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Electronic consent in a COVID-19 vaccine implementation trial in South Africa: Participant perspectives

The COVID-19 pandemic has warranted modifications to clinical research implementation to ensure adherence to public health and safety measures. Often, this modification has necessitated a deviation from the traditional face-to-face approach to an electronic or hybrid consent process. We assessed the acceptability and preference for electronic consent and explored understanding of the electronic consent information – an outcome which is vital in providing reassurance that consent is provided with full appreciation of the risks and benefits of study participation. In this descriptive study, healthcare professionals (HCPs) were invited, through a database of HCP contacts, snowball sampling and advertisement, to participate in an online survey between 14 July 2021 and 17 September 2021, to explore their experiences of providing electronic consent for enrolment into the largest implementation trial of a COVID vaccine in South Africa (SISONKE Trial). Descriptive analysis was used to characterise respondents and categorical data were expressed as frequencies. The prevalence of recurring responses to open-ended questions allowed for the identification of themes. A total of 1025 HCPs completed the online survey. Access to a COVID-19 vaccine was the strongest motivating factor for enrolment (82.3%) into the SISONKE Trial. Over a third of participants (38.6%) were not able to discuss the study with research staff. While the majority of participants (85.2%) indicated that online consent was acceptable, it was recognised that acceptability was context specific. Although 64% indicated awareness that reporting both a positive COVID test and adverse events were requirements, a significant percentage (32%) did not recall that the reporting period was 2 years. The electronic consent process was easily navigated by educated HCPs with access to electronic devices and data. Vaccine access was the most important motivation for participation, thus raising questions about how voluntary the consent process was and the role of desperation in deciding to participate.

Significance:

- Navigation of the electronic consent process for participation in a COVID-19 vaccine implementation trial is not a challenge for educated healthcare professionals with access to electronic devices and data. However, technical skills and access to technology may impact the integrity of the informed consent process for lay research participants.
- Motivation to join research studies for access to scarce resources impacts negatively on the authenticity of the consent processes, as participation may be informed but not truly voluntary, and is an issue that ethics committees and researchers should address.

Background

The COVID-19 pandemic has negatively impacted the implementation of clinical trials, specifically, and clinical research in general. Research and related operational activities have had to be modified to comply with COVID-19 related public health and safety measures.¹ At the same time, researchers have had to ensure adherence to ethical, legal, scientific and good clinical practice guidelines for clinical research.

Multiple guidelines and publications address the ethical and legal requirements of informed consent.^{2,3} The consent process involves providing information on the research study in question and the implications of participation on the potential volunteer. Implications include the appreciation of risks, obligations and benefits, time, inconvenience and expenses, compensation for possible injury, confidentiality and protection of personal information.^{4,5} Informed consent has rightfully been described as a dynamic process and not a single event.^{6,7} New information that could impact the risk–benefit ratio of the study must be communicated so that an informed decision can be made about ongoing study participation. It is also a requirement that a copy of the signed consent form be made available to the study participant.^{2,8}

Methods of obtaining consent have included traditional face-to-face interactions with signing of a paper consent form, to alternative methods including online consent with an electronic signature and a hybrid method of online/ telephonic discussions followed by the signing of a paper form.⁹ Traditional methods of obtaining consent may not be practical in the setting of implementation or pragmatic clinical trials that are evaluating or comparing different standards of care.⁹ Implementation and pragmatic trials serve to provide information to policymakers on mechanisms to streamline delivery processes of effective health interventions rather than to evaluate the efficacy or safety of the interventions.⁹ Although South African guidelines do not address the use of altered consent, this approach may be used in implementation/pragmatic trials as per guidelines in the USA if the research meets the requirements of minimal risk and does not impact the rights or welfare of participants, if participants will be provided additional information after study procedures are completed, and if obtaining traditional consent is not

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practical.⁸ Logistical reasons alone – such as cost, convenience and need for study implementation to be fast-tracked – are not legitimate reasons for use of altered consent.¹⁰ US Food and Drug Administration regulations allow for use of altered consent in emergency situations in which there is immediate threat to life and an alternative to the test product is not available.¹¹

To assist in understanding of the content of the informed consent form, supplemental material, in the form of interactive exercises, quizzes and links to relevant information, is often used. In studies evaluating user experiences, it has been found, that even when electronic consenting was supplemented with various links to informational material, respondents rarely opted to look at this material.¹²

Research has been undertaken on the perspectives of research ethics committees and researchers on electronic consent processes.^{7,13,14} However, the perspectives of research participants have not been explored in depth, especially in sub-Saharan Africa. A scoping review identified published research on electronic informed consent in North America, Europe, Asia and Oceania, but not from sub-Saharan Africa.¹²

We assessed the preferences, acceptability and understanding of the electronic consent information and process among healthcare professionals (HCPs) from a diverse range of health science disciplines enrolled in a phase 3b COVID-19 vaccine trial (SISONKE) in South Africa between February 2021 and May 2021. The SISONKE Trial was one of the largest ‘implementation’ trials conducted in South Africa, under pandemic conditions and in a context of no vaccine availability for general roll-out.^{15,16} At the time of trial implementation, it was a high-risk study conducted with a vaccine that had only emergency use authorisation in some countries.¹⁷ To date, significant serious or special interest adverse events have been reported.¹⁸ Therefore, an assessment, post-consent, of participants’ motivation to enrol in the trial and their understanding of adverse event reporting requirements is of relevance.

Method

We undertook an independent descriptive survey amongst a sample of healthcare professionals (HCPs) and academics who had enrolled in the SISONKE Trial. Between 14 July 2021 and 17 September 2021, we invited trial enrollees to participate in an online survey on the electronic consent process of the SISONKE Trial. Recruitment of participants was through a database of HCP contacts maintained by the Centre for Medical Ethics and Law (Stellenbosch University), snowball sampling, and advertisement via professional bodies (Colleges of Medicine of South Africa, South African Medical Association, and Independent Practitioner Associations), an academic institution (Stellenbosch University’s Faculty of Medicine and Health Sciences), a public tertiary level teaching hospital (Tygerberg Hospital), and a private hospital group (Mediclinic). A broader sample of HCPs from public and private hospitals and institutions across South Africa were invited via a weekly medical news digest. All HCPs participated in their personal capacities and provided online consent prior to completion of the survey.

Ethics approval was received from Stellenbosch University’s Faculty of Medicine and Health Sciences Health Research Ethics Committee (reference number: N21/06/018_COVID-19) and the research ethics committee of Mediclinic SA (reference: 20210727). Institutional approval was received from Stellenbosch University and the Western Cape Provincial Department of Health.

The design and content of the survey questionnaire were based on a literature review and the researchers’ experience with factors that are likely to influence understanding, acceptability and preference for electronic consent. The survey was created using SUNsurveys Checkbox® 7 Version 2018 Q2. To confirm relevance, validity and reliability, the survey was piloted among seven HCPs and researchers with experience in the design of online surveys and research ethics. The final survey consisted of open and closed questions.

Data analysis

Survey responses were exported to Statistical Package for Social Science (IBM SPSS Statistics 27.0) for analysis. Descriptive analysis

was used to characterise respondents and categorical data were expressed as frequencies. An online proportion calculator was used to calculate 95% confidence intervals using frequencies.

NVivo qualitative data analysis software (QSR International Pty Ltd. Version 12, 2018) was used to analyse the data. The prevalence of recurring responses to open-ended questions allowed for inductive coding and subsequently the identification of themes. During the analysis, two authors independently analysed the data. The generated themes were compared and discussed until consensus was reached. Trustworthiness was achieved by sharing and discussing themes among the study team.

Table 1: Characteristics of survey participants (*n*=1025)

Characteristic	<i>N</i> (%)
Age (years)	
18–29	80 (7.8)
30–39	265 (25.9)
40–49	276 (26.9)
>50	404 (39.4)
Location (province)	
Eastern Cape	18 (1.8)
Free State	23 (2.2)
Gauteng	177 (17.3)
KwaZulu-Natal	89 (8.7)
Limpopo	2 (0.2)
Mpumalanga	11 (1.1)
Northern Cape	6 (0.6)
North West	3 (0.3)
Western Cape	696 (67.9)
Type of healthcare facility/institution	
Public healthcare facility	469 (45.8)
Private healthcare facility	236 (23.0)
Independent practice	53 (5.2)
Academic institution	187 (18.2)
Other	80 (7.8)
Position/role	
Healthcare worker	653 (63.7)
Academic staff	123 (12.0)
Both healthcare worker and academic staff	249 (24.3)
Previous experience as a research participant	
Yes	426 (41.6)
No	599 (58.4)
Previous experience as part of a research team	
Yes	514 (50.1)
No	511 (49.9)

Results

Respondent characteristics

A total of 1025 HCPs completed the online survey. The majority of respondents were younger than 50 years of age (621/1025, 60.6%). Responses were received from all nine provinces of South Africa, with the majority of responses received from the Western Cape (67.9%) followed by Gauteng (17.3%) and KwaZulu-Natal (8.7%) (Table 1).

HCPs comprised 63.7% of the sample, 12% were academics and 24.3% identified as occupying both roles. Half of the respondents reported having been part of a research team previously (Table 1).

Motivation to join the SISONKE Trial

The majority of respondents indicated that they enrolled in the SISONKE Trial to access a COVID-19 vaccine (844/1025, 82.3%), to protect themselves (757/1025, 73.9%) or to prevent inadvertent exposure of family members through themselves (780/1025, 76.1%) to SARS-COV-2. This finding is supported by the following anonymised responses:

Being in the clinical field, it really left no options for not taking the vaccine. It can't really be considered a trial in which we had great choice; we had no choice of the vaccine we could take (would have preferred a mRNA based vaccine) as the government had no clear plan. (PID 1337636)

People consented for fear of losing their lives and were desperate for protection. (PID 1333708)

Very grateful to be included in the trial. (PID 1334644)

A further 65.9% (625/1025) regarded it as a duty to receive a COVID-19 vaccine for the public good, to allow the country to reach herd immunity. Pressure from family members, peers, community members (30/1025, 2.9%), negative impact on employment (25/1025, 2.4%) or positive impact on employment (123/1025, 12%) impacted the decision to participate the least.

Technical enablers or challenges

The majority of respondents used their own electronic devices (961/1025, 93.8%), had Internet/data access (963/1024, 94%) and the technical skills to complete the electronic informed consent process independently (989/1024, 96.5%). Over three quarters (907/1025, 88.5%) agreed that both the electronic consent document and the information leaflet were easily accessible. Whilst 6.7% (69/1024 respondents) indicated that they did not access the consent form at all. Trust and confidence in the research process compensated for difficulty in accessing study related information:

But I could not access/see/find the actual study information or text about the consent. When I tried to go back and search for it I still couldn't see it. But I trusted in the research process. (PID 1337168)

Characteristics of the consent process

In total, over two thirds of respondents (733/1019, 71.9%) indicated that they had thoroughly read the consent document. Access to the consent form and ability to discuss the content of the form or the study procedures prior to providing consent are annotated in Table 2. The lack of opportunity for the majority of SISONKE Trial participants (59.5%) to discuss the consent document with the study staff or doctors is reflected by the following participants' comments:

Information was lacking. I needed vaccine and had no choice as to agree. No consent, no vaccine is the rule. So, I had no choice. (PID 1335027)

Not informed that participation in this vaccine study would exclude me from receiving vaccination as part of the national vaccination

rollout. I am now not eligible to receive the (likely) more effective Pfizer vaccine because I have been 'vaccinated' with an incompletely validated vaccine. I will NEVER participate in such a study again as I believe that this has compromised my ability to optimally protect myself. (PID 1337815)

Three quarters of survey respondents (784/1025, 76.5%) indicated that being able to discuss the study with their colleagues increased the acceptability of the electronic consent process. The majority were aware of and able to access additional study material that impacted the risk-benefit ratio when it was made available, while half read this new information (Table 2).

Some respondents expressed dissatisfaction with the timeliness of or paucity of study updates:

I have received no updates on the preliminary trial findings as a study participant and health worker. I feel that I was used as a participant, but the investigators did not have the courtesy to provide updates on vaccine effectiveness to participants, even as data accumulated on symptomatic infections, hospital admissions and deaths during the third wave. (PID 1336993)

It would be helpful if the trial heads provided feedback from time to time to all Sisonke participants on how the Janssen-J&J vaccine is doing in relation to new variants in the population, e.g., the delta variant seems not to be well-controlled by this vaccine in terms of re-infections and even transmission from such re-infections. (PID 1337013)

Table 2: Access to consent material

	Number (%) of affirmative responses
Able to print or save a copy of the consent form	166/280 (59.3)
Able to access a copy of the consent form at a later time	89/175 (50.9)
Able to access a copy to discuss with own doctor or family	134/384 (34.9)
Able to discuss concerns with study doctor or other study staff	270/666 (40.5)
Received SMS notification of availability of new study information related to change in risk/benefit assessment	680/1025 (66.3)
Easily accessed the online new information	607/680 (59.1)
Read the new information	510/680 (49.8)

Acceptability, preference and understanding

Acceptability

The majority (873/1025, 85.2%) [95% CI: 83, 87.3] indicated that online consent was acceptable while 5.5% thought it was not (56/1025) [95% CI: 4.1, 6.9] and 9.4% opted to provide a neutral response (96/1025) [95% CI: 7.6, 11.1].

An overwhelming majority of respondents to this survey indicated that online consent was acceptable and commented on some of the advantages:

I can read through the information in my own time, and I don't feel obliged to participate in order not to disappoint the person taking the informed consent. I can think as long as I want, 'Google'



aspects of care, ask opinions from friends and formulate questions. I can re-read the information as many times as I want. (PID 1337857)

Online consent was appropriate in this case due to the nature of Covid-19 and reducing contact with people and can accommodate the big numbers and spread across the whole country easily. (PID 1337410)

Others recommended a hybrid process or that other printed or audiovisual material be used to strengthen the online consent process:

Online consent must be preceded with printed pamphlets regarding the trial to allow better decision making. (PID 1337294)

The consent form was very long and most people I know did not read it page for page. Perhaps if consent is read aloud in a video it would lead to better uptake. (PID 1338552)

Over 90% (930/1025, 90.7%) of participants were confident that the personal information shared as part of providing consent would remain confidential.

Preference

When asked if online consent should be implemented rather than face-to-face consent, even if the possibility of adverse events was high, less than half (447/1025, 43.6%) [95% CI: 40.6, 46.6] agreed. A slightly lower number thought that consent should not be obtained online if risk of adverse events was high (330/1025, 32.2%) [95% CI: 29.3, 35.1], while approximately one quarter were neutral (248/1025, 24.2%) [95% CI: 21.6, 26.8].

Online consent is acceptable for minimal risk research such as questionnaires. I feel that for all other research, especially including participants who do not have a research and/or medical background, face to face and in depth discussion is non-negotiable. (PID 1337963)

Understanding

One quarter of respondents were aware of the expected duration of study participation of 2 years (256/1025, 25%); while 90% (923/1025) [95% CI: 88.2, 91.9] understood that that they were required to report side effects, fewer participants were aware of the reporting duration (221/923, 23.9%) [95% CI: 21.2, 26.7]. Of the 37.6% of respondents who believed they experienced side effects, 16.5% indicated that they did not remember to report side effects while a further 3.1% logged a report only when reminded to do so. In comparison to reporting side effects, fewer participants were aware of the requirement to report a positive COVID test (685/1024, 66.8%) [95% CI: 64.0, 69.8] and a similar number (659/1024, 64.4%) [95% CI 61.4, 67.3] understood that reporting both a positive COVID test and adverse events was a requirement. About two thirds of participants (634/1025, 61.9%) [95% CI: 58.9, 64.8] were aware of the overall efficacy in preventing any infection and efficacy in preventing severe infection of the SARS-COV-2 vaccine dispensed in the SISONKE Trial.

While the majority of participants were aware of their obligations to report adverse events, some experienced challenges when attempting to log reports:

My wife developed severe side effects from the vaccine but there was no avenue to report. (PID 1336930)

Colleagues who had vaccine adverse effects were initially unable to register complaints at Sisonke site – no one picked up phone or took the issue seriously initially. (PID 1334487)

A clear portal to report adverse events was not available/frustrating. The Sisonke hotline was very regularly jammed/overcrowded. I would have found a link to report symptoms/positive covid tests very helpful. (PID 1338552)

Respondents recognised that acceptability and understanding were context specific, as borne out by the following comments:

Online consent is a good idea when dealing with educated and affluent study participants (like the health workers in this study). I don't think it would be adequate if the study involved uneducated and poverty-stricken participants as there would be problems with understanding the information clearly (especially potential negative effects). (PID 1338018)

Online consent should only be done if level of education allows. Participants should be educated (at least gr12 education level) and researchers need to verify the level of computer literacy. (PID 1340990)

The target group for J&J vaccine was mostly highly knowledgeable. They can access information for themselves, and I think many made informed decisions. However, the low income employees such as cleaners and other low levels of education staff may have not understood and could have benefitted from face to face consent. (PID1337344)

Discussion

While the informed consent document and information leaflet were easily accessible by the majority of participants, and electronic literacy, access to and confidence with use of technology was not a deterrent, approximately 28% of respondents indicated that they had not read the consent information completely. A survey of electronic/online consent among healthcare workers in the UK demonstrated similar results, with 33% indicating that they had not read all of the consent information.⁷ Enrolling in the SISONKE Trial without reading the consent material in its entirety could be related to several factors, including motivation for enrolling in the trial to access a SARS-COV-2 vaccine, confidence in the research team and the informed consent process, pre-existing knowledge about SARS-COV-2 vaccines, the ability to supplement knowledge gaps through online searches, social media and discussion with knowledgeable HCP colleagues.

Context influences motivation and contributes to decision-making related to trial participation. Over 80% of respondents – many of whom are frontline health workers – were desperate to access any SARS-COV-2 vaccine, even though they may have had preferences, in a setting in which there was no other mechanism of access with the South African government's vaccine roll-out programme not having started. Volunteers expressing their autonomy to participate in clinical trials to access scarce resources or interventions still under investigation is not a new phenomenon and has been a historical mechanism to access scarce treatment resources.¹⁹ This impacts negatively on the authenticity of consent processes as participation may be informed but not truly voluntary.²⁰

As seen in this survey as well, fear of being infected with SARS-COV-2 and desire to protect family members from inadvertent exposure were strong motivating factors for COVID-19 vaccine uptake among employees of a Czech tertiary level hospital.²¹

A large proportion of respondents in this survey also appreciated the urgency to increase vaccine uptake in the public interest. Pressure from peers, the community and employers was not a significant motivating factor; this finding could be attributable to the survey being conducted prior to poor vaccine uptake among South Africans with the subsequent calls for mandatory vaccination in some sectors.

Other studies have noted that research participants in certain situations would decide to participate in research, even before the consent process, based on trust alone²² or confidence in professional recommendation²³. Participants in the SISONKE Trial may have drawn on their own experiences as HCPs, academics and researchers when obtaining consent that meets ethical and legal requirements and this may have increased acceptability.

Three quarters of respondents indicated that being able to discuss the study with colleagues increased online consent acceptability and this is consistent with findings from the UK study of healthcare workers.⁷ However, there is the risk of independent decision-making being influenced by strong opinions of colleagues and others in positions of authority, such as managers within the clinical work space.²⁴

Among other factors, a review of current practice for use of e-consenting, identified the use of hyperlinks to digital media and websites to provide more information useful in engaging users and enhancing comprehension of the consent document.²⁵

As per the Belmont Report, comprehension is one of the three conditions for ensuring that consent is informed; the others being information provision and voluntariness.²⁶ While current good clinical practice guidelines do not require a test of comprehension of the risks and benefits of study participation, it is important to have reassurance that intention to participate is based on sound consideration of all the relevant information, including safety data. At the same time, not trusting the participant's capacity to make an informed choice should be avoided if study participants do not demonstrate comprehension of all aspects of the study but are able to understand key elements and possible risks associated with participation.²

While a test of comprehension as part of the consent process is not mandatory, assessing computer literacy in addition to comprehension of the consent document should be part of the electronic consent process in non-professional populations, and this opinion was expressed by respondents in this study. However, this suggestion raises the challenge of access to various electronic consent platforms and training in the use thereof in developing countries. Costs related to hardware and data access will be prohibitive if not covered by the study budget. Theft of expensive devices and subsequent possible harm to participants located in indigent communities must also be considered. In contrast to South African guidelines, international guidelines stipulate that study participants must have options to provide consent.³ To control for issues related to lack of Internet or e-literacy, printed material should be available. Some study participants may prefer a printed copy which they can refer to while going through the consent process with a member of the research team²², irrespective of whether consent is face to face or via teleconsent. Other material such as pamphlets and audiovisual material should be used to decrease the content in the consent document and enhance understanding.²⁵

Consent to participate in a clinical trial initially, and throughout the duration of the study, is a dynamic ongoing process. In addition to discussions between researcher and participant initially, key elements of the consent form and the study, in addition to new information that changes the risk–benefit ratio or advises of the availability of other therapeutic/preventative options, should be discussed at every study visit by the research team, with the option for the participant to withdraw consent at any time.^{7,27,28} This ongoing process is not only an opportunity to remind participants of key study facts, including requirements for reporting adverse events, but to allay fears around side effects and address myths and misconceptions. Accessibility to the research team – whether face to face or via telephone, video call or teleconference – builds trust in researchers and in the research itself. In the context of high-risk studies, preference for face-to-face consultation with researchers was expressed in this survey, and was a sentiment expressed in other studies as well.^{28–30} However, access to the research team, to provide clarification and reminders to report both adverse events and a positive COVID-19 test, proved challenging for some participants of the SISONKE Trial.

While international guidelines allow for an altered consent process for implementation/pragmatic trials¹⁰ as well as under emergency conditions¹¹, this is not addressed by South African guidelines. These waivers would not have been applicable to the SISONKE Trial as it did not meet the accepted definitions of an implementation or pragmatic trial or complete stipulations for an emergency situation. It is, however, worth noting that multiple research ethics committees in South Africa reviewed the SISONKE protocol and accepted and approved the research team's categorisation of the trial as a pragmatic trial as well as the altered consent process. This raises important questions around how research ethics committee members' training and research ethics guidelines in South Africa incorporate discussion of implementation trials and altered consent processes.

Limitations

This survey was implemented between 2 and 4 months after enrolment in the SISONKE Trial was completed and recall bias may have impacted responses. For South African HCPs at the time, this trial provided the only means of accessing a vaccine to protect themselves and their families against a life-threatening infection. In light of this, factors that influenced the acceptability of the consent process used in the SISONKE Trial may have been of little relevance to trial participants who felt coerced to enrol in the trial to access a vaccine. It is possible that they may have regarded the consent process merely as a means to an end. Therefore, the high acceptability of electronic consent seen in this survey may be inflated. The number of neutral responses received may be attributable to social desirability bias, with survey participants wanting to express their gratitude for access to a vaccine and to avoid being critical of the consent process or SISONKE Trial researchers. The target population of this survey is not representative of the general population who would be enrolled into a clinical trial in South Africa or any other country in sub-Saharan Africa.

Conclusion

Obtaining consent remotely is an invaluable option allowing the possibility of enrolling a large number of study participants quickly and efficiently from scattered geographical locations under conditions that preclude close contact. In the SISONKE Trial, the electronic consent process was easily navigated by educated HCPs with access to electronic devices and data. However, a significant percentage (32%) did not recall that breakthrough infections and adverse events had to be reported for a 2-year period after receiving the vaccine. Vaccine access was the most important motivation for participation, raising questions about how voluntary the consent process was. With the high likelihood of increased transmissibility of the Omicron variant of SARS-COV-2, HCPs find themselves once again in a position of no choice with respect to accessing a second vaccine via the SISONKE booster trial. At the time of writing, although recent policy changes allow for a Pfizer booster shot following one dose of the Johnson & Johnson's vaccine, HCPs who received two doses of the Johnsons & Johnson's vaccine via SISONKE, are currently not able to receive a Pfizer booster.

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Competing interests

We have no competing interests to declare.

Authors' contributions

K.M. conceptualised the study, reviewed and edited the survey instrument and protocol, was involved in participant recruitment and reviewed and edited the manuscript. G.N. developed the content of the survey instrument and the protocol, submitted the protocol for ethics committee reviews, was involved in participant recruitment and led the development



of the manuscript. S.M.K. designed the online survey instrument and was responsible for data capturing. M.M.M.J.A. undertook the data cleaning and analysis. A.E.A.O. contributed to the literature review. M.G.M.C. provided expert advice on statistical analysis. All authors read and approved the final manuscript.

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