Innovations for Resource-Constrained Settings: Opioid Crisis and Wound Care

By

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Thesis

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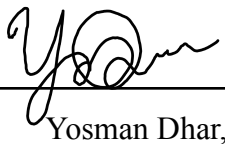
Date 04/29/2022 

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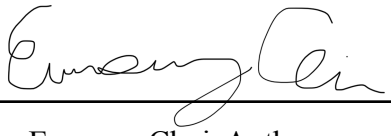
Date 04/29/22 

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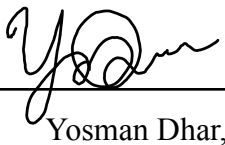
Date 04/29/2022 

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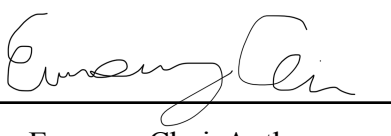
Date 04/29/22 

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This thesis by Yosman Dhar and Eunsung (Ally) Choi is accepted in its present form by the Center for Biotechnology as satisfying the thesis requirements for the degree of Master of Science

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Author Contributions

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This provides a brief introduction to the inspiration for the thesis project and its components

Yosman Dhar

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The Opioid Crisis and NaloxBox

Adapted and edited from Disease Fundamentals and Final Paper from the design courses ENGN1930/1L: Biomedical Engineering Design and Innovation I & II. This project was introduced by Dr. Geoff Capraro and began in the design course. Norbesida Bagabila, a biomedical engineering undergraduate student at Brown University (Class of 2021), was involved during ENGN1931L and conducted sound research.

Yosman Dhar: Clinical Need, Design Documentation (Design Requirements) Final Prototype, Functionality, Design Consideration (Intellectual Property), Discussion, Figures (1-5), Table (1-3)
Ally Choi: Design Documentation, Functionality, Design Considerations

Chapter 3

Wound Care and Negative Pressure Wound Therapy

This project was introduced by Aayush Setty, an undergraduate student in applied math and economics and the accelerated medical degree program at Brown University (Class of 2026).

Yosman Dhar: Clinical Need, Design Documentation, Final Prototype, Functionality, Figures (6,8,9,11,12), Table (4,5)
Ally Choi: Final Prototype (Carrier), Design Considerations, Discussion, Figures (7,10)

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Conclusion

A brief summary of the projects and final concluding remarks on what we have gained from these projects.

Yosman Dhar and Ally Choi

Abstract

Innovations for Resource-Constrained Settings: Opioid Crisis and Wound Care

Yosman Dhar, ScM, Brown University, May 2022

Eunsung (Ally) Choi, ScM, Brown University, May 2022

Resource-constrained settings can be defined as areas facing severe inequities, areas with limited access to basic necessities, and low to middle-income countries. Addressing clinical needs in these settings requires overcoming unique challenges and thinking outside of the box, which is all the more reason why innovation in these settings is so important. In this thesis, we examine two pain points, the opioid crisis and wound care, in the hopes of developing solutions with resource-constrained settings and their' needs in mind. For the first component of our thesis, we worked with Dr. Geoff Capraro and his company NaloxBox. NaloxBox produces opioid overdose emergency kits containing naloxone, a drug that reverses opioid overdoses. These boxes are placed in obscure locations with limited access to medical services in the hopes of improving naloxone access. To supplement NaloxBox, we proposed developing a voice prompt system to encourage proper naloxone administration. Such a system has been shown to improve bystander intervention in other emergency kits. We surveyed the impact of the voice prompt system (n=102) and gained preliminary user feedback to determine that a voice prompt system may be beneficial, but not critical. For the second part of our thesis, we worked to develop a negative pressure wound therapy (NPWT) device for Tenwek Mission Hospital in Kenya. NPWT devices promote chronic wound healing by creating a negative pressure environment under a tightly sealed dressing; however, NPWT can be expensive, require a sustained energy source, and are not always portable. Our proposed solution consists of a repurposed aspirator that was tested to function as an NPWT device. This aspirator was modified to include an optional solar-powered battery source and tamper-proof case to improve the device's portability. We also explored the design and use of an NPWT tip with better flexibility for wounds located on joints. Preliminary wound models demonstrated that the device provided a constant, reliable pressure, suggesting that aspirators could be repurposed for use as an NPWT. Overall, these projects have expanded our perspective and understanding of resource-constrained settings and we are excited to apply the skills we developed to future endeavors.

Chapter 1: Introduction

Resource-constrained settings present pressing health challenges that urgently require creative solutions. These settings have been broadly defined as low-to-middle income countries, regions with poor access to basic resources, and areas with limited access to quality care.[3,4] The conditions defining a resource-constrained setting all directly or indirectly influence health outcomes. In rural areas where access to healthcare and other resources may be limited, residents were reported to have a higher rate of preventable diseases and risky behaviors.[5] Areas located in food swamps, regions with a high density of high-calorie "junk" food, and food deserts, regions with a low density of healthy food options, were reported to have higher obesity rates and a greater risk of acquiring chronic diseases.[6] Overall, individuals living in resource-constrained settings tend to experience a higher burden of disease.[7] Therefore, it is critical to push for innovative approaches by improving technologies, infrastructure, and even workflow in resource-constrained settings. Doing so successfully, however, requires a deep dive into the unique factors associated with these settings and understanding how they may impact the design process. It also requires seamlessly integrating the opinions of key stakeholders to target the true underlying need and an open mind to the trial-and-error process. In this thesis, we explore and discuss two such solutions to target the challenges of resource-constrained settings.

For the first component of the thesis, our team examined the opioid crisis, which is considered a national health emergency in the United States despite the availability of naloxone, a drug that reverses the fatal effects of an opioid overdose. Organizations such as NaloxBox, producers of an emergency kit that contains naloxone, have increased access to naloxone by placing their NaloxBoxes in locations that may have limited access to immediate health services; however, other factors such as lack of bystander intervention due to stigma and improper naloxone administration due to a lack of awareness may contribute to overdose deaths. Developing a way to improve naloxone administration and awareness of opioid overdoses could reduce opioid overdose deaths. Our proposed solution was to create an Arduino-based voice prompt system that can be integrated into NaloxBoxes and will provide prompts on how to administer naloxone. The success of voice prompts in automated external defibrillators (AED) suggests similar benefits if implemented in NaloxBoxes. We surveyed the impact of the voice prompt system and gained preliminary user feedback to determine that a voice prompt system may be beneficial, but not critical.

For the second component of our thesis, we investigated negative pressure wound therapy (NPWT) devices for the treatment of chronic wounds. Chronic wounds are long-lasting, non-healing wounds that can be expensive, time-consuming, and difficult to treat especially in areas with limited resources. NPWT devices work by creating a negative pressure environment under a tightly sealed dressing and have been reported to improve healing and prevent infections. Unfortunately, these devices can be expensive to rent and require a sustained energy source to function. Our proposed solution is to develop a take-home NPWT that will be piloted in Tenwek Mission Hospital in Kenya, where resource limitations related to hospital beds, cost, and energy make advancements in this therapy critical. The proposed device consists of a repurposed aspirator that was tested to function as an NPWT device. This aspirator was modified to include an optional solar-powered battery source and a tip for wounds located on joints, all of which can be carried in a tamper-proof case we developed.

We hope to garner more awareness of clinical needs in various communities and inspire others to design with the patient in mind. By including public and global health principals into engineering design, it is possible to develop a new outlook and study the challenges faced in resource-constrained settings and the ways to overcome them.

Chapter 2: NaloxBox and the Opioid Crisis

Clinical Need

Opioids are analgesics, or pain-relieving medications, that can be prescribed to patients with diseases such as cancer.[8] While providing short-term comfort, opioids can be highly addictive and dangerous if abused. The abuse of opioids has grown into an epidemic that was declared a public health emergency in the United States in 2017.[9] This epidemic can be traced back to the 1990s when pharmaceutical companies and public health initiatives began campaigning against patient discomfort. These campaigns contributed to the over-prescription of opioids as hospitals did not want to be labeled "inhumane" by withholding pain medications and were often pushed through monetary incentives by pharmaceutical companies.[8-10] The addictiveness of opioids was also downplayed and reported inaccurately in initial research publications.[9] As a result, policies, and training evolved to encourage physicians to prescribe opioids as a basic pain management protocol, initiating the opioid crisis.[9,11]

The addictiveness and risks associated with opioid abuse are related to the pathways they impact. Opioids bind onto opioid receptors and obstruct pain processing by reducing synaptic transmission from the peripheral nervous system to the central nervous system.[12] Pain processing is not the only thing opioid receptors influence (Figure 1). The specific binding of opioids to Mu receptors acts as a double-edged sword. Mu receptors cause feelings of sedation and euphoria through the release of endorphins, making opioids addictive. however, repeated activation of Mu receptors has been shown to promote recreational drug use by slowing the release of endorphins and thus increasing opioid tolerance.[13] Additionally, Mu receptors may also impact self-control, behavior, and brain stem function.[13] This is important because the brain stem regulates breathing and opioids intercept signals that set the respiratory rhythm, causing opioid-induced respiratory depression. [12,14] In some cases respiratory depression is short-lived; however, during opioid overdoses, it can be fatal.[15]

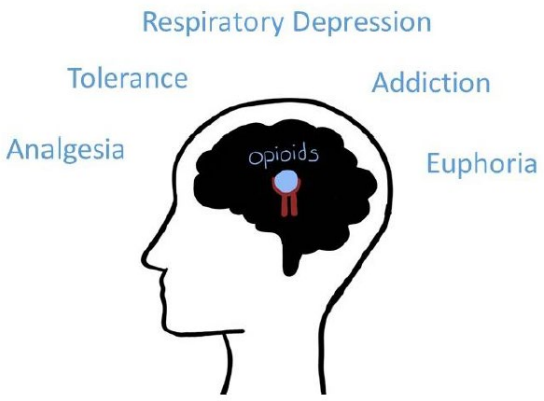

Figure 1 Effects of opioid receptor activation because of opioid binding.

Figure 2 NaloxBox with alarm system, CPR mask, instructions, and Naloxone.[1]

The current gold standard of treatment for an opioid overdose is naloxone, an opioid antagonist that binds to opioid receptors and restores normal functioning by inhibiting receptor activation.[15] Compared to opioids, naloxone has a stronger affinity for opioid receptors, which allows it to replace opioid molecules.[15] Currently there are three FDA-approved formulas of naloxone that can be injected, auto-injected, or sprayed into the nostril. Generally, naloxone is a prescription drug; however, some states and distribution programs have made it accessible without a prescription in hopes of reducing overdose deaths. These programs have allowed increased access to naloxone and inspired Dr. Geoff Capraro to develop an opioid emergency kit called NaloxBox (Figure 2). NaloxBoxes are similar to AED kits and can be placed in public areas, especially those with high rates of opioid abuse or limited access to care. Each box costs up to US$ 300 depending on what it contains; components include an alarm system, a cardiopulmonary resuscitation mask, and written instructions. Although there is room for naloxone, it has to be purchased by the NaloxBox owner themselves due to state regulations regarding non-prescription purchasing of naloxone. Currently, about 700 NaloxBoxes have been manufactured by Amos house and sold to governments, schools, homeless shelters, and other organizations.

Despite the increasing availability of naloxone through organizations like NaloxBox and state-run programs, from 1999 to 2018 a total of 450,000 people have died from prescription and synthetic opioid overdoses.[16] Opioid abuse is also expensive, costing the United States US$ 78.5 billion in 2013; of this, US$ 28 billion included health care and treatment spending from insurance companies.[17] Therefore, it can be concluded that the continued growth of opioid overdose deaths may not be due to the absence of a successful treatment, but due to a variety of different factors. Naloxone inaccessibility and improper administration may make it difficult to treat opioid overdoses in an emergency situation. Additionally, limited knowledge and stigma surrounding opioid abuse may also contribute to overdose deaths by reducing bystander intervention during an

overdose. While the ideal goal would be to address addiction from the source, a first step may be to improve bystander intervention and naloxone administration. To address this issue, we teamed up with NaloxBox and General Electric (GE) to improve various components of NaloxBox. GE worked on one of our ideas to develop a tracking system that alerts a NaloxBox owner of when a NaloxBox has been used and needs restocking, creating a log of areas with higher opioid overdoses and higher naloxone need. For our project, we developed a voice prompt system to encourage bystander intervention and better naloxone administration.

Design Documentation

In the process of developing our final prototype, we examined different solutions that could target the opioid epidemic while being compatible with NaloxBox. Ultimately, we selected a voice prompt system as it best met our solution requirements (Figure 3).

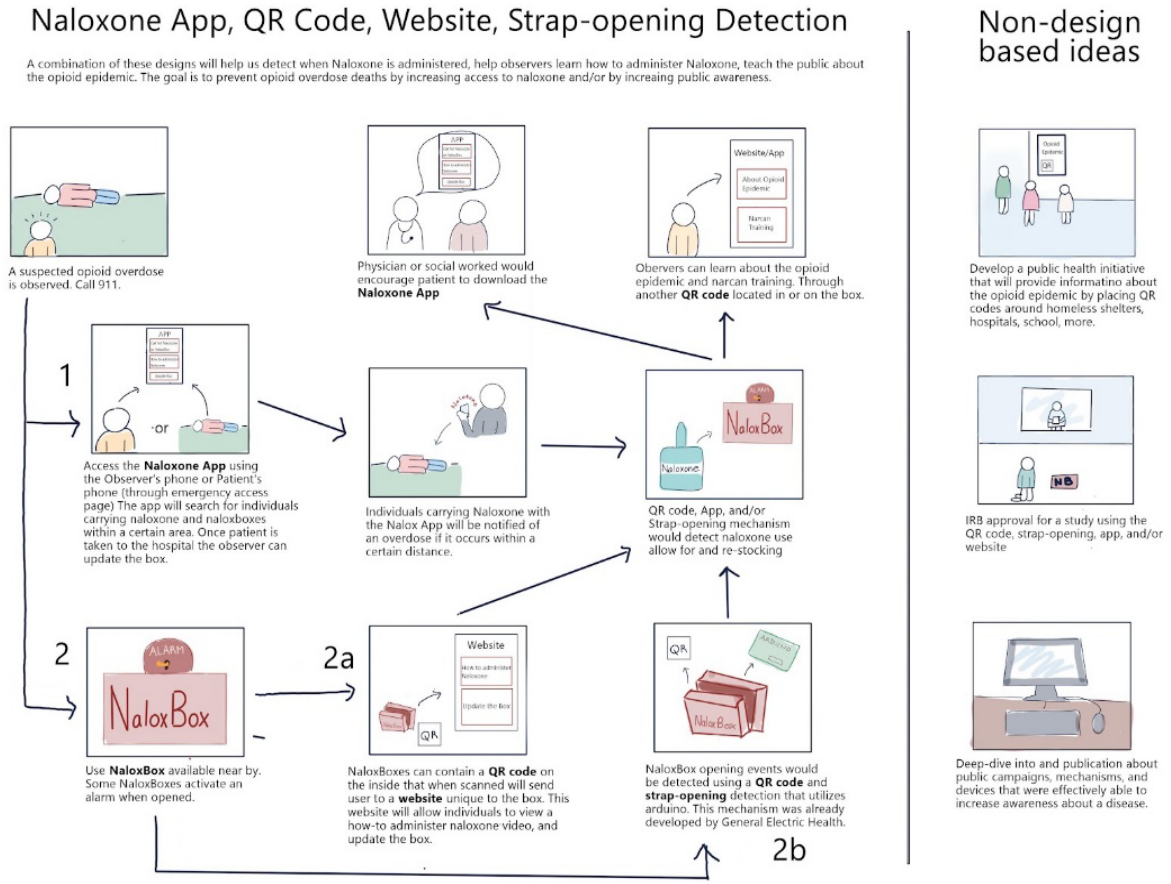

Figure 3 The design ideation process indicates solution areas that were considered (1) Use of a naloxone app that notifies naloxone carriers of an overdose. (2) Use of an app that notifies naloxone carriers and locates NaloxBoxes (2a) Involves a QR-based tracking of NaloxBoxes (2b) Involves a QR and SMS-based tracking of NaloxBoxes.

First, we considered an app that can locate naloxone in individual carriers and NaloxBoxes nearby. The app could include naloxone video instructions for emergency and non-emergency training. Opioid abusers and their family and friends would be encouraged to download the app, which would help them easily detect naloxone when in need. Many opioid abusers who die from overdose have a history of being hospitalized for previous overdose incidents.[18] Hospitals could encourage opioid users to download the app before getting discharged and educate them on how they may use it. However, it would not be effective at increasing public awareness and improving bystander intervention. It would be difficult to persuade the general public to download and keep the app on their phones. It may also not be intuitive in emergencies.

Another solution that was considered to promote bystander intervention and also keep track of NaloxBox use was a QR code that is linked to a website containing an instructional video and various educational materials. The QR code would be placed on NaloxBoxes and could be scanned in an emergency to be directed to the instructional video. Following the emergency, the website would encourage the bystander to provide an update of the NaloxBox status: how many doses of naloxone were used or if the box is damaged? Each NaloxBox would have a unique QR code for automatic box-specific tracking. This feature is useful because it would be inexpensive to add to future NaloxBox production and existing NaloxBoxes. There are limitations to this solution as well. The QR code is not self-explanatory and would require extensive labeling on the NaloxBox to encourage the bystander to utilize the QR code. This solution also introduces other problems as the bystander may not have a smartphone or know how to use QR codes, and there could be a language barrier if the labeling is only in English. Also, not all bystanders may follow through with updating the box status after the emergency, resulting in inaccurate records. To improve on this idea, GE created an SMS-based system instead, which will automatically track and update the owner when a NaloxBox has been opened. There is also a QR code within the box that will allow users to fill out an update on the box's status. Providing this automated system allows for more accurate tracking of NaloxBoxes; however, it does not address the issue of low bystander intervention and limited knowledge on naloxone administration.

Thirdly, another solution was a campaign-based idea that could promote public awareness through developing a public health initiative poster with a QR code. The QR-code could present information about the opioid epidemic, how naloxone can reduce overdose-related mortality and naloxone administration instructions. These QR codes could be placed around homeless shelters,

hospitals, and schools, and would be very effective for helping during non-emergency situations. However, this approach does not address the immediate need for training necessary during emergencies. Though this is a future supplemental component that could help address the overall problem, it was deprioritized over other solutions.

After the thorough ideation process, the final solution selected was a voice prompt system that will explain how to administer naloxone properly. This voice prompt system can be installed into NaloxBoxes and will begin playing when a NaloxBox is opened. This design was chosen after research on human responses during an emergency. We believe the voice prompts would decrease choice paralysis and reduce the time between shock and action. Additionally, this solution could increase bystander intervention and naloxone administration. A device that addresses a similar need for concise on-site administration instructions is the voice prompts in automated external defibrillators (AEDs). The ZOLL AED Plus, which includes voice prompts, has been proven to more than double the chance of survival in an emergency situation.[18] A study by Williamson et al. even demonstrates that voice prompts in AED boxes improved the quality of cardiopulmonary resuscitation (CPR) in subjects familiar with CPR and made unfamiliar subjects more willing to perform CPR.[19] Thus by developing a voice prompt system we may improve bystander intervention and reaction time during an emergency, especially in bystanders who are unfamiliar with naloxone administration.

To determine the design requirements necessary to examine the functionality of the prototype, discussions with GE and Dr. Geoff Capraro were conducted and analyzed (Table 1). From these conversations, it was clear that NaloxBox manufacturing has already been established via Amos House so any additional components have to be inserted easily and fit within a designated area. Secondly, given that NaloxBoxes are used in emergencies, keeping the voice prompts as hands-off and easy-to-use as possible is important. A button-based design that starts the voice prompts had been considered, but this system would add unnecessary steps and the button may be overlooked especially in an emergency. One iteration that can be considered in the future is issuing a button-based design to change the language settings. In addition to how the voice prompts are initiated, the actual content of the voice prompts needs to be considered. Narcan Naloxone instructions were condensed after speaking to Dr. Jeffrey Bratberg from the University of Rhode Island College of Pharmacy who is familiar with regulations related to opioid abuse initiatives. Discussions concluded that this was more effective than writing instructions from

scratch as they have been thoroughly examined for clarity and directly relate to the product and company that is usually purchased for NaloxBoxes. After condensing the voice prompts, the speed and clarity of the prompts had to be considered. The voice prompts must be slow enough that the user has enough time to perform the designated tasks. It would also be useful to confirm if the voice prompts are more effective than written instructions. Additional requirements that were discussed include battery usage. Since NaloxBoxes are often placed in obscure locations or not checked upon, NaloxBoxes need to be powered without requiring frequent battery changes. Lastly, NaloxBoxes that are placed in crowded areas may be difficult to hear therefore the voice prompts need to be loud enough to be heard. The voice prompt system would also need to be compatible with GE's electronics and design, which were all Arduino-based.

Final Prototype

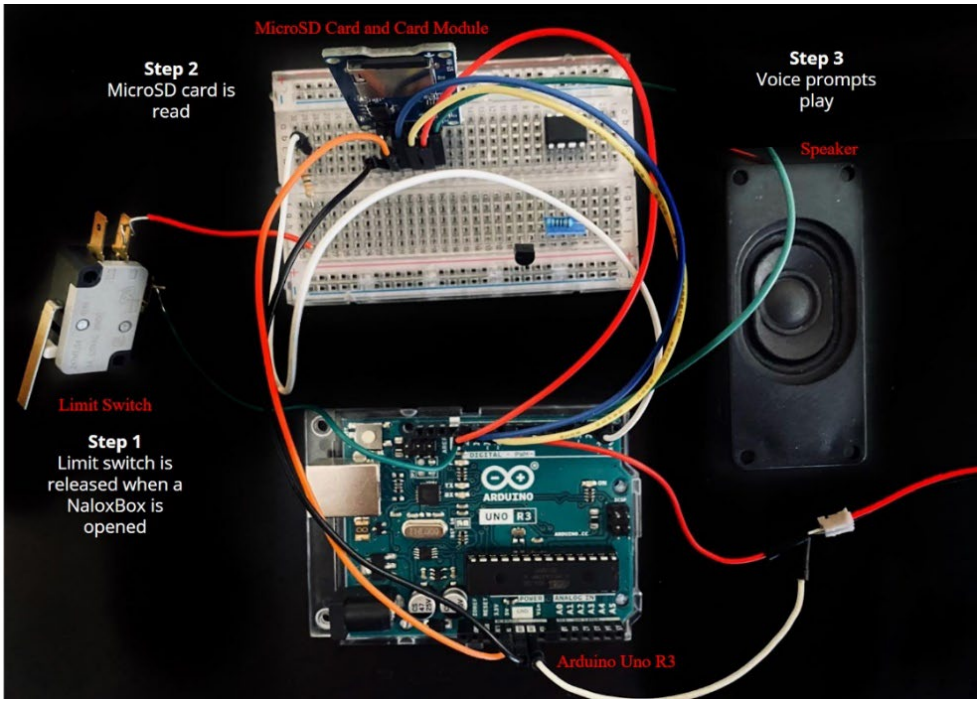

Figure 4 Final prototype and steps of Arduino-audio player that plays voice prompts when a NaloxBox is opened.

The hardware and software for the final prototype were developed based on Sarvagnya Purohit's audio player.[20] The hardware component includes an Arduino Uno Rev3, breadboard, MicroSD card module, MicroSD card, and limit switch purchased from Adafruit. The software was developed on Arduino IDE. The final prototype was formatted so that the voice prompts will begin playing when a NaloxBox is opened and the limit switch is released (Figure 4).

Hardware

The MicroSD card and MicroSD card module store and read the voice prompts. The voice prompts were converted from text to an artificial voice using Notevibes software. The voice prompts were stored as a .wav file and were formatted to have an 8bit resolution, 16000 Hz sampling rate, and a mono audio channel. The MicroSD card module was linked to the Arduino Uno Rev3 through the breadboard to circumvent the need for soldering. To read the MicroSD card, the MicroSD card module's chip select was connected to pin four and integrated into the code (Figure 5).

Hardware Component	Pin Number
MicroSD Card Module	MOSI- pin 11 MISO- pin 12 CLK- pin 13 CS - pin 4
Limit Switch	Pin 2
Speaker	Pin 9

Figure 5 Hardware setup for the voice prompt system.

A limit switch is an on/off dual-modality that can signal whether an event occurred In our prototype, the limit switch will be off and depressed when a Naloxbox is closed and on and released when a NaloxBox is opened. A released limit switch allows the MicroSD card module to be read. The limit switch was connected to pin two and integrated into the code. The speaker is connected to the Arduino through pin nine and will play the voice prompts when the limit switch is released and the MicroSD card has been successfully read (Figure 4). Overall, this system will be able to integrate into GE's current hardware as they use a limit switch as well.

Software

The code begins by including Arduino IDE's SD card library and Sarvagnya Purohit's Arduino audio player TMRpcm library. The code then recognizes the MicroSD card module, speaker, and limit switch on pins four, nine, and two, respectively. The limit switch was defined as the input and the ChipSelect (CS) pin is defined as the output, allowing the limit switch to determine whether the SD card is read. For troubleshooting, if the MicroSD card module is unable to be read, "SD fails" will be printed on the serial monitor. Volume can be set from one to ten but is dependent on the speaker's maximum limit. The function play allows the voice prompt file to be read and outputs "file works" to confirm that the .wav is properly formatted. The code includes a loop that requires the box to be opened again for the voice prompts to play. The software was developed to stand alone after being integrated into GE's software.

Script

The script for the voice prompts was based on Narcan Naloxone instructions that were condensed (Figure 6). Notevibes was chosen to convert the script to speech as pauses, speed, and voice could be easily controlled. For the same reason, the script uses an artificially generated voice. The current script plays in 82 seconds at 101 words per minute. Pauses between paragraphs are 1.5 seconds long and pauses after periods are 1 second long.

Abbreviated Audio Voice Prompts

Voice prompts for Naloxone administration. Spanish prompts will play after English prompts. Check the written instructions manual inside the box for additional details and diagrams.

Step 1. Get Naloxone nasal spray from the box. Peel back tab to open.

Step 2. Hold the naloxone nasal spray with your thumb on the bottom of the plunger. Place your pointer and middle fingers on either side of the nozzle.

Step 3. Tilt the person's head back and provide support under the neck with your hand. Fully insert the spray nozzle into one nostril. Firmly press the plunger to administer Naloxone.

Step 4. Call 911 then lay the person on their side. Every 2 to 3 minutes, check for responsiveness. If unresponsive, administer another dose of naloxone nasal spray until emergency help arrives. To listen to instructions again, close and open the box.

Figure 6 Voice prompt script condensed from Narcan Naloxone instructions.

Functionality

Table 1 Design requirements, testable variables, and verifications used to determine the outcomes of the proposed voice prompt system.

Design Requirement	Testable variables	Verification
Should fit within $185 \boldsymbol{in^3}$	Speaker, Arduino	Testing
Should play 95% of the time when the limit switch is depressed	Limit switch, Arduino	Testing
Greater than 90% of users should consider the voice prompts easy to understand	Wording, pauses	Survey
Greater than 90% of users would like the addition of the voice prompts	Instruction manual	Survey
The battery should withstand 10 voice prompt starts	Hardware	Testing
The volume of the voice prompts should be greater than $80 db$	Speaker, code, amplifier	Testing

To determine the functionality of the prototype, the design requirements were outlined to assist in achieving the goal of an effective voice prompt system (Table 1). The requirements are listed according to priority and the testable variables are based on different hardware and script components that can be adjusted. Design verifications were performed using testing and a survey sent through snowball sampling.

The first design requirement involves the size of the prototype, which must fit within 185 in^3 or ⅙ the volume of a NaloxBox; the weight of the electronics is negligible. Accomplishing this requirement was significant to ensure the voice prompt system can be installed in a NaloxBox. This size requirement was determined based on the other components that must be placed within a NaloxBox, including naloxone, the CPR mask, and GE's hardware, which includes batteries that would power our system as well. The testable variables were different materials we could utilize; for example, one option considered was Adafruit's Music Maker Arduino which can directly store voice prompts, allowing us to bypass the need for a MicroSD card and reader; however, this system would be difficult to integrate with GE's hardware. The final prototype and its components were able to fit within the desired measurements based on their overall individual volume.

The second design requirement states that the voice prompts must be able to play greater than 95% of the time after the limit switch is depressed. This requirement confirmed that the voice prompts and the prototype is functional and reliable. To verify the prototype's functionality, ten consecutive trials were performed to determine whether the voice prompts would play after the limit switch is depressed. The voice prompts were able to play 100% of the time, verifying our requirement. For long-term testing up to 100 consecutive trials could be performed, although opening a NaloxBox these many times may be rare, it would confirm that the system works. Additionally, testing the switch over a month or more to see if it still functions could be considered.

The third design requirement states that greater than 90% of users should consider the voice prompts easy to understand (Table 2). Through a survey we conducted with 102 survey participants, 96 participants chose to answer the question: how do you feel about the speed of the voice prompts? In total, 86% of survey participants considered the voice prompts easy to understand, but around 36% believed the voice prompts were too slow. The current speed of the voice prompts is 101 wpm. Slow speech is regarded as less than 110 wpm and conversational speech is regarded as 120 to 160 wpm. We would want the voice prompts to be a little slower than a conversational rate to ensure that users have enough time to process and perform the action stated

by the prompt. To test for the optimal pace, we could record prompts at speeds of 106 wpm, 111 wpm, and 116 wpm and choose the prompt with the highest preference. It is also possible since the participants were simply listening to the voice prompts and not performing the actions states, that their gauge of the speed was inaccurate. Additionally, some participants thought the prompt was clear but did not like the AI's voice. As this choice was for prototype purposes to control speed and pause parameter, another survey could be conducted using a prompt with a live narrator.

Table 2 Outcomes of the survey to understand the effectiveness of NaloxBox voice prompts.

How do you feel about the speed? (n=96)				
Needs to be Faster	Needs to Slower	Speed is Fine	N/A	Other
36%	3%	57%	1%	2%
How do you feel about the clarity? (n=96)				
Voice prompts are clear and easy to understand	Voice prompts are unclear and hard to understand.	Not Applicable	Other	
86%	4%	1%	6%	
How do you feel about the pauses (n=94)				
Pauses are perfect	More pauses between words	More pauses between each step	B and C	Needs less/are distracting
62%	0%	0%	3%	35%
Do you think voice prompts will help you administer Naloxone if you are unfamiliar with its administration? (n=99)				
Yes	No	Prefer not to answer		
90%	9%	1%		
Do you think voice prompts are more effective than the instruction manual? (n=97)				
Yes	No	They were similar	Prefer not to answer	
32%	31%	33%	4%	
Do you think you would prefer the voice prompts or instruction manual during an emergency opioid overdose? (n=99)				
Just voice prompts	Just instruction manual	Voice prompts and instruction manual	Prefer not to answer	
3%	29%	66%	2%	

The fourth design requirement was that greater than 90% of users would like the addition of voice prompts. This design requirement was tested through the survey questions that asked the user if they believe the voice prompts will help them administer Naloxone if they are unfamiliar with its administration. 90% of participants did believe it would help and 66% of participants preferred for NaloxBox to have both the instruction manual as well as the automated voice

prompts. Only 32% of participants believed the voice prompts were more effective than the instruction manual, while 33% believed they were similar. Though these results reveal that voice prompts cannot completely replace the instruction manual, it may still be beneficial for them to be included.

A design requirement that is still in development is that the battery should withstand 10 voice prompt starts. The current prototype runs on the power sourced by the computer it is connected to and a battery would source the power for actual implementation. For manufacturing, the audio prompt system will be incorporated into GE's parts, and the two components would share an Arduino and battery source. This would alter the battery requirements down the line. There are two methods the battery could be tested to determine if it meets the requirements. The first method involves getting different batteries with different capacities, and testing if each battery can support ten iterations of the audio prompt getting triggered and playing all the way through. NaloxBoxes are opened around twice a year, and this would ensure the battery would be sufficient for at least 5 years before needing to be replaced. An alternative testing method would be to use a battery indicator that depicts the percentage of battery drained with each box opening event, which accurately gauges how many iterations each battery can support. For manufacturing purposes, the latter method would be the optimal way to test the battery requirement.

The last design requirement was that the volume of the voice prompts should be greater than 80 decibels, which is the average street volume. The volume of the reported noise level in New York was averaged with the measured sound level in parts of Providence at varying times of the day. These results revealed that the noise level ranges from 64 decibels to 120 decibels, which is how it was determined that the audio prompt should play at greater than 80 decibels so it can be heard at different potential NaloxBox locations. This requirement was not achieved as the current speaker with the prototype cannot play audio above 80 decibels, and different speakers need to be tested to find one that can reach that volume. To maintain the size constraints, the speaker would still need to be small enough to be enclosed by the holder.

An overarching and more comprehensive design requirement would determine if naloxone administration was carried out effectively. This experiment may be conducted by using NaloxBoxes with written instructions as a historical control over a year, and then installing voice prompts in the NaloxBoxes and tracking them for a year. This study would be limited to a designated area with high opioid overdoses and effectiveness could be quantified based on a post-

administration survey taken by the initial emergency responder to understand whether the voice prompts and written instructions, written instructions-only, or voice prompts-only were considered to have better outcomes. It could also be measured by patient outcomes, although this may be more difficult to track.

Design Considerations

Intellectual Property

To conduct the intellectual property search, the terms "Emergency box, emergency kit, first-aid, voice prompts" were used on Google Patent, United States Patent and Trademark Office's (USPTO) website, and Google. The purpose of using these search terms was to find patents and prior art related to the voice prompt system and/or NaloxBox. Based on the search terms, both the voice prompt system and NaloxBox are obvious and non-novel, therefore there would freedom to develop and operate the voice prompt system. The notable prior art includes voice prompts integrated into automated external defibrillator (AED) emergency boxes. Other devices include talking glucose meters and voice recognition systems.[21] Prior art for NaloxBox includes multiple emergency kits and community response systems for emergencies.[22] Marketplace competition for NaloxBoxes and voice prompts is limited, but there are other initiatives targeting the opioid epidemic. To improve naloxone administration and bystander intervention there are public health initiatives and petitions to pass legislation for naloxone accessibility.[22] There are also devices to improve rapid drug testing and monitoring.[23] Although competition is minimal, it may be worthwhile to collaborate with other organizations to address the opioid epidemic to create a seamless and multidimensional tracking system.

Regulatory Pathway

Per this guidance, our device is a voice recording that can be assimilated to the category of a mobile app that incorporates device software functionality that meets the definition of device in section 201(h) of the FD&C Act11; and either is intended: The intended use of software determines whether it meets the definition of a "device." As stated in 21 CFR 801.4,12 intended use may be shown by labeling13 claims, advertising materials, or oral or written statements by manufacturers or their representatives[1]. According to the FDA, when the intended use of software is for the diagnosis of disease or other conditions, or the cure, mitigation, treatment, or prevention of disease, or is intended to affect the structure or any function of the body of man, this software will then be categorized as a device under section 520(o) of the FD&C Act[1].

FDA's oversight approach to software functions is focused on their functionality, just as we focus on the functionality of conventional devices. Their oversight is not determined by the platform, in this case, naloxone. Therefore, under this guidance, FDA would not regulate the sale or general/conventional consumer use of our device. FDA's oversight applies to software functions performing medical device functions, such as when a mobile medical app or software application transforms a mobile platform or a general-purpose computing platform into a medical device[1]. Based on the FDA classification of medical devices, it was determined that our device is qualified for the class I category. A class I category devices are simple devices, with minimal risk to the user. Such definition applies to devices and therefore is subject to the general regulatory controls of medical devices and typically does not require any premarket submission.

Payers

The product that we are developing is intended to provide supplemental instruction for NaloxBox. Unlike other medical alert systems, our device will not be reimbursable by either Medicare or Medicaid. According to Medicare and Medicaid guidance, medical alert systems allow you to get help if you're alone and have an emergency or injury. Typically, a button on the device sends a signal to the alert company to let them know you need assistance. Although our devices can provide peace of mind and help in emergencies, Medicare doesn't consider them necessary medical devices. Medicare does not usually cover the costs of purchasing or maintaining an alert system. However, there are few provisions in Medicare plans that could allow health insurance providers to purchase some coverage for a medical alert system and how to choose one if you're purchasing it on your own. For instance, Medicare part C or Medicare Advantage is a plan provided by private insurance companies. Some plans offer additional benefits and services that traditional Medicare does not. In some plans, this may include medical alert systems.

Since our product will be mostly purchased by Public Health entities, neither Medicare nor Medicaid have plans in place to reimburse institutions. However, our device qualifies for the Health Maintenance Organization (HMO) Plans. The HMO plans offer additional coverage for institutions and organizations such as the NaloxBox organization. Based on the HMO reimbursement guidance, it will reimburse up to 100% of the cost if the organization demonstrates through a specialist that the case is vital in solving a public health crisis. An additional way to get reimbursed for our device is organizing fundraising and reaching out to NGOs for donations to support our initiative. Lastly, as mentioned earlier, naloxone purchasing would be independent of

NaloxBox purchasing and depends on state guidelines, some of which freely distribute naloxone while others require a prescription.

Estimated Manufacturing Costs

Materials	Price per unit	Comment
Enclose Box	US$ 60	We have decided to use a combination of stainless steel and an ABS plastic electrical case. This is the best material for the box because it is waterproof, dustproof, and has shockproof built-in. Fixing the box to the naloxbox will be easy because the box comes with a mounting plate. The necessary modification will not be hard
Arduino	US$ 30	This is the central component of the device. It is an easily accessible piece and not very costly for the work that is intended for.
Speaker	US$ 20	The speaker should be small, no bigger than 2 inches long. And able to emit a sound louder than 80db
Miscellaneous	US$ 20	Extra wires, pines, and joints
Total	US$ 130	

Based on the price per unit breakdown, if NaloxBox was not a non-profit, we believe that que can market our device at a flat price of $150. The $20 margin profit on each device is acceptable as it will exponentially grow when we will figure out a way to get a wholesale price of each piece of the device. We are expecting our device to be sold in bulk because it will be sold to a unique organization, the NaloxBox.

Market Analysis

NaloxBox and subsequently the proposed voice prompt system can penetrate a large market. In 2016, it was reported that there are 100 million individuals suffering from chronic and acute pain in the United States putting them at risk for opioid abuse due to the previously less monitored prescribing protocols.[24] Similarly, in 2015, it was estimated that 2 million Americans aged 12 and older have abused pain medications.[25] While opioid abuse impacts individuals across all socioeconomic statuses, those of lower statuses are the most affected.[26] This suggests there is a great need for NaloxBox and more information about the opioid crisis.

Discussion

The opioid crisis is a multidimensional problem that will require creative solutions to address all of its components. One way to target its needs is by exploring methods for improving naloxone administration through voice prompts. Based on our survey results it can be concluded that although beneficial, voice prompts in NaloxBox are not critical; however, additional investigations may be helpful to understand this conclusion. Future work could examine the use of a narrator instead of AI prompts for a smoother and less distracting delivery. The actual survey questions could be optimized and participants recruited could be more diverse and have the opportunity to practice naloxone administration using the voice prompts or the instruction manual. Such a study could reveal results in a larger context, including human behaviors and reactions in emergencies. Another avenue for addressing the opioid crisis includes developing a public health campaign that would provide information about naloxone and its administration. From our survey, 42.4% of participants (n=102) did not know what naloxone was and 60.8% of participants did not know how to administer it. This is concerning since 36% of participants reported knowing someone who uses or has used prescribed opioids and 10% of participants reported knowing someone who uses or has used unprescribed opioids. Even if voice prompts may not be the solution, other methods such as placing QR codes around stores, schools, and other public areas could provide simple, quick, and interesting videos about the opioid crisis. Not only would this be useful for the layman, but it could also provide resources for opioid abusers and their families who may be seeking help. From this project, we gained a broader understanding of some of the skills required to examine such a complex problem. We are hopeful that in the future more efforts will be invested in addressing the challenges surrounding the opioid crisis beyond naloxone administration and accessibility to the misunderstanding and stigma associated with opioid abusers.

Chapter 3: Negative Pressure Wound Therapy and Wound Care

Clinical Need

Chronic wounds have an immense economic, social, and health impact. In the United States alone costs of chronic wound care exceed US$ 1 billion and 1-2% of the population is expected to experience a chronic wound during their lifetime.[27] In the United Kingdom about 33-41% of a nurse's time reportedly accounts for the costs of wound care.[28] Worldwide it is estimated that 15 million people suffer from chronic wounds; however, unlike the United States and the United Kingdom, not all nations have the resources to effectively treat them.[29] In Cameroon, for example, doctors have been reported to reject patients with chronic wounds because of the complicated and lengthy treatment. Many patients also tend to avoid care due to cost and time demands.[29] Above all else, chronic wounds greatly alter a patient's quality of life, making them a critical health problem to address.[29,30]

Unlike acute or normal wounds, chronic wounds deviate from typical wound healing, which consists of four overlapping steps. The first step is coagulation where platelets and blood clotting factors gather to prevent excessive bleeding. These cells produce growth factors that attract leukocytes and phagocytes leading to the next stage, inflammation. During the inflammation stage, antimicrobial agents and protective actions are taken to mitigate the risk of infection. The last two stages are proliferation followed by scar tissue formation during which extracellular matrix deposition occurs and cell proliferation is accelerated.[31] Chronic wounds are characterized by a prolonged inflammation phase and a persistent infection; they include vascular ulcers, diabetic ulcers, and pressure ulcers.[32,33] Chronic wounds can grow from small traumatic injuries, including scratches or penetrating injuries, to nonhealing chronic wounds because of exogenous factors like diabetes, obesity, or improper care.[34] If not addressed immediately, acute wounds are at risk of growing into chronic wounds, and chronic wounds are at risk of developing biofilm infections, which are extremely difficult to treat, antibiotic-resistant infections. Once developed wounds are characterized according to the size, depth, edge characteristics, and wound exudate. Wound exudate components include water, fibrin, glucose, platelets, micro-organisms, cellular debris, and more. Wound exudates are classified into serous wounds which have a thin, clear, and watery exude, serosanguinous which appear watery and tinted pink, sanguineous which contains fresh blood, and purulent which appear yellow and pus-filled. Wound exudate can also

be understood by the volume of exudate produced: minimal has a dry dressing, medium has a wet dressing, and heavy has a soaked dressing.[35] Wound types can impact the rate of exudate production which can range from .17-.86 $g/cm^2/24hr$.[36]

One way to address chronic wounds and prevent acute wounds from developing into chronic wounds is negative pressure wound therapy (NPWT) (Figure 6). There are several NPWT devices on the market and most function by applying localized pressure around wounds. NPWT devices contain a pump that is connected to a canister through a tube, creating a negative environment by sucking the air out of the canister. This allows a second tube, connected to the canister and the wound site, to aspirate fluids. The second tube is also placed in a wound dressing that creates a tight seal, which is important to keep wounds warm and moist and decrease bacterial penetration. Localized pressure caused by NPWT has been reported to stretch and activate cells to increase angiogenesis and cell division, while also decreasing necrotic tissue and excess fluid, which often contain pro-inflammatory mediators or infective agents.[37] Removal of these factors can encourage wound healing by facilitating movement from the inflammation stage to proliferation.[38] NPWT also decreases the frequency of wound dressing changes, which can decrease the risk of infection and patient discomfort.[39]

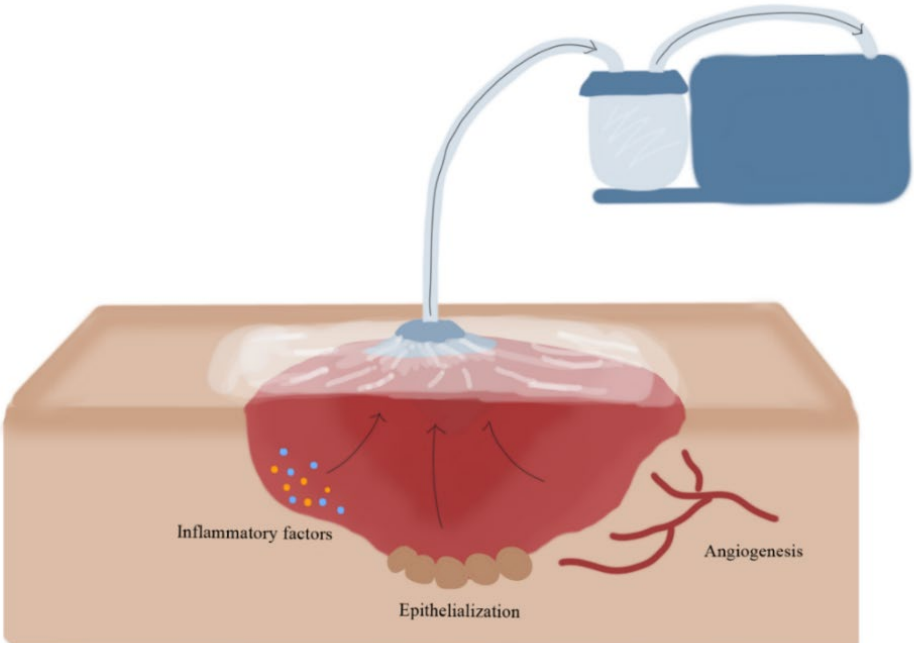

Figure 6 Placement of the negative pressure wound therapy devices and their benefits on chronic wounds. A sealed environment is necessary for appropriate aspiration and needs to cover the wound. Within the wound environment fluid aspiration and mechanical stimulation promotes healing.

Studies on NPWT have proven its effectiveness. A randomized control trial on 60 patients demonstrated improved skin graft acceptance and shorter hospital duration.[40] Other studies also reported faster healing and decreased total costs.[39,40] Scholars even suggest bringing NPWT devices home to reduce costs associated with hospitalization and to improve patient comfort.[38] Such a take-home device would be extremely beneficial in low-to-middle income countries, where access to care is limited due to costs, lack of resources, and transportation difficulties.[41] Additionally, such a take-home device could also allow more patients to be admitted and treated as it would free up beds that would otherwise be occupied for days. At the same time, however, NPWT devices and the resources that they require may make them difficult to be take-home. Costs for NPWT are especially high with individual devices costing upwards of US$ 300, and the average daily costs of renting a device around US$ 94.01.[42] Other than cost, energy resources may be limited in clinics and especially at home where inconstant electricity can make providing quality care difficult.[42]

Current take-home NPWT devices include the V.A.C.VIA™ Therapy System (Kinetic Concepts, Inc.). This disposable, .7lbs device comes with its own wound dressing and contains a 250mL canister. It works well for low exuding wounds (<80mL/day) and has an external power supply of 100-240 VAC at 50/60 Hz, but it costs US$ 595.00 for a starter kit.[43,44] Another more cost-saving, take-home, and disposable device is the PICO (Smith and Nephew Healthcare, Hull, UK). This device weighs .17 lbs and delivers a pressure of 80 mmHg for 7 days using a single battery power; however, it was developed for wounds with low to no exudate and costs about US$ 200.[45,46] One key fact to note about these devices is that they are one-time use and disposable, so costs for treating ten patients with them amount to US$ 5,950 for V.A.C.VIA™ Therapy System and US$ 2,000 for PICO. Inpatient NPWT devices, on the other hand, can cost up to US$ 25,000, and although these can be used multiple times, a new canister for each patient costs about US$ 35 and there are further costs for staying in the hospital.[45] In addition to these devices, there have been NPWT devices designed with resource-constrained settings in mind. These devices move away from typical NPWT designs that require energy. Gravity is an NPWT device that is hung on the wall and uses weight to create a constant pressure of 125mmHg. This device operates for approximately five hours before needing to be reset. Gravity is disposable and costs only US$ 7.22. The downside with this device is that it does require being hung and may be difficult to set up.[47] Another device utilizes a bellow-like mechanism that produces a negative pressure

environment when compressed. One con to this system was that training and proper dressing are critical to prevent leaks that compromise effectiveness.[48,49] These devices demonstrate that NPWT can be modified using creativity and the constraints of an environment in mind; however, instead of exploring options like the ones discussed above, which take a different perspective of NPWT devices, we wanted to focus on developing a typical NPWT device. We believe its technology is simple and reliable enough that it can be made cheaper and more accessible.

Design Documentation

The clinical need was proposed by a team of physicians and students associated with Tenwek Mission Hospital in Kenya. The team had asked for an NPWT device that can be operated as a take-home device for Tenwek Mission Hospital and eventually scaled up to be operated elsewhere. The primary communication facilitator was Aayush Setty from Brown University, who gave us access to the design parameters and resource limitations observed by the team (Table 3). The proposed solution was documented to require a pressure ranging from 40 mmHg to 200 mmHg. While this pressure can be variable, it must be constantly applied, simply controlled, and readable through a pressure gauge. Other than the pump, the canister, tubing, and dressing must be easily disposed of and replaced to account for wounds that produce a great deal of fluid. The dressing must also provide a tight seal to ensure effective aspiration and prevent external environmental factors from drawing in. Features of a resource-constrained environment also influence the design requirements. The NPWT device is preferred to be take-home and portable as it would save both patients and the hospital money and open beds up for additional patients. This suggests that the device would be required to be tamper-proof and have an alternative energy source to address the unreliable and limited access to energy and concerns with theft. The device would have to run for about 72 hours, after which the patient would need to return to the hospital to get their wound dressing changed. In addition to this, the overall initial and maintenance costs of the device must be low, and bear in mind international regulations.

Based on this information we examined different design options before selecting to move forward in one direction. For the development of the NPWT device, deliberations were to build the device from the bottom-up. This would require obtaining a vacuum pump with an easily controllable and readable pressure gauge, compressor, and fan. This device would also require a canister holder and tubing that could be easily replaced while creating a tight seal. Additionally,

adequate power source, durability, and variability in the pressure would have to be measured. For prototyping, utilizing an Arduino compatible negative pressure suction pump was considered. A benefit of this design was that there would be more control over the individual components and the size of the device, however, there would also be more room for failure with no significant cost benefits. The second option considered was repurposing an already existing device. Aspirators are often used in laboratories and homes for a variety of purposes; they can be small and affordable devices, but durability may be a concern. After researching different aspirators, we decided on Drive Heavy Duty Suction Machine by Drive Medical. Although this device may be larger than a bottom-up device, it has already existing components such as a canister holder, tubing, pressure gauge, and power cable. Its canister and tubing could be replaced by the company, and since it is an already existing device it would not have as many regulatory hurdles in Kenya where regulations allow existing devices to be repurposed for medical use. After consideration of our general requirements (Table 3), we ultimately chose to repurpose and test the aspirator.

Another important component of NPWT is developing a seal-tight environment. One way to ensure this is by customizing the tip of the tubing to be placed in the wound dressing and against the patient's skin so that it is flush and sealed. Our first design was flat, circular, and reminiscent of traditional NPWT tips; however, as we continued to innovate, we realized that this flat design would not be effective on wounds located around joints as it would limit mobility and patient comfort. We, therefore, created a tip based on band-aid designs with narrow and then wide components that can be bent. We also determined that ensuring that the tips attach tightly to the tubing is necessary through a force fit and seal as aspiration quality may be compromised. Therefore, the tip could be attached by either being placed inside the tup or over the tube end. To test the design of the tips a variety of flat versions were printed using PLA filament on Prusa i3 MK3S+ 3D printers. The tips were then printed using Flexfill 98A filament; given the flexible nature of Flexfill material, this tip would be able to bend and contort around joints and may further result in a better suction environment. While standard NPWT tips can be used, these tips were examined in further detail to understand if they may provide a more secure sealed environment for smaller wounds.

Another component of the design is the energy source, where we spent the bulk of our time researching sustainable energy options for the selected aspirator, which has the electrical requirements: AC 115V, 60 Hz, and 70 W. For the proposed NPWT device a light battery pack

will be required. A powerful battery that can run the proposed NPWT may be heavier and more expensive, so one solution is to have a battery that can be disposable battery-powered, hand-cranked-powered, or solar-powered. The first two options are feasible but were not prioritized because they may not be strong enough to power the aspirator for 72 hours and could require additional resources like money and time to crank or replace the batteries. The last option was to use a solar-powered based battery, which would provide a continuous almost hands-off energy supply. Although this would also be more costly and bulkier to carry, it would be re-usable and could save costs over time. For this reason, we selected Westinghouse's iGen200 portable power station that is compatible with a foldable solar panel.

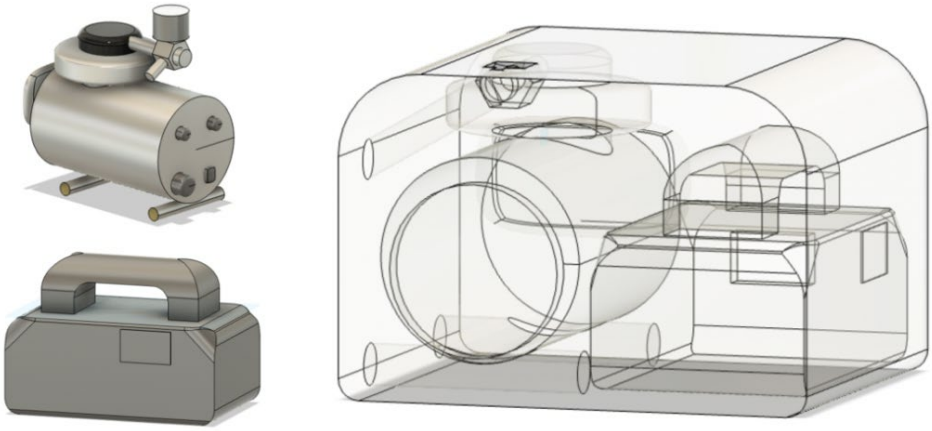

Figure 7 Design of the aspirator and battery that was used to create the carrier.

While deliberating these design considerations, it became clear that a take-home device would need a compact way to carry all components. These components are also expensive and although it would not be detrimental, the settings of the aspirator should not be changed. Therefore, the carrier should be semi-tamper-proof. The power switch, tubing, and canister should be easily accessible to operate the proposed NPWT and replace parts if necessary; however, the battery and pressure gauge should only be accessible by the healthcare provider. Making the entire device completely tamper-proof would reduce the risk of theft but also reduce usability, thus patients will be asked to provide a refundable deposit when taking the device home. Overall, this carrier would include the aspirator, battery, and solar panel (Figure 7). It would need to be covered with foam to ensure the device does not get damaged when carried. For this reason, polyurethane foam was considered, as it can withstand the heating of the proposed NPWT device and is commonly used to provide a cushion. Based on the size and shape of the aspirator and battery, a carrier for the

device was 3D printed using PLA. For the solar panel, an external Velcro strap design was considered in case the panel is required.

Final Prototype

Figure 8 Schematic of the proposed negative pressure wound device, the Drive Heavy Duty Suction Machine from Drive Medical.[2]

The final selected aspirator is the Drive Heavy Duty Suction Machine by Drive Medical. This device consists of a canister, the main pump device, and tubing (Figure 8). The canister has an 800cc capacity, which should allow for enough fluid aspiration without the container having to be replaced often. The device also contains a knob that allows the pressure to be adjusted and read on the pressure gauge. Other features include a carry handle, a filter in case fluid is aspirated into the wrong tubing, and power cord storage. The final tip designs were selected to ensure a proper sealed environment and attachment to the tubing. The first tip consists of a flat circular design for more general wounds, the second tip consists of a bent design that allows for more movement for wounds located on joints (Figure 9). Both tips are printed using Flexfill 98A filament. The final tamper-proof carrier designs were selected to hold all the components of the device together. A CAD model of the aspirator and power bank was created using Autodesk Fusion 360 (Figure 10), then they were negatively extruded from a box.

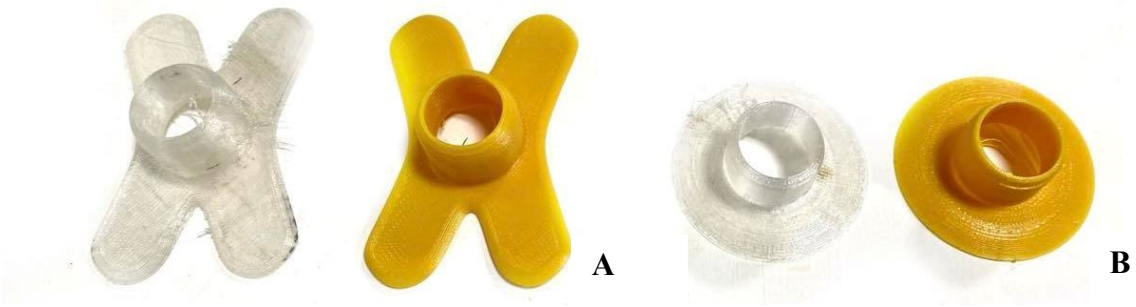

Figure 9 Final tip designs. (A) Design for wounds located on joints made from clear Flexfill 98A and yellow PLA (B) Circular designs for wounds located on flat surfaces made from clear Flexfill 98A and yellow PLA.

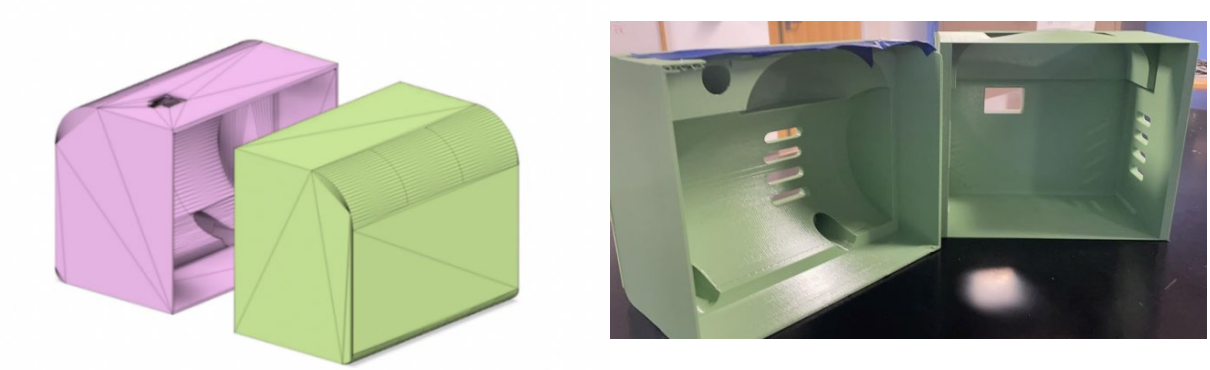

Figure 10 3D printed carrier (A) Design for fitting the carrier together (B) Printed carrier slots to allow the tubing, ventilation, and canister to sit within.

Functionality

Table 3 Design requirements, testable variables, and verifications used to determine the outcomes of the proposed NPWT device. These requirements were based on observations by the student and physician team associated with Tenwek Hospital in Kenya.

Design Requirement	Testable variable	Verification
Constant pressure ranging from 40mmHg to 200mmHg and durable	Device, Tips	Run device for 24h
Tips should create an appropriate negative pressure environment	Tips	Run device on silicone model
Canister, tubing, and dressing must be easily replaced	Device	Research
Device should be less than 20 pounds and portable	Device, power sources	Weigh device
Device should have an alternative energy source	Power source	Run device on battery

The purpose of initial testing was to determine whether the proposed NPWT device would have appropriate functionality and durability to fulfill design requirement one. This test was also developed to assist in "failing fast" and to confirm whether we should continue with the proposed NPWT. A crude watermelon model was selected because of its low cost, porous and soft flesh that mimics the interior of a wound environment, and natural fluids that mimic fluids in a wound (Figure 11). Seram wrap and tape were used to imitate the wound dressing and ensure a negative pressure environment. For this experiment, the unmodified proposed NPWT tube was sealed against the watermelon model. The proposed NPWT was switched on and adjusted to run at 125mmHg for 10 minutes. We observed the device aspirate fluids at low quantities without outwardly damaging the flesh of the watermelon. For the second test, the watermelon model was crushed to create a section containing watermelon fragments and fluid. The proposed NPWT device was adjusted to run at 125 mmHg, but within 1 minute and 23 seconds the device had aspirated the fragments and fluids. This suggests that the NPWT device may aspirate free tissue fragments in a human wound model while slowly aspirating contained fluids. Additionally, while testing and administering this experiment, it was noted that the proposed NPWT did not function if the Seram wrap and tape did not effectively create a tight seal. This confirms the importance of an invulnerable seal for a negative pressure wound environment and the need for design requirement two. It was also apparent that the pressure levels could not be set until the device was turned on and the tube was placed in the wound model. This suggests that the pressure would have to be adjusted each time it is placed in a new wound or the wound is rebandaged; however, once easily adjusted the pressure remained constant. Further testing confirmed the consistency of the pressure and the durability of the device. For this experiment, the device was run at 125 mmHg for 24 hours, with it being checked at 2 hours, 8 hours, and then 24 hours. The device was able to run for 24 hours at a constant pressure Although this experiment was not

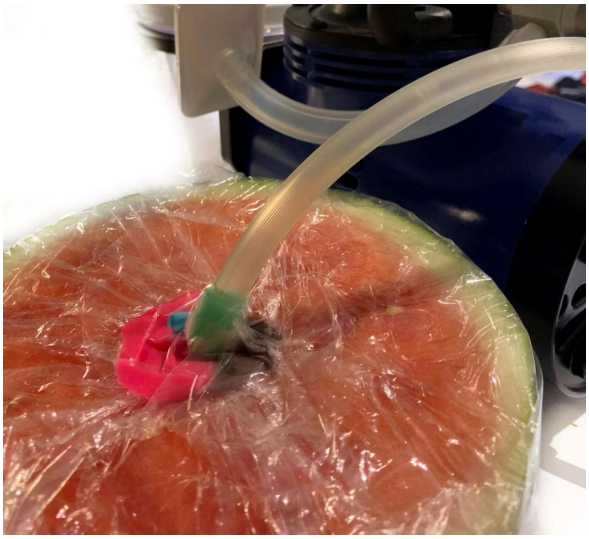

Figure 11 Watermelon model and aspirator tube sealed in using putty

repeated, the device has run for approximately 115 hours to complete additional testing, suggesting the device can be used for multiple patients.

Figure 12 Silicone sponge model that was soaked in water. The tip was attached to the model using Seram to ensure a tight seal. This was further confirmed by the compression of the entire model due to the negative pressure environment.

For more in-depth testing of design requirement one and design requirement two a silicone model with a sponge interior was chosen (Figure 12. The purpose of this test was to provide a quantitative understanding of the proposed NWPT's ability and to understand the functionality of different tips. This model was chosen as the exterior silicone, which is often used to practice suturing and punctures better mimicked the feel and grip of skin than the watermelon model. The sponge's porous texture mimicked the inner wound environment and could hold onto fluid as a wound may. The dimensions of this model were 4.9 x 3.6 x 1.2 inches for the sponge, and 4.9 x 3.6 x .31 inches for the silicone skin top, which is adequate to represent the range in size and depth in wounds. On average this model held 20g of water which would be equivalent to a small, serous wound exudate. For this experiment, the weight of the wound model was measured before the model was thoroughly soaked in water and weighed again. The proposed NPWT with varying tips was placed on the wound model and was run for 5h at 125mmHg. The final weight was measured after 24 hours and the wound model was wrapped in Seram wrap to create a sealed environment but to also prevent solution loss through evaporation. In addition to the fabricated tips, a standard NPWT tip was purchased and tested as a control. Overall, test results revealed that the proposed NPWT and tips were able to aspirate majority of the fluid present in the wound model, especially when compared to the standard of care. This suggests that the aspirator would be effective for small wounds and potentially larger ones, since the fluid from this small and low serous wound

exudate model was almost completely aspirated in 5 hours; however, more testing and a larger sample size are needed to confirm this and demonstrate significance between the bent tip and standard of care.

Table 4 Test results of a silicone sponge model that was soaked in water after 5 hours.

Tip Type	Starting Weight(g)	Weight Soaked (g)	Ending Weight (g)	Percent Difference (%)
PLA Circular	132	150	136	97%
Flex Circular	131	153	131	100%
PLA Circular	131	152	133	98.5%
Flex Bent	131	153	132	99.2%
Standard of Care	131	151	131	100%

Design requirements three, four, and five were confirmed during material selection. The proposed NPWT contains an easily replaceable tube and canister that can be ordered from Drive Medical directly or purchased in bulk elsewhere. Only tubing connected to the negative pressure pump has to be removed, allowing the canister and the rest of the tubing to be released and disposed of. The pump may then be disinfected using an alcohol wipe if necessary. In terms of design requirement three, the weight of the proposed NPWT is 12.1 lbs and the weight of the battery is 3.8 lbs, resulting in a total weight of 15.9 lbs. With a solar panel, the total weight can increase from 10 to 15 lbs, increasing the total weight to 25.9-30.9lbs. Although this is over initial weight considerations, the tamper-proof carrier works to make the device more portable. For design requirement five, the electrical requirements of the aspirator are AC 115V, 60 Hz, and 70 W which are compliant with the electrical outputs in the United States. Thus, for this initial testing, Westinghouse's iGen200 portable power station was utilized, which has 120 V and has the dimensions of 8 x 3.6 x 7.36 inches. The aspirator ran at 125 mmHg for 3 hours using this power source; however, with the solar power attached it would be able to provide continuous power. Before purchasing a more powerful battery, however, we consulted with Aayush and determined such a battery could be purchased in Kenya.

Design Considerations

Intellectual Property

To determine existing patents and devices in this field, the terms "Negative pressure wound therapy, portable, and alternative energy" were searched on Google Patent, United States Patent, and Trademark Office's (USPTO) website, and Google. There are many existing patents on portable negative pressure wound therapy devices as well as wound dressing technology. There is an existing patent for a wound therapy system that relies on subatomic pressure rather than an external energy source. Though this could be useful in a low-resource setting, it would not be able to maintain a specific and reliable pressure on the wound. [50] However, a portable device that relies on alternative energy that can be used in a low resource setting is a novel direction.

Reimbursement

The negative pressure wound therapy device in consideration is for use in low-income settings and is intended for countries outside of America. Thus, the device would not be reimbursable by Medicare or Medicaid. The device would be purchased by governments, public health entities, hospitals, or foreign aid organizations. There are no reimbursement avenues within America for funding overseas device costs. Thus, the cost of manufacturing and product development would mostly need to be reimbursed through fundraisers, NGO donations, or potentially government for the country the device is implemented in.

Estimated Manufacturing Costs

Materials	Price per unit	Comment
Enclose Box	US$ 75	3D printed PETG and polyurethane foam for the enclosure of the entire device. It could change from 3D printing to alternate methods for the PETG manufacturing process. This material was chosen for its lightweight property with a high melting temperature
Aspirator	$190	This is the central component of the device which is the vacuum source.
Accessories	$20	There is a cost of parts including the medical tubing, canister, and aspirator tips which would need to be replaced for sanitary reasons.
Power bank	$175	The power source for the device
Total	$460	

The total cost of the device ends up being $460 for each patient which is high. There would also be an additional cost for the solar power device which would be stored at the hospital to charge the power banks. Though the costs add up to be high, they would be a capital investment and worth the cost over time since the device is reusable over multiple patients and years. Only the accessories would need to be replaced, which would end up being around $20 per patient. Thus costs for ten patients would be $660 if the device is used as is without cost reductions due to bulk purchasing. Even with this model, over time, the profit margin of the device would be high enough and sustainable for a nonprofit company.

Market Analysis

Negative pressure wound therapy has a huge global market projected to reach $3.2B by 2025. This is in part due to increasing evidence supporting the use of negative pressure wound therapy on chronic, surgical, and acute wounds. In America specifically, there are increasing government initiatives to prevent supplemental security income programs as well as an increased rate of cesarean section procedures, making North America the highest NPWT consumers. However, many key market players are expected to become more involved including the UK, Sweden, Germany, Switzerland, and China. In 2019, the use of NPWT devices in-home care accounted for the largest portion of the market. There is an even bigger market for our specific product as there is an increasing demand for alternative energy technologies and affordable technologies for use in developing countries. 2% of the North American population are affected by chronic wounds and 1-2% are in developed countries. Though there are limited statistics on that developing countries, chronic wounds are a much more prevalent problem in developing countries since most of the wounds, like diabetic ulcers, vascular ulcers, and pressure ulcers, result from infection. The COVID-19 outbreak has negatively impacted the market due to limited healthcare providers, minimal staffing, factory shutdowns, and resources. But COVID-19 is expected to improve in the next couple of years, and with it, the wound therapy market will be on the rise again as the consequences are life-threatening. This business would follow a capital investment model which has value for low-resource areas that cannot make repeated expensive purchases. The primary stakeholders involved are the physicians involved in the project, my partner, and me. The device would benefit most from being sold to a nonprofit organization for distribution. Overall, our device meets most of the primary stakeholder expectations as it fulfills all of the requirements

requested except the cost. But that high cost is offset by the fact that most of the device is reusable across multiple patients.

Discussion

Negative pressure wound therapy (NPWT) is an effective way to treat chronic wounds to increase angiogenesis and cell division, decrease necrotic tissue and excess fluid, and generally promote wound healing. The device in question demonstrates that a portable alternative energy NPWT device can easily be built using a medical aspirator. This makes NPWT more accessible to patients with varying incomes, resources, and settings.

One of the primary ways that this take-home device is designed for resource-constrained settings is the power source. Medical aspirators are high-power devices and are unable to handle different voltages. The prototype developed is suitable if the device is to be utilized in a low-resource setting in the USA and other countries with AC 120V outlets. However, Kenya uses a G plug that operates on a 240V supply voltage and 50Hz which means modifications need to be made to the device prototype to ensure compatibility. There are various approaches to the problems that dictate the appropriate modifications to be made. The device can be manufactured using devices from America and explicitly powered through an alternative power source such as a solar panel. Since the medical aspirator used is compatible with the power bank and the solar panel, no modifications need to be made. There are a few more solutions if the device is built using devices from America. Another approach is using a multi-voltage power supply that can take an input of AC 100V-240V, but this solution is unideal since it would add unnecessary cost and weight to the device. It is also possible to switch a motor that has two 120V windings between being wired for 240V or 120V to power the device. A less ideal solution that would be immediately compatible with the existing prototype is to use a step-down voltage converter. This solution could potentially result in 10-30% efficiency loss which is detrimental for such a high-power device. Alternatively, the device design can be maintained but made by repurposing medical aspirators from Kenya or other countries that utilize 240V which can then be powered through various 240V-compatible power supplies. This approach is the most straightforward for optimizing efficiency, minimizing weight, and best for powering through various options including solar panels and standard residential outlets.

Limited preliminary testing was performed on the device due to time constraints. Some modifications can be made for future testing including changing wound fluid, and wound model

wound filler. A silicone sponge model with water was utilized for preliminary testing purposes. However, this method has shortcomings in accurately representing the varying viscosity of different types of wound fluid. Artificial wound fluid exudate can be used in future testing, either purchased commercially or prepared by combining 5.844g sodium chloride, 3.360g sodium hydrogen carbonate, 0.298g potassium chloride, 0.277g calcium chloride, 33.00g bovine albumin, and 1000mL deionized water. The tests were performed on a silicone model with a sponge interior, but future tests can be performed on multilayered artificial skin with a fatty and muscle layer underneath. The curved aspirator tip design can be tested on skin models that emulate specific non-flat body parts. The tests can be performed with fine-tuned prototype designs that are professionally manufactured with ideal materials. The aspirator tips were 3D printed using FlexFill on Prusa printers. The tips are expected to be more effective if manufactured through highly flexible synthetic materials such as PVC plastic or neoprene, materials that are conventionally used for suction cups. The mechanical strength and flexibility of those materials will reliably create a tighter seal through the tip design. The device casing, which was 3D printed using PETG, would also be manufactured for quick and reliable parts that can be shipped off to be assembled.

Chapter 4: Conclusion

For the first year of our thesis, we worked with NaloxBox to address the opioid crisis. While GE developed an SMS and QR-based tracking system, we developed a voice prompt system to encourage bystander intervention and proper naloxone administration. To verify the voice prompts we conducted a survey (n=102) for user feedback and determined that the voice prompts were not vital, but may be beneficial. For the second year of our thesis, we worked to develop an NPWT device for Tenwek Hospital in Kenya. After testing the proposed NPWT device and examining various tip options, we ultimately concluded that aspirators could be repurposed as NPWT devices.

The design projects we pursued were valuable in teaching us about the many steps involved in product development. We learned to prioritize making a product that meets the actual needs of the user and to specifically think about the challenges in resource-constrained settings. In addition to furthering our skills in engineering methods pertinent to our projects, such as CAD, 3D printing, and Arduino hardware and software, we also learned public and global health principles that are not usually emphasized in the engineering curriculum. We hope to apply the skills and broader perspective we have developed during the span of these two projects to focus our future work on user-centered innovation and frugal technologies.

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