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CourseSource

Lesson

Mock Drug Activity Enhances Student Learning About the Challenges of HIV/AIDS Therapy

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Abstract

While traditional didactic coursework is important for learning about the scientific aspects of HIV/AIDS, it is difficult to convey social aspects of the epidemic. Due to effective drug therapies, an HIV diagnosis is now considered a chronic lifelong health condition if medication is taken properly and on time. Despite scientific advances, stigma and discrimination are still directed against people living with HIV/AIDS in part due to misinformation about the current state of the HIV/AIDS epidemic. This mock drug therapy lesson was designed to allow students to experience how easy or difficult it is to adhere to drug therapy. The goal of this experience is to enhance understanding of HIV drug therapies and highlight the challenges faced by people living with HIV. In this activity students are assigned to one of three drug regimens that have been used to treat HIV/AIDS throughout history. Over six days, students take Tic Tac® mints or Kool-Aid® drink mix as replacements for medication and record their adherence, taking the "medication" properly and on time. Students then complete a reflective written assignment to report adherence and discuss challenges of the activity. In the following class period on HIV drug treatments, students engage in small group and class discussion about their experiences. Adherence data from the activity is examined during class to discuss the challenges of medication adherence. This lesson increased student learning of HIV drug therapies and medication adherence while successfully highlighting some of the social aspects of the HIV/AIDS epidemic.

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Supporting Materials: Supporting Files Supporting File S1. Mock Drug Therapy- Protocol Data Sheet; Supporting File S2. Mock Drug Therapy- Slides Class Session 1; Supporting File S3. Mock Drug Therapy- Drug Protocol Report; and Supporting File S4. Mock Drug Therapy- Slides Class Session 2.

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Learning Goals

Students will:

- explain the development and mechanism of HIV medications.
- demonstrate the importance of medication adherence.
- highlight the challenges faced by people living with HIV

Learning Objectives

Students will be able to:

- define how common HIV drugs block HIV replication.
- describe how poor adherence leads to the evolution of drug resistant virus.
- identify the challenges of adhering to a HIV drug regimen and design an adherence plan.
- describe and develop a plan to overcome medical and social challenges of people living with HIV.

INTRODUCTION

HIV/AIDS currently affects 38 million people worldwide with an estimated 32.7 million people having died from the disease (1). In the United States about 38,000 people are diagnosed with HIV each year with one in seven HIV+ Americans unaware of their HIV status (2). An HIV diagnosis is now considered a chronic lifelong health condition due to the development of highly effective drug therapies. One challenge for people living with HIV is adhering to their drug regimen by taking the medication properly and on time. Adherence to antiretroviral drug therapies is important to prevent HIV transmission and development of drug resistant HIV strains (3). Despite advances in HIV treatment, stigma and discrimination are still associated with an HIV diagnosis (4). Stigma is defined as having negative beliefs about people living with HIV. For example, the belief that people deserve to get HIV based on their decisions or by belonging to a specific group. Discrimination against people living with HIV can stem from these beliefs, from being socially isolated to being refused medical care or other services. People living with HIV may also internalize these attitudes or fear disclosure of their HIV status which is detrimental to mental and physical health. Unfortunately, fear of judgement or discrimination associated with an HIV diagnosis remains a significant barrier to people seeking the HIV testing and treatment needed to stay healthy and prevent new infections. Stigma and discrimination are partially due to a lack of education about the current state of the HIV/AIDS epidemic (4).

While traditional didactic coursework is important for learning about the scientific aspects of the HIV/AIDS epidemic, it is difficult to convey the challenges associated with an HIV diagnosis. The mock drug therapy activity described here was designed to allow

students to experience issues in adherence to drug therapy. The goal of this experience is to generate interest in HIV drug treatments, enhance understanding of the development and mechanism of HIV medications, demonstrate the importance of medication adherence, and highlight the challenges faced by people living with HIV. In this activity students are assigned to one of three drug regimens that have been used to treat HIV/AIDS throughout history. The three HIV treatment protocols vary in complexity. Over the course of six days, students take Tic Tac® mints or Kool-Aid® drink mix as replacements for medication and record their adherence to the medication schedule. The Tic Tac® mints serve as a substitute for pills. The Kool-Aid® drink mix represents an injectable medication and mimics the extra preparation time needed for this drug compared to taking a pill. Students then complete a reflective written assessment of the activity where they report adherence and answer questions about the challenges of the activity. The drugs in this activity are referenced in the following class period covering HIV drug treatments. Students engage in small group and class discussion about their experiences with the lesson. We also examine adherence data from the current and past semesters to compare the drug regimens and discuss challenges of adherence.

This lesson is a modified version of an activity developed by the Howard Hughes Medical Institute (HHMI) as part of the 2007 Holiday Lecture Series in Science (5). For approximately 10 years this activity was provided by HHMI on their BioInteractive website with other free science education materials. The activity has since been archived as more up-to-date information on HIV/AIDS has become available and is not currently searchable on the BioInteractive website. A different modification of the HHMI activity increased learning about HIV drug treatments and empathy in pharmacy students (6). In general, mock drug protocol activities have been effective at facilitating understanding of medication adherence and increasing empathy in medical and pharmacy students (7). This lesson builds on these studies but focuses on undergraduate learning with respect to the HIV/AIDS epidemic by modeling HIV drug therapy regimens over an extended time period.

This lesson aligns with the sixth core competency outlined in the Vision and Change Report, "ability to understand the relationship between science and society" (8). HIV/AIDS is a global health problem. Scientific advances in understanding HIV infection, treatment, and prevention have turned a viral infection that was once a death sentence into a chronic lifelong health condition. This lesson highlights some of these advances by looking at the change in HIV treatment strategies over time. Public perception of HIV/AIDS affects the everyday lives of people living with HIV. During this lesson, students often discuss the mock drug therapy activity and the HIV/AIDS epidemic with family and friends to directly observe attitudes about HIV/AIDS. In addition to being members of the public, many undergraduate biology students are interested in health science careers where they will likely treat HIV+ patients. Therefore, this lesson offers students the opportunity to perceive social aspects of a prominent infectious disease that lies at the intersection of science and society.

Intended Audience

The intended audience of this lesson is undergraduate students with a basic background in biology. This lesson was taught to undergraduate students (sophomore level and above) at a public four-year university. Students were science majors with a large proportion interested in health careers. The only course specific prerequisite was an introductory general biology or human biology class. However, this lesson may be relevant for introductory first-year biology classes if the prerequisite student knowledge is covered earlier in the course.

Required Learning Time

This lesson was taught in a class that met for one hour and fifty minutes once a week. Students completed the hands-on activity outside of class over the six-day period between two class sessions. Part of these two class sessions were required to complete the lesson. About 15 minutes of the first class session was used to assign the activity. About one hour of the second class session was devoted to HIV drug treatments and class discussion of the lesson.

Prerequisite Student Knowledge

Students should have a taken an introductory biology class. Students should also have a basic understanding of the biology of HIV infection and the steps of HIV replication. During the lesson students will learn about HIV treatments and medication adherence.

Prerequisite Teacher Knowledge

Instructors should understand the progression of HIV infection to AIDS, steps of HIV replication, how medications prevent HIV replication, and how mutations can cause resistance to these drugs. Any virology or microbiology textbook should have sufficient information on HIV infection, replication cycle, and drug treatments. General background and resources on HIV drug treatments and adherence are found in the Lesson Plan. HIVinfo is a service from the United States Department of Health and Human Services that is maintained by the National Library of Medicine. The HIVinfo website contains a series of Fact Sheets on HIV/AIDS and Infographics that are regularly updated. Additional information about HIV/AIDS is available from the National Institutes of Health and Centers for Disease Control. Avert is an excellent website for background on all aspects of HIV/AIDS and offers the option of navigating through the website as a professional or member of the general public.

SCIENTIFIC TEACHING THEMES

Active Learning

This lesson involves a hands-on activity that students complete independently over a six-day period to experience adhering to a medication regimen. Students then complete a writing assignment before the next class period to reflect on the activity. The following class period students engage in small group discussion to compare their experiences. We then have a class discussion about the activity and examine adherence data.

Assessment

Learning was assessed by the reflective writing assignment and student responses in the class wide discussion. Students were tested for knowledge of drug treatments and adherence on a quiz and final exam. The number of correct answers on three common questions was assessed and compared between students that completed the mock drug activity (four semesters) and students that did not (two semesters). Students completed an anonymous course evaluation using the using the Student

Assessment of Learning Gains (SALG) survey system and could leave comments on the mock drug activity. Student also had the option of completing a post-course survey to assess learning objectives which was collected using the Qualtrics survey system in accordance with IRB approval at Missouri State University (IRB-FY2020-42).

Inclusive Teaching

In small groups, students answer questions about the drug activity to compare their experience with other students in the group. Student experiences could be different based on several factors, including drug therapy protocol assigned, previous experience taking regular medication, and class/work schedules. The small group discussion allows students to appreciate how their experience was different from other students in the group even if they were assigned to the same drug protocol. In the class wide discussion students can compare their group responses to the rest of the class. Most recently, I have used the response software Poll Everywhere (polleverywhere.com) to survey the class on these questions. Response software allows students to contribute to the discussion that may otherwise not feel comfortable speaking to the whole class. Students also often discuss this activity with family and friends and can observe public attitudes about HIV/AIDS through these interactions. In the United States HIV/AIDS disproportionally affects members of the LGBTQ, Black/African American, and Hispanic/Latino communities (9). Therefore, this activity reveals the impact of science in diverse communities.

LESSON PLAN

Background on HIV Drug Treatments

There are seven classes of HIV drugs that target different steps in viral replication (Figure 1; 10). HIV replication proceeds through multiple steps involving both viral and cellular proteins. In the first step of viral replication, the HIV virion binds to the cellular CD4 and CCR5 receptor proteins on the cell surface. The viral membrane then fuses with the cell membrane to release the contents of the virus into the cell. In the cytoplasm the viral RNA genome is converted to double stranded DNA by the viral enzyme reverse transcriptase. This viral DNA enters the nucleus. The viral protein integrase then inserts the viral DNA into the host chromosomal DNA. The host cell transcription and translation machinery makes multiple copies of viral RNA and proteins. Viral proteins and RNA then assemble at the cell membrane to form new virions. These new virions bud off the cell but are uninfectious. In the final step of viral replication, the viral enzyme protease cleaves viral structural proteins to form a mature infectious virus. The steps in HIV replication currently targeted by different classes of HIV drugs are virus binding to the cell (binding inhibitors), fusion of the viral and cellular membranes (fusion inhibitors), reverse transcription of the viral RNA to DNA (reverse transcriptase inhibitors), integration of viral DNA into the chromosomal DNA (integrase inhibitors), and maturation of newly formed virus (protease inhibitors; Figure 1; 11). Of these steps, reverse transcription, integration, and maturation are mediated by the viral enzymes. These steps are especially attractive as drug targets as inhibition of viral enzymes should not disrupt host cell proteins or normal cellular processes.

The HIV reverse transcriptase is error prone and will randomly generate mutations during reverse transcription. HIV also has a high turnover rate to produce a large number of infectious virions in a relatively short time. This combination of characteristics increases the chance of a random mutation being generated that can confer drug resistance to a progeny virus (12). The presence of HIV medication in an individual will then select for this drug resistant virus. Drug resistance can rapidly arise in HIV patients taking only one or two antiretroviral medications (12). Therefore, the standard drug regimen for HIV is treatment with three drugs from at least two different drug classes (10). This strategy greatly reduces the chance of drug resistant virus evolving as random mutations would have to be simultaneously generated in three distinct drug targets (12).

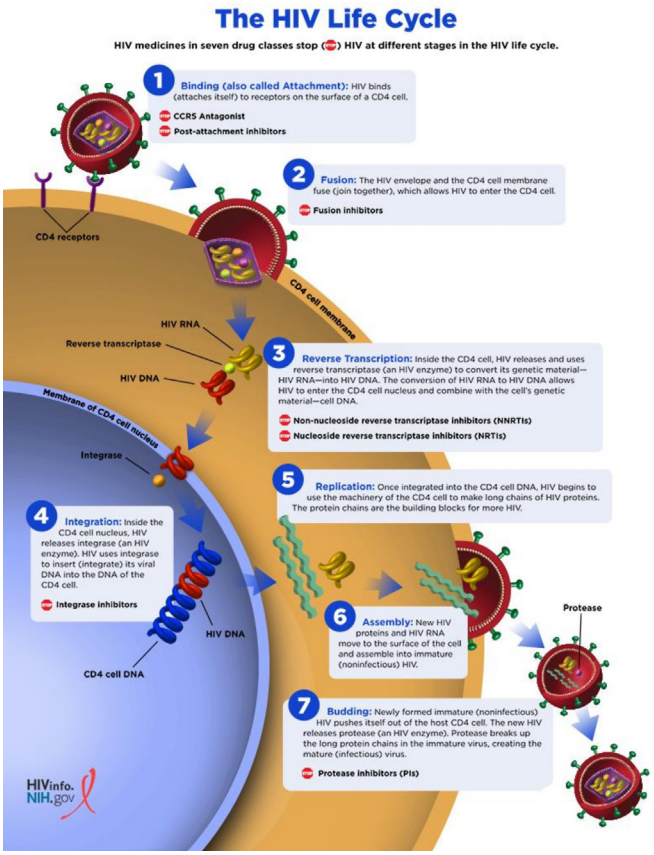

Figure 1. Model of how different drug classes block steps of HIV replication. Image is courtesy of HIVinfo and is maintained by the National Library of Medicine (10).

Medication adherence is taking medication at the correct time and under the correct conditions. While adherence is important for any medication, it is particularly important for HIV treatments to prevent the evolution of drug resistant strains of the virus (12). Ideally a person would not miss a single dose of medication to keep viral replication to a minimum. When a dose of medication is missed, the drug concentration in the body drops below the effective dose needed to prevent viral replication. This situation allows virus to replicate and randomly generate mutations that may confer drug resistance (3). When the patient resumes taking their medication, a population of virus may then be resistant to one or more of the drugs. Drug resistant virus will be able to replicate in the presence of drug and the amount of virus in the body will increase. To regain control of HIV infection, the patient will have to switch a different drug regimen. Studies have shown that 95% adherence is recommended to control

HIV infection and prevent drug resistant virus under older HIV regimens, while 80-90% adherence is needed for newer HIV drug regimens (13, 14).

Prepare Materials

Table 1 shows the teaching timeline for this lesson. In this activity students are randomly assigned to one of three different drug regimens that have been used to treat HIV/AIDS. Table 2 outlines each drug protocol, including background information and notes. Over the course of six days, students take Tic Tac® mints and drink mix to serve as replacements for pills and injectable medication, respectively. I assign the same number of students to each drug protocol. If there is an odd number of students, I assign additional Protocols 1 and 2 as these regimens are more complex. Tic Tac® mints are purchased in multipacks. The Tic Tac® colors are arbitrary, but three colors are needed for three uniquely colored pills in Protocol 2 (Table 2). The assignment of colors to different medications in Table 2 also allows equal amounts of each color to be purchased. I assemble each student's Tic Tac® "pills" for the 6-day activity in a sterile 50 ml conical tube. The drink mix is single serving Kool-Aid® mix or the generic equivalent and is only used in Protocol 1. The conical tube of pills and drink mix (if needed) is placed into a brown paper lunch sack with the corresponding Protocol Data Sheet (Supporting File S1. Mock Drug Therapy- Protocol Data Sheet).

Class Session 1: Assign Mock Drug Therapy Activity

This activity is assigned during the class session prior to when HIV drug treatments are discussed. I inform students that they will be participating a mock drug therapy protocol for the next six days, which is modeled after HIV drug treatments of the past. I give a short background on HIV drug treatments and adherence (Supporting File S2. Mock Drug Therapy- Slides Class Session 1). Students then open the paper sack and are randomly assigned to a drug protocol by whatever "medication" is in the bag (Table 2). The Protocol Data Sheet includes dosing guidelines for each drug protocol and what to do if a dose is missed (Supporting File S1. Mock Drug Therapy- Protocol Data Sheet). If a student has dietary or medical restrictions about eating candy, they should not take the "medication", but dispose of it at the time they would have taken it. After reading about their assigned drug protocol, students plan the best time(s) of day to take their medication and mark this time(s) on the Protocol Data Sheet. I encourage students to think of a way to remember to take the medication without making specific recommendations so they develop a system on their own. I also emphasize that their grade is not dependent on adherence so that students will be honest about whether or not they took the medication. The first few semesters a common student comment was lack of motivation to take the medication because of they did not have HIV and did not "feel sick." I acknowledge this viewpoint when assigning the activity by telling students to put themselves in the frame of mind that this medication is important for their health. I also remind them that people living with HIV often do not "feel sick" but must take medication for the rest of their lives to stay healthy.

Finally, we discuss the three drug protocols and what step in HIV replication is targeted by each medication (Table 2, Supporting File S2. Mock Drug Therapy- Slides Class Session 1). I briefly cover this information as this topic is discussed in more detail during the next class session on HIV drug treatments. To ensure that students develop their own strategy for adherence, I do not discuss the dosing information in detail for each protocol but will answer specific questions from students.

Intersession: Students Complete Activity

Over six days students participate in the mock drug therapy activity by taking the medication. On the Protocol Data Sheet they record the actual time each drug is taken (Supporting File S1. Mock Drug Therapy- Protocol Data Sheet). When students finish the activity, they complete a Drug Protocol Report to record their adherence and answer discussion questions (Supporting File S3. Mock Drug Therapy- Drug Protocol Report). These questions ask for reflection on challenges of the activity, methods for adherence, comparison of the drug protocols, and any interesting insights or situations. The completed report is due on the learning management system a few hours before the next class session to allow sufficient time to record and graph the adherence data. For each protocol I count the number of doses missed by each student. This data is graphed as a histogram representing the number of doses missed overall and the number of doses missed per protocol. I also combine this data with adherence data from previous semesters. These histograms are presented during the next class session.

Class Session 2: Discussion and Reflection

The next class period is focused on drug treatments. Before discussing the mock drug therapy activity, I cover the major classes of HIV drugs, their mode of action, and mutations that confer drug resistance. During class I specifically describe the drugs that were part of the mock drug therapy activity, especially in cases where two drugs inhibit the same step in HIV replication (Supporting File S4. Mock Drug Therapy- Slides Class Session 2). For example, Atripla in Protocol 3 contains three reverse transcriptase inhibitors (Efavirenz, Emtricitabine, and Tenofovir; 11) which seems to violate the general principle of targeting more than one step in HIV replication for effective drug therapy. However, there are two classes of reverse transcriptase inhibitors that block reverse transcription in different ways (Figure 1). Efavirenz is a nonnucleoside reverse transcriptase inhibitor which binds to reverse transcriptase to inhibit activity (11). Emtricitabine and Tenofovir are both nucleoside reverse transcriptase inhibitors and block reverse transcription by being incorporated into the newly synthesized viral DNA (11). In addition, Emtricitabine resembles the nucleotide cytosine, while Tenofovir resembles the nucleotide adenine, therefore it is unlikely that a single mutation would produce resistance to both drugs.

Next, the students meet in groups of 4-6 and compare the results of their mock drug therapy. I provide a list of discussion questions about the challenges of the activity, methods of adhering, and comparing the drug protocols (Supporting File S4. Mock Drug Therapy- Slides Class Session 2). After allowing 10-15 minutes for small group discussion, the groups share with the class. I have varied the format of this class wide discussion in different semesters. Some semesters different groups will volunteer group answers for discussion. Most recently I have used Poll Everywhere (polleverywhere.com) to poll the class for some discussion questions. The word cloud feature is especially useful as it allows individuals to submit short phrase answers and builds word clouds of the responses. Finally, I will ask the class a few follow-up questions to highlight social aspects of HIV/AIDS (Supporting File S4. Mock Drug Therapy- Slides Class Session 2). I ask if anyone had to travel during the activity, if they remembered their medication, and if they were worried about

explaining Tic Tac® mints in a conical tube to airport security. I ask if anyone felt self-conscious about taking medication in public or around family and friends. I also ask if anyone encountered misinformation about HIV/AIDS during the activity. I have developed this list of questions over time in response to student reported situations.

We then discuss why adherence is especially important for HIV/AIDS medications due to the potential development of drug resistant strains (Supporting File S4. Mock Drug Therapy- Slides Class Session 2). I then review each of the three protocols to emphasize the varying degree of difficulty and effect of ongoing drug research. Protocol 1 is the oldest and most complex drug regimen, while Protocol 3 is the newest and least challenging. I present graphed adherence data for the class and then show the aggregate data from all semesters I have taught the class. We examine the data in class to observe how well students adhered to their protocols and compare adherence between the three protocols. A study on older HIV drug regimens (most similar to Protocol 1) showed that 95% adherence is needed to control HIV infection and prevent drug resistant virus (13). Since this activity takes place over 6 days, a student missing only 1 dose in that time is analogous to the conditions that allow drug resistance to arise. An analysis of newer drug regimens (most similar to Protocol 3) suggested that the required level of adherence is lower at 80-90% (14). This is equivalent to a student missing 2 doses of Protocol 1 during this activity.

TEACHING DISCUSSION

Overview

The reaction of the students to this activity has overwhelmingly been positive. Students generally enjoy completing an interactive assignment to connect with the material learned in class. In fact, former students will mention the activity to me semesters after they have taken the class. Here are some quotes when students were asked how the mock drug activity influenced their learning in the course:

- *"I thought the mock drug trial was very cool! I really enjoyed actually experiencing what others had to go through and see the difficulties with sticking to the drug regimen."*
- *"The activity was helpful and fun. I feel it did a good job reinforcing things we had discussed in lecture."*
- *"I thought the activity was different from anything I've ever done in a class before. I loved the idea and thought it was a great assignment for the course."*
- *"I thought that this activity was one of the best activities to enhance my learning. It showed me what an actual patient would go through and that was really beneficial for my learning."*
- *"It was cool, keep this going! Us college students don't get to have fun with school work very often."*
- *"I LOVED the mock drug regimen. I thought it was very fun and interesting way to help us see the difficult life HIV+ people face."*

Student learning as related to the learning objectives was assessed in multiple ways and is discussed below. General trends were observed from student responses in the class wide discussion and reflective writing assignment. Students were tested for knowledge of drug treatments and adherence on a quiz and final exam. The number of correct answers on three common exam questions was compared between students that completed the mock drug activity (four semesters, 169 students) and students that did not (two semesters, 64 students) using a chi-square test of independence to determine statistical significance. Students also completed an anonymous course evaluation and could leave comments on the mock drug activity. Finally, 24 students in two semesters completed an optional post-course survey about what they had learned from the mock drug therapy activity and adherence success. The survey questions asked students to rate how much the mock drug activity increased their understanding of HIV drug treatments and adherence on a Likert scale. Student could also leave comments about the activity in this survey.

HIV Drug Treatments

To assess learning about HIV drug treatments, students were surveyed and asked to rate how much the mock drug activity increased their understanding of different aspects of HIV drug treatments in a post-course survey. In this survey, 79% of students reported that the mock drug therapy activity highly or moderately increased their understanding of HIV drug treatments (Figure 2). The three drug protocols in the activity reflect the change in HIV regimens over time, to emphasize the importance of developing less challenging drug therapies that also require a lesser degree of adherence. This purpose was successful as 71% of students self-reported moderate or high gains in their understanding of the history of HIV medications due to the mock drug therapy activity (Figure 2). In addition, 88% of students surveyed found the activity highly or moderately increased their understanding of the importance for research and development of new drug therapies (Figure 2).

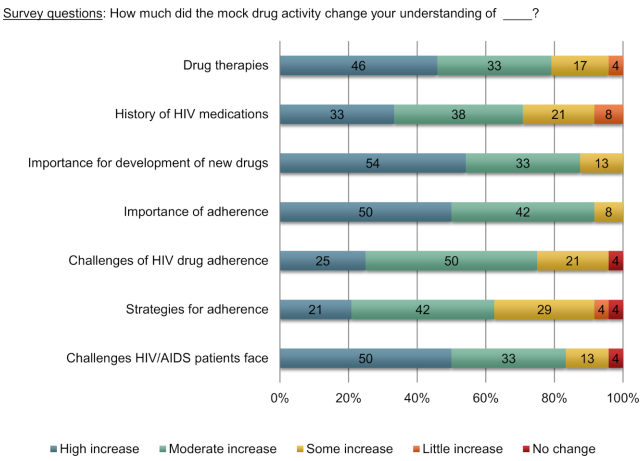

Figure 2. Students report significant increases in learning about various aspects of HIV/AIDS in an optional post-course survey available for two semesters (n=24 students). Students were asked to rate how much the mock drug therapy activity increased understanding of the specific aspects of HIV/AIDS by choosing one of the response choices listed in the key. The general survey question is present at the top of the figure with a blank to be filled in for each specific question. Numbers in each bar are the percentage of responses for that choice.

These student perceptions of learning are supported by exam data. In all semesters, students received the same information about HIV replication, types of HIV drug treatments, and adherence in a traditional lecture format. Two exam questions on HIV drug treatments were identical between multiple semesters of the class, including semesters in which the mock therapy activity was not used. These questions asked students to identify the target proteins for HIV medications and which

drug inhibited various steps in HIV replication. Students who participated in the mock drug activity answered these questions correctly more often than students that did not participate in the activity (Figure 3). This result was statistically significant for the second question asking about the replication step with 83% of students answering this question correctly in semesters with the drug activity compared to 72% of students in semesters without the drug activity (Figure 3). Therefore, this mock drug activity enhanced student learning about HIV drug treatments.

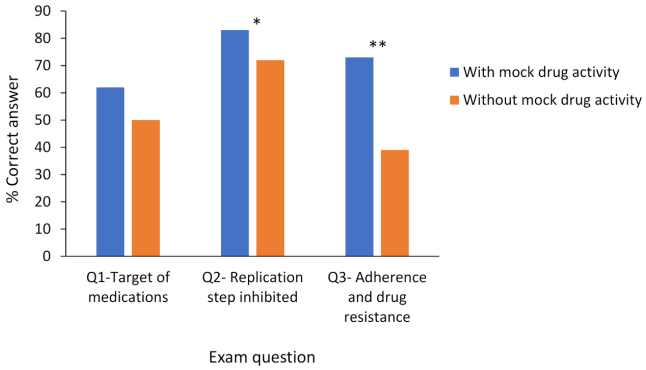

Figure 3. Effect on mock drug therapy activity on student learning. Three exam questions (Q1, Q2, Q3) on HIV drug treatments and adherence were identical between multiple semesters of the class. The number of correct and incorrect responses to these questions was compared between four semesters that completed the mock drug activity (n = 169 students) and two semesters that did not (n = 64 students) using a Chi square test of independence. *p<.05, **p<.0001

Adherence

In post-course surveys, 92% of students reported moderate to high increases in understanding about the importance of adherence (Figure 2). This perception is supported by data from a repeated exam question on the importance of adherence to prevent drug resistant virus. From the exam data, 73% of students that participated in the mock drug activity answered this question correct while only 39% of students got this question correct in semesters who did not participate in the activity (Figure 3). This difference was found to be statistically significant. Therefore, this activity enhanced student learning about adherence.

The lesson was also successful at demonstrating the challenges of adherence, which can be difficult for students to grasp. Most students think that taking medication will be easy without considering the attention needed to adhere to the drug protocol. In fact, 75% of students in the post-course survey said they thought they would take all doses of medication before starting the activity (Figure 4). However, only 38% of students reported taking all doses in the post-course survey, while 46% of students missed 1 or 2 doses of medication and 16% missed more than 2 doses (Figure 4). Therefore, adhering to a drug therapy activity is more challenging than the students anticipate, making this activity a worthwhile learning experience.

In the post-course survey, students were also asked to choose how much the activity increased their understanding of different aspects of drug adherence. In this survey, 75% of students stated that the activity moderately or highly increased their learning about the challenges of adhering to a HIV drug regimen (Figure 2). These challenges depend on the student and the drug protocol they were assigned. Students typically identify the challenge of

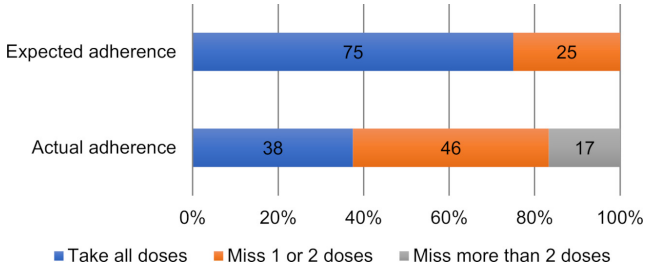

Figure 4. Students overestimate their ability to adhere to drug therapy. In the optional post-course survey students were asked how many doses they expected to miss before starting the activity and how many doses they actually missed (n=24 students). Response choices are listed in the key. Numbers in each bar are the percentage of responses for that choice.

taking the drug correctly within their normal routine. Additional challenges arise when their normal routine varies based on work schedule, class schedule, or day of the week. Students also have different previous experience taking medication. In general, students that regularly take a daily medication or vitamins typically report fewer challenges completing the assignment without missing doses, especially if their current medication routine overlaps with the timing of the assigned drug protocol. The chance for the small group and class wide discussion allowed students to reflect on how their experience was different from their classmates' even if they received the same drug protocol. In general, I have observed the following adherence trends for each drug protocol:

- Protocol 1- Students consistently identify Protocol 1 as the most difficult based on taking medication twice a day and having to combine the drink mix with water before consuming it. Therefore, it is not surprising that there is less adherence (or more missed doses) associated with Protocol 1.
- Protocol 2- Responses to Protocol 2 have varied. Students find it easier than Protocol 1. However, some students also feel that Protocol 2 is easier than Protocol 3 because the medication does not have to be taken on an empty stomach. Most students realize that all pills can be taken at the same time and must be taken with food for Reyataz to be effective. Therefore, the main challenge identified is eating at a consistent time to take the medication. Another challenge unique to Protocol 2 is the doubled dosage for Reyataz (2 tablets) compared to Truvada and Norvir (1 tablet each). Some students find it difficult to remember which pill is the doubled dose.
- Protocol 3- Protocol 3 is often perceived as the easiest protocol as one pill is taken once a day. Protocol 3 usually has the highest levels of adherence. The main challenge adhering to this protocol is taking the medication on an empty stomach. Students who eat dinner late or snack in the evening often prefer Protocol 2.

Finally, many of the students who participated in this activity are interested in health professions where they may prescribe medication, fill prescriptions, or work with patients. The challenges that students face when completing this homework assignment allow them to relate to the challenge a patient may face when taking medication. Indeed, 63% of students felt that the mock drug therapy activity moderately or highly increased their understanding of strategies for adherence (Figure 2). Most students used reminders/alarms on their phone and the support of family/friends to remember to take the medication at the correct

times. These methods are broadly applicable and could be recommended to a future patient. Students found experiencing adherence helpful for learning as seen in their comments:

- *"I learned that adherence is more difficult than I presumed. I probably got the easiest protocol and it was still a challenge. It helped me empathize with HIV patients."*
- *"It was helpful to see the different ways medicine is administered and how their schedules require concise planning in order to adhere properly."*
- *"The drug therapy highlighted how challenging drug adherence is and how important drug adherence is. I take a daily medication and I struggle with adherence for several reasons so this really impacted my view on how living with HIV/AIDS impacts people on a daily basis."*
- *"It was very hard for me to keep up with the drugs I had to take, one in the morning and one at night and I had to let the drink mix stand ten minutes before ingesting it. I understand how important it is to take these drugs all at the correct time everyday so a stronger strain does not develop and that person can stay healthy for as long as possible."*
- *"The mock drug activity helped me understand how hard it could be adhering to a drug regimen and how hard it can be doing daily activities when you have drugs to take."*
- *"Luckily, I was given the easiest plan to adhere to. Even though it was the easiest did not mean that it was entirely easy. I am definitely someone who learns by doing, and this assignment allowed for that."*
- *"This activity enhanced my learning because it made me realize how difficult it can be to adhere to multiple treatments at one time. It is incredibly important to not miss a dose and risk mutations in the virus, so it just made the regimen patients have to take more real and personal."*

Challenges of HIV Diagnosis

As discussed above, many students overestimate their ability to adhere to a drug protocol, which is one of the challenges faced by people living with HIV. In the post-course survey, students reported a 83% moderate or high increase in understanding of the challenges of faced by HIV/AIDS patients (Figure 2). The interactions students have with family and friends while completing this activity is an important experience as reported by the students in the reflective writing assignment or in class discussion. Because most students use an alarm or reminder system on their phone to remember to take their pills, at least one student a semester has mentioned having a family member or friend observe the alert with "HIV meds" come up on their phone, followed by the reaction of that family member. This situation shows how HIV status could accidentally be disclosed and the reaction of family/friends to such news. This activity has also served as a discussion point for the HIV/AIDS epidemic with friends and family members. Students educate others about the epidemic and dispel common myths/misinformation about HIV/AIDS in the process. Therefore, this lesson is successful in highlighting some of the social aspects of the epidemic that are difficult to teach in a traditional format, which is seen in comments from students:

- *"I loved this activity! It was fun and really gave true insight to how difficult drug adherence can be for those living with HIV."*
- *"This activity really put into perspective what HIV/AIDs patients in the past and present had to deal with. This activity expanded my understanding of what it means to have HIV/AIDs."*
- *"At first I did not think this activity would create much of a difference but it really helped me understand the life of someone with HIV."*
- *"I learned a lot about how difficult this is to follow and also had reactions from family members that gave perspective on how hard this would be to have and be successful treating."*
- *"You felt weird about taking the medicine just how there's stigma around HIV."*
- *"It was a great activity that I think was very helpful in increasing the empathy for those who are HIV+ and their life has been changed forever."*
- *"Drug adherence was truly the main concept I will take with me from this class, as well as understanding how to break HIV stigmas. People infected with HIV are just like normal humans, and do not need to be discriminated!"*

Modifications

This lesson is a preparatory activity to increase interest and learning about HIV medications and adherence (Figure 2). The timing sparks student curiosity in these topics as the mode of action of the different drugs and consequences of adherence are revealed during the subsequent class period. However, the mock drug therapy activity could be used after discussing HIV drug treatments in class. The original activity from HHMI was conducted over 10 days, but I shortened the timeframe to 6 days given my class schedule (5). I do not recommend further reducing this timeframe as often it is easy for students to remember the medication for the first few days but becomes more challenging to remember over additional days. The length of my class (1 hour and 50 minutes) is extended compared to most classes. However, the time required for the second class session could still be accommodated by a more traditional length class (Table 1). If necessary due to time constraints, it would be possible to have small group and class discussion of the assignment during one class session (session 2) and then discuss the adherence data in the next class session (session 3). This lesson could be further modified to include different medication regimens, either by adding a fourth protocol or replacing one of the protocols. The HHMI activity was developed before the drug class of integrase inhibitors were available to treat HIV (Figure 1). In addition, there are advertisements for new HIV medications in the media. These newer medications could be added to highlight advancements in treating HIV. Given the level of difficulty of Protocol 1 and the more complex dosing directions for Protocol 2, I recommend replacing Protocol 3. Importantly, the current lesson allows participation for all students even if one has dietary restrictions or medical conditions that prevent them from consuming the Tic Tacs® or drink mix.

This lesson is currently taught as a part of a one credit hour undergraduate class on the biology of HIV/AIDS. This lesson could easily be incorporated into undergraduate or graduate level microbiology, virology, or public health classes that discuss HIV/AIDS. Given the focus on drug treatments this lesson could also be useful in a pharmacology class although this may require additional background on HIV/AIDS. This lesson could be modified to highlight complex drug therapy for other challenging diseases like Tuberculosis or HIV/Tuberculosis coinfection in

the courses mentioned above. Finally, as HIV/AIDS is a global health concern this activity could be incorporated into classes that discuss global health, the intersection of science and society, or even a non-majors science class.

Various aspects of this lesson could be emphasized to provide more depth for upper level undergraduate or graduate level classes. Students could research the drugs used in this activity and then present on the mode of action, side effects, and drug resistance mutations. The random nature of mutation and evolution of drug resistance could be discussed in more detail. A quick class activity would be to have all the students who did not adhere to the drug therapy at a 95% level (miss 1 dose or more) draw playing cards. You could then randomly choose a number and any student with that number would develop drug resistant virus. This activity could lead to a discussion of having to change drug therapy for those that develop drug resistance. Finally, students could collate and/or graph the class adherence data to gain more experience with data analysis and presentation.

SUPPORTING MATERIALS

- Supporting File S1. Mock Drug Therapy- Protocol Data Sheet
- Supporting File S2. Mock Drug Therapy- Slides Class Session 1
- Supporting File S3. Mock Drug Therapy- Drug Protocol Report
- Supporting File S4. Mock Drug Therapy- Slides Class Session 2

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REFERENCES

1. UNAIDS. 2020. Global HIV & AIDS statistics- 2020 fact sheet. https://www.unaids.org/en/resources/fact-sheet. Accessed May 28, 2021.
2. Centers for Disease Control and Prevention. 2020. HIV in the United States and Dependent Areas. https://www.cdc.gov/hiv/statistics/overview/ataglance.html. Accessed May 28, 2021.
3. HIVinfo. 2020. HIV Treatment Adherence. https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-treatment-adherence. Accessed May 28, 2021.
4. Centers for Disease Control and Prevention. 2020. HIV Stigma and Discrimination. https://www.cdc.gov/hiv/basics/hiv-stigma/index.html. Accessed May 28, 2021.
5. Howard Hughes Medical Institute. 2007. Classroom Activities: Drug Adherence Activity. https://www.biointeractive.org/classroom-resources/classroom-activities-drug-adherence-activity. Accessed May 28, 2021.
6. Wesche-Szollosi DE, Ghoneim O, Edafiogho IO, Ofosu JR. 2016. Developing pharmacy student empathy using mock HIV antiretroviral therapy regimens: A learning activity. Currents in Pharmacy Teaching and Learning 8:240–246.
7. Witry MJ, LaFever M, GuX. 2017. A narrative review of medication adherence educational interventions for health professions students. Am J Pharm Educ 81:95.
8. AAFTA of Science and Others. 2011. Vision and change in undergraduate biology education: call to action. Washington, DC.
9. Centers for Disease Control and Prevention. 2021. HIV Basics: Basic Statistics. https://www.cdc.gov/hiv/basics/statistics.html. Accessed May 28, 2021.
10. HIVinfo. 2020. The HIV Life Cycle. https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-life-cycle. Accessed May 28, 2021.
11. HIVinfo. 2021. FDA-Approved HIV Medicines. https://hivinfo.nih.gov/understanding-hiv/fact-sheets/fda-approved-hiv-medicines. Accessed May 28, 2021.
12. HIVinfo. 2020. Drug Resistance. https://hivinfo.nih.gov/understanding-hiv/fact-sheets/drug-resistance. Accessed May 28, 2021.
13. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, Wagener MM, Singh N. 2000. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Annals of Internal Medicine.
14. Bezabhe WM, Chalmers L, Bereznicki LR, Peterson GM. 2016. Adherence to antiretroviral therapy and virologic failure: A Meta-Analysis. Medicine 95:e3361.

Table 1. Mock Drug Therapy lesson plan timeline.

Activity	Description	Estimated Time	Notes
Preparation of materials			
Prepare materials to hand out in class	1. Prepare one brown paper lunch bag containing "medication" and a handout for each student. 2. Make one copy of Supporting File S1. Mock Drug Therapy- Protocol Data Sheet for each student assigned to that Protocol. 3. Add the correct number of Tic Tacs® to a sterile 50ml conical tube. 4. Assemble the correct number of drink mix packets for each student assigned to Protocol 1. 5. Put the conical tube, drink mix (Protocol 1 only), and matching Protocol data sheet in bag.	1 – 1.5 hours for 40 students	• Each student is assigned one drug protocol. • Handout is in Supporting File S1. Mock Drug Therapy- Protocol Data Sheet. • Numbers of Tic Tacs® and drink mix needed for each day of each protocol are listed in Table 2. • Give the students the protocol specific data sheet and "medication" at the same time, so they get the correct materials for their assigned protocol.
Class session 1			
Handout lesson materials	Students pick a bag so that the Protocols are assigned randomly.	3 minutes	More efficient when done at the beginning of class as students arrive
Assign mock drug therapy activity	1. Give brief introduction to HIV drug treatments and adherence. 2. Give directions for completing the assignment. 3. Have students open bag to look at their drug protocol. 4. Give overview of each drug protocol, pointing out classes of each drug.	15 minutes	• PowerPoint slides are in Supporting File S2. Mock Drug Therapy- Slides Class Session 1. • Do not discuss drug treatments in detail as this topic is the focus of the next class.
Analyze adherence data			
Record and graph adherence data	1. Using assignments submitted through the Learning Management System, record the number of doses missed by each student, per protocol. 2. Use Excel to make histograms: • Frequency of number of doses missed. • Frequency of doses missed per protocol. • Graphs for current class and combined data from multiple semesters. 3. Insert graphs into PowerPoint slides to present in next class session.	1 – 1.5 hour for 40 students	Students submit completed assignment using Supporting File S3. Mock Drug Therapy- Drug Protocol Report.

Activity	Description	Estimated Time	Notes
Class session 2			
Lecture on HIV drug treatments	1. Use PowerPoint slides to present the mode of action and how resistance mutations prevent drug action for each drug class. 2. Specifically mention each drug in the mock drug therapy activity. 3. Briefly review drug protocols.	20 minutes	PowerPoint slides are in Supporting File S4. Mock Drug Therapy- Slides Class Session 2.
Small group discussion	Break students into groups of 4-6 and provide list of questions for discussion.	10-15 minutes	Small group discussion questions are found in Supporting File S4. Mock Drug Therapy- Slides Class Session 2.
Class discussion	1. Allow groups to volunteer answers to the Discussion questions or use response software. 2. Ask class additional discussion points.	10-15 minutes	• The word cloud function of PollEverywhere response software (PollEverywhere is free for class size <40 students). • For class sizes of >40 students have groups volunteer answers or use response software (iClickers). • Additional class wide discussion questions are found in Supporting File S4. Mock Drug Therapy- Slides Class Session 2.
Lecture on adherence	Use PowerPoint slides to discuss the importance of adherence	5 minutes	Slides about adherence are in Supporting File S4. Mock Drug Therapy- Slides Class Session 2.
Present adherence data	1. Use PowerPoint slides to present histograms with adherence data from class and cumulative data. 2. Determine how adherence relates to difficulty of protocol. 3. Highlight that 95% adherence is not missing any doses for this activity.	5 minutes	

Table 2. Overview of the three assigned drug protocols. Drug class, dosing guidelines, and notes about each protocol are included. The amount and type (Tic Tac® Mints or Kool-Aid® drink mix) of each medication is noted.

Drug	Drug Class	Represented By	Dose Instructions	Notes on Protocol
Protocol 1				
Kaletra	Protease inhibitor	White Tic Tac®	Take 1 pill every 12 hours.	Fuzeon is an injectable drug. It is represented by a drink mix packet to mimic the extra preparation time needed compared to taking a pill.
Fuzeon	Fusion inhibitor	Drink mix	Take one dose every 12 hours. Mix one drink packet with 8 oz water. Let stand for 10 minutes before drinking.	
Combivir	Reverse transcriptase inhibitor	Green Tic Tac®	Take 1 pill every 12 hours.	
Protocol 2				
Truvada	Reverse transcriptase inhibitor	White Tic Tac®	Take 1 pill once a day with or without food	The "with and without food" instructions sometimes confuse students into thinking that they must take some pills without food. Unless a student asks, I do not clarify that all pills can be taken once a day with food because Truvada can be taken with or without food.
Reyataz	Protease inhibitor	Orange Tic Tac®	Take 2 pills once a day with food	
Norvir	Protease inhibitor	Green Tic Tac®	Take 1 pill once a day at the same time as Reyataz	
Protocol 3				
Atripla	Reverse transcriptase inhibitor	Orange Tic Tac®	Take 1 pill once a day at bedtime on an empty stomach	Atripla is a combination pill of three reverse transcriptase inhibitors. I define an empty stomach as 4 hours after eating for the students.