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Affordable Medical Care: Using Chemistry Concepts to Lower Consumer Cost for Medications and Vaccines

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Introduction and Rationale

The cost of healthcare is one of the largest personal expenditures worldwide, with residents of the United States spending upwards of $10,000 each year[1] . Moreover, the cost of healthcare seems to be rising in most countries[2] . With real wages remaining relatively stagnant over the past several decades in the United States[3] and other countries[4] , this presents growing concern for policy makers and citizens worldwide. A significant portion of healthcare costs in the United States and many other countries comes from paying for pharmaceuticals[5] . For students who represent the next generation of scientists, economists, politicians, and medical professionals it is imperative they have an intimate understanding of healthcare costs, healthcare technologies and the measures we can take to lower costs to the consumer.

With the new Next Generation Science Standards (NGSS) in Connecticut there is a push for instructional methods that encourage students to tackle real world problems. Under NGSS students are thought to develop deeper understanding of content and related issues via activities that promote inquiry, collaboration, and problem solving[6] . Lessons of this sort encourage use of so-called 21st century skills designed to prepare students to successfully navigate the modern world. Several of the NGSS standards for high school chemistry in Connecticut address evaluating a real-world issue from social and economic perspectives and designing a solution using concepts of engineering. Additionally, there is an NGSS standard in the chemistry curriculum that asks students to analyze a global challenge using qualitative and quantitative data that reflect societal wants and needs. Consequently, I believe a unit in which students study the economics of the healthcare system and then use chemistry concepts to design a technology to help make pharmaceuticals more affordable would beautifully hit upon several desired learning outcomes. The students will be provided with some foundational knowledge to give them ideas before they begin their own research and start the design process.

This unit will be designed for an 11th grade, high school chemistry class in New Haven, CT. According to data from 2017 on Census.gov, New Haven's per capita income is about 79% of the national average and its median household income is only about 68% of the national median[7-8] . Many of the students I teach come from a low-income households, which means saving on the cost of their healthcare and prescription

medications could be very meaningful and a topic they may find great interest in. Additionally, Connecticut consistently seems to have higher costs for healthcare procedures when compared to the national average. For instance, according to data from the Healthcare Cost Institute, cesarean childbirths and x-rays in Connecticut are on average 26% and greater than 33% more expensive than the national averages respectively[9] . Consequently, lowering healthcare costs may be especially important to my students. During the unit, an effort will be made to make such connections between the content and the community to encourage student investment.

Unit Description

In order for students to have a stake in the topic, apply their chemistry knowledge and put together a well thought out project, students will need to be exposed to some background on the healthcare and the pharmaceutical industries. Students will get a brief overview of the costs of healthcare and prescription medications as well as several ways costs of medications could potentially be decreased including the repurposing old drugs, improving stability, the design and use of biosimilars, or improving production efficiency. In order for students to research and/or design one of these cost reduction methods they will need a foundation of certain chemistry concepts which will likely include a combination of the following; the relationship between structure and function, pH, activation energy, the relationship between temperature and reaction rate, catalysts, inhibitors, among additional concepts. Students will also likely need to be able to use the periodic table to make predictions on the properties of various elements and how they may react with one another based on valence electrons. In their research, students will need to be able to access and analyze information they find including how to read and interpret charts and graphs. Depending upon the focus of their project, basic knowledge of other topics such as stoichiometry, electromagnetic radiation or cell culture may be necessary.

Students will be required to choose one method (repurposing old drugs, improving stability of current drugs, the design and use of biosimilars, or improving production efficiency) of reducing the cost of prescription drugs and research it. Students may choose a method not included in the list above but will be required to receive teacher approval before beginning. Students will both write a three-page research paper on their proposed method and will design a new strategy or technology. Teacher approval will be required once a focus for their research and design project has been decided upon. The research focus must be deemed reasonable and related to chemistry in some way. Students will present their research and designs in a 5 minute presentation in front of the class using a slideshow, poster board, video, demonstration, or other means of presentation. Regular teacher checks will be required along the way to ensure projects meet requirements and the students are on pace to finish.

The project along with the prerequisite material will be scaffolded over several weeks so that students are adequately prepared for the task and have enough time to complete what is asked of them. A significant part of the grade for this project will be determined by student’s ability to prove that their technology or strategy is viable. Students will need to provide references for their research and will spend one class in the library learning how to properly conduct research online and cite their sources. In the research paper students will need to provide calculations for their predictions on the cost savings to consumers of their proposed strategy or technology. If students would like to build a prototype or model of their technology they will need to submit a list of materials with their topic proposal and an approval decision will be made based on the availability of such materials.

Background

Healthcare Spending

As mentioned above healthcare costs continue to rise at a significant rate[2] . The Center for Medicare and Medicaid Services (CMS) projects that healthcare spending with rise 5.5% annually over the next decade reaching close to $6 trillion by 2027[10] . This rate significantly exceeds both the recent nominal gross domestic product (GDP) and nominal wage growth rates[11-12] . Approximately 10% of total healthcare expenditures originates from pharmaceuticals in the United States, with the average American spending over $1,000 on their prescriptions each year[5] . Cost of prescription medications is cited as a major reason for patient nonadherence to medications with as many as 14% of those skipping prescriptions attributing their actions to the high cost. That figure rises to 24% when asking low-income Americans why they skip prescriptions and as high as 33% for uninsured Americans[5] . Nonadherence to prescribed medications is thought to cause about 125,000 deaths in the United States each year[13] . According to Viswanathan et al, nonadherence is thought to cost the American healthcare system between 100 and 289 billion dollars annually[13] . High prices of pharmaceuticals, leading to nonadherence and eventually much higher medical costs later due to this lack of preventative care creates somewhat of a positive feedback cycle costing the system, and thus consumers, more and more money. Much of the cost of pharmaceuticals is due to the large sums pharmaceutical companies are willing to put into research and development for new drugs. It's estimated that the average price for the development of each new drug costs pharmaceutical companies about 800 million dollars[14] . Fully automating new drug development may be far off but there are still ways we can save money and reduce costs to consumers.

While the United States and other developed countries of the west struggle with high pharmaceutical prices, the problem with access to adequate and affordable healthcare persists in the rest of the world as well. As of 2001, some less developed countries, like Liberia for instance, had an annual per capita healthcare expenditure of only about 1 U.S. dollar[15] . Not only do the residents of less developed countries not have the funds for proper healthcare, they do not have the access for it and in many ways are less fortunate than even the low-income residents of more developed countries. For years the United Nations (UN) has been dedicated to the development of less fortunate countries, publishing their Millennium Development Goals (MDGs) in an effort to reduce poverty and to improve medical care and general quality of life[16] . Although, often forgotten, the purpose of science is to improve our quality of life. For these developing countries and for the low-income residents of more fortunate countries, it is essential that the pharmaceutical and healthcare industries achieve a higher efficiency in order to allow for greater affordability and, therefore, access. Through the development of new technologies and improving the efficiency of production methods, we increase the quality of care and purchasing power of the dollar respectively. With increased purchasing power, we increase the affordability of proper medical care and other life essentials. While it is the general trend in most industries that as technologies improve the cost to consumers decreases, the cost of pharmaceuticals remains out of reach for many, especially citizens of developing countries and those of lower income levels in developed countries. Consequently, it should be a goal of biotechnologists and pharmaceutical scientists to increase the efficiency of production in order to lower the cost to consumers.

Rising costs is not necessarily the norm across industries. In his book "The Cost Disease," William Baumol discusses how the prices of other technologies get cheaper while medical care and pharmaceuticals continue

to get more expensive[17] . Baumol argues that many industries have become largely automated and thus are more efficient resulting in lower prices. Industries such as healthcare and education, however, remain labor-intensive, which is one reason their prices remain high. The questions remains, what can we do to change this trend and lower costs? Although the focus of this paper will be to discuss scientific measures to reduce costs of prescription medications it is important to note that the most effective way to lower healthcare costs at least in the short term may indeed be through changes in political policy. From a scientific perspective, however, there are many avenues of research that may lead to more affordable pharmaceuticals. Improving the thermostability of drugs and vaccines, repurposing existing drugs for new applications, and developing cheaper or more efficient cell culture media used for drug production are all viable routes to lower costs to consumers.

Competition and Generics

Competition in a market is one of the best way to drive down prices. Unfortunately patents prevent competition for a new medication for as many as 20 years in the drug industry. In some circumstances, companies can effectively extend their monopoly on a recently off-patent drug by arranging “pay to delay” agreements with competitor companies. Such agreements involve paying rival companies to hold off on developing a generic version of the name-brand drug for a specified amount of time so as to maintain full market share for said drug.

Once generics begin to be produced they save consumers and governments a great deal of money. The Association for Accessible Medicines estimated that generic drugs lowered pharmaceutical spending by $253 billion in the U.S. in 2016, with $2.9 billion saved in Connecticut[18] . The cost difference is quite significant with generic drugs priced about 85% less than their brand-name counterparts.[19] To demonstrate this cost difference another way, generics have 84% market share of U.S. pharmaceutical industry by volume but only 28% by value[20] . Interestingly, generics seem to be grasping more of the market share both in value and volume over the last 13 years in several EU countries at least, perhaps as more popular drugs come off patent[20] . New consumer facing software can also help lower costs on pharmaceuticals by exposing individual consumers to competitive or alternative products with a lower price. Companies like Rx Savings Solutions notify users of any more competitively priced generic products as well as prompt them to talk with their doctors about alternative medications for their condition that may decrease costs. A more expensive class of drugs, called biologics also have their own type of ¨generic” to increase competition in the market.

Biologics and Biosimilars

Biologics, also known as biopharmaceuticals, are a class of drugs produced from living organisms Biologics are typically large macromolecules with tens of thousands of atoms making them much larger than typical pharmaceuticals like aspirin, which has 21 atoms for instance (Figure 1). Administration of biologics are often via infusion or injection, and largely because of the size of the molecules, biologics are typically much less stable than typical pharmaceuticals. Most of their applications are in complex disease states such as cancer and autoimmune disorders. One of the most important pieces of information about biologics is their price tag. Biologics accounted for 38% of U.S. drug spending in 2015[21] . The annual cost for a single biopharmaceutical prescription is typically in the tens of thousands, with the average cost of $16,425 annually for biologics compared to an average of $730 annually for traditional pharmaceuticals as of a 2008 analysis[22] . Despite biologics being so expensive there has been little evidence to suggest that use of biologics lead to downstream financial offsets; things like reduction in doctors visits or length of hospital stay[23] .

Just as generics provide a lower cost off-brand option to many off-patent pharmaceuticals, so-called "biosimilars" can provide a lower cost alternative to off-patent biologics. A notable difference between generics and biosimilars, however, is that whereas generics contain chemically identical active ingredients compared to the brand name products, biosimilars may not be the exact same molecule as the name brand biologic they were designed to emulate. Because biologics have complex structures, are less stable, and are sensitive to the varying productions processes of different labs, biosimilars will likely consist of a combination of subspecies that may be slightly different than the original producer's formulation (Figure 2). Developers of biosimilars must demonstrate that although the structure varies slightly compared to the reference product, the biological response remains safe and effective. For this reason and others, developing biosimilars can be somewhat of gamble for biopharmaceutical companies. Biologics demand a high price which represents a large potential reward, however, the initial financial investment required can be quite substantial, representing a large risk. For example, with expensive laboratory supplies and costs associated with obtaining Federal Drug Administration (FDA) approval it can cost $100-250 million to develop a biosimilar[24] , compared to a measly $1-4 million to develop a new generic. The time for development represents a large investment as well, taking approximately 7 to 8 years to develop a new biosimilar[24] . Interestingly, federal regulations in the European Union (EU) seem to have made it easier for companies to develop biosimilar products. Because of this, the EU has more data on how much biosimilars might save consumers. Their data suggests that biosimilar products are discounted an average of 15-30% when compared to reference products[25] . Mulcahy et al. have used such data to predict that Americans could potentially save $54 billion in 10 years between 2017-20[26] on their biologics spending by using biosimilars[26] .

Figure 1: The relative size of a traditional small molecule pharmaceutical, like aspirin, compared to a large macromolecule like a monoclonal antibody, a potential example of a biologic drug[27] .

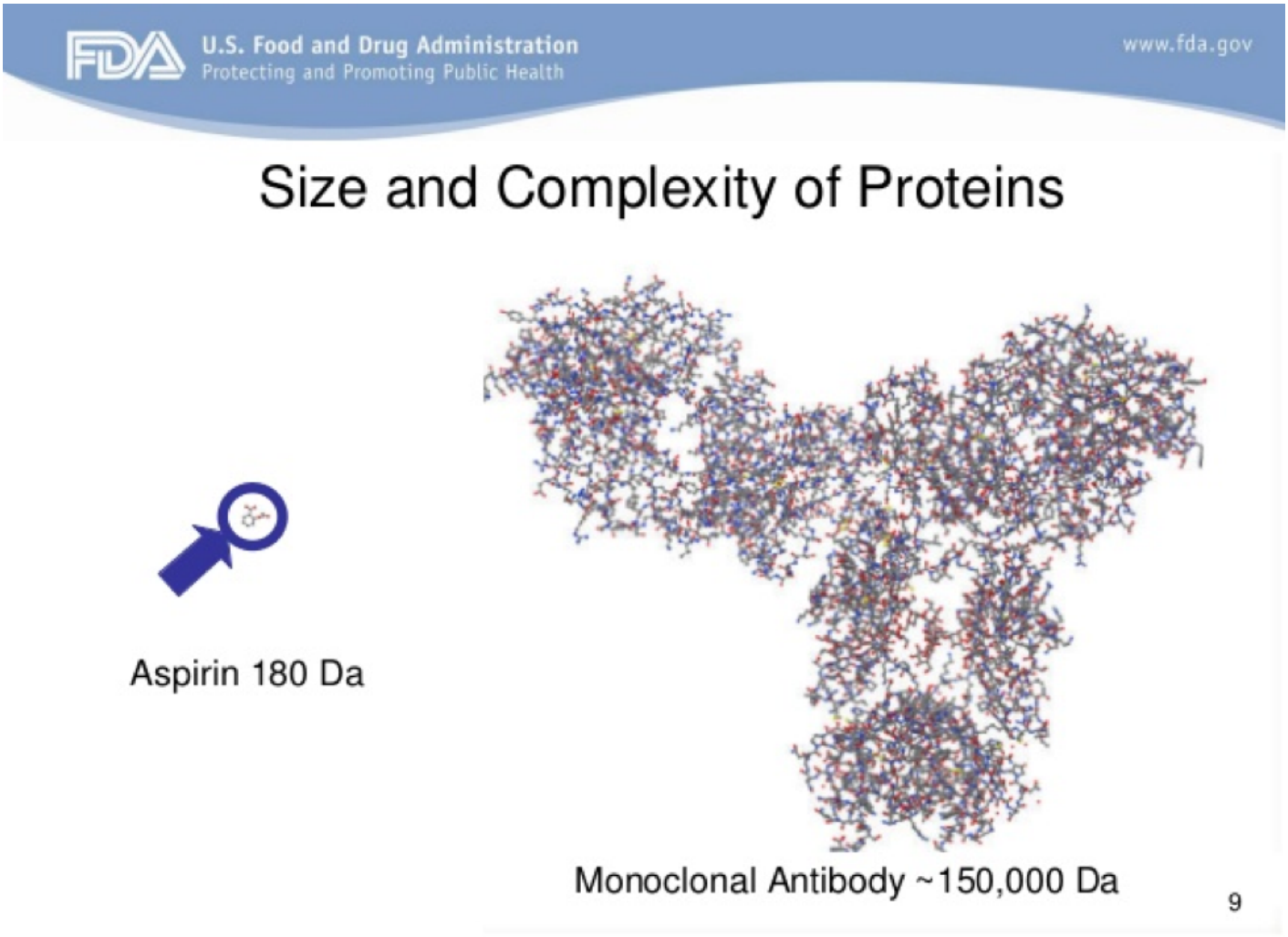
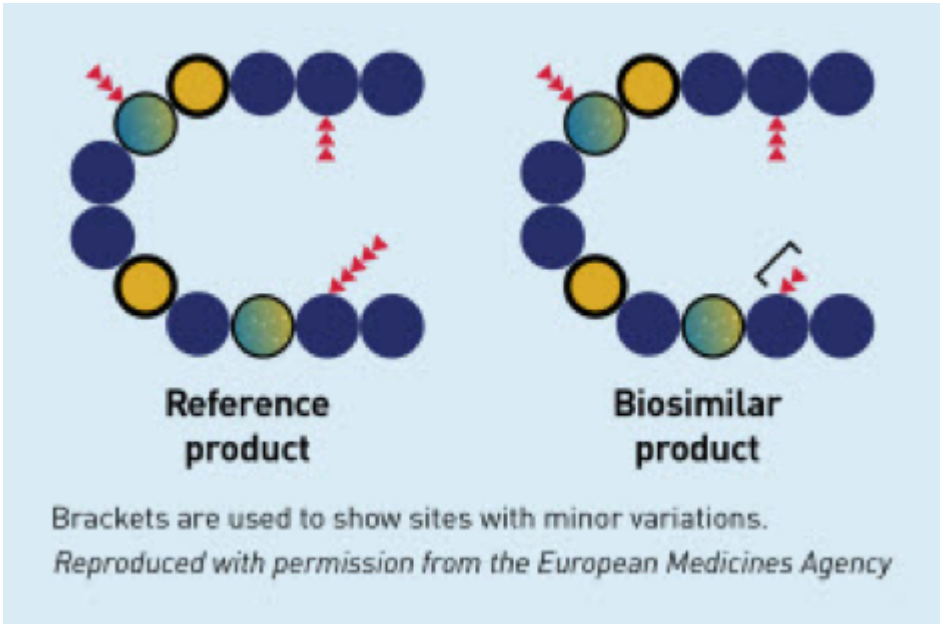


Figure 2: Visual representation of potential minor difference between biosimilar and reference products[28] .



Repurposing Old Drugs

Repurposing already-approved, off-patent drugs can present an incredible opportunity to lower prescription and healthcare costs. This strategy may be particularly valuable in the developing world since pharmaceuticals companies have little monetary incentive to develop drugs targeted for these areas. Repurposing old drugs can potentially do a great service if they can fill a need in developing countries where new medications are not affordable. In these countries, funds available to spend on healthcare are extremely limited as mentioned earlier. Access to many, especially newer, medications may be very little, in which case people will need to make do with what they have, requiring what has been termed “lean” thinking[29] . Finding new applications for old, cheap drugs that are on hand can be tremendously innovative and valuable to society.

Repurposing old drugs can potentially be useful to reduce costs in western medicine as well. In particular, it can significantly decrease funds required for companies to get through the FDA approval process. Compared to the roughly $800 million it takes to get a new drug on the market, it only costs $40 million to $80 million for FDA approval of a new use on an old drug[30] . Additionally, there appears to be great untapped potential for many old drugs. The Repurposing Drugs in Oncology (ReDO) project, for example, has identified 230 drugs (over 75% of which are off-patent) that currently have applications other than cancer but have shown evidence for anti-cancer activity[31] . Considering the cost of many cancer treatments, repurposing old drugs may have significant financial benefits.

Increasing Shelf Life

In the 1980s the U.S. military had billions of dollars of stockpiled pharmaceuticals that were about to expire and the FDA decided to test batches of the drugs to determine if expiration date extensions were warranted. Upon testing 122 different medications, the FDA determine 90% of them had high enough active ingredients levels to warrant extensions[32] . In another study of medications that expired 28 to 40 years earlier, 12 of 14 active ingredients were still present at levels 90% of that listed33. Considering the fact that hospitals like Tufts Medical Center in Mass throw out about $200,000 of expired medications per year, extending expiration dates can save hospitals a great deal of money; savings that could then be passed on to patients and insurance companies[32] . Extrapolate out that example considering there are over 6,000 hospitals in the U.S. and it's not difficult to believe that $2 billion are lost each year in US from expired pharmaceuticals as estimated by Lenzer in 2014[34] .

Inappropriately over-extending expirations is certainly unwise of course, and such extensions are far from all we can do to increase shelf life and save on wasted medications. Additions to formulations to improve stability and optimized storage protocols/technologies are other strategies that can improve shelf life. Biologics and vaccines are much more vulnerable to deterioration and thus have shorter shelf lives as well as stricter storage instructions. For example, according to a Canadian publication, most Canadian vaccines need to be stored between a narrow range of 2°C and 8°C, yet up to 20% of healthcare facilities in Ontario fail to meet this requirement or others[35] . Additionally, about 4% of vaccines in Ontario expire before they can be used contributing to $3 million in wasted vaccines each year[35] . Evidently, technologies to improve stability and innovative storage devices may have tremendous cost saving potential.

Production Efficiency

There are potentially many other ways to increase the efficiency of the drug production process in order to

lower costs. Just as Baumol explains, other industries have cut costs through automation, and technologies can be developed to help the pharmaceutical and biopharmaceutical industries become more automated. This effort has long been underway with labs integrating robotics for automation starting in the 1980s. One of the most productive uses of automation is in high-throughput screening, the ability to screen many drug candidates at once. Still there is room for increased automation. It's estimated that with more and optimized automation, drug companies could potentially screen 100,000 compounds per day compared the average 25,000 per week they currently are able to screen[36] . With that in mind, improvements in automation could potentially save us millions in an industry where it costs close to $1 billion to discover and develop a new drug.

In the biopharmaceutical industry where living organisms are required for the manufacturing process, improvements in growth medias or cellular habitats, for instance, may be an additional line of research to pursue in the effort to increase production efficiency and, thereby, lower costs. Unfortunately, it does not appear there is an incredible amount of research being done in the area. From all the information discussed above, students should have many jumping off points and ideas to be able to start their research and design projects.

Lesson Plans

Overview

This research project is to be used as a culminating activity in the last three to four weeks (seven 80 minute class periods) of marking period four. Researching and designing technologies or strategies to reduce the cost of prescription drugs will engage students while incorporating various chemistry concepts they havelearned throughout the year (the relationship between structure and function, pH, activation energy, the relationship between temperature and reaction rate, catalysts, inhibitors, etc.). Costs of healthcare and prescription medications continue to rise and remain a significant portion of individual's annual spending. Students will work to solve this problem by researching and designing their own technology or strategy to lower the costs of prescription medications to consumers. They may choose one of many way to tackle this including repurposing old drugs, improving stability of current drugs, the design and use of biosimilars, and improving production efficiency. Students will need to present their findings and their plans in a research paper and will also be required to present this research to the class. Students will work individually or in pairs to complete these tasks. A significant portion of their grade will be determined by their ability to effectively demonstrate that their technology or strategy may have a potential use case. Consequently, students will need to provide calculations in their paper showing how much their technology/strategy is estimated to save consumers. Learning objectives, a timeline of the unit, materials needed, the components of the research paper, and an example grading rubric for the unit have all been provided below.

Learning Objectives

SWBAT identify and understand basic economic factors that influence healthcare and drug costs

SWBAT research the drug industry and potential ways to lower costs

SWBAT use chemistry concepts to design money saving technologies and/or strategies in the drug industry

SWBAT discuss the value of repurposing old drugs for new uses

SWBAT calculate estimated cost savings to consumers

SWBAT analyze potential benefits and limitations to their proposed technologies

SWBAT effectively present their findings to their classmates

Timeline

Teacher checks will be required after completion of each of the following stages to help keep students on pace.

Stage 1: Research on their technology or technologies of interest and submission of proposal (1 day)

Stage 2: Writing of research paper and submission of rough draft (2 days)

Stage 3: Preparation for presentations (designing of PowerPoints, building of models, etc) (1 day)

Stage 4: Presentations and submission of final paper (1 days)

Two preparatory days will be included before the start of these stages to help prepare students for the research component and to help inspire ideas. To prepare for their research, one day will be spent in the library learning the effective research techniques and proper citation methods. Additionally, one day will be spent doing a lab, ideas for which are discussed below.

Students will investigate drug degradation in a one day laboratory activity. There are several possibilities for analytes and methods of decomposition and measurement. No one method will be suggested here, but rather several methods will be discussed and example protocols will be referenced. One option is to degrade hydrogen peroxide (H_2O_2) by heating and to measure the remaining H_2O_2 via titration with Potassium Permanganate ($KMnO_4$). Heating causes H_2O_2 to decompose into water (H_2O) and oxygen (O_2). The amount of H_2O_2 can be determined through calculation based on the volume of 0.2M KMnO4 required to titrate with the H2O2. An example protocol can be found on Microsep's website37. Another option is to again use heat to decompose Aspirin (acetylsalicylic acid) into salicylic acid and acetic acid. The amount of salicylic acid formed can be measured through spectroscopy. For every one mole of acetylsalicylic acid decomposed, one mole of salicylic acid will form, making calculation of the percentage degraded quite simple. An example protocol written by Dr. Stephanie Farrell may be found at pharmahub.org[38] . In the absence of a UV spectrometer it may be possible to detect degradation via subtle pH changes using a well calibrated pH meter. The goal of an activity such as one of those mentioned above is to get students thinking about drug stability, what affects it and how it can be measured. Coupled with the addition of a stabilizing factor, one of these methods could be used to help determine interventions that may improve the stability of a drug.

Another optional lesson that could be included would be to have students read an article on examples of old drugs that have been repurposed to help give them some ideas. The article can then be discussed as a class. An article such as "Repurposing Old Drugs, like Ketamine, Saves Time and Money," written by David Potter and posted on StatNews.com on April 26th, 2016, would be a good example[39] .

Materials

It is recommended to have students work in no more than pairs (individually if they prefer) to maximize engagement. Chromebooks or other computers will be necessary for students to conduct research on their technology or strategy. Necessary materials for the laboratory activity will depend on the analyte and methods chosen. Comprehensive lists can be found within the referenced protocols[37,38] .

Research Paper and Presentations

Research papers are expected to be between 3-5 pages with included calculations and figures. The following components must be included in their research papers:

- Description of the general problem at hand and a rationale behind their efforts
- Introduction to their technology/strategy
- Detailed description of how their technology/strategy could be implemented
- Justification for why their technology or strategy would theoretically work based on chemistry concepts they learned throughout the year
- Discussion of potential societal or safety concerns related to their technology/strategy, as well as any other challenges or limitations they predict may be an issue
- Calculation of estimated cost savings their technology/strategy would bring to consumers

Students will present their findings and their technologies/strategies to the class. Presentations are expected to be 5 minutes in length. Presentations could include a demonstration, a poster board, a video, a PowerPoint, or other means of presentation. The following components must be included in their presentations:

- A professional nature in terms of preparedness and conduct during presentation
- A description of their technology/strategy, how it may help, and a discussion of how chemistry is related
- An estimation for cost savings to consumers and how they reached this estimate
- A significant effort to teach the class something new

Grading Rubric

Component	**Percentage**
Proposal	10
Research Paper	-
Rationale	5
Introduction to Technology / Strategy	
Implementation	10
Discussion ofChemistry Concepts	15
Limitations	5
Cost Reduction Analysis	15
Presentation	-
Professionalism	10
Discussion of ChemistryConcepts	5
Cost Reduction Analysis	5
Novelty	10

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Appendix

Next Generation Science Standards (NGSS) for Chemistry

HS-PE-ETS1-1: Analyze a major global challenge to specify qualitative and quantitative criteria and constraints for solutions that account for societal needs and wants.

Healthcare costs are a major global issue and in their research papers students will analyze the issue before offering their own solution.

HS-PE-ETS1-2: Design a solution to a complex real-world problem by breaking it down into smaller, more manageable problems that can be solved through engineering.

Students will focus on one method of addressing high prescription drug costs and will design a novel solution, describing its potential application in great detail.

HS-PE-ETS1-3: Evaluate a solution to a complex real-world problem based on prioritized criteria and trade-offs that account for a range of constraints, including cost, safety, reliability, and aesthetics as well as possible social, cultural, and environmental impacts.

Students will assess the viability of their proposed new technology or strategy to reduce prescription drug costs considering all of the concerns listed above. They will provide mathematical analysis to estimate costs savings to consumers.