinical features besides profuse diarrhea (more than three loose stools per day) to establish a cholera diagnosis include abdominal and muscle cramps and frequent vomiting [20,27]. Without treatment the case-fatality rate (CFR) may reach 50% [2].

1.5 Treatment of cholera

Timely rehydration with compensation of electrolyte loss (i.e., potassium, sodium, calcium and chloride) is the mainstay of treatment. According to WHO guidelines, rehydration of cases depends on the severity of dehydration and includes (i) giving oral rehydration solutions (ORS) after each stool even if no dehydration is apparent, (ii) giving ORS in larger amounts if moderate dehydration[7] is apparent, or (iii) using intravenous drips[8] for severely dehydrated patients[9] [20,27]. Antibiotics can be administered to shorten episodes in severe cases, to diminish the amount of intravenous fluids required and to reduce shedding of *V. cholerae*. In addition to WHO guidelines, researchers have suggested that carefully timed use of antibiotics also include moderately dehydrated cases [28].

1.6 Cholera control strategies

Cholera control is based on prevention—safe water, improved sanitation and education of people on the importance of hygiene and diarrheal diseases (WASH)—health system preparedness and a timely response to provide appropriate treatment in the event of an outbreak. Recognizing that the occurrence of cholera in a specific setting is essentially a structural issue,[10] improving water supply and sanitation, i.e., making sure that bacterial contamination of drinking water is no longer possible due to a careful separation of water supply systems and sewage, would be *the* most effective solution to permanently protect a population from cholera (and also other fecal-orally transmitted waterborne diseases).

In spite of cholera's tendency to occur in outbreaks, the public health literature has been distinguishing *endemic*, i.e., based on recurrence in time and place, from *epidemic* cholera, i.e., based on relatively unpredictable occurrence in settings that have been cholera-free for some time. To better guide control strategies, the Strategic Advisory Group of Experts on Immunization to the WHO (SAGE) has recently defined endemic cholera as "the occurrence of fecal culture-confirmed cholera diarrhea in a population in at least 3 of the past 5 years." [30] (p. 526)

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[7]Two or more of the following signs have to be present: sunken eyes, absence of tears, dry mouth and tongue, patient is thirsty and drinks eagerly, skin pinch goes back slowly

[8]Ringer's Lactate, Hartmann's solution or saline

[9]In addition to the above signs, a severely dehydrated patient is lethargic, unconscious or floppy, is unable to drink, has a weak radial pulse and a skin pinch that goes back very slowly

[10]Because low- and middle-income countries are characterized by a poor or absent infrastructure, they bear the brunt of the global cholera burden [29]. Before heavy investments were made in their infrastructure, cholera had once also been endemic in today's high-income countries [1]. The few cases that are currently reported in North America or Europe have usually been imported from cholera-endemic countries (Figure 1-1).

1.6.1 From classical prevention to consideration of oral cholera vaccines as public health tool

With the advent of two promising oral cholera vaccines (OCVs),[11] the WHO for the first time recommended vaccination for cholera prevention in acute emergency situations in 1995 [11,12]. This recommendation was drafted against the background of several large outbreaks that had happened in the early 1990s. Subsequent WHO meetings of experts in 1999 [31], 2002 [23] and 2005 [32] reevaluated the evidence regarding use of OCVs in emergencies. Because of cholera's persistence after decades of promoting WASH activities, the use of OCVs in endemic settings was also recommended in 2002 [23]. Following a demonstration project in Beira, Mozambique, where feasibility and effectiveness of a mass OCV vaccination campaign in an endemic environment was shown [33,34], the WHO reinforced the role of OCVs as a supplementary measure for endemic cholera control in 2005, but requested that more research be done under field conditions to validate the findings from this project [32].

1.6.2 WHO recommendations for use of OCVs in endemic settings

Text box 1-2 summarizes the current WHO position on the use of OCVs for endemic cholera control [30]. These recommendations were proposed by SAGE in October 2009 based on a comprehensive background paper that reviewed recent evidence regarding cholera burden, epidemiology and use of OCVs [35].

Scope
Vaccination should not target the whole population, but focus on high-risk areas and populations.

Criteria for vaccination
Two out of the following criteria have to be met: (i) detection of culture-confirmed cholera in ≥ 3 of the past 5 years, (ii) incidence ≥ 1 per 1,000, (iii) in the absence of surveillance data, high-risk areas/groups have been identified by local public health officials.

Target groups
Even though all age groups are vulnerable to cholera, priority should be given to children and older age groups if resources are limited.

Vaccine delivery strategy
Periodic mass vaccination campaigns are the preferred option for delivery.

Frequency of vaccination
Booster vaccinations are recommended every second year based on the maximum duration of protection of currently available OCVs.

Text box 1-2: WHO recommendations for use of OCVs for cholera control in endemic settings

Source: SAGE [30]

[11] An earlier parenteral vaccine that was developed soon after *V. cholerae* had been detected as causative agent in the 19th century has never been recommended by the WHO for public health use due to its limited protective efficacy and considerable side effects [1,8].

Vaccination should not disrupt the provision of safe water and sanitation to prevent or contain cholera outbreaks. Vaccination should only be considered as supplement to WASH activities. Cholera control should ideally be a multisectoral approach involving different ministries and research institutes as well as local (and international) non-governmental organizations (NGOs) that coordinate activities towards improvement of structural issues (water supply and sanitation), disease surveillance and reporting, case management, food safety, and health and hygiene education.

1.7 Oral cholera vaccines

Development and production of several oral cholera vaccines started in the 1980s and led to licensure of the first OCVs in the 1990s. Two types of OCVs—based on killed whole-cells (WCs) and on live, attenuated strains—have been available in the market [9]. Until very recently only one OCV, Dukoral®, was prequalified by the WHO and thus available for public health use in low- and middle-income countries. Dukoral® was initially designed as a traveler's vaccine containing not just killed WCs, but also recombinant cholera toxin (CT) B subunit for faster protection among immunologically naïve people and because this component also provides some cross-protection against traveler's diarrhea caused by enterotoxigenic *Escherichia coli* [36]. Because this composition was not a viable option for use in low- and middle-income countries, the technology was transferred to Vietnam to manufacture a simpler and cheaper variant containing only the killed WCs. However, because the Vietnamese regulatory agency is not approved by the WHO, this OCV has never been prequalified by the WHO. Another transfer was thus made to manufacture this WC vaccine in India, where WHO prequalification is possible. The Indian OCV was licensed under the trade name of Shanchol™ in 2009 and received WHO prequalification on September 29, 2011.[12]

The main characteristics of the three currently available OCVs, and of promising candidates at different stages of development, are presented in Table 1-1. Not mentioned are several other less advanced candidates.

[12] http://www.who.int/immunization_standards/vaccine_quality/pq_250_cholera_1dose_shantha/en/index.html

Table 1-1: Main characteristics of currently available and future OCVs

Type	WC-rCT B	WC	Modified WC[a]	CVD 103-HgR[b]	Peru-15
Trade name	Dukoral®	Shanchol™	mORC-Vax®	NA	CholeraGarde®
Description	Inactivated[c]	Inactivated[c]	Inactivated[c]	Live, attenuated	Live, attenuated
Components	Whole-cell *V. cholerae* O1 and recombinant CT B subunit	Whole-cell *V. cholerae* O1/O139	Whole-cell *V. cholerae* O1/O139	*V. cholerae* O1, with 94% deletion of gene encoding CT A1 subunit and mercury resistance marker	*V. cholerae* O1, genetically engineered to be nontoxigenic, nonmotile and nonrecombinational
Number of doses	2, given 7-14 days apart	2, given 14 days apart	2, given 14 days apart	1	1
Formulation/Buffer	Liquid/yes	Liquid/no	Liquid/no	Lyophilized/yes	Lyophilized/yes
Administration	Diluted in ~1.5 dl buffer using cup	Undiluted, using oral syringe	Undiluted, using oral syringe	Diluted in 1 dl buffer using cup	Diluted in 20-45 ml of buffer
Shelf life (years)	3[d]	2+[d]	2[d]	2[d], 3[e]	>1[d]
Protective efficacy (PE) (%)	~60-85	66-67	67	79	NA
Duration of protection (years)	~2	2-3	2	NA	NA
Age groups (years)	≥2	≥1	≥2	≥2	>9 months
Price/dose[f]	~5[g]	≤1.85	~0.75	~1 (target price)	NA
WHO prequalification	Yes	Yes	No	No	No
First licensure	1993	2009	1997 (old formulation), 2009 (new formulation)	Clinical trials planned	Clinical trials ongoing
Licensed in	>60 countries	India	Vietnam	USA in 2014	NA
Use since licensure	>14 million doses	NA	>20 million doses	NA	NA
Manufacturer	Crucell/SBL Vaccines, Sweden	Sanofi/Shanta Biotech, India	Vabiotech, Vietnam	PaxVax, USA	VTI, USA, China

[a]Based on Dukoral and technology transfer to Vietnam, several formulations followed since first vaccine was licensed in 1997 as ORC-Vax®; [b]Manufactured by Berna Biotech AG, Bern, Switzerland, as Orochol/Mutachol until 2004; [c]By heat or formalin; [d]At 2-8°C; [e]At -30°C; [f]Purchase price in USD considered for use by UN agencies; [g]Depending on the agreement with the implementing institution. Source: Chowdhury *et al.* [37], Qadri *et al.* [38], Shin *et al.* [39], Sur *et al.* [40,41], WHO [35]

1.8 Research on social, cultural and economic features of cholera and vaccine acceptance

1.8.1 Population perceptions of illness and vaccination

Successful public health interventions for disease control are in principle based on three pillars: (i) an efficacious intervention, such as a drug, a treatment plan or a vaccine, (ii) a functional health system to deliver or implement the intervention, and (iii) willingness among the target population to accept the intervention.

Ironically, public perception of the importance of vaccination, especially against childhood diseases, has been waning in many high-income countries in Europe and North America due to the immensely positive impact vaccination has had on people's lives over the past ~100 years. Because vaccination programs against previously much-feared child killers like measles, diphtheria or pertussis have been so successful, many people no longer believe in the benefit of vaccines or even oppose them [42]. The collective memory of the once terrible impacts of pathogens such as polio and tetanus on all ages has diminished dramatically over the past ~30 years. Instead of being concerned about the negative consequences caused by vaccine-preventable diseases, fears of people living in the industrialized world have mainly shifted away to the alleged severe side effects of vaccines [43]. Anti-vaccine movements ignore the scientific evidence regarding safety and efficacy of modern vaccines and often base their resistance on unethical or even fraudulent research.[13] They have become powerful players and negatively influence public perception on vaccination by using the internet or engaging stars of film and TV to fuel resentment and resistance against vaccines [42,45]. As a consequence of such activities that undermine previous efforts to control, eliminate or even eradicate disease, measles morbidity and mortality, for example, has recently increased in the USA and the plan to eliminate this disease from Europe by 2010 failed [46].

Compared to the industrialized world however, vaccines seem to be much more appreciated in low- and middle-income countries because many people still see or experience the serious consequences of infection with vaccine-preventable diseases every day. Meningococcal meningitis, for instance, contributes substantially to child morbidity and mortality in sub-Saharan African countries that belong to the so-called *meningitis belt*.[14] But vaccination programs have also suffered in the developing world, especially when not enough attention was

[13]See the recent 'MMR Scare' [40-42] as an extreme example of fraudulent research that has had a significant negative impact on global MMR vaccination coverage and consequently morbidity and mortality [44].

[14]http://www.who.int/immunization/topics/meningitis/en/

paid to potential unwillingness or even resistance of communities to accept vaccines [47-49]. Rumors about tetanus toxoid causing infertility have hampered national vaccination efforts in Africa [50,51]; programs were even brought to a halt because of an ignorance of local realities, as was the case with the global polio eradication campaign in Northern Nigeria [52,53].

Hence, in addition to recognizing the importance of infrastructural, logistical and political issues for the success of immunization programs in low-income countries [54], consideration of local cultural concepts of illness among potential vaccine recipients and how these may affect vaccine acceptance is crucial [49,55,56].

The influence of policy makers' and communities' perceptions on vaccine acceptance was assessed in various recent studies for cholera, shigellosis and typhoid fever in several Asian countries [55,57-65]. This research reaffirmed the importance of investigating the social and cultural contexts into which vaccines are introduced in order to better understand their effects on improving vaccination coverage [66]. However, no studies have been published yet that examine the influence of social and cultural features of cholera on vaccine acceptance in African settings. This includes attention to cultural variation within and across local communities and in gender dynamics [67].

1.8.2 Economic evaluation of oral cholera vaccine use

Economic evaluations are conducted to guide decision makers on making choices in the health sector between potentially available alternatives in the context of scarce resources. Economic evaluations compare the costs and outcomes of at least two alternative programs [68] (Table 1-2).

Table 1-2: Costs and consequences in economic evaluations

Type of study	Measurement/valuation of costs in both alternatives	Identification of consequences	Measurement/valuation of consequences
Cost analysis	Monetary units	None	None
Cost-effectiveness analysis	Monetary units	Single effect of interest, common to both alternatives, but achieved to different degrees	Natural units, e.g., life-years gained, disability-adjusted life-years (DALYs) saved, points of blood pressure reduction, etc.
Cost-utility analysis	Monetary units	Single or multiple effects, not necessarily common to both alternatives	Healthy years, typically measured as quality-adjusted life-years (QALYs)
Cost-benefit analysis	Monetary units	Single or multiple effects, not necessarily common to both alternatives	Monetary units

Source: Adapted from Drummond *et al.* [68]

A series of studies have been published over the past two decades on the economic evaluation of using different OCVs in endemic and epidemic settings throughout the world [69-74]. More recently, the Disease of the Most Impoverished (DOMI) program has been at the forefront of economic evaluation research for cholera by conducting private demand studies, COI studies and examining cost-effectiveness (CE) and cost-benefit for OCV across several endemic settings [21,75-86]. Despite DOMI studies have shown that OCVs can be cost-effective in certain settings according to WHO criteria [87], further country-specific studies are required to provide national policy makers with local data on cholera-related costs and CE of OCVs before they can make an informed decision regarding the use of OCVs for cholera control [88].

Relating costs and consequences to determine economic efficiency, however, is not the only criterion for decision making on public spending for health; additional economic criteria as well as ethical and political criteria are relevant for priority-setting [89]. Since cost-effective interventions, for example, are not always affordable, it is important to differentiate cost-effectiveness (value for money) from affordability (financial resources required). To determine affordability, budget impact analyses are required. Additional economic criteria are related to whether an intervention is a public good and whether it yields substantial externalities, which are classical justifications for public health intervention, because private markets could not supply them efficiently, just as in other sectors. Ethical considerations that may affect priorities include poverty, horizontal equity (equal treatment for people in equal circumstances), vertical equity (priority for people with worse problems) and the *rule of rescue* (priority of saving lives over interventions that do not make a big difference). The political criterion is related to the adequacy of demand, public attitudes and needs.

1.9 Overview of research approaches

1.9.1 Cultural epidemiology

Although many studies in the published literature have examined people's perceptions and behavior regarding diarrheal diseases, most of them have been done with a strong disciplinary focus, based on either medical anthropology [90-92] or classical or social epidemiology.

Following the central paradigm of epidemiology that "patterns of disease in populations may be analyzed systematically to provide understanding of the causes and control of disease" [93], epidemiologists are mainly concerned with the collection of quantitative data and use of statistical tools. Epidemiological studies typically work with random samples drawn from a defined population and apply standardized questionnaires and/or use clinical examinations, laboratory analyses of biological specimens, etc., to acquire numerical information needed for

statistical analysis. Anthropologists, on the other hand, are primarily concerned with qualitative data and use methods for data collection based on ethnographic research. They focus more on local knowledge and contextual data to gain a deeper understanding of the perspective of patients or affected people and how consideration of their social, cultural, political and natural environment may affect illness- or health-related behavior. Research in anthropology involves focus group discussions, open-ended interviews, participatory mapping, participant observation, etc., and typically does not require large sample sizes as in epidemiological studies since the focus is clearly on in-depth information rather than on making decisions for public health based on statistical inferences.

Despite the important contributions both disciplines have made to international public health, attempts to connect them have been limited [94]. A methodological approach called *cultural epidemiology*[15] has been developed and implemented over the past two decades to address a persistent gap between both traditional disciplines [95,96]. This approach integrates qualitative and quantitative methods for interdisciplinary health research in order to harness the explanatory power of epidemiology *and* the local validity of anthropology.

Cultural epidemiology is defined as the study of the distribution of locally valid representations of illness-related experience, meaning and behavior—i.e., sociocultural features of illness—in a population [96]. On the one hand it draws on medical anthropology, most notably Arthur Kleinman's concept of illness explanatory models [98]. On the other, it uses tools and statistical techniques common to epidemiology to answer locally relevant descriptive, analytical or comparative questions for the benefit of public health (Figure 1-3). But compared to classical epidemiology that typically adopts the professional or outsider's, i.e., *etic*, perspective, cultural epidemiology examines people's ideas on illness and health-related behavior from the vantage point of the affected persons, thus making it an *emic* approach [99].

[15]The framework of cultural epidemiology that was used in this study refers to the work of Mitchell Weiss [95,96]. Other formulations of cultural epidemiology for health social science research have been described by James Trostle [94,97].

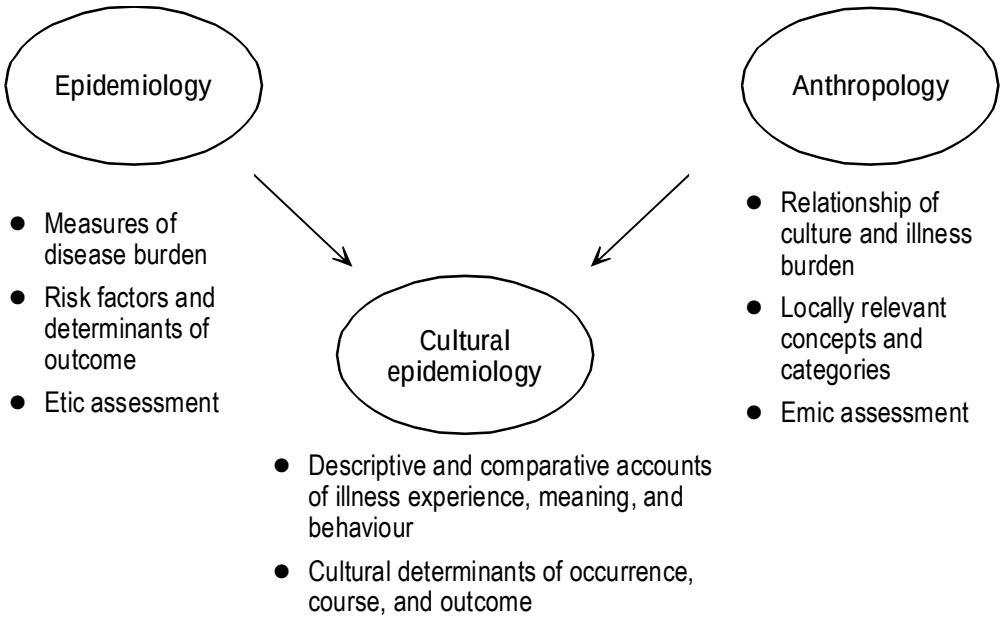

Figure 1-3: Multidisciplinary framework: contributions of epidemiology and anthropology to cultural epidemiology

Source: Adapted from Weiss *et al.* [100]

Semi-structured interviews based on the Explanatory Model Interview Catalogue (EMIC) constitute the principal tool for cultural epidemiological research. The EMIC framework provides a guide based on Kleinman's original eight questions for eliciting patient explanatory models [98] (p. 106). EMIC interviews are used to assess sociocultural features of illness, operationalized as patterns of distress, perceived causes and help seeking (Table 1-3). EMIC interviews produce numerical and narrative data for integrated quantitative and qualitative analysis.

Table 1-3: Operational formulation of sociocultural features of illness for cultural epidemiology

	Experience	Meaning	Behavior
Operationalized as	Patterns of distress	Perceived causes	Help seeking
Categories related to	Problems and concerns; name of illness, symptoms, anticipated outcome; psychological, social, and economic impact; stigma, disclosure, and self-esteem; marriage prospects and marital relations, etc.	Ingestion, psychological factors, psychosocial stressors and victimization; sanitation, hygiene, contamination, and health habits; infection, prior illness, constitutional factors; magico-religious forces; heredity; retribution of previous deeds, etc.	Family support and home remedies; private practitioners and public clinics; Western-styled health professionals, paraprofessionals, and specialists; traditional healers of various types; past experience and current preferences, etc.

Source: Adapted from Weiss [95]

The design of a cultural epidemiological study typically includes an ethnographic component to derive locally valid categories—i.e., to adapt the EMIC interview to the local context and the

illness of interest—and a survey component to interview patients, community members, health care personnel and so forth. The first step in cultural epidemiological analysis is descriptive and clarifies the distribution of categories of distress, perceived causes and help seeking. In a second step, comparative analysis based on statistical testing examines which categories are similar or different between genders or between sites, etc. The analytical step involves uni- and/or multivariable testing, i.e., linear or logistic regression, to study how sociocultural features of illness affect health-related behavior, e.g., treatment delay, appropriate treatment seeking, vaccine acceptance, etc., or stigma.

Integrated analysis of cultural epidemiological data requires importation of numerical variables and narrative texts into qualitative data analysis software and follows a deductive and inductive strategy to coding [101]. Narratives are transcribed from respondents' accounts and imported in a precoded structure that reflects major interview items. This helps retrieve relevant text segments to clarify categories and their context and explain the nature of associations found in statistical analysis. Additional issues emerging from statistical or qualitative analysis may require coding of further themes.

Cultural epidemiological studies using EMIC interviews have been conducted in a variety of settings in high-income as well as middle- and low-income countries to inform policy makers and public health professionals in the fields of mental health [102-106], chronic [107] and infectious diseases [108-110] as well as stigma and gender [111-116].

1.9.2 Cost-effectiveness analysis

The most commonly used method to measure the value of an intervention is the cost-effectiveness analysis (CEA). CEA links costs and effects of a health intervention with reference to doing nothing or current practice by comparing the differences in costs with the differences in health outcomes. The difference in program costs between two alternatives that compete for the same resources divided by the difference in health outcomes, i.e., the additional cost required per additional unit of health benefit, is expressed as incremental cost-effectiveness ratio (ICER) [117]. The ICER to evaluate immunization programs is calculated by dividing incremental costs—calculated as the difference between costs of the vaccination program and costs of treatment saved due to the vaccination—by the difference in deaths, cases or disability-adjusted life-years (DALYs) averted. DALYs represent an aggregate measure combining mortality and morbidity by quantifying the number of years lost due to premature death and the number of years lived with disability.

Recommendations endorsed by the WHO commission on Macroeconomics and Health are frequently used to guide decision making about whether an intervention is cost-effective or not compared to one or several alternatives [117]. Results of CEAs, if expressed in ICERs per DALY averted, can be classified with regard to national per capita GDP [87]: an intervention is considered *highly cost-effective* if the ICER is less than per capita GDP, *cost-effective* if the ICER is between one and three times per capita GDP, and *cost-ineffective* if the ICER exceeds three times per capita GDP.

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2

STUDY DESCRIPTION

2.1 Rationale and framework for research

Cholera remains a serious public health burden in low- and middle-income countries despite the promotion of safe water, improved sanitation, and health education (WASH) over the past decades. The World Health Organization (WHO) recommends the use of oral cholera vaccines (OCVs) as a supplementary measure for epidemic and endemic cholera control. In 2006, the WHO received a grant from the Bill & Melinda Gates Foundation, Seattle, USA, to work on the preemptive use of OCVs in populations at risk. Following an earlier demonstration project in urban cholera-endemic Mozambique [1-7], this grant made it possible to further examine how OCVs—in addition to WASH—can be used in a sustainable manner in countries with endemic cholera and to gain more evidence on the usefulness of establishing a global OCV stockpile.

Zanzibar has been regularly affected by cholera since 1978. The government has proposed using OCVs for populations living at risk of recurrent outbreaks as a strategy for enhancing disease control. As a result, an agreement to establish a collaborative research project was signed in 2008 between the WHO, the International Vaccine Institute (IVI), Seoul, Korea, the Swiss Tropical and Public Health Institute (Swiss TPH), Basel, Switzerland, and the Ministry of Health and Social Welfare of Zanzibar (MoHSW).

The project's overall goal was twofold: (i) to reduce the burden of cholera on Zanzibar by vaccinating a target population of 50,000 residents living in cholera hotspots and (ii) to complement this intervention with a series of studies to address key research questions that remained unanswered from the demonstration project in Mozambique [8].

In response to the need for detailed data on a variety of epidemiological aspects, and to inform public health policy regarding the use of OCVs for endemic cholera control, the project

embarked on a series of classical epidemiological studies under the scientific leadership of the IVI.[1]

Consideration of social and cultural features of diarrheal illness and of people's intention and actual behavior to use a vaccine is essential to improve and sustain community vaccination coverage of mass vaccination campaigns. Since no such studies for cholera and OCVs have yet been conducted in African settings, a socioeconomic and behavioral (SEB) study was conceived among the MoHSW, the WHO and the Swiss TPH. The latter assumed scientific leadership of this component of the project.

2.2 Aims

The overall aims of this thesis research were (i) to study social and cultural features of OCV acceptance from a community perspective and (ii) to assess the cost-effectiveness (CE) of the 2009 OCV mass campaign in Zanzibar.

Findings presented here should inform governments and ministries, in particular the Ministry of Health and Social Welfare of Zanzibar, regarding the introduction of an OCV as part of a sustainable and financially viable strategy to improve prevention and control of endemic cholera.

2.3 Research questions and objectives

Based on the two aims, this thesis project addressed the following general and specific research questions in the context of an OCV mass campaign in cholera-endemic communities in Zanzibar:

- What are the social and cultural features of OCV acceptance?
  - What are the perceptions and essential features of cholera in the context of diarrheal diseases?
  - What is the anticipated OCV acceptance?
  - What is the actual OCV acceptance, i.e., uptake?
  - What are the social and cultural determinants of anticipated OCV acceptance and uptake?
  - What are the barriers to OCV uptake?

[1]Studies on cholera epidemiology, vaccine effectiveness, vaccine safety for pregnant women, herd protection etc., were conducted and have either been published [9-11] or are being written up for publication.

- Does use of an OCV in a mass vaccination campaign in Zanzibar provide value for money?
  - What are the public and private costs of illness (COI) due to cholera?
  - What are the costs of the OCV mass campaign?
  - What is the CE of using an OCV?

Based on these questions, five objectives were defined that are reported in the next chapters:[2]

Part I: Social and cultural features of OCV acceptance in Zanzibar[3]

1. To clarify the social and cultural features of cholera with reference to diarrheal diseases, in particular shigellosis, among community residents before the vaccination campaign (Chapter 3).

2. To identify the social and cultural determinants of anticipated acceptance of an OCV among community residents before the vaccination campaign (Chapter 4).

3. To identify the social and cultural determinants of OCV uptake among community residents (Chapter 5).

4. To evaluate the influence of social and cultural factors on OCV uptake and to identify the logistical, medical, social and system-related barriers to OCV uptake among community residents (Chapter 6).

Part II: CE of oral cholera mass vaccination in Zanzibar

5. To estimate public and private COI due to cholera, costs of the OCV mass campaign, and the CE of using OCVs in an endemic setting from a health care provider and a societal perspective (Chapter 7).

[2]These chapters constitute the core of this thesis and report findings as self-contained papers that have either been published in international peer-reviewed journals or are under review or have been prepared for submission.

[3]Findings presented in Part I come from studies done among community residents in Zanzibar. Additional data on cholera and vaccine use that have been collected on the level of policy makers, allopathic and traditional health care professionals and formal and informal community leaders are currently being analyzed and written up and will be published as separate papers (lead investigator: Dr. Al Pach, IVI, Seoul, Korea).

2.4 Study setting

Zanzibar consists of two major islands, Unguja (also named Zanzibar) and Pemba, and is situated in the Indian Ocean ~40 to 60 km off the coast of Tanzania, East Africa (Figure 2-1). In 1964, shortly after independence from the British colonial powers, the archipelago of Zanzibar and Tanganyika formed the United Republic of Tanzania. As a semiautonomous polity within Tanzania, Zanzibar consists of five regions which are subdivided into ten districts, 50 constituencies and 296 communities (so-called Shehias). The main islands cover ~2,557 km² (Unguja: ~1,651 km², Pemba ~906 km²). Unguja is mostly flat and sandy while Pemba has hilly terrain that is fertile and heavily vegetated. The climate is humid tropical with a long (March to June) and a short rainy season (October to December). Mean temperature on Unguja varies between 21 and 33°C and monthly rainfall between 25 and 434 mm [10].

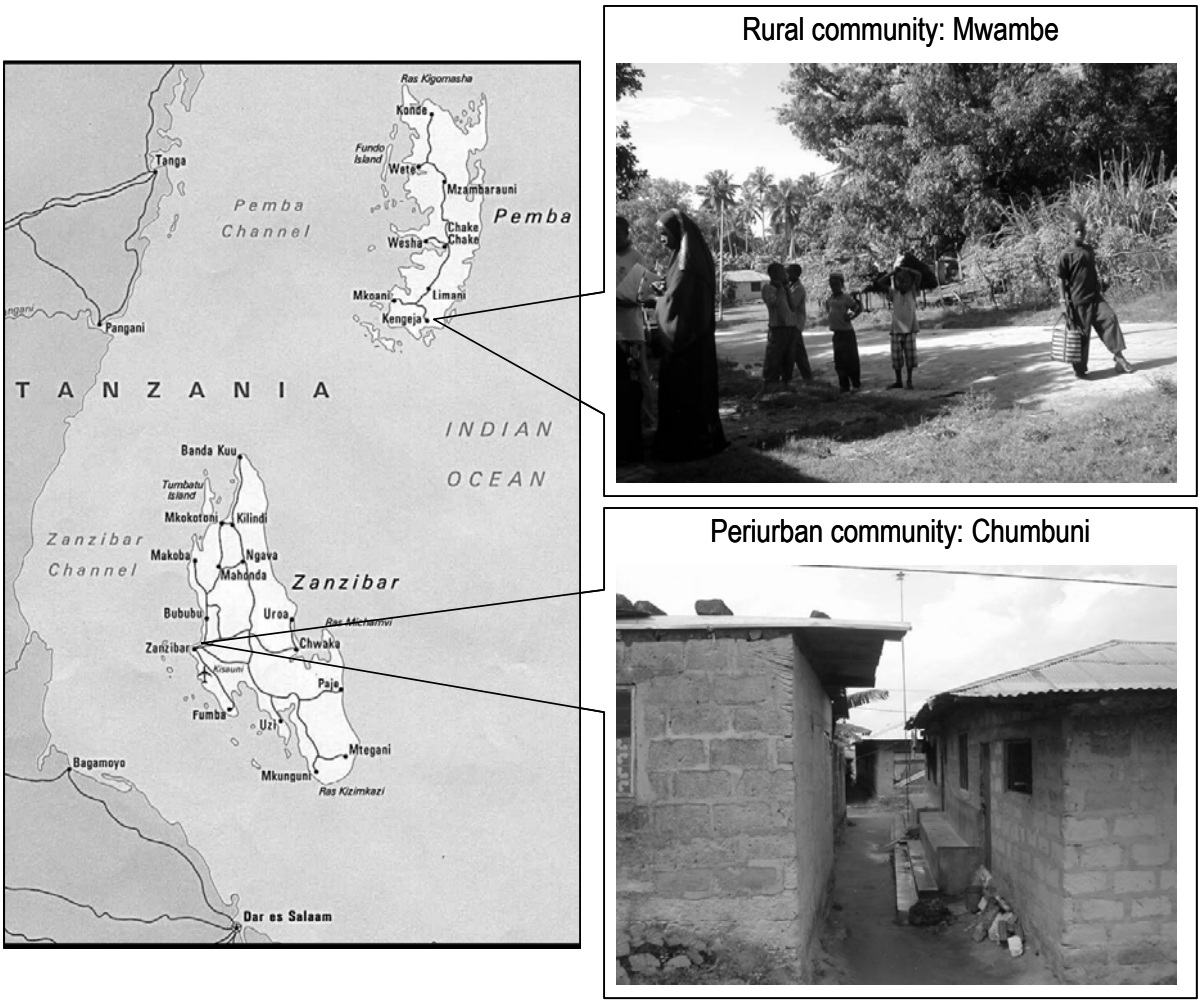

Figure 2-1: Map of Zanzibar with the two main islands and the periurban and rural sites selected for study of social and cultural features of OCV acceptance

Map: courtesy of the University of Texas Libraries (The University of Texas at Austin); Photos: C. Schaetti

Approximately 1.2 million people live in Zanzibar and the population is growing rapidly.[4] The inhabitants are predominantly Muslim and the main language is Kiswahili, but English is also widely used. According to the most recent household budget survey from 2004/2005, one-fourth of the population had not received any education and the primary education net enrolment ratio amounted to 77% [13]. The majority (71 %) had access to piped water while a minority relied on drinking water from wells (27 %) and other sources like street vendors, rainwater, spring water, and open water sources (2 %) [13]. Fifty-three percent had access to pit latrines and 12 %, mainly living in urban areas, used a flush toilet. As a possible consequence of poor water supply and sanitation, street food sold in Pemba was found to be bacteriologically contaminated and unsafe for consumption [14].

Top three causes of admission to Zanzibar hospitals in 2007 were due to malaria (27.4% of all admissions), gastroenteritis (12.7%) and pneumonia (9.9%) [15]; in 2008, pneumonia was the top cause of admission (12.2%), followed by malaria (10.8%) and gastroenteritis/diarrhea (8.6%) [16]. Main causes of death in 2007 in rank order were related to malaria (18.4%), hypertension (8.5%), pneumonia (7.9%) and gastroenteritis (7.5%). In 2008, pneumonia (11.8%), hypertension (7.6%) and septicemia (7.0%) were the three top causes of death [16]. Main sources of help consulted are primary health care units (PHCU) which are situated within four kilometers of households for over 90% of the population. Monthly mean per capita expenditure for all goods and services was TZS 21,000 (~USD 18) in 2004/2005 with a 2.1% share for health-related expenditures [13]. Life expectancy at birth rose from 47 years in 1988 to 57 years in 2002 [12].

Zanzibar has been affected by cholera since the days of the first pandemic in 1821. It was again reported in 1978 when an outbreak with 411 cases and 51 deaths affected two fishermen villages [17]. Thirteen outbreaks followed since then with almost annual episodes since the year 2000 and with case-fatality rates (CFRs) ranging from 0% to 17%. Reyburn *et al.* reported an annual incidence of 0.5 cases per 1,000 population based on a review of routine surveillance data for the years 1997 to 2007 [11]. A seasonal pattern can be observed that follows the rainy seasons when widespread flooding occurs; this has recently been confirmed by a study that linked cholera incidence to rainfall and temperature [10]. Such environmental conditions, together with the scarcity of safe drinking water and a generally poor, and sometimes even lacking sanitation infrastructure, frequently expose the majority of inhabitants on both islands to an increased risk of waterborne diseases.

[4]Intercensal annual growth rates (1988-2002) varied from 2.1% to 4.5% [12].

2.5 Research instruments and data analysis strategies

The following sections give an overview of the instruments and data analysis approaches used. Detailed descriptions are included in the respective chapters in Part I and II.

All instruments were developed in English. Translation into Kiswahili and back translation into English was done by language teachers from the State University of Zanzibar. Instruments were only finalized after pilots had been done in areas adjacent to the study communities and any remaining issues had been resolved.

2.5.1 Part I: Social and cultural features of OCV acceptance

A semi-structured interview based on the Explanatory Model Interview Catalogue (EMIC) was employed to study social and cultural features of cholera and shigellosis. The EMIC interview was developed based on a series of focus group discussions with community residents and several meetings with local social scientists and health care professionals (Appendix 9.2). Since people without current diarrhea, rather than patients, were the focus of research, clinical vignettes were developed and formulated in an easily understandable language to describe a local person suffering from cardinal somatic symptoms of cholera and shigellosis, respectively (Appendix 9.3).

The EMIC interview examined illness-related experience, meaning and behavior operationalized as categories of distress, perceived causes and help seeking [18]. Categories of distress were elicited in relation to somatic symptoms not mentioned in the vignette, psychosocial problems and financial issues that may have an impact on patients. To elicit perceived causes, respondents were questioned about their views and opinions on why and how they think one can get the illness with regard to ingestion- and behavior-related factors, and environmental and traditional/magico-religious causes. To find out more about sources of help seeking, respondents were asked to identify and assess health care providers, including locally available allopathic and traditional forms of treatment, which patients described in the vignette would likely consult. Possible options for self treatment at home were also elicited. Separate sections inquired about sociodemographic characteristics, previous experience with vaccines and whether respondents would swallow a vaccine against cholera if it was made available at no cost, which was the case during the mass vaccination campaign, and at three different price levels. The prevaccination EMIC interview was slightly adapted to the postvaccination phase and a new section on potential barriers to vaccination included.

Quantitative data were double-entered in Epi Info and cleaned before importation into statistical analysis software (Stata, SAS). Clarification of the relative prominence of categories of

distress, perceived causes and help seeking involved a weighted coding of responses, based on the approach and rationale used in many cultural epidemiological studies and recommended for analysis of EMIC interviews [18]. A value of 3 was assigned if a category was identified as most troubling, most important or most useful; a value of 2 if a category was reported spontaneously without probe; a value of 1 if a category was reported after probing only; and a value of 0 for no response. This coding facilitated calculation of the mean prominence for each category.

Descriptive analyses compared mean prominence for each category between site and gender using the nonparametric Wilcoxon test. Numerical variables were compared using the t test; categorical variables were compared using the Pearson Chi^2 of Fisher's exact test. Analysis of determinants of vaccine acceptance used uni- and multivariable logistic regression analysis.

Narratives for each question were written down in Kiswahili during the interview, translated into English and typed in word processor software by using templates with a precoded structure according to interview items. Narratives were then automatically coded upon importation into qualitative data analysis software (MAXQDA). Importation of selected quantitative variables into MAXQDA enabled integrated analysis of numerical findings based on statistically significant relationships.

2.5.2 Part II: CE of oral cholera mass vaccination

Treatment of cholera patients in Zanzibar is usually done in temporary cholera treatment centers (CTCs) that are erected in public health facilities in the vicinity of the outbreak. Questionnaires were developed based on WHO guidelines [19] to elicit fixed and variable public COI from health care providers and public health officials; private direct and indirect COI were elicited from patients (or their caregivers) (Table 7-1). To estimate costs of the mass vaccination campaign, relevant records were reviewed and reports collected from local and international public health experts and non-governmental organizations (NGOs). Parameters on epidemiology and vaccine performance, such as protective efficacy, duration of protection etc., were obtained from the mass vaccination database developed by the IVI, or if unavailable, from published studies or experts.

All data were entered into Microsoft Excel for analysis of total and average costs and to develop a CE model based on a study from Bangladesh [20]. Incremental cost-effectiveness ratios (ICERs) per death, per case and per disability-adjusted life-year (DALY) averted were calculated from the health care provider and the societal perspective. Incremental costs from the health care provider perspective were calculated as the difference between costs of the vaccination program and public COI saved due to the vaccination. Private direct COI saved were added to

the model from the societal perspective. The number of deaths, cases or DALYs averted was equal to the difference in numbers with and without the vaccination program. Relevant CE model parameters like incidence, protective efficacy, OCV purchase price etc. were varied in one-way sensitivity analyses to assess the influence of parameter uncertainty on outcomes.

2.6 Study design

2.6.1 Part I: Social and cultural features of OCV acceptance

Based on a review of epidemiological data from recent cholera outbreaks in Zanzibar, the mass vaccination campaign was planned to take place in selected periurban and rural districts on both islands. The periurban Shehia of Chumbuni (Unguja) and the rural Shehia of Mwambe (Pemba), both representing core areas of the mass vaccination campaign, were selected as study communities (Figure 2-1). Both sites are described in detail in Table 3-1.

A cross-sectional cultural epidemiological study was repeated in the designated periurban and rural study communities (Figure 2-2). The study began in 2008 with a preparatory phase to develop and test an EMIC interview for the prevaccination survey. A random sample of community residents aged ≥18 years with an equal gender ratio was drawn. After completion of the mass vaccination campaign in early 2009, two new samples of vaccinated and unvaccinated adults were randomly drawn from the same two communities based on the vaccination database; the prevaccination EMIC interview was modified and piloted before use in the postvaccination survey.

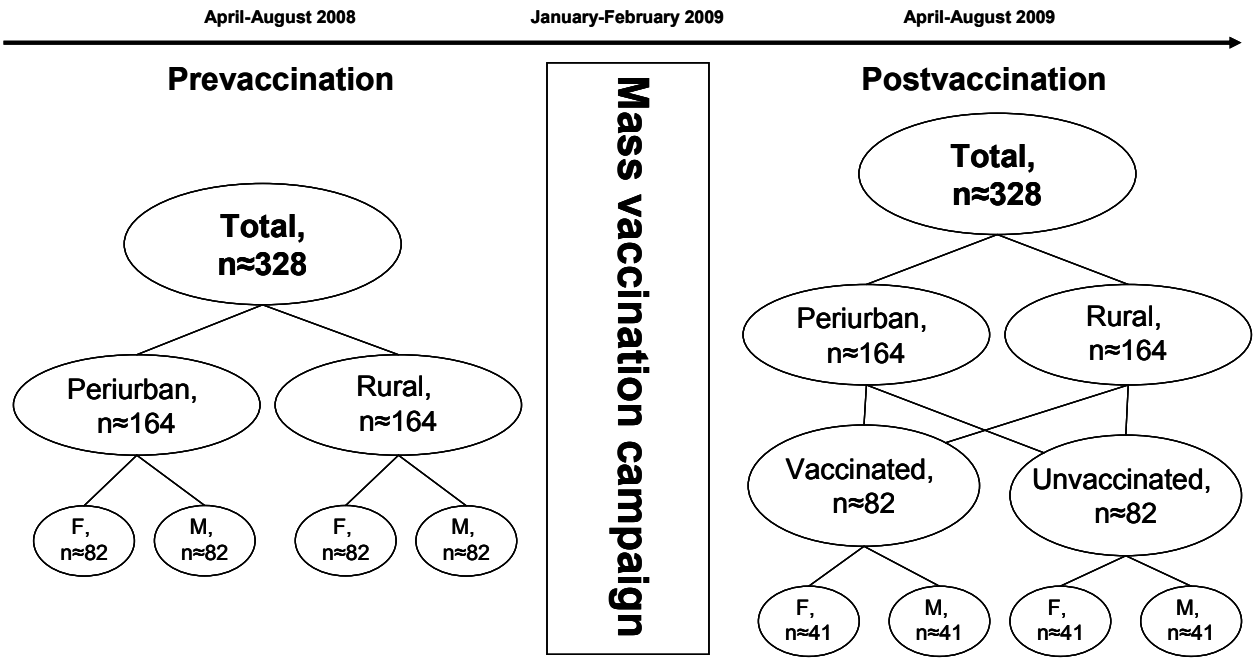

Figure 2-2: Outline of the repeated cross-sectional design for community study with EMIC interviews
F: female gender, M: male gender

The sample size calculation for the pre- and postvaccination EMIC interview surveys was based on the comparison of mean prominence of categories of distress, perceived causes, and help seeking between periurban and rural sites and between female and male gender. To detect a difference of 0.5 between prominence means with equal standard deviations of 1.5, at a level of 95% significance and 80% power, a sample size of at least 164 respondents for each group was required. This calculation was based on a two-sample t test assuming a worst-case scenario, i.e., no underlying distribution in the data, which requires that the sample size derived from the t test (n=142) be divided by 0.864 [21].

2.6.2 Part II: CE of oral cholera mass vaccination

Cost data were collected in 2009 based on primary and secondary data sources. Private COI were collected from a sample of ~100 laboratory-confirmed cholera cases from Pemba. Public COI from three cholera outbreaks were obtained from local experts and public health officials. Costs of the mass vaccination campaign were obtained from implementers, i.e., from the WHO (headquarters and consultants) and the local Expanded Program on Immunization (EPI).

2.7 Ethics

The work presented in this thesis has been reviewed by internal and external scientific experts. The protocol on social and cultural determinants of OCV acceptance [22] and the protocol on

the CE of using OCVs in Zanzibar have both been reviewed and approved by the WHO Research Ethics Review Committee and the MoHSW Ethics Committee. The Ethics Committee of Basel (EKBB) was also informed about both protocols and no ethical concerns were raised.

Participants were informed about study aims and objectives and written consent was obtained from all respondents from the general population and from patients and caregivers. All data were handled with utmost care and confidentiality and made anonymous before analysis and reporting.

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PART I

SOCIAL AND CULTURAL FEATURES OF ORAL CHOLERA VACCINE ACCEPTANCE IN ZANZIBAR

3

SOCIAL AND CULTURAL FEATURES OF CHOLERA AND SHIGELLOSIS IN PERIURBAN AND RURAL COMMUNITIES OF ZANZIBAR*

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Abstract

Background

Responding to the high burden of cholera in developing countries, the WHO now considers vaccination as a supplement to the provision of safe drinking water and improved sanitation in the strategy for cholera control in endemic settings. Cultural concepts of illness affect many aspects of public health. In the first step of a two-step strategy to examine determinants of cholera vaccine acceptance, this study identified social and cultural features of diarrheal illness for cholera control in endemic communities.

Methods

A cultural epidemiological study with locally adapted vignette-based interviews was conducted in two cholera-endemic communities of Zanzibar. A random sample of unaffected periurban (n=179) and rural (n=177) adults was interviewed to study community ideas of cholera and shigellosis, considering categories of distress, perceived causes, and help-seeking behavior.

Results

Cholera was recognized by 88%. Symptoms of dehydration were most prominent in reports at the periurban site. Interference with work leading to strain on household finances was frequently emphasized. Dirty environment was the most prominent perceived cause, followed by unsafe drinking water and germ-carrying flies. Causes unrelated to the biomedical basis of cholera were reported more often by rural respondents. Rural women had more difficulty (20%) to identify a cause than men (7.1%, p=0.016). Periurban self treatment emphasized rehydration; the rural community preferred herbal treatment and antibiotics. Shigellosis was recognized by 70%. Fewer regarded it as very serious compared with cholera (76% vs. 97%, p<0.001) and regarded it as less likely to be fatal (48% vs. 78%, p<0.001). More respondents could not explain causes of shigellosis (23%) compared with cholera (7.3%, p<0.001). Community respondents less frequently identified dehydration and contagiousness for shigellosis. Government facilities were preferred health care providers for both conditions.

Conclusions

This study clarified local views of cholera and shigellosis relevant for diarrheal disease control in Zanzibar. The finding that rural women were less likely than men to specify causes of cholera suggests more attention to them is required. Better health education is needed for cholera in rural areas and for shigellosis in general. This study also identified variables for subsequent analysis of social and cultural determinants of cholera vaccine acceptance.

3.1 Background

Cholera is an intestinal disease characterized by acute and profuse watery diarrhea, caused by the bacterium *Vibrio cholerae* O1 or O139. A total of 190,130 cases and 5,143 deaths globally were reported to the World Health Organization (WHO) in 2008 [1], which is an underestimate; the annual burden is likely to exceed 3 million episodes and over 100,000 deaths [2,3]. The approach to control involves treatment of patients with rehydration and prevention of new cases, based on improved sanitation, hygiene and safe water supply. Because of persistence of cholera as a public health problem, the WHO now recommends vaccines as an additional tool to control cholera in endemic areas [3].

Cultural concepts about illness and how to treat and prevent it are important for many aspects of public health. The role of various social and cultural factors (e.g., sociodemographic characteristics, gender, urban and rural setting, and cultural concepts of illness and treatment) has practical implications for behavior, public health, and disease control that need to be considered. Such factors are also likely to be especially important considerations for the acceptance and demand for vaccines [4-7]. Effective disease control with a vaccine requires not only an efficacious vaccine and health system to deliver it, but also recognition among the general population of its benefits and their willingness to use such a vaccine [8]. Consideration of cultural concepts of cholera and of a comparable serious disease, such as shigellosis, which has both similar and distinctive features, may help to formulate effective strategies, general and specific, for cholera control.

Studies have begun to address questions of vaccine acceptance and demand for diarrheal diseases, including recent research on typhoid fever and shigellosis in Asian countries [9-13], but not yet for cholera in Africa. Such research requires consideration of how cultural concepts of cholera affect acceptance and demand for a vaccine. To achieve that, two steps are essential: First, it is necessary to identify social and cultural features of the disease, and in a second step to explain how these features of cholera influence vaccine acceptance. This study was concerned with the first of these two questions, and the second will be addressed in a subsequent paper.

Fieldwork was undertaken in Zanzibar, motivated by the interest of the Ministry of Health and Social Welfare (MoHSW) in using a cholera vaccine for control in endemic periurban and rural areas of the archipelago. Because shigellosis, caused by enteropathogenic *Shigella* spp., is also endemic, and it has a profile of symptoms different from cholera, it was included for comparative study of local experience, meaning and preferred sources of help for diarrheal illness.

Specific aims of the study were (i) to examine the variety and distribution of social and cultural views of cholera, (ii) to compare these views in periurban and rural endemic communities, and (iii) to identify common and distinctive features of cholera and shigellosis that clarify how well differentiated these conditions are in these communities.

3.2 Methods

3.2.1 Setting and study sites

The survey was conducted from June to August 2008 in Zanzibar, United Republic of Tanzania. This Indian Ocean archipelago consists of two major islands—Unguja and Pemba—inhabited by a rapidly growing population of ~1.2 million Kiswahili-speaking people, who are predominantly Muslim. Medical morbidity in the population of Zanzibar mainly results from communicable diseases like upper respiratory tract infections, including pneumonia (33% of outpatient visits to primary and secondary hospitals in 2008), malaria (9.7%) and diarrheal diseases (8.6%) [14]. According to the latest Tanzanian national census (2002), the health situation on the islands has been improving, and the life expectancy at birth rose from 47 to 57 years between 1988 and 2002 [15].

A periurban and a rural community (locally termed Shehia) in core areas for a subsequent mass vaccination campaign were selected as study sites. This campaign with the killed whole-cell oral cholera vaccine Dukoral® was conducted in January and February 2009. Interviews for this study were conducted simultaneously in the periurban Shehia of Chumbuni and the rural Shehia of Mwambe. A description of the study sites is given in Table 3-1. Both Shehias are served by a primary health care unit within walking distance, which is staffed with nurses and stocked with basic drugs and equipment mainly for outpatient treatment [16].

Table 3-1: Overview of study sites

	Periurban site	Rural site
Administrative structure		
Community (Shehia)	Chumbuni	Mwambe
District	Urban[a]	Mkoani
Island	Unguja	Pemba
Population estimates		
Number of inhabitants[b]	10,869	8,164
Population density	15,300/km^2	800/km^2
Characteristics		
Environment	Unplanned, slum-like extension of the capital, situated along a main road, narrow alleys, sandy ground, few trees and shrubs, few plots for farming	Coastline community with widely scattered hamlets, lush green vegetation, livestock, cassava, banana, paddy rice and coconuts
Main housing structure	Brick houses, corrugated iron roofs	Mud houses, thatched roofs
Access to[c] (%)		
Electricity	34	6.2
Private or community piped water	84	59
Public wells	8.1	39
Latrines	70	32
No access to toilet facilities	7.0	57
Economy[c]		
Main economic activities	Informal business, government employees	Fishing, farming
Monthly median per capita expenditure	USD 22.6	USD 17.5
Annual incidence of cholera per 1,000 population[d]		
Mean (standard deviation)	2.9 (1.7)	2.5 (6.0)
Median (range)	2.2 (1.3-5.7)	0 (0-14.8)
Annual incidence of shigellosis per 1,000 population[e]		
Mean (standard deviation)	4.6 (1.6)	1.9 (0.3)
Median (range)	4.9 (2.9-6.1)	2.0 (1.7-2.2)

[a]Despite belonging to the Urban district, this community is of periurban character; [b]Census data from cholera control research project, 2008; [c]District-level data from Zanzibar Household Budget Survey, 2004/5 [16]; [d]Estimates (2002-2007) from Reyburn *et al*. (unpublished data) and WHO Cholera Country Profile for Zanzibar, 2006; [e]District-level estimates (2006-2008) from health facility-based surveillance [14,36]

3.2.2 Research framework and instrument

Among the various formulations of cultural epidemiology for health social science research [17], this study is based on an approach for examining the distribution of community ideas of illness-related experience, meaning and behavior [18,19]. A semi-structured Explanatory Model Interview Catalogue (EMIC) interview was developed to study community views of cholera and shigellosis in a periurban and rural community of Zanzibar. These EMIC interviews produce complementary data sets with numeric data for quantitative analysis and illness narrative data for qualitative analysis [20].

A first version of the interview was drafted in English during several scientific workshops and translated locally into Kiswahili. A series of focus group discussions and a field assistant training workshop with piloting of the instrument among people living adjacent to the study communities followed. This was crucial to further refine the EMIC interview with regard to clarity, field applicability and questions concerning translation. Because people without a current diarrheal disease were interviewed, rather than cases, the conditions that were the focus of the interview were introduced as clinical vignettes. For each condition, the respondent was asked to consider the case of a person typical of community residents with pathognomonic somatic symptoms presented in simple, easily understandable terms (see Appendix 9.3). The sex of the vignette and respondent were matched. All questions of the interview that was based on the vignette referred to the diarrheal illness of the person described in the vignette.

Selected sociodemographic variables were recorded at the outset before enquiring about illness-related experience, meaning and behavior operationalized as categories denoting patterns of distress (referring to additional somatic symptoms not mentioned in the vignettes and psychosocial problems), perceived causes, self treatment at home, and outside help seeking. The selection of the most relevant locally valid categories of distress, perceived causes, and help-seeking behavior required for a meaningful description of the insider's perspective was based on discussions with local researchers, field workers and focus group discussions among purposively selected community residents.

3.2.3 Study design and participant selection

This cross-sectional survey was conducted prior to a mass oral cholera vaccination campaign to provide baseline data on community views of diarrheal illness in areas of Zanzibar at high risk for cholera among unaffected adults [21]. A simple random sample of 180 houses per site was drawn based on enumerated houses from an existing geographic information system for the periurban and a census database for the rural site. Sampled periurban houses were approached with the help of aerial photographs and a global positioning system device. Sampled houses in the rural community were located through census house numbers nailed on doorframes. If the house selected for sampling did not contain dwellings (e.g. if it was a business place, mosque or under construction), then the field teams would move on to the house which was closest to the front door of the originally selected house. If the second house was not inhabited either, then a third house was identified following the above procedure, and so forth until a household with eligible participants was found. A household is defined by people sharing the same kitchen or pot. Eligible participants had to be 18 years or older and willing enough to give time for an interview of approximately one hour duration.

Three field teams plus a coordinator on both islands were recruited by the MoHSW and trained in a ten-day workshop to conduct this survey. Each team consisting of an interviewer and a note taker completed on average two interviews per day. Written informed consent was obtained from all participants prior to the interview and no compensation was offered to them.

3.2.4 Data management and analysis strategy

For cholera, the categories related to illness experience, meaning and help-seeking behavior were coded for their prominence with a value of 2 after a spontaneous response, a value of 1 after a probed response and a value of 0 if not considered at all to reflect the response style. An additional value of 3 was assigned to the category of response if the category was considered the most troubling category of distress, the most important perceived cause or the most helpful self treatment or source of help. The cumulative prominence by respondent (ranging from 0-5) was then used to calculate the mean prominence for each category. Thematically similar individual categories were grouped under specific headings (e.g. related to dehydration among somatic symptoms) for the analysis of broader concepts of experience, meaning and behavior. Calculation of the grouped prominence followed the same procedure as with the individual variables. To identify significant differences for cholera between the two sites and between sexes, a non-parametric statistic, the Wilcoxon rank-sum test, was used when comparing prominence variables; the Pearson Chi^2 and Fisher's exact test were applied when comparing proportions. This particular approach to comparing prominence, which has been widely used in other cultural epidemiological studies, takes more information about a category into account than a simple comparison of frequencies of report without considering how they are reported.

A similar series of questions were asked to elicit shigellosis-related illness experience, meaning and help-seeking behavior. The same categories that were coded for cholera were also coded for shigellosis. Comparative analysis between the two conditions considered only spontaneously reported categories, because the interview coded only spontaneous responses for shigellosis. The proportion of positive responses by category was tabulated individually for each vignette, and for a report in both vignettes. To determine whether a category was associated more with one vignette than the other, McNemar's Chi^2 test for paired data was used. To examine whether or not individual categories were differentiated between both conditions, Cohen's kappa was calculated. The kappa statistic indicates the strength of agreement for a categorical assessment, corrected for agreement by chance. The analysis identified the two conditions as distinct for a category if the kappa coefficient was below 0.4, a level commonly accepted as a threshold for moderate agreement [22].

Narrative information was written down during the interview in Kiswahili, then translated into English and typed in a word processor. The qualitative software MAXQDA, version 2007, was

used for managing the textual data and to facilitate further analyses of findings from quantitative data. Quantitative data was entered twice and verified in Epi Info software, version 3.4.3, and cleaned. Statistical analyses were done with Stata, version 10.

3.2.5 Sample size

The sample size calculation was based on comparison of mean prominence of categories of distress, perceived causes, self treatment and outside help seeking for periurban–rural and female–male differences. The detection of a difference of 0.5 between prominence means with equal standard deviations of 1.5 at 95% significance and 80% power required a sample size of at least 164 individuals per independent group. This calculation was based on a two-sample t test assuming no underlying distribution in the data [23]. Ten percent was added to this sample size to compensate for missing data.

3.2.6 Ethics

The protocol describing the study presented here was cleared by the WHO Research Ethics Review Committee and the MoHSW Ethics Committee in Zanzibar and later published in an open access journal to make it freely available to the research community [21]. Only individuals who gave written informed consent were interviewed. All data were handled with strict confidentiality and made anonymous before analysis.

3.3 Results

3.3.1 Sample characteristics

A total of 356 interviews were conducted, with very few people among the visited households who refused to be interviewed. The sociodemographic characteristics of the sample are summarized by site in Table 3-2. All respondents were Tanzanians and Muslims except a 22-year-old woman from Chumbuni who was Christian. The majority of the periurban sample consisted of married housewives and men doing small businesses. Periurban residents lived in bigger families than their rural counterparts and were also better educated. The rural sample in contrast consisted primarily of married persons mostly active in farming, fishing and also small informal businesses.

Table 3-2: Sample characteristics of study respondents from the general adult population of Zanzibar, n=356

	Periurban site, n=179	Rural site, n=177
Sex (%)		
Female	48.6	52.0
Age (years)		
Mean (standard deviation)	36.5 (14.1)	34.4 (14.9)
Median (range)	35 (18-85)	30 (18-90)
*Marital status[a] ** (%)*		
Never married	23.5	11.9
Married	68.7	84.2
Separated	0.6	0.0
Divorced	4.5	3.4
Widowed	2.8	0.6
*Household size[b] *** (number of persons)*		
Mean (standard deviation)	7.4 (3.2)	6.2 (2.7)
*Occupation[a] *** (%)*		
Agriculture	4.5	57.1
Fishing	2.2	12.4
Self-employment	22.3	11.9
Formal employment	11.7	4.0
Housewife	33.5	9.0
Casual labourer	2.2	0.6
Student	14.5	4.0
Not active/retired	8.9	1.1
*Highest educational level attained[c] *** (%)*		
No education	9.5	4.5
Koranic school	10.1	34.5
Primary school	23.5	33.9
Secondary school	54.2	25.4
Higher education	2.8	1.7
*Education[c] *** (years)*		
Median (range)	10 (0-16)	6 (0-20)
Household income (%)		
More regular and dependable	59.8	52.0
Less regular and dependable	40.2	48.0

[a]Pearson Chi² or Fisher's exact test; [b]t test; [c]Wilcoxon test; *p≤0.05, **p≤0.01, ***p≤0.001

3.3.2 Recognition and importance of illnesses and past episodes

The vignette describing an adult person with symptoms of acute watery diarrhea was named by 88.2% of the sample as *kipindupindu*, which is the Kiswahili name for the disease entity cholera. The rural villagers recognized cholera less often than the periurban residents (80.8% vs. 95.5%, p<0.001, Chi² test). Other names given by rural villagers were *kuharisha kawaida* for normal diarrhea (6.2%) and *kuharisha maji* for watery diarrhea (4.0%) while 6.2% could not identify the condition at all. The condition described in the shigellosis vignette was identified by 69.9% of the respondents as *kuharisha damu*, which refers to the disease entity bloody diarrhea. While

12.9% could not name it at all, 19 individuals (5.3%) confused the case presented in the shigellosis vignette with cholera.

The perceived severity and likely fatality for cholera and shigellosis vignettes was assessed in the periurban and rural areas. Cholera was more frequently said to be “very serious” (96.6%) than shigellosis (76.1%, $p<0.001$, McNemar’s Chi^2 test). Cholera was also more often anticipated to be “usually fatal without treatment” (77.5%) than shigellosis (47.8%, $p<0.001$, McNemar’s Chi^2 test). Although there was no difference in perceived severity for cholera at the two sites, for shigellosis more periurban respondents considered it very serious (86.0%) than rural respondents (66.1%, $p<0.001$, Chi^2 test). Periurban respondents more frequently anticipated fatality for cholera (84.4%) than rural respondents (70.6%, $p=0.002$, Chi^2 test), and periurban respondents were also more likely to anticipate fatality for shigellosis (65.4%) than rural respondents (29.9%, $p<0.001$, Chi^2 test).

When asked about previous experiences of the condition described in the cholera vignette, 5.3% of the total sample reported an individual episode. Stratified analyses revealed a significant difference between the periurban and rural community (2.8% vs. 7.9%, $p=0.032$, Chi^2 test), but not between women and men (3.4% vs. 7.3%, $p=0.094$, Chi^2 test).

3.3.3 Patterns of distress for cholera

Weakness was reported as the most prominent somatic symptom by the total sample (Table 3-3, upper panel). Categories related to dehydration, none of which were mentioned in the vignette, featured more prominently in the periurban site. This difference was primarily due to unconsciousness, a symptom which was identified by almost one-third of the periurban sample as most troubling. The respondents’ views regarding this category were related to the loss of body fluid or the advanced stage of the illness. Almost one-fifth could not report any other somatic symptom apart from the ones described in the vignette. Symptoms related to shigellosis were probed for consistency under the cholera vignette but were less often mentioned spontaneously or identified as most troubling and hence yielded a lower prominence than symptoms of general gastroenteritis or dehydration.

Table 3-3: Somatic symptoms and psychosocial problems for a cholera vignette in periurban and rural Zanzibar, n=356

	Periurban site, n=179				Rural site, n=177				
	How reported?[b]				How reported?[b]				
Category[a]	Total reported %	Fraction spon.	Most troubling %	Mean prom.[c]	Total reported %	Fraction spon.	Most troubling %	Mean prom.[c]	
Somatic symptoms									
Related to general gastrointestinal illness	98.9	0.81	14.5	2.23	99.4	0.67	16.4	2.15	
Abdominal pain/discomfort	91.1	0.47	2.8	1.42	88.7	0.06	6.2	1.13	***
Headache	64.8	0.02	0.0	0.66	55.4	0.02	0.6	0.58	
Loss of appetite	92.2	0.20	1.7	1.16	83.6	0.06	1.1	0.92	***
Nausea	87.7	0.04	0.6	0.93	88.1	0.03	0.6	0.93	
Weakness	96.6	0.69	9.5	1.92	97.7	0.64	7.9	1.84	
Related to shigellosis	97.2	0.20	3.9	1.28	96.0	0.10	13.0	1.45	
Abdominal cramps	76.5	0.11	2.8	0.93	75.1	0.08	6.8	1.01	
Bloody stool	23.5	0.14	0.6	0.28	50.3	0.03	2.8	0.60	***
Fever	82.7	0.11	0.6	0.93	87.0	0.03	1.7	0.95	
Pus in stool	8.9	0.06	0.0	0.09	37.9	0.00	0.0	0.38	***
Rectal pain	69.3	0.00	0.0	0.69	73.4	0.00	1.7	0.79	
Related to dehydration	98.3	0.31	46.9	2.70	98.3	0.51	18.6	2.04	**
Confusion	87.7	0.01	2.2	0.95	81.9	0.01	2.3	0.89	
Palpitations	84.4	0.03	9.5	1.16	73.4	0.02	1.7	0.80	***
Loose skin	90.5	0.17	1.1	1.09	88.1	0.24	0.6	1.11	
Sunken eyes	93.9	0.21	0.6	1.15	96.0	0.41	0.6	1.37	***
Unconsciousness	92.7	0.04	32.4	1.94	90.4	0.06	11.3	1.30	***
Very thirsty	76.5	0.03	1.1	0.82	78.5	0.06	2.3	0.90	
Miscellaneous	25.1	1.00	1.7	0.55	38.4	1.00	1.7	0.82	**
Other symptoms	10.1	1.00	1.1	0.23	16.4	1.00	0.6	0.34	
Cannot say	15.1	1.00	0.6	0.32	22.0	1.00	1.1	0.47	
Psychosocial problems									
Social impact	99.4	0.88	36.9	2.97	99.4	0.91	50.3	3.41	**
Disruption of health services	48.0	0.01	1.7	0.54	88.1	0.01	1.7	0.94	***
Fear of infecting others	83.8	0.28	2.2	1.14	72.9	0.22	6.8	1.09	
Fear of isolation from others	62.6	0.36	8.4	1.10	53.1	0.12	14.7	1.03	
Interference with social relationships	65.4	0.08	3.9	0.82	74.6	0.60	2.8	1.28	***
Interference with work/daily activities	96.6	0.73	20.7	2.30	97.2	0.72	24.3	2.40	
Emotional impact	100.0	0.75	10.1	2.06	94.9	0.45	11.3	1.72	***
Sadness, anxiety, worry	100.0	0.75	10.1	2.06	94.9	0.45	11.3	1.72	***
Financial impact	99.4	0.62	52.5	3.18	99.4	0.73	38.4	2.88	
Costs (transport, food, drugs)	97.2	0.08	34.1	2.07	96.0	0.32	13.6	1.67	
Loss of family income	98.3	0.58	18.4	2.11	92.7	0.52	24.9	2.16	

[a]Categories ordered alphabetically within each group (bold). Categories reported by less than 5% not listed; [b]Columns indicate percentage of reported categories, fraction of spontaneously mentioned categories and whether a category was identified as most troubling; [c]Mean prominence based on values assigned to each reported category (0=not reported, 1=reported after probing, 2=reported spontaneously, 3=identified as most troubling); Wilcoxon test used to compare mean prominence between both sites (*p≤0.05, **p≤0.01, ***p≤0.001)

When assessing the potential impact of cholera on a person's life, interference with work or daily activities was ranked as the highest category in both sites, followed by financial and emotional distress (Table 3-3, lower panel). The disruption of local health services was rated as the least important problem overall, but it was seen more as a problem in the rural community. The spontaneous account of a 75-year-old man from Chumbuni indicates how respondents describe the impact of cholera:

> "It affects life in general. Emotionally, the patient thinks that he is going to die. Also, financially, he will spend a lot of money to buy medicine and at the same time he cannot work because of the disease."

The emotional impact was more prominently expressed in the periurban community, where the fraction of spontaneous replies for this category was higher. Despite this significant difference, the dangerousness of cholera, especially in relation to the possibility of death as exemplified in the statement above, featured equally in both communities.

3.3.4 Perceived causes for cholera

A dirty environment (*mazingira machafu*), related to general in- and outdoor dirtiness, was by far the most prominently reported perceived cause overall, but particularly notable in the periurban site (Table 3-4). Among the causes related to ingestion, which were the second most prominent group in both sites, drinking contaminated water was ranked highest. This category was coded when respondents mentioned drinking unboiled or dirty water, or water containing feces—some respondents explicitly mentioned cholera bacteria. Drinking contaminated water ranked as the second most prominent cause in total followed by flies, which were seen as disease transmitters in both communities. Flies, which can actually transmit *V. cholerae* [24,25], were mostly mentioned in connection with uncovered, i.e. unprotected, food, which was more prominently reported in the periurban community:

> "Yes, because usually flies carry dirt and spread it everywhere, especially in the food." (Housewife from Chumbuni, 32 years old).

> "It is possible that the flies coming from the toilet contaminate the food." (Male coffee seller from Mwambe, 50 years old).

Table 3-4: Perceived causes for a cholera vignette in periurban and rural Zanzibar, n=356

	Periurban site, n=179				Rural site, n=177				
	How reported?[b]				How reported?[b]				
Category[a]	Total reported %	Fraction spon.	Most important %	Mean prom.[c]	Total reported %	Fraction spon.	Most important %	Mean prom.[c]	
Ingestion	98.3	0.61	17.3	2.11	96.6	0.37	22.6	2.00	*
Drinking contaminated water	96.1	0.40	10.1	1.65	94.4	0.24	16.4	1.66	
Eating unprotected/spoiled food	95.5	0.45	7.3	1.60	94.4	0.18	5.1	1.27	***
Eating forbidden food	27.4	0.00	0.0	0.27	54.8	0.00	1.1	0.58	***
Eating soil	36.9	0.00	0.0	0.37	48.6	0.01	0.0	0.49	*
Behavior	96.1	0.28	4.5	1.36	94.4	0.44	11.3	1.69	**
Contact with contaminated water	85.5	0.20	1.7	1.07	91.0	0.42	9.6	1.58	***
Not washing hands	92.2	0.14	2.8	1.13	88.1	0.12	1.7	1.03	
Environment	100.0	0.89	70.9	4.02	98.3	0.68	37.3	2.77	***
Dirty environment	99.4	0.84	61.5	3.68	96.0	0.62	24.9	2.30	***
Flies	99.4	0.34	9.5	1.62	94.4	0.28	12.4	1.58	
Malaria	15.1	0.00	0.0	0.15	48.0	0.02	0.0	0.49	***
Worms	13.4	0.00	0.0	0.13	46.9	0.00	0.0	0.47	***
Magico-religious causes	94.4	0.07	7.3	1.23	91.0	0.16	28.8	1.92	***
God's will	93.3	0.07	7.3	1.22	86.4	0.16	27.7	1.83	***
Witchcraft	20.7	0.00	0.0	0.21	45.8	0.01	1.1	0.50	***
Miscellaneous	5.0	1.00	0.0	0.10	27.1	1.00	0.0	0.54	***
Other	3.9	1.00	0.0	0.08	13.6	1.00	0.0	0.27	**
Cannot say	1.1	1.00	0.0	0.02	13.6	1.00	0.0	0.27	***

[a]Categories ordered alphabetically within each group (bold), except "cannot say". Categories reported by less than 5% not listed; [b]Columns indicate percentage of reported categories, fraction of spontaneously mentioned categories and whether a category was identified as most important; [c]Mean prominence based on values assigned to each reported category (0=not reported, 1=reported after probing, 2=reported spontaneously, 3=identified as most important); Wilcoxon test used to compare mean prominence between both sites (*p≤0.05, **p≤0.01, ***p≤0.001)

Among the causes not related to the fecal-oral route of transmission, God's will was the most prominent category and ranking higher among rural residents. A statement from a 30-year-old female farmer from Mwambe helps to explain the commonly expressed notion regarding this finding, i.e. that God overrules people's prevention efforts if only it wished:

> "There is no cause except God's will, which cannot be changed; and it is not caused by dirty environment because there are some dirty places where people do not get the disease."

Further perceived causes not linked to cholera disease etiology—like witchcraft, malaria and worms—had lower prominence ratings since they were almost never mentioned spontaneously nor identified as most important. And these categories were more characteristic for the rural compared with the periurban community. A substantial proportion of the respondents from Mwambe—more than one-tenth, compared to only two periurban residents—had no idea what could have made the person suffer from the symptoms described in the vignette (coded as cannot say). Among rural respondents who could not spontaneously identify a cause, women

featured significantly more often than men (19.6% vs. 7.1%, p=0.016, Wilcoxon test) (not shown in Table 3-4).

3.3.5 Self treatment and help seeking for cholera

The most prominent self treatment at home in the rural community was herbal treatment, followed by giving antibiotics or other drugs like pain killers or antacids and then home-made or ready-to-use oral rehydration solution (ORS) (Table 3-5, upper panel). In contrast, the periurban residents' preference for herbal treatment was less pronounced as they primarily suggested giving someone like the person described in the cholera vignette more water or other liquids, like tea or porridge, or ORS. For most respondents, local herbal treatment, used for relief or cure of symptoms, comprised concoctions of water with locally grown spices like cumin or cloves, or with leaves, barks and roots of herbs and trees (e.g., *mpatakuva* (*Plectranthus* spp.), neem tree, guava). Doing nothing at home, i.e., sending the person described in the cholera vignette immediately to allopathic health care facilities, was considered as the least prominent category in the rural community, while it ranked fourth in the periurban community and was regarded as the most helpful thing one can do at home. The following statement from a housewife, aged 47 years, from Chumbuni is typical for what the communities would do for people with cholera at home:

> "At home we give water and other people give local treatment. […] and if the condition becomes worse, we will send the patient to the hospital."

Table 3-5: Self treatment and help seeking for a cholera vignette in periurban and rural Zanzibar, n=356

	Periurban site, n=179				Rural site, n=177				
	How reported?[b]				How reported?[b]				
Category[a]	Total reported %	Fraction spon.	Most helpful %	Mean prom.[c]	Total reported %	Fraction spon.	Most helpful %	Mean prom.[c]	
Self treatment at home									
Antibiotics/drugs	44.7	0.26	15.6	1.03	72.3	0.14	24.9	1.57	***
Doing nothing at home	27.9	1.00	22.9	1.25	19.8	1.00	4.5	0.53	**
Drinking more water or liquids	68.7	0.45	19.6	1.58	69.5	0.10	9.6	1.05	**
Herbal treatment	49.7	0.75	14.0	1.29	83.1	0.73	28.8	2.31	***
Oral rehydration therapy/solution	59.8	0.28	21.2	1.40	72.9	0.07	23.7	1.49	
Prayers	55.9	0.02	5.6	0.74	47.5	0.00	8.5	0.73	
Outside help seeking									
Faith healers	11.7	0.00	0.0	0.12	18.1	0.00	2.3	0.25	
Health facilities	100.0	1.00	95.5	4.87	100.0	1.00	80.2	4.41	***
Informal help from health worker/friend	38.5	0.00	4.5	0.52	73.4	0.00	15.8	1.21	***
Pharmacy/OTC	27.4	0.00	0.0	0.27	40.7	0.00	1.1	0.44	**
Traditional healers	3.9	0.00	0.0	0.04	9.6	0.06	0.6	0.12	*

[a]Categories ordered alphabetically. Categories reported by less than 5% not listed; [b]Columns indicate percentage of reported categories, fraction of spontaneously mentioned categories and whether a category was identified as most helpful; [c]Mean prominence based on values assigned to each reported category (0=not reported, 1=reported after probing, 2=reported spontaneously, 3=identified as most helpful); Wilcoxon test used to compare mean prominence between both sites (*p≤0.05, **p≤0.01, ***p≤0.001)

Public primary health care units and hospitals were mentioned by all respondents (Table 3-5, lower panel). More than 95% of the periurban residents identified health facilities as most helpful source of treatment, while the rural residents' preference was around 15% lower. Faith healers and traditional healers were of little importance and probing revealed that they would only be consulted after allopathic treatment had failed.

3.3.6 Shigellosis versus cholera

Similar to the cholera vignette, weakness was also rated as the most prominent somatic symptom for the shigellosis vignette (Table 3-6, top panel). Among symptoms related to dehydration, only loose skin and sunken eyes were mentioned; and both categories were reported significantly less for shigellosis than for cholera. The remaining symptoms of dehydration fell under the 5% threshold. All categories of somatic symptoms were differentiated on the individual level in both sites.

Table 3-6: Symptoms, perceived causes, and self treatment for a cholera and a shigellosis vignette in Zanzibar, n=356

Category[a]	Only cholera vignette[b] %	Only shigellosis vignette[b] %	Both cholera & shigellosis vignette[c] %	p value[d]	Kappa coefficient[e] Estimate	95% CI
Somatic symptoms						
Abdominal pain/discomfort	24.2	38.2	13.2	<0.001	0.18	0.08 - 0.28
Loose skin	18.3	5.6	3.4	<0.001	0.21	0.09 - 0.34
Loss of appetite	11.8	13.5	3.1	0.467	0.14	0.01 - 0.26
Sunken eyes	29.5	8.4	5.1	<0.001	0.16	0.06 - 0.25
Weakness	64.9	57.0	45.2	0.008	0.34	0.25 - 0.44
Other somatic symptoms	13.2	12.4	2.5	0.726	0.08	-0.04 - 0.20
Cannot say	18.5	22.8	9.8	0.087	0.34	0.23 - 0.46
Psychosocial problems						
Costs (transport, food, drugs)	19.1	20.8	12.6	0.405	0.54	0.43 - 0.65
Fear of infecting others	19.7	2.0	1.1	<0.001	0.07	-0.01 - 0.15
Fear of isolation from others	14.3	4.2	2.0	<0.001	0.16	0.03 - 0.29
Interference with social relationships	24.7	15.2	12.6	<0.001	0.55	0.44 - 0.65
Interference with work/daily activities	70.5	61.8	53.9	0.001	0.46	0.35 - 0.55
Loss of family income	52.8	43.5	34.0	0.001	0.44	0.35 - 0.53
Sadness, anxiety, worry	59.3	58.7	47.2	0.827	0.51	0.42 - 0.60
Perceived causes						
Contact with contaminated water	27.5	2.8	1.7	<0.001	0.06	-0.01 - 0.13
Dirty environment	71.6	32.6	28.4	<0.001	0.17	0.11 - 0.25
Drinking contaminated water	30.6	21.6	9.6	0.003	0.15	0.04 - 0.26
Eating unprotected/spoiled food	30.1	29.8	12.1	0.929	0.15	0.04 - 0.26
Flies	30.3	13.2	5.9	<0.001	0.11	0.01 - 0.21
God's will	10.1	13.8	3.9	0.085	0.24	0.10 - 0.38
Not washing hands	11.5	9.0	1.1	0.264	0.01	-0.10 - 0.12
Cannot say	7.3	23.0	5.6	<0.001	0.29	0.18 - 0.41
Self treatment at home						
Antibiotics/drugs	11.0	20.5	3.4	<0.001	0.08	-0.03 - 0.19
Doing nothing at home	23.9	20.2	10.4	0.154	0.32	0.21 - 0.44
Drinking more water or liquids	18.8	10.7	5.9	<0.001	0.31	0.18 - 0.43
Herbal treatment	49.2	55.6	35.7	0.035	0.33	0.24 - 0.43
Oral rehydration therapy	11.0	5.9	2.8	0.004	0.28	0.12 - 0.44

[a]Categories ordered alphabetically, except "cannot say". Categories reported by less than 5% of the sample for each vignette not listed; [b]Proportion of categories reported spontaneously for either cholera or shigellosis vignette; [c]Proportion of categories reported spontaneously for both vignettes; [d]McNemar's Chi^2 test used to compare population proportions between both vignettes. Bold figures ($p \leq 0.05$) indicate significant differences; [e]Kappa coefficients (presented with 95% confidence intervals) greater than or equal to 0.4 suggest no differentiation of illness categories (bold figures)

Notable among psychosocial problems was fear of infection and fear of isolation from others. Both categories were reported considerably less for shigellosis than for cholera, and were also well-differentiated (Table 3-6, second panel). All the other categories, which represent general features of diarrheal illness, i.e. costs, loss of family income, interference with social

relationships and with daily activities, and being sad, anxious or worried, were not differentiated between both conditions (kappa coefficient greater than 0.4).

A dirty environment was perceived to be the most prominent cause of shigellosis (Table 3-6, third panel). The percentage of this category, however, was less than half the percentage for cholera, and was closely followed by the category of eating unprotected or spoiled food. All categories of perceived causes that showed a significant difference between the two conditions were mentioned less frequently for shigellosis, with the exception of cannot say, which was reported three times more often for shigellosis than for cholera. Kappa coefficients for all categories were below the threshold of 0.4 suggesting differentiation of the meaning of cholera from shigellosis.

The distribution of respondents' answers for self-treatment options showed that the population proportions related to rehydration were higher for cholera (Table 3-6, bottom panel). Conversely, a likely benefit for shigellosis was reported for antibiotics/drugs and for herbal treatment. Kappa coefficients were also below the threshold of 0.4 for all help-seeking categories.

Similar to the observed preponderance in the case of cholera, health facilities were regarded as the sole source of outside help for treating people with shigellosis (354 out of 356 respondents).

3.4 Discussion

Findings from both periurban and rural areas of Zanzibar were notable for the high perceived severity and anticipated fatality of cholera. Even though the condition described in the cholera vignette was similarly regarded as very serious in both communities, it was more often named as cholera and considered as a serious life-threatening illness in the periurban community. The lower recognition of the condition described in the cholera vignette in the rural community, which is consistent with lower prominence of reported signs and symptoms of dehydration and higher prominence for the two most conspicuous shigellosis signs (bloody stool, pus in stool), may be explained by poorer education. It cannot be explained by less personal illness experience of cholera, however, since rural residents reported the occurrence of an individual episode 2.8 times more often than periurban residents.

The severity of the condition in the cholera vignette was also elaborated with reference to its impact on affected persons and household livelihoods. Absence from work was felt to be the major effect at both sites leading to strain for household finances because of reduced or lost income and treatment costs. Compared to the shigellosis vignette, the condition described in the

cholera vignette was more often perceived as a severe and potentially fatal health problem in both communities. This finding is consistent with another study comparing the two conditions; unaffected community residents, confirmed shigellosis patients and health care providers in Bangladesh considered cholera to be more severe than shigellosis [26].

Although a variety of causes were acknowledged, respondents clearly regarded the condition depicted in the cholera vignette as a disease linked to a dirty environment and to ingesting microbiologically contaminated water and food. The relevance of this concept of dirtiness and of sanitation and hygiene in connection with diarrhea was also found in a qualitative study of childhood diarrhea among mothers living in Chake-Chake district on Pemba [27]. The role of a dirty environment as a cause of cholera was especially highlighted by periurban residents living in an area with better water supply and sanitation. While it can be expected that better water supply and sanitation would result in less importance of dirty environment, the periurban emphasis in this study may be explained by the 19 times higher population density and the higher number of persons living in the average Chumbuni household. Most people reported magico-religious causes, but the relative priority was higher in the rural site. Other causes unrelated to the biomedical basis of cholera (i.e. worms and malaria) were less frequently mentioned in both sites and were also more prominent in the rural site. These findings are consistent with the lack of knowledge of cholera causes in the rural community, which was especially prominent among the women there.

Besides using various allopathic and traditional home remedies, respondents also recommended immediate hospital treatment when queried about what they would do at home with someone like the person described in the cholera vignette. Periurban community responses emphasized rehydration; rural community responses emphasized herbal treatment and use of antibiotics and other drugs. Certain herbs and plants, most of which were also reported as herbal treatment in the childhood diarrhea study from Chake-Chake [27], were frequently recommended as home-based treatment. Reasons for that may include their availability to people, who collect them freely in the bush and woods, and their beneficial effect against cholera and other bacterial gastrointestinal diseases [28-30]. Periurban recommendations for self-treatment more frequently referred to health education and awareness, which probably results from exposure to public health activities. Periurban respondents also more frequently considered the value of immediate hospital treatment for the condition in the cholera vignette. Rural respondents, on the other hand, emphasized magico-religious and other unrelated causes of cholera.

In both sites, help seeking outside the household for the person described in the cholera vignette essentially meant going to public health care facilities, with little mention of traditional healers and faith healers. This finding of reliance on hospital treatment is remarkable compared with

other studies from low- and middle-income countries, which emphasize traditional treatment for childhood and adult diarrhea [31-33]. Several factors may help explain this priority: Many people in these communities have experience and a high regard for cholera treatment camps, which have been established when needed for outbreaks by the district administration and provide free treatment. Traditional health care providers, on the other hand, charge for their services. These communities have also been exposed to health education from public health action of the MoHSW and international non-governmental organizations in the wake of cholera outbreaks. Ethnographic field study also indicates that traditional healers in the study communities support hospital treatment (A. Pach, unpublished data).

The analysis of disagreement showed illness concepts for the two conditions were distinct with respect to reported patterns of distress, perceived causes and self treatment. For outside help seeking, however, reference to the value of hospital treatment was the same for both conditions. Differentiation of the two conditions may be explained by community and personal experience with cholera and shigellosis, resulting in the awareness of particular features of the two conditions. Both conditions occur with similar rates in the study communities (Table 3-1).

Health educational activities for cholera, in response to the priority arising from outbreaks making heavy demands on the health system in Zanzibar, are more extensive than for shigellosis. Less emphasis on shigellosis control may account for the finding that fewer respondents could explain the cause of shigellosis (23% reporting cannot say) compared with cholera (7.3%). The finding that fewer respondents identified houseflies as a cause of shigellosis may also result from the lower priority of public health action for shigellosis control, inasmuch as houseflies are recognized agents of transmission for shigellosis [34]. Dehydration and contagiousness are two other features of both conditions that community respondents identified more with cholera only. Dehydration is also an important feature of shigellosis, and shigellosis is more contagious than cholera [35].

The differentiation of the two conditions is reflected by appropriate differences in treatment recommended by respondents. Community self-treatment priorities emphasized rehydration for cholera and herbal and antibiotic treatment for shigellosis.

3.4.1 Strengths and limitations

This study shows how EMIC interviews can be used to assess explanatory models of diarrheal illnesses among unaffected community residents and how to compare them among sub-groups. The specific approach employed in this cultural epidemiological study to comparing prominence allowed the ranking of categories according to their relative priority and not just according to their reported frequency. This weighted approach represents a more sensitive method to clarify

differences between groups and has implications for explaining cultural priorities and potential effects on health behavior.

The findings presented here are specific for cholera and shigellosis in one culture and focus on variation between periurban and rural areas. Thus, any generalizations made to countries outside the target populations have to be examined cautiously as the results presented here are inherently linked to the context. Some may argue that the differences in community views are due to education rather than to residence. However, analysis of the patterns of distress, perceived causes, self treatment and help seeking, stratified by educational status, showed that the cross-site differences reported here were not confounded by education.

It should also be noted that findings reported here are cross-sectional and may change over time, possibly in response to access to health services, a vaccine campaign or other social changes. Furthermore, the data are based on respondents' ideas about the condition of a clinical vignette, representing community views of illness experience, meaning and behavior, but not necessarily an account of personal or family history.

The sampling included only community residents who were at home when the field teams visited. The study could be biased if the views of the respondents available for interviews at home and persons unavailable because of other responsibilities differed. The age distribution at both sites, however, mitigates this concern, inasmuch as all age groups were represented in the sample.

3.5 Conclusions

This study has clarified local periurban and rural views of cholera among the general population with practical significance for cholera control in Zanzibar. Cholera was recognized as a serious and potentially fatal condition, a priority that makes such communities receptive to community health education programs. The overwhelming preference for public health care facilities to treat cholera and shigellosis indicates the importance of strengthening health systems to ensure they are capable of fulfilling expectations. Notwithstanding this appropriate community preference for hospital treatment, this study also suggests that better health education is needed for cholera in rural areas and for shigellosis in general. The finding that rural women were more likely than men to be unable to specify a cause of cholera indicates the need to ensure a gender-sensitive approach to control.

Although sanitation, hygiene and safe water are critical issues for diarrheal disease control, recent consideration of vaccines in endemic areas suggest an appealing complementary

intervention. It is an approach that has been of considerable interest to policy makers in Zanzibar, where a cholera vaccine campaign was implemented in January and February 2009. Research is needed to identify not only health system capacities to deliver vaccines but also social and cultural factors affecting community acceptance of vaccines. Factors influencing the willingness and enthusiasm of communities for a recommended vaccine can be expected to affect the success of a vaccine intervention program. The interests and findings of this study are likely to inform such efforts to clarify social and cultural features of vaccine acceptance and demand.

Although not used in planning the cholera vaccine campaign in Zanzibar, findings from this study identified variables for a subsequent analysis of social and cultural determinants of vaccine acceptance and demand. Further analysis is also needed to explain the impact of the vaccine campaign on community views of cholera and risk-related behavior. This study indicates directions and enables further research, and it has also clarified important issues for cholera control.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Conception and design of this study: CS, AMK, SMA, RH, CLC and MGW. Supervision of data collection and data entry: CS. Analysis of data: CS and MGW. Writing of manuscript: CS and MGW. Revision and final approval of manuscript: CS, AMK, SMA, RH, CLC and MGW.

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4

SOCIAL AND CULTURAL DETERMINANTS OF ANTICIPATED ACCEPTANCE OF AN ORAL CHOLERA VACCINE PRIOR TO A MASS VACCINATION CAMPAIGN IN ZANZIBAR*

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Abstract

Despite improvements in sanitation and water supply, cholera remains a serious public health burden. Vaccination is included among recommendations for cholera control. Cultural concepts of illness are likely to affect vaccine acceptance. This study examined social and cultural determinants of anticipated acceptance of an oral cholera vaccine (OCV) prior to a mass vaccination campaign in Zanzibar. Using a cultural epidemiological approach, 356 unaffected adult residents were studied with vignette-based semi-structured interviews. Anticipated acceptance was high for a free OCV (94%), but declined with increasing price. Logistic regression models examined social and cultural determinants of anticipated acceptance at low (USD 0.9), medium (USD 4.5) and high (USD 9) price. Models including somatic symptoms (low and high price), social impact (low and medium) and perceived causes (medium and high) explained anticipated OCV acceptance better than models containing only sociodemographic characteristics. Identifying thirst with cholera was positively associated with anticipated acceptance of the low-priced OCV, but acknowledging the value of home-based rehydration was negatively associated. Concern about spreading the infection to others was positively associated at low price among rural respondents. Confidence in the health system response to cholera outbreaks was negatively associated at medium price among periurban respondents. Identifying witchcraft as cause of cholera was negatively associated at medium and high price. Anticipated acceptance of free OCVs is nearly universal in cholera-endemic areas of Zanzibar; pre-intervention assessments of community demand for OCV should not only consider the social epidemiology, but also examine local sociocultural features of cholera-like illness that explain vaccine acceptance.

4.1 Introduction

Despite improvements in infrastructure, cholera remains a serious public health burden in Africa and South Asia [1,2]. The World Health Organization (WHO) recommends vaccination as a supplement to improved sanitation, supply of safe water and hygiene education for the prevention of cholera in populations at risk [3]. Recent studies have assessed the use of oral cholera vaccines (OCV) in endemic areas and in emergency situations, with a focus on vaccine characteristics, herd protection and economic aspects [4].

To maximize the public health impact of immunization, however, more than a safe and efficacious vaccine is needed. In addition to an effective health system optimizing access to immunization, it is also crucial to better understand local cultural concepts of illness among potential vaccine recipients as these are likely to affect vaccine acceptance [5-7]. The bulk of literature on determinants of vaccine acceptance, however, has mainly considered sociodemographic characteristics, with an emphasis on vaccines for human papillomavirus, and seasonal or pandemic influenza [8-10]. In industrialized countries, acceptance of these vaccines by health care workers has also been a focus of research [11]. Despite the need to assess local community views of illness and their relationship with vaccine acceptance, only few studies have been conducted in low- and middle-income countries. A series of studies on social and cultural determinants of cholera vaccine acceptance was conducted by the International Vaccine Institute in cholera-endemic Asian countries [12-14], but no such studies have been published for Africa.

Cultural epidemiological studies using vignette-based semi-structured interviews have been employed to empirically describe community views of illness among general populations [15,16]. Cultural epidemiology [17], which is an integrated methods approach based on Arthur Kleinman's concept of illness explanatory models [18], is using qualitative and quantitative methods to clarify locally valid sociocultural features of illness experience with reference to patterns of distress, meaning with reference to perceived causes, and behavior with reference to help seeking. These three areas of interest are examined through study of the distribution of categories of distress (which include signs, symptoms and other features of illness experience), perceived causes (a feature of illness meaning of particular interest) and self treatment at home and outside help seeking for health problems. Cultural epidemiological studies have been particularly useful in examining the link between the distribution of sociocultural features of illness and designated outcomes of importance for disease control and public health for infectious and chronic illnesses [19-22].

This study was performed in Zanzibar within a project managed by the WHO. The project's main objective was to vaccinate community residents in selected cholera hotspots on both islands of Zanzibar to assess the effectiveness of OCV under real-life conditions. Complementary research studies examined additional epidemiological, sociobehavioral and economic aspects regarding the use of OCV in endemic settings in Africa. A mass vaccination campaign, which was implemented in early 2009 by the Ministry of Health and Social Welfare of Zanzibar (MoHSW) with assistance from the WHO, offered an OCV without cost to a target population of ~50,000 people living in periurban and rural communities. The campaign used Dukoral®, a recombinant cholera toxin B subunit, killed whole-cell OCV that has to be administered in a buffer solution in two doses at least one week apart; it should not be given to children younger than two years and to pregnant women [3]. Dukoral® is currently the only OCV that is prequalified by the WHO; thus it is the sole OCV that can be used for cholera control in countries that have no capacity or limited resources to license vaccines. Another OCV, Shanchol™, is a simpler variant of Dukoral® that is being produced in India and likely to be cheaper and thus more attractive for use in low- and middle-income countries, but it is still pending WHO prequalification [3,4].

The results presented here are based on descriptive findings from a previous report that clarified similarities and differences of community views of cholera in the periurban and rural target populations in Zanzibar [23].

This study aimed to assess social and cultural determinants of anticipated oral cholera vaccine acceptance prior to a mass vaccination campaign in a periurban and a rural community of Zanzibar. Because of the reported high awareness of cholera in the study communities [23], it was hypothesized that anticipated acceptance of the free vaccine would also be high, and that determinants of anticipated acceptance would not only include sociodemographic and economic characteristics, especially for high-priced vaccines [24-26], but also sociocultural features of illness. Social and cultural determinants of anticipated OCV acceptance were investigated with regard to the OCV at no cost, and at three distinct price levels. The latter were defined on the basis of pragmatic considerations of using vaccines as a public health tool to improve cholera control.

4.2 Methods

4.2.1 Setting and study design

This cross-sectional survey took place from June to August 2008 in two communities selected for the 2009 cholera mass vaccination campaign in Zanzibar. The community of Chumbuni,

located on the outskirts of the capital Stonetown on Unguja island, was selected as the periurban, and the community of Mwambe, located on the southeastern tip of Pemba island, as the rural study site. In both sites only a basic sanitation infrastructure and a sporadic water supply exist. Monthly mean per capita expenditure for all goods amounted to USD 28.3 in the periurban and to USD 20.1 in the rural site in 2004/2005 [30]. Further details of both study sites have been presented elsewhere [23].

A simple random sample of 180 houses per site was drawn from existing geographic information system data in the periurban site and from census information in the rural site. Eligible participants who were selected from households identified in the sampled houses needed to be 18 years or older and capable to stand an interview of approximately one hour duration. An equal number of men and women were approached for the interviews.

4.2.2 Instrument

Semi-structured illness explanatory model interviews are the principal tool for cultural epidemiological research. These EMIC (Explanatory Model Interview Catalogue) interviews enable assessment of locally valid features of illness-related experience, meaning and behavior, operationalized as categories of distress, perceived causes, and help seeking [35]. Since this study's objective was to examine the influence of community views of cholera illness on anticipated vaccine acceptance, only residents without an apparent diarrheal illness at the time of the study were interviewed.

Interviews were introduced with clinical vignettes describing a person with cardinal somatic symptoms of cholera. Categories of somatic symptoms (in addition to the ones mentioned in the vignette), social impact, perceived causes, self treatment at home and outside sources of help seeking were elicited first with open questions followed by explicit probing of remaining categories. After each section, a summary question was asked to identify the most troubling category of distress, the most important category of perceived causes and the most helpful category of help seeking. Further details about interview development and the vignettes used in this study have been presented elsewhere [23].

The interview also inquired whether respondents would swallow a vaccine against cholera if it was made available at no cost, since Dukoral® was administered for free during the subsequent mass vaccination campaign. However, since a vaccine for free might have been considered less useful by respondents, interviews also asked about acceptance of the OCV at a *low* price of TZS 1,000 (~USD 0.9), a *medium* price of TZS 5,000 (~USD 4.5) and a *high* price of TZS 10,000 (~USD 9). The low price level was chosen to be close to the threshold of USD 1 reported by Asian

policy makers as “the maximum acceptable price the government would pay for new-generation enteric vaccines.” [13] The high price level approximated the manufacturing costs of Dukoral® at the time of the study; the medium level represented 50% of it.

4.2.3 Data management and analysis

Explanatory variables

Explanatory variables for the analysis of anticipated OCV acceptance included categories of distress, perceived causes, and help seeking. Categories mentioned spontaneously were assigned a value of 2. After screening for remaining categories, those that were reported affirmatively were assigned a value of 1. Categories identified as most troubling, most important or most helpful were assigned an additional value of 3. The cumulative prominence by respondent (range 0-5) was then used to calculate the mean prominence for each category. This prominence-based approach enabled examination of the relative significance of each category in the local cultural concepts of cholera. The distribution and prominence of these categories with reference to their similarities and differences in the periurban and the rural study community has been presented extensively in the baseline study [23]. Sociodemographic characteristics were also recorded and, if needed, categorized for regression analysis.

Outcome variables

Anticipated acceptance of the OCV for free, at low, medium and high price was elicited with a series of four questions at the end of the interview. Respondents’ positive answers were coded with “yes” or “possibly” in the event of a qualified answer and with “no” and “uncertain,” respectively, for a negative answer. These variables were then dichotomized into outcome variables denoting acceptance or non-acceptance of the OCV for logistic regression analysis using SAS 9.2 (SAS Institute, Cary, NC, USA).

Focal and comprehensive models of anticipated OCV acceptance

Only explanatory variables reported by 5-95% were considered for analysis. Second, only variables whose crude association with the outcome had a p value less than 0.2 were retained for subsequent multivariable models. Third, *focal* multivariable logistic regression models were run for each subset of categories related to somatic symptoms, social impact, perceived causes, self treatment at home and outside sources of help seeking, while adjustment was made for sociodemographic characteristics. Focal models addressed the question of how specific subsets of sociocultural features of cholera-like illness are associated with anticipated OCV acceptance. Fourth, to examine which factors affect anticipated OCV acceptance from an exclusively social epidemiological standpoint [31], additional focal models were calculated that considered only

sociodemographic characteristics. Among these focal models, consideration of the difference (Δ) in the Akaike Information Criterion corrected for sample size (AICc) between each model and the model with the lowest AICc helped to examine which of these models explain anticipated OCV acceptance better. Models of sociocultural features of cholera-like illness were considered better than the sociodemographic model if their Δ(AICc) value was noticeably below the latter's value. Finally, *comprehensive* multivariable models examined determinants of anticipated OCV acceptance, taking into account only variables with $p<0.2$ from focal models. Respondents' residence (rural vs. periurban site at baseline) was assessed as an effect modifier. Interaction between each explanatory variable and site was initially tested in focal models and interaction terms only retained in final focal and comprehensive models if $p<0.1$. Models report regression coefficients and their 95% confidence intervals and p values. In case of significant effect modification by site, site-specific estimates are presented. This staged variable reduction strategy ensured that the final models were not overfitted.

Qualitative data for integrated analysis

Qualitative data were used to help explain quantitative associations found in adjusted analyses. Narratives written down in Kiswahili during the interview were translated into English and typed in word processor software using a pre-coded structure that reflected interview items. Deductive coding of themes was done based on open-ended questions and probing in the interview. Transcripts were imported into MAXQDA 10 (VERBI Software, Consult. Sozialforschung. GmbH, Marburg, Germany) together with explanatory and outcome variables. This enabled selective retrieval of narrative segments based on analytically relevant relationships. Further themes were coded inductively based on additional relevant issues emerging from analysis.

4.2.4 Ethics

Written informed consent was obtained from all study participants and no incentives were provided to them. The protocol of this study was cleared by the WHO Research Ethics Review Committee and the MoHSW Ethics Committee [36]. Interviews were recorded without names and all data were handled with strict confidentiality and anonymized for analysis.

4.3 Results

Of the 356 interviews that were conducted in total, 179 took place in the periurban and 177 in the rural site. The sample consisted of 50.3% women. Mean age was 35.5 years (median 33 years) and the majority of respondents was married (76.4%). Mean household size was 6.8 persons (median 7 persons) and major occupations were farming (30.6%), being a housewife

(21.4%) and working in the informal economy (17.1%). More than half (55.9%) reported a regular and dependable household income. All respondents were Muslims, except one Christian woman.

4.3.1 Anticipated acceptance of OCV

Figure 4-1 presents the anticipated acceptance rates for the OCV at no cost and at the three designated price levels.

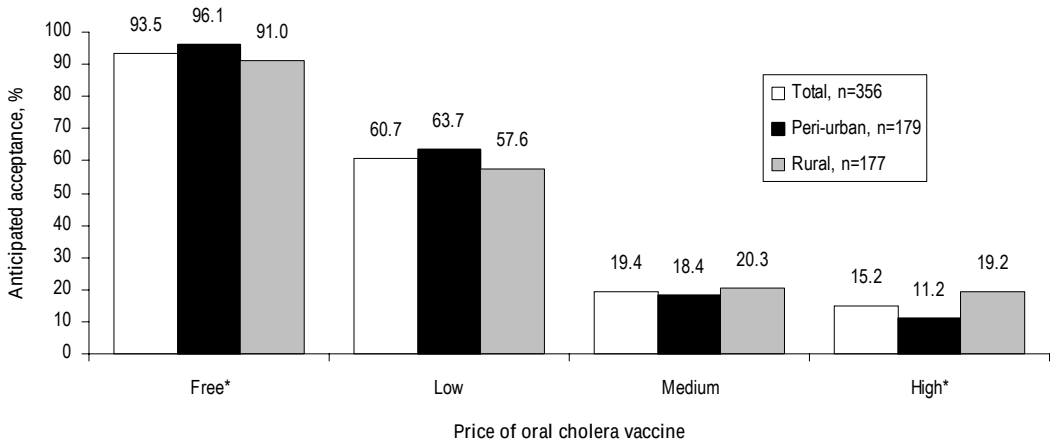

Figure 4-1: Anticipated oral cholera vaccine acceptance at different prices in Zanzibar, stratified by site

Low price: TZS 1,000 (~USD 0.9), medium price: TZS 5,000 (~USD 4.5), high price: TZS 10,000 (~USD 9). Approximate exchange rate of TZS 1,140 per USD 1 as of August 1, 2008 (www.oanda.com); *p<0.05

Anticipated acceptance of the free vaccine was greater than 93% for the pooled sample of periurban and rural sites. These acceptance rates dropped with increasing price level to a minimum of 15%. Differences between sites were significant at the no cost and high price level.

In addition to a high demand for free vaccination, respondents also stated the importance of other preventive measures for cholera control when asked for advice at the end of the interview. The following narrative of a 47-year-old man from the rural site represents these community-perceived needs:

> "The ministry of health should provide health education. They should also tell us how to build and use latrines. The provision of safe water is also important, especially during the rainy season. The ministry of health should give us vaccines and inform the community about the importance of using vaccines that ought to be provided free of charge."

Because intention to take the free OCV was almost 95%, subsequent statistical analysis of determinants of anticipated OCV acceptance considered only low, medium and high price as

outcome variables. Tables 4-1 to 4-6 present explanatory variables that were identified in crude analyses together with the respective focal and comprehensive models. Focal models analyzed specific subsets of explanatory variables to examine the influence of categories of distress, perceived causes, self treatment at home and outside help seeking on anticipated OCV acceptance. Each of these models was adjusted for sociodemographic characteristics and compared to the respective model containing only sociodemographic characteristics by using the Akaike Information Criterion corrected for sample size (AICc). Focal models were also used to select explanatory variables for analysis of social and cultural determinants of anticipated OCV acceptance in comprehensive models.

4.3.2 Determinants of anticipated OCV acceptance at low price

Two categories of distress—being very thirsty and being concerned about spreading the infection to others—were positively associated with anticipated OCV acceptance, though the former with borderline significance (p=0.056) and the latter only at the rural site (Table 4-1).

Table 4-1: Crude and adjusted analysis (focal models) of social and cultural determinants of anticipated oral cholera vaccine acceptance at low price in Zanzibar, n=356

	Crude analysis[a]		Adjusted analysis[b]			
	Coefficient (95% CI)[c]	p value[d]	Coefficient (95% CI)[c]	p value[d]	Int[e]	Δ(AICc)[f]
Categories of distress: somatic symptoms						*0.34*
Very thirsty	0.31 (-0.05; 0.68)	0.09	0.37 (-0.01; 0.75)	0.06		
Categories of distress: social impact						*0*
Fear of infecting others	0.22 (-0.02; 0.46)	0.07				
Fear of infecting others (periurban site)			-0.14 (-0.54; 0.26)	0.49		
Fear of infecting others (rural site)			0.41 (0.07; 0.75)	0.02	**	
Perceived causes						*5.91*
Unprotected/spoiled food	0.29 (0.04; 0.54)	0.03	0.16 (-0.11; 0.43)	0.23		
Not washing hands	0.40 (0.02; 0.77)	0.04	0.11 (-0.28; 0.50)	0.59		
Witchcraft	-0.45 (-0.85; -0.05)	0.03	-0.25 (-0.68; 0.19)	0.27		
God's will	-0.14 (-0.30; 0.03)	0.10	-0.03 (-0.22; 0.15)	0.73		
Cannot say	-0.49 (-0.90; -0.08)	0.02	-0.40 (-0.85; 0.05)	0.09		
Self treatment at home						*2.12*
Drinking more water or liquids	-0.10 (-0.24; 0.05)	0.19	-0.18 (-0.34; -0.02)	0.03		
Oral rehydration therapy	0.11 (-0.02; 0.25)	0.10	0.04 (-0.10; 0.18)	0.56		
Prayers	-0.21 (-0.41; -0.01)	0.05	-0.13 (-0.35; 0.09)	0.23		
Outside help seeking						*2.98*
Faith healers	-0.35 (-0.76; 0.07)	0.10	-0.31 (-0.75; 0.13)	0.17		
Sociodemographic characteristics[g]						*2.25*
Gender (male vs. female)	0.31 (-0.12; 0.74)	0.15	0.36 (-0.11; 0.83)	0.14		
Site (rural vs. periurban)	-0.25 (-0.68; 0.17)	0.24	-0.43 (-1.11; 0.24)	0.21		
Age	-0.02 (-0.04; -0.01)	0.01	-0.01 (-0.03; 0.00)	0.11		
Primary school vs. no education	0.67 (0.12; 1.23)	0.02[h]	0.54 (-0.06; 1.14)	0.08		
Secondary school and above vs. no education	1.18 (0.65; 1.70)	<0.01[h]	1.05 (0.42; 1.68)	<0.01		
Regular and dependable household income	0.59 (0.16; 1.02)	0.01				
Regular and dependable household income (periurban site)			0.11 (-0.55; 0.78)	0.74		
Regular and dependable household income (rural site)			0.91 (0.27; 1.56)	0.01	*	

[a]Only variables with univariable association (p<0.2) listed, except for site; [b]Focal models adjusted for sociodemographic characteristics (see footnote [g]). Effects of adjustment variables not presented since similar to model containing only sociodemographic characteristics (bottom block); [c]Logistic regression coefficient with 95% confidence interval; [d]Figures in bold if p<0.05; [e]Interaction of rural with periurban site (baseline) considered if p<0.1 for interaction term (*p<0.1, **p<0.05); [f]Difference of corrected Akaike Information Criterion (AICc) between each model and the *best* model, designated with Δ(AICc)=0. Bold figures indicate models that are better than the model containing only sociodemographic characteristics (bottom block); [g]Variables used for adjusting each focal model. Figures reported in adjusted analysis refer to model containing only sociodemographic characteristics; [h]Variable with three categories, overall p<0.01

In crude analysis, categories of perceived causes related to biomedical risk factors for cholera were significantly positively associated; attribution of cholera to witchcraft or inability to identify a cause was negatively associated. These effects, however, were reduced in the focal model probably because they were partly explained by sociodemographic factors. Rehydration as self treatment at home was negatively associated with anticipated OCV acceptance. Among sociodemographic characteristics, having completed at least secondary school, and reporting a

regular and dependable household income in the rural site, were highly significant determinants of anticipated OCV acceptance. According to their Δ(AICc) values, both models related to categories of distress explained anticipated acceptance better than the model containing only sociodemographic characteristics.

All variables that showed a significant association with anticipated acceptance of the low-priced OCV in the focal models were also present in the comprehensive model (Table 4-2). Effects were similar, but *very thirsty* turned significant (p=0.034) and the interaction with rural site was no longer present for regular and dependable household income.

Table 4-2: Adjusted analysis (comprehensive model) of social and cultural determinants of anticipated oral cholera vaccine acceptance at low price in Zanzibar, n=356

	Adjusted analysis[a]		
	Coefficient (95% CI)[b]	p value[c]	Int[d]
Categories of distress: somatic symptoms			
Very thirsty	0.41 (0.03; 0.80)	0.03	
Categories of distress: social impact			
Fear of infecting others (periurban site)	-0.20 (-0.60; 0.20)	0.33	
Fear of infecting others (rural site)	0.38 (0.02; 0.74)	0.04	*
Perceived causes			
Cannot say	-0.34 (-0.81; 0.14)	0.16	
Self treatment at home			
Drinking more water or liquids	-0.22 (-0.38; -0.05)	0.01	
Outside help seeking			
Faith healers	-0.19 (-0.64; 0.26)	0.41	
Sociodemographic characteristics			
Gender (male vs. female)	0.32 (-0.16; 0.81)	0.19	
Site (rural vs. periurban)	-0.70 (-1.49; 0.10)	0.09	
Age	-0.02 (-0.03; 0.00)	0.11	
Primary school vs. no education	0.59 (-0.03; 1.21)	0.06	
Secondary school and above vs. no education	0.97 (0.34; 1.61)	<0.01	
Regular and dependable household income	0.57 (0.10; 1.05)	0.02	

[a]Only variables identified in focal models (p<0.2) included in comprehensive model; [b]Logistic regression coefficient with 95% confidence interval; [c]Figures in bold if p<0.05; [d]Interaction of rural with periurban site (baseline) considered if p<0.1 for interaction term (*p<0.05)

4.3.3 Determinants of anticipated OCV acceptance at medium price

In the periurban site, disruption of health services was negatively associated with anticipated OCV acceptance at medium price (Table 4-3).

Table 4-3: Crude and adjusted analysis (focal models) of social and cultural determinants of anticipated oral cholera vaccine acceptance at medium price in Zanzibar, n=356

	Crude analysis[a]		Adjusted analysis[b]			
	Coefficient (95% CI)[c]	p value[d]	Coefficient (95% CI)[c]	p value[d]	Int[e]	Δ(AICc)[f]
Categories of distress: somatic symptoms						*4.90*
Abdominal pain/discomfort	-0.31 (-0.67; 0.05)	0.09	-0.30 (-0.71; 0.10)	0.14		
Pus in stool	0.43 (-0.15; 1.00)	0.14	0.55 (-0.11; 1.21)	0.10		
Categories of distress: social impact						*0*
Fear of infecting others	0.18 (-0.07; 0.44)	0.16	0.19 (-0.08; 0.47)	0.16		
Disruption of health services	-0.33 (-0.79; 0.13)	0.16				
Disruption of health services (periurban site)			-1.11 (-2.02; -0.20)	0.02		
Disruption of health services (rural site)			0.28 (-0.44; 0.99)	0.45	**	
Interference with social relationships	-0.27 (-0.58; 0.04)	0.08	-0.22 (-0.56; 0.12)	0.20		
Perceived causes						*1.51*
Witchcraft	-0.60 (-1.19; -0.01)	0.05	-0.79 (-1.45; -0.14)	0.02		
Self treatment at home						*6.22*
Prayers	-0.21 (-0.51; 0.09)	0.17	-0.19 (-0.50; 0.12)	0.24		
Outside help seeking						*6.00*
Pharmacy/Over-the-counter drugs	-0.39 (-0.94; 0.16)	0.17	-0.37 (-0.93; 0.20)	0.20		
Sociodemographic characteristics[g]						*4.80*
Household size	-0.06 (-0.15; 0.03)	0.19				
Household size (periurban site)			-0.20 (-0.34; -0.06)	0.01		
Household size (rural site)			0.08 (-0.06; 0.23)	0.26	***	
Marital status (married vs. not married)	1.37 (0.49; 2.24)	<0.01	1.26 (0.36; 2.17)	0.01		
Site (rural vs. periurban)	0.12 (-0.40; 0.65)	0.65	-1.05 (-2.74; 0.65)	0.23		
Regular and dependable household income	0.98 (0.39; 1.56)	<0.01				
Regular and dependable household income (periurban site)			1.67 (0.63; 2.70)	<0.01		
Regular and dependable household income (rural site)			0.56 (-0.21; 1.34)	0.15	*	

[a]Only variables with univariable association (p<0.2) listed, except for site; [b]Focal models adjusted for sociodemographic characteristics (see footnote [g]). Effects of adjustment variables not presented since similar to model containing only sociodemographic characteristics (bottom block); [c]Logistic regression coefficient with 95% confidence interval; [d]Figures in bold if p<0.05; [e]Interaction of rural with periurban site (baseline) considered if p<0.1 for interaction term (*p<0.1, **p<0.05, ***p<0.01); [f]Difference of corrected Akaike Information Criterion (AICc) between each model and the *best* model, designated with Δ(AICc)=0. Bold figures indicate models that are better than the model containing only sociodemographic characteristics (bottom block); [g]Variables used for adjusting each focal model. Figures reported in adjusted analysis refer to model containing only sociodemographic characteristics

Narratives among acceptors and non-acceptors, however, did not differ and acknowledged the impact of outbreaks on the primary health care system:

> "Yes, health services can stop because health workers will deal only with the outbreak for that time." (Male student, 21 years)

A 39-year-old jobless man even gave a reason why health care services would be interrupted:

> "Yes, if the primary health care unit provides treatment for cholera patients, other patients will not be treated there to avoid infection."

Attribution of witchcraft as a cause of cholera was identified as negative determinant in both the crude and adjusted analysis. The larger the household was in the periurban site, the lower the willingness for buying medium-priced OCV. A statement by a male, 33-year-old carpenter represents a likely reason behind this:

> "It is hard because what we earn is not enough to pay for a vaccine for the fifteen people who are living in this house."

Being married and reporting a regular and dependable household income in the periurban site were positively related sociodemographic factors. Focal models of social impact and perceived causes explained anticipated OCV acceptance better than the sociodemographic model.

All variables from the focal models, except witchcraft, were retained as significant determinants with similar effects in the comprehensive model (Table 4-4).

Table 4-4: Adjusted analysis (comprehensive model) of social and cultural determinants of anticipated oral cholera vaccine acceptance at medium price in Zanzibar, n=356

	Adjusted analysis[a]		
	Coefficient (95% CI)[b]	p value[c]	Int[d]
Categories of distress: somatic symptoms			
Abdominal pain/discomfort	-0.27 (-0.69; 0.15)	0.21	
Pus in stool	0.54 (-0.14; 1.22)	0.12	
Categories of distress: social impact			
Fear of infecting others	0.15 (-0.13; 0.43)	0.30	
Disruption of health services (periurban site)	-1.14 (-2.07; -0.22)	0.02	
Disruption of health services (rural site)	0.26 (-0.50; 1.01)	0.51	**
Perceived causes			
Witchcraft	-0.63 (-1.31; 0.05)	0.07	
Outside help seeking			
Pharmacy/Over-the-counter drugs	-0.16 (-0.71; 0.39)	0.58	
Sociodemographic characteristics			
Household size (periurban site)	-0.22 (-0.37; -0.07)	<0.01	
Household size (rural site)	0.08 (-0.07; 0.24)	0.28	***
Marital status (married vs. not married)	1.40 (0.47; 2.33)	<0.01	
Site (rural vs. periurban)	-1.89 (-3.88; 0.11)	0.06	
Regular and dependable household income (periurban site)	1.66 (0.58; 2.75)	<0.01	
Regular and dependable household income (rural site)	0.45 (-0.35; 1.25)	0.27	*

[a]Only variables identified in focal models (p<0.2) included in comprehensive model; [b]Logistic regression coefficient with 95% confidence interval; [c]Figures in bold if p<0.05; [d]Interaction of rural with periurban site (baseline) considered if p<0.1 for interaction term (*p<0.1, **p<0.05, ***p<0.01)

4.3.4 Determinants of anticipated OCV acceptance at high price

In the focal models for high price, no interactions with site were present (Table 4-5).

Table 4-5: Crude and adjusted analysis (focal models) of social and cultural determinants of anticipated oral cholera vaccine acceptance at high price in Zanzibar, n=356

	Crude analysis[a]		Adjusted analysis[b]		
	Coefficient (95% CI)[c]	p value[d]	Coefficient (95% CI)[c]	p value[d]	Δ(AICc)[e]
Categories of distress: somatic symptoms					*0.38*
Abdominal pain/discomfort	-0.40 (-0.81; 0.02)	0.06	-0.29 (-0.76; 0.17)	0.22	
Pus in stool	0.75 (0.15; 1.36)	0.02	0.68 (-0.00; 1.36)	0.05	
Categories of distress: social impact					*1.01*
Fear of infecting others	0.23 (-0.04; 0.50)	0.10	0.23 (-0.05; 0.52)	0.11	
Perceived causes					*0*
Eating soil	0.41 (-0.16; 0.98)	0.16	0.36 (-0.26; 0.98)	0.25	
Malaria	0.42 (-0.15; 1.00)	0.15	0.43 (-0.26; 1.13)	0.22	
Witchcraft	-0.52 (-1.17; 0.13)	0.11	-0.90 (-1.66; -0.14)	0.02	
Self treatment at home					*2.29*
Prayers	-0.24 (-0.58; 0.11)	0.18	-0.19 (-0.56; 0.17)	0.30	
Sociodemographic characteristics[f]					*1.40*
Site (rural vs. periurban)	0.64 (0.04; 1.23)	0.04	0.80 (0.12; 1.48)	0.02	
Marital status (married vs. not married)	1.51 (0.46; 2.56)	<0.01	1.41 (0.33; 2.49)	0.01	
Primary school vs. no education	0.79 (-0.00; 1.57)	0.05[g]	0.82 (-0.00; 1.64)	0.05	
Secondary school and above vs. no education	0.37 (-0.40; 1.15)	0.34[g]	0.87 (0.00; 1.74)	0.05	
Regular and dependable household income	0.94 (0.30; 1.59)	<0.01	0.98 (0.30; 1.66)	0.01	

[a]Only variables with univariable association (p<0.2) listed; [b]Focal models adjusted for sociodemographic characteristics (see footnote [f]). Effects of adjustment variables not presented since similar to model containing only sociodemographic characteristics (bottom block); [c]Logistic regression coefficient with 95% confidence interval; [d]Figures in bold if p<0.05; [e]Difference of corrected Akaike Information Criterion (AICc) between each model and the *best* model, designated with Δ(AICc)=0. Bold figures indicate models that are better than the model containing only sociodemographic characteristics (bottom block); [f]Variables used for adjusting each focal model. Figures reported in adjusted analysis refer to model containing only sociodemographic characteristics; [g]Variable with three categories, overall p=0.14

But site itself was a confounding factor, indicating that rural respondents were more likely to accept the vaccine. Besides marital status, education and regular and dependable household income, which were all positively associated, attribution of cholera to witchcraft, similar to the medium price focal model, was a negative determinant of anticipated OCV acceptance. Another positive determinant was pus in stool, an unrelated symptom of cholera, which was probed for in the interview to compare community views of cholera and shigellosis [23]. Perceived causes and somatic symptoms explained anticipated OCV acceptance better than the sociodemographic model.

The only significant variables in the comprehensive model at high price were sociodemographic characteristics: being married and depending on a regular household income were positive determinants of anticipated OCV acceptance (Table 4-6). Belonging to rural site (p=0.052) and having attained primary school education (p=0.057) were also positive predictors, though with borderline significance.

Table 4-6: Adjusted analysis (comprehensive model) of social and cultural determinants of anticipated oral cholera vaccine acceptance at high price in Zanzibar, n=356

	Adjusted analysis[a]	
	Coefficient (95% CI)[b]	p value[c]
Categories of distress: somatic symptoms		
Pus in stool	0.64 (-0.06; 1.33)	0.07
Categories of distress: social impact		
Fear of infecting others	0.16 (-0.14; 0.45)	0.29
Perceived causes		
Witchcraft	-0.69 (-1.43; 0.05)	0.07
Sociodemographic characteristics		
Site (rural vs. periurban)	0.73 (-0.01; 1.47)	0.05
Marital status (married vs. not married)	1.44 (0.36; 2.53)	<0.01
Primary school vs. no education	0.82 (-0.02; 1.67)	0.06
Secondary school and above vs. no education	0.73 (-0.17; 1.63)	0.11
Regular and dependable household income	0.91 (0.22; 1.60)	0.01

[a]Only variables identified in focal models (p<0.2) included in comprehensive model; [b]Logistic regression coefficient with 95% confidence interval; [c]Figures in bold if p<0.05

4.4 Discussion

This cross-sectional study using the cultural epidemiological framework clarified social and cultural determinants of anticipated OCV acceptance before a mass vaccination campaign in Zanzibar. Reported anticipated acceptance of a free OCV was very high (94%). Fewer were willing to pay for it: 61% at low, 19% at medium and 15% at high price. Sociocultural features of cholera-like illness—that is, how people perceive and understand the acute watery diarrhea described to them in a clinical vignette—were identified as determinants of anticipated acceptance if the OCV was offered at some cost. Individual features of respondents, i.e., their sociodemographic and economic status, were also important determinants, and they became more influential as prices increased.

This study examined willingness to accept a free vaccine for cholera, or to pay for the vaccine, which may be regarded as a surrogate for demand. Anticipated acceptance of the free OCV was at the upper end of the range of 60-99% reported by studies that have assessed people's intention to receive vaccines for shigellosis, other dysentery and typhoid fever in several Asian countries [27-29]. High levels of intention to receive free vaccination against cholera in Zanzibar may be explained by high levels of reported severity and fatality in the sample [23]. The fact that 60% of respondents willing to spend more for the low-priced OCV than the mean monthly per capita out-of-pocket expenditure on health (~USD 0.44 in 2004/2005) [30] indicates the priority of cholera. The finding that less than 20% would pay for the medium- or high-priced OCV indicates that despite this priority the cost was insurmountable. Other studies highlight the problem of cost as a barrier to use of desired OCVs [24-26]. If free vaccination becomes possible

for cholera control in Zanzibar, findings from this study of high community demand for a free OCV suggest it will be effective. This demand for an accessible vaccine complemented demand for classical preventive interventions, such as improved infrastructure, better services and health education from the government.

The positive association of sociodemographic and economic factors with anticipated acceptance if the OCV was offered at some cost was represented by respondents who reported a regular and dependable income, which was used as a proxy for economic status, who had attained a good educational level and were married. The effects of income, present throughout all models, and education, present at low and high price, are supported by Lucas *et al*. who studied private demand for Dukoral® in the city of Beira, Mozambique [26]. In contrast to findings from Beira, increasing household size was identified as a negative determinant of willingness to pay for medium-priced OCV in the periurban community, probably reflecting limited financial capabilities there.

As hypothesized, sociocultural features of illness, i.e., somatic symptoms (at low and high price), categories of social impact (at low and medium price) and perceived causes (at medium and high price), explained anticipated vaccine acceptance better than models containing only sociodemographic and economic characteristics. This finding demonstrates the explanatory power of sociocultural features of cholera-like illness as determinants of anticipated OCV acceptance. It shows that to enhance effectiveness of mass vaccination programs for cholera, pre-intervention assessments of community demand for OCV should not only consider the social epidemiology [31], but also examine local concepts of cholera-like experience, meaning and behavior. With particular reference to Zanzibar, consideration of social and cultural determinants of OCV acceptance may be especially important if the vaccine is offered at some cost. Even though overwhelming willingness to receive the free OCV made it impossible to study determinants, in settings where anticipated acceptance is lower, sociocultural features of illness are also likely to be important.

The use of cultural epidemiological methods enabled the identification of explanatory variables based on empirical associations, rather than just relationships based on the insight of respondents. The finding that thirst was associated with anticipated acceptance of the low-priced vaccine suggests a relationship between an important feature of dehydration from cholera, and the perceived value of a vaccine to prevent it, even though respondents did not explain it that way explicitly. Community solidarity to prevent spread of the infection to others—though it was only identified in the rural site—also increased priority of the low-priced vaccine.

On the other hand, an alternative intervention to vaccination—rehydrating the patient with cheap liquids at home—was preferred to spending even a little money on vaccines.

Although a disruption of local health care services was identified as the least prominent problem in both communities [23], this factor was a significant determinant of non-acceptance at medium price, but only among periurban respondents. This finding might indicate that periurban villagers who reported adequate government response to cholera outbreaks were less willing to spend money on a vaccine to prevent an illness that, in their eyes, can be dealt with in treatment camps. Such camps, where patients are treated at no cost in Zanzibar, are usually set up in primary health care facilities by district health authorities. These facilities were identified by everybody as the preferred place to seek help for cholera patients; and they were perceived as more helpful in the periurban community [23].

The appeal of perceived causes that compete with biomedical explanations of cholera made respondents less willing to buy an OCV at medium and high price. This suggests the relevance of people's beliefs in witchcraft be taken into account as a factor if mass vaccinations are planned that require recipients to contribute fees that exceed ~USD 1.

Based on the variation of the distribution of sociocultural features of cholera-like illness in both communities, interaction with site (rural vs. periurban site at baseline) was tested in all models. The only sociocultural feature that interacted with site at low price was fear of infection; at medium price, the only interacting factor was disruption of health services. At high price, no interaction terms remained in the models, implying that a financial level was reached that canceled out any community-specific characteristics. However, site itself was a main factor at this price level; it predicted higher anticipated OCV acceptance among rural respondents who also expressed higher willingness than their periurban counterparts to purchase the vaccine at its manufacturing costs of ~USD 9.

Previous experience of illness episodes was positively associated with vaccine acceptance for cholera in Vietnam [25], and negatively for dysentery in six Asian countries [29]. Owing to the fact that personal or household episodes of the condition described in the cholera vignette were reported by 15.5% of the sample, crude analysis also examined previous experience as an additional explanatory variable. But since no suggestive relationship with any of the outcome variables was found ($p>0.2$), *previous experience* was not included as independent variable in subsequent adjusted analyses. Similarly, no statistically relevant relationship between previous experience of cholera and vaccine demand was reported in the private demand study from Mozambique [26].

Although anticipated that research as presented here should guide future cholera immunization campaigns, recommendations that may follow from this prevaccination survey were not part of the design for the 2009 mass vaccination campaign in Zanzibar since analyses were only completed after the campaign had been implemented.

It should also be noted that findings reported here indicate people's intention to vaccinate but not necessarily their actual behavior. Study of determinants of actual acceptance is required to explain what actually influenced vaccine uptake. Recognizing this as a limitation of any pre-intervention research, an additional study following the mass vaccination campaign in Zanzibar was conducted to retrospectively examine social and cultural determinants of uptake. Preliminary findings from that study, which is currently being written up, confirm the importance of considering sociocultural features of illness vis-à-vis a solely social epidemiological approach to explain vaccine acceptance.

It may be regarded as another limitation that this study assessed the influence of illness explanatory models on vaccine acceptance. Another approach might also have considered how perceived features of OCVs, such as their effectiveness, duration of protection and/or side effects, affect acceptance [25,32]. Studying vaccine-related barriers to acceptance might thus also be required to explain their impact on immunization campaigns. A separate postvaccination study was conducted to analyze barriers of actual acceptance; details of these findings will be reported in a subsequent paper. Investigation of other factors that likely influence vaccine acceptance (e.g., national and regional policy contexts [33], other political–macroeconomic factors, access and equity issues, client–health care provider communication and geographical features [12,34]) might also warrant attention, but consideration of these factors was beyond the scope of this study.

In conclusion, findings of this prevaccination survey suggest that anticipated acceptance of a free OCV is nearly universal in cholera-endemic areas of periurban and rural Zanzibar, and the vaccine also appears acceptable at an affordable price of ~USD 1. This study indicates the salience of considering not only sociodemographic characteristics but also locally valid sociocultural features of cholera-like illness as potentially relevant determinants of anticipated OCV acceptance. When planning mass vaccination campaigns, knowing more about local ideas of illness and how they may influence vaccination behavior is likely to be useful to increase participation for maximum community effectiveness.

Conflicts of interest

The authors declare that no conflicts of interest exist.

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5

SOCIAL AND CULTURAL DETERMINANTS OF ORAL CHOLERA VACCINE UPTAKE IN A MASS VACCINATION CAMPAIGN IN ZANZIBAR*

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Abstract

Introduction

Improving mass vaccination campaigns for cholera control requires not only consideration of technical and financial feasibility, but also consideration of social and cultural factors of vaccine acceptance in target populations. This study empirically examined how local community views of cholera influenced oral cholera vaccine (OCV) uptake in the 2009 mass vaccination campaign in Zanzibar.

Methods

Data from a baseline study that had elicited local community views of cholera with semi-structured interviews was used. Uni- and multivariable logistic regression models identified social and cultural determinants of OCV uptake.

Results

Less than half of the 356 interviewed adult respondents (49.7%) drank two doses of OCV. Nonspecific features of cholera related to malaise were negative determinants. Recognition of unconsciousness as a serious sign of dehydration and concern that cholera outbreaks could negatively impact the local health care system in the rural area were positive determinants of acceptance. Female gender, rural residence and older age were also positive determinants of OCV uptake.

Conclusions

OCV uptake in a mass vaccination campaign in periurban and rural Zanzibar was lower than reported anticipated acceptance. Consideration of sociocultural features of cholera-like illness explained uptake better than a purely social epidemiological analysis. Planning of future cholera mass vaccination and sensitization campaigns in Zanzibar may directly benefit from findings presented here. The likely potential of cholera as a cause of severe dehydration should be emphasized vis-à-vis nonspecific symptoms of diarrheal illness. Rural recognition of the cholera-related burden on the local health care system was reflected by a priority for oral cholera vaccination. This indicates community appreciation of vaccination for cholera control and a perceived need to strengthen health care services in Zanzibar, particularly in rural areas. Findings recommend particular efforts to increase cholera immunization coverage among young adults, in periurban areas and for men.

5.1 Introduction

In 2009, 45 countries mainly from Africa and Asia reported a global total of 221,226 cases and 4,946 deaths attributable to cholera [1]. Recognizing difficulties with limited surveillance and under-reporting, the World Health Organization (WHO) estimates annual morbidity and mortality to be in excess of 3 million cases and 100,000 deaths [2].

Besides timely rehydration and administration of antibiotics to patients who suffer from acute watery diarrhea caused by *Vibrio cholerae* O1 or O139, cholera control also involves preventive activities that center on the provision of safe water in sufficient quantities, sanitation and health education (WASH). Using oral cholera vaccines (OCV) has also been recommended to supplement WASH in an integrated strategy to reduce the public health burden of cholera in affected countries [3]. In endemic settings, community-based mass vaccination campaigns in selected hotspot areas have been the preferred route for efficient deployment of OCV.

Following research examining key epidemiological parameters and characteristics of available OCVs in different populations and contexts [4-7], studies have investigated the practical feasibility and economic aspects of using OCVs in vulnerable populations that are at risk of recurrent cholera outbreaks [8-13]. Effective use of OCVs for maximum impact on morbidity and mortality depends on a variety of factors: in addition to the availability of a safe and efficacious vaccine and a well-functioning health system with sufficient capacity to implement mass immunizations, local views of potential respondents about cholera, and how these affect whether or not they would accept a vaccine, have to be considered for maximum coverage, but have often been neglected [14].

Recently published studies addressing the relationship between local perceptions of severe enteric diarrheal illness and willingness or desire to receive vaccines have mainly focused on shigellosis and typhoid fever [15-21]. Studies on cholera have assessed social factors of vaccine acceptance [22] or have considered policy makers' views [23], but empirical study of cultural factors of cholera and how they affect OCV uptake is lacking.

Research reported in this paper took advantage of a mass vaccination campaign that was conducted in cholera-endemic areas of periurban and rural Zanzibar in 2009. Approximately 50,000 inhabitants were targeted for vaccination with Dukoral®, which was the only OCV prequalified by the WHO at that time. This two-dose vaccine was offered without charge in two rounds in January and February 2009 [24]. Nine temporary vaccination posts were set up on

each island in the target communities; posts were open daily for at least eight hours and staffed with local health personnel and villagers.

A baseline survey, which was conducted six months before the mass vaccination campaign, examined social and cultural determinants of anticipated OCV acceptance [25]. Findings from that study showed that 93.5% of the interviewed adults intended to take a vaccine if offered without charge. However, when offered at three different prices levels—approximately USD 0.9, USD 4.5 and USD 9—acceptance rates dropped to 60.7%, 19.4% and 15.2%, respectively. Multivariable models examining factors that affect vaccine acceptance if the OCV was offered at various levels of cost showed that sociocultural features of illness explain anticipated acceptance better than social epidemiological models [26] containing only sociodemographic characteristics.

Since intention to be vaccinated does not always predict vaccination [27-29], examination of how cultural concepts of cholera determine actual OCV acceptance (or uptake) is much-needed. Findings from such research may contribute essential information to increase coverage of OCV in future mass vaccination campaigns for the benefit of cholera control in Zanzibar.

This study used the integrated methods framework of cultural epidemiology [30]. This research approach has been valuable in determining how local cultural concepts of illness—i.e., how people experience an illness, what causes they attribute it to and what they do for help seeking—affect health-related behavior [31-33]. The aim of this work was to identify social and cultural determinants of OCV uptake based on a random sample of adults that was interviewed before the 2009 mass vaccination campaign in Zanzibar [34].

5.2 Methods

5.2.1 Setting and study participants

Zanzibar belongs to the United Republic of Tanzania and consists of two major islands, Unguja and Pemba, just off the coast between Dar-Es-Salaam in the south and the Kenyan border in the north. Zanzibar has been regularly affected by cholera since the 1970s, and the government therefore recently decided to vaccinate major hotspots on both islands with assistance from the WHO. Two out of the six cholera-endemic communities that had been identified as mass vaccination targets were visited six months before the campaign was conducted in January and February 2009. The periurban community of Chumbuni on Unguja and the rural community of Mwambe on Pemba, both representing core areas of the campaign, were chosen for this baseline survey. Diarrhea-free adults aged 18 years or older were randomly selected for interviews. An

equal number of men and women were approached at each study site. A detailed description of both sites and more information on sampling has been presented elsewhere [34].

5.2.2 Instrument

Semi-structured interviews based on the Explanatory Model Interview Catalogue (EMIC) are the principal instrument of inquiry in cultural epidemiological research [35]. EMIC interviews enable empirical clarification of how locally valid features of illness-related experience, meaning and behavior are distributed in a population [36-38]. Since adults who were apparently unaffected by cholera were the focus of this study, the EMIC interview began with the presentation of a clinical vignette that described a local person with cardinal somatic symptoms of cholera [34]. The interview also recorded sociodemographic characteristics and asked about anticipated acceptance of the OCV if it was offered without charge and at three different levels of cost.

5.2.3 Data management and analysis

Explanatory variables for analysis of actual determinants of OCV acceptance were obtained from the baseline study [34]. These included sociodemographic characteristics and sociocultural features of cholera-like illness, operationalized as patterns of distress referring to categories of somatic symptoms and social, emotional and financial impact, categories of perceived causes, self treatment at home and help seeking outside households of affected persons. The outcome variable, respondents' vaccination status, was obtained from the mass vaccination database that had been compiled with the use of personal digital assistants by the International Vaccine Institute, Seoul [24]. Receipt of two complete doses of OCV was coded with a value of 1 and receipt of one or zero doses with a value of 0.

Determinants of uptake were identified in a staged process that involved uni- and multivariable logistic regressions in SAS 9.2 (SAS Institute, Cary, NC, USA). Crude analysis examined associations between OCV and explanatory variables that were reported by 5-95% of respondents. Only variables with $p<0.2$ were retained for multivariable analyses to calculate *focal* models of sociocultural features of illness, adjusted for sociodemographics. Variables identified in focal models with $p<0.2$ were then used for calculating a *comprehensive* model. Assessment of which focal model explained vaccine uptake better than the focal model containing only sociodemographic characteristics was based on the corrected Akaike Information Criterion (AICc). The difference (Δ) of AICc between each model and the model with the lowest AICc was calculated; any focal model with a Δ(AICc) noticeably lower than the one containing sociodemographics only was considered better. Interaction of rural or periurban site with each variable was tested individually in focal models; interaction terms were only

retained if their p values were below 0.1. Only interaction terms present in the focal models were assessed for inclusion in the comprehensive model based on the same threshold of $p<0.1$.

Anticipated acceptance if the OCV was offered without charge, and at low, medium and high price, respectively, were also considered as potential explanatory variables; however, only acceptance for free was included in models because crude analysis showed no associations between intention to buy an OCV and uptake in the campaign ($p>0.2$). Because 15.5% of the sample had reported a personal or household episode of cholera [25], previous illness experience was also considered as potential explanatory variable, but not included in further analyses since crude analysis showed no suggestive association ($p=0.44$).

This study was approved by the Research Ethics Review Committee of the World Health Organization and the Ethics Committee of the Ministry of Health and Social Welfare of Zanzibar. All study participants gave written consent before being interviewed. No compensation was offered to them.

5.3 Results

5.3.1 Sample characteristics

A total of 356 interviews were completed, 179 in the periurban and 177 in the rural site. Slightly more than half of the study participants were women (50.3%). Mean age was 35.5 years, 76.4% were married and the mean household size was 6.8 persons. Major occupations were farming (30.6%), being housewife (21.4%) and working in the informal economy (17.1%). The sample consisted of Muslims, with the exception of one Christian woman. A majority (55.9%) reported a regular and dependable household income. Further details of sample characteristics have been described elsewhere [34].

5.3.2 OCV uptake

Less than half of the respondents (49.7%) actually drank two doses of OCV, as documented in the mass vaccination database. More rural than periurban respondents drank the vaccine (58.8% vs. 40.8%, $p<0.01$, Chi^2 test); and more women than men (54.8% vs. 44.6%), though with borderline statistical significance ($p=0.056$, Chi^2 test).

5.3.3 Social and cultural determinants of OCV uptake

Crude analysis and focal models

Table 5-1 presents all variables that were identified in crude analysis together with focal models of sociocultural features of illness (i.e., patterns of distress, perceived causes and self treatment at home), of intention to receive the OCV and of sociodemographic characteristics.

Table 5-1: Crude analysis and focal models of social and cultural determinants of oral cholera vaccine uptake in a community mass vaccination campaign in Zanzibar, 2009, n=356

	Crude analysis[a]		Focal models[b]			
	Coefficient (95% CI)[c]	p value[d]	Coefficient (95% CI)[c]	p value[d]	Int[e]	Δ(AICc)[f]
Categories of distress: somatic symptoms						*0*
Loss of appetite	-0.34 (-0.70; 0.02)	0.07				
Loss of appetite (periurban site)			0.15 (-0.33; 0.62)	0.54		
Loss of appetite (rural site)			-0.58 (-1.22; 0.06)	0.08	*	
Nausea	-0.49 (-0.99; 0.02)	0.06	-0.65 (-1.22; -0.08)	0.03		
Palpitations	-0.19 (-0.44; 0.06)	0.14	-0.03 (-0.31; 0.24)	0.81		
Unconsciousness	0.11 (-0.05; 0.27)	0.18	0.21 (0.04; 0.38)	0.02		
Categories of distress: social impact						*3.06*
Fear of isolation from others	-0.11 (-0.27; 0.05)	0.18	-0.12 (-0.29; 0.05)	0.16		
Disruption of healthcare services	0.36 (0.01; 0.70)	0.04				
Disruption of healthcare services (periurban site)			-0.07 (-0.53; 0.38)	0.75		
Disruption of healthcare services (rural site)			1.01 (0.15; 1.87)	0.02	**	
Perceived causes						*10.77*
Unprotected/spoiled food	-0.15 (-0.38; 0.07)	0.18	-0.02 (-0.26; 0.22)	0.86		
Contact with contaminated water	0.19 (-0.03; 0.41)	0.08	0.13 (-0.11; 0.37)	0.28		
Witchcraft	0.50 (0.08; 0.91)	0.02	0.26 (-0.18; 0.69)	0.25		
Cannot say	0.35 (-0.07; 0.77)	0.10	0.21 (-0.24: 0.66)	0.36		
Self treatment at home						*5.83*
Drinking more water or liquids	-0.16 (-0.30; -0.01)	0.04	-0.12 (-0.28; 0.03)	0.12		
Intention to receive OCV						*4.44*
Anticipated acceptance of a free OCV	0.87 (-0.05; 1.78)	0.06	0.91 (-0.06; 1.87)	0.07		
Sociodemographic characteristics[g]						*6.05*
Gender (male vs. female)	-0.41 (-0.82; 0.01)	0.06	-0.48 (-0.97; 0.01)	0.05		
Site (rural vs. periurban)	0.73 (0.31; 1.15)	<0.01	0.73 (0.15; 1.31)	0.01		
Age	0.02 (0.00; 0.03)	0.01	0.02 (0.01; 0.04)	0.01		
Marital status (married vs. not married)	0.68 (0.18; 1.19)	<0.01	0.31 (-0.25; 0.88)	0.27		
Main occupation (housewife/student/retired vs. farmer/fisherman)	-0.58 (-1.07; -0.09)	0.02[h]	-0.02 (-0.70; 0.66)	0.96		
Main occupation (informal business/formally employed vs. farmer/fisherman)	-0.56 (-1.09; -0.03)	0.04[h]	-0.04 (-0.70; 0.61)	0.90		

[a]Only variables with univariable association at p<0.2 listed; [b]Each model adjusted for sociodemographic characteristics, see footnote g; [c]Logistic regression coefficient with 95% confidence interval; [d]Figures in bold if p<0.05; [e]Interaction of rural with periurban site (baseline) considered if p value of interaction term less than 0.1 (*p<0.1, **p<0.05); [f]Difference of corrected Akaike Information Criterion (AICc) between each model and the *best* model, designated with Δ(AICc)=0. Bold figures indicate models that explain vaccine acceptance better than the sociodemographic model only; [g]Variables used for adjusting. Figures reported in adjusted analysis refer to model with sociodemographic characteristics alone; [h]Variable is nominal with 3 categories, overall p=0.04

According to their Δ(AICc) values, focal models of somatic symptoms and social impact and the model containing the intention-to-vaccinate variable explained uptake better than the model containing only sociodemographic characteristics. Respondents who identified unconsciousness as a priority symptom and those among the rural respondents who strongly believed that cholera patients may cause a disruption in the local health care services were more likely to drink the OCV. Rural respondents and older respondents were also more likely to become vaccinated; and women tended to accept it more than men, though with borderline significance (p=0.053). Nausea was the only negative determinant of OCV uptake identified in any focal model.

Comprehensive model

All sociocultural features of illness identified as significant determinants of OCV uptake in the focal models (Table 5-1) were retained with similar effects in the comprehensive model that includes interactions with site (Table 5-2). An additional somatic symptom, loss of appetite, showed a negative association, but only in the rural site. Sociodemographic characteristics were also the same as in the focal model, with female gender clearly a significant positive determinant of OCV uptake (p=0.03). Anticipated acceptance for a free OCV appears to influence uptake; the adjusted regression coefficient is 0.91, but only marginally significant (p=0.078).

Table 5-2: Comprehensive model of social and cultural determinants of oral cholera vaccine uptake in a community mass vaccination campaign in Zanzibar, 2009, n=356

	Comprehensive model[a]		
	Coefficient (95% CI)[b]	p value[c]	Int[d]
Categories of distress: somatic symptoms			
Loss of appetite (periurban site)	0.12 (-0.36; 0.59)	0.63	
Loss of appetite (rural site)	-0.67 (-1.34; -0.00)	0.05	*
Nausea	-0.64 (-1.21; -0.08)	0.03	
Unconsciousness	0.19 (0.02; 0.37)	0.03	
Categories of distress: social impact			
Fear of isolation from others	-0.08 (-0.26; 0.09)	0.35	
Disruption of healthcare services (periurban site)	-0.06 (-0.52; 0.39)	0.79	
Disruption of healthcare services (rural site)	0.91 (0.00; 1.81)	0.05	*
Self treatment at home			
Drinking more water or liquids	-0.13 (-0.29; 0.03)	0.12	
Intention to receive OCV			
Anticipated acceptance of a free OCV	0.91 (-0.10; 1.92)	0.08	
Sociodemographic characteristics			
Gender (male vs. female)	-0.51 (-0.97; -0.05)	0.03	
Site (rural vs. periurban)	0.83 (-0.41; 2.07)	0.19	
Age	0.03 (0.01; 0.04)	<0.01	

[a]Only variables identified in focal models at p<0.2 included in comprehensive adjusted model; [b]Logistic regression coefficient with 95% confidence interval; [c]Figures in bold if p<0.05; [d]Interaction of rural with periurban site (baseline) considered if p value of interaction term less than 0.1 (*p<0.1)

The overall effect of site (adjusted regression coefficient: 0.94, 95% confidence interval: 0.47 to 1.42, p<0.01) showed that rural respondents were more likely to accept the OCV (main effects model, not shown).

5.3.4 Comparing social and cultural determinants of intention and uptake for a free OCV

Because intention to be vaccinated with a free OCV was almost 95%, a multivariable logistic regression of determinants of this outcome would be inappropriate. Nevertheless, to address the question of whether determinants of intention and of uptake are similar or different, univariable logistic regression was conducted to compare results for each outcome. Table 5-3 shows the variables that were associated in crude analysis (p<0.05) with respondents' intention to vaccinate themselves with a free OCV, including borderline results for gender and site.

Table 5-3: Crude analysis of social and cultural determinants of intention to vaccinate with a free oral cholera vaccine in Zanzibar, n=356

	Crude analysis[a]	
	Coefficient (95% CI)[b]	p value
Categories of distress: social impact		
Fear of infecting others	0.86 (0.19; 1.54)	0.01
Disruption of healthcare services	0.89 (0.06; 1.72)	0.04
Perceived causes		
God's will	-0.37 (-0.64; -0.10)	<0.01
Self treatment at home		
Drinking more water or liquids	0.55 (0.05; 1.04)	0.03
Sociodemographic characteristics		
Gender (male vs. female)	-0.89 (-1.81; 0.02)	0.06
Site (rural vs. periurban)	-0.89 (-1.81; 0.02)	0.06
Regular and dependable household income	1.14 (0.22; 2.05)	0.02

[a]Only variables listed with univariable association with anticipated acceptance for a free OCV at $p<0.05$, except gender and site; [b]Logistic regression coefficient with 95% confidence interval

Similar to the crude analysis of uptake (Table 5-1), categories related to social impact, perceived causes, self treatment at home and sociodemographic variables were identified as significant determinants. Reported disruption of health care services was a positive determinant in both analyses, and fear of infecting others was another positive factor, but only in the intention analysis. Among perceived causes, instead of witchcraft as positive determinant of uptake, God's will was related to intention, but negatively. Rehydration at home featured as positive determinant in the intention-to-vaccinate analysis, but was a negative determinant of uptake. Among sociodemographics, only women and site were identified in both analyses, but periurban site was positively associated with intention and rural site with uptake. Increasing age, being married and being a farmer/fisherman were only positively associated with uptake. Although the vaccine was offered for free, regular and dependable income was a positive determinant of intention to be vaccinated.

5.4 Discussion

To improve the use of vaccines in endemic communities, public health planners need not only know coverage rates of vaccination campaigns, but also what social and cultural factors may have contributed to the achieved coverage [39]. By empirically examining the relationship between cultural concepts of illness and OCV uptake, a connection which has rarely been considered by classical epidemiologists and public health officials [40], this study developed an approach for contributing relevant information to help local decision makers to improve cholera control.

Prevaccination study results showed a high rate of anticipated acceptance (94%) across both islands. Despite this and the local organization and implementation of the 2009 mass vaccination campaign that attempted to minimize other access-related issues, uptake of the OCV was notably lower (50%). This uptake rate was between rates of two recent mass vaccination campaigns conducted in Africa and Asia. The 2003/2004 campaign using Dukoral® in an urban endemic neighborhood in the coastal town of Beira, Mozambique, estimated coverage of ~41% for people 15 years and older [8]. Coverage with a locally produced two-dose OCV in a campaign conducted in 1998 in 13 communes of coastal Hue City, Vietnam, amounted to 74% for people aged 20 and above, and with significantly higher coverage among women [13].

Demotivating factors for OCV uptake were related to symptoms of malaise: priority for getting a vaccine was reduced when people associated cholera with nausea and loss of appetite, which are not cholera-specific symptoms.

Higher OCV uptake in the rural site was further reinforced by the fact that concern about the detrimental impact of cholera outbreaks on local health care services was a positive determinant of uptake among rural respondents only. Rural villagers feared that the local health care system would be overburdened with cholera cases; this might explain their preference for vaccination, although supplementary WASH activities were also frequently demanded [25]. This finding and the previously reported higher rural than periurban willingness to buy the OCV at a price of almost USD 10 [25] suggest a higher priority for using OCV in rural Zanzibar.

Perceived severity of illness may influence desire for enteric vaccines [15-17]. Because cholera was almost universally reported in both communities as “very serious” (97%) and “usually or sometimes fatal without treatment” (96%) (not shown), the influence of illness-related severity and fatality could not directly be analyzed as potential determinants of OCV uptake. Perceptions regarding severity and potential fatality were nevertheless related to vaccine acceptance in these communities because unconsciousness, a feature of dehydration and thus an advanced stage of cholera, was not only reported as one of the most prominent somatic problems [34], but it was also identified as positive determinant of OCV uptake.

Increasing age and female gender were further positive determinants of OCV uptake. In contrast, Ali *et al.*, who studied how sociodemographic and spatial variables influenced participation in a cholera vaccination trial in Kolkata, India, found that younger age was positively related [22]. Although previous personal or household illness experience was not associated with OCV uptake, older people might have drunk the vaccine more often because of their higher likelihood to have witnessed the grave consequences of cholera. In line with the

Kolkata study [22] and the 1998 mass vaccination campaign in Vietnam [13], men were less likely to accept oral cholera vaccination. As in Zanzibar, it is not clear whether this reflects more responsibility or self-perceived vulnerability among women.

In addition to focusing on sociocultural features of cholera, anticipated acceptance of the free OCV was also assessed and found to be a tentative positive predictor of uptake. However, evidence that intention to vaccinate is directly related to vaccination behavior is still inconclusive [28,29,41]; because of this and because no studies have yet firmly established such an association for cholera, further research is warranted to investigate this relationship.

Social and cultural determinants of anticipated acceptance and uptake of an OCV in a mass vaccination campaign in Zanzibar were not directly comparable because of almost universal willingness for free immunization. Recognizing this statistical limitation, comparison of crude associations nevertheless showed that categories related to social impact, perceived causes, self treatment at home and sociodemographics are relevant determinants for both intention to be vaccinated and actual behavior.

5.4.1 Conclusions

Uptake of a free OCV in the 2009 mass vaccination campaign in a periurban and a rural endemic area of Zanzibar was lower than anticipated acceptance. This study showed that consideration of sociodemographic and economic factors is necessary but not sufficient to explain coverage, because sociocultural features of cholera-like illness determined vaccine acceptance better than purely social epidemiological models.

Planning of future cholera mass vaccination and sensitization campaigns in Zanzibar should benefit from findings presented here. Cholera as a cause of severe dehydration should be emphasized vis-à-vis its moderate malaise-related symptoms. Rural recognition of the cholera-related burden on the local health care system was reflected by a priority for oral cholera vaccination; this shows not only the importance of vaccination for cholera control but also the need to strengthen health care services in Zanzibar, particularly in rural areas. Inasmuch as resources for public health are generally scarce in Zanzibar, findings recommend particular efforts to increase cholera immunization coverage among young adults, in periurban areas and for men.

Conflict of interest

The authors declare that no conflict of interest exists.

Authors' contributions

All authors contributed to the study design. CS organized and supported data collection. SMA, RH, AMK and CLC facilitated data collection and field activities. CS and MGW analyzed the data and drafted the first version of the manuscript. All authors read and approved the final manuscript.

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6

IMPROVING COMMUNITY COVERAGE OF ORAL CHOLERA MASS VACCINATION CAMPAIGNS: LESSONS LEARNED IN ZANZIBAR*

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Abstract

Background

Recent research in two cholera-endemic communities of Zanzibar has shown that a majority (~94%) of the adult population was willing to receive free oral cholera vaccines (OCVs). Since OCV uptake in the 2009 campaign reached only ~50% in these communities, an evaluation of social and cultural factors and of barriers was conducted to understand this difference for future cholera control planning.

Methodology/Principal Findings

A random sample of 367 adult periurban and rural community residents (46.6% immunized vs. 53.4% unimmunized) was studied with a semi-structured interview that inquired about social and cultural features of cholera depicted in a vignette and barriers to OCV uptake. Symptoms (rectal pain, loose skin only in rural community) and perceived causes (uncovered food, contact with contaminated water) specific for severe diarrhea were associated with uptake. Purchasing drugs from pharmacies to stop diarrhea and vomiting was negatively associated with uptake. Increasing household size, age and previous enteric illness episode were positively related to uptake, the latter only at the rural site. The most prominent barrier to uptake was competing obligations or priorities (reported by 74.5%, identified as most important barrier by 49.5%). Next most prominent barriers were lacking information about the campaign (29.6%, 12.2%), sickness (14.3%, 13.3%) and fear of possible vaccine side effects (15.3%, 5.6%). The majority of unvaccinated respondents requested repetition of the vaccination with free OCVs.

Conclusions/Significance

Factors associated with uptake indicated a positive impact of the vaccination campaign and of sensitization activities on vaccine acceptance behavior. Unlike communities opposed to cholera control or settings where public confidence in vaccines is lacking, identified barriers to uptake indicated a good campaign implementation and trust in the health system. Despite prospects and demand for repeating the vaccination, local decision makers should reconsider how careful logistical arrangements may improve community coverage and thus effectiveness of vaccination campaigns.

6.1 Introduction

Cholera control in populations living at risk of recurrent cholera outbreaks is based on timely treatment and a preventive strategy, mainly promoting supply of safe water in sufficient quantities, improved sanitation, and health education (WASH) [1]. Despite these recommendations, cholera has remained a global public health concern; the World Health Organization (WHO) assumes that annual estimates for morbidity and mortality exceed 3 million cases and 100,000 deaths [2]. The WHO also recommends the use of mass oral cholera vaccination as a supplementary prevention measure to WASH [3].

Cholera is an enteric bacterial disease caused by *Vibrio cholerae* serogroup O1 or O139. People living in unsanitary conditions without access to safe drinking water and sanitation are at greatest risk of becoming infected with *V. cholerae*, which is mainly transmitted through the fecal-oral route. Major clinical features, which usually start abruptly after an incubation period of a few hours to five days, include profuse watery diarrhea and vomiting [4]. Without treatment, case-fatality rates may rise to 50% or above. Rehydration is the mainstay for treatment and includes administration of oral rehydration solution (ORS) to patients with mild to moderate symptoms and intravenous fluids to severely dehydrated cases. Antibiotics should also be administered to severe cases to shorten episodes, diminish the amount of intravenous fluids required and reduce shedding of *V. cholerae* [2]. Some studies suggest that antibiotics should also be used for moderate cases [5].

While recent research on the use of oral cholera vaccines (OCVs) in mass vaccination campaigns in endemic communities has focused on epidemiologic parameters [6,7] and economic aspects [8-13], relatively little is known about local perceptions of cholera, intentions to accept OCVs and how such factors are associated with uptake. Even though detailed knowledge of epidemiologic and economic aspects is indispensable for a successful introduction of vaccines, social and cultural factors should also be examined to improve and sustain vaccination coverage [14,15]. In the past, a lack of attention to community views of illness and prevention has proven to be fatal not only for disease control in certain populations but also for national or international public health goals, e.g., to eradicate polio in Africa [16,17].

Up to date, only articles on policy makers' views of cholera [18,19] and on social factors of oral cholera vaccine uptake [20] have been published, and studies on the feasibility and costs of community mass vaccination campaigns have examined why people might not have taken the OCV [8,21,22]. However, an assessment of mass vaccination campaigns to more systematically

evaluate social and cultural factors associated with OCV uptake and to identify potential barriers is still missing, but likely to be very useful for the benefit of local (and even international) vaccination campaign planning.

Recent research in two cholera-endemic communities of Zanzibar, conducted within the framework of a WHO study to evaluate the use of OCV in endemic settings, has shown that a vast majority (~94%) of the population targeted for the campaign was in principle willing to receive free vaccines against cholera [23]. Since actual OCV acceptance (or uptake) reached only ~50% in this prevaccination sample, an evaluation of social and cultural factors and of barriers to OCV uptake was needed to understand this difference for future cholera control planning in Zanzibar.

Findings reported here are based on the research approach of cultural epidemiology, which was used in prevaccination studies to examine social and cultural determinants of anticipated and actual OCV acceptance [23,24]. Cultural epidemiology is a research approach in health social sciences that integrates quantitative and qualitative data [25] to study community views of illness [26-30] and how these influence health-related behavior [31-33].

This study examined data from a periurban and a rural community targeted in the 2009 OCV mass vaccination campaign in Zanzibar. It aimed to evaluate the influence of social and cultural factors on OCV uptake and to identify logistical, medical, social and system-related barriers to uptake.

6.2 Methods

6.2.1 Ethics statement

The Research Ethics Review Committee of the World Health Organization and the Ethics Committee of the Ministry of Health and Social Welfare of Zanzibar approved this study. Participants were informed orally about this study and also given a detailed information sheet. Only those who gave written consent were interviewed. No compensation was offered for the interview. Interview data sheets did not bear the names of respondents and all data were anonymized before analysis.

6.2.2 Setting

The east African archipelago of Zanzibar belongs to the United Republic of Tanzania and is inhabited by ~1.2 million people who are predominantly Muslim. Kiswahili is the main language, but English is also widely used. The archipelago is located ~60 km off the coast of

mainland Tanzania and consists of two major islands—Unguja in the south and Pemba in the north—and several islets; it can be reached from the coast by ferry or air within 20 minutes to 2 hours. Zanzibar has been regularly affected by cholera; the first cases in recent times were detected in 1978 [34,35].

This study was conducted in the periurban Shehia of Chumbuni (population ~11,000) in Unguja and the rural Shehia of Mwambe (~8,000) in Pemba. Both Shehias (administrative term for community in Zanzibar) were among the core areas of a mass vaccination campaign that was conducted in early 2009 by the Ministry of Health and Social Welfare of Zanzibar (MoHSW) with support from the WHO. The sample for this study was drawn from these two Shehias because they had been studied in a prevaccination survey in 2008 [23,24].

6.2.3 Mass vaccination campaign

The mass vaccination campaign aimed to vaccinate ~50,000 inhabitants with Dukoral®, a two-dose OCV containing killed *V. cholerae* O1 bacteria and recombinant cholera toxin B subunit protein [36]. Dukoral® was the only OCV prequalified by the WHO at the time of vaccination. It requires a cold chain for storage and safe water (~1.5 dl per dose) for its administration. It was offered without charge in two rounds from January 17 to 26 and February 7 to 16, 2009, to residents aged two years or older from six Shehias from Unguja and Pemba that had been identified as recent cholera hotspots. Nine vaccination posts were set up on each island that operated daily for at least eight hours and were staffed with local health care workers and villagers.

Information activities for the campaign started with a meeting with district officials on December 23, 2008 followed by three meetings to inform leaders, Shehia committee members and mobilizers from each community (January 5 and 10, 2009) and general community residents (January 15, 2009) (MoHSW, Health Promotion Unit, OCV Social Mobilization Report, February 20, 2009). A refresher meeting in the communities followed shortly before the second round on February 5, 2009. Social mobilization used posters, leaflets, street banners and T-shirts to disseminate information on the OCV campaign and to reinforce general hygiene and sanitation messages in the six Shehias. Messages were continuously broadcast on national TV and radio from the first until the last day of the campaign. The local press was also briefed and newspaper articles reported from the campaign to promote participation. The campaign was officially launched by the Minister of Health who drank the vaccine publicly at the Chumbuni Primary Health Care Unit (*Zanzibar Today*, January 18, 2009). Mobilizer teams were formed for each Shehia and delivered information from house to house and by megaphone. Each team consisted of five to six community residents representing also women's groups, youth, religious

groups and members of the opposition party. Key messages highlighted not only the importance of vaccination for cholera prevention, but also promoted hygiene messages to prevent other diarrheal diseases, and explained administration of the OCV, its characteristic features and potential for mild side effects.

6.2.4 Design and sampling

This was a cross-sectional survey designed as a case-control study. Data were collected in June and July 2009 from vaccinated and unvaccinated community residents, six months after the mass vaccination campaign. The sampling frame for this study was derived from the census database that had been compiled by the International Vaccine Institute shortly before the mass vaccination campaign implementation in early 2009 [37]. Names, age, sex, OCV vaccination status and a unique house identification number were extracted for both study Shehias. Respondents' houses in Chumbuni were located with the help of aerial photographs indicating house numbers; houses in Mwambe were located with the help of local assistants.

Approximately 380 adults, based on a sample size of 330 [38] with 15% compensation for missing data, were identified following a stratified random sampling procedure. After exclusion of respondents who had been interviewed before the vaccination for the baseline study [24], all respondents aged 18 years and older were selected. Second, periurban and rural respondents were separated and groups of women and men created among them. Third, of the ~95 women and 95 men required per site, 50% were selected from those who had received two doses of the OCV, 40% from those who had not received a single dose and 10% from those with one dose only. Only residents who were physically and mentally fit to stand an interview of approximately one hour duration were included in the sample. Women who had not taken the vaccine because of pregnancy during the mass vaccination campaign were not interviewed.

6.2.5 Instrument

Semi-structured interviews based on the Explanatory Model Interview Catalogue (EMIC) are the principal instrument for cultural epidemiological studies and elicit locally valid representations of illness-related experience, meaning and behavior [25,39]. An EMIC interview for study of diarrhea-free community residents was developed based on the prevaccination survey [24]. A ten-day workshop was conducted shortly before the survey to train field workers and pilot the EMIC interview in Shehias adjacent to the study communities.

After recording relevant sociodemographic characteristics, interviews began with the telling of a brief story in easily understandable terms, making use of a clinical vignette that described a cholera patient with cardinal somatic symptoms. To study sociocultural features of cholera-like

illness, respondents were asked a series of open and closed questions. These elicited respondents' opinions on (i) what additional physical symptoms the cholera patient described in the vignette might suffer from, (ii) how the illness might impact him/her socially, emotionally and financially, (iii) what causes the illness may be attributed to and (iv) what would usually be done at the patient's home for self treatment and (v) what sources of help would be consulted outside the household.

Respondents who did not swallow two doses of the OCV during the mass vaccination campaign were queried about their reasons against vaccination by specifically inquiring about barriers related to logistical, social and system-relevant and medical aspects.

6.2.6 Data management and analysis

Data entry

Quantitative data were recorded by interviewers on data sheets, double entered in Epi Info 3.5.1 (CDC, Atlanta, GA, USA) by data entry clerks and cleaned for statistical analysis in SAS 9.2 (SAS Institute, Cary, NC, USA). Qualitative data, i.e. narratives from selected items of the interview, were written down during the interview by note takers in Kiswahili (or in English in a few cases). Narratives were typed in a pre-coded word processor template after translation into English. This enabled automatic importation of entire interviews with codes into the qualitative data analysis software MAXQDA 10 (VERBI Software, Consult. Sozialforschung. GmbH, Marburg, Germany). For integrated analysis of quantitative and qualitative data, relevant quantitative variables were imported into MAXQDA 10; this made it possible to retrieve narrative segments based on analytically relevant findings or statistical relationships.

Multivariable analysis of factors of uptake

Sociodemographic characteristics were coded as numeric or categorical variables and, if needed, dichotomized for logistic regression analysis. Categories of sociocultural features of cholera-like illness were assigned a value of 2 if they were mentioned spontaneously and a value of 1 if they were mentioned only after probing. Those among the reported categories that were identified as single most troubling (among patterns of distress), most important (perceived cause) or most helpful (help seeking) were given an additional value of 3. A cumulative prominence was then calculated for each category ranging from 0 to 5. This approach based on the ranked prominence of responses has been widely used in analytic cultural epidemiological studies, which have examined how sociocultural features of illness affect health behavior [31,33].

To identify social and cultural factors explaining OCV uptake, a multivariable logistic regression model was calculated. OCV uptake was obtained from mass vaccination campaign data that had been compiled electronically during the campaign [37]; fully immunized respondents were coded as 1 and those who had received only one or no dose were coded as 0. The regression analysis included interaction with site as suggested by site-specific findings from the prevaccination survey [24] and because OCV uptake was higher in the rural than in the periurban site (58.8% vs. 40.8%, p=0.001).

Only explanatory variables reported by 5-95% were considered for analysis. First, variables were identified whose univariable association with OCV uptake had a $p<0.2$. Second, multivariable regression models were run for each subset of categories related to patterns of distress, perceived causes and help seeking, and each of these models was adjusted for sociodemographic characteristics. To calculate the final model, only those variables which were retained with a $p<0.2$ in these sub-models were considered. Interaction between each explanatory variable and site (rural vs. periurban site at baseline) was tested in sub-models; only interaction terms retained with a $p<0.1$ in sub-models were used in the final model. The final model reports logistic regression coefficients with 95% confidence intervals and p values. In case of significant interaction with site, site-specific estimates are presented.

Descriptive analysis of barriers to uptake

Coding and calculation of variables related to barriers followed the approach used for sociocultural features of illness. Unvaccinated respondents' spontaneous and probed answers for each barrier and the barrier they identified as most important were recorded. Thematically similar barriers were subsumed under groups of logistical, medical and social/system-related barriers. The nonparametric Wilcoxon test was used for identifying statistically significant differences of prominence between both sites and between genders.

6.3 Results

6.3.1 Sample characteristics

A total of 378 respondents were interviewed. Eleven interviews were excluded from analysis due to pregnancy. Of the remaining 367 respondents, 46.6% were vaccinated with two doses, 9.3% with one dose only and 44.1% had not drunk any dose of OCV. Their characteristics are presented in Table 6-1. All respondents were Muslims and of Tanzanian nationality.

Table 6-1: Sociodemographic characteristics and vaccination status of a sample interviewed after a community mass vaccination campaign in Zanzibar, stratified by site and gender

	Total	Periurban site	Rural site		Women	Men	
Number (%)	367 (100)	189 (51.5)	178 (48.5)		180 (49.0)	187 (51.0)	
Age (years)							
Mean (SD)	35.4 (14.6)	33.1 (13.5)	37.8 (15.4)	**	35.7 (13.8)	35.1 (15.4)	
Median (range)	32 (18-90)	28 (18-75)	36.5 (18-90)	**	33 (18-90)	30 (18-80)	
Marital status (%)							
Never married	30.5	42.9	17.4	***	21.1	39.6	***
Married	59.4	49.7	69.7	***	61.1	57.8	
Separated	0.5	0.0	1.1		0.0	1.1	
Divorced	6.5	6.9	6.2		12.2	1.1	***
Widowed	3.0	0.5	5.6	**	5.6	0.5	**
Household size (number of persons)							
Mean (SD)	6.9 (3.0)	7.6 (3.2)	6.3 (2.6)	***	6.8 (3.0)	7.1 (2.9)	
Median (range)	7 (1-15)	7 (1-15)	6 (1-13)	***	7 (1-14)	7 (1-15)	
Main occupation (%)							
Agriculture	30.8	3.2	60.1	***	35.0	26.7	
Fishing	6.0	0.0	12.4	***	0.0	11.8	***
Self-employment	23.7	36.0	10.7	***	18.3	28.9	*
Formal employment	8.2	13.2	2.8	***	3.3	12.8	***
Housewife	12.3	18.0	6.2	***	25.0	0.0	***
Casual laborer	0.8	1.1	0.6		0.0	1.6	
Student	12.5	18.0	6.7	**	12.2	12.8	
Not active/retired	5.7	10.6	0.6	***	6.1	5.3	
Highest education (%)							
No education	8.4	4.8	12.4	*	10.6	6.4	
Koranic school	23.7	10.1	38.2	***	30.6	17.1	**
Primary school	26.4	21.2	32.0	*	19.4	33.2	**
Secondary school	36.8	56.1	16.3	***	35.6	38.0	
Above secondary school	4.6	7.9	1.1	**	3.9	5.3	
Vocational school	1.4	1.6	1.1		0.6	2.1	
Higher education	3.3	6.3	0.0	***	3.3	3.2	
Household income (%)							
More regular and dependable	39.8	54.0	24.7	***	41.1	38.5	
Less regular and dependable	60.2	46.0	75.3		58.9	61.5	
Vaccination status							
Receipt of 2 doses, number (%)	171 (46.6)	86 (45.5)	85 (47.8)		85 (47.2)	86 (46.0)	
Receipt of 1 dose, number (%)	34 (9.3)	18 (9.5)	16 (9.0)		17 (9.4)	17 (9.1)	
Receipt of 0 doses, number (%)	162 (44.1)	85 (45.0)	77 (43.3)		78 (43.3)	84 (44.9)	

SD: Standard deviation, t test used for comparing means, Wilcoxon test used for comparing medians, Fisher's exact test used for comparing proportions (*p<0.05, **p<0.01, ***p<0.001)

6.3.2 Social and cultural factors associated with OCV uptake

Multivariable logistic regression analysis identified sociocultural features of cholera-like illness associated with OCV uptake, adjusted for sociodemographic characteristics (Table 6-2).

Table 6-2: Social and cultural factors associated with oral cholera vaccine uptake in a community mass vaccination campaign in Zanzibar, n=367

	Adjusted analysis[a]		
	Coefficient (95% CI)[b]	p value[c]	Int[d]
Categories of distress: somatic symptoms			
Pus in stool	0.30 (-0.14; 0.75)	0.18	
Rectal pain	0.60 (0.16; 1.05)	0.01	
Sunken eyes	0.18 (-0.15; 0.51)	0.29	
Loose skin (periurban site)	-0.48 (-1.15; 0.18)	0.16	
Loose skin (rural site)	0.70 (0.17; 1.22)	0.01	**
Perceived causes			
Unprotected/spoiled food	0.22 (0.00; 0.43)	0.05	
Contact with contaminated water	0.36 (0.06; 0.65)	0.02	
Outside help seeking			
Pharmacy/Over-the-counter drugs	-0.61 (-1.08; -0.13)	0.01	
Sociodemographics and previous illness episode			
Age	0.03 (0.01; 0.04)	<0.01	
Household size	0.09 (0.01; 0.17)	0.03	
Site (rural vs. periurban)	-1.29 (-2.32; -0.26)	0.01	
Previous enteric illness episode (periurban site)	-0.38 (-1.73; 0.98)	0.59	
Previous enteric illness episode (rural site)	1.11 (0.13; 2.09)	0.03	*

[a]List of variables with univariable association at p<0.2 that were included in adjusted models; [b]Logistic regression coefficient with 95% confidence interval; [c]Figures in bold if p<0.05; [d]Interaction of rural with periurban site (baseline) considered if p value of interaction term less than 0.1 (*p<0.1, **p<0.01)

Among categories of distress, two of the somatic symptoms that were mentioned in connection with the cholera vignette were positively associated with OCV uptake: rectal pain and loose or shriveled skin, which is a sign of dehydration. Rectal pain was spontaneously reported by 1.9% and mentioned by 68.7% upon probing. Vaccinated and unvaccinated respondents explained that this symptom meant that frequent passing of stool may be painful to the person described in the vignette. Loose or shriveled skin was only associated with vaccine uptake among rural respondents. It was reported by 86.6% of the total sample; 88.8% reported it in the rural and 84.7% in the periurban site and more rural respondents mentioned it spontaneously (33.1%) compared to periurban respondents (5.8%). Accounts from vaccinated and unvaccinated respondents were similar, saying that frequent diarrhea leads to loss of water in the body, which in turn was seen as the reason for dehydration manifested by the sign of loose skin.

Among categories of perceived causes, two categories were positively associated with OCV uptake: eating food that has not been covered properly and contact with contaminated water. The first category was mentioned by 89.4% of the total sample and identified by 8.2% as most important cause for cholera. Among those who reported this category, the majority said that if food is not covered properly, flies or other insects that carry germs may contaminate it. A 22-year-old farmer from Pemba, who had ingested both doses, explained it this way:

> "Yes, this is the area where one can get it [the illness described in the vignette], because the flies are carrying feces and land with it on the food."

Such explanations were not only typical for the vaccinated group because narratives from unvaccinated respondents also frequently showed flies as main disease vector.

Fewer respondents (69.2%) reported that contact with contaminated water was a cause for cholera, and only 1.9% identified it as most important cause. Both vaccinated and unvaccinated respondents referred to dirty water as a potential cause because it contains bacteria or other disease-causing organisms that can be transmitted through the fecal-oral route. The following example from a 19-year-old fully immunized male student from Unguja illustrates this reasoning:

> "Yes, because it is already contaminated with bacteria. If you have touched the water and not washed your hands with soap and then you eat food you will get the disease."

Among categories of help seeking outside the home, consulting pharmacies was negatively associated with OCV uptake. While everybody reported spontaneously that a patient with cholera-like illness should be sent to professional health facilities, 32.4% of the sample also reported getting drugs from the pharmacy as a means to stop diarrhea and vomiting, though none of them identified this category as most helpful. Primarily antibiotics like tetracycline or septrine were mentioned among both vaccinated and unvaccinated groups.

Among sociodemographic characteristics, increasing household size and increasing age was positively related to OCV uptake. A total of 9.5% reported a household episode of the illness described in the cholera vignette. No gender differences were found, but rural respondents reported more such episodes than their periurban counterparts (13.5% vs. 5.8%, p=0.013). This variable was also positively associated with OCV uptake, but only at the rural site.

6.3.3 Barriers to OCV uptake

All 196 respondents who were not completely immunized were asked the following open question: "Can you tell us the reasons why you did not swallow two doses of the cholera vaccine?" Individual and grouped barriers are presented for the overall sub-sample of unvaccinated respondents (Table 6-3), and stratified by site (Table 6-4) and by gender (Table 6-5).

Most prominent barriers

Logistical factors were reported as paramount barriers, followed by medical issues; social and system-related factors were the least prominent barriers (Table 6-3).

Table 6-3: Barriers to uptake of an oral cholera vaccine in a community mass vaccination campaign in Zanzibar

	Pooled sample, n=196 How reported?			
Barriers to uptake[a]	Total[b] %	Spon.[c] %	Most important[d] %	Mean prom.[e]
Logistical barriers	76.5	71.4	63.3	3.38
Competing obligations/priorities	74.5	69.4	49.5	2.92
Lacking information about campaign	29.6	9.7	12.2	0.76
Vaccination post open days/hours limited	13.8	3.1	1.5	0.21
Costs apart from vaccine	3.6	0.5	0.0	0.04
Organizational problems at vaccination post	0.5	0.0	0.0	0.01
Medical barriers	31.1	23.5	23.5	1.25
I was sick (not due to vaccine)	14.3	14.3	13.3	0.68
Fear of possible side effects from vaccine	15.3	6.1	5.6	0.38
Doubted effectiveness of vaccine	9.2	5.6	4.6	0.29
Social/system-related barriers	12.2	4.1	3.6	0.27
Vaccine free of charge (useless medicine)	5.6	2.6	1.0	0.11
Fear of infertility	3.1	0.0	1.5	0.08
Mistrust motives of campaign	5.1	2.0	0.0	0.07
Social pressure against taking vaccine	3.1	1.0	0.5	0.06
Lacking confidence in government	2.6	1.0	0.5	0.05
Prior bad experience with health system	0.5	0.0	0.0	0.01
Miscellaneous	8.7	8.7	6.6	0.37
Other barriers	7.1	7.1	5.6	0.31
Cannot say/Nothing	1.5	1.5	1.0	0.06

[a]Barriers ordered according to descending mean prominence (see footnote e), grouped barriers in bold; [b]Percentage of barriers reported spontaneously and after probing; [c]Percentage of barriers reported spontaneously only; [d]Percentage of barriers that were identified as single most important among all the reported barriers. Six respondents who only received one dose identified barriers that were not among the ones listed as most important: four respondents reported "Experience of side effects from first dose of vaccine," two respondents reported "Did not have information about timing of second dose;" [e]Mean prominence based on values assigned for each barrier (3=identified as most important, 2=reported spontaneously, 1=reported after probing, 0=not reported)

The most prominent individual barrier to OCV uptake, i.e., the one having the highest mean prominence, was competing obligations or priorities, which was reported by almost three-quarters (74.5%) of the unvaccinated respondents and identified by nearly half (49.5%) as the most important barrier. Analysis of qualitative data from these respondents indicated that they had mostly been away for a longer time on the mainland or another island and thus were less able to reach the vaccination posts. Activities included working in farms, going on month-long fishing trips and some visited their relatives or were away from home for study or exams.

The second most prominent barrier was *lacking information about the campaign*, reported by 29.6% and identified as most important barrier by 12.2%. Almost everyone who did not have

information about the campaign also reported his/her absence because of other activities. The following accounts illustrate how lacking information and being away together prevented vaccine uptake. Respondents were either away during both rounds, as illustrated by the account of a 36-year-old man from Chumbuni:

> "I was not here during the campaign and I didn't know when the campaign started and finished. I am a seaman. My wife informed me that all the people in the house got the vaccine. The day I arrived here I was advised to take the vaccine but I didn't take it because I was tight with other activities. And on the second day my boss asked me to go to Mombasa."

Or they were only in their village during the second round, but not given the vaccine:

> "I was not around because I had traveled to Wete. And when I came back I went to the vaccination post and the workers told me that I cannot get it because I missed the first dose." (Housewife from Mwambe, 50 years old)

Sickness, which was reported by 14.3% of unvaccinated respondents in total and identified by 13.3% as the single most important reason, was the third most prominent barrier to uptake. Respondents who reported a sickness were either uncomfortable to take the vaccine, concerned about a potential negative impact of vaccination on their health, or simply not able to access vaccination posts because of a physical handicap or a recent delivery or surgery.

Fear of possible side effects was the fourth most prominent barrier against vaccination, reported by 15.3% in total and identified by 5.6% as most important. People were afraid of side effects such as diarrhea, vomiting, nausea, skin reactions after injection, and exacerbations of underlying diseases due to interaction with the vaccine. Also, something free of charge was believed to cause problems. Three respondents were afraid of side effects if the vaccine was administered concurrently with other drugs—they were also among those who reported being sick as main barrier to vaccination.

Besides fear of side effects, *doubted effectiveness of the vaccine* was reported by 9.2% as another vaccine-related barrier; and for 4.6% this category was the main reason against taking the OCV. Respondents were not sure about the benefit for their own health or the effectiveness of the vaccine.

Least prominent barriers

The four least prominent barriers to OCV uptake were related to *lacking confidence in the government* (reported in total by 2.6% of the unvaccinated sub-sample), *costs apart from the*

vaccine (3.6%), *prior bad experience with health system* (0.5%), and *organizational problems at vaccination post* (0.5%) (Table 6-3).

Other barriers related to social issues were reported by 5% or less: *mistrust motives of the campaign* were reported by 5.1% and *social pressure against vaccination* and *fear of infertility* by 3.1%. Nobody reported that discouragement by authoritative persons made them refuse vaccination.

Site- and gender-specific barriers

Among the most prominent barriers, *lacking information about the campaign* was more often reported and identified as most important barrier among rural than periurban respondents (p=0.012) (Table 6-4). Narratives indicated that rural respondents were away from their homes for longer times and several went fishing for months, which made it difficult for them to be home at the right time slot needed for the vaccination:

> "I had traveled to Unguja for fishing for a period of one month and fifteen days. And I had no information about the vaccine campaign." (Unvaccinated rural fisherman, 35 years old)

Table 6-4: Barriers to uptake of an oral cholera vaccine in a community mass vaccination campaign in Zanzibar, stratified by site

	Periurban site, n=103 How reported?				Rural site, n=93 How reported?				
Barriers to uptake[a]	Total[b] %	Spon.[c] %	Most important[d] %	Mean prom.[e]	Total[b] %	Spon.[c] %	Most important[d] %	Mean prom.[e]	
Logistical barriers	79.6	75.7	68.0	3.59	73.1	66.7	58.1	3.14	
Competing obligations/priorities	76.7	73.8	55.3	3.17	72.0	64.5	43.0	2.66	
Lacking information about campaign	20.4	8.7	11.7	0.64	39.8	10.8	12.9	0.89	*
Vaccination post open days/hours limited	8.7	4.9	1.0	0.17	19.4	1.1	2.2	0.27	*
Costs apart from vaccine	2.9	0.0	0.0	0.03	4.3	1.1	0.0	0.05	
Organizational problems at vaccination post	0.0	0.0	0.0	0.00	1.1	0.0	0.0	0.01	
Medical barriers	27.2	22.3	23.3	1.19	35.5	24.7	23.7	1.31	
I was sick (not due to vaccine)	15.5	15.5	14.6	0.75	12.9	12.9	11.8	0.61	
Fear of possible side effects from vaccine	10.7	4.9	5.8	0.33	20.4	7.5	5.4	0.44	
Doubted effectiveness of vaccine	5.8	3.9	2.9	0.18	12.9	7.5	6.5	0.40	
Social/system-related barriers	8.7	2.9	1.0	0.15	16.1	5.4	6.5	0.41	
Vaccine free of charge (useless medicine)	1.9	1.0	0.0	0.03	9.7	4.3	2.2	0.20	*
Fear of infertility	1.9	0.0	0.0	0.02	4.3	0.0	3.2	0.14	
Mistrust motives of campaign	1.9	1.0	0.0	0.03	8.6	3.2	0.0	0.12	*
Social pressure against taking vaccine	3.9	1.9	1.0	0.09	2.2	0.0	0.0	0.02	
Lacking confidence in government	0.0	0.0	0.0	0.00	5.4	2.2	1.1	0.11	*
Prior bad experience with health system	0.0	0.0	0.0	0.00	1.1	0.0	0.0	0.01	
Miscellaneous	6.8	6.8	5.8	0.31	10.8	10.8	7.5	0.44	
Other barriers	5.8	5.8	4.9	0.26	8.6	8.6	6.5	0.37	
Cannot say/Nothing	1.0	1.0	1.0	0.05	2.2	2.2	1.1	0.08	

[a]Barriers ordered according to descending mean prominence for the pooled sample (see Table 6-3), grouped barriers in bold; [b]Percentage of barriers reported spontaneously and after probing; [c]Percentage of barriers reported spontaneously only; [d]Percentage of barriers that were identified as single most important among all the reported barriers; [e]Mean prominence based on values assigned for each barrier (3=identified as most important, 2=reported spontaneously, 1=reported after probing, 0=not reported), *p<0.05 (Wilcoxon test for comparison of mean prominence between site)

Four more barriers were more prominent in the rural area: *limited open days/hours of vaccination post* (p=0.045), *vaccine free of charge is useless* (p=0.020), *mistrust motives of the campaign* (p=0.037) and *lacking confidence in government* (p=0.019). Three out of these five rural barriers were also reported with more prominence by men (in the total sub-sample): *Limited open days/hours of vaccination post* (p=0.032), *vaccine free of charge is useless* (p=0.008) and *lacking confidence in government* (p=0.030).

The analysis of grouped categories showed that men reported significantly more logistical, social and system-related barriers than women (Table 6-5). Narratives indicated that men had their business or were committed to fishing and farming and mostly away during the daytime or for months. These commitments limited access to vaccination posts because open hours were too limited or because the duration of the campaign itself was not long enough. Even though women reported fewer such problems, they also explained their absence as being too busy with work and thus unable to reach the posts in time. Mostly rural men, compared to only one woman

from the periurban site, complained about why the vaccine was offered free of charge despite the fact that other drugs require purchase. This and the finding that only rural men were not confident about the government's intentions is illustrated by the account of a 40-year-old man from Pemba:

> "I did not drink the medicine because I felt it does not help and drugs are not given free. Also when they give it to you free of charge there is some reason for doing that."

Table 6-5: Barriers to uptake of an oral cholera vaccine in a community mass vaccination campaign in Zanzibar, stratified by gender

	Women, n=95 How reported?				Men, n=101 How reported?				
Barriers to uptake[a]	Total[b] %	Spon.[c] %	Most important[d] %	Mean prom.[e]	Total[b] %	Spon.[c] %	Most important[d] %	Mean prom.[e]	
Logistical barriers	66.3	62.1	56.8	2.99	86.1	80.2	69.3	3.74	*
Competing obligations/priorities	65.3	61.1	47.4	2.68	83.2	77.2	51.5	3.15	
Lacking information about campaign	26.3	7.4	8.4	0.59	32.7	11.9	15.8	0.92	
Vaccination post open days/hours limited	8.4	1.1	1.1	0.13	18.8	5.0	2.0	0.30	*
Costs apart from vaccine	2.1	0.0	0.0	0.02	5.0	1.0	0.0	0.06	
Organizational problems at vaccination post	0.0	0.0	0.0	0.00	1.0	0.0	0.0	0.01	
Medical barriers	38.9	32.6	32.6	1.69	23.8	14.9	14.9	0.83	**
I was sick (not due to vaccine)	26.3	26.3	24.2	1.25	3.0	3.0	3.0	0.15	***
Fear of possible side effects from vaccine	15.8	6.3	5.3	0.38	14.9	5.9	5.9	0.39	
Doubted effectiveness of vaccine	5.3	3.2	3.2	0.18	12.9	7.9	5.9	0.39	
Social/system-related barriers	7.4	0.0	1.1	0.11	16.8	7.9	5.9	0.43	*
Vaccine free of charge (useless medicine)	1.1	0.0	0.0	0.01	9.9	5.0	2.0	0.21	**
Fear of infertility	2.1	0.0	1.1	0.05	4.0	0.0	2.0	0.10	
Mistrust motives of campaign	2.1	0.0	0.0	0.02	7.9	4.0	0.0	0.12	
Social pressure against taking vaccine	3.2	0.0	0.0	0.03	3.0	2.0	1.0	0.08	
Lacking confidence in government	0.0	0.0	0.0	0.00	5.0	2.0	1.0	0.10	*
Prior bad experience with health system	0.0	0.0	0.0	0.00	1.0	0.0	0.0	0.01	
Miscellaneous	9.5	9.5	7.4	0.41	7.9	7.9	5.9	0.34	
Other barriers	8.4	8.4	6.3	0.36	5.9	5.9	5.0	0.27	
Cannot say/Nothing	1.1	1.1	1.1	0.05	2.0	2.0	1.0	0.07	

[a]Barriers ordered according to descending mean prominence for the pooled sample (see Table 6-3), grouped barriers in bold; [b]Percentage of barriers reported spontaneously and after probing; [c]Percentage of barriers reported spontaneously only; [d]Percentage of barriers that were identified as single most important among all the reported barriers; [e]Mean prominence based on values assigned for each barrier (3=identified as most important, 2=reported spontaneously, 1=reported after probing, 0=not reported), *p<0.05, **p<0.01, ***p<0.001 (Wilcoxon test for comparison of mean prominence between gender)

Sickness was equally prominent in both sites, but the majority who reported this barrier were women (26.3% vs. 3.0%, p<0.001). Qualitative data showed that many of those women had actually been eager to receive the vaccine, but could not because of troubling symptoms or because they were afraid that the vaccine could make their present condition worse. A 30-year-old housewife from Chumbuni explained why she could not take the vaccine because of her severe fever:

> "I came home during the vaccination days but I had severe fever and I left soon after the campaign. While I was there I heard an announcement about the vaccination on the radio. But because of my condition—I was still sick—I was unable to come and take the vaccine."

Three men only reported sickness, but identified it as the most important barrier; they exclusively referred to a perceived harmful interaction between drugs and the OCV:

> "I was sick with severe fever. And they told me it was [high blood] pressure. I was using many drugs and therefore I was told not to mix drugs because of harmful effects." (50-year-old farmer in Mwambe)

Since the majority of respondents (76.5%) had missed the vaccination due to logistical constraints (Table 6-3), further analysis of their views was deemed necessary. At the end of the interview, respondents were encouraged to share any additional comments, advice or suggestions about the health problems and vaccines that had been discussed or needed to be emphasized. Based on the assumption that these respondents did not object to receiving the OCV in principle, thematic analysis of their concluding statements was done.

Most of the respondents who missed the complete course of vaccination because of logistical barriers requested the government repeat the vaccination to make them fully immunized and to vaccinate those people who did not get the vaccine during the campaign. They also emphasized the need to make the vaccine available free of charge and frequently demanded more health education in the communities. Even though men reported logistical barriers more prominently (Table 6-5), themes identified in male and female narratives were very similar. A businessman from Chumbuni, aged 28 years, gave the following advice:

> "I would like to advise the Ministry of Health and Social Welfare to provide free vaccines. They should also sensitize the community by providing health education. This will make the community aware of the importance of vaccines."

A female student from Mwambe, aged 18 years, also suggested how to improve the campaign:

> "The vaccination should be repeated so that I can also make it. But I suggest that we should be better informed about the real date of the second dose."

6.4 Discussion

This postvaccination survey clarified social and cultural factors of uptake of an oral cholera vaccine in a periurban and a rural community of Zanzibar. Sociocultural features of cholera-like

illness and sociodemographic factors were identified, and logistical, medical and social and system-related barriers were examined among unvaccinated community residents.

6.4.1 Influence of social and cultural factors on uptake

Compared to the prevaccination analysis of determinants of OCV uptake where nonspecific symptoms of cholera determined uptake negatively, rectal pain was positively associated with OCV uptake in this survey. Even though cholera-related purging is usually painless [4], this finding may indicate a priority for vaccines not only for cholera but also for severe diarrhea in general. Features of dehydration were identified as promoting factors for vaccination in both pre- and postvaccination surveys. However, while unconsciousness determined uptake positively in the prevaccination study in both sites, reporting a loose or shriveled skin influenced only rural respondents to take the OCV.

Recognizing biomedical risk factors for cholera, i.e., the potential risk for infection with germs when leaving food uncovered or when coming into contact with contaminated water, prompted respondents to take the OCV. This may reflect the positive impact of the mass vaccination campaign on people's ideas and behavior. Neither biomedical nor alternative factors that had been perceived to cause cholera were identified as determinants of OCV uptake in the prevaccination survey.

Despite offering the OCV for free and despite no significant direct costs were likely to be incurred in accessing the vaccination posts, purchasing drugs to stop vomiting and diarrhea in pharmacies competed with vaccines. This finding may indicate that the idea of treating cholera with drugs seemed to be more attractive than prevention with vaccination, or that the appeal of well-known powerful antibiotics was so valued that they overrode vaccination as a new and more uncertain intervention for cholera in Zanzibar.

Reporting a previous enteric illness episode at the rural site was positively associated with uptake. This confirms results from a study in Vietnam [11], but contrasts the prevaccination study in Zanzibar, where reporting of such episodes did not determine vaccine uptake. This finding nevertheless suggests a higher perceived need for vaccination in the rural area, which is supported by the higher OCV uptake among rural respondents and the finding from the prevaccination study that fear of disruptions of health care services during cholera outbreaks was a positive determinant of OCV uptake in the rural area. Consistent with the prevaccination study is the finding that older people were more likely to drink the OCV. A higher household size, which had made people less willing to pay for an OCV before the campaign, was positively

associated with uptake; this might demonstrate the higher perceived need for vaccines if no costs are attached to it.

6.4.2 Assessment of barriers to uptake

Logistical issues were paramount barriers against taking the vaccine. Issues around social pressure or mistrust in the government or the vaccine, which have been identified as major factors against cholera control [40] or vaccination in other developing countries [17,41], did influence campaign coverage in Zanzibar only slightly. The importance of logistical issues confirms findings from a mass vaccination campaign in the cholera-endemic city of Beira, Mozambique, where main reason against OCV uptake were traveling (mentioned by 58% of non-acceptors) and being busy (26%), while the rest reported pregnancy (5.2%), refusal (3.7%), long waiting time (3.1%) and taking medication (2.6%) [8].

People's own busy daily schedules and obligations, which made it also less likely for them to receive timely information about the planned mass vaccination campaign, were limiting factors to receive vaccines. Qualitative data clearly indicate that those residents who had been away during the campaign still wished to receive the vaccine. Thus, it can be expected that an earlier start of the mobilization—media broadcasts and meetings with community leaders started only shortly before the campaign in January 2009—is likely to increase coverage because people would have more time to plan their activities around the campaign. Alternative ways to administer the vaccine may have to be considered as well to better reach those population groups that are in principal willing to get vaccinated but whose daily schedules or professional activities make it difficult to receive vaccines.

Fears about possible side effects were a substantive barrier to uptake; this needs to be addressed in future campaigns. The usually mild and transient side effects of Dukoral® (or other OCVs) [7,36] should be explained more properly versus the benefit of protection against cholera. Such information may also re-emphasize that the vaccine is administered orally and not through injections.

Rumors about sterility have been reported in many immunization campaigns in Africa [42]. However, contrary to studies reporting that Muslims believe vaccines might cause infertility or could have been adulterated with anti-fertility agents [41-43], issues around fertility were not an important barrier to vaccine uptake. This suggests that future cholera campaigns in Zanzibar are somewhat less likely to suffer from such potentially sensitive issues.

The site and gender analysis of barriers to uptake showed that logistical challenges to access vaccination posts, and a tendency to question the value of vaccination against cholera, were primarily prominent among rural men. Despite differing logistical challenges, a clear demand for OCVs or a repetition of the mass vaccination campaign was reported among both genders, highlighting the local priority and demand for vaccination for cholera control in endemic areas of Zanzibar. Because sickness prevented more than one-fourth of women (regardless of site) from accessing posts or accepting the vaccine, further study may be needed to examine whether women are in general more often sick than men in Zanzibar, or whether this gender difference occurred by chance.

Study limitations may include a potential selection bias because respondents were chosen from only two instead of all the six villages of the mass vaccination campaign. It should also be borne in mind that this was a cross-sectional survey, where only associations and no causal relationships could be examined.

6.4.3 Lessons learned and recommendations

Despite a high willingness to receive free vaccines, coverage was less than satisfying in the 2009 oral cholera mass vaccination campaign in Zanzibar. Complementing a prevaccination community survey that identified predisposing social and cultural factors as determinants of OCV uptake, this postvaccination survey examined which social and cultural factors were associated with uptake and assessed barriers to uptake among unvaccinated community residents.

Factors associated with uptake indicated a positive impact of the mass vaccination campaign and of community sensitization activities on vaccine acceptance behavior. Unlike in other circumstances, where communities opposed cholera control or where public trust of vaccines was damaged, the evaluation of barriers to uptake also indicated a good implementation of the mass vaccination campaign and trust in the health system.

High community awareness of cholera and a positive attitude towards receiving OCVs, especially if they are provided without charge, suggest little opposition to vaccination as a supplementary means to cholera control in Zanzibar. Despite such encouraging prospects and demand for repeating vaccination in cholera-endemic populations, local policy makers and public health officials still need to know how community coverage of mass campaigns could be improved. Even though the following recommendations are in principle limited to cholera-endemic communities in Zanzibar, national and international cholera control experts may also benefit from them.

First, campaigns should be announced earlier, at least a few months before vaccination posts open, with repeated reminders in the target communities. Second, campaign planners may also consider an extension of daily open hours or numbers of days for the vaccination especially in rural areas. Third, information about the campaign should not only cover dates and venues, specific requirements and inclusion criteria, but, fourth, also reinforce again more general health education on hygiene and diarrhea to interrupt fecal-oral transmission and, fifth, particularly point out the value of vaccination versus treatment of cholera with antibiotics. Sixth, although side effects of OCVs are usually mild, they should not only be specified, but also explained versus the benefit of vaccination. Finally, identification of alternative solutions to mass vaccination campaigns may be needed for population groups that recognize the value of vaccination in principal but are harder to reach due to their daily or professional activities.

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PART II

COST-EFFECTIVENESS OF AN ORAL CHOLERA MASS VACCINATION CAMPAIGN IN ZANZIBAR

7

COSTS OF ILLNESS DUE TO CHOLERA, COSTS OF IMMUNIZATION AND COST-EFFECTIVENESS OF AN ORAL CHOLERA MASS VACCINATION CAMPAIGN IN ZANZIBAR*

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Abstract

Background

Despite efforts to improve water supply and sanitation, cholera still represents a serious public health burden in low- and middle-income countries. The World Health Organization (WHO) recommends oral cholera vaccines (OCVs) as a supplementary public health tool to conventional prevention and treatment in endemic and epidemic settings. Dukoral®, a killed whole-cell two-dose OCV was used in a mass vaccination campaign in 2009 in Zanzibar. This study estimated public and private costs of illness (COI) due to endemic cholera and costs of the 2009 mass vaccination campaign to assess the cost-effectiveness (CE) of OCVs in Zanzibar from both the health care provider and the societal perspective.

Methodology/Principal Findings

Estimates for public COI were obtained from interviews with local experts and patients and from reports and record review. Cost data for the mass vaccination campaign were collected based on real expenditure and planned budget data. Private direct and indirect costs were collected through patient interviews from three outbreaks. A static cohort of 50,000 individuals was examined. Primary outcome measures were incremental cost-effectiveness ratios (ICERs) per death, per case and per disability-adjusted life-year (DALY) averted. One-way sensitivity and threshold analyses were conducted and the ICER evaluated with regard to widely used WHO criteria for CE. Base-case ICERs were USD 1,878,142 per death averted, USD 16,171 per case averted and USD 119,339 per DALY averted, with negligible differences between the health care provider and the societal perspective. Threshold analyses using Shanchol™, the second OCV that is currently prequalified by the WHO for public use, indicated that the purchase price per course would have to be as low as USD 1.10 to render the mass vaccination campaign cost-effective from a health care provider perspective (or USD 1.15 from a societal perspective).

Conclusions/Significance

The 2009 mass oral cholera vaccination campaign with Dukoral® was not cost-effective mainly due to the expensive OCV and the low incidence. However, mass vaccination campaigns in Zanzibar to control endemic cholera may meet WHO criteria for CE under certain circumstances, especially in high-incidence areas and when OCV prices are reduced to levels at USD 1.10 to 1.15.

7.1 Introduction

Despite efforts to improve water supply and sanitation, cholera still represents a serious public health burden in low- and middle-income countries. In 2009, more than 220,000 cases and almost 5,000 deaths were reported to the World Health Organization (WHO) [1]. Due to underreporting and difficulties with surveillance, however, the true burden is likely to exceed 3 million cases and 100,000 deaths per year [2]. A recent review of official cholera-related morbidity and mortality data from the WHO Africa region also indicated a potential economic burden of cholera for families and the health sector [3].

Cholera is an enteric bacterial disease caused by *Vibrio cholerae* serogroup O1 or O139 that usually occurs in sudden epidemics. Main features include acute, profuse watery diarrhea and vomiting that may lead to dehydration with concurrent electrolyte loss and eventually death if timely treatment is unavailable. Even though case-fatality rates (CFRs) may reach 50%, a rate below 1% has been realistic with proper case management [2,4]. Treatment is based on prompt rehydration with oral rehydration solution (ORS) for mild to moderate cases and intravenous (IV) fluids for severe cases [2]. Antibiotics are recommended for severe, and also moderate cases, to reduce the duration of episodes and shedding of infectious *V. cholerae* [2,5].

Traditionally, cholera control has been based on prevention, i.e., adequate water supply, improved sanitation and health education, and timely treatment. The role of vaccination for cholera control has recently received increased attention from public health officials; the WHO recommends oral cholera vaccines (OCVs) as a supplementary public health tool to traditional prevention and treatment in endemic and epidemic settings [6].

A series of research studies, done as part of the Diseases of the Most Impoverished (DOMI) project coordinated by the International Vaccine Institute (IVI), evaluated the use of OCVs in Asia and Africa for control of endemic cholera. Private demand for cholera vaccines was examined through willingness-to-pay studies [7-10], costs of illness (COI) and mass vaccination data were collected [11-13], and cost-effectiveness and cost-benefit analyses were performed [14,15]. Besides the recent article by Poulos *et al*. [12], published information about COI due to cholera is lacking even though patient-level data is needed for economic evaluations to improve local planning of cholera control.

A joint initiative between the WHO, the IVI and the Ministry of Health and Social Welfare of Zanzibar (MoHSW) implemented a mass vaccination campaign with an OCV in two selected

cholera-endemic areas of Zanzibar in 2009. This intervention-cum-research project provided the opportunity to assess costs of immunization in an endemic setting. Public COI were estimated from three outbreaks that happened in 2009 outside the mass vaccination target communities. Private direct and indirect COI (borne by patients and their families) were elicited from a sample of patients admitted to cholera treatment centers during these outbreaks.

This study aims to estimate (i) public and private COI due to cholera, (ii) costs of an oral cholera mass vaccination campaign, and (iii) the cost-effectiveness (CE) of using OCVs in endemic regions of Zanzibar from a health care provider and a societal perspective.

7.2 Methods

7.2.1 Study setting

Zanzibar consists of two major islands, Unguja (also named Zanzibar) and Pemba, which are situated in the Indian Ocean about 40-60 km off the coast of Tanzania. Zanzibar, a semiautonomous entity within the United Republic of Tanzania, consists of five regions, which are subdivided into ten districts, 50 constituencies and 296 Shehias, the latter being the smallest administrative unit. The main islands cover ~2,557 km² (Unguja: ~1,651 km², Pemba ~906 km²). The archipelago is inhabited by a fast-growing population of ~1.2 million Kiswahili-speaking Muslim people. Monthly mean per capita expenditure for all goods and services was TZS 21,000 (~USD 18) in 2004/5 with a 2.1% share for health-related expenditures [16]. Life expectancy at birth has risen from 47 years in 1988 to 57 years in 2002 [17]. The economy of the islands depends on agriculture (primarily cloves, coconuts/copra and seaweed), fishing and tourism.

The public health care delivery structure in Zanzibar comprises two zones, Unguja and Pemba, each with three levels: the primary, the secondary and the tertiary level. Each zone is headed by a zonal medical officer. Most of the health care services are provided at the primary level through Primary Health Care Units (PHCU) (n=124). The majority of these units is open during the day to outpatients and provides basic services. Primary Health Care Centers (PHCC) (n=4) are additional facilities on the primary level; they operate on a 24-hours basis and can admit up to 30 patients. At the secondary level, three district hospitals (only in Pemba) are operational while the country's only tertiary level hospital (Mnazi Mmoja) is located in the capital Stonetown in Unguja. The top causes of primary- and secondary-level outpatient visits in 2008 were upper respiratory tract infections (23%), pneumonia (10%), malaria (10%) and diarrhea (9%) [18].

In recent times, the first cholera outbreak with 411 cases and 51 deaths was reported in 1978 from two fishermen villages in Zanzibar [19]. More than a dozen outbreaks followed since then with almost annual episodes since the year 2000. Reyburn *et al*. reported an annual incidence of 0.5 cases per 1,000 population based on a review of routine surveillance data for the years 1997 to 2007 [20]. A seasonal pattern can be observed that follows the rainy seasons (usually from March to June and from October to December) during which widespread flooding occurs. Such deteriorating environmental conditions subsequently expose the majority of inhabitants on both islands to an increased risk of waterborne diseases due to the scarcity of safe drinking water supplies and a generally poor or lacking sanitation infrastructure in periurban and rural areas.

Based on a consideration of areas of recent cholera activity, three Shehias per island, adjacent to each other, were selected as sites for the mass vaccination campaign. In Unguja, the Shehias of Chumbuni and Karakana in Urban district and Mtopepo in West district were targeted for the campaign; in Pemba, the Shehias of Kengeja, Mwambe and Shamiani, all located in the rural southeastern Mkoani district, were chosen.

Dukoral®, the only OCV that was prequalified by the WHO in 2009, was used in the mass vaccination campaign. Dukoral® is a *V. cholerae* serogroup O1 whole-cell, killed vaccine containing recombinant cholera toxin (CT) B subunit protein; it has to be administered in two doses at least one week apart and requires a cold chain (2-8°C) [21]. This OCV was originally designed for immunologically naïve travelers from the north to tropical countries; it is licensed for use from two years of age and above and was shown to be 60-90% protective for up to three years [22-24]. One 3-ml vial of Dukoral® contains $1x10^{11}$ killed *V. cholerae* O1 (biotype classical and El Tor) and 1 mg of the CT B subunit protein in a suspension. Because the CT B subunit protein is not gastric acid-fast, the suspension has to be mixed with 1.5 dl of drinking water and a buffer sachet containing effervescent granules of sodium bicarbonate for ingestion. Recipients need to fast one hour before and after ingestion.

7.2.2 Cost data collection

Table 7-1 describes cost components (and sources) of data collected for this study. Estimates for public COI were obtained from interviews with local experts and patients and from reports and record review. Cost data for the mass vaccination campaign were collected based on real expenditure and planned budget data. Private direct and indirect costs were collected through patient interviews done on Pemba. All costs are reported in 2009 USD from an economic perspective, based on mid-year exchange rates obtained from http://www.oanda.com.

Table 7-1: Cost components for cholera collected in Zanzibar, 2009

Cost components	Description	Source
Public COI		
Fixed costs	CTC set up and running including top up payments and personnel opportunity costs	Questionnaire for zonal and district medical officers, MoHSW, NGOs, reports, record review
Variable costs	Treatment costs including drugs and material	Interview with laboratory-confirmed cases and health care personnel, questionnaire for zonal and district medical officers, chief pharmacist, NGOs
Private COI		
Direct	Medical, non-medical costs	Interview with laboratory-confirmed cases
Indirect	Loss of income	Interview with laboratory-confirmed cases
Mass vaccination campaign costs		
Material	Purchase, transport and storage of vaccine, water and cups	Reports and documents from WHO HQ, WHO consultants, EPI
WHO consultants	Compensation, travel	Communication from WHO HQ
Training of vaccinators and social mobilizers	Staff compensation, transport, material, refreshment, venue	Reports and documents from WHO consultants, EPI
Implementation	Staff compensation, transport, material, communication	Reports and documents from WHO consultants, EPI

COI: Costs of illness, CTC: Cholera treatment center, MoHSW: Ministry of Health and Social Welfare of Zanzibar, NGO: Non-governmental organization, WHO HQ: World Health Organization headquarters, EPI: Expanded program on immunization in Zanzibar

Public COI

Usually, cholera treatment centers (CTCs) are set up in Zanzibar once a cholera outbreak has been declared. Any person with acute watery diarrhea will be admitted and treated with IV fluids (Ringer's lactate, Hartmann's solution) and/or ORS, antibiotics and other drugs (Zinc for children) depending on the dehydration level. Community help-seeking behavior for cholera in peri-urban and rural Zanzibar also favors professional treatment in public health care facilities [25]. Thus, assuming that the majority of cases that occur during outbreaks are treated in CTCs, this study collected treatment costs incurred at CTCs to estimate public COI.

Public COI data from three outbreaks (one from Unguja and two from Pemba) that happened after the mass vaccination campaign were collected prospectively and retrospectively from local health care personnel and experts. All three centers were visited for an overview of how they were set up and being run. Fixed COI related to set up and running of centers, but considered independent of the number of cholera cases, included permanent material, consumables, transportation and personnel, i.e., extra payments for personnel and opportunity costs due to personnel diverted from other health services. Variable COI incurred for cholera cases included drugs (resource use obtained from patient interviews) and material used for patient treatment. Current unit costs for drugs and material were provided by the chief pharmacist and the medical store department.

In Unguja, a CTC was opened on September 22, 2009, in PHCU Chumbuni after a cholera outbreak had been declared in one of the districts where the mass vaccination was conducted. A total of 161 patients were admitted over the course of 63 days before the CTC was closed on November, 29, 2009. Patients were treated in military tents (at the beginning of the outbreak) and in premises belonging to the PHCU. During the period while the CTC was operational, only suspected cholera cases were treated; patients with other illnesses were sent to adjacent clinics.

The first outbreak on Pemba occurred in Wete district, which is located between Micheweni district in the north and the Pemban capital Chake-Chake in the center of the island; the PHCU in Kiuyu Minungwini was turned into a CTC during 88 days from May 11 until August 7, 2009, when 88 patients were admitted and treated. The second outbreak on Pemba happened in Micheweni district in the northeast of the island. A school adjacent to PHCC Micheweni was turned into a CTC with male and female and pediatric wards. This center was first open from June 18 until August 11, 2009, to admit 349 patients over the course of 54 days. After another surge in cholera cases, the center was reopened on August 30, 2009, and run for an additional 31 days to treat another 32 patients until it was closed on September 30, 2009.

Private COI

Private COI data were collected with questionnaires from laboratory-confirmed cholera patients. A convenience sample of ~100 respondents was selected based on a list of positive cases from outbreaks kept at the Public Health Laboratory (PHL) in Chake-Chake, Pemba. Health care providers were then contacted at the respective CTC where the patients had been admitted to confirm details and to contact the patient or the caregiver for an interview.

Based on WHO guidelines [26], a questionnaire was constructed in an adult and a child version to elicit out-of-pocket costs for cholera cases borne by patients and affected households. After pretesting, the questionnaire was administered in face-to-face interviews to inquire about direct medical and non-medical costs and indirect costs, i.e., productivity losses to the patient or caregiver and other household members. Patients aged 18 years or older were directly interviewed while caregivers were interviewed if the patient was younger than 18 years. Questionnaires were administered between July and November 2009, predominantly at respondents' homes. Questionnaire data were entered into Microsoft Excel for analysis.

Mass vaccination campaign costs

The mass vaccination campaign with Dukoral® was implemented in the six selected Shehias in two rounds from January 17 to 26, 2009, and from February 7 to 16, 2009. Vaccination posts were erected within easy reach for the targeted population. Posts were run by local health care

workers and villagers and open daily for at least eight hours. For each round, a total of 21 teams were needed to run the nine vaccination posts on each island. Each team consisted of six vaccinators. In addition, eight supervisors were deployed to Unguja and five to Pemba. The campaign was planned and implemented by the local Expanded Program on Immunization (EPI) team and international consultants deployed by the WHO. Social mobilization was done before and during both rounds by the MoHSW Health Promotion Unit.

Cost data on material (purchase, transport and storage of vaccines, cups and water), training and implementation required for the campaign were obtained locally from consultants and EPI. Because the campaign was planned and implemented within the scope of the research project, raw data were adjusted to exclude costs related to research. These costs were mostly incurred to train and compensate people at vaccination posts collecting data with electronic devices for parallel and subsequent epidemiological studies [27].

7.2.3 Cost-effectiveness analysis

Based on a previous study for Bangladesh [28], a model was developed in Microsoft Excel to estimate the costs and health effects of a mass vaccination campaign program compared to standard treatment in CTCs in Zanzibar. A static cohort of 50,000 individuals, reflecting the target population of the 2009 mass vaccination campaign in Zanzibar, was examined from a health care provider and a societal perspective considering input parameters related to vaccine characteristics and vaccination costs, burden and impact of cholera, and public and private COI. Private providers were not considered since the majority of patients would visit public facilities in case of an outbreak [25]. The base-case model considered costs and effects of a one-time vaccination program over the duration of protection, i.e., three years. Annual number of cases without vaccination was obtained by multiplying the population size times the mean annual cholera incidence obtained from a review of cases per Shehia. The number of annual deaths was calculated by multiplying the CFR with the annual number of cases. The annual number of cases under the vaccination program was calculated by multiplying the annual number of cases without vaccination with (1 – protective efficacy). The number of deaths with vaccination was calculated similarly by using the same CFR.

Incremental cost-effectiveness ratios (ICER) calculated as incremental costs per death, per case and per disability-adjusted life-year (DALY) averted were used as outcome measures. Incremental costs were calculated as the difference between costs of the vaccination program and public COI saved due to the vaccination from the health care provider perspective. Private direct COI saved were added in the base-case model adopting the societal perspective. Private indirect COI saved were not included in the base-case model [29]. The number of deaths, cases

or DALYs averted was equal to the difference in numbers with and without the vaccination program. DALYs, which are an aggregate measure combining morbidity (i.e., years of life lived with disability) and mortality (years of life lost), were calculated according to Jeuland *et al.* [14], assuming no age weighing and a disability weight of 0.105 for diarrheal diseases [30]. Life expectancy at average age of onset based on patient data was obtained from WHO life tables for Tanzania [31]. The vaccine was directly purchased from the manufacturer at a UN rate. Future effects were discounted at a rate of 3% for the base case. Costs were not discounted since the mass campaign happened over one single year.

Cost-effectiveness was examined according to widely-used WHO criteria that define an intervention as *cost-effective* if the ICER is less than three times per capita gross domestic product (GDP) per DALY averted and as *highly cost-effective* if the ICER is less than per capita GDP per DALY averted [32].

One-way sensitivity analyses were done to estimate the influence of changes in potentially influential input parameters on model outcomes. Such key parameters included vaccine purchase price and delivery costs, protective efficacy (PE), duration of protection, incidence, CFR and so forth [14]. Plausible ranges were based on public health considerations (for vaccine purchase price and delivery costs, incidence), guidelines (discount rate) and variation for local data (PE, CFR, coverage, number of ill days, public and private COI). Base-case values and plausible ranges are presented in Table 7-2. Threshold analyses examined at which vaccine purchase price the intervention would become cost-effective.

Table 7-2: Model input parameters with plausible ranges

Parameters	Base case	Minimum	Maximum	Assumptions, References
Vaccine costs and characteristics				
Vaccine purchase price, 2009 USD per 2 doses	10.28	2.06	12.34	Base case: this study; range: 20-120% of base case based on policymaker and expert data [33,34]
Vaccine delivery, 2009 USD per 2 doses [a]	2.66	1.06	3.19	Base case: this study; range: from USD 0.5 per dose to 120% of base case [14,34]
Protective efficacy of vaccine, %	77.0	30.0	93.0	Base case and range (95% CI): this study (Khatib *et al.*, unpublished manuscript)
Campaign coverage, %	57.9	53.5	66.8	Base case: this study; range: minimum and maximum among the 6 targeted Shehias
Duration of protection, years	3	2	4	Jeuland *et al.* [14]
Discount rate, %	3	0	5	Constant, for effects [35], no discounting of costs
Life expectancy at average age of onset, years	44.9	36.4	55.5	Life tables for WHO member states [31]; base case: based on mean age of onset (18 years) from patient data; range: based on life expectancy [31] at IQR of age of onset from patient data
Risk for cholera				
Cholera incidence, annual cases/1,000 population	0.65	0.5	4.0	Base case: mean from review of surveillance reports from Unguja for 2002-2010; range: minimum (Beira), maximum (Jakarta) (Deen *et al.* [36])
Impact of illness on patients				
Case-fatality rate, %	0.86	0.52	1.86	Base case: 14 deaths/1626 cases treated in CTCs in Unguja and Pemba during three outbreaks between June 2009 and April 2010; range: minimum and maximum (ZMO Unguja); same rate assumed for vaccinated and unvaccinated cases
Duration of illness episode, days	5	4	6	Base case: median illness duration from patient data; range: IQR from patient data
Costs of illness, 2009 USD				
Public fixed costs of treatment per episode	51.41	20.64	88.00	Base case: mean from this study (seeTable 7-3); range: minimum and maximum from this study (see Table 7-3)
Public variable costs of treatment per episode	9.15	4.57	18.29	Base case: mean from this study (see Table 7-3); range: 50-200% of base case [14]
Private direct costs per episode[b]	11.39	4.23	16.50	Base case: mean from this study (see Table 7-4); range: based on IQR from patient data
Private indirect costs per episode[b]	31.46	4.44	46.32	Base case: mean from this study (see Table 7-4); range: based on IQR from patient data

[a]Excluding costs for international consultants (see Table 7-5); [b]Estimates only used in analysis from societal perspective; CI: Confidence intervals, IQR: Interquartile range, ZMO: Zonal medical officer

7.2.4 Ethics

Written informed consent was obtained from all study participants interviewed for private COI. No incentives were provided to them. The protocol of this study was cleared by the WHO Research Ethics Review Committee and the MoHSW Ethics Committee. All data were handled confidentially and made anonymous before analysis.

7.3 Results

7.3.1 Public COI

Table 7-3 presents the fixed and variable mean public COI at the three CTC sites. Fixed costs of USD 51.41 accounted for 84.9% of public COI, with mean fixed costs ranging from USD 20.64 to USD 88.00. Direct and indirect human resources costs accounted for the majority of fixed costs; they were highest in Kiuyu Minungwini (86.3%), medium in Micheweni (84.9%) and lowest in Chumbuni (80.0%). The remaining fixed costs were used for setting up and running the centers. Health care personnel working in Unguja received higher top up payments than in Pemba, but the latter were given food to cater for themselves while on shift. Variable costs of USD 9.15 were mainly driven by IV fluid use as patients were administered on average 8.8 liters, which cost USD 7.08. Further details on public variable costs for treatment can be found as supporting information in Table 9-1.

Table 7-3: Public costs of illness for cholera, Zanzibar, 2009

	Description	2009 USD	%
Fixed costs[a]		51.41	84.9
CTC at PHCU Chumbuni (Unguja)		88.00	100.0
Permanent material	*Beds, canvas, ropes, basins, buckets, further utensils*	*6.37*	*7.2*
Consumables	*Water, detergent, kerosene*	*2.54*	*2.9*
Transport	*Fuel for DHMT cars*	*8.67*	*9.9*
Personnel	*Top up payments*	*27.28*	*31.0*
Personnel diverted from other health care services	*Opportunity costs based on functions and official salaries*	*43.13*	*49.0*
CTC at PHCC Micheweni (Pemba)		20.64	100.0
Permanent material	*Water drum*	*0.01*	*0.0*
Consumables	*Detergent, kerosene*	*1.15*	*5.6*
Transport	*Fuel for DHMT cars*	*1.94*	*9.4*
Personnel	*Top up payments and food allowance*	*6.01*	*29.1*
Personnel diverted from other health care services	*Opportunity costs based on functions and official salaries*	*11.52*	*55.8*
CTC at PHCU Kiuyu Minungwini (Pemba)		45.59	100.0
Permanent material	*Water tank, cooking utensils etc*	*1.88*	*4.1*
Consumables	*Chlorinated lime*	*1.71*	*3.8*
Transport	*Car use*	*2.64*	*5.8*
Personnel	*Top up payments and food allowance*	*13.46*	*29.5*
Personnel diverted from other health care services	*Opportunity costs based on functions and official salaries*	*25.89*	*56.8*
Variable costs[b]		9.15	15.1
Total		60.56	100.0

[a]Mean costs per treated patient at each CTC; [b]Mean costs per treated patient from patient interviews (n=95), including drugs and material, see supporting information (Table 9-1) for more details; CTC: Cholera treatment center, PHCU: Primary health care unit, PHCC: Primary health care center, DHMT: District health management team

7.3.2 Private COI

A total of 95 individuals were interviewed. All but one of the interviewed patients had been admitted at the CTC at Micheweni PHCC. Total direct and indirect mean private COI amounted to USD 42.85, with almost three-fourth (USD 31.46) being indirect costs, i.e., productivity losses to the patient or caregiver and other household members (Table 7-4). Among direct costs, which amounted to USD 11.39, feeding the patient at the CTC accounted for the biggest share (USD 8.29, 19.4% of total costs). Other direct costs, incurred for treatment (mainly for plastic sheets needed to cover cots), transport and communication, were reported by less than 3%.

Table 7-4: Private direct and indirect costs of illness for cholera, Zanzibar, 2009

	2009 USD*		%
Direct costs	11.39	(9.13)	26.6
Medical	1.21	(1.6)	2.8
Food	8.29	(6.64)	19.4
Transport	1.23	(2.66)	2.9
Communication	0.65	(1.36)	1.5
Indirect costs (i.e., lost productivity)	31.46	(34.97)	73.4
Total	42.85	(40.08)	100.0

* Mean costs (standard deviation in brackets) per treated patient from patient interviews (n=95)

7.3.3 Mass vaccination campaign costs

Total mass vaccination campaign costs amounted to USD 755,192, with USD 513,901 (68.0%) spent on vaccine purchase and USD 241,291 (32.0%) on delivery (Table 7-5). The vaccine was purchased from SBL Vaccin AB, Sweden, at a price of USD 10.28 per course (2 doses). Delivery costs comprised transport of the vaccine from Stockholm to Zanzibar and procurement of cups and water required for the buffer solution (6.0% of campaign costs), the work of two experienced international consultants (14.4%), training of locally recruited implementers (1.3%) and the implementation (social mobilization and vaccination) itself (10.4%). More details on delivery costs are presented as supporting information in Table 9-2.

Table 7-5: Costs of a mass oral cholera vaccination campaign, Zanzibar, 2009

	Total[a]	Mean[b]	%
Vaccine (purchase price USD 10.28 per 2 doses)	513,901	17.73	68.0
Delivery[c]	241,291	8.32	32.0
Vaccine transport, storage, water and cups	45,128	1.56	6.0
International consultants	108,432	3.74	14.4
Training	9,461	0.33	1.3
Implementation	78,270	2.70	10.4
Total	755,192	26.05	100.0

[a]Total costs (2009 USD) to vaccinate a target population of 49,980 people; [b]Mean costs (2009 USD) per fully immunized individual based on actual coverage (58.0%); [c]Based on real expenditure or planned budget data from 2009 mass vaccination campaign, see supporting information (Table 9-2) for more details

At a vaccine purchase price of USD 10.28 per course, the estimated total costs per fully immunized individual amounted to USD 26.05, with mean costs per vaccine course of USD 17.73 and mean costs for delivery of USD 8.32. Mean costs were adjusted for actual coverage of 58.0%, relating to 29,666 fully immunized individuals out of 51,151 targeted during the mass vaccination campaign (Khatib *et al.*, unpublished manuscript).

7.3.4 Cost-effectiveness analysis

Base-case results

Table 7-6 presents the results of the cost-effectiveness analysis (CEA) from the health care provider perspective using base-case parameter estimates obtained from primary and secondary data sources from Zanzibar. Annual costs to immunize 50,000 people, if the OCVs cost USD 10.28 per course, were USD 371,850, assuming one campaign per three years at a cost of USD 1,115,549. Annual public COI averted by vaccination amounted to USD 1,515. Incremental costs, the difference between total annual costs (i.e., vaccination program and public COI) with and without vaccination, amounted to USD 370,334. ICERs were USD 1,878,142 per death averted, USD 16,171 per case averted and USD 119,339 per DALY averted.

Table 7-6: Key outcomes from model of mass oral cholera vaccination (health care provider perspective) in Zanzibar, 2009[a]

	No vaccination	Vaccination	Difference
Effects			
Annual number of cases	30	7	23
Annual number of deaths	0.26	0.06	0.20
Annual number of YLD averted			0.02
Annual number of YLL averted			3.08
Annual number of DALY averted			3.10
Total number of DALY averted over duration of protection			8.78
Costs of outcome indicators, 2009 USD			
Annual costs of vaccination program[b]	0	371,850	-371,850
Annual public costs of illness	1,968	453	1,515
Annual costs of treatment and vaccination program	1,968	372,302	-370,334
Costs per death averted with vaccine		1,885,827	
Costs per case averted with vaccine		16,237	
Costs per DALY averted with vaccine		119,828	
Incremental costs and cost-effectiveness ratios (ICER), 2009 USD			
Incremental costs[c]			370,334
ICER (death): Incremental costs/death averted			1,878,142
ICER (case): Incremental costs/case averted			16,171
ICER (DALY): Incremental costs/DALY averted			119,339

[a]Base-case results from population of 50,000, with 3% annual discounting of effects; [b]Costs for international consultants excluded; [c]Costs of vaccination program minus public COI averted by vaccination (cost savings); YLD: Years of life lived with disability, YLL: Years of life lost, DALY: Disability-adjusted life-year, ICER: Incremental cost-effectiveness ratio

Logistical on-site support from the WHO headquarters was provided since the campaign was conducted within a research project that aimed to assess also epidemiological and sociobehavioral aspects of OCV use in endemic settings. Thus, costs incurred for international consultants were excluded from the analysis on the assumption that the campaign would also have been possible without intensive external help.

The predicted ICER was much greater than three times the per capita GDP for Tanzania (USD 1,509 in 2009) per DALY averted [37], suggesting that mass immunization with OCV in Zanzibar was not cost-effective. Even if the OCV was offered at no cost, the vaccination would still cost more than the avoided public COI due to the delivery costs and the ICER would be USD 24,127.

Compared to the health care provider perspective, key outcomes of the CEA from the societal perspective (Table 9-3), which included private direct COI, differed only minimally. Annual private COI averted by vaccination amounted to USD 285; the ICER decreased to USD 119,247 per DALY averted. With the OCV offered at no cost, the vaccination would still cost more than the avoided public and private COI and the ICER would be USD 24,035.

Sensitivity analyses

One-way sensitivity analyses were performed with all input parameters presented in Table 7-2 from the health care provider perspective. This analysis does not account for the effects of non-linearity and interactions between uncertain parameters as it varies parameters one at-a-time while keeping other parameters at base-case values, and the ranges specified for each parameter may not reflect equivalent ranges of uncertainty [38]. Varying base-case values over plausible ranges helped to estimate the influence of each parameter on the ICER per DALY averted (see supporting information, Figure 9-1), and per death (Figure 9-2) and case (Figure 9-3) averted. The most influential parameters on the ICER per DALY averted were PE, CFR, incidence, discount rate and vaccine purchase price.

Threshold analyses

Another two-dose OCV was licensed for use in India in 2009. Shanchol™ (Shanta Biotechnics, Hyderabad, India) is a bivalent variant of Dukoral®, containing killed *V. cholerae* O1 and O139, but no CT B subunit. It has recently been prequalified by the WHO for UN use; at its current price of USD 1.85 per dose to the public sector, it may become an attractive alternative for future OCV campaigns [21]. Interim analysis from two-year follow-up of a randomized controlled trial from Kolkata, India, showed that Shanchol™ is safe and has a PE of 67% across all age groups, which is similar to Dukoral® [39]. Repetition of the OCV campaign in Zanzibar with Shanchol™ at USD 3.70 per course and PE=67% while keeping vaccine delivery with USD 1.06 at the minimum level—and CFR (1.86%) and cholera incidence (4/1,000) as the most influential parameters at the maximum level—would reduce the ICER considerably to USD 3,600 per DALY averted from the health care provider perspective and to USD 3,557 per DALY averted from the societal perspective.

Based on these assumptions the purchase price of Shanchol™ per course would have to be as low as USD 1.10 to render the mass vaccination campaign cost-effective from a health care provider perspective (or USD 1.15 from a societal perspective).

7.4 Discussion

This study estimated public and private COI due to endemic cholera in Zanzibar and costs of the 2009 mass vaccination campaign to assess CE from a health care provider and a societal perspective. The analysis presented here suggests that COI averted by a mass vaccination campaign with an OCV were negligible to the public health sector and the society and that such an intervention was not cost-effective based on the stated assumptions. However, mass vaccination campaigns in Zanzibar to control endemic cholera may meet WHO criteria for CE under certain circumstances of highly optimistic assumptions about vaccine purchase price, delivery costs, incidence and CFR.

Private cost were higher than in Beira, Mozambique [12], where Dukoral® had also been used in a mass campaign in endemic settings. Despite mean public and private COI of ~USD 104 per episode were higher than the ~USD 47 for hospitalized cases in Beira, the mass vaccination campaign was not cost-effective in Zanzibar.

Relative costs for the vaccine and for delivery were comparable to findings from two campaigns in Vietnam with the bivalent Vietnamese OCV where this ratio was 25 vs. 75% in 1997 [40] and 21 vs. 79% in 1998 [13], respectively. However, mean costs per fully immunized individual were much higher than previously reported costs of USD 0.5 to 10.0 from Sudanese refugee settlements in northern Uganda (1997) [41], USD 2.09 from Beira, Mozambique (2003), where the vaccine was provided free of charge [11], and USD 7.1 from Darfur, Sudan (2004), where the vaccine course cost USD 3.8 [42]. Mean costs per immunized individual of USD 17.6 for a mass immunization campaign in post-tsunami Aceh, Indonesia (2005), were also still lower than in Zanzibar, even though the vaccine had been purchased at a comparable rate of USD 9.4 per course [43].

ICERs were well above any results reported for cholera mass vaccination campaigns [14,28,44-47]. The main reason why mass vaccination with Dukoral® was cost-ineffective in Zanzibar may be due to using an expensive OCV in a low incidence setting. Another reason may be that the present model used local data on costs of immunization. Other CE models that were not based on locally available data generally assumed much lower immunization costs, using (subsidized) vaccine prices of ~USD 1 and delivery costs of ~USD 1 per course; this made them propose

vaccination is economically more viable than standard treatment [14]. Threshold analyses indicated that mass vaccination may also become cost-effective in Zanzibar if OCVs were procured at prices of ~USD 1, a price level acceptable by many public health policy makers in Asia [33].

This study has several limitations. First, even though uncertainty in input parameters was considered in one-way sensitivity analyses, an assessment of whether an intervention was cost-effective or not should ideally be based on outcomes obtained from probabilistic sensitivity analysis that include confidence intervals and not only on point estimates [35]. Second, herd protection may play a considerable role in cholera vaccination [48] and was shown to make community-based programs in three Asian and one African setting cost-effective regarding the per capita GDP criterion [14]. Since relevant epidemiological data to model herd protection were not available for Zanzibar, indirect effects were not included in the model. Third, non-diarrhea patients were usually not treated or admitted by their local public health care facility during the time it operated as a CTC. Patients who need treatment, e.g., for malaria, will have to bear extra direct and indirect costs related to additional travel or potential serious complications due to delayed treatment. These additional costs have not yet been included in the CEA.

7.4.1 Conclusions

The analysis presented here suggests that costs averted by a mass vaccination campaign with an OCV in endemic areas of Zanzibar were negligible when compared to standard treatment in decentralized cholera treatment centers. Mass vaccination was not cost-effective based on the stated assumptions, mainly due to the high purchase price and the low cholera incidence in Zanzibar. However, mass vaccination campaigns in Zanzibar for endemic cholera control may meet WHO criteria for CE under certain circumstances, especially in high-incidence areas and when OCV prices are reduced to levels at USD 1.10 to 1.15.

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8

General discussion and implications

Cholera control is primarily a structural issue demanding a strong commitment and considerable investments by governments to overhaul and/or maintain a safe water supply and an appropriate sanitation infrastructure [1]. Even though great strides have been taken over the last two decades to increase the access of the global population to improved drinking-water sources, 40% of the people in sub-Saharan Africa still lived without safe water in the year 2008 [2]. Recognizing that a reduction of the proportion of people without access to safe drinking water will remain a huge challenge, mainly because of the unprecedented population growth in low- and middle-income countries, which bear the brunt of the global cholera burden, developing and testing of complementary measures to protect peoples' health from epidemic-prone diarrheal diseases is crucial.

Inasmuch as use of vaccines has been shown to reduce cholera-related morbidity and mortality in several settings [3], research presented in this thesis was conducted to provide practical information to local and international policy makers towards improving cholera control through vaccination in endemic settings.

Findings and implications presented here come at a particularly appropriate time. They reiterate that the present public health burden due to cholera is still intolerable and that difficulties to tackle this disease have not been sufficiently addressed by the global community. On May 24, 2011, the 64th World Health Assembly adopted a new resolution urging member states to more actively engage in the global fight against cholera and "to undertake planning for and give consideration to the administration of vaccines, where appropriate, in conjunction with other recommended prevention and control methods and not as a substitute for such methods." [4]

This thesis benefited greatly from the opportunity to conduct studies before and after a mass vaccination campaign in Zanzibar. Knowing whether the people of Zanzibar would like to take a vaccine against cholera, and what actually made them take it (or not take it), is likely to be relevant and represents important information to maximize the impact of future vaccination campaigns on cholera.

However, the decision to use oral cholera vaccines (OCVs) as a complementary measure for routine cholera control in endemic settings not only relies on community willingness for vaccination, but also on macroeconomic considerations. Such information is especially needed in settings where efforts and resources in the health sector have to be employed with utmost care and sensitivity to situation factors. In the effort toward achieving a sustainable cholera control strategy, policy makers and public health officials need to know whether health-related benefits and cost savings due to vaccinating their people is worth the monies invested.

This thesis aimed to examine social and cultural features of OCV acceptance from a community perspective *and* to evaluate the cost-effectiveness (CE) of the 2009 OCV mass campaign in Zanzibar. In the following sections, major findings and methodological issues that are particularly relevant with reference to the research questions are discussed before overall conclusions are presented. Implications for local and global cholera control with OCVs and directions for future research follow.

8.1 Discussion of major findings

8.1.1 What are the social and cultural features of OCV acceptance in Zanzibar?

The first research question was addressed from different angles in Chapters 3 to 6. Community views of cholera were clarified prior to examining rates and social and cultural determinants of anticipated and actual OCV acceptance and barriers to uptake were examined.

Community-perceived burden and views of cholera

Chapter 3 documents local perceptions of cholera in relation to shigellosis, another enteric diarrheal illness. It was shown that cholera was more often recognized as serious illness that may be fatal without appropriate treatment than shigellosis. Features of distress were primarily related to the negative social and financial impact cholera can have on a patient's life. Interference with work- or income-related activities was the most prominent category of distress. The most prominent somatic symptoms were related to dehydration and to general gastrointestinal features. Cholera was mainly attributed to a dirty environment and microbiological contamination while causes unrelated to the biomedical basis were also identified, but with less prominence. Even though rehydration of the patient (primarily in the periurban community) and use of herbal treatment and antibiotics (rural community) were the preferred self-treatment options, professional health facilities were universally recommended at both sites. This survey showed that cholera represented a significant perceived illness burden in

periurban and rural Zanzibar. Because of community preference for professional treatment for cholera and shigellosis, the importance of strengthening local health systems to improve enteric disease control was highlighted; health education efforts for cholera were suggested particularly for rural areas and with a focus on women, and for shigellosis in general.

Social and cultural features of OCV acceptance

To date, no studies on social and cultural features of OCV acceptance in Africa have been published. Thus it was necessary to study whether and how community views of cholera, as presented in Chapter 3, determined anticipated OCV acceptance. The almost universal willingness (94%) to accept an OCV at no cost (Chapter 4) confirmed that the perceived high severity and fatality of cholera required preventive action in addition to existing treatment practices in endemic communities in Zanzibar. Fewer community residents, however, were willing to pay if the OCV was offered at some cost. The same pattern, but with a much less pronounced gradient, was found in studies using a similar EMIC interview in western Kenya and in southeastern Democratic Republic of Congo (DRC) (Figure 8-1).

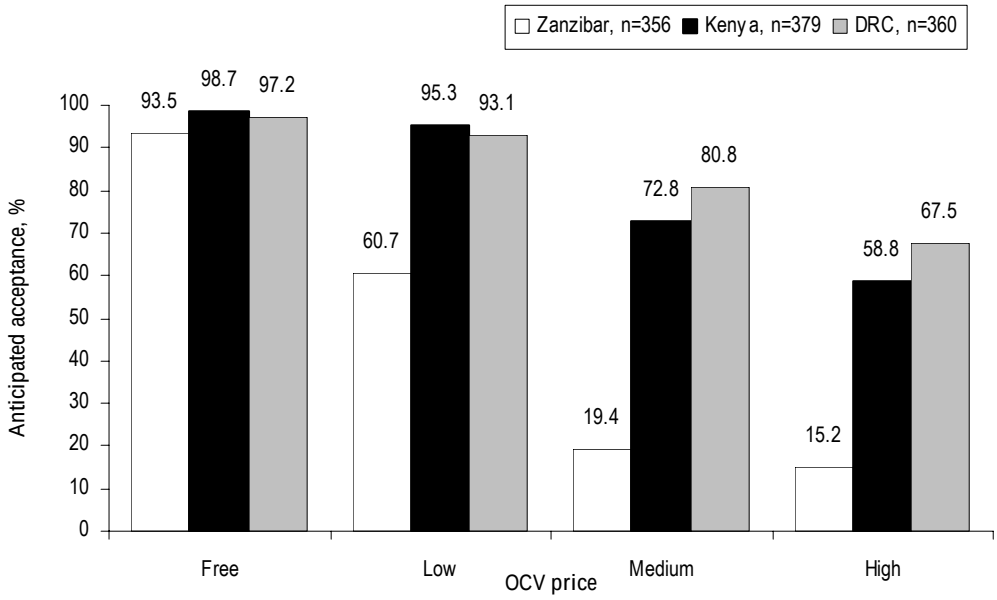

Figure 8-1: Anticipated OCV acceptance in cholera-endemic communities in three African countries

Low price: ~USD 1, medium price: ~USD 5, high price: ~USD 10. OCV: Oral Cholera Vaccine; DRC: Democratic Republic of Congo. Source: Zanzibar: Chapter 4, Kenya: Sundaram [5], DRC: Merten *et al*. [6]

The influence of vaccine-related costs on reported and actual health behavior was reflected in the analysis of social and cultural determinants of anticipated OCV acceptance (Table 8-1): the higher the OCV price, the fewer categories of sociocultural features of illness determined

anticipated acceptance (Chapter 4). Economically more stable conditions, represented by households that depended on a regular budget or by married respondents, were the main drivers behind the willingness to buy the medium- and high-priced OCV.

Table 8-1: Social and cultural features of anticipated and actual OCV acceptance (uptake) before and after a mass vaccination campaign in Zanzibar

	Prevaccination				Postvaccination
	Anticipated acceptance			Actual	Actual
Category[a]	Low price, ~USD 0.9	Medium price, ~USD 4.5	High price, ~USD 9	acceptance (uptake)	acceptance (uptake)
Categories of distress: somatic symptoms					
Loose skin					(+)[rural]
Loss of appetite				(–)[rural]	
Nausea				(–)	
Rectal pain					(+)
Unconsciousness				(+)	
Very thirsty	(+)				
Categories of distress: social impact					
Disruption of health services		(–)[periurban]		(+)[rural]	
Fear of infecting others	(+)[rural]				
Perceived causes					
Contact with contaminated water					(+)
Unprotected/spoiled food					(+)
Self treatment at home					
Drinking more water or liquids	(–)				
Outside help seeking					
Pharmacy/Over-the-counter drugs					(–)
Sociodemographic characteristics/ previous illness episodes					
Age				(+)	(+)
Gender (male vs. female)				(–)	
Household size		(–)[periurban]			(+)
Married vs. not married		(+)	(+)		
Previous illness episode					(+)[rural]
Regular/dependable household income	(+)	(+)[periurban]	(+)		
Secondary school or above vs. no education	(+)				
Site[b] (rural vs. periurban)			(+)	(+)	

[a]Only significant positive and negative determinants ($p \leq 0.05$) listed that were identified in comprehensive models including interaction with periurban site as baseline if p(interaction term)<0.1. Superscript text refers to site at which effects were significant; [b]Overall effect of site assessed from main effects model. Source: Chapter 4 to 6.

Because intention to accept a free vaccine was almost universal, only determinants of anticipated acceptance of the low-, medium- and high-priced OCV could be studied. Thus, subsequent study of determinants of vaccine uptake was needed (Chapter 5), which showed the influence of sociocultural features of illness on vaccine acceptance if no direct cost were attached. The decision to take preventive action against cholera was to a large extent influenced

by categories of distress, referring to illness experience. This supported the findings from analysis of focal models suggesting that categories of illness experience, meaning and behavior explained anticipated and actual OCV better than purely social epidemiological models (Chapter 4 and 5). Postvaccination study of factors associated with OCV uptake also confirmed this relative importance of sociocultural features of illness (Chapter 6). While proxy variables for economic status had no effect on people's decision to drink the free OCV, increasing age was a positive predictor to prevent cholera with vaccination. Contrary to the medium-price analysis, showing that a higher household was a negative determinant of anticipated acceptance in the periurban community, OCV uptake was not limited, but rather reinforced by a higher household size; this indicated the priority for free OCVs in both periurban and rural households. The finding that economic considerations are important in these poor communities was not surprising and confirmed contingent valuation exercises that studied private demand for cholera vaccines [7-9]. Studies presented in Chapter 4 to 6 showed the relevance of vaccine price on community willingness for cholera vaccination and highlighted the need to study sociocultural features of cholera-like illness in addition to sociodemographic and economic characteristics when assessing determinants of OCV acceptance.

Passive acceptance rather than active resistance or refusal

Despite a high willingness to receive free vaccines, the achieved coverage of 50% among prevaccination respondents (Chapter 5) was less than satisfying, even lower than community anticipation for a low-priced OCV. In the continuum from active resistance or refusal of vaccination to active demand [10-12], findings from the prevaccination studies did not suggest that there would be much active or passive resistance against cholera vaccination in Zanzibar. Also noteworthy with regard to the often reported allure of *exotic* reasons for refusal of vaccination was the complete absence of magico-religious causes as determinants of vaccine acceptance. Overall, these studies indicated passive community acceptance of OCVs, apparently uninfluenced by concepts of illness meaning.

Retrospective study of determinants of uptake, and in particular analysis of barriers to uptake among unvaccinated community members (Chapter 6), confirmed this conclusion. Analysis of barriers revealed logistical issues as main reasons for the low coverage, with people's own busy daily schedules as the most prominent feature. It is in principle possible that—under the pretext of "having a lot of things to do"—the real reasons why vaccination against cholera had a low priority for some people were confounded or not discernible by the approach taken. However, analysis of qualitative data indicated that those who did not drink the required two doses of Dukoral® did so because of daily commitments to either feed their families or support their households or because they were studying. Thus, despite the vaccine being offered at no cost

and mitigation of factors likely to limit access (e.g., travel distances), engagement in daily economic activities was identified as the major obstacle to getting immunized against cholera.

One may ask, why were people apparently unwilling to sacrifice a few hours from mostly informal work to queue for the vaccine? Research on economic systems and behaviors in low- and middle-income countries may offer an explanation. In their recent book *Poor Economics*, Duflo and Banerjee [13] point out that even though many families run an informal business (e.g., petty trading, village shop, selling street food, etc.) in these countries, they earn almost nothing due to poor organization, lack of capital and limited entrepreneurship. Little diversity in the local informal economy—most of the village shops have the same goods in stock and women are virtually selling the same street food every day to passers-by and commuters—means that the return is meager even though investment in working time every day is high.

Barriers related to concerns about the vaccine were much less prominently reported than logistical challenges. Nevertheless, fears about side effects or the doubted effectiveness of the vaccine should not be neglected in future campaign planning as rumors about allegedly adulterated vaccines may spread quickly with devastating consequences for immunization campaigns [14-16].

8.1.2 Does use of an OCV in a mass vaccination campaign in Zanzibar provide value for money?

The study presented in Chapter 7 estimated public and private costs of illness (COI) due to cholera and costs of a mass vaccination campaign including the benefits in terms of cases and deaths prevented and disability-adjusted life-year (DALY) averted.

Because the incremental cost-effectiveness ratio (ICER) of ~USD 119,000 per DALY averted exceeded three times the national per capita gross domestic product, use of OCVs was not considered a cost-effective strategy in comparison to the current practice of treatment in cholera treatment centers (CTCs). Mass vaccination costs were not offset by public and private COI in Zanzibar. In contrast, the Beira mass vaccination campaign was cost-effective, but only when herd protection was taken into account [17].

The main reason why mass vaccination was not found to be cost-effective in Zanzibar may be due to use of an expensive OCV in a relatively low incidence setting. Vaccine and delivery costs of ~USD 26 per fully immunized individual were higher than in any other published study on costs of immunization with OCVs. The high purchase price of Dukoral® accounted for 68% of these costs. The second-most costly item, hiring of international consultants (14%), was not

included in the CE model because a repetition of the campaign will likely be done without technical help from abroad. Despite this reduction to ~USD 22 per fully immunized individual, the mass vaccination was still not cost-effective. The impact of the vaccination campaign on morbidity and mortality, i.e., absolute reduction in numbers of cases and deaths, was limited because cholera incidence was too low and because the current case management was efficacious enough to keep the case-fatality rate (CFR) at ~1%.

The vaccine purchase price is the only influential parameter policy makers or implementers can manipulate directly to improve the CE of vaccination. A threshold analysis with Shanchol™, the second OCV that is currently prequalified for use by UN agencies, indicated that only a substantial reduction in vaccine purchase price—from the USD 10.28 offered for Dukoral® for the 2009 campaign to USD 1.10—would make the intervention cost-effective (i.e., ICER<USD 1,509 per DALY averted). This estimation was based on the health care provider perspective and maximum rates used in the CE model for incidence (4 per 1,000) and CFR (~1.9%) and minimum delivery costs of USD 1.06.

Other short-term measures like chlorination of water kept at home or point-of-use water treatment may prove to be more cost-effective than use of OCVs [18], and long-term benefits of investments in water and sanitation were shown to be cost-beneficial [19]. While efforts at improving the sanitation infrastructure in Zanzibar are underway,[1] repeating mass vaccination campaigns with OCVs may be considered as a supplement to current cholera control activities until improvements in the water and sanitation systems are realized. These proposed water and sanitation interventions, however, were beyond the scope of this thesis project.

8.1.3 Is it affordable countrywide?

In the following paragraphs, results presented in Chapter 7 are discussed to assess whether countrywide use of OCV mass campaigns may be an economical *and* affordable strategy for the government of Zanzibar.

Cost-effectiveness is not the only criterion to decide whether OCV mass campaigns should be integrated into the national cholera control strategic plan. Affordability has to be considered as well to estimate whether the national health budget would be able to cover immunization expenses and/or whether and how much co-funding from international institutions is required.

[1] http://www.unhabitat.org/content.asp?cid=7728&catid=5&typeid=6&subMenuId=0

A basic budget impact analysis using data from Chapter 7 shows that if Dukoral® were used to vaccinate 50% of the population of Zanzibar at the current public price of USD 10.28, the annual cost to the government would be ~USD 2.6 million. This would translate into 14.8% of the annual Zanzibar health budget for 2008 [20] (Figure 8-2). Whether this level of the health budget is affordable and should be allocated to cholera vaccination has to be decided by Zanzibar decision makers. If Shanchol™ were used at its current public price of USD 3.70, it would still cost the government between USD 1.1 and 1.2 million, equal to 6.6 and 6.9% of the annual health budget.

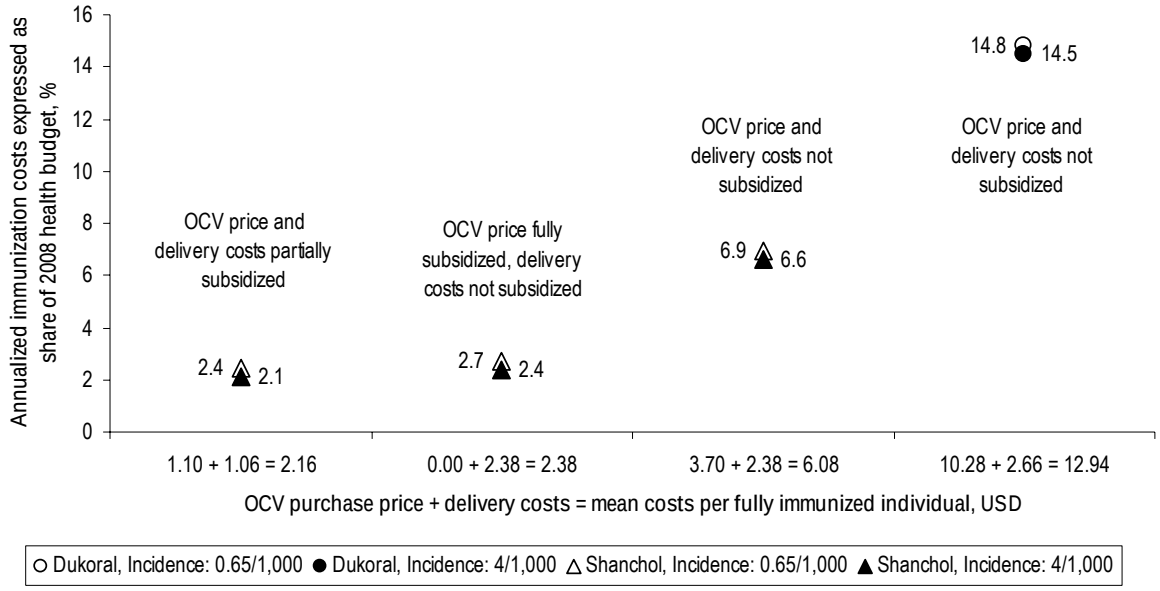

Figure 8-2: Estimation of the impact of subsidized and unsubsidized OCV purchase prices and delivery costs for countrywide mass vaccination on the 2008 health care budget for Zanzibar

Assumptions: Duration of protection of three years; vaccination needed for people living at risk of recurrent cholera outbreaks (50% of the entire population of Zanzibar). Current price for use by UN agencies is USD 3.70 for one course of Shanchol™ and USD 10.28 for one course of Dukoral®. Mean delivery costs for Dukoral® (USD 2.66) are higher than for Shanchol™ (USD 2.38) because the latter does not require cups and drinking water for administration.

Hence, international support for cholera vaccination may be needed if the government of Zanzibar decides to use vaccination for endemic cholera control. Co-funding from the GAVI Alliance[2] and other donors like the Bill & Melinda Gates Foundation—and/or price negotiations through OCV bulk purchase by mechanisms such as the UNICEF procurement system[3] and the PAHO Revolving Fund[4]—could improve the CE of OCVs in Zanzibar and make their use more affordable to the government.

[2]The GAVI alliance is not supporting cholera vaccination until 2013 [21], but recommendations may be revised given the renewed global interest in cholera control.

[3]http://www.unicef.org/supply/index_immunization.html

[4]http://new.paho.org/hq/index.php?option=com_content&task=view&id=1864&Itemid=2234&lang=en

The following two scenarios illustrate how cholera vaccination may become economically and financially attractive to the government of Zanzibar if external support or price negotiations are considered: first, if Shanchol™ is sold at a reduced price of USD 1.10 to Zanzibar, and if delivery costs are also partly subsidized to make the intervention cost-effective, annual countrywide vaccination of hotspots would cost the government ~USD 374,000. This would be equal to 2.1% of the annual health budget for 2008 (Figure 8-2). Second, if Shanchol™ would be fully subsidized, but delivery costs were borne by the government, immunization of hotspots would cost the government ~USD 420,000 to 475,000, or 2.4 to 2.7% of the annual health budget, depending on the annual incidence.

Local health policy makers may also decide to continue with the current practice of reactive treatment, which was shown to be capable of keeping the average CFR of cases seen at facilities at reasonable levels. However, responses to outbreaks always represent a stress on the local health care system in Zanzibar, which is already constrained by shortage of qualified personnel and resources; this may affect general primary health care services negatively. The priority for cholera vaccination, especially among rural residents who feared that health care would be negatively affected by cholera outbreaks (Chapter 5), is an indication that community concerns about the health care system need also be taken into consideration when revising the current cholera control strategy in Zanzibar from an economic perspective.

8.2 Methodological issues

8.2.1 Bridging epidemiology and anthropology for the benefit of diarrheal disease control

Despite numerous attempts to bring the disciplines of epidemiology and anthropology together for the benefit of public health [22-25], James Trostle stated in his book *Epidemiology and Culture* [26] that "culture is less widely appreciated in the epidemiological worldview, but it has explanatory power and effectiveness comparable to the concept of society." (p. 5) He thus argued "for a complementary alternative to social epidemiology, one that focuses attention on disease classification, meaning, risk, and behavior in addition to social variables such as income, marital status, and occupation." (*ibid*.)

Cultural epidemiology was developed in an effort to enhance the interface of anthropology and epidemiology. It was first implemented over 20 years ago in studies of diarrheal illnesses and oral rehydration solution (ORS) promotion [27]. An early validation of this approach was later done in Thailand when EMIC interviews were used to describe local diarrheal illnesses for public health policy recommendations [28]. Since then, however, few studies that systematically

integrated quantitative and qualitative methods have been published on the topic of diarrhea control.

Findings presented in this thesis provided evidence for the hypothesis that cultural concepts of illness have equal or even more explanatory power than if only results from social epidemiology were used. Statistical methods enabled formal testing of this hypothesis by using the Akaike Information Criterion. Comparing focal models of illness experience, meaning and behavior with models containing only sociodemographic variables clearly demonstrated that categories of patterns of distress and perceived causes for cholera explained anticipated and actual OCV acceptance better than social epidemiology alone. Preliminary results from the OCV acceptance study from Kenya [29] and DRC [6] confirmed this finding, suggesting also considerable influence of cultural concepts of cholera on vaccination behavior in endemic sites. Findings reported in this thesis provide strong validation for Trostle's call to integrate cultural concepts of illness into research for the benefit of public health planning.

Limitations that need to be addressed in future studies

Limitations in the presented studies (Chapter 3 to 6) require more attention for improving future studies of cultural epidemiology and vaccine acceptance.

First, assessment of whether intention to take the vaccine is a (strong) predictor of uptake could not be firmly established. Because of this and because the literature, which is mostly reporting on social cognition models to examine the relation between attitudes and behavior [30], is mixed regarding whether intention to take a vaccine predicts uptake [31-34], further research is needed. Prevaccination assessments would benefit cholera control greatly if future studies conducted along with OCV mass vaccination campaigns would support the hypothesis that intention predicts acceptance.

Second, based on research experience and observations in Zanzibar, complementing EMIC surveys with in-depth interviews would be an asset. Doing such interviews with the study population, and also other stakeholders in the community, would help contextualize the results better. Stakeholders, namely policy makers, allopathic and traditional health care professionals and formal and informal community leaders, were also studied within the framework of the OCV project in Zanzibar, but analysis is still ongoing. Once available, narrative data obtained from these interviews may be imported into the qualitative data analysis software MAXQDA; this would allow additional and potentially instructive comparisons between stakeholders' views on cholera and vaccination and the community views presented in this thesis.

Third, on a more technical note, EMIC interviews require rigorous training of research assistants [35]. Despite regular supervision and technical input, working with EMIC interviews has been quite challenging to field workers in Zanzibar who had been more used to administering a questionnaire than to interview members of the general community. Data quality, especially narrative content, could be improved by the use of digital voice recorders. Provided respondents give consent, interviews should be recorded and at least verbatim transcription of key questions done.[5] Even though this procedure requires more time for data entry, it would improve the explanatory power of cultural epidemiology, which is to a large extent based on the integrated analysis of quantitative and qualitative data.

Finally, due to the increasing number of cholera outbreaks worldwide, development of tools for rapid prevaccination assessment of community willingness to vaccinate and of social and cultural determinants of OCV acceptance may become useful. Surveys using several hundred semi-structured interviews where each interview takes one hour or more to complete require a lot of time, financial resources and skilled manpower that are hardly available in most circumstances. Thus, future research for cultural epidemiological study of OCV acceptance should therefore focus on developing a scaled-down version of the EMIC interview that was used here.

8.2.2 Estimating the CE of OCVs for endemic cholera control

The current CE model has several limitations that need to be addressed in the next steps.[6]

First, CE outcomes were reported as point estimates. To avoid making suggestions solely based on point estimates, the revised model should employ probabilistic sensitivity analysis, which takes into account the uncertainty around parameter estimates and enables computation of CE acceptability curves for easier interpretation of findings [36,37].

Second, indirect effects of OCVs on the public health impact need to be considered. Besides direct protection of vaccinees, vaccination may also induce protection in unvaccinated populations through indirect effects known as *herd immunity* or *herd protection* [38,39]. Herd immunity occurs only when live vaccines are administered to people; shedding of these organisms by vaccinees may then induce a protective immune response in unvaccinated people. Herd protection relates to the reduction of disease transmission by the fact that the probability of susceptible people to infection is reduced when they are surrounded by or live with

[5]Full transcripts are of course better, but require much more time (1 hour of interview typically requires about 5-6 hours of transcription, and more if translation is required) and are too costly for many research projects.

[6]It should be noted that making modifications to the cost-effectiveness model has to improve it considerably; else the time and financial resources invested are forgone to help other more important research needs.

immunized people. Herd protection is a feature of both live and inactivated vaccines, but only works if the pathogen is transmitted through person-to-person contacts. Herd protection was shown to play a role in a reanalysis of data from a trial using OCVs in Bangladesh [40]. After development of a mathematical model with these data, Longini *et al*. concluded that OCV mass campaigns may be useful to reduce endemic cholera even with moderate coverage levels [41]. This evidence has led to the consideration of herd protection effects in economic evaluation studies using OCVs [17,42-44]. In an economic evaluation of community-based vaccination programs in four countries (Bangladesh, India, Indonesia, Mozambique), Jeuland *et al*. showed that the use of OCVs was only cost-effective if herd protection was taken into consideration [17]. Although herd protection was not included in the present cost-effectiveness analysis (CEA) due to unavailability of relevant epidemiological data, it can be assumed that indirect effects would also decrease the ICER in Zanzibar.

Third, economic indicators suggested that vaccination with Dukoral® was not cost-effective in Zanzibar when compared to the current practice of erecting CTCs in public health care facilities. This treatment approach may also cause additional costs that have not yet been included in the CEA. Such costs would mainly be related to non-diarrhea patients who are not treated or admitted by their local public health care facility during the time it caters exclusively for cholera patients (Chapter 7). For example, patients who need treatment for malaria will have to bear extra direct and indirect costs, e.g., related to additional travel or to the higher probability of serious complications due to delayed treatment, which may contribute to public costs and also increase inequity.

Finally, provided that relevant data are obtainable, a *generalized* CEA that examines costs and effects of all possible cholera-related interventions to select the mix that ensures maximum population health within the context of constrained resources may be warranted [45]. Generalized CEA examines the CE of vaccination, other prevention activities like provision of safe water, sanitation and hygiene education etc., and treatment with regard to *doing nothing*. This would allow researchers to clearly determine the CE of different mutually exclusive cholera prevention and treatment packages and give health policy makers more comprehensive information to help them decide how to allocate resources most effectively.

8.3 Conclusions

Research presented in this thesis assessed the use of OCV mass campaigns for endemic cholera control in Zanzibar.

From the *perspective of the affected population*, this thesis suggests **good prospects to use an OCV offered at no cost in mass vaccination campaigns for endemic cholera control in Zanzibar** for the following reasons:

- People's perceptions showed that cholera was distinct from shigellosis and represented a serious and potentially fatal illness that requires professional help;

- Community willingness to receive an OCV at no cost was almost universal;

- Even though uptake of an OCV offered at no cost was lower than anticipated acceptance, analysis of sociocultural features of illness identified relevant determinants of acceptance that may be addressed in future campaigns;

- Community behavior regarding OCVs was characterized by passive acceptance rather than active resistance or refusal;

- Sociocultural features of illness associated with OCV uptake indicated a positive impact of the mass vaccination campaign and of sensitization activities on vaccine acceptance behavior;

- Study of barriers to OCV uptake indicated a good campaign implementation and trust in the health system, but also highlighted the importance of logistical factors for future campaign planning.

From an *economic perspective*, this thesis suggests **limited prospects to use OCV mass campaigns under current conditions for endemic cholera control in Zanzibar** for the following reason:

- Mass vaccination with OCVs at a purchase price of ~USD 10 and with annual incidence of 0.65 per 1,000 was cost-ineffective compared to the current practice of responding to cholera outbreaks with decentralized treatment centers;

However, OCV mass campaigns may become an alternative, and potentially also a financially affordable, option to treatment in Zanzibar if price negotiations would reduce OCV costs and/or if external financial support would be available. At a subsidized purchase price of ~USD 1 and subsidized delivery costs of ~USD 1 per immunized individual, OCV mass campaigns may become feasible for cholera control in high-incidence areas of Zanzibar.

8.4 Implications for endemic cholera control with OCVs

In general, future mass vaccination campaigns in endemic areas may be planned according to recently published practical guidelines compiled by the WHO.[7] Findings reported here are directly applicable to periurban and rural cholera-endemic areas of Zanzibar; but they may in principle also be helpful to public health professionals and decision makers in mainland Tanzania and other African countries.

8.4.1 Local level

To maintain or improve campaign effectiveness in Zanzibar, planning for future OCV mass campaigns in cholera-endemic areas should consider the following points:

- Campaigns should
    - offer OCVs at no cost to the target population;
    - be announced at least a few months before vaccination posts open, with repeated reminders in the target communities;
    - extend daily open hours or numbers of days for the vaccination, especially in rural areas;

[7] *Oral cholera vaccines in mass immunization campaigns: guidance for planning and use* [46]

- concentrate efforts among young adults, periurban areas, and men.

- Information material for community sensitization and mobilization should
  - emphasize cholera as a cause of severe dehydration;
  - particularly point out the value of vaccination versus treatment of cholera with antibiotics;
  - better explain (the usually mild) side effects of OCVs versus the benefit of vaccination.

CEA suggested the OCV mass campaign was not cost-effective in the base-case scenario with an OCV priced at ~USD 10; but this may change with the availability of cheaper OCVs.

Thus, if cholera control through countrywide preemptive vaccination is envisaged in Zanzibar, such programs should focus on communities (Shehias) where incidence rates are highest, i.e., in settings characterized by a high population density and where inhabitants are less likely to benefit from an upgrade in their sanitation system in the near future. Such a revised cholera control strategy might also be more equitable because vaccination programs that tackle cholera in defined hotspots areas are more affordable to governments or donors and thus more likely to be implemented in the mid-term than water supply and sanitation interventions [19].

8.4.2 Global level

High community appreciation for OCVs in Zanzibar matches the recently reinforced global strategy to promote OCVs for endemic and also epidemic cholera prevention and control. Fuelled by large cholera outbreaks in Zimbabwe, Pakistan and Haiti [47-49], and by recent progress made in the field of OCV development, governments from low- and middle-income countries have become more and more interested in using OCVs for an integrated cholera control strategy. Efforts by the WHO and academic institutions, with strong financial, practical and scientific support by international and non-governmental organizations, recently led to a series of innovative clinical, public health and economic evaluation studies to reassess the use of OCVs as a supplement to classical prevention activities [44,50-53]. Trials with Shanchol™ are ongoing [54] and further mass vaccination campaigns are planned for preemptive or reactive vaccination in endemic or epidemic situations in Haiti, the Solomon Islands and Thailand.

It is likely that global use of OCVs will rise notably in the near future because of three reasons: first, a growing number of cases worldwide coupled with increasing urbanization urging more and more people to reside in crowded and unsanitary informal housing conducive to cholera [55]; second, the availability of now two prequalified OCVs, which means more competition and thus probably lower prices and bigger flexibility for international agencies and donors. Finally, a proposal dating back to 1999 to create a global stockpile to better respond to cholera outbreaks [56] has now been declared a priority in a recent international meeting convened by the WHO.[8] It was in principle agreed to take action and develop a plan to finance and implement such a mechanism.

Findings presented in this thesis may be particularly useful for future projects that intend to employ OCVs for endemic cholera control. Based on the premise that a strong government commitment is required and that willingness to receive OCVs in communities targeted for mass vaccination campaigns is pivotal to ensure maximum coverage, the following points merit attention:

- Prevaccination assessments of community willingness should not only consider sociodemographic characteristics but also examine sociocultural features of cholera as potential determinants of OCV acceptance;

- In communities that welcome OCVs in principle, campaign planners also need to carefully consider logistical arrangements and start community mobilization activities with repeated reminders well in advance of campaigns;

- Alternative solutions to mass campaigns may be needed for population groups that value vaccines in principle but are more difficult to reach due to their specific daily or professional activities.

8.5 Directions for future research

The cultural epidemiological framework for *study of vaccine acceptance in endemic communities* may benefit from the following considerations:

- Further research is needed to assess whether intention to take vaccines might be a predictor of uptake;

[8]Consultation on *Oral Cholera Vaccine Stockpile Strategic Framework: Potential Objectives and Possible Policy Options*, September 6-7, 2011, World Health Organization, Geneva.

- In-depth interviews with community residents and other stakeholders should be considered to complement findings from EMIC surveys;

- Voice recording with verbatim transcription of key questions may improve narrative data quality;

- A shorter version of the EMIC interview used in Zanzibar may be developed as tool for rapid assessment of social and cultural determinants of OCV acceptance.

Further studies are required to gain more evidence on the *economic viability of using OCVs for endemic cholera control through mass vaccination campaigns.*

- The current CE model developed for Zanzibar should be revised and extended according to the following points:

    - In addition to one-way sensitivity analyses, probabilistic sensitivity analyses should be employed to generate an empirical distribution of the ICER based on multiple input parameters and to compute CE acceptability curves;

    - Herd protection effects should be included to examine the extent to which base-case results presented here would change. Assessing herd protection effects would essentially require more data on local cholera incidence and vaccine protective efficacy and a more sophisticated approach to modeling [57];

    - Direct and indirect costs incurred by the limited availability of services to non-diarrhea patients during outbreaks should be included among public COI;

    - The revised model should be calculated for two scenarios, one with use of Dukoral® and one with use of Shanchol™;

- Results from the revised model should be examined with regard to generalizability towards other cholera-endemic settings in Africa;

- A sectoral priority setting exercise might be conducted to determine the CE of different mutually exclusive cholera prevention and treatment packages under varying assumptions

by using the generalized CEA approach.

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9

APPENDIX

9.1 Supporting information for Chapter 7

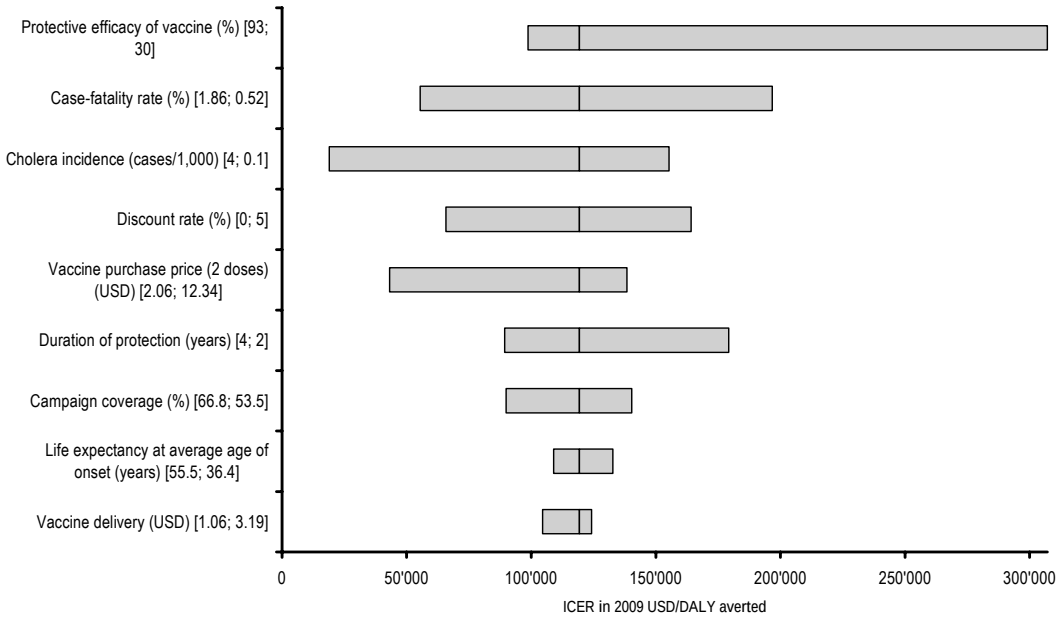

Figure 9-1: One-way sensitivity analysis of the influence of key parameters on ICER in 2009 USD per DALY averted from model of mass oral cholera vaccination (health care provider perspective) in Zanzibar, 2009

Tornado diagram presents parameters that were varied over their plausible ranges, as shown in brackets. Vertical line indicates base-case ICER of USD 119,339 per DALY averted. ICER: Incremental cost-effectiveness ratio, DALY: Disability-adjusted life-year

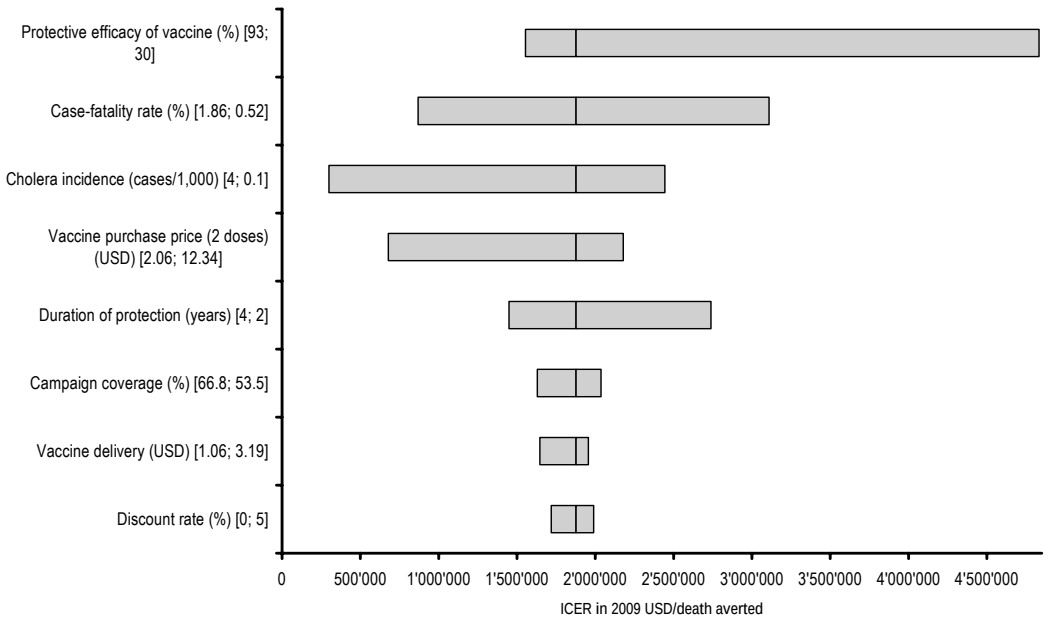

Figure 9-2: One-way sensitivity analysis of the influence of key parameters on ICER in 2009 USD per death averted from model of mass oral cholera vaccination (health care provider perspective) in Zanzibar, 2009

Tornado diagram presents parameters that were varied over their plausible ranges, as shown in brackets. Vertical line indicates base-case ICER of USD 1,878,142 per death averted. ICER: Incremental cost-effectiveness ratio

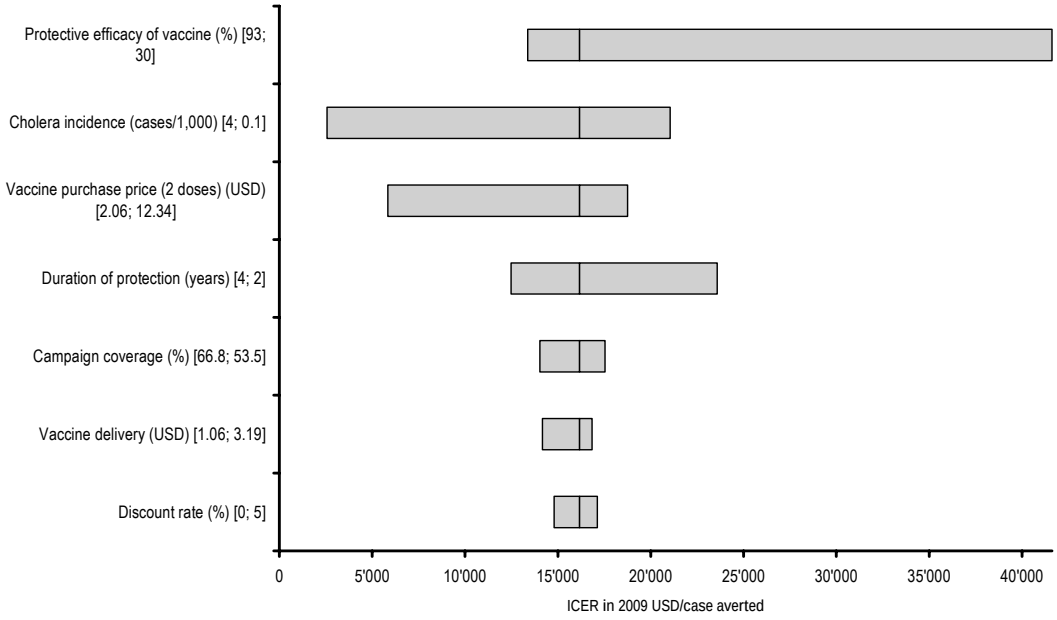

Figure 9-3: One-way sensitivity analysis of the influence of key parameters on ICER in 2009 USD per case averted from model of mass oral cholera vaccination (health care provider perspective) in Zanzibar, 2009

Tornado diagram presents parameters that were varied over their plausible ranges, as shown in brackets. Vertical line indicates base-case ICER of USD 16,171 per case averted. ICER: Incremental cost-effectiveness ratio

Table 9-1: Public variable costs of illness for cholera, Zanzibar, 2009

	2009 USD[a]		%
Drugs[b]	8.03	(7.92)	87.8
Antibiotic: Ciproxine	0.01	(0.08)	0.1
Antibiotic: Doxycycline	0.01	(0.13)	0.1
Antibiotic: Erythromycine	0.52	(0.41)	5.6
Antibiotic: Erythromycine syrup	0.10	(0.48)	1.1
Antibiotic: Metronidazole	0.01	(0.04)	0.2
Antibiotic: Septrine	0.01	(0.04)	0.1
IV fluid	7.08	(7.74)	77.3
Oral rehydration solution	0.25	(0.14)	2.8
Other drugs: Mebendazole (antihelminthic)	0.01	(0.01)	0.1
Other drugs: Zinc sulphate	0.03	(0.07)	0.3
Material[c]	1.12	(0)	12.2
Cannula (adults)	0.34	(0)	3.8
Examination gloves	0.52	(0)	5.7
IV giving set	0.20	(0)	2.1
Zinc oxide plaster	0.05	(0)	0.6
Total	9.15	(7.92)	100.0

[a]Mean costs and standard deviation in brackets; [b]Drug resource use based on patient interviews (n=95), drug unit costs include 6% for storage at medical store department and distribution; [c]Standard resource use per patient based on expert interview: cannula (1-2 pieces), examination gloves (8 pairs), IV giving sets (1 piece) and Zinc oxide plaster (30 cm); IV: Intravenous

Table 9-2: Delivery costs for a mass oral cholera vaccination campaign, Zanzibar, 2009

	Total[a]	Mean[b]	%
Vaccine transport, storage, water and cups	45,128	1.56	18.7
International transport of vaccine[c]	19,803	0.68	8.2
Purchase of cups and international transport[d]	9,326	0.32	3.9
Purchase of bottled water[e]	4,628	0.16	1.9
Storage and local transport of vaccines, cups and water[f]	11,370	0.39	4.7
International consultants[g]	108,432	3.74	44.9
Compensation, travel	108,432	3.74	44.9
Training	9,461	0.33	3.9
Training vaccinators	5,803	0.20	2.4
Training social mobilizers	3,658	0.13	1.5
Staff allowances	*2,090*	*0.07*	*0.9*
Staff transport	*290*	*0.01*	*0.1*
Material	*642*	*0.02*	*0.3*
Refreshment	*527*	*0.02*	*0.2*
Venue	*108*	*0.00*	*0.0*
Implementation	78,270	2.70	32.4
Vaccination	66,054	2.28	27.4
Staff allowances	*33,047*	*1.14*	*13.7*
Staff transport	*7,104*	*0.25*	*2.9*
Material	*25,552*	*0.88*	*10.6*
Communication	*351*	*0.01*	*0.1*
Social mobilization[h]	12,217	0.42	5.1
Total	241,291	8.32	100.0

[a]Total delivery costs (2009 USD) to vaccinate a target population of 49,980 people; [b]Mean delivery costs (2009 USD) per fully immunized individual based on actual coverage (58.0%); [c]Vaccine transported from Stockholm, Sweden; [d]Disposable paper cups purchased at a price of 8 US cents and transported from Shanghai, China; [e]15,000 liters of drinking water procured from a local agent in 1.5 liter plastic bottles at TZS 600 (USD 0.5) per bottle; [f]Costs for storage of vaccines, cups and water at the medical store department including cold room facilities and generator maintenance and transport to vaccination posts; [g]Involvement of two international consultants; [h]Includes material (T-shirts, posters, leaflets, banners, radio/TV programs) and staff costs

Table 9-3: Key outcomes from model of mass oral cholera vaccination (societal perspective) in Zanzibar, 2009[a]

	No vaccination	Vaccination	Difference
Cholera burden			
Annual number of cases	30	7	23
Annual number of deaths	0.26	0.06	0.20
Annual number of YLD averted			0.02
Annual number of YLL averted			3.08
Annual number of DALY averted			3.10
Total number of DALY averted over duration of protection			8.78
Costs of outcome indicators, 2009 USD			
Annual costs of vaccination program[b]	0	371,850	-371,850
Annual public costs of illness	1,968	453	1,515
Private costs of illness (direct)	370	85	285
Annual costs of treatment and vaccination program	2,338	372,388	-370,049
Costs per death averted with vaccine		1,888,555	
Costs per case averted with vaccine		16,260	
Costs per DALY averted with vaccine		119,828	
Incremental costs and cost-effectiveness ratios (ICER), 2009 USD			
Incremental costs[c]			370,049
ICER (death): Incremental costs/death averted			1,876,696
ICER (case): Incremental costs/case averted			16,158
ICER (DALY): Incremental costs/DALY averted			119,247

[a]Base-case results from population of 50,000, with 3% annual discounting of effects; [b]Excluding costs for international consultants; [c]Costs of vaccination program minus public and private COI averted by vaccination (cost savings); YLD: Years of life lived with disability, YLL: Years of life lost, DALY: Disability-adjusted life-year, ICER: Incremental cost-effectiveness ratio

9.2 EMIC interview for cultural epidemiological study of cholera

OCV SEB Study: Explanatory Model Interview Catalogue (EMIC)

Survey Phase: 1, Study Level: IV
Ministry of Health and Social Welfare of Zanzibar,
in collaboration with
World Health Organization, Geneva, and Swiss Tropical Institute, Basel

English Version of 27/06/2008 (Final)

Date interview (dd-mm-yyyy)	

EMIC ID (1-X-yyy) *X: 1=Unguja, 2=Pemba*	1-____-____ ____ ___

General information

Tick appropriate:

Sex	*1* F	*2* M

Approximate age (years)	

Tick one only:

Site	*1* Unguja	*2* Pemba
Pregnant	*1* Yes	*2* No

Introduction

Thank you for letting me speak with you today. I will be asking you questions about health problems that could affect people in your community. You may recognize these conditions, or they may be unfamiliar. In either case I would like to understand your ideas about it. Your answers and thoughts will help us to assist people who have these problems. But first, a few questions about your background.

Socioeconomic and demographic information

1. Marital status

Tick one only:

1 Sijawahi kuoa au kuolewa *Never married*	*2* Nimeoa au nimeolewa *Married*	*3* Nimetengana *Separated*	*4* Nimeachik a *Divorced*	*5* Tunaishi pamoja *Living together*	*6* Nimefiliwa na mume au mke *Widowed*	*7* Siwezi kusema *Cannot say*

2. Household size

Idadi ya watu unaishi nao *Number of people living in the household* ☐

3. Children living in the household

Enter 0 when answer is none for a given category:

Idadia ya watoto *Number of children*	Chini ya miaka 5 *< 5 yrs*	Miaka 5 mpaka 10 *5-10 yrs*	Miaka 10 mpaka 17 *10-17 yrs*
Wavulana *Boys*			
Wasichana *Girls*			

4. Relationship with household head

Tick one only:

1 Mwenyewe *Self*	*2* Mke/mume *Spouse*	*3* Wazazi *Parent*	*4* Ndugu *Sibling*	*5* Mtoto *Offspring*	*6* Uhusiano mwingine *Other specify:*

Tick sex of household head:

Sex	*1* F	*2* M

5. Main occupational status

Tick one only:

1 Kilimo *Agriculture*	*2* Uvuvi *Fishing*	*3* Nimejiajiri *Self-employment (not 1&2)*	*4* Kuajiriwa rasmi *Formally employed*	*5* Mama wa nyumbani *Housewife*
6 Mfanyakazi wa nyumbani *Housemaid*	*7* Kibarua *Casual labourer*	*8* Mwanafunzi *Student*	*9* Sifanji kazi/nimestaafu *Not active/retired*	*10* Mengine, eleza *Other specify:*

6. Education

Tick highest achieved level only:

1 Sijasoma *No education*	*2* Madrassa ya Koran *Koranic school*	*3* Elimu ya msingi *Primary school*	*4* Elimu ya sekondari *Secondary school*	*5* Elimu amali *Vocational school*	*6* Elimu juu *Higher education*

7. Years of education

☐ Siwezi kusema *Cannot say* ☐

8. Religion

Tick one only:

1 Mwislamu *Muslim*	*2* Mkristo *Christian*	*3* Mengine, eleza *Other specify:*	*4* Sielezi *Undisclosed*

9. Nationality

Tick one only:

1 Mtanzania *Tanzanian*	*2* Raia wa nchi nyingine, eleza *Other specify:*

10. Is your household income usually reliable (and dependable)?

Tick one only, not disclosed means uncertain:

Ndio *Yes 3*	Labda *Possibly 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

If "yes" or "possibly", enquire further, otherwise go to Q 12:

11. What main sources of income are there in your household?

Narrative: _____

Tick all that apply:

Sources of income	Own	Others
1 Kuajiriwa kwa mshahara *Employment for cash*		
2 Kuajiriwa kwa namna nyingine *Employment in kind*		
3 Kujiajiri mwenyewe katika sekta yoyote isiyo ya kilimo *Non-farm self-employment*		
4 Kuuza mayao ya kilimo *Selling agricultural produce*		
5 Kuuza samaki na mazao ya baharini *Selling fish and seafood*		
6 Kukodisha (nyumba, shamba, duka) *Rent*		
7 Msaada kututoka nje *Remittances (money sent from outside)*		
8 Pensheni *Pension*		
98 Nyinginezo, eleza *Other specify:* /		
99 Siwezi kusema *Cannot say*		

12. How much money did you make during the last month on your own? And what about your spouse and other household members?

Narrative: _____

Query for items not mentioned, clarify if needed. If there is no income, enter 0 in TSh column. If respondent is widowed, then tick "cannot say" for category 2:

Monthly income	TSh		
1 Chake mwenyewe *Own*		Siwezi kusema *Cannot say*	
2 Cha mume/mke wake *Spouse*		Siwezi kusema *Cannot say*	
3 Cha watu wengine wanaoishi katika nyumba hii hii *Additional household income*		Siwezi kusema *Cannot say*	

Introduction to vignettes

I appreciate your willingness to talk to me about a few health problems that affect people in your community. I want to understand how you think about it. It is your ideas that I am interested in so please don't feel shy to tell me your personal opinion. I will tell you two different stories about persons who are having a particular problem.

Vignette A

Let me tell you the story about this [person]...

13. What is the name of this disease?

Specify name, summary term or short description in his/her own words. If 'other', specify term and explain here:

Narrative: _____

Types of diarrhoea	
1 Kuharisha kawaida *Normal diarrhoea*	*5* Kipindupindu *Cholera*
2 Kuharisha maji *Watery diarrhoea*	*6* Mchanganyiko *Multiple*
3 Kuharisha marenda *Mucous diarrhoea*	*98* Mengineyo, eleza *Other, specify*:
4 Kuharisha damu *Bloody diarrhoea*	*99* Siwezi kusema *Cannot say*

Code the name from the above numbered list: ☐

Use the name as identified for this disease instead of referring to disease/problem and use the name of the person mentioned in the vignette in the following questions.

14. Can you think of any other symptoms that this [person] is likely to experience besides the ones we already mentioned?

Summarize the respondent's account of problem in his/her own words:

Spontaneous narrative: _____

Based on the respondent's account tick problems which are mentioned under the Spon *column indicating a* spontaneous *response to the open-ended question above. Continue by probing for any categories not yet mentioned and tick them in the* Prob *column, indicating a* probed *response to screening. Make a cross when "no" or "cannot say" was the reply to probed categories. Shaded cells must not be probed.*

Physical symptoms	**Spon**	**Prob**		**Spon**	**Prob**
1 Kusokotwa na tumbo *Abdominal cramps*			*13* Kunyauka, kukauka ngozi *Skin (loose, dry, shrivelled)*		
2 Kuumwa na tumbo *Abdominal pain/discomfort*			*14* Kutokuwa na hamu ya kula *Loss of appetite*		
3 Kuumwa na misuli *Muscle cramps*			*15* Maumiva ya kitchwa *Headache*		
4 Kutapika *Vomiting*			*16* Kichefuchefu *Nausea*		
5 Choo kingi kupita kiasi *Large amounts of stool*			*17* Homa *Fever*		
6 Kuharisha mara kwa mara *Frequent passing of stool*			*18* Udhaifu *Weakness*		
7 Choo kama maji ya mchele *Rice water-like stool*			*19* Kupaparikwa na moyo *Palpitations*		
8 Choo chenye usaha *Pus in stool*			*20* Fadhaisha *Confusion*		
9 Choo chenye damu *Bloody stool*			*21* Kupoteza fahamu *Unconsciousness*		
10 Maumivu sehemu ya kunyea *Rectal pain*			*98* Dalili nyingine mwilini *Other physical symptoms*		
11 Kiu kali *Very thirsty*			*99* Siwezi kusema *Cannot say*		
12 Macho kuingia ndani *Sunken eyes*					

Probed narrative: _____

If respondent has mentioned more than one category, enquire further, otherwise go to Q 16:

15. Among all these symptoms which one do you consider the single most troubling?

Narrative: _____

Code the most troubling category from the above numbered list of patterns of distress: ☐

16. How do you think that this [disease] will affect [this person] emotionally, socially and financially in his/her daily life?

Summarize the respondent's account of problem in his/her own words:

Spontaneous narrative: _____

Based on the respondent's account tick problems which are mentioned under the Spon *column indicating a* spontaneous *response to the open-ended questions above. Continue by probing for any categories not yet mentioned and tick them in the* Prob *column, indicating a* probed *response to screening. Make a cross when "no" or "cannot say" was the reply to probed categories.*

Impact	**Spon**	**Prob**		**Spon**	**Prob**
Social impact			*Emotional impact*		
1 Kutengwa na watu wengine *Isolation from others*			*6* Huzuni, kukosa raha, wasiwasi *Sadness, anxiety, worry*		
2 Woga wa kuambukiza wengine *Fear of infecting others*			*Financial impact*		
3 Kusitisha huduma za afya *Disruption of health services*			*7* Kuongezeka kwa gharama za maisha *Costs (transportation, foods, drugs)*		
4 Kuathiri shudhuli za kila siku *Interference with work/daily activities*			*8* Kupoteza kipato cha familia *Loss of family income*		
5 Kuathiri uhusiano na watu wengine katika jamii *Interference with social relationships*			*Miscellaneous*		
			98 Mengine, eleza *Other, specify:*		
			99 Siwezi kusema *Cannot say*		

Probed narrative: _____

If respondent has mentioned more than one category, enquire further, otherwise go to Q 18:

17. Which of these problems that you have mentioned do you consider the single most troubling?

Narrative: _____

Code the most troubling category from the above numbered list of impacts: ☐

18. How serious is this [disease] for [this person]?

Tick one only:

Mbaya sana *Very serious 3*	Mbaya kiasi *Moderately serious 2*	Haitabiriki *Uncertain 1*	Si mbaya *Not serious 0*

Narrative: _____

19. What is the most likely health outcome of this [disease] for [this person] without appropriate treatment from outside?

Tick one only:

Kifo *Usually fatal 4*	Wakati mwingine inaweza kusababisha kifo *Sometimes fatal 3*	Hali mbaya sana, lakini haisababishi kifo *Serious but not fatal 2*	Haitabiriki *Uncertain 1*	Kupona vizuri na haraka *Full/quick recovery 0*

Narrative: _____

20. Have you or somebody else in your household ever had this [disease]?

Tick one only:

Ndio *Yes 3*	Inawezekana *Possibly 2*	Hakuna hakika *Uncertain 1*	Hapana *No 0*

Narrative: _____

If yes *or* possibly, *enquire further otherwise go to Q 22:*

21. Who was that?

Tick all that apply:

1 Mimi mwenyewe *Self*	*2* Mke/Mume *Spouse*	*3* Wazazi *Parent*	*4* Watoto *Children*	*5* Dada/kaka/mdogo wangu *Sibling*	*6* Watu wengine wanaoishi ndani ya nyumba hii *Other household member*	*99* Siwezi kusema *Cannot say*

Narrative: _____

22. In general, who is most likely to get this [disease]? Is it men or women? Adults or children? Rich or poor people?

Enquire about the following categories if not clear from response and tick all that apply:

Jinsia *Sex*	*1* Wanaume *Men*	*2* Wanawake *Women*	*3* Si yeyote *Neither*
Umri *Age*	*1* Watu wazima *Adults*	*2* Watoto *Children*	*3* Si wowote *Neither*
Hali ya maisha *Social class*	*1* Matajiri *Rich*	*2* Watu masikini *Poor*	*3* Si yoyote *Neither*

Narrative: _____

23. Each of us may explain something that happens in various ways. What do you think has caused this [person]'s problem?

Summarize the respondent's ideas about causes in his/her own words:

Narrative: _____

Based on the respondent's account tick perceived causes in the Spon *column indicating a* spontaneous *response to the open-ended question above. Continue by probing for any category not yet mentioned and tick them in the* Prob *column, indicating a* probed *response to screening. Make a cross when "no" or "cannot say" was the reply to probed categories.*

Perceived causes	**Spon**	**Prob**		**Spon**	**Prob**
Ingestion			*8* Nzi *Flies*		
1 Kunywa maji machafu *Drinking contaminated water*			*9* Malaria		
2 Chakula ambacho hakijahifadhiwa/kimeoza *Unprotected/spoiled food (biological)*			*10* Minyoo *Worms*		
3 Chakula kilichokatazwa *Forbidden food (taboo)*			*Magico-religious causes*		
4 Kula udongo *Eating Soil*			*11* Uchawi *Witchcraft*		
Behaviour			*12* Rehema ya *Mungu God's will*		
5 Kugusa maji machafu *Contact with contaminated water*			*Miscellaneous*		
6 Kutoosha mikono *Not washing hands*			*98* Mengine, eleza *Other, specify:*		
Environment			*99* Siwezi kusema *Cannot say*		
7 Mazingira machafu *Dirty environment*					

Probed narrative: _____

If respondent has mentioned more than one category, enquire further, otherwise go to Q 25:

24. Which one of these causes that you have mentioned do you consider the main cause?

Narrative: _____

Code the most important category from the above numbered list of perceived causes: ☐

25. What do people do at home for a [person] with this [disease] before looking for treatment or help outside their homes?

Summarize the respondent's account of home-based treatment in his/her own words:

Spontaneous narrative: _____

Based on the respondent's account tick home-based treatment categories in the Spon *column indicating a* spontaneous *response to the open-ended question above. Continue by probing for any home-based treatment categories not yet mentioned and tick them in the* Prob *column, indicating a* probed *response to screening. Make a cross when "no" or "cannot say" was the reply to probed categories.*

Home-based treatment	**Spon**	**Prob**
1 Kunywa maji mengi au vinywaji vingine *Drinking more water or liquids*		
2 Dawa za mitishamba (mizizi, magamba, majani) *Herbal treatment (roots, bark, leaves)*		
3 Kunywa dawa za vipaketi (ORS) zinazouzwa madukani *Oral rehydration therapy*		
4 Kuomba dua *Prayers*		
5 Kutumia dawa za antibiotics za kujinunulia mwenyewe *Self-administered antibiotics/drugs*		
6 Hapana *Nothing*		
98 Mengine, eleza *Other, specify:*		
99 Siwezi kusema *Cannot say*		

Probed narrative: _____

If respondent has mentioned more than one category, enquire further, otherwise go to Q 27:

26. Which one of all these things people do at home do you think is likely to be most helpful?

Narrative: _____

Code the most helpful category from the above numbered list of home-based treatments: ☐

27. Where will this person usually go for treatment outside his/her home?

Summarize the respondent's account of outside treatment in his/her own words:

Spontaneous narrative: _____

Based on the respondent's account tick outside treatment categories in the Spon *column indicating a* spontaneous *response to the open-ended question above. Continue by probing for any outside treatment categories not yet mentioned and tick them in the* Prob *column, indicating a* probed *response to screening. Make a cross when "no" or "cannot say" was the reply to probed categories.*

Outside treatment	**Spon**	**Prob**
1 Hospitali *Health facilities*		
2 Waganga wa kienyeji *Traditional healers*		
3 Maduka ya madawa *Pharmacy or over-the-counter drugs*		
4 Viongozi vya dini *Faith healers (Imams, Sheikh)*		
5 Ushauri kutoka kwa ndugu/jamaa na marafiki wanaofanya kazi vituo vya afya *Informal help from health-worker, friend/relative*		
98 Sehemu nyinginezo, eleza *Other, specify:*		
99 Siwezi kueleza *Cannot say*		

Probed narrative: _____

If respondent has mentioned more than one category, enquire further, otherwise go to Q 29:

28. Which one of these people they might consult do you think is most helpful?

Narrative: _____

Code the most helpful category from the above numbered list of outside treatments: ☐

29. Do you think [this person] should not disclose [this disease] beyond his/her closest family?

Tick one only:

Ndio *Yes 3*	Labda/mchanganyiko *Possible/mixed 2*	Haijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

30. If they knew, do you think some people might make [this person] feel ashamed or embarrassed because of [this disease]?

Tick one only:

Ndio *Yes 3*	Labda/mchanganyiko *Possible/mixed 2*	Haijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

31. Would others finding out about [this disease] cause problems for [this person]?

Tick one only:

Ndio *Yes 3*	Labda/mchanganyiko *Possible/mixed 2*	Haijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

32. Would others finding out about [this disease] cause problems for the family of [this person]?

Tick one only:

Ndio *Yes 3*	Labda/mchanganyiko *Possible/mixed 2*	Haijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

33. Might there be someone in the household who would hesitate to bring [this person] to treatment because they did not want the [disease] to be known?

Tick one only:

Ndio *Yes 3*	Labda/mchanganyiko *Possible/mixed 2*	Haijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

34. Is it likely that others outside the family finding out about [this disease] would be helpful to [this person]?"

Tick one only:

Ndio *Yes 0*	Labda/mchanganyiko *Possible/mixed 1*	Haijulikani *Uncertain 2*	Hapana *No 3*

Narrative: _____

35. What can be done to prevent this [disease]?

Summarize the respondent's account of prevention options in his/her own words:

Spontaneous narrative: _____

Based on the respondent's account tick prevention categories in the Spon *column indicating a* spontaneous *response to the open-ended question above. Continue by probing for any prevention categories not yet mentioned and tick them in the* Prob *column, indicating a* probed *response to screening. Make a cross when "no" or "cannot say" was the reply to probed categories.*

Prevention	Spon	Prob
1 Kuosha mikono *Wash hands*		
2 Maji yaliyochemshwa au yenye dawa *Safe water*		
3 Chakula safi na salama *Clean/safe food*		
4 Utupaji na uwekaji wa takataka vizuri *Safe disposal of garbage*		
5 Uhifadhi wa kinyesi vizuri *Safe disposal of stool*		
6 Dawa za kinga *Preventive drugs*		
7 Chanjo *Vaccines*		
8 Elimu ya afya *Health education*		
98 Mengine, eleza *Other, specify:*		
99 Siwezi kusema/hapana *Cannot say/Nothing*		

Probed narrative: _____

If respondent has mentioned more than one category, enquire further, otherwise go to Q37:

36. Which one of these ways of prevention do you think is most useful?

Narrative: _____

Code the most useful way from the above numbered list of preventive measures: ☐

Vaccines

37. Have you or anyone in your household received any type of vaccine?

Tick one only:

Ndio *Yes 3*	Labda *Possibly 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

If "yes" or "possibly", enquire further, otherwise go to Q 39:

38. Who got it?

Tick all that apply:

1 Mimi mwenyewe *Self*	*2* Watoto *Children*	*3* Watu wazima wanaokaa nyumba hii *Adults in household*

Narrative: _____

39. Based on your experience, do you think vaccines are generally helpful?

Tick one only:

Ndio *Yes 3*	Wakati mwingine *Sometimes 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

40. Do you think some vaccines are also likely to cause problems?

Tick one only:

Ndio *Yes 3*	Labda *Possibly 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

If "yes" or "possibly", enquire further, otherwise go to Q 42:

41. Please tell me about that.

Tick all that apply:

Problems caused by vaccines	Tick
1 Kuvimba/maumivu sehemu iliyochomwa sindano *Pain/swelling at injection site*	
2 Homa *Fever*	
3 Majipu/kidonda *Infection/abscess*	
4 Kovu *Scar*	
5 Mtoto kulia sana *Crying baby*	
98 Mengine, eleza *Other, specify:*	

Narrative: _____

42. If a vaccine that you swallow becomes available to prevent cholera, would you take it if it was made available without charge?

Tick one only:

Ndio *Yes 3*	Labda *Possibly 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

If "yes" or "possibly", enquire further, otherwise go to next vignette.

43. If the vaccine were to cost 1,000 TSh would you still take it?

Tick one only:

Ndio *Yes 3*	Labda *Possibly 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

If "yes" or "possibly", enquire further, otherwise go to next vignette.

44. If the vaccine were to cost 5,000 TSh would you still take it?

Tick one only:

Ndio *Yes 3*	Labda *Possibly 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

If "yes" or "possibly", enquire further, otherwise go to next vignette.

45. If the vaccine were to cost 10,000 TSh would you still take it?

Tick one only:

Ndio *Yes 3*	Labda *Possibly 2*	Hakijulikani *Uncertain 1*	Hapana *No 0*

Narrative: _____

Vignette B

Let me tell you the story about this [person]...

46. What is the name of this disease?

Specify name, summary term or short description in the respondent's own words. If 'other', specify term and explain here:

Narrative: _____

Types of diarrhoea	
1 Kuharisha kawaida *Normal diarrhoea*	*5* Kipindupindu *Cholera*

Types of diarrhoea	
2 Kuharisha maji *Watery diarrhoea*	*6* Mchanganyiko *Multiple*
3 Kuharisha marenda *Mucous diarrhoea*	*98* Mengineyo, eleza *Other, specify*:
4 Kuharisha damu *Bloody diarrhoea*	*99* Siwezi kusema *Cannot say*

Code the name from the above numbered list: ☐

Use the name as identified for this disease instead of referring to disease/problem and use the name of the person mentioned in the vignette in the following questions.

47. Can you think of any other symptoms that this [person] is likely to experience besides the ones we already mentioned?

Narrative: _____

Tick all that apply:

Physical symptoms	Tick		Tick
1 Kusokotwa na tumbo *Abdominal cramps*	■	*13* Kunyauka, kukauka ngozi *Skin (loose, dry, shrivelled)*	
2 Kuumwa na tumbo *Abdominal pain/discomfort*		*14* Kutokuwa na hamu ya kula *Loss of appetite*	
3 Kuumwa na misuli *Muscle cramps*		*15* Maumiva ya kitchwa *Headache*	
4 Kutapika *Vomiting*		*16* Kichefuchefu *Nausea*	
5 Choo kingi kupita kiasi *Large amounts of stool*		*17* Homa *Fever*	■
6 Kuharisha mara kwa mara *Frequent passing of stool*		*18* Udhaifu *Weakness*	
7 Choo kama maji ya mchele *Rice water-like stool*		*19* Kupaparikwa na moyo *Palpitations*	
8 Choo chenye usaha *Pus in stool*	■	*20* Fadhaisha *Confusion*	
9 Choo chenye damu *Bloody stool*	■	*21* Kupoteza fahamu *Unconsciousness*	
10 Maumivu sehemu ya kunyea *Rectal pain*	■	*98* Dalili nyingine mwilini *Other physical symptoms*	
11 Kiu kali *Very thirsty*		*99* Siwezi kusema *Cannot say*	
12 Macho kuingia ndani *Sunken eyes*			

48. How do you think that this [disease] will affect [this person] emotionally, socially and financially in his/her daily life?

Narrative: _____

Tick all that apply:

Impact	Tick		Tick
Social impact		*Emotional impact*	
1 Kutengwa na watu wengine *Isolation from others*		*6* Huzuni, kukosa raha, wasiwasi *Sadness, anxiety, worry*	
2 Woga wa kuambukiza wengine *Fear of infecting others*		*Financial impact*	
3 Kusitisha huduma za afya *Disruption of health services*		*7* Kuongezeka kwa gharama za maisha *Costs (transportation, foods, drugs)*	
4 Kuathiri shudhuli za kila siku *Interference with work/daily activities*		*8* Kupoteza kipato cha familia *Loss of family income*	
5 Kuathiri uhusiano na watu wengine katika jamii *Interference with social relationships*		*Miscellaneous*	
		98 Mengine, eleza *Other, specify:*	
		99 Siwezi kusema *Cannot say*	

49. How serious is this [disease] for [this person]?

Tick one only:

Mbaya sana *Very serious 3*	Mbaya kiasi *Moderately serious 2*	Haitabiriki *Uncertain 1*	Si mbaya *Not serious 0*

Narrative: _____

50. What is the most likely health outcome of this [disease] for [this person] without appropriate treatment from outside?

Tick one only:

Kifo *Usually fatal 4*	Wakati mwingine inaweza kusababisha kifo *Sometimes fatal 3*	Hali mbaya sana, lakini haisababishi kifo *Serious but not fatal 2*	Haitabiriki *Uncertain 1*	Kupona vizuri na haraka *Full/quick recovery 0*

Narrative: _____

51. Each of us may explain something that happens in various ways. What do you think has caused this [person]'s problem?

Narrative: _____

Tick all that apply:

Perceived causes	**Tick**		**Tick**
Ingestion		*8* Nzi *Flies*	
1 Kunywa maji machafu *Drinking contaminated water*		*9* Malaria	
2 Chakula ambacho hakijahifadhiwa/kimeoza *Unprotected/spoiled food (biological)*		*10* Minyoo *Worms*	
3 Chakula kilichokatazwa *Forbidden food (taboo)*		*Magico-religious causes*	
4 Kula udongo *Eating Soil*		*11* Uchawi *Witchcraft*	
Behaviour		*12* Rehema ya *Mungu God's will*	
5 Kugusa maji machafu *Contact with contaminated water*		*Miscellaneous*	
6 Kutoosha mikono *Not washing hands*		*98* Mengine, eleza *Other, specify:*	
Environment		*99* Siwezi kusema *Cannot say*	
7 Mazingira machafu *Dirty environment*			

52. What do people do at home for a [person] with this [disease] before looking for treatment or help outside their homes?

Narrative: _____

Tick all that apply:

Home-based treatment	**Tick**
1 Kunywa maji mengi au vinywaji vingine *Drinking more water or liquids*	
2 Dawa za mitishamba (mizizi, magamba, majani) *Herbal treatment (roots, bark, leaves)*	
3 Kunywa dawa za vipaketi (ORS) zinazouzwa madukani *Oral rehydration therapy*	
4 Kuomba dua *Prayers*	
5 Kutumia dawa za antibiotics za kujinunulia mwenyewe *Self-administered antibiotics/drugs*	
6 Hapana *Nothing*	
98 Mengine, eleza *Other, specify:*	
99 Siwezi kusema *Cannot say*	

53. Where will [this person] usually go for treatment outside his/her home?

Narrative: _____

Tick all that apply:

Outside treatment	**Tick**
1 Hospitali *Health facilities*	

2	Waganga wa kienyeji *Traditional healers*	
3	Maduka ya madawa *Pharmacy or over-the-counter drugs*	
4	Viongozi vya dini *Faith healers (Imams, Sheikh)*	
5	Ushauri kutoka kwa ndugu/jamaa na marafiki wanaofanya kazi vituo vya afya *Informal help from health-worker, friend/relative*	
98	Sehemu nyinginezo, eleza *Other, specify:*	
99	Siwezi kueleza *Cannot say*	

Concluding advice from respondent

Is there anything else you can tell me about the health problems we have discussed or about vaccinations from your experience? Any further comments, advice or suggestions will be appreciated.

Narrative: _____

9.3 Clinical vignettes for community study of cholera and shigellosis

9.3.1 Vignette A—Cholera

Jecha[1] from Chumbuni[2] who is 40 years old did not feel like going to visit his friends one morning last week. All of a sudden he had to run to the latrine. He became more and more concerned after the second and third time of running to the latrine that morning because he was passing lots of stool which looked like rice water. It was as if he were urinating instead of defecating. He also felt very miserable because he was vomiting terribly and the muscles in his arms and legs were very painful.

9.3.2 Vignette B—Shigellosis

When 25-year-old Makame[1] woke up on Monday last week in his house in Chumbuni[2] he was feeling feverish and also had pangs of pain in his belly. He was having a loose stool and when he looked at it he noticed red drops, probably blood, and a whitish substance like pus. He went to the toilet another 3 times that day but he did not feel better afterwards. The day after, he still felt the same urge to go to the toilet many times. But with each time he produced less and less stool although he strained a lot and his anus was painful.

[1]Local people's names were used to make the story sound more familiar to the respondents. The names were always adapted to match the respondent's sex. *Jecha* was the male and *Sharifa* the female name used in the cholera vignette while *Makame* (male) and *Fatma* (female) were featuring in the shigellosis vignette.

[2]*Chumbuni* was used as the community name for Unguja and *Mwambe* for Pemba reflecting the respondents' addresses.