

Students Need More than Content Knowledge To Counter Vaccine Hesitancy

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To better prepare undergraduate students as informed citizens, they need skills to evaluate and interpret scientific data that are relevant to real world scenarios. Socioscientific issues are typically complicated or debatable issues that require individuals to evaluate their background knowledge and make decisions with respect to social and cultural contexts. Incorporation of socioscientific issues into a course allows students opportunities to demonstrate their argumentation skills. In this study, we investigated the relationship between students' biological content knowledge and their argumentation skills. We evaluated students' content knowledge of primary research articles on mRNA vaccine development and clinical trials. There was no correlation of content knowledge and students' argumentation skills to counter vaccine hesitancy. While most students demonstrated understanding of the primary research articles, almost half the students did not include specific biological knowledge in their arguments, indicating they had difficulty in applying their knowledge to the real world. These results suggest there is a need to provide students with additional opportunities to practice and develop their argumentation skills with respect to socioscientific issues.

KEYWORDS socioscientific issue, scientific literacy, argumentation skills, vaccine hesitancy

INTRODUCTION

With information being more readily accessible, science education must consider not only teaching students scientific concepts but also developing their critical thinking skills to analyze and interpret scientific data to make decisions which may be applicable to their lives (1). Decision-making on social issues requires students to evaluate their content knowledge or evidence in the social or cultural context to support their reasoning (2). Student's content knowledge plays a significant role in their ability to discuss and reason key issues (3–5). However, decision-making is not based solely on one's understanding of content. A number of other factors, including personal experiences, family perspectives, morality, social contexts, and emotions, influence informal reasoning and decision-making in students (6–8). In navigating this complex network of decision-making, it is unclear what level of science literacy is necessary to help individuals make informed decisions on social issues (9).

In the classroom, science educators may introduce, integrate, and evaluate social issues from a science perspective, which is also known as the Socioscientific Issue (SSI) approach (10). SSIs focus

on integrating science into a dynamic network where students have different moral, political, social, and economical perspectives, and they are encouraged to apply their content knowledge in their reasoning, argumentation, and decision-making on social issues (8, 10, 11). SSIs encourage students to expand their views and consider societal and global perspectives in their reasoning (12). Informal reasoning involves thinking and evaluating an issue and making a claim or decision and typically occurs when the issue is more open-ended, complicated, or debatable (13, 14).

A key component of informal reasoning includes the use of argumentation skills (5, 13). Argumentation is a fundamental practice in science as scientists use evidence to support or justify their claims. Learning argumentation skills is a critical part of science education (15). The quality of an argument or justifications used in an argument is also associated with content knowledge and rationalistic informal reasoning, characterized by the use of logic and reason (16, 17).

Argumentation involves discussing and writing science and reflecting about self and society, which supports scientific literacy and critical thinking skills (18). Writing in courses can be used to not only assess but also improve students' learning, critical thinking, reasoning, and argumentation skills (19–23). Students who apply their content knowledge in weekly essays exhibit improved critical thinking skills, with highest gains in their analytical and inference abilities (21).

Argumentation skills align with the ability to apply the process of science, which is emphasized as a core competency for biological literacy. In higher education, the emphasis in biology education reform has been focused on knowledge (core concepts) and practice of science (core competencies) (1). One of the other core competencies is the understanding of the

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relationship between science and society. SSIs in biology courses provide students with the opportunity to practice their informal reasoning and argumentation skills in the larger societal and cultural context. However, only a few higher education research studies have involved the use of SSIs (24), suggesting there is a need to evaluate how societal issues are integrated into higher education biology courses.

With the 2019 coronavirus disease pandemic (COVID-19), there has been a call to action to integrate SSIs into courses to increase science literacy and immune literacy (25). Here, we introduced vaccine hesitancy as an SSI in a scientific writing course for undergraduate students who were primarily biology majors. In this writing course, students were asked to write about scientific concepts as well as reflect on societal issues, including racism, climate change, and vaccine hesitancy. Vaccine hesitancy has been defined as the “delay in acceptance or refusal of vaccines despite availability of vaccine services. Vaccine hesitancy is complex and context specific, varying across time, place, and vaccines” (26). Major determining factors for vaccine hesitancy are confidence, complacency, constraints, calculation, and collective responsibility (27). Racial factors, including racial fairness and racial consciousness, are more likely to contribute to vaccine hesitancy for people of color compared to white people (28). At the time of the study in early June 2021, 47.3% of the population in California (location of the study) had completed the vaccination series (2 doses) and 56.9% had been administered one dose of the vaccine, according to the Centers for Disease Control and Prevention (29). COVID-19 vaccination rates varied depending on a number of factors, including race/ethnicity, employment status, religious beliefs, gender, education, and age, among others (30).

Strategies to address vaccine hesitancy include educating people about how vaccines work, how vaccines are tested, and being transparent about any conflicts of interests (31). The most common reasons cited for vaccine hesitancy involve the speed of vaccine development and potential side effects or safety concerns (32, 33). In the scientific writing course, we address these two main concerns by reading five primary research articles ranging from the development of mRNA vaccines to testing the Moderna and Pfizer COVID-19 vaccines in clinical trials. After providing students with the background knowledge and skills to analyze and interpret data from these primary papers, we asked the following research questions:

1. What is the content knowledge of vaccines and argumentation skills of students? Are there differences in students from different backgrounds (gender, first-generation status, marginalized groups, or socioeconomic status)?
2. Is there a correlation between students' knowledge of vaccines and their argumentation skills to counter vaccine hesitancy?
3. In their counterargument to vaccine hesitancy, do students justify their claims with specific knowledge about vaccines?

TABLE I
Demographic characteristics of students

Category and characteristic	% (n)
Gender	
Female	58.8% (50)
Male	41.2% (35)
Race/ethnicity	
Asian	48.2% (41)
Black or African American	3.5% (3)
Native Hawaiian or other Pacific Islander	10.6% (9)
Latinx	20.0% (17)
White	16.5% (14)
Decline to state	1.2% (1)
Low income	27.1% (23)
First generation	49.4% (42)
Transfer	36.5% (31)
STEM major	95.3% (81)

METHODS

Study participants

The study was conducted in the Spring quarter of 2021 at a large public university with a Carnegie basic classification of Doctoral University: Highest Research Activity. It is a Hispanic-serving institution with at least 25% of the undergraduate student population identifying as Hispanic or Latinx.

This study was conducted under the guidelines of the Institutional Review Board (protocol number 2808).

Scientific writing course

All participants ($n = 85$) were enrolled in a scientific writing course in Spring 2021. The scientific writing course was a required course for students majoring in the biological sciences, and 95.3% of the students were science, technology, engineering, and mathematics (STEM) majors. Prerequisites for the course included cell biology and organismal biology, ecology and evolutionary biology, genetics, and biochemistry. Molecular biology may have been taken as a corequisite. Most students enrolled in the scientific writing course in their third year or later (75%, $n = 64$). Twenty-five percent of students ($n = 21$) were at the end of their second year. Demographic information for students enrolled in the course is provided in Table I.

The learning goals of the course were as follows: (i) describe the elements found in each section of a scientific paper or lab report; (ii) read a paper and research its components enough to be able to describe in writing the background, hypothesis, and the findings to a peer; and (iii) communicate scientific ideas through writing skills. The course met three times a week for 50 min each class period for one quarter (10 weeks). The course

was designed to be high structure with a primary research article annotated on Perusall and 2 additional assignments completed each week. During class, active learning strategies were emphasized as students discussed a specific section of the article and worked on their assignments with facilitation by a teaching assistant or learning assistant. One of the assignments allowed students to practice their science writing with respect to the primary research article before a summative quiz each week.

During the first half of the course, the topics of the research articles changed every 1 to 2 weeks, including aposematism, aging and exercise, and sea organism responses to changes in temperature and microplastics. In the second half of the course, the research articles focused on mRNA vaccine development and the clinical trials of Pfizer and Moderna vaccines (see Appendix S1 in the supplemental material). Students were assessed on the content of the article at the end of the week with short-answer quizzes (5 to 7 questions). Short-answer quiz questions included asking students to identify the hypothesis of the paper, provide rationale for experiments, draw conclusions based on a figure, explain how one finding is related to another, or identify limitations of a study (see Appendix 2 for example quiz questions). Average quiz scores were used to assess mRNA vaccine content knowledge.

Finally, in addition to content-focused assignments, there were three required assignments that asked students to share their opinions on social issues, including racism in academia, climate change, and vaccine hesitancy. With respect to racism and climate change, students were asked how they might address these issues after reading papers on these topics.

Argumentation skills analysis

For the vaccine hesitancy assignment, at the end of the quarter, students were asked to answer one or more of the following questions: (1) Does someone you know (or you) have concerns about getting the COVID-19 vaccine? What concerns do they (or you) have about the vaccine? (2) Having read the research papers on the COVID-19 mRNA vaccine, how would you talk to someone who had concerns about the speed of the mRNA vaccine development? Safety of the vaccine? Distrust of science and/or medical communities? (3) In the future, how can science and medical communities improve their relationship with communities of color? Students were told that the assignment would be graded for completion and should be written entirely in their own words. Most students chose to answer questions 1 and 2, and a few students focused on question 3.

Responses to question 2 were analyzed to determine how students argued against vaccine hesitancy. Argumentation skills of students were determined by the number of justifications and types of justifications (14). A justification was considered to be a reason that the student provided for someone to receive the vaccine. Justifications provided by students addressed different aspects of vaccine hesitancy, including speed of vaccine development, safety, efficacy, and herd immunity, among others. The number of justifications was coded as 0 (no justification provided

or no argument made), 1 (one justification), 2 (two justifications), or 3+ (three or more justifications). Examples of 1 to 3+ justifications (in italics) are provided below.

Examples of students' justifications and further categorization

(i) Example with one justification. *"In an effort to convince him to get the vaccine, I try to persuade him that although he may think he doesn't 'need' it, he can also be helping others by receiving immunity from COVID-19."* (Student 7)

(ii) Example with two justifications. *"Many members of my family were wary of the vaccine mainly because of how quickly it was developed. They believed that the vaccine was not truly tested for any long term damage. My sister and I did our best to explain vaccine research. We explained the differences between DNA and mRNA, what is the normal process for vaccine development, how we have knowledge and data bases for other viruses and vaccines. Also, everyone's body is different and can react differently to a vaccine. This does not mean the vaccine does not work."* (Student 21)

(iii) Example with three or more justifications. *"Having read the research papers on the Covid-19 mRNA vaccine, I would tell someone who has concerns about the speed of its development that there are many benefits to utilizing mRNA to protect ourselves from SARS-CoV-2, and many trials have been conducted to ensure its effectiveness. I would also emphasize that, because so much is known about the properties of mRNA, and combining that knowledge with new technology, this allows for speedy vaccine development. To individuals who have concerns about the safety of the vaccine, I would discuss with them that many trials were performed on, not just animals, but also people to test its safety. Furthermore, I would say that mRNA does not alter anyone's DNA (or anything else)—it helps us produce proteins to prevent us from infection."* (Student 36)

Justifications were further categorized as one of the following: (i) no biological knowledge is considered; (ii) consideration of nonspecific biological knowledge; (iii) correct consideration of specific biological knowledge (14). Justifications were considered to have no biological knowledge when students did not include or refer to biological concepts in their arguments. Justifications were considered to be nonspecific biological knowledge when students referred to general biological concepts without providing detailed information about the science, research, or vaccine. Justifications were considered to be of specific biological knowledge when students provided detailed information about the science, research, or vaccine. Students who made 2 or more justifications may have had justifications coded into more than one category. Examples of types of justifications are provided in Table 2.

To ensure interrater reliability, coding of the number of justifications and types of justifications were done by two individuals. Both individuals coded the entire data set independently. For the number of justifications, there was 80.2% agreement between the two raters and Cohen's kappa was 0.73, indicating

TABLE 2
Types of justifications provided by students

Category	Description	% (n)	Example
No biological knowledge is considered	Did not include or refer to any biological concepts	27.0% (40)	"I would talk to them that the COVID-19 vaccine is safe to use as a semiprofessional student majoring in biology." (Student 62)
Consideration of nonspecific biological knowledge	Provided a general statement, but does not provide any details about the science, vaccine, or research	34.5% (51)	"I have tried talking my coworkers into getting the vaccine by explaining how the mRNA vaccine works, but they remain skeptical that the long-term effects have not been documented (for obvious reasons)." (Student 77)
Consideration of specific biological knowledge	Provided detailed information about the science, vaccine, or research	38.5% (57)	"One recent study investigated the effects of mRNA vaccination in nonhuman primates, which resulted in successful combatant against SARS-CoV-19. This is important because the genetics of nonhuman primates are similar to that of humans, so this discovery was beneficial towards the development of the vaccines in human trials." (Student 79)

substantial agreement (34). For the types of justifications, there was 81.6% agreement between the two raters and Cohen's kappa was 0.72, indicating substantial agreement. Subsequent discussions occurred until 100% agreement was met on the number and types of justifications.

Statistical analysis

All statistical analyses were performed using R. One-way analysis of variance was used to determine if there was an overall difference in average quiz scores or number of justifications by race/ethnicity. Welch's *t* test was used to determine significant differences in average quiz scores or number of justifications by gender, first-generation status, marginalized groups, or socioeconomic status. Marginalized groups included Latinx, Black/African-American, Native Hawaiian/Pacific Islander, American Indian, and Alaskan Native. Pearson's correlation test was used to determine correlations between average quiz score and number of justifications and between average quiz score and types of justifications.

RESULTS

Content knowledge of mRNA vaccines

To assess students' content knowledge, students took a short-answer quiz after reading a primary research article on mRNA vaccine development or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccine clinical trials. Student's average scores on quizzes ranged from 83.66% to 94.60% (Fig. 1). Quiz 1 (mean score 85.14%, standard deviation [SD] 10.55, *n* = 76), quiz 2 (mean score 83.66%, SD 11.53, *n* = 79), and quiz 3 (mean score 89.17%, SD 10.39, *n* = 74) were

focused on primary research articles about mRNA vaccine development. Quiz 4 (mean score 89.05%, SD 10.01, *n* = 63) and quiz 5 (mean score 94.60%, SD 4.98, *n* = 49) were focused on primary research articles about SARS-CoV-2 mRNA vaccine clinical trials by Moderna and Pfizer, respectively. In the course, the two lowest quiz scores were dropped for their final course grade, and some students opted to not take quizzes 4 and 5, as they were administered in the last 2 weeks of the course.

Further analysis revealed that there were no overall differences in average scores for all 5 quizzes by race/ethnicity [$F_{(5, 75)} = 1.844, P = 0.12$]. The average scores for the 5 quizzes were the following: Asian (mean 89.23%, SD 7.03, *n* = 40), Black/African-American (mean 82.31%, SD 5.83, *n* = 3), Latinx (mean 87.47%, SD 5.79, *n* = 16), Native Hawaiian/Pacific Islander (mean 89.94%, SD 3.34, *n* = 9), and white (mean 84.43%, SD 6.83, *n* = 12). There was no significant difference in average quiz scores by gender [$t_{(54.97)} = -0.54, P = 0.59$], first-generation status [$t_{(70.76)} = 0.03, P = 0.98$], or marginalized status [$t_{(69.35)} = 0.36, P = 0.72$].

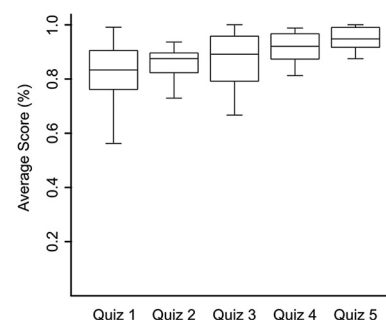


FIG 1. Student performance on short-answer quizzes. Quiz 1 (*n* = 76), quiz 2 (*n* = 79), and quiz 3 (*n* = 74) tested students' knowledge on primary research articles about mRNA vaccine development. Quiz 4 (*n* = 63) and quiz 5 (*n* = 47) tested students' knowledge on primary research articles on SARS-CoV-2 mRNA vaccine clinical trials.

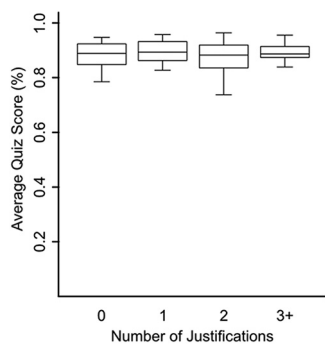


FIG 2. Student performance on short-answer quizzes and number of justifications to counter vaccine hesitancy. Students who had 0 ($n = 14$), 1 ($n = 12$), 2 ($n = 37$), or 3 or more justifications ($n = 18$) in their arguments to counter vaccine hesitancy performed similarly on quizzes that evaluated their knowledge of mRNA vaccine development and SARS-CoV-2 mRNA vaccine clinical trials.

There was a significant difference in average quiz scores by students who self-identified as non-low income (mean 87.25%, SD 6.92, $n = 59$) and as low income (mean 90.20%, SD 5.19, $n = 22$) [$t_{(50.25)} = -2.07$, $P < 0.05$].

Analysis of students' arguments to counter vaccine hesitancy

To determine if students used evidence or data in their arguments, students ($n = 81$) were asked to address common vaccine hesitancy concerns after reading primary research articles on the development, safety, and efficacy of the COVID-19 mRNA vaccine. The quality of their argument was based on the number of justifications included in their argument and whether they considered biological knowledge as part of their justification.

(i) Number of justifications. The number of justifications ranged from 0 justifications to 3 or more justifications. There were students who did not attempt to provide a counterargument for vaccine hesitancy. They expressed uncertainty about how to have the discussion and whether they themselves were knowledgeable enough to make an argument. "Sometimes I feel like I should educate themselves but I am worried that I do not have enough knowledge about the subject or enough of a backbone to talk to them like that." (Student 81).

Seventeen percent of students ($n = 14$) did not include any justification or provide an argument to counter vaccine hesitancy; 15% of students ($n = 12$) provided 1 justification; most students (46%, $n = 37$) included 2 justifications; 22% of students ($n = 18$) provided 3 or more justifications in their argument. Further analysis revealed that there were no overall differences in the number of justifications by race/ethnicity [$F_{(5, 75)} = 0.712$, $P = 0.62$]. There was no significant difference in number of justifications by gender [$t_{(71.05)} = 1.44$, $P = 0.15$], first-generation status [$t_{(74.94)} = 1.36$, $P = 0.18$], marginalized status [$t_{(47.52)} = 0.66$, $P = 0.51$], or socioeconomic status [$t_{(51.57)} = -0.63$, $P = 0.53$].

Regardless of the number of justifications in their arguments, students performed similarly on the content knowledge quizzes (Fig. 2). Students who gave 0 justification received an average

score of 87.65% (SD 5.90) on all five quizzes. Students who gave 1 justification received an average score of 89.82% (SD 4.40), and those with 2 justifications received an average score of 87.01% (SD 8.17) on all five quizzes. Finally, students who gave 3 or more justifications received an average score of 89.44% (SD 4.13). There was no correlation between the number of justifications in their arguments and their knowledge of mRNA vaccines [$r_{(79)} = 0.03$, $P = 0.77$].

There were students ($n = 16$) who opted out of 2 of 5 quizzes. Though they did not take the quizzes, all students were required to annotate the readings and complete other writing assignments about the papers. However, it is possible that these students may not have had as much content knowledge to be confident in creating arguments. To determine whether this was the case, we analyzed data from students who completed 4 out of the 5 quizzes, and there was no correlation between the number of justifications in their arguments and their content knowledge [$r_{(63)} = 0.03$, $P = 0.84$].

(ii) Types of justifications. The justifications provided by students were divided into 3 categories based on whether students considered biological knowledge (Table 2). Most students provided more than one justification, and types of justifications were categorized into potentially more than one category.

(a) No biological knowledge was considered. Twenty-seven percent of justifications were categorized as no biological knowledge was considered. Students who did not include biological knowledge in their justification primarily provided reasons that were not directly related to the biology, science, or research of the vaccine. Some students focused on addressing the speed of vaccine development with the amount of resources and with scientists working together to develop a vaccine. A subset set of students also argued for getting the vaccine to return back to a normal way of life (prepandemic), while others argued for a need to trust scientists and experts who developed the vaccine. Finally, some students made brief and vague statements about the vaccine being safe or effective without further explanation.

(b) Consideration of nonspecific biological knowledge. A total of 34.5% of justifications were categorized as consideration of nonspecific biological knowledge. Students provided general biological statements about how they might counter vaccine hesitancy but did not include any details about the science, research, or vaccine. Students mentioned that they might explain how the mRNA vaccine works or tell them more about the research about the vaccine but did not provide more specific information. Students also made general statements about sharing knowledge of the benefits and risks of the vaccine.

(c) Consideration of specific biological knowledge. A total of 38.5% of justifications were categorized as consideration of specific biological knowledge. Students provided specific statements about how they might counter vaccine hesitancy, including details about the science, research, or vaccine. Some students discussed details about biological knowledge relevant to the vaccine, including differences between mRNA and DNA. Some students provided information about past research on

coronaviruses and the development of mRNA vaccines. Some students explained the experimental design or results from the vaccine trials in animal models and in humans.

Of the students ($n = 67$) who provided justifications, 32 students (47.7%) did not include specific biological knowledge in their arguments to counter vaccine hesitancy. Seven students (10.4%) provided only one justification where no biological knowledge was considered; they did not refer to nonspecific or specific biological knowledge in their argument. There was no correlation between their knowledge of mRNA vaccines and types of justifications: no biological knowledge [$r(64) = 0.05$, $P = 0.67$]; nonspecific biological knowledge [$r(64) = 0.11$, $P = 0.39$]; specific biological knowledge [$r(64) = -0.06$, $P = 0.66$].

DISCUSSION

In this study, we assessed students' content knowledge about mRNA vaccine development and clinical trials from primary research articles. Quiz scores were similar among students of various backgrounds (gender, first-generation status, marginalized groups, or socioeconomic status). The absence of opportunity gaps may be reflective of the course design and instructional practices. The high-structure course emphasized active learning strategies with facilitation from teaching assistants and learning assistants, which have been shown to reduce opportunity gaps in students of different genders and races or ethnicities (35–37). With assignments related to climate change and vaccine hesitancy, students were able to connect content to their personal life, which has also been reported to reduce opportunity gaps for students from marginalized and first-generation backgrounds (38, 39).

We showed that students' content knowledge was not correlated with their argumentation skills to counter vaccine hesitancy. The number of justifications used in their arguments was similar regardless of their content knowledge from primary research articles. Most students provided at least two or more justifications in their arguments, indicating they were able to formulate an argument.

As STEM majors, students were expected to be able to apply the process of science by formulating arguments and citing evidence or data to support their arguments. Students read and interpreted data from primary research articles; however, almost half the students did not apply their specific biological knowledge into their arguments to counter vaccine hesitancy. Interestingly, more than half of the justifications provided by students did not include biological knowledge or included general, nonspecific biological knowledge. This is consistent with previous studies that have shown that undergraduate students struggle with transferring and applying their knowledge to real world scenarios (40, 41). For example, in one study, biology major students had sufficient background knowledge but did not include molecular and cellular processes in their explanation of genetically modified organisms (41).

A number of factors dictate whether students are able to apply their knowledge to real world scenarios, including their

prior knowledge and expertise (40). While the students were able to answer questions about mRNA vaccine development and clinical trials, their knowledge of vaccines and the immune system may have been insufficient to provide students with the confidence to present robust arguments to counter vaccine hesitancy. Undergraduate students' prior knowledge of vaccines is highly variable, and over half of the students' explanations of how vaccines work include misconceptions (42). Additionally, a recent urged educators to integrate immune literacy into scientific literacy learning goals through the use of SSIs (25).

In conjunction with students' content knowledge, recent efforts have focused on developing competencies in students, including the ability to apply the process of science (1). Scientists use data as their evidence to support their claims in their research papers. However, without explicit instruction, students have difficulty identifying which data are relevant and applicable to support their arguments (43). In science education, more efforts need to be made to allow students to cultivate their argumentation skills (44). Students who are provided with opportunities to practice and develop their argumentation skills are more likely to include data into their arguments (14, 45, 46).

Limitations

In this study, we did not assess the students' baseline level of argumentation skills. We assessed and analyzed their argumentation skills at the end of the course. During the course, students discussed a number of SSIs, including racism in academia, climate change, and vaccine hesitancy. Previous studies have shown SSIs positively influence students' argumentation skills (16, 47). It is unclear what the impact of the course itself was on their argumentation skills.

Further studies are needed to identify how to best integrate SSIs into courses to develop students' argumentation skills and how they apply these skills within their social network.

Given the lower vaccination rates in marginalized communities, the application of argumentation skills from students may be particularly beneficial to their communities. People of color have lower trust in vaccines and the vaccine process due to historical exploitations (28), and students have the potential to increase vaccine rates in their communities by sharing their knowledge about vaccines and countering vaccine hesitancy. In this study, there was no difference in argumentation skills in students from marginalized backgrounds. However, the sample size of different populations (Black/African-American, $n = 3$; Latinx, $n = 16$; Native Hawaiian/Pacific Islander, $n = 9$) was small, and further studies are needed to better understand the development and application of argumentation skills of students from marginalized backgrounds.

Conclusions

Results from this study indicate that students have difficulty applying their content knowledge to address vaccine hesitancy. While integrating SSIs into a biology course provides students with opportunities to engage in argumentation skills, these

findings suggest that students would benefit from additional instructional support in developing their argumentation skills with respect to SSIs.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, DOCX file, 0.02 MB.

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We do not have any conflicts of interest.

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