Trials

Animated, video entertainment-education to improve vaccine confidence globally during the COVID-19 pandemic: an online randomized controlled experiment with 24,000 participants

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Animated, video entertainment-education to improve vaccine confidence globally during the COVID-19 pandemic: an online randomized controlled experiment with 24,000 participants

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Abstract

Background: Science-driven storytelling and entertainment-education (E-E) media demonstrate potential for promoting improved attitudes and behavioral intent towards health-related practices. Months after the outbreak of coronavirus disease 2019 (COVID-19), emerging research highlights the essential role of interventions to improve public confidence in the COVID-19 vaccine. To improve vaccine confidence, we designed three short, animated videos employing three research-informed pedagogical strategies. These can be distributed globally through social media platforms, because of their wordless and culturally accessible design. However, the effectiveness of short, animated storytelling videos, deploying various pedagogic strategies, needs to be explored across different global regions.

Methods/design: The present study is a multi-site, parallel group, randomized controlled trial (RCT) comparing the effectiveness of (i) a storytelling-instructional-humor approach (ii) a storytelling-analogy approach (iii) a storytelling-emotion-focused approach and (iv) no video. For our primary outcomes, we will measure vaccine hesitancy and for secondary outcomes, we will measure behavioral intent to seek vaccination and hope. Using online platforms, we will recruit 12,000 participants (aged 18-59 years) from the USA and China respectively, yielding a total sample size of 24,000.

Discussion: This trial uses innovative online technology, reliable randomization algorithms, validated survey instruments and list experiments to establish the effectiveness of three short, animated videos employing various research-informed pedagogical strategies. Results will be used to scientifically support the broader distribution of these short, animated video as well as informing the design of future videos for rapid, global public health communication.

Keywords: COVID-19, randomized controlled trial, vaccine hesitancy, vaccine acceptance, protocol, hope, list experiment, vaccine confidence

Trial registration: DRKS #00023650

Administrative information

Title	Animated, video entertainment-education to improve vaccine confidence globally during the COVID-19 pandemic: an online randomized controlled experiment with 24,000 participants
Trial registration	DRKS #00023650
Funding	This study is funded by an Alexander von Humboldt Foundation (Prize recipient: Dr. Till Bärnighausen) and the Sino-German Center for Research Promotion (Project C-0048), which is funded by the German Research Foundation (DFG) and the National Natural Science Foundation of China (NSFC).
Name and contact information for the trial sponsor	https://www.humboldt-foundation.de/en/ https://www.dfg.de/en/dfg_profile/head_office/dfg_abroad/beijing/index.html
Role of sponsor	The funders will have no role in the collection, management, analysis, and interpretation of data; writing of the report or submission decisions.

Background and rationale

In the midst of the COVID-19 pandemic, research highlights the critical role of interventions to increase vaccine confidence, even before vaccines for COVID-19 become universally available.[1, 2] The WHO has dubbed vaccine hesitancy one of the greatest threats to global health[3] yet we are lacking interventions that effectively promote vaccine confidence in ways that are accessible and globally scalable. Many existing interventions have focused on providing information in the form of scientific data, a strategy which has proven ineffective for key target audiences[4].

Designing effective interventions has become even more important during the COVID-19 pandemic as misinformation has spread rapidly around the world.[5] Negative claims about vaccines often appeal to the emotions of the target audiences, eliciting vaccine doubt and hesitancy. This observation – that emotion-focused messages resonate and affect health behaviors[4, 6] – can also potentially be used to the advantage of health communicators. Research suggests that activating positive emotions, like hope and altruism, can actually bolster vaccine education interventions [6].

Other promising pedagogical strategies, including the use of instructional humor [7], analogies [8, 9] and storytelling could also be leveraged to promote vaccine confidence and researchers have advocated for a transdisciplinary approach to successful health communication on vaccines [4]. By integrating different fields of expertise, including those outside of academia - like entertainment and marketing - we may be able to design more effective vaccine promotion

interventions. Animated E-E videos, developed using transdisciplinary approaches, could be an especially effective method for distributing evidence-based health messages globally through social media platforms [10].

To improve vaccine confidence, we designed three videos, employing three research-informed pedagogical strategies: (i) a storytelling-instructional-humor approach (ii) a storytelling-analogy approach (iii) a storytelling-emotion-focused approach.

The first prototype video was released on Stanford Medicine's YouTube channel (https://youtu.be/Ut_6GInouYg) on October 19th, 2020 and was viewed 27,290 times within the first three weeks. This video belongs to a collection of science-driven, storytelling COVID-19 animations that have already reached several million viewers globally. Because all of the videos contain no spoken words, these interventions can be rapidly distributed to global audiences without translation. We believe that such video interventions could play an important role in improving vaccine confidence during the COVID-19 pandemic, but there is a need to evaluate the efficacy of such interventions.

A secondary aim of the intervention videos is to convey hope, a measurable parameter which research suggests is related to improved health, psychosocial and academic outcomes [11]. Recent research even suggests that leveraging positive emotions, including hope, may be leveraged as part of COVID-19 vaccine education interventions [6]. Hope has been defined as the perceived capacity to build pathways towards our goals and motivate ourselves to use those

pathways. Hope theory proposed by Snyder CR [11] has been likened to the theories of optimism, self-efficacy and self-esteem. Especially during the COVID-19 pandemic, a period characterized by widespread emotional distress [12], bolstering hope could have meaningful positive effects on the mental health of the global public.

Despite the potential for short, animated videos to reach the general public globally, through social media, we have yet to systematically evaluate the efficacy of such interventions, including different pedagogical approaches to their design, for: a) reducing vaccine hesitancy, b) increasing behavioral intent to get vaccinated and c) increasing hope. Here, we propose an online experiment in which the video intervention and a survey will be randomly ordered and assigned to 24,000 participants between the age of 18 and 59, living in China or the USA. Results will be used to scientifically support the ongoing distribution of these interventions as well as optimizing the design of future animated, E-E videos for public health communication.

Objective

Our study aims to achieve the following objectives. To:

1. Establish the effectiveness of each of the intervention videos in reducing COVID-19 vaccine hesitancy.
2. Establish the effectiveness of each of the intervention videos in increasing behavioral intent towards COVID-19 vaccination.
3. Establish the effectiveness of each of the intervention videos in increasing participants' level of hope

Methods: participants, interventions, and outcomes

Study setting

This trial will be conducted online, using the SPIRIT reporting guidelines [13]. For the United States, we will use the research platform created and managed by Prolific Academic Ltd (ProA: https://www.prolific.co/) to recruit participants and an online web platform Gorilla (www.gorilla.sc) to host and deploy our study; for China, we will use Kurundata, which recruits members in a variety of ways, including through its own platform (https://www.kurundata.com/), partnerships with other websites, and encouraging registered members to recruit new members through the popular mobile application Wechat (Figure 1).

Figure 1. Schedule of enrolment, interventions, and assessments for the study

	STUDY PERIOD		
	Enrolment	**Allocation**	**Post-allocation**
TIMEPOINT	$-t_0$ *Minute 1*	t_0 *Minute 0*	t_1 *Minute 1-10*
ENROLMENT:			
Eligibility screen	×		
Informed consent	×		
Allocation		×	
INTERVENTIONS:			×

Arm a			✕
Arm b			✕
Arm c			✕
Control			✕
ASSESSMENTS:			✕
Questionnaire survey			✕

Trial Design

Our study is a multi-site, parallel group, randomized controlled trial (RCT) comparing the effectiveness each of the short intervention videos with each other and with no video (the control condition). Via the online research platforms, participants will be randomly assigned to four intervention arms (Video A: storytelling-instructional-humor approach, Video B: storytelling-analogy approach, Video C: storytelling-emotion-driven approach) and a control arm (no video). Participants will be randomized at a 1:1:1:1 ratio (Figure 2). In each trial arm, there is a questionnaire survey, arranged in the following order. *Intervention arm a*: participants will receive the storytelling-instructional-humor video, followed by the survey. *Intervention arm b*: participants will receive the storytelling-analogy video, followed by the survey. *Intervention arm c*: participants will receive the storytelling-emotion-focused video, followed

by the survey. *Control arm*: participants will first receive the survey. After survey responses are submitted, participants in the control arm will be given access to the video interventions arranged in a single loop (to ensure post-trial access to treatment).

Eligibility criteria

To be eligible, participants must be between the age of 18 and 59, living in China or the USA. Since this video is wordless and culturally inclusive, therefor accessible to participants of all language and cultural groups. The English questionnaire will be translated into Chinese, so participants from the USA must have reading competency in English and participants from China must have reading competency in Chinese to complete the trial questionnaire.

Ethical approval

Ethics approval was obtained from the Stanford University IRB on January 12th, 2021, protocol #59503, and from the Chinese Academy of Medical Sciences & Peking Union Medical College IRB on March 10th, 2021.

Who will obtain informed consent?

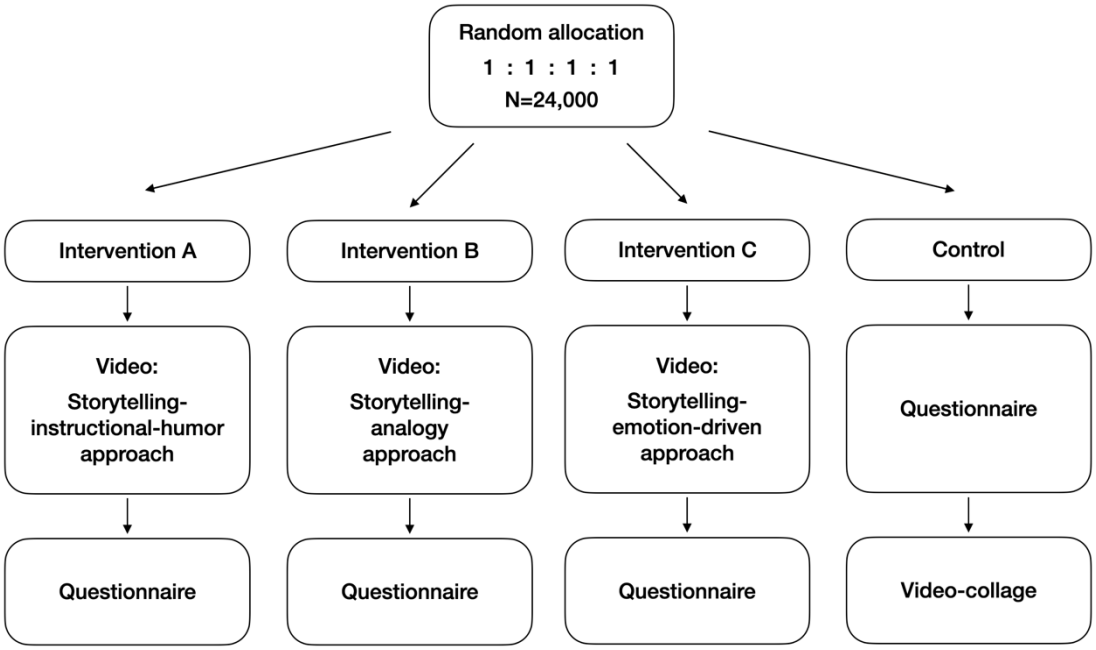
Participants must preview an information and consent form before they can begin the survey. The form explains the purpose of the study, the risks and benefits of the research, and how to contact the study investigators (or the Stanford University ethics review board). By clicking the link, participants consent to participate in our study, and will be redirected to the Gorilla or Kurundata platform, where additional information is given. Participants can exercise their

freedom to participate (or decline participation) at recruitment or at any point during the study.

Criteria for discontinuing or modifying allocated interventions

Since this is a minimal risk study of an online educational video intervention, we do not anticipate needing to discontinue or modify the allocated interventions during the course of the study. Participants can withdraw from the study at any time and participants will not be compensated for incomplete surveys.

Figure 2. Study design with 24,000 participants randomized to receive the video and questionnaire (treatment arm) or questionnaire and video (control arm).



Interventions

Intervention description

The video interventions are a short (2-3 minute) animated E-E videos about vaccines. All videos use a storytelling approach, but each video differs slightly in its pedagogical approach. *Intervention arm a* will view a video that uses a storytelling-instructional-humor approach.

Intervention arm b will view a video that uses a storytelling-analogy approach and *intervention arm c* will view a video that uses a storytelling-emotion-focused approach. The videos were developed with input from advisors at the Immunization Action Coalition, Vaccinate Your Family (formerly, Every Child by Two), the Stanford University Pediatrics Dept. Division of Infectious Diseases, the Icahn School of Medicine, the University of Texas Rio Grande Valley School of Medicine and the Heidelberg Institute of Global Health. The video interventions have no words, speech, or text, but incorporate soundtracks consisting of music and sound effects. The videos demonstrate how COVID-19 has impacted lives around the world and how a vaccine could catalyze a partial return to pre-pandemic lifestyles. The videos are designed for universal reach and optimized for release on social media. The interventions can be viewed at the links below in countries that allow access to YouTube:

Video A: https://youtu.be/ap8xpyREaTc

Video B: https://youtu.be/fYYBJ0d6gl0

Video C: https://youtu.be/WH5KUhGtfa8.

Explanation for the choice of comparators

The comparators are similar-length E-E videos, all animated in the same styles by the same animator. They all convey the same message (i.e., vaccines work) using a storytelling approach, without the use of spoken or written language. Each intervention arm video uses a slightly different pedagogical approach. The control arm receives no video intervention. Comparing the *intervention arms a, b* and *c* with the control arm will allow us to quantify the effect of each intervention on the primary and secondary outcomes. Comparing *intervention arms a, b* and *c* with each other will allow us to explore the differential effect of these pedagogical approaches

on the primary and secondary outcomes. We will use list experiments, also referred to as the unmatched count technique [14], to eliminate social desirability bias regarding vaccine-seeking behavioral intent. For the list experiments, we will use the control list as the comparator.

Outcomes

Primary outcome measures

Our primary outcome is vaccine hesitancy (including COVID-19 vaccine hesitancy). We will ask participants how much they agree or disagree with statements related to perceived vaccine safety as well as their attitudes, preferences, beliefs, and hesitancies regarding regular vaccines and the COVID-19 vaccine, respectively [15]. In the statistical analysis process, we will use nine questions to measure the degree of vaccine hesitancy in general and seven questions to measure the COVID-19 vaccine hesitancy specifically. Then we will normalize the final score to a range of 1-5 for both measures for comparison, which higher scores indicate higher degrees of vaccine hesitancy. These questions are shown in **Table 1** and the data elicited from this survey will enable us to achieve objective 1.

Table 1. The (COVID-19) vaccine hesitancy items

Vaccine Hesitancy	**COVID-19 Vaccine Hesitancy**
L1. Vaccines are important for my health	L1. COVID-19 vaccines are important for my health
L2. Vaccines are effective	L2. COVID-19 vaccines are effective
L3. Having myself vaccinated is	L3. Having myself vaccinated with a COVID-19

important for the health of others in my community	vaccine is important for the health of others in my community
L4. All vaccines offered by the government programme in my community are beneficial.	L4. All COVID-19 vaccines offered by the government program in my community are beneficial
L5. New vaccines carry more risks than older vaccines	L5. COVID-19 vaccines from other countries carry more risks than vaccines from my country
L6. I trust the information I receive about shots	L6. The information I receive about COVID-19 vaccines from the vaccine program is reliable and trustworthy
L7. Getting vaccines is a good way to protect myself from disease	L7. Getting COVID-19 vaccines is a good way to protect myself from COVID-19
L8. I am able to openly discuss my concerns about shots with my doctor	L8. Generally, I do what my doctor or health care provider recommends about COVID-19 vaccines for myself
L9. I am concerned about serious adverse effects of vaccines	L9. I am concerned about serious adverse effects of COVID-19 vaccines
L10. People do not need vaccines for diseases that are not common anymore	L10. I do not need COVID-19 vaccines if it's not a pandemic anymore
L11. I believe that many of the illnesses shots prevent are severe	L11. I am concerned that COVID-19 vaccines might not prevent the disease
L12. It is better to get fewer vaccines at	L12. I am concerned that COVID-19 vaccines

the same time	might not be safe
L13. People get more shots than are good for them	
L14. It is better to develop immunity by getting sick than to get a shot	

*Note: the survey tool was designed based on [15], which requires the level of agreement from "strongly disagree" to "strongly agree"

Secondary outcome measures

Our secondary outcomes include participants' behavioral intent to get vaccinated as well as participants' level of hope. In order to reduce the social desirability bias often associated with direct questioning about sensitive items [14], we will use the unmatched count or list randomization approach to devise a series of list experiments [16]. Four list experiments will be used, as shown in **Table 2**. For each experiment, the control group will receive a list of three items. Participants are asked how many items they are likely to do in the coming months without stating which ones they chose. The treatment group will get the identical item lists but with one additional "sensitive" item relating to their behavioral intent to get vaccinated or encourage their loved ones to do so. For example, imagining that the control group select 1 out of the 3 items on average while the treatment group select 1.3 out of the 4 items, with the assumption that the average acceptance of these two cohorts is the same, we can conclude that the prevalence of participants who would get vaccinated against COVID-19, is 20%. We have designed the list experiments in accordance with published best practices[16], and these data will be used to assess objective 2.

Table 2. List experiments in the trial.

List 1: COVID vaccine -self uptake	**List 3: routine vaccine – self uptake**
1. Brush my teeth at least twice daily	1. Wash my hands before eating
2. Begin learning a new language	2. Take up a new sport
3. Smoke cigarettes or vape	3. Have unprotected sex with someone who is not my long-term partner
4. Get vaccinated against COVID-19 when the vaccine is available for me*	4. Get a routine vaccine (for example flu vaccine, tetanus booster shots, Hepatitis B Vaccine, etc.) if the doctor recommends it*
List 2: COVID vaccine – recommendation	**List 4: routine vaccine -recommendation**
1. Recommend a show or movie to my friend	1. Try to get my family to eat more fruits and vegetables
2. Encourage a friend to seek routine dental care	2. Perform a routine check of the batteries in our smoke detectors
3. Allow a friend to drive home even though I think they may have had too much to drink	3. Encourage a friend to get a tattoo or body piercing
4. Encourage a friend or family member to get vaccinated against COVID-19 when the vaccine is available for them*	4. Encourage a friend or family member to get a routine vaccine (for example flu vaccine, tetanus booster shots, Hepatitis B Vaccine, etc.) if the doctor recommends it*

Note: In each trial arm, both groups will receive four lists. For each list, the control group will get the first three items only; the treatment group will receive the three items and the fourth sensitive item, indicated by an asterisk (*). Each list experiment will be preceded by the question: "In the coming 3 months, how many of the following things are you likely to do? I do not need to know which of these things you are likely to do, just how many."

Second, we will assess participants' level of hope using the Adult Hope Scale [17], a 12-item scale measuring participants' level of hope (**Table 3**). The Adult Hope Scale is comprised of two subscales relating to Snyder's cognitive model of hope: (1) Agency (goal-directed energy) and (2) Pathways (planning to accomplish goals) [11]. The 12 items include 4 Agency items, 4 Pathways items and 4 distractors. Participants are asked to respond using an 8-point Likert-type scale ranging from Definitely False to Definitely True. As recommended in the literature, we will refer to the scale as "The Future Scale" within the survey experiment.

Table 3. The Future Scale

Items	**Response**
I1. I can think of many ways to get out of a jam.	1. = Definitely False
I2. I energetically pursue my goals.	2. = Mostly False
I3. I feel tired most of the time.	3. = Somewhat False
I4. There are lots of ways around any problem.	4. = Slightly False
I5. I am easily downed in an argument.	5. = Slightly True
I6. I can think of many ways to get the things in life that are important to me.	6. = Somewhat True

I7. I worry about my health.	7. = Mostly True
I8. Even when others get discouraged, I know I can find a way to solve the problem.	8. = Definitely True
I9. My past experiences have prepared me well for my future.	
I10. I've been pretty successful in life.	
I11. I usually find myself worrying about something.	
I12. I meet the goals that I set for myself.	

Note: Items 2, 9, 10, and 12 make up the agency subscale. Items 1, 4, 6, and 8 make up the pathway subscale. Researchers can either examine results at the subscale level or combine the two subscales to create a total hope score.

We also aim to measure the difference of the outcomes above between the three *intervention arms a* (storytelling-instructional-humor) *b* (storytelling-analogy) and *c* (storytelling emotion-focused). These data will be used to assess objective 3.

Sample size

To calculate the sample size needed for pairwise comparison between three groups, we used a one-way analysis of variance (ANOVA). The formula is as follows. [18]

$$n_A = \left(\sigma_A^2 + \frac{\sigma_B^2}{\kappa}\right)\left(\frac{Z_{1-\frac{\alpha}{\tau}} + Z_{1-\beta}}{\mu_A - \mu_B}\right)^2$$

Where κ, the matching ratio, is equal to 1 in our study; μ_A and μ_B are the means of group A and group B; σ_A and σ_B are the standard deviations; $\alpha = 0.05$ and $\beta = 0.2$ are the type-I

and type-II error respectively; Z is the quantile function and $\tau = 2$ is the number of comparisons to be made. For vaccine hesitancy (and COVID-19 vaccine hesitancy), we assume that the means of two arms are 2.00 and 2.01, which represents the level of vaccine acceptance of this arm (1 means total acceptance and 5 means complete refusal), the standard deviations are the same, 0.10. To detect a difference of 0.01 between the vaccine hesitancy between arms, we can calculate the total minimal sample size is $n_A = n_B = n_C = n_D = 1{,}570$, so the $N = 6{,}280$. To test the sensitivity of the result, we can change our assumption and increase the standard deviation to 0.12, i.e., $\sigma_A = \sigma_B = 0.12$. Then we have $n_A = n_B = n_C = n_D = 2{,}260$ and $N = 9{,}040$. To achieve a higher level of accuracy, we will recruit 12,000 participants in each country for this study.

Recruitment

We will recruit participants from the ProA and Kurundata platforms. A potential study participant must open an account on ProA or Kurundata and provide his or her personal information. Participants must agree to ProA's or Kurundata's data privacy terms and conditions. ProA or Kurundata will assign each participant a unique, anonymized ID. Because ProA and Kurundata handle the interaction between the study investigators and participants, the participants will be anonymous to the study investigators.

Assignment of interventions: allocation

Using a web-based randomization algorithm, Gorilla and Kurundata will randomly allocate participants to the intervention arm a, intervention arm b, intervention arm c, or control arm

(sequence generation) at a 1:1:1:1 ratio.

Assignment of interventions: blinding

The study investigators and those involved in the data analyses and statistics will be blinded to the group allocation.

Data collection and management

Plans for assessment and collection of outcomes

The study investigators will be responsible for data collection. Data will be collected on the either the Gorilla or Kurundata platforms. The data retrieved from the platforms will be anonymous. Data downloaded will be stored on an encrypted and secure server. The data will be deleted two years after the study has been completed.

Plans to promote participant retention and completion

Participants will be automatically timed-out from the online platform if they take more than 45 minutes to complete the study. Though participants can withdraw the study at any time, they will not be compensated for incomplete survey participation. Incomplete data will be excluded from our analyses. Since the participants are anonymous to us, there is no way to initiate follow-up in the time limit.

Data management

Data will be collected on the Gorilla or Kurundata platforms. Third parties except for ProA or

Kurundata will not have access to the data. The data will be downloaded and safely stored for statistical analysis on a computing system maintained by the University of Heidelberg in Germany.

Confidentiality

Because of the anonymized participant IDs, the study investigators can never meet or know the identity of the study participants. The study investigators will only have access to the participants' anonymized ID and no other personal or confidential information, and the data will be deleted two years after the study has been completed. The study investigators will keep this information confidential.

Statistical methods

Descriptive measures

We will use descriptive statistics to obtain summaries of the demographic data (age, sex, education status, country of residence, etc.).

Primary outcomes

For each participant, we will calculate their (COVID-19) vaccine hesitancy score based on their survey responses. Let $\overline{K_k}$ denote the mean vaccine hesitancy for each trial arm, where $k \in \{a, b, c\}$ such that a represents the intervention arm a (video with storytelling-instructional-humor approach), b represents the intervention arm b (video with storytelling-analogy approach), c represents the intervention arm c (video with storytelling-emotion-focused

approach) and *d* represents the control arm. We will use generalized linear mixed models (GLMM) for the analysis of our endpoints. We use ordinary least squares (OLS) regression for our continuous endpoints; we will use (modified) Poisson regression for our binary endpoints; we will use negative binomial regression for our count endpoints. The reason for the choice of modified Poisson regression for our binary endpoints is that this analysis has good statistical properties and generates risk ratios, which are far easier and safer to interpret than the effect size measures generated by alternative methods (such as odds ratios or marginal effects) [19-22].

Secondary outcomes

For the vaccination plan in the list experiment, we will calculate the mean score for the control list and treatment list, denoted by $\overline{C_\iota}$ and $\overline{T_\iota}$ respectively, where i is the index of the list. Then we can calculate the mean difference between control list and treatment list within each trial arm, which is considered as the participants' behavioral intent to get vaccinated in this trial arm, denoted as $\overline{D_{\iota k}} = \overline{T_{\iota k}} - \overline{C_{\iota k}}$. Analogous to difference-in-difference analyses, we can identify the effect of each treatment.

For other secondary outcomes, we can use the same statistical procedure described above to assess the effectiveness of our E-E video. We will use R statistical software to undertake the analysis.

Interim analyses

No interim analyses are planned.

Methods for additional analyses (e.g., subgroup analyses)

Since we will conduct the trial in the USA and China, we will conduct both country-specific and cross-country pooled analyses for further comparison.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data

Participants who decide to withdraw from the trial will not be replaced

Plans to give access to the full protocol, participant level-data, and statistical code

This document is the full protocol. Anyone interested in other data or documentation should contact the corresponding author.

Oversight and monitoring

Composition of the coordinating center and trial steering committee

The trial will be overseen by a trial steering committee (TSC). The TSC will have an independent chairperson and members but also includes the trial collaborators. Two TSC meetings are planned.

Adverse event reporting and harms

As this is an online survey, there is very minimal risk for study-related injury or harm. We will present non-threatening video interventions and questions about vaccine attitudes. There are no foreseeable risks to participating in the online study.

Dissemination plans

The results of this study will be disseminated through presentations at international conferences and publications in peer-reviewed journals. Results will be used by the study collaborators and their institutions (Stanford School of Medicine, Heidelberg University, Chinese Academy of Medical Sciences and Peking Union Medical College) to improve the design and universal appeal of future educational and health promotion videos. All investigators who meet authorship criteria will be included as co-authors and anyone who contributed, but does not meet the criteria for authorship, will be acknowledged. No professional author services will be used.

Discussion

Global government and health authorities have actively engaged in efforts to combat the COVID-19 pandemic, including imposing a variety of strict lockdown policies on regions and countries. Also, since the World Health Organization (WHO) is currently orchestrating the global campaign to fight against the spread of the SARS-CoV-2 virus, the progress of vaccination has dramatically accelerated and it is foreseeable that numerous safe and effective vaccines will come to market by 2022[23]. However, previous research has indicated that vaccine availability does not guarantee vaccine acceptance, especially given global variations in cultural and educational backgrounds[24]. In this study, we propose using animated, E-E videos to decrease general vaccine hesitancy globally and to evaluate their effectiveness using three innovative approaches.

First, we will use the latest online technology to conduct our multi-site, parallel, randomized controlled trial. ProA, the online platform, enables researchers to connect with individuals around the world who are interested in participating in online studies[25]. Kurundata fills a similar function in in China. Second, we will host and deploy our study on the Gorilla platform, which is an experiment builder that provides users with the tools for undertaking online behavioral research. The Gorilla randomization algorithm, which demonstrates the platform's capability to implement innovative trial designs, will guide us in randomly assigning participants at two levels: (1). Participants will be randomized to the storytelling-instructional-humor video arm, the storytelling-analogy video arm, the storytelling-emotion-focused video arm or no video arm. (2). Within each arm, participants will be randomized to control list or treatment list within the list experiment portion of the survey.

Third, we will deploy list experiments to reduce the social desirability bias associated with sensitive questions such as intention to seek vaccination. Prior research highlights the documented discrepancies between publicly declared vaccine intentions and privately held reservations, including safety and efficacy concerns. [24]. Therefore, we have designed the list experiment to minimize social desirability bias toward the behavioral intention questions.

This study is expected to establish the effectiveness of short, animated, E-E videos, using different pedagogical approaches, for improving vaccine confidence. We hope to document a reduction in vaccine hesitancy and guide future E-E video development strategies to support education and health communication campaigns globally.

Trial status

The protocol version number is 1.0 and the date is March 15th, 2021. Recruitment is expected to end by 31 May, 2021.

Supplementary information

Acknowledge

Not applicable

Funding

This study is funded by the Alexander von Humboldt Foundation and the Sino-German Center for Research Promotion (Project C-0048), which is funded by the German Research Foundation (DFG) and the National Natural Science Foundation of China (NSFC). This study is also funded by an Alexander von Humboldt University Professor Prize awarded to Dr. Till Bärnighausen.

Availability of data and materials

Data will be collected and stored on the Gorilla and Kurundata platform. The study investigators own and have complete control of the research data, which can be accessed at any time. For statistical analysis, the data will be downloaded and safely stored on a computing system maintained by the University of Heidelberg.

Ethics approval and consent to participate

Ethics approval was obtained from Stanford University in the United States (ID#59503) and from Chinese Academy of Medical Sciences and Peking Union Medical College in China (ID#0622021). Participants must preview an information and consent form before they can begin the survey. The form explains the purpose of the study, the risks and benefits of the research, and how to contact the study investigators (or Stanford University ethics review board). By clicking the link, participants consent to participate in our study, and will be redirected to the Gorilla or Kurundata platform, where additional information is given. Participants can exercise their freedom to participate (or not) at recruitment or at any point

during the study. Protocol amendments will be promptly communicated with the relevant ethics committees and the TSC.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

Authors' contributions

SC, MA, TB and SF conceived the trial. SC, MA, SF and FY wrote the first draft of the manuscript. SC, MA, JG, SF, and TB designed the survey. SC and FY conducted the quantitative data analysis. SC, JY, CW and TB obtained funding. All authors provided critical revisions to the manuscript.

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25. **How it works** [https://www.prolific.co/#researcher-content]

Appendix

SPIRIT Checklist for *Trials*

Complete this checklist by entering the page and line numbers where each of the items listed below can be found in your manuscript.
Your manuscript may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please state "n/a" and provide a short explanation. **Leaving an item blank or stating "n/a" without an explanation will lead to your manuscript being returned before review.**
Upload your completed checklist as an additional file when you submit to *Trials*. You must reference this additional file in the main text of your protocol submission. The completed SPIRIT figure must be included within the main body of the protocol text and can be downloaded here: http://www.spirit-statement.org/schedule-of-enrolment-interventions-and-assessments/
In your methods section, please state that you used the SPIRIT reporting guidelines, and cite them as:
Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page and Line Number	Reason if not applicable
Administrative information				
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 1, Lines 1-3	
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 4, Line 58	
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a	We have a trial identifier and registry name. The DRKS collects all items from the World Health Organization Trial Registration Data Set https://www.who.int/clinical-trials-registry-platform/network/primary-registries/german-clinical-trials-register-(germanctr)
Protocol version	#3	Date and version identifier	Page 26, Lines 430-432	
Funding	#4	Sources and types of financial, material, and other support	Page 5 - Line 59	
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	Page 1-2, Lines 5-33	

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	Page 5, Line 59	
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Page 5, Line 59	
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Page 24, Lines 370-374	
Introduction				
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Page 6-8 – Lines 60-116	
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	Page 6-8 – Lines 60-116	
Objectives	#7	Specific objectives or hypotheses	Page 8, Lines 118-125	
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	Page 10, Lines 139-152	
Methods: Participants, interventions, and outcomes				
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Page 9, Lines 128-135	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 11, Lines 154-159	

Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Pages 12-13, 180-209	
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	Pages 12-13, Lines 180-209	
Interventions: adherence	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests). Also relevant for non-pharmacological RCTs.	Page 9, Lines 128-135	The online academic research platforms used in this study have rigorous, ethically sound strategies for recruiting members and optimizing adherence to intervention protocols. Our team has previously used these survey platforms, which have excellent response rates.
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a	Since this trial involves viewing online health animations, there is little to no risk in the trial.
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 14, Lines 211-221 and Page 16, Lines 227-241	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Page 9-10, Line 136	
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Pages 19-20, Lines 265-281	
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 20, Lines 282-288	
Methods: Assignment of interventions (for controlled trials)				

Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Page 20, Lines 290-293	
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Page 20-21, Lines 295-297	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enroll participants, and who will assign participants to interventions	Page 20, Lines 290-293	
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 20-21, Lines 295-297	
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a	Unblinding is not permissible in this study due to its setting: the study takes place 100% online using established, online academic research platforms.
Methods: Data collection, management, and analysis				
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Page 21, Lines 299-318	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	Page 21, Lines 306-311	

Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Page 21, Lines 313-317	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Page 22-23, Lines 326-254	
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Page 23, Lines 359-361	
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Page 24, Line 365	
Methods: Monitoring				
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Page 24, Lines 370-374	
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Page 11-12, lines 179-183	
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Page 24, lines 376-379	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Page 24, lines 379-380	
Ethics and dissemination				
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	Page 11, Lines 161-154	

		including the committee's reference number (if applicable)		
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	Page 27, 454-455	
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 11, Lines 166-172	
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a	No ancillary studies are planned.
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Page 22, Lines 319-324	
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 29, Lines 456-457	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Page 28, Lines 440-444	
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a	There is very minimal to no risk of study-related harm in this study.
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Page 24-25, Lines 381-389	
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	Page 25, lines 392-395	
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Page 24-25, Lines 381-389	

Appendices				
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorized surrogates	We include the Stanford consent as an appendix	
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a	No biological specimens will be collected in this study.