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A standardized instrument quantifying risk factors associated with bi-directional transmission of SARS-CoV-2 and other zoonotic pathogens: The COVID-19 human-animal interactions survey (CHAIS)

Jonathon D. Gass Jr. [a,1], Kaitlin B. Waite [b,1,*], Nichola J. Hill [c], Kathryn R. Dalton [b], Kaitlin Sawatzki [a], Jonathan A. Runstadler [a,2], Meghan F. Davis [b,d,2], CHAIS Expert Review Group[3]

[a] Dept. of Infectious Disease and Global Health, Cummings School of Veterinary Medicine, Tufts University, United States
[b] Dept. of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, United States
[c] Department of Biology, University of Massachusetts Boston, United States
[d] Dept. of Molecular and Comparative Pathobiology; Division of Infectious Diseases, Johns Hopkins School of Medicine, United States

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ABSTRACT

Similar to many zoonotic pathogens which transmit from animals to humans, SARS-CoV-2 (CoV-2), the virus responsible for the COVID-19 pandemic, most likely originated in Rhinolophus bats before spreading among humans globally. Early into the pandemic, reports of CoV-2 diagnoses in animals from various countries emerged. While most CoV-2 positive animals were confirmed to have been in close contact with CoV-2 positive humans, there has been a paucity of published evidence to-date describing risk factors associated with CoV-2 transmission among humans and animals. The COVID-19 Human-Animal Interactions Survey (CHAIS) was developed to provide a standardized instrument describing human-animal interactions during the pandemic and to evaluate behavioral, spatiotemporal, and biological risk factors associated with bi-directional zoonotic transmission of CoV-2 within shared environments, predominantly households with limited information about human-wildlife or human-livestock interactions. CHAIS measures four broad domains of transmission risk: 1) risk and intensity of infection in human hosts, 2) spatial characteristics of shared environments, 3) behaviors and human-animal interactions, and 4) susceptible animal subpopulations. Following the development of CHAIS, with a One Health approach, a multidisciplinary group of experts ($n = 20$) was invited to review and provide feedback on the survey for content validity. Expert feedback was incorporated into two final survey formats—an extended version and an abridged version for which specific core questions addressing zoonotic and reverse zoonotic transmission were identified. Both versions are modularized, with each section having the capacity to serve as independent instruments, allowing researchers to customize the survey based on context and research-specific needs. Further adaptations for studies seeking to investigate other zoonotic pathogens with similar routes of transmission (i.e. respiratory, direct contact) are also possible. The CHAIS instrument is a standardized human-animal interaction survey developed to provide important data on risk factors that guide transmission of CoV-2, and other similar pathogens, among humans and animals.

* Corresponding author.
E-mail address: Kwaite2@jh.edu (K.B. Waite).
[1] These authors should be considered joint first authors
[2] These authors should be considered joint senior authors
[3] Edward Baker, South Bay Veterinary Group, USA; Anne Barnhill, Johns Hopkins University, USA; Nicola Decaro, University of Bari, Italy; Janet Forrester, Tufts University, USA; Charles Frevert, University of Washington, USA; Gregory Gray, Duke University, USA; David Lee-Parritz, Tufts University, USA; Deborah Linder, Tufts University, USA; Julianne Meisner, University of Washington, USA; Dan Morris, University of Pennsylvania, USA; Megan Mueller, Tufts University, USA; Felicia Nutter, Tufts University, USA; Danielle Ompad, New York University, USA; Peter Rabinowitz, University of Washington, USA; Marieke Rosenbaum, Tufts University, USA; Ron Rubenstein, Washington University, USA; Adam South, Tufts University, USA; Jean Van Seventer, Boston University, USA; Lee Wetzler, Boston University, USA; and Eugene White, Tufts University, USA.

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1. Introduction

SARS-CoV-2 (herein CoV-2) most likely emerged from closely related bat coronaviruses before first detection in human populations and spawning the catastrophic global COVID-19 pandemic with millions of human deaths worldwide [1–3]. Since the initial emergence of the virus, many CoV-2 cases in animals have been reported, including in domestic dogs, cats, hamsters and ferrets, farmed mink, wild mink, captive felids (including puma, cougar, snow leopard, lions, and tigers), white-tailed deer, and other captive wildlife including gorillas and otters [4–8] (Fig. 1). Domestic mink infections (see OIE map) are particularly important as mink may show clinical signs, have potential for high mortality rates [4,9,10], and have played crucial roles in multiple disease transmission pathways (including human-to-mustelid, mustelid-to-mustelid, mustelid-to-human, and mustelid-to-feline). There is also a larger concern that mustelids and now perhaps white-tailed deer, could serve as CoV-2 reservoirs [8,9].

The probability of interspecies transmission of infectious pathogens is influenced by interactions among human, animal, and environmental dimensions [11]. While most CoV-2 positive animals were in close contact with CoV-2-positive humans in households and other shared environments [12], little published evidence to-date has identified direct human-to-animal transmission events, nor described behavioral, spatiotemporal, and biological risk factors associated with CoV-2 transmission between humans and animals. In fact, this is a knowledge gap for many zoonoses [11]. A deeper understanding of the human-animal interface and potential risk factors associated with CoV-2 transmission between humans and animals is critical for risk

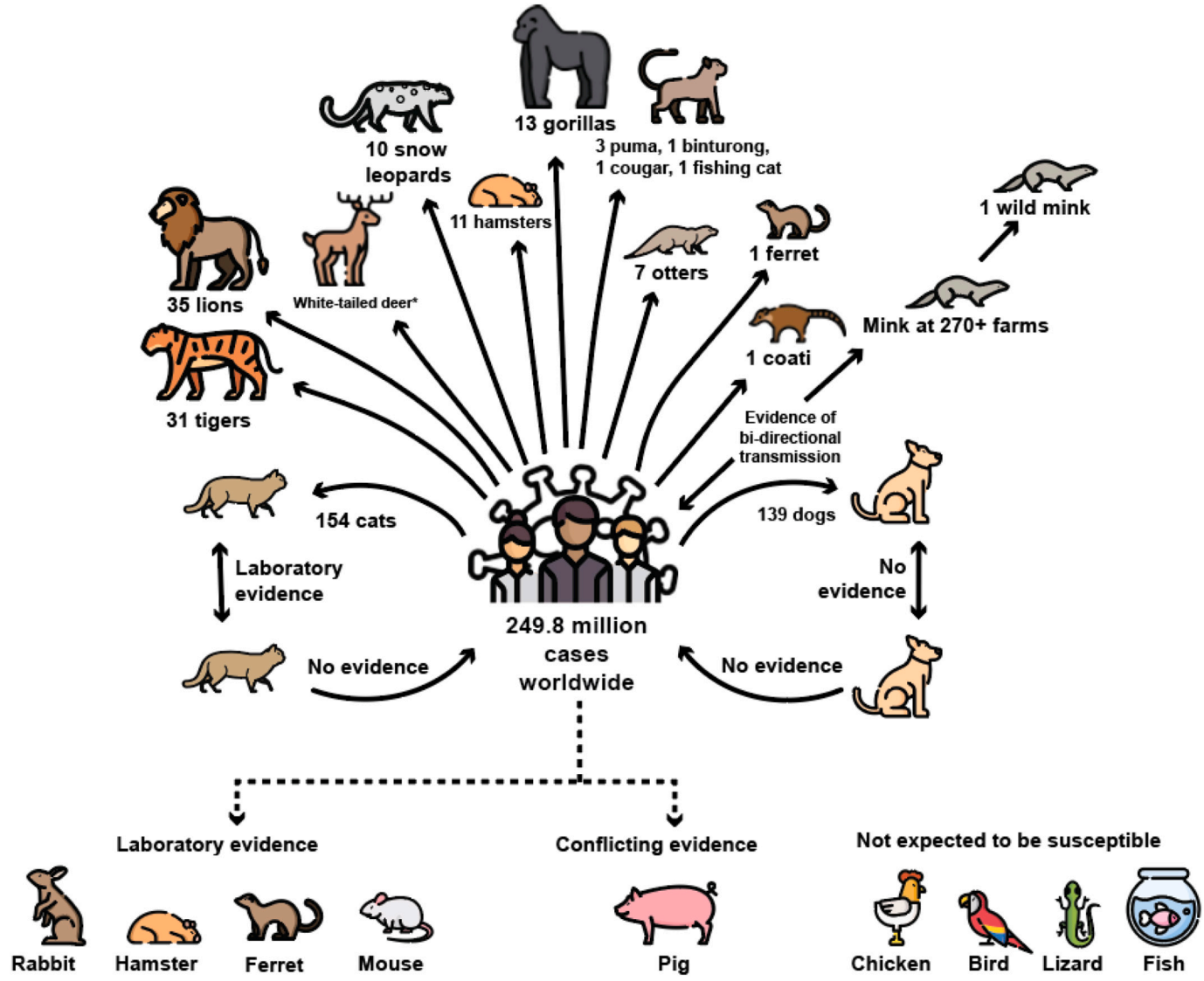

Fig. 1. Global evidence to-date of CoV-2 transmission and susceptibility among common household pets and other animals.
As of March 15, 2022, there have been 462.1 million human cases of COVID-19 globally [2]. Multiple natural cases have been confirmed by PCR in animals since January 2020 in 31 countries worldwide. In addition, many CoV-2 outbreaks at mink farms have occurred in the Netherlands, Spain, Denmark, Italy, Sweden, Poland, Latvia, Greece, France, and Canada including secondary transmission from mink back to humans in Denmark [4,47]. In December 2020, the first free-ranging native wild animal, a wild mink, was confirmed with SARS-CoV-2 near a mink farm in the state of Utah, USA [48], and since additional cases among wildlife have been detected, including white-tailed deer in the US [49]. Laboratory evidence has confirmed that cats are infectious to other cats while there is no evidence of ongoing transmission in dogs [43]. There is no evidence that household pets, including cats and dogs, act as ongoing reservoirs for transmission back to humans. Laboratory studies have demonstrated common household animals such as rabbits, hamsters, ferrets, and mice as susceptible to infection [50]. Multiple studies have concluded that pigs, chickens, other birds, reptiles, and fish are not expected to be susceptible to the virus [51–55]. Figure includes modified icons originally made by Freepik from www.flaticon.com.

prevention and mitigation. While much human-animal interaction data is collected utilizing questionnaires, no standard instrument currently exists for zoonoses. A standard human-animal interaction instrument will allow researchers the opportunity to pool data across studies, which is needed as routine CoV-2 testing in animals is not currently recommended [13,14] and information regarding animal infections are isolated and sparce.

Acknowledging the factors that drive interspecies transmission and the need for a standardized tool, the COVID-19 human-animal interactions working group (CHAI-WG) was established to develop the COVID-19 Human-Animal Interactions Survey (CHAIS). The objective of CHAIS is to describe human-animal interactions and evaluate risk factors associated with bi-directional zoonotic transmission of CoV-2 and other similarly transmitted zoonotic pathogens within households and other shared settings. CHAIS evaluates four broad domains of transmission risk: 1) risk and intensity of infection in human hosts, 2) spatial characteristics of shared environments, 3) behaviors and human-animal interactions, and 4) susceptible animal subpopulations (Fig. 2). In this article, we report on the development of this standard instrument evaluating human-animal interactions in the context of COVID-19, though with broad applicability to multiple zoonotic pathogens, and offer guidance on its many applications in research.

2. Methods

2.1. The COVID-19 human-animal interactions working group (CHAI-WG)

The National Institute of Allergy and Infectious Disease (NIAID) Centers of Excellence for Influenza Research and Surveillance (CEIRS) comprises a network of multidisciplinary collaborating institutions engaged in international surveillance and targeted research on host immune response, viral pathogenesis, emergence, and transmission of influenza viruses. In early 2020 our CEIRS-funded laboratories formed the CHAI-WG to harness both teams' expertise and develop a standardized survey instrument given the increasing number of reported cases of domestic and captive animals testing positive for CoV-2 globally. The CHAI-WG comprised scholars from the fields of virology, epidemiology, infectious disease ecology, veterinary medicine, and environmental microbiology.

2.2. Development of the CHAIS instrument

First, we determined the structure, types of questions, and intended use for the instrument, including that it be adaptable for use across multiple contexts in which animals and humans share contact. Next, we identified human, animal, and environmental dimensions of importance to transmission pathways for CoV-2 and other similar zoonotic pathogens in the context of close human-animal interaction. Two One Health-focused research groups independently drafted survey questions specific to these pathways, removed areas of overlap, and added questions based on emergent evidence during the evolving pandemic.

A multi-disciplinary panel of experts ($n = 20$), outside of the CHAI-WG, were invited to critique and provide feedback on the questionnaire for content validation purposes [15,16]. This panel represented multiple disciplines including veterinary medicine, infectious disease, farm- and lab-animal medicine, One Health, virology, microbiology, occupational health, biostatistics, epidemiology, pulmonology, environmental health, human-animal behavior, and bioethics. Reviewers completed a worksheet for structured feedback, offered new questions and edits for existing questions. The goals of this expert-driven pretesting exercise, utilizing the modified Delphi Technique and multi-stakeholder iterative feedback [17,18], were to pinpoint problem areas, reduce measurement error and respondent burden, and ensure consistent question interpretation. Edits and feedback from expert reviewers were incorporated into the final survey by consensus among CHAI-WG members.

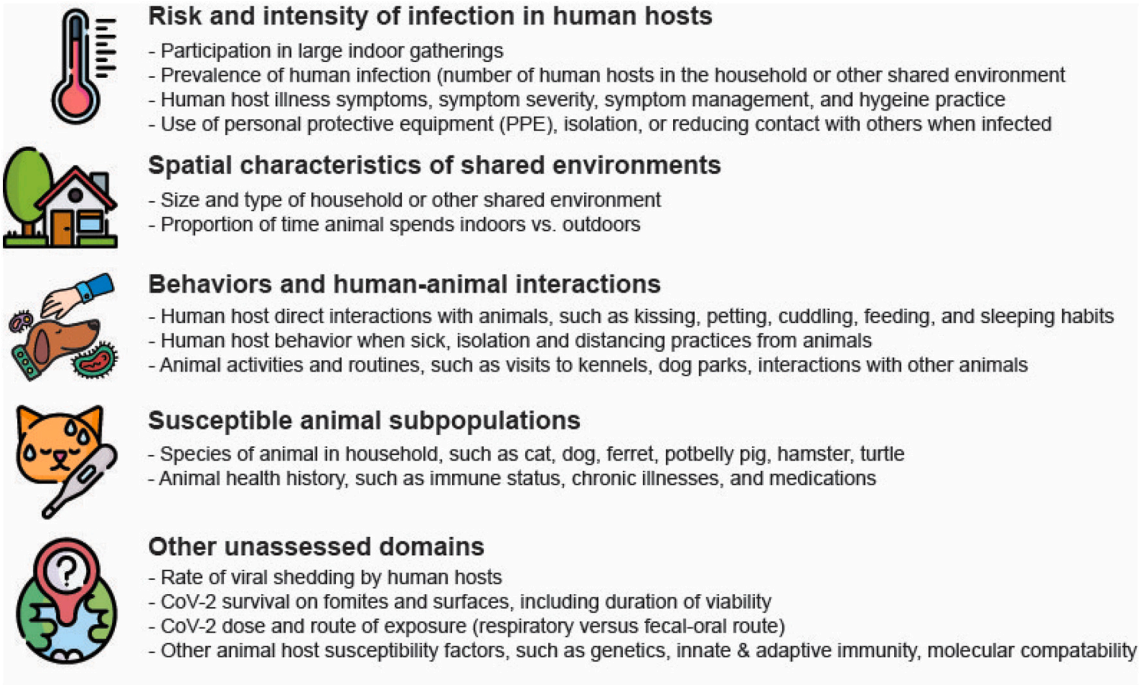

Fig. 2. CHAIS domains evaluating bi-directional zoonotic transmission of CoV-2 in households and other shared environments.
The CHAIS instrument focuses on measuring four broad domains which in part are likely to determine bi-directional zoonotic transmission risk in household settings and other shared environments. Additional domains which the CHAIS instrument does not measure are also described. Figure adapted from Plowright, et al. Pathways to Zoonotic Spillover, Nature, August 2017. Icons made by Freepik from www.flaticon.com.

3. Results

3.1. The CHAIS instrument

The CHAIS instrument is offered in two formats, an extended version, *E*-CHAIS (Supplemental file 1), and an abridged version, A-CHAIS (Supplemental file 2). Both versions encompass ten modularizable sections that capture multiple levels of human-animal interactions within the four domains of transmission risk referenced above (Fig. 2). Each section can be used as independent instrument modules and can be adapted to capture other zoonotic and reverse zoonotic pathogens with similar transmission pathways to CoV-2. The questionnaire comprises closed-ended questions with multiple choice responses, and logic-driven follow-up questions based on respondent answers. The questionnaire also incorporates time-bound questions that encompass important timepoints in the COVID-19 pandemic, which can be modified to reflect local context or to capture events associated with pathogen transmission during outbreaks of other zoonoses (Supplemental table 1). Several questions also ask whether events occurred, or behaviors were performed in the last six, three, and one-month time-period to contextualize responses outside of any calendar-bound period for COVID-19 or other zoonotic disease outbreaks.

All 10 sections of the CHAIS instrument focus on human subjects' interactions with close-contact animals in commonly shared environments (Fig. 3). Here we provide a brief overview of each CHAIS section and how each contributes to the aims of the questionnaire (Supplemental table 2).

The first section, *Household Demographics* [DEM], captures human demographic information for the respondent and each member of the respondent's household including zip code and employment status. Given that individual members within a household may contribute uniquely to risk factors of disease transmission to household animals,

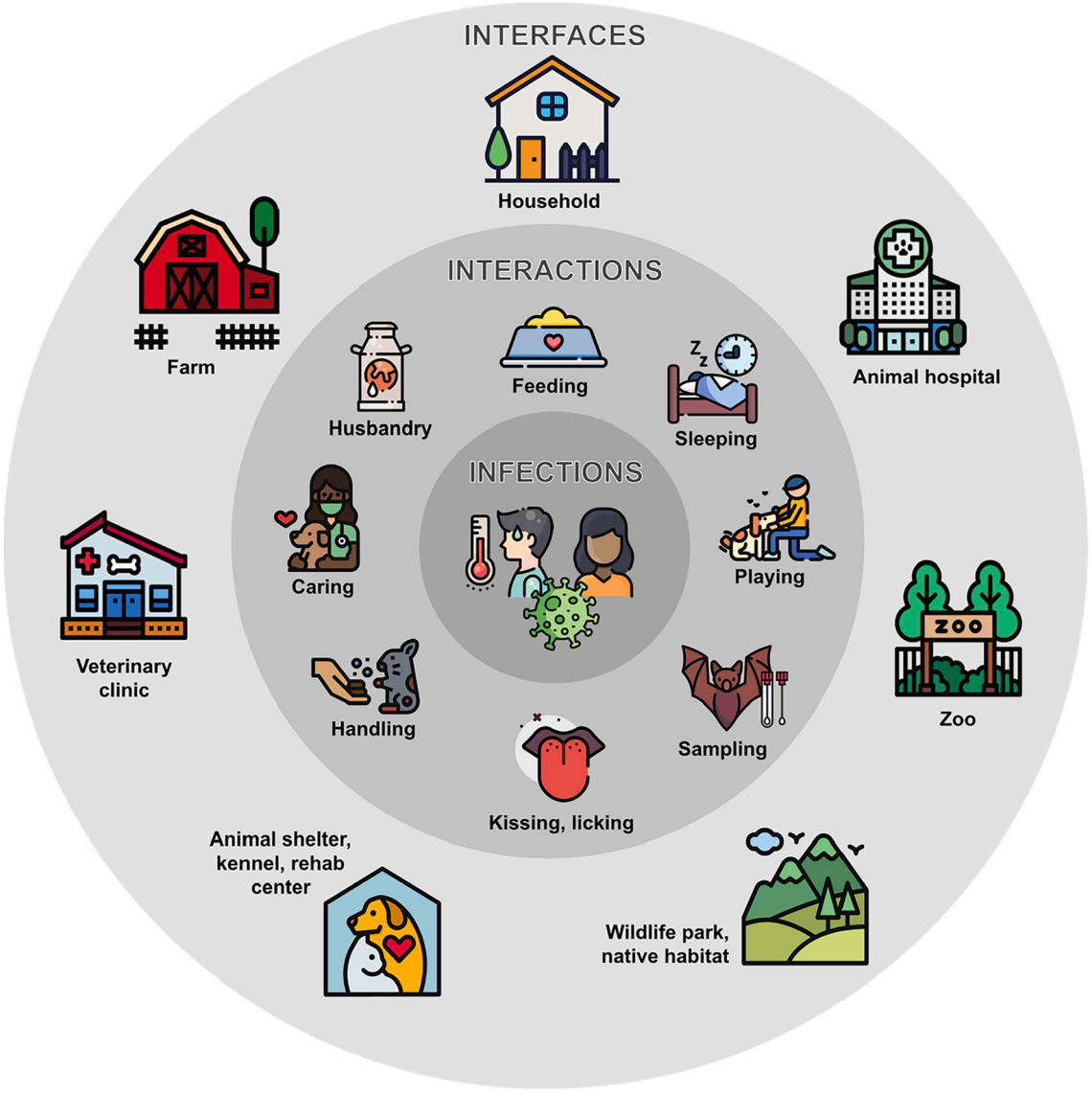

Fig. 3. Common interfaces for human-animal interactions associated with bi-directional zoonotic transmission of respiratory pathogens.
The CHAIS instrument focuses on interfaces where animals and humans share close contact, including households, and limited farms and veterinary settings. The CHAIS instrument can be expanded to further capture other common interfaces including wildlife, zoos, and shelter settings. Reverse zoonotic transmission events of CoV-2 and other zoonotic pathogens have been postulated to be due to direct interactions between human hosts and animals, specifically kissing, cuddling, playing, feeding, and sleeping habits. Given widespread prevalence of COVID-19 in human populations, the CHAIS instrument seeks to uncover behavioral risk factors and important interfaces for reverse zoonotic transmission events as well as potential zoonotic events. Not pictured here, the CHAIS instrument also addresses biological and spatiotemporal risk factors underlying these events. Icons made by Iconixar, Photo3idea_studio, Smalllikeart, Pixelmeetup, and Freepik from www.flaticon.com.

and vice versa, such factors may be attributed to individual household members throughout the questionnaire. This section also captures information at the household level, including household type and spatial factors. Additional adaptations may be possible for non-household environments where humans and animals share contact, including farms, zoos, wildlife, veterinary clinics and shelter settings. In addition, spatial analyses at a broader scale may be possible, from descriptive mapping of participant zip codes with geographically relevant meta-data to spatial statistics for potential infection clustering or quantification of spatio-temporal risk factors.

The *Pet Demographics and Behavior* [PetDEM] section compiles baseline information about all animals in the household. Pets refer to animals kept primarily for a person's company, entertainment, and/or specified tasks, rather than as livestock or laboratory animals; however, differing definitions for pets across cultures may require further adaptation depending on the context. To enable data attribution for individual animals, subsequent sections of the instrument ask that responses are reported individually for each animal in the shared environment. This section addresses factors related to companion or working animals. Working animals, such as service and emotional support animals, may have different exposures based on differences in their contact with humans. As working animals have varying roles tied to risks for disease transmission, the CHAIS instrument asks the participant to describe these roles (Supplemental table 2).

The Occupation [Occ], *Human Travel and Activities* [Travel], and *Animal Worker* [AW] *Sections* include specific questions that help capture the human risk of exposure to CoV-2 through either work, personal- or work-related travel, or exposure to household members who have a high risk of occupational exposure. Questions about biosafety, hand hygiene, and social distancing are also included. *The Animal Worker Section* [AW] targets individuals who work with animals, primarily those in small and large animal health and husbandry professions.

The Human Illness History section [HMNill] gathers information about health status and medical history with respect to chronic illnesses and other underlying health conditions that are associated with increased risk of severe COVID-19 illness. The *COVID-19 Testing/Symptoms section* [CoV2] captures important information about COVID-19 symptomatology, while the *Human Animal Interaction while sick section* [HAIill] evaluates human-pet interactions during during periods when respondents or household members had potential COVID-19 illness. The *Pet Health History Section* [PetHlth] evaluates illnesses and underlying health conditions that may play a role in the susceptibility and infection severity of COVID-19 in animals. This section also serves to measure pet health outcomes relative to human illness in shared environments.

Building on other works that have examined zoonoses and risk of pathogen transmission among humans and household pets based on intensity and frequency of human-animal contact [19–21], the *Human-Animal Interaction Section* [HAI] captures the intensity and frequency of human-animal contact. To quantify the closeness of human and animal interactions, the CHAIS instrument includes an interactions index which weighs individual behaviors relative to zoonotic transmission risk [20] (Table 1).

4. Discussion

The CHAIS instrument is a standardized data collection tool to describe human-animal interactions and measure risk factors associated with bi-directional transmission of CoV-2 and similarly transmitted pathogens between humans and animals. The CHAIS instrument serves to evaluate behavioral, spatiotemporal, and biological risk factors associated with zoonotic and reverse zoonotic transmission events in household and related settings (Fig. 2), with a goal to facilitate the harmonization of data collection across studies for future data-pooling and meta-analysis of findings. Through citation of the CHAIS instrument (Supplemental table 3, 4), cross-study data-pooling and meta-analysis will a) improve our understanding of pathogen exposure and transmission, b) provide a basis for predictive models of bi-directional transmission of SARS-CoV-2 among humans and animals in shared environments, and c) provide an evidence-base for public health guidance and the design of protective interventions to minimize exposure and disease risks. To expand usability, the CHAIS instrument encompasses two formats, an extended (*E*-CHAIS) version detailing human-animal interactions, and an abridged version (A-CHAIS), which only includes core questions addressing zoonotic and reverse zoonotic risk factors for transmission of CoV-2.

4.1. Guidance for the application of CHAIS in research

Both versions of CHAIS contain modularizable sections that can be stand-alone instruments. Individual studies may deploy and use the survey in several ways: 1) incorporate either extended or abridged versions of the survey en bloc; 2) select individual modules from either the extended and/or abridged versions of CHAIS and use them independently or in conjunction with another instruments; 3) use individual modules in their entirety with the selection of individual questions from other modules; 4) select individual questions and cite the CHAIS instrument to track the instrument's usage (Supplemental table 4). Researchers who use *E*-CHAIS or A-CHAIS will name one or both instruments with citation, whereas researchers who use a modular approach, such as those already conducting research with need for only certain types of questions covered in specific modules, are encouraged to name the individual modules with citation (Supplemental table 3,4). The CHAIS instrument also allows for minor amendments to identified questions to best serve studies of varying regionality, population, temporality, and cultural diversity, including adjustments to time-bound questions (Supplemental table 1). The CHAIS instrument can be implemented within a broad range of research studies, with some examples described below.

CHAIS as a standard instrument for other zoonotic pathogens: The CHAIS instrument was designed to be adapted to support studies investigating bi-directional transmission of zoonotic pathogens in settings where animals and humans share close contact, such as zoonotic strains of influenza viruses, *Chlamydophila felis*, *Bordetella bronchiseptica, Y. pestis*, *Streptococcus* group A, and methicillin-resistant *Staphylococcus aureus* (MRSA), among others [22–28]. While there may be important pathological and immunological differences between CoV-2 and other zoonotic pathogens, the CHAIS instrument measures transmission risks which have broad epidemiologic applicability. Zoonotic influenza virus transmission, for instance, is understudied in household environments [29,30] and the CHAIS instrument may enable an increased understanding of the factors that impact human and animal exposure and infection.

Research studies that do not include concurrent sampling of humans or animals: The CHAIS instrument can be administered as an epidemiological survey to gather data from community members on human-animal interactions during the COVID-19 pandemic or other zoonotic outbreaks and can rely on self-reported illness history by respondents. Survey questions evaluating human cases of COVID-19 allow for multiple methods to define a human case based on date of onset and duration of individual symptoms, or self-report of a laboratory-confirmed diagnosis, notification by healthcare professional of confirmed diagnosis, or suspect case. Studies without concurrent sampling may not confirm but describe potential transmission risks and may be used to describe human-animal interactions prior to and during the pandemic. Survey questionnaire data can be used to guide future sampling criteria in humans and animals, an important consideration for limited-resource studies.

Surveillance and research studies featuring specimen collection from animals and/or humans: The CHAIS instrument can contextualize results in studies that include viral and/or antibody testing. For studies in which samples are only collected from animals, the CHAIS instrument may elucidate factors associated with the animal's exposure and may

Table 1
Human-animal interactions closeness index.

					Maximum index item value
Respondent or other household members are the primary care provider for the pet (feeding, giving medication to, cleaning bedding, taking for exercise, playing)					
Yes = 1	No = 0				1
Respondent or other household members hold pet in arms, lay, or cuddle with					
Yes = 1	No = 0				1
Respondent or other household members allow pet to kiss or touch their face with pets its face: mouth, lips, nose, or beak					
Yes = 1	No = 0				1
Washing hands before touching pet					
Yes = 0	No = 1				1
Wash your hands after touching your pet					
Yes = 0	No = 1				1
Pet sleeps with the respondent or other household members					
Always = 3	Most of the time = 2	Sometimes = 1	Never = 0		3
Perceived average intensity of contact with humans:					
Heavy-handed petting with hands (i.e. vigorous or strong petting/scratching/rubbing of pet), allowing pet on lap, hugging, bringing close to face, intimate contact =3	Somewhat assertive petting with hands, allowing pet on lap, holding pet in hand(s) = 2	Light, gentle petting with hand only = 1	No Contact =0		3
Respondent or other household members kiss pets on the face: mouth, lips, nose, beak, head					
Multiple times a day, once per day, A few times a week =4	Once per week =3	A few times in last 30 days = 2	Once in last 30 days = 1	No = 0	4
Respondent or other household members allow pets to lick their face:					
Multiple times a day, once per day, A few times a week =4	Once per week =3	A few times in last 30 days = 2	Once in last 30 days = 1	No = 0	4
Respondent or other household members allow pets to lick hands:					
Multiple times a day, once per day, a few times a week = 4	Once per week =3	A few times in last 30 days = 2	once in last 30 days = 1	Never = 0	4
Perceived time spent directly touching or having direct contact with pets:					
Greater than 8 h/day = 4	6–8 h/day = 3	2–5 h/day = 2	Less than 1 h/day = 1	No Contact = 0	4
Total maximum index value					27

use survey questions for human case ascertainment. For studies with paired human and animal testing, the CHAIS instrument may be used to measure risk factors associated with zoonotic and reverse zoonotic transmission events. Additionally, studies that include antibody testing of humans and/or animals may use the CHAIS instrument to evaluate transmission risks for particular time periods based on time-bound questions. Researchers should take into consideration the current limitations of antibody testing, including antibody duration and accuracy in humans and animals [31–33]. Researchers also should consider vaccination status of people and animals and are encouraged to add questions as needed. Studies conducted in environments where infected humans interact with multiple animal species may build upon laboratory animal model studies by elucidating natural-world differences in susceptibility and transmission patterns.

5. Limitations

While the CHAIS instrument incorporates spatial characteristics of shared environments and was developed with contributions from experts in environmental health, it alone does not serve as a robust assessment of the built environment and its effects on infectious pathogen spread. We encourage scientists who are interested in investigating the built environment's role in CoV-2 and other pathogens to acknowledge the guidelines set forth for environmental assessments and One Health studies, like COHERE [34]. To better characterize household and workplace environmental risk factors of CoV-2 spread, researchers may want to include questions that capture information about air ventilation systems, sanitary plumbing, types of home surfaces, and others [35]. For studies in which environmental sampling will be conducted, additional questions about frequency of sanitation, cleaning products used, type-of heating and cooling systems used, and other environmental modifiers in the home such as air purifiers or humidifiers may be included.

Similarly, the CHAIS instrument does not fully capture information about human-wildlife and wildlife-domestic animal interactions. For researchers focusing on these interfaces, we recommend expanding upon what is provided in the current version of the CHAIS instrument to gather complete information and enhance surveillance efforts of not only CoV-2 but other infectious diseases at wildlife/human/domestic animal interfaces. Likewise, expansion and further adaptions are recommended for working dog populations, human-livestock interactions, and other interfaces CHAIS does not fully capture including farms, zoos, shelters, and veterinary spaces.

Finally, the CHAIS instrument is limited during the times in which overlapping seasonal pathogens with similar symptoms to CoV-2 are in circulation (i.e. influenza viruses). Though we believe that there is great value in symptom-based reporting for CoV-2 and other diseases [36], symptoms due to other respiratory diseases (i.e. influenza viruses) may confound associations between human-animal interactions and zoonotic transmission of CoV-2. For studies that do not include the use of confirmatory testing, we recommend that researchers account for co-circulation of known seasonal and endemic pathogens with CoV-2 and acknowledge this when reporting findings.

While this instrument is yet to be fully validated, it was modeled on previously published instruments [19–21] and followed an extensive expert review process, satisfying content validation, which can be viewed as the initial step in complete instrument validation [37]. Given the urgent need to identify risk factors associated with zoonotic and reverse zoonotic transmission of CoV-2, including emergent and potentially heterogenous CoV-2 strains, the CHAI-WG determined that content validation of the instrument was sufficient for public dissemination in anticipation that data collected from multiple studies which adopt CHAIS will inform construct validity of the instrument for CoV-2 and other pathogens. This instrument is available to use in REDCap [38] by request.

We recommend researchers use validated instruments where additional questions or adaptations are needed to mitigate confounding variables. Given the multitude of potential settings and geographies where the CHAIS instrument is deployed, we encourage researchers to consider and anticipate biases when designing research studies that use the CHAIS instrument so that this may be accounted for in the analysis.

6. Future directions

Though the CHAIS instrument may be adapted for other pathogens, we suggest that the research community prioritize questions related to 1) risk factors associated with transmission in animal care worker environments (e.g. zoos, animal shelters); 2) species-specific, biological, behavioral, and spatiotemporal risk factors for bi-directional transmission among human and animal populations; 3) risk identification and mitigation for spillover interfaces; and 4) impact of vaccination in humans and animals on transmission. Finally, despite a growing number of CoV-2 animal surveillance studies [39–44], CoV-2 testing in animals remains inconsistent among animal groups (domestic, farmed, and wild), and active animal surveillance may be needed to describe animal roles as potential reservoirs or intermediary hosts of CoV-2 [9,45,46].

7. Conclusion

The CHAIS instrument is a standardized tool for evaluating risk factors associated with transmission of CoV-2 and other similarly transmitted pathogens in environments where humans and animals share contact and addresses gaps in knowledge of behavioral, spatiotemporal, and biological factors underlying transmission from humans to pets and other animals. We ask that researchers cite and provide data for meta-analysis across studies for a more precise understanding of factors associated with zoonotic and reverse zoonotic exposure and transmission of CoV-2 and other zoonotic pathogens.

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Declaration of Competing Interest

The authors declare that they have no conflicts of interest in relation to this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2022.100422.

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