ARTICLE

https://doi.org/10.1057/s41599-022-01246-w

OPEN

Check for updates

Pre-graduate teaching of human parasitology for medical laboratory technologist programs in Japan

Sho Sekine₁[™]

Parasitic diseases continue to exist in many developing countries. In most cases, medical laboratory technologists (MLTs) detect parasitosis, which is then diagnosed and treated by medical doctors. However, parasitological education in medical schools has been declining, particularly in developed countries, leading to a decline in diagnostic ability. Therefore, the role of MLTs has become more critical. However, the current status of parasitology education in MLTs has not been investigated. In this study, a questionnaire survey of 93 schools and the students that are members of the Japanese association of medical technology and offer MLTs training programs was conducted. The educators were asked about the time and content of lectures and practical training, and the students were asked about their understanding of parasitology and the areas they found difficult. A series of χ^2 distribution analyses were employed to analyze the data, and the Benjamini-Hochberg method was subsequently used to correct the p-values. This study included 62 out of 93 schools and 1043 students as participants. The results revealed a significant decrease in lecture hours in parasitology compared to 1994, and the trend that may continue in the future. In addition, after attending the lectures, students tended to disregard parasitology as a necessary subject. Pre-study interest was found to have an impact on post-study comprehension. This study is the first to report on the current status of parasitology education in MLTs parasitology training programs in parasite-free countries and can serve as a model for similar studies in other regions in the future.

¹Morinomiya University of Medical Science, 1-26-16 Nankokita, Suminoe-ku, Osaka-shi, Osaka 559-8611, Japan. 🖾 email: sho_sekine@morinomiya-u.ac.jp

Introduction

s Norman Stoll described, in his 1947 paper, *This Wormy World* (Stoll, 1947), that parasitic diseases remain the most common chronic infections globally, and the majority of affected patients live in developing countries with poor sanitation (Palmieri et al., 2011). Parasitic diseases wreak havoc on the health of the residents of endemic areas and exacerbate poverty by robbing them of their labor. The negative spiral that hinders development must be broken (Wijerathna et al., 2018; Khuu et al., 2019). To this end, non-government organizations, such as Doctors Without Borders, and a few pharmaceutical companies have provided support, but the problem remains unsolved (Fitzmaurice et al., 2019; Zitko and Doležal, 2016).

In contrast to developing countries, sanitation in developed countries has improved tremendously, and the majority of the people now live parasite-free lives (Bethony et al., 2006). Many parasitic diseases have been grouped together as neglected tropical diseases and are frequently overlooked, especially in developed countries, despite the fact that over a billion people are infected worldwide (Bodimeade et al., 2019; Molyneux et al., 2017, Engels and Zhou, 2020). However, parasitic diseases are likely to increase in this age of globalization and changing diets, even in developed countries. For instance, in 2015, France reported domestic cases of bilharziasis (Beltrame et al., 2015), while in 2017, Italy reported cases of non-imported falciparum malaria (Boccolini et al., 2020); these two countries are classified as parasite-non-endemic countries.

Particularly in parasitic diseases, the detection of parasite eggs and their bodies, is directly related to the diagnosis; hence, the role of medical laboratory technologists (MLTs) has become critical (Garcia et al., 2018). However, the qualifications and systems for MLTs vary significantly from country to country (Sakamoto, 2012). For example, in the United States (US), in addition to each state, the American Society for Clinical Pathology (ASCP), American Medical Technologies (AMT), and the American Association of Bioanalysis (AAB) conduct MLT examinations. The MLTs in the US are characterized by the fact that they solely perform specimen testing (e.g., blood or urine). In Japan, MLTs are specialists who analyze the components of a patient's specimen at a medical facility. Additionally, they conduct tests ranging from electrocardiography to microbiology and pathology and they provide medical doctors (MDs) the accurate data necessary to make a diagnosis.

The training of MLTs in Japan began in 1959. At that time, they were called public health laboratory technicians, and their one of main job was to improve public health through testing for parasites, which were prevalent in 60–80% of the population due to poor sanitation after World War II (Mimura, 2015).

Initially, the main focus was on training through 2- or 3-year programs at technical colleges, where it was hoped that personnel who could be immediately effective in the clinical field would be trained. Later, however, as public health conditions improved, and the scope of work expanded with the development of medical technology, 4-year education at universities became the norm. Therefore, in 2004, all national universities in Japan that offer clinical technologist training programs shifted from 3-year to 4-year programs.

Currently, 69 of the 93 schools registered with the Japanese association of medical technology offer 4-year programs, and more than 80% of these schools also offer graduate programs (Matsuda, 2017).

In teaching programs for medical students who will treat parasitic diseases, the number of hours devoted to parasitological lectures is decreasing. Several countries are concerned about the decline in the ability of MDs to diagnose parasitic diseases (Bruschi, 2009; Takahashi et al., 2010; Janovy, 2014). As a result, the role of MLTs in detecting parasites in clinical settings is expected to grow worldwide. However, there are many aspects of parasitology education in MLT training programs that have not been clarified. Several papers on parasitology education are being reported (Hillver, 2020; Jabbar et al., 2021), but these are studies regarding the impact of COVID-19 on parasitology education and the trial of new teaching methods using e-leaning. Regarding parasitology education in China, Zhao et al. (2012) reported on lectures and lab hours, but these were mainly for medical or nursing students, and there is little information on MLT programs. In Japan, only one survey was conducted on parasitology education in MLT training programs (Sano et al., 1994). However, this survey was conducted before the transition to a 4-year program for training MLTs at all national universities in Japan. At that time, 4-year education was offered at only 9 out of 81 schools, so it is unlikely to reflect the current status. Therefore, the purpose of this study is to investigate the lecture and practical training hours in MLT training programs in Japan to clarify the changes since 1994. In addition, a questionnaire survey was conducted to determine the level of interest in and understanding of parasitology among students in MLT training programs.

This study not only sheds light on the current status of parasitological education in MLT training schools in Japan but it can also serve as a model for future studies in many other countries.

Methods

Data collection and sample size. The current status of parasitology education was investigated using a questionnaire survey of educators and students at Japanese universities and colleges that offer MLT training programs. In this study, "university" was defined as a 4-year bachelor's degree program and "college" as a 3-year tertiary institution. "School" is used as a generic term for both university and college. The questionnaire, which included a Q.R. code for answering online and a request form for students to participate in this study, was mailed to educators or the educational affairs division of each school. They were then asked to fill out the questionnaire and return it to the researcher or answer it online. In addition, educators were asked to encourage students from each school to participate in this study. The survey was conducted from April through June 2021. If multiple educators were in charge of a lecture, only one representative was asked to complete the questionnaire.

The target sample size (*N*) was determined using the formula below, where *d* represents the confidence level, *p* is the response ratio, λ denotes tolerance, and *n*' represents the total number of participants. In this study, d = 5%, p = 95%, and $\lambda = 50\%$. The number of schools, university students, and college students were 93, 15,892, and 2880, respectively. The number of students was estimated based on the number of students who took the national examination for MLT held in 2020.

$$n = \lambda^2 \frac{p(1-P)}{d^2}, \qquad N = \frac{nn'}{n+n'-1}$$

Participation in this study was voluntary, and no personally identifiable information, such as names, was collected.

Questionnaire. Three comprehensive questionnaires, which included open-ended questions, single and multiple-choice questions, and scale questions (four-point Likert scale), were developed for educators and students who had previously taken parasitology as well as those who had not. The questionnaire for educators included information about the hours and content of lectures or practical training, number of full-time or part-time

educators, curriculum, and their opinions on existing parasitology education. The questionnaire for students collected data on grade level, parasitology enrollment, and interest in and understanding of parasitology.

Data analysis. A series of χ^2 distribution analyses were employed to analyze the relationship between school (university or college) and the understanding of parasitology. Furthermore, the relationship between students (completed or uncompleted) and their perceptions of the importance of parasitology was also analyzed. The Benjamini–Hochberg method was subsequently used to correct the *p*-values. The *p*-value information should be interpreted descriptively because of the exploratory nature of this study. The analysis of the importance of parasitology was scored on a four-point scale (4 = very important), and an unpaired t-test was used. In this study, *p* < 0.05 was considered statistically significant and all tests were conducted using a two-tailed test.

Descriptive and exploratory inferential statistics were computed using js-STAR, a free website for statistical analysis (http:// www.kisnet.or.jp/nappa/software/star/index.htm). The correlation coefficient (r) was calculated after replacing the level of understanding with a ten-point scale (1–10) and the importance of parasitology with a four-point scale (1–4). The calculation was also performed using js-STAR. In this study, r < 0.2 was considered as no correlation, $0.2 \le r < 0.4$ as weak, $0.4 \le r < 0.7$ as moderate, and $0.7 \le r$ as strong correlation. Results are shown as mean \pm standard deviation (SD).

Results

Questionnaire collection. The study's target sample sizes were 76, 376, and 340 for the schools (educators), university students, and college students, respectively. A total of 93 schools were surveyed, resulting in 62 (67.4%) educators responding but not reaching the target sample size. Of the 1043 students who participated in the study, 663 (63.6%) were university students and 380 (36.4%) were college students. Both of them yielded the target sample size. Of the students, a total of 525 (50.3%) completed their parasitological courses. This group was compared to the group that did not complete parasitological courses (n = 518) (Table 1). In this study, students who had completed at least 75% of the course were treated as having completed the course.

Time spent on lectures and practical training. In the parasitological course, the average lecture duration was 1136 ± 384 min (maximum: 2070 min, minimum: 450 min). The average amount of time spent on practical training was 904 ± 665 min (maximum: 2700 min, minimum: 0 min) (Table 2). Four institutions (two universities and two colleges) reported that they did not offer practical training.

The lecture duration was deemed adequate by 46 schools, whereas it was deemed excessive and insufficient by four and 12 schools, respectively. The schools that responded excessively had 1350 min of lectures and 2003 ± 507 min of practical training, while the schools that responded insufficiently had 970 ± 401 min of lecture and 659 ± 397 min of practical training. In addition, 10 schools in the survey indicated that they had reduced the number of parasitology classes in the past 5 years, with the average reduction being 484 ± 199 min (maximum: 675 min, minimum: 270 min) for lectures and 576 ± 362 min (maximum: 990 min, minimum: 540 min) for practical trainings. Furthermore, two schools indicated that they plan to reduce the number of lectures in the near future, although the details thereof have not yet been determined.

Table 1 Affiliations and grades of students who participatedin this study.

| | 1st grade | 2nd grade | 3rd grade | 4th grade | Total |
|-------------|-----------|-----------|-----------|-----------|-------|
| Completed | 33 | 125 | 192 | 175 | 525 |
| Uncompleted | 249 | 152 | 117 | 0 | 518 |

Table 2 Time of lectures and practical training inparasitology and working style of lecturers.

| | Lecture time (min) | Training time (min) | No. of full- time educators | No. of part- time educators |
|---------|-----------------------|------------------------|-----------------------------------|-----------------------------------|
| Average | 1136 | 904 | 1.0 | 0.8 |
| SD | 384 | 665 | 1.1 | 0.7 |
| Max. | 2070 | 2700 | 4.0 | 3.0 |
| Min. | 450 | 0 | 0.0 | 0.0 |

SD standard deviation, Min. Minimum, Max. Maximum

 Table 3 Students' grades for whom parasitological lectures

 and practical training were offered.

| | Lecture | | Training | |
|-------------------------------------|---------------|--------------|---------------|-------------|
| | University | College | University | College |
| 1st grade 2nd grade 3rd grade | 3 20 23 | 12 4 0 | 2 17 25 | 7 7 0 |

Table 3 shows the grades in which lectures and practical training were given. All results are expressed as mean \pm SD. If the SD is zero, it is not shown.

Educators. The average number of educators working full-time was 1.0 ± 1.1 (with a maximum of 4 and a minimum of 0). The mean number of part-time educators was 0.8 ± 0.7 (maximum: 3, minimum: 0) (Table 2). There were no full-time educators in 24 schools (38%, 14 universities, and 10 colleges). The most common specialty of lecturers in 34 schools was parasitology, followed by microbiology (12 schools), public health, and pathology (3 schools each).

Changes in students' perceptions of parasitology before and after the course. Mean scores were calculated for completed and uncompleted students, with "very important" receiving a score of 4 and "not important at all" receiving a score of 1. The mean score was 3.20 ± 0.62 for completed students and 3.35 ± 0.57 for uncompleted students, which was significantly lower ($p = 7.28 \times 10^{-5}$) for completed students (Fig. 1). This is because "very important" decreased significantly (adjusted residual value: 2.990, p = 0.0028) and "not important" increased significantly (adjusted residual value: 2.958, p = 0.0031) among students who had already taken the course (Supplementary Fig. 1)

Correlation coefficients (*r*) were calculated for three items: performance at the time of questionnaire response, comprehension, and importance of parasitology (Table 4). The results showed no correlation between grade and level of understanding (r = -0.089). There was, however, a weak negative correlation (r = -0.226) between grade and importance and a weak positive correlation (r = 0.250) between comprehension and importance.



Fig. 1 Comparison of the perception of importance before and after the parasitological course. Students who had taken parasitology (n = 525) and those who had not (n = 518) were asked how importantly they perceived parasitology. The students were asked to rate the importance of parasitology on a four-point scale (4 = "very important" and 1 = "not important at all").

Table 4 Correlation coefficients between students' grade, level of understanding, and perception of the importance of parasitology.

| | Students' grade | Level of understanding | Importance of parasitology |
|--|-----------------|---------------------------|-------------------------------|
| Students' grade Level of understanding | -0.089 | -0.889 | -0.226 0.250 |
| Importance of parasitology | -0.226 | 0.250 | |

Discussion

Of the 93 educators, 62 (67.4%) participated in the research, which was slightly less than the target of 76. This is due to the fact that many educators are in charge of multiple schools, and some are retired or work part-time, making communication difficult. While this is one of the limitations of this study, receiving responses from more than two-thirds of the relevant Japanese educators is a significant achievement. Furthermore, several schools held remote lectures due to the COVID-19 measures during the survey collection period (Bahri and Read, 2021; Jabbar et al., 2021), but a sufficient number of students cooperated in this study.

Sano et al. (1994) reported that all lectures on parasitology in MLT training programs in Japan were given by experts. Lectures lasted a maximum of 5520 min and a minimum of 3120 min, and practical training lasted a maximum of 3960 min and a minimum of 1200 min. The results of this study showed that in 2021, lecture and practical training time decreased to 1136 ± 353 and 904 ± 665 min, respectively (Table 2), and not all educators were parasite experts. The amount of time devoted to parasitology education in MLT training programs in Japan has decreased significantly over the past 20 years, and two schools (one university and one college each) are planning to further reduce lecture hours, which may further diminish parasitology in the future. One of the reasons for the large decrease in lecture hours in parasitology is presumably the decrease in parasite examinations, with 231,276 parasite examinations conducted by the Tokyo Health Service Association in 1994, but only 957 conducted in 2021 (Annual report of Tokyo Health Service Association, 2021).

In this survey, there was more variation in the practical training than in the lectures. This was most likely due to the fact that four schools did not offer practical training. One of the reasons for not conducting practical training is that 38% of the schools lacked full-time educators who specialize in parasitology. While collecting the questionnaires, several points were made: the aging of educators and the lack of young educators (Supplement table). The development of educators capable of leading lectures and practical training is also considered critical for parasitology education's future stability. Another reason for the lack of practical training could be that obtaining samples becomes more difficult every year as parasitosis declines. Japanese medical schools have a project proposal to promote the collective management and sharing of samples (Takahashi et al., 2010), but there is still no way to realize it. Such a project must also be implemented in MLT training programs.

In this study, no significant differences in understanding of parasitology were found between university students and college students (Supplementary Fig. 2). Regarding the comprehension levels of students, 5.1% of university students and 12.5% of college students responded with a comprehension level of 11–20%, and the residual analysis confirmed significant differences only in this column. One reason for this is that lectures on parasitology are often given in the third year at universities, however, at colleges they are often given in the first year (Table 3), resulting in a lack of knowledge of other basic medical sciences necessary for understanding parasitology. One educator in this survey took issue with this point (Supplementary Table).

After attending lectures, students indicated that they tended to somewhat disregard parasitology (Fig. 1). This is presumably because, through the lectures, they have come to regard parasitic diseases as rare in Japan and irrelevant to them. However, there was a positive, albeit somewhat weak, correlation (r = 0.250)between students' perceptions of the importance of parasitology and their level of understanding (Table 4). Therefore, highlighting the importance of parasitology globally by introducing MLTs working for international organizations such as the Japan International Cooperation Agency (JICA) may also help to increase students' understandings. It was also suggested that the interest of the students before attending the lecture may affect their understanding of the lecture afterward. (Supplementary Figs. 3 and 4). However, due to this finding, it is possible that students may not have been interested in this project, and more detailed research is needed. Due to COVID-19, not only traditional faceto-face lectures but also online lectures have been actively conducted. In particular, e-learning-based education is gaining traction and has been incorporated into parasitology education (Jabbar et al., 2016, 2021). Furthermore, the use of digital materials has been shown to reduce learning time (Shomaker et al., 2002). However, it is being argued that excessive reliance on digital materials should be avoided and face-to-face lectures are necessary (Gunn and Pitt, 2003; Jabbar et al., 2016). Since these are considered an important method to compensate for the everdecreasing number of lectures, it is necessary to explore ways to utilize digital materials effectively to stimulate student interest.

Conclusion and prospects

The results revealed that parasitology education has been shrinking in MLT training programs in Japan as well as in medical schools. In particular, parasitology education in MLT training programs has decreased significantly compared to 1994. Additionally, this study found that students who had taken parasitology were somewhat more likely to disregard it than those who had not. In addition, it is also suggested that the interest of the students before attending the lectures may affect their understanding of the lecture afterward. Therefore, it is crucial to provide lectures in which students unfamiliar with parasites can develop an interest in and appreciation for the subject. This study is the first to report the impact of declining parasite prevalence on parasitology education in MLT training programs and provides essential data for future curriculum evaluation in various countries.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. All data were collected in Japanese and translations into other languages can be provided on request. In this study, I used js-STAR, the website for statistical processing (http://www.kisnet. or.jp/nappa/software/star/index.htm). Anyone can use this site without registration. It is also possible to check the R code used for the analysis.

Received: 5 November 2021; Accepted: 23 June 2022; Published online: 02 July 2022

References

- Bahri R, Read L (2021) Perspectives of medical student interviewers conducting online interviews during the COVID-19 pandemic. Med Sci Educ. https://doi. org/10.1007/s40670-021-01341-8
- Beltrame A, Zammarchi L, Zuglian G et al. (2015) Schistosomiasis screening of travelers from Italy with possible exposure in Corsica, France. Emerg Infect Dis 21(10):1887–1889
- Bethony J, Brooker S, Albonico M et al. (2006) Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm. Lancet 367(9521):1521–1532
- Boccolini D, Menegon M, Di Luca M et al. (2020) Non-imported malaria in Italy: paradigmatic approaches and public health implications following an unusual cluster of cases in 2017. BMC Public Health 20(1):857
- Bodimeade C, Marks M, Mabey D (2019) Neglected tropical diseases: elimination and eradication. Clin Med 19(2):157–160
- Bruschi F (2009) How parasitology is taught in medical faculties in Europe? Parasitology, lost. Parasitol Res 105(6):1759–1762
- Engels D, Zhou XN (2020) Neglected tropical diseases: an effective global response to local poverty-related disease priorities. Infect Dis Poverty 28 9(1):10
- Fitzmaurice C, Abate D, Abbasi N et al. (2019) Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2017: a systematic analysis for the global burden of disease study. JAMA Oncol 5(12): 1749–1768
- Garcia LS, Arrowood M, Kokoskin E et al. (2018) Practical guidance for clinical microbiology laboratories: laboratory diagnosis of parasites from the gastrointestinal tract. Clin Microbiol Rev 31(1):e00025–00017
- Gunn A, Pitt S (2003) The effectiveness of computer-based teaching packages in supporting student learning of parasitology. Biosci Educ 1(1):1-14
- Hillyer JF (2020) Parasites and parasitology in this SARS-CoV-2, COVID-19 World: an American Society of Parasitologists Presidential Address. J Parasitol 106(6):859-868. https://doi.org/10.1645/20-158
- Jabbar A, Gasser RB, Lodge J (2016) Can new digital technologies support parasitology teaching and learning. Trends Parasitol 32(7):522-530
- Jabbar A, Gauci CG, Anstead CA (2021) Parasitology education before and after the COVID-19 pandemic. Trends Parasitol 37(1):3-6
- Janovy J (2014) Why American higher education needs parasitologists. J Parasitol 100(6):700-707
- Khuu D, Eberhard ML, Bristow BN et al. (2019) Economic impact of malariarelated hospitalizations in the United States, 2000–2014. J Infect Public Health 12(3):424–433
- Matsuda H (2017) Graduate School Education of clinical laboratory scientist. J Junshin Gakuin Univ 2017(6):23-30
- Mimura K (2015) Rinshou kensa gishi kyouiku no rekisho wo tsumugu (Weaving a history of medical laboratory technologist education). Jpn Assoc Med Technol Educ 7:16–23
- Molyneux DH, Savioli L, Engels D (2017) Neglected tropical diseases: progress towards addressing the chronic pandemic. Lancet 389(10066):312-325

- Palmieri JR, Elswaifi SF, Fried KK et al. (2011) Emerging need for parasitology education: training to identify and diagnose parasitic infections. Am J Trop Med Hyg 84(6):845–6
- Sakamoto H (2012) Kaigai ni okeru rinnsyoukensagishi no shikaku seido (Qualification systems for clinical laboratory technicians abroad). Modern Media 58(12)
- Sano MH, Wang W, Chen K et al. (1994) Takeda a training on clinical parasitology and medical zoology in the College of Medical Technology. Med Technol 38:849–852
- Shomaker TS, Ricks DJ, Hale DC (2002) A prospective, randomized controlled study of computer-assisted learning in parasitology. Acad Med 77(5):446–449 Stoll NR (1947) This wormy world. J Parasitol 33(1):1–18
- Takahashi YY, Oku T, Aoki et al. (2010) Igaku kyouiku no henkaku ni muketeno kiseichugaku idoubutugaku kyouiku (Parasitology and Medical Zoology Education for the Transformation of Medical Education.). Igaku kyouiku (Med Edu) 41(1):17-21
- Tokyo Health Service Association (2021) Annual report 2021. https://www. yobouigaku-tokyo.or.jp/nenpo/pdf/2021/03.pdf. Accessed 11 March 2022
- Wijerathna T, Gunathilaka N, Gunawardena K (2018) The economic impact of cutaneous leishmaniasis in Sri Lanka. Biomed Res Int 2018:3025185
- Zhao G, He S, Chen L et al. (2012) Teaching human parasitology in China. Parasit Vectors 5:77. https://doi.org/10.1186/1756-3305-5-77
- Zitko J, Doležal M (2016) Enoyl acyl carrier protein reductase inhibitors: an updated patent review (2011–2015). Expert Opin Ther Pat 26(9):1079–1094

Acknowledgements

I would like to thank all the people who participated in the questionnaire survey for conducting this study. I also thank our colleagues at Morinomiya University of Medical Sciences and Osaka Metropolitan University Graduate School of Medicine for their advice in conducting this study. I would like to thank Editage (www.editage.com) for English language editing. This work was supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI Grant Number 21K02817.

Author contributions

As this is a single-authored paper, all research was carried out by one.

Competing interests

The author declares no competing interests.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent

Before the questionnaire survey, the participants were given a document to explain the purpose of this study. Afterwards, only those who understood the study aims and were willing to cooperate were asked to respond. The authors' contact details were included in the handout, and questions about the study and withdrawal of cooperation were accepted. From this, I believe that informed consent was obtained from all participants. Approval to conduct this research has been obtained from the ethics committee of the author's institution (details in the cover letter). Before carrying out the questionnaire survey, a document explaining the purpose of this research was distributed and responses were requested only if the participants understood the purpose of this study. Moreover, the questionnaire does not contain any personally identifiable information.

Consent for publication

I have also provided informed consent to publish the data obtained through this study at academic conferences and papers. This study did not contain any information that could identify individuals or schools.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1057/s41599-022-01246-w.

Correspondence and requests for materials should be addressed to Sho Sekine.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/ licenses/by/4.0/.

© The Author(s) 2022