Orbis

Opioid Reporting and Biosensor Integration System

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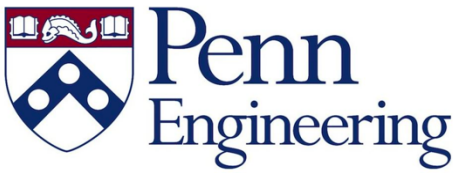

Abstract

Orbis addresses the opioid epidemic by aiding clinicians with the diagnosis and treatment of opioid use disorder (OUD), which affects over 2 million Americans. Currently, OUD is diagnosed using the Clinical Opiate Withdrawal Scale (COWS) score, which integrates physiological measurements of 11 symptoms to determine withdrawal severity and appropriate treatment. The COWS score is subjective, time-consuming to assess, and its misuse is potentially dangerous. Orbis automates COWS score data collection and calculation through continuous measurements of real-time physiological data (tremor intensity, heart rate, and galvanic skin conductance or GSC). In its current form, Orbis is a lightweight silicone wearable encasing three biosensors. Raw data is processed in MATLAB with custom algorithms to output a COWS score, which is then sent to a Firebase database. This score is accessible through an accompanying mobile application. Individual biosensor and overall COWS score accuracy were evaluated with various studies on healthy volunteers. Three sets of trials were performed to assess the accuracy of Orbis in measuring heart rate, severity of wrist tremors, and change in GSC. Results show Orbis can sufficiently measure heart rate within five beats per minute and distinguish between baseline and various levels of tremor and anxiety. In addition, Orbis demonstrated comparable accuracy to a clinician in generating a COWS score for tremor, heart rate, and anxiety. Further testing is required to evaluate the efficacy of Orbis in a clinical setting on OUD patients. Next steps for implementation include printed circuit board manufacturing, establishing wireless connectivity, and implementing software alert functionality.

Introduction

The opioid epidemic is the deadliest drug crisis in American history. In 2016, 12 million Americans misused prescription opioids, heroin, and fentanyl, 2.5 million had opioid use disorder (OUD),[1] and more than 42,000 Americans died from an opioid overdose.[2] In addition to lives lost, the opioid crisis has led to increased incarceration, unemployment, and crime, resulting in an estimated $504 billion in costs in 2015.[3] OUD is defined as clinically significant opioid-induced impairment and distress, increased tolerance to opioids, and withdrawal symptoms when use is abruptly discontinued.

Amid a steadily rising number of OUD-affected individuals, healthcare providers lack the capacity to provide evidence-based opioid addiction treatment in the form of medication-assisted treatment (MAT). MAT with buprenorphine, methadone, naltrexone, or a combination of these, is currently the most effective treatment method for OUD. Typically, these medications are combined with behavioral counseling, which has been found to significantly decrease opioid use, overdose deaths, and criminal activity. In a study conducted where buprenorphine was made available in the city of Baltimore, heroin overdose deaths decreased by 37%.[4] Additionally, patients treated with MAT are more likely to remain in therapy and continue treatment. However, less than half of privately-funded substance-use treatment programs offer MAT, and only one-third of the patients with opioid dependence in these programs receive MAT.[5] Despite pressing demand, MAT remains in short supply for several reasons. First, clinicians are required to complete additional training to prescribe certain anti-opioid therapeutics to patients. Second, the process of diagnosing withdrawal, a step required in the administration of anti-opioids, is time-consuming and subjective in nature. Third, clinicians and patients are afraid of inducing and

experiencing precipitated withdrawal, a painful and dangerous condition resulting from the rapid onset of all withdrawal symptoms following premature dosing of an anti-opioid therapeutic.

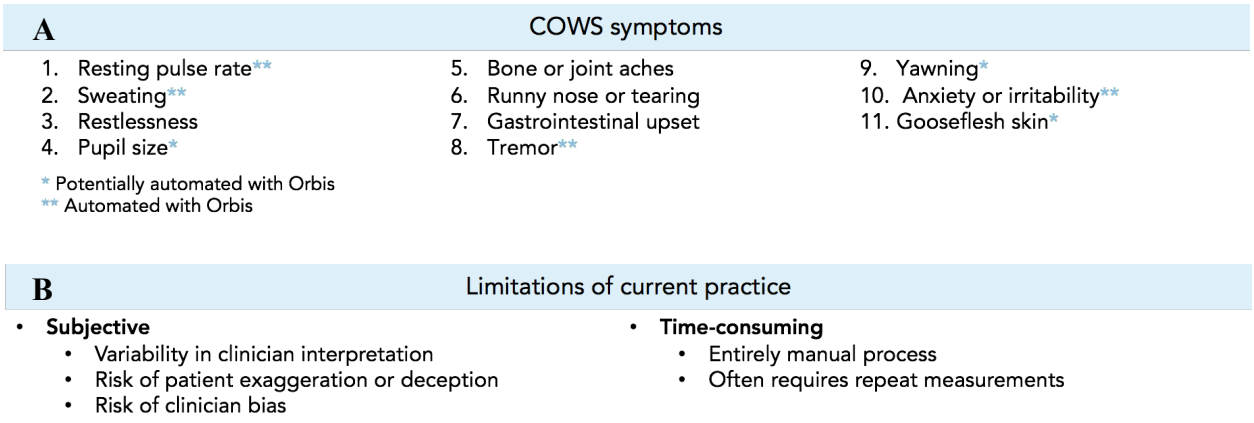

Figure 1. A) Summary of the 11 COWS symptoms and their potential to be automated with Orbis. **B)** Limitations of the current COWS treatment paradigm.

Currently, opioid withdrawal is manually diagnosed using the Clinical Opiate Withdrawal Scale (COWS score), which sums the subjective measurements of 11 withdrawal symptoms (resting pulse rate, sweating, restlessness, pupil size, bone or joint aches, runny nose or tearing, gastrointestinal upset, tremor, yawning, anxiety or irritability, and gooseflesh skin) and ascribes a numerical score to the severity of withdrawal **(Fig 1)**. The COWS score helps the clinician determine if the patient is far enough in withdrawal to receive an anti-opioid medication while avoiding precipitated withdrawal. In a clinical setting, the COWS score must be taken repeatedly until it is high enough to administer an anti-opioid, a requirement that is both labor-intensive and time-consuming. Furthermore, due to the subjective nature of the COWS score, assessments may vary widely from clinician to clinician, and may be influenced by the patient.

The potential impact of Orbis is far-reaching: opioid use disorder affects almost 30 million people worldwide.[1] Orbis will decrease the burden on the health care system by eliminating inefficiencies in the current MAT paradigm and facilitating the patient journey to sobriety. Reduced risk of precipitated withdrawal, lowered risk of relapse, and more accurate dosing of anti-

opioid therapeutics will lead to better patient outcomes. Additionally, Orbis will reduce the economic costs associated with the administration of anti-opioid therapeutics by freeing up capacity, increasing throughput of patients in the hospital system, and lowering hospital readmission. Orbis would have the societal impact of reduced crime and recidivism, decreased familial burden, and increased economic activity due to the return of formerly addicted individuals to the workforce.

Objectives and Approach Overview

Orbis, the Opioid Reporting and Biosensor Integration System, is composed of a wrist-based wearable device and an accompanying mobile application. The wearable contains three biosensors (accelerometer, LED-based pulse sensor, and galvanic skin response sensor) which measure four physiological symptoms of opioid withdrawal: tremor, heart rate, sweating, and anxiety. Galvanic skin response was used to determine both sweating and anxiety, as both factor share a common physiological manifestation. The raw analog voltage signals from the sensors are read from Arduino into MATLAB, where the data is filtered, processed, and translated to a COWS score. During data collection, the COWS score is periodically and automatically "pushed" to an online database, where it is retrieved by a clinician using the mobile application. The user (a clinician performing a COWS evaluation) then completes the remaining elements of the COWS score in the mobile application, and a final COWS score is output. In the ideal use case, the patient's COWS score would be continuously monitored during the "waiting" period, allowing a clinician to see other patients instead of repeatedly assessing the same patient's withdrawal. The clinician would be alerted when the four "automated" COWS parameters (tremor, anxiety, sweating, and heart rate) reach a threshold that indicate a patient being monitored is experiencing

severe withdrawal, and only then would they complete the remainder of the COWS assessment **(Fig 2)**.

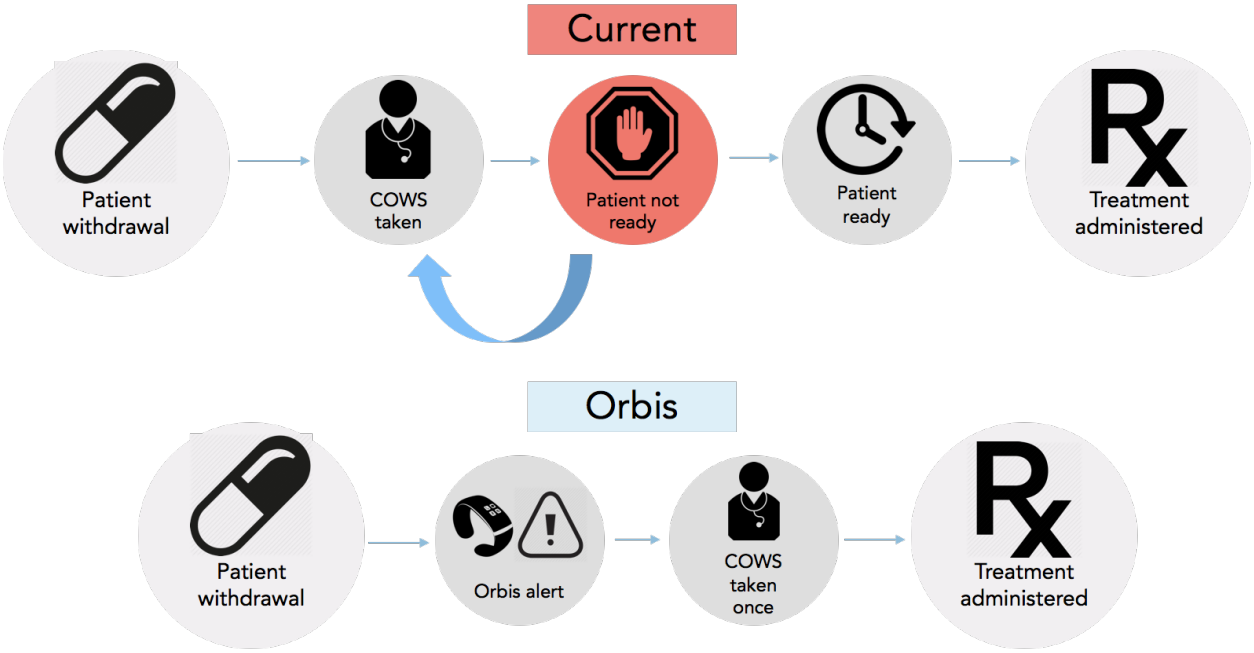

Figure 2. Workflow of diagnosing withdrawal using current methods versus Orbis.

To meet the needs of our stakeholders and address the identified problem, we established three primary design goals. First, to create time savings for clinicians, enabling them to treat more patients and increasing the availability of MAT via increased provider throughput. Orbis accomplishes this by eliminating the need for repeated COWS assessments on a given patient. Based on pooled results of stakeholder surveys, this can result in time savings of up to 65 minutes per patient, eventually leading to lower resource costs. Second, Orbis improves patient outcomes by objectively monitoring the COWS score, decreasing subjective bias and clinician-to-clinician variability, and increasing the accuracy of withdrawal diagnosis and treatment. We hypothesize that proper use of Orbis would lead to decreased incidence of precipitated withdrawal and faster time to treatment with MAT. Third, Orbis will reduce the societal burden of the opioid epidemic

by reducing relapse rates and criminal activity, and facilitating the patient journey to sobriety, allowing former OUD patients to re-enter the workforce and re-integrate into society.

Currently, there are no objective technology-based solutions for opioid withdrawal diagnosis. Orbis is innovative in that it is the first solution to (1) objectively and continuously monitor the symptoms of opioid withdrawal using biosensors, and (2) process and interpret biosensor data to output a clinically meaningful and actionable score. Furthermore, Orbis is tailored to a clinical setting, providing the most relevant physiological data to clinicians in a digestible format that fitness trackers and research-grade devices cannot replicate.

Specifications, Design Goals, and Constraints

The technology-enabled solution for OUD diagnosis and treatment needs to be accurate, user-friendly, and practical for inpatient use in order to reduce the likelihood of precipitated withdrawal and decrease the time to treatment with MAT. Design specifications were grouped into three categories: software, hardware, and clinical viability (**Table 1**). Hardware specifications focused on portability and durability, which are critical qualities for a medical device used in a clinical setting. Software specifications targeted high-speed data updates and application usability, necessary for physician adoption and accrual of time savings.

Parameter	**Value/Design Description**
COWS Score Accuracy	± 2 scaled points (out of 48)
Portability	Less than 60g
Application features & UI	User prompting using logic tree, calculation based on sensor data, and freeform text option
Durability	Withstand constant use/turnover (inpatient use case)
Wireless Connectivity	Real-time updating; <1-minute sync time

Table 1. Key design specifications for Orbis.

The most important specification was overall COWS score accuracy, given its centricity to Orbis's clinical viability and value proposition. This parameter encompasses the accuracy of measurements from all three biosensors used to calculate the COWS score. An accuracy specification of ± 2 scaled COWS points relative to a trained clinician was chosen because the COWS scale is out of 48 points; therefore, 2 points represent a 5% error. A 2-point difference in the COWS score does not change treatment recommendations drastically in the majority of cases. This specification was tested with trials involving healthy volunteers.

As the device is meant to be worn by patients in an inpatient setting, the wearable was specified to mimic a compact wristwatch. 60g, or approximately 2oz, was chosen as a key specification to ensure patient comfort. In addition, the range of weights of wristwatch wearables available for purchase was considered in determining the final value of this specification. For context, the Fitbit weighs 22g and the largest Apple watch weighs 128g.

The user interface (UI) was designed to help clinicians use data collected from the wearable in combination with manual inputs of the remaining COWS score factors. Therefore, full step-by-step COWS score prompting (with auto-fill for measured physiological parameters) and calculation of the overall COWS score was integrated into the application. The UI was designed to balance functionality with simplicity; a limited number of features were provided to prevent complexity and increase ease-of-use. In regards to durability, Orbis was built to withstand normal daily "wear and tear," including scratches, bumps, and drops. Ultimately, the wearable was designed for repeated use among subjects during benchtop testing. Lastly, backend algorithms were built to enable <1 minute sync-time among MATLAB, the database, and the mobile application.

Three specifications, battery life, temperature sensor accuracy, and FDA Device Class were removed in the second semester, as the final device did not possess an external battery or temperature sensor. Since the device was built with a focus on accuracy rather than wireless capability, the specification for a battery was removed. FDA Device Class was also removed because the device did not reach the FDA approval process.

The device was designed with several key constraints in mind. Economic constraints included the limited budgets of hospitals and pain clinics. Additionally, government funding of opioid addiction research and management is limited by politics and partisan budgeting. The current administration has not substantially increased the funding offered to aid the opioid epidemic and has not classified the epidemic as a national emergency.[6] Private hospitals have their own funding mechanisms, which allow them to serve the crisis better. However, they too must allocate finite resources and thus do not have unlimited capital to devote to tackling opioid addiction. Furthermore, there are few physicians interested in offering the appropriate treatment because physicians are only allowed to prescribe limited amounts of MAT and must complete an 8 hour training prior to prescribing.

A major societal constraint to addressing the opioid crisis is stigma surrounding addiction. Individuals are unlikely to seek help or treatment until the disorder has progressed to the point where it interferes with activities of daily life such as work or family interaction, causes severe physical discomfort during withdrawal, and/or motivates irrational and extreme actions to obtain drugs. Society has historically looked down upon addiction as a weak individual's affliction, and only recently has medical research begun to sway opinion towards classification of addiction as a disease. Unfortunately, this stigma is likely to change more slowly in the demographics most commonly affected by opioid use disorder. Orbis was designed to help OUD patients, providers,

and caregivers realize the importance and effectiveness of medication-assisted treatment early in disease progression.

Most ethical considerations in the design of Orbis relate to privacy in patient monitoring. Measures must be taken to ensure patient data is confidential and that physicians are appropriately using the device to help patients access MAT. Health and safety was considered when designing an electronic device that was intended to be placed on patients. Faulty electronics have small, but still relevant, potential to harm patients. This was also considered in the manufacturability constraints, thought they were not major inputs to the design of a proof-of-concept prototype. Environmental and sustainability considerations were not assessed for the purposes of this project.

FDA guidelines for medical devices will have a major impact on the device beyond the prototyping phase. Orbis will need to prove safety and effectiveness in addressing its intended use, helping patients with OUD access treatment through the automation of the COWS score. 21 Code of Federal Regulations (CFR) 800 identifies all medical devices which have been classified into three categories: Class I, II, and III. Orbis would likely fall into Class I or II, which are categorized as generally low-risk devices with a long clinical history of safe and effective use, and more complex devices that must be equivalent to currently marketed device with safety and effectiveness based on equivalence and/or compliance with technical standards, respectively.

Design and Testing

Design Process

The design process began with envisioning the solution: specifically, which parameters of the COWS were best suited for quantification and automated collection. Out of the 11 COWS parameters, heart rate, anxiety, sweating, and tremor were chosen as the most suitable for a proof-

of-concept prototype. Heart rate is easily measured using off-the-shelf sensors, easily quantified and interpreted in beats per minute (BPM), and is assigned a COWS score based on raw numerical data. Tremor, while not as readily quantified as heart rate, can be measured using an inexpensive, easy-to-use 3-axis accelerometer, and is perhaps not as easily visible to a clinician. Anxiety and sweating can be parameterized via galvanic skin conductance (GSC), or the ability of the skin to conduct electric current, which can be read through a voltage divider circuit with electrodes. Other COWS symptoms, such as pupil size or gastrointestinal upset, would be more difficult to quantify and can be easily accessed by a clinician's eye in a matter of seconds.

After deciding which symptoms to measure, the appropriate biosensors were purchased, along with an Arduino microcontroller to read in data from each individual biosensor and pass the signals to a computer via USB for data collection and analysis. The three biosensors used in the final design were a Grove - GSR_Sensor V1.0, Pulse Sensor Amped, and ADXL335 tri-axial accelerometer. Initially, to test the output and accuracy of each sensor, sensors were powered and wired separately from each other, and analog input was wired to an Arduino Uno for collection on a computer (**Fig 3A**). Data transfer from the Arduino Uno to MATLAB, the chosen software for signal processing, was complicated by two major challenges: reading data from Arduino into MATLAB (via a virtual "handshake") and converting raw analog values into voltage. Due to the lack of documentation of the GSR sensor, an equation converting raw analog signal to GSR was derived based on a simple voltage divider circuit. Once all three biosensors were transferring accurate data to MATLAB, the design focus shifted to signal processing, COWS score mapping, and accuracy testing, which are discussed in the following section.

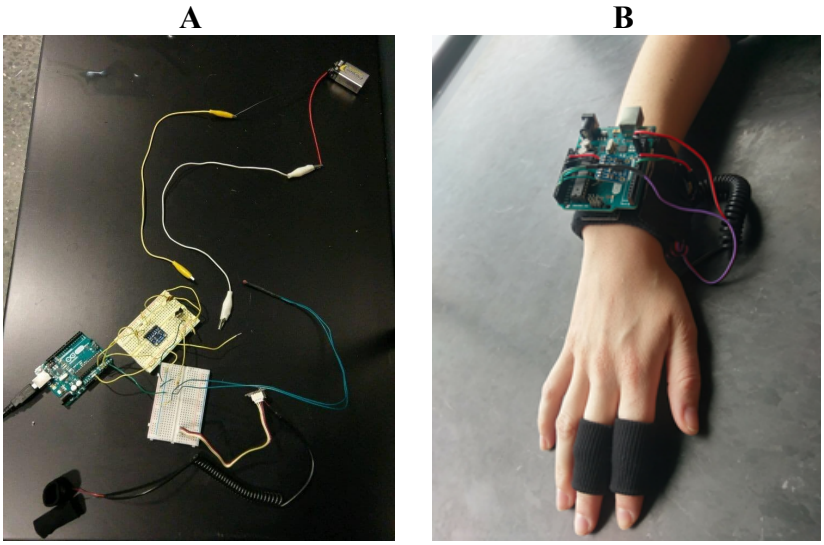

Figure 3. (**A**) Preliminary and (**B**) Version 1.3 Orbis prototypes. In V1.3, the user wears the Arduino mega and attached accelerometer mounted on a wrist sprain support. The pulse sensor is in contact with the wrist, and the GSR electrodes with the index finger and thumb. When plugged into a computer, the Arduino USB cord runs away from the user's hand in the direction of the fingers.

Design Solutions: Software

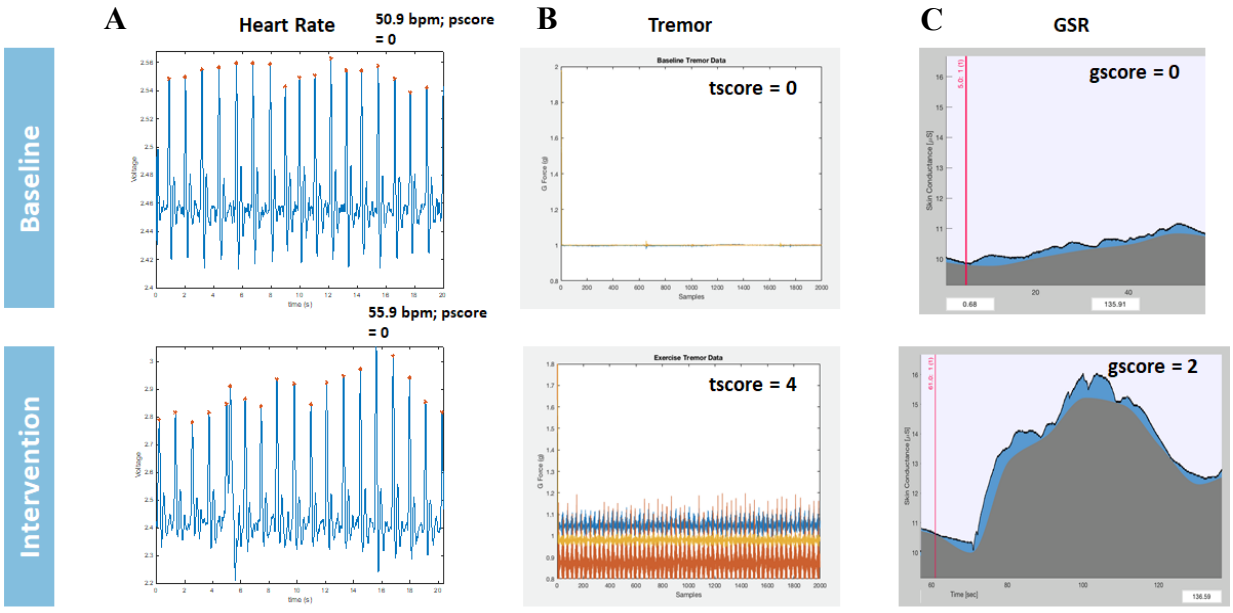

Figure 4. Visualization of biosensor data as processed in MATLAB, for both "normal" and "withdrawal" states (please see *Design Testing* section for more detail. **A)** Raw voltage signal from the pulse sensor with peaks detected by the Orbis algorithm overlaid in red, calculated heart rate in BPM, and corresponding COWS score. **B)** Raw voltage signal from each axis (blue, yellow, and orange) of the accelerometer, with corresponding tremor score. **C)** Ledalab graphs of tonic (gray) and phasic (blue) components of the filtered, decomposed GSC signal, with an anxiety-inducing "event" represented by a red line, and the corresponding anxiety and sweating score.

Heart rate was calculated from the raw pulse sensor voltage signal using a custom peak detection algorithm summarized as follows. First, the raw voltage signal is smoothed with a Savitzky-Golay FIR filter (in MATLAB, `sgolayfilt`) with polynomial order seven and frame length 21. The `findpeaks` function in MATLAB is used to find peaks in the smoothed voltage signal with a minimum peak prominence of 0.02. Following initial peak detection, several conditional statements remove false peaks based on the following criteria: the value of the current peak is less than 99% of the mean of the prior two peaks and itself, or the peak is within 15 samples of the prior peak. The peak locations are converted from samples to seconds via the sampling rate, and the number of beats per minute is calculated as the total beats over the time elapsed divided by 60 seconds per minute. A COWS score is assigned to heart rate following the COWS criteria: 0, BPM <= 80; 1, 80 < BPM <= 100; 3, 100 < BPM <= 120; and 4, 120 < BPM.

Tremor magnitude was calculated from accelerometer tri-axial (x-, y-, and z-axis) voltage data using a custom scaling and filtering algorithm. First, 200 baseline voltage values are passed with all subsequent accelerometer voltage data into a separate MATLAB script designed to compare the differences between baseline and in-treatment tremor values. After separating the baseline and subject data, each data set is filtered with a low-pass of 20 Hz and the Fourier Transform (FFT) is determined in MATLAB. The FFTs' power spectra are then calculated using the transforms, and areas under the power spectra are determined for both baseline and subject data. These areas are compared in each axis and then summed to obtain a final total difference between baseline and subject readings. This is then converted to a final COWS score based upon the following criteria: 0, power area difference (PAD) < 0.02; 1, 0.02 <= PAD < 0.25; 2, 0.25 <= PAD < 1; and 4, 1 < PAD.

Numerical values for skin resistance and conductance were calculated using an equation derived from a simple voltage divider circuit (**Eq 1**).

$$(\mathbf{1})\ R_{skin} = \frac{1}{C_{skin}} = -\frac{(R_{GSR} \times V_{GSR})}{(V_{GSR} - V_{in})}$$

Where C_{skin} is skin conductance, R_{skin} is skin resistance, R_{GSR} is the internal resistance of the sensor, V_{GSR} is the voltage read from the sensor as analog input, and V_{in} is the voltage supplied to the sensor from the GSR's internal circuit (2.5V).

The internal resistance of the GSR was measured using a digital multimeter, and for the testing-grade prototype, was 0.1 mOhms. The analog scaling factor (ASF) for all sensors was 5V/1032, given an Arduino-regulated power of 5V provided to all sensors corresponding to the maximum value of 1032 on the Analog scale.

Interpreting an individual's numeric GSR values and translating the conductance value to a COWS score required a thorough search of the literature and collecting human GSR data. A number of papers and previous experiments catalogue changes in GSR under stress-inducing situations.[7] These papers cite two types of GSR: (1) tonic, or the baseline GSR, and (2) phasic, or event-driven GSR. Tonic GSR characterizes the long-term, base level GSR of an individual. This is referred to as the Skin Conductance Level (SCL), and generally ranges between 10-50 S. The SCL is highly individual and varies due to overall physiological characteristics in the body (such as height, weight, gender). It is primarily derived from the autonomic nervous system. Phasic GSR, on the other hand, refers to short-term responses to environmental stimuli (sight, smell, sound, etc.) and is referred to as a Skin Conductance Response (SCR). SCRs only last 10-20 seconds before returning to baseline levels. For the purposes of the COWS score, we believe that tonic GSR is more informative than phasic. While phasic GSR may measure more rapid changes in skin resistance, tonic GSR reflects overall physiological condition of the patient. This is much more applicable to a patient experiencing withdrawal because anxiety levels will be elevated for a longer

period of time, exhibited in GSR data as an elevated Skin Conductance Level. Over time, tonic GSR can indicate an increase or decrease in overall anxiety and stress that phasic GSR cannot capture given its short time scale. Therefore, subject testing was designed to better understand shifts in tonic GSR over time, and ultimately derive an algorithm that tracks and scores GSR shifts of longer (minutes, rather than milliseconds) periods of time.

In our research, we discovered a MATLAB-based software called Ledalab for the visualization and analysis of skin conductance data, which uses deconvolution to separate the tonic and phasic components of GSR, and computes several useful metrics based on event-related GSR changes.[8] This software, and the metrics it outputs, has been used in numerous GSR-anxiety mapping research studies. Ledalab source code was adapted to analyze event-related changes in skin conductance in data collected using Orbis. One specific metric that we analyzed using Ledalab was integrated skin conductance response (ISCR), the area (time integral) of the phasic GSR driver within a response window of 1 - 4 seconds from the stimulus. This metric was chosen because, in subject testing, we presented a subject with an anxiety-producing stimulus at a known time point and wanted to understand the event-driven data based on the stimulus. Ledalab was used in patient testing to visualize data and as validation of our testing technique and our devices ability to detect a difference in the key numerical skin conductance metrics. We also used Ledalab's ISCR metric to determine which anxiety study intervention (asking questions with emotional content or showing disturbing video content) most elevated GSC (**Fig 5**). Based on this information, we used disturbing video content to elevate anxiety in the COWS accuracy study. However, Ledalab is not used in the final prototype to derive a COWS score. While Ledalab was helpful for visualizing and understanding GSR data, ultimately, we developed our skin conductance to anxiety to COWS mapping based on a normalized distribution of baseline and percentage change in GSC.

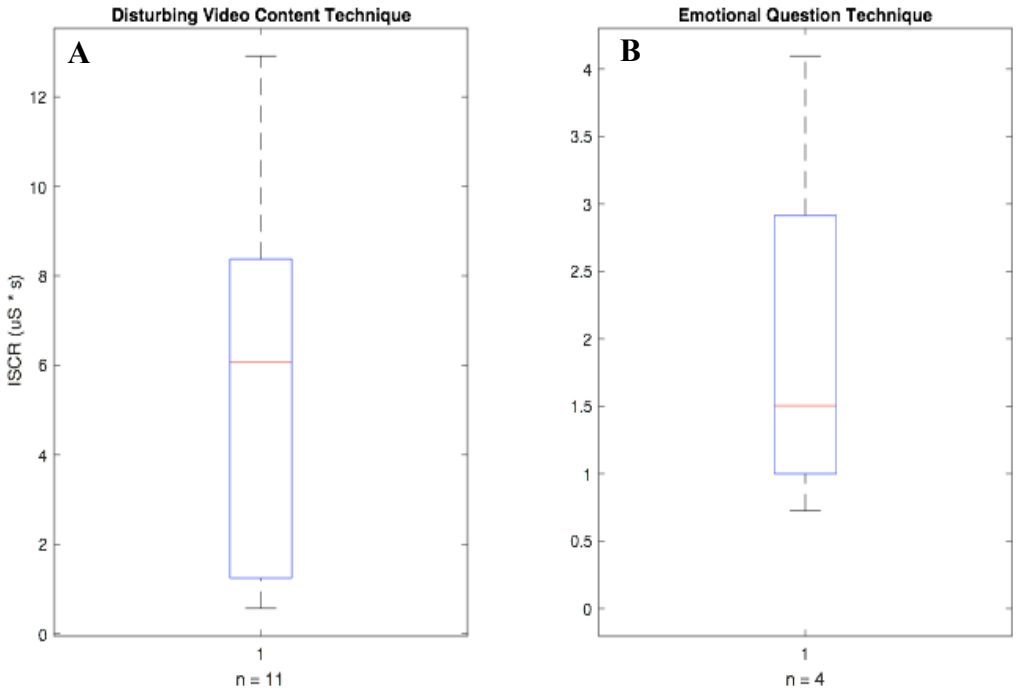

Figure 5. Boxplot of mean ISCR (integrated skin conductance response) for **(A)** Disturbing video content intervention and **(B)** emotional question technique intervention, calculated from the filtered GSC signal and Continuous Decomposition Analysis (CDA) technique in Ledalab. Because the mean and range of values for ISCR are higher, disturbing video content was used in all subsequent studies.

A MATLAB GUI was created to collect patient information (see screenshot below) prior to data collection in all subject trials. The main data collection script pulls the patient information collected, and after collection of raw data, writes an Excel file that contains patient data for that trial. The script automatically calculates sampling rate and trial duration based on the length of the loop. After each physiological data point is converted into a segment of the total COWS score, the subject's first and last name, and final scores are compiled and passed through a backend cascade to be stored in Google Firebase for use in the mobile application. The database obtains data from the MATLAB script with the use of Node.JS, a coding language specifically used for web-based communication.

First, MATLAB accumulates the relevant data and compiles a uint8 cell array of converted strings and numbers (firstname, lastname, individual COWS scores). A TCP, or private host

connection, is instantiated in MATLAB to access local web connection services. In Javascript, Node.JS simultaneously generates an open local port and listens for data on the server. Once pushed by MATLAB, data transfer is detected, and the subject data is obtained for further processing in Javascript code. The cell array is separated and rearranged for placement in Google Firebase. To account for a subject with data already populated in Firebase, code was written to perform a user check on incoming data and, if not already populated in Firebase, create a new subject.

Finally, data added to Firebase was pulled by Swift once a front-end user input the first and last name of the target subject into the mobile iOS application. Once found, the already-calculated portions of the COWS score are shown to the front-end user, and then this user is prompted to input the remaining seven COWS score segments. Backend design and code compile these seven inputs with the four scores found in Firebase to calculate a final COWS score for the user, which is displayed on the screen.

Design Solutions: Hardware

In the V1.1-1.3 prototypes, an accelerometer, pulsometer, and galvanic skin response sensor (GSR) are connected to an Arduino Mega, all attached to a wrist sprain guard. V1.2 and V1.3 prototypes have streamlined designs, each iteration working to minimize the number of exposed and/or loosely attached sensors and wires. V1.2 onward include the accelerometer placed on the Arduino to minimize detachment issues, the pulsometer placed on the inner wrist to mimic final design specifications, and the GSR attached to the side of the device and the fingers.

In the V2 prototype, the wristband and circuitry were miniaturized to achieve durability and wearability specifications as well as to test data quality of a smaller device more reflective of

a minimum viable product. In the miniaturization process, we encountered a tradeoff between data accuracy and form factor. Since signal quality was tied to the use of full size sensors, miniaturizing the sensors to fit in the wristwatch wearable with an Arduino Micro was a significant challenge. To complete wearable design, off-the-shelf sensors wires were cut and re-soldered into a more compact form, reducing the signal-to-noise ratio. Ultimately, a streamlined wearable was designed in SolidWorks, and the corresponding injection mold was 3D printed using a MakerBot (Replicator 3D printer (5th Generation) by MakerBot) (**Fig 6**). The mold was injected with silicone (Smooth-On - Dragon Skin FX Pro Trial Size Special Effects Silicone Rubber) and the miniaturized circuit was placed inside.

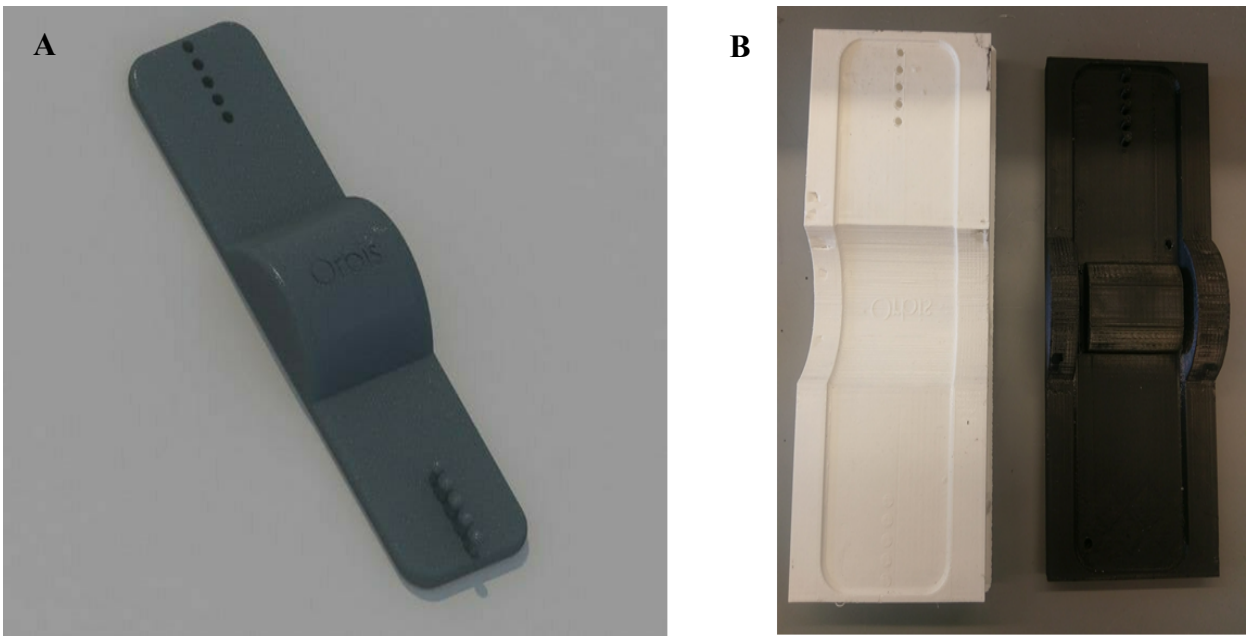

Figure 6. **A**) Solidworks design of Orbis wristband. **B**) 3D-printed molds for silicone injection molding, created by subtracting the shape of the wristband from a solid block and adding holes for injection of silicone and venting of air.

Design Testing

	Heart Rate	Tremor	Galvanic Skin Conductance
Subjects (pooled)	n = 11	n = 12	n = 32
Design	Intervention vs. Control	Intervention vs. Control	Interventions (x3) vs. Control
Intervention	Exercise	Vibrating hand-held device Mock tremor	Exercise, Interrogation, or Disturbing videos
Endpoint	Accuracy of BPM for Orbis vs. pulse-ox	Detect statistically significant change from baseline	Detect statistically significant change from baseline
Statistical Analysis	T-test	T-test	Paired t-test

Table 2. Design, intervention, endpoint, and statistical testing of studies for the evaluation of biosensor accuracy.

To maintain agility and efficiency in prototyping, we adopted a modular approach to design testing, evaluating the accuracy of each individual biosensor prior to overall COWS score accuracy. Biosensor accuracy testing was conducted on a total of 32 healthy volunteers between the ages of 18 and 22. After pooling across studies, 11 subjects were tested for heart rate, 12 subjects were tested for tremor, and 32 subjects were tested for GSC. Study design, endpoint, and statistical evaluation for each of the three parameters are summarized in **Table 2**. Interventions included exercise to elevate heart rate, a hand-held vibrating device and mock tremor / shaking to induce tremor, and disturbing video content and interrogation techniques to elevate GSC. For tremor and GSC, the primary endpoint was the ability of Orbis to detect a statistically significant change from baseline. A change from baseline is appropriate for these parameters because the COWS evaluates tremor and GSC categorically, rather than numerically. In the clinical context, anti-opioid treatment is administered based on whether or not the patient's anxiety is elevated, not his or her actual numerical skin conductance reading. Similar logic applies for tremor scoring.

Thus, the accuracy study endpoints reflect the need to translate raw numerical biosensor data into categorical assignments. Orbis' heart rate calculation was compared to a pulse oximeter output, while GSR and tremor values were compared to a resting baseline. All biosensor accuracies were evaluated with t-tests to determine if Orbis was accurate versus its comparison (**Table 2**). The difference in values between baseline and intervention conditions demonstrates the ability of Orbis to accurately detect heart rate, tremors, and GSC (**Table 3**).

	Heart Rate	Tremor	GSR
Goal	Accuracy of ORBIS BPM vs. pulse-ox	Detect change from baseline	Detect change from baseline
Result	Mean difference of pulse-ox vs. ORBIS < 5 bpm	Distinguishes between rest and tremor	Distinguishes between baseline and anxiety
P-Value	.0801	.0206	.0100
COWS Mapping	Raw BPM → 4 COWS buckets	Change in magnitude of power of Fourier transform → COWS score	Quantiles of % change in GSC from baseline → COWS score

Table 3. Results and statistical analysis of individual biosensor studies.

Tremor and GSC accuracy endpoints were met, with Orbis meaningfully distinguishing between baseline and various levels of tremor and anxiety. Accuracy of Orbis's calculated heart rate was within 5 beats per minute for most subjects, but the result was not statistically significant due to a small sample size and limitations of the peak detection algorithm at elevated heart rates. In addition to testing accuracy, the data from the individual biosensor tests, specifically the distribution of baseline GSC and typical changes in GSC upon induced anxiety (and the analogous metrics for tremor), was used to develop the algorithms for mapping biosensor data to the COWS score for these parameters.

While not statistically significant, heart rate testing and data analysis proved illuminating. The mean absolute difference between heart rate measured with Orbis and with a pulse oximeter was 6.29 beats per minute. Additionally, measurements using the control pulse-ox and Orbis were compared and relatively linear trend (**Figure 7**). This indicates that Orbis, although unsuccessful at the desired level of significance to accurately match a pulse-ox, trends towards accuracy. Further development of data collection techniques during testing, as well as refinement of the heart rate MATLAB algorithm could improve accuracy moving forward.

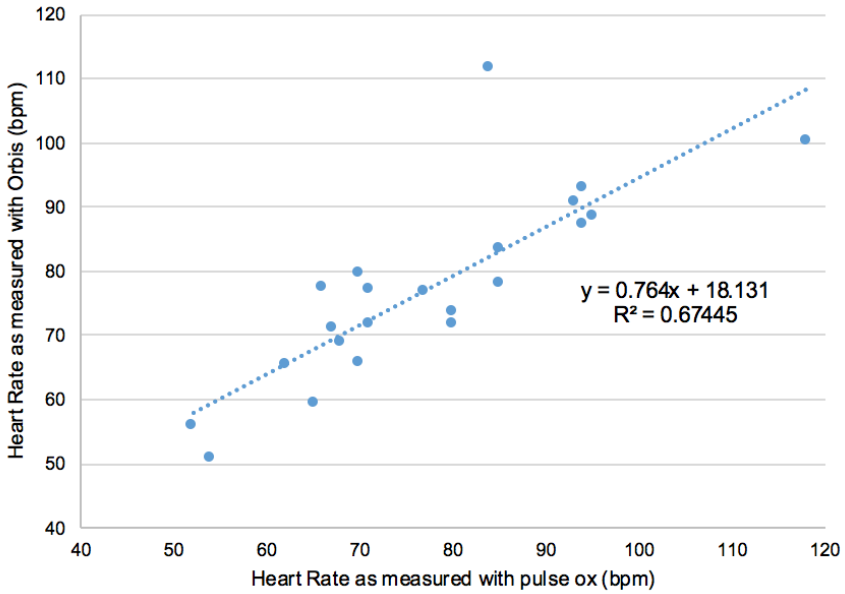

Figure 7. Scatter plot of heart rate measurements using a pulse-ox (x-axis) and Orbis (y-axis).

The difference between baseline values for x-, y-, and z-axis acceleration and parallel subject values, compared by calculating the area under the Fourier transform power spectrum of each voltage dataset, was used to assign a COWS score (0, 1, 2, or 4) for tremor. In patient testing, baseline data was accumulated over the span of three minutes and a "rest baseline" for power area on each axis, used as the benchmark for COWS score determination, was set as: 1.62 (x-axis); 1.81 (y-axis); 1.83 (z-axis). The Fourier transform for each subject retained a consistent circular shape due to the continued oscillatory experienced by the accelerometer during tremor (**Figure 8)**. The

data could be converted to a polar orientation and made linear, although unnecessary given the power function does not change based on coordinate system. Transforms were then converted to power spectra, consistently characterized by greater power at lower frequencies (**Figure 8)**.

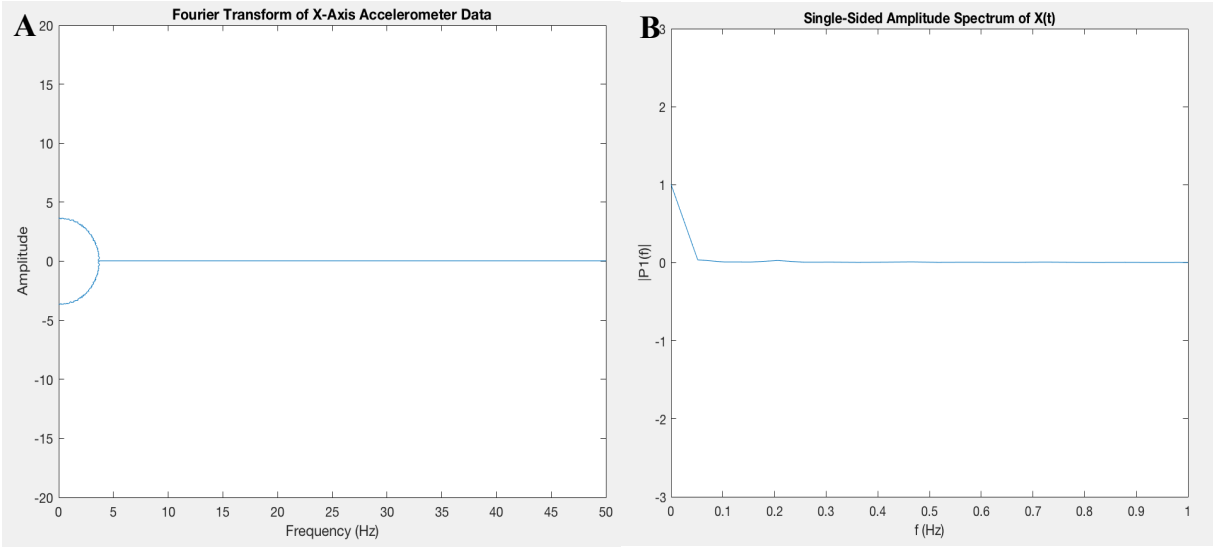

Figure 8. A) Example subject data for the Fourier Transform of x-axis accelerometer voltage readings. **B)** Power spectrum of the Fourier transform shown on the left.

Baseline was compared to subject treatment data and translated into a final COWS score. A selection of this analysis can be seen below (**Table 4**), wherein the power area for treatment data is significantly larger than that for baseline data and a COWS score greater than 0 is determined.

Subject	**X-Axis Power Area**	**Y-Axis Power Area**	**Z-Axis Power Area**	**Total Baseline Power Area**	**Power Area Difference**	**COWS Score**
2248.1	1.5104	1.6977	1.7538	4.9619	-0.3031	0
2248.2	1.5021	1.6944	1.7581	4.9545	-0.3104	0
2247.1	1.5086	1.7294	1.7078	4.9458	-0.3191	0
2247.2	2.2139	1.9880	1.6937	6.4051	0.6306	2
2245.1	1.4482	1.7290	1.4490	4.9295	-0.3355	0
2245.2	3.4561	3.6697	3.5649	10.6907	5.4257	4

Table 4. Sample of tremor measurements from three subjects at rest (xx.1) and at treatment (either rest or exercise with tremor, xx.2). Subject 2248 remained at rest during treatment, while Subject's 2247 and 2245 maintained induced tremors during treatment. Difference in power area shows a significant change from baseline values, and calculates a COWS score accordingly.

The distribution of baseline and percentage change in GSC from baseline from the data collected in these studies (**Table 4)** was used to assign COWS scores (either 0, 1, 2, or 4) to the numerical value of galvanic skin conductance. The use of previously collected subject data as a benchmark for another patient is justified because the distribution of baseline skin conductance appears normal (**Fig 10**) and would likely prove statistically normal if a greater sample size were obtained. Because there is a slight positive skew to the distributions, the threshold GSC values for COWS scoring (e.g. the value of GSC at which the score changes from a "2" to a "4") were adjusted upwards from the first, second, and third quartile values. The process by which the Orbis algorithm assigns COWS score for anxiety and sweating based on collected GSC data is described below (**Fig 9**). After a period of ~5min, or if a known baseline exists for that patient, the patient's own GSC data is used as baseline, and the COWS is assigned based on percentage change from baseline.

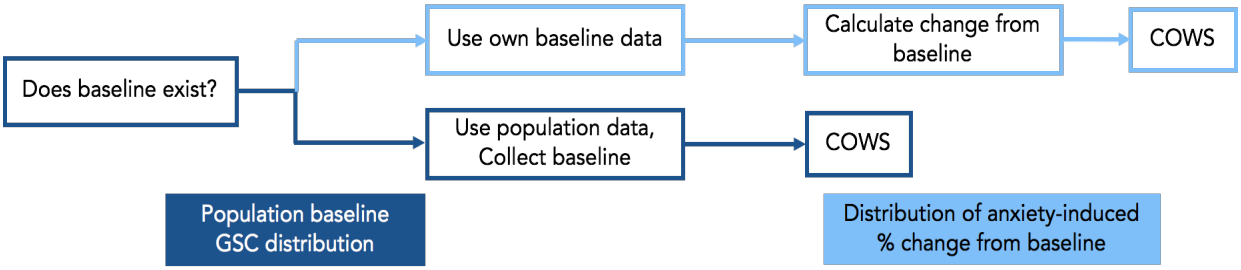

Figure 9. Logic tree for assigning a COWS score to anxiety and sweating from skin conductance data.

	Min	Q1	Median	Mean	Q3	Max	SD
Baseline	6.629	12.433	12.246	19.495	22.983	59.926	11.59
Anxiety	7.143	11.635	15.922	18.821	25.159	33.282	8.34
Change	-0.308	0.0291	0.51431	1.820	2.176	9.074	2.76
% Change	-4.65%	0.23%	4.20%	9.34%	9.47%	15.14%	

Table 5. Summary statistics for baseline (n=32), maximum GSC (n=19), and change in GSC (n=19). Q stands for quantile, and SD for standard deviation. All numerical values are in units of micro Siemens.

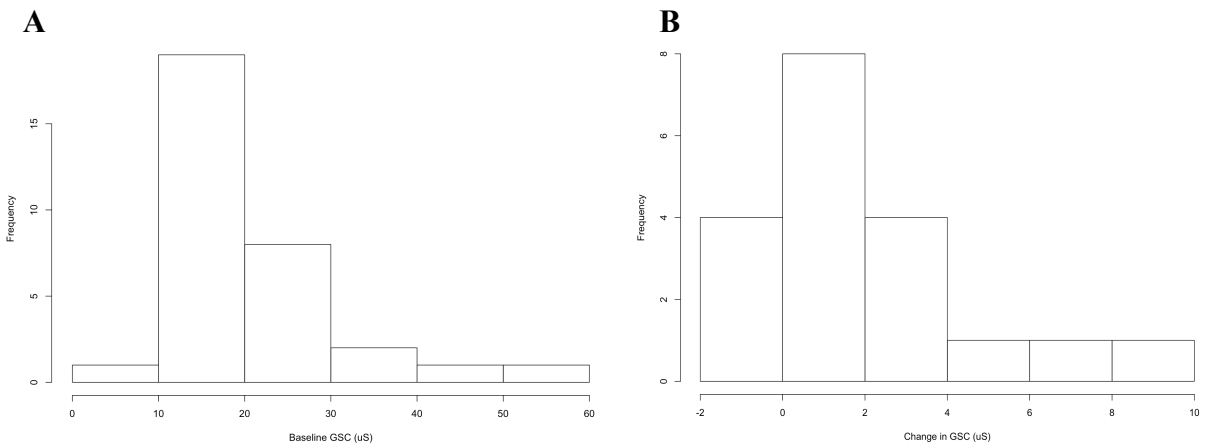

Figure 10. Histograms of **A)** baseline galvanic skin conductance (n = 32) and **B)** change in skin conductance upon induced anxiety (n = 19). The histograms appear mostly normal with a slight positive skew.

Optimal Design Performance and Project Impact

To test the most important specification, COWS score accuracy, Rachel McFadden (BA BSN R.N.), a nurse with significant COWS experience, assessed a subject experiencing mock withdrawal using the traditional COWS method while the subject wore Orbis at the same time. Exercise, mock tremor, and disturbing video content was used to elevate heart rate, tremor, and anxiety.

Orbis met the accuracy goal of within 2 points on the COWS scale for our device compared to a trained clinician for each of the five trials we conducted **(Fig 11)**. In addition, Orbis met specifications for portability, weighing less than 60 grams, durability, as it was used for repeated testing, connectivity, as Orbis COWS score values were integrated quickly and rapidly with a application, and UI usability, as a user-prompting logic tree enabled the quick calculation of the COWS score.

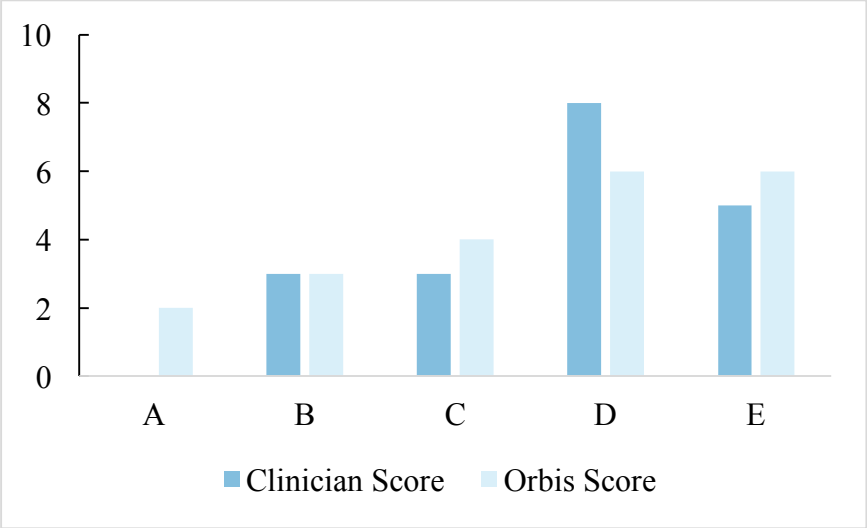

Figure 11. Calculated COWS scores for Orbis (light blue) compared to a trained clinician (dark blue) for 5 trials of a patient experiencing mock withdrawal. Orbis COWS output is within +/- 2 points for each of the 5 trials conducted.

There were many qualitative takeaways from the comparison of Orbis to a clinician. The most important was that in many cases, continuous monitoring of physiological symptoms leads to a different score than a clinician would give for a snapshot in time. While continuous monitoring of the COWS score is potentially more informative, for the sake of comparison with a clinician's score, it may be preferable to obtain a very short (~30s) sample of patient data. In addition, it was noted that the subjective nature of the COWS score means that the clinician relies on verbal feedback from the patient to determine anxiety, a parameter determined solely by a biosensor currently in Orbis. Lastly, timestamping each entry in the database is crucial for repeated patient assessments, so that data from earlier time points, where withdrawal symptoms might be more severe, is not overwritten for the same patient.

Display of Final Product

The final "looks-like" Orbis prototype integrates a miniaturized circuit with the three biosensors into a molded silicone band that fits snugly onto the wrist (**Fig 12**). With data collected from the wearable analyzed in MATLAB and translated to COWS score outputs, the wearable

efficiently monitors patient withdrawal continuously. Once the COWS score is collected, it is transferred to an application developed in Swift for iOS through Node.js and Firebase, a database storing trial information. Overall, the COWS score updates repeatedly and rapidly through a combination of software and hardware tools.

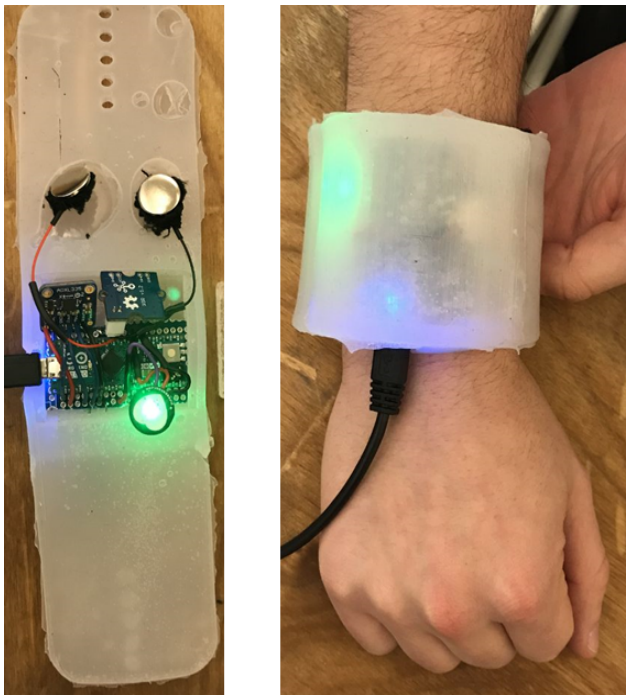

Figure 12. Final "looks-like" Orbis prototype consisting of a silicone injection-molded wristband and a miniaturized circuit with all three biosensors (left). The band fits snugly onto the users wrist.

Project Illustration

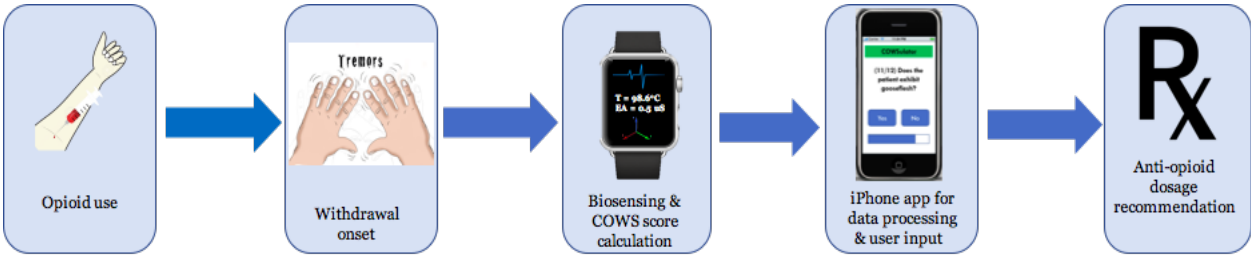

Figure 13. Revised project illustration. Following withdrawal from abuse of short-acting opioids, a patient seeks treatment in a hospital emergency department (due to the severity of withdrawal symptoms), a substance abuse treatment facility (motivated by the desire to detox from opioids and achieve sobriety), or a primary care physician (for one or both of the aforementioned reasons). The patient's physiological symptoms of withdrawal are tracked using Orbis until the patient's symptoms indicate withdrawal is severe enough to receive anti-opioid treatment, at which point a provider is alerted and prompted to complete the remainder of the COWS assessment. Afterwards, the Orbis mobile application displays the calculated COWS score and, in future iterations, a treatment recommendation (e.g. "administer 8 mg SL buprenorphine").

Budget

A

Component	Prototype Costs Quant.	Unit Cost	Budgeted	Actual
Microcontrollers				
Arduino Mega	1	$45.29	$45.29	$90.58
A-Male to B-Male USB Cable	1	$4.99	$4.99	$9.98
Sensors				
Pulse Sensor	1	$24.99	$24.99	$124.95
Grove GSR Sensor	1	$21.88	$21.88	$131.28
ADXL 335 3-axis Accelerometer	1	$0.00	$0.00	$0.00
Software				
Firebase database	1	$0.00	$0.00	$0.00
MATLAB student license	4	$0.00	$0.00	$0.00
Xcode for SWIFT	1	$0.00	$0.00	$0.00
Prototype Fabrication				
Wrist Sweatband	1	$7.99	$0.00	$7.99
Wrist Stabilizer	2	$9.99	$0.00	$19.98
Command Hanging Strips	2	$5.79	$0.00	$11.58
Soft Silicone (DragonSkin)	1	$34.99	$0.00	$34.99
Total Budgeted Cost '17-'18			**$97.15**	---
Total Actual Cost '17-'18			---	**$431.33**

B

Component	Cost
Wristband, injected-molded polycarbonate & silicone	$1.45
Main enclosure, injection-molded plastic	$1.08
Low-Power Microcontroller (MCU)	$7.91
Bluetooth Low Energy IC	$2.50
BTLE Wireless MCU with USB	$4.50
Charging cable	$2.08
Gyroscope + Accelerometer + Compass	$4.95
Infrared LEDs	$0.36
Op Amp	$1.63
Electrodes	$0.38
LCD Display	$1.01
Li-ion power management IC	$2.30
Printed Circuit Board Fabrication	$0.31
Printed Circuit Board Assembly	$1.00
Direct Materials	$31.5
Labor (Contract Manufacutring Services)	$2.3
Total Cost, Hardware	$33.7

Figure 14. **A)** 2017-2018 budget, projected and actual. Quantities are listed in units needed per prototype made, not total units ordered. **B)** Projected costs of a production-grade Orbis minimum viable product.

The total budgeted cost to build and prototype Orbis was estimated to be $97.15, while actual total cost for the year was $431.33, remaining under the $600 limit **(Fig 14)**. Of the $431.33 spent, $250 was obtained from the Rothberg Catalyzer and the remaining $181.33 was spent from the BE Senior Design budget. The initial budgeted cost of $97.15 only accounted for one prototype of Orbis. The additional cost incurred was due multiple iterations of Orbis, which required additional sensors and the creation of multiple prototypes for subject testing. Ultimately, three fully functioning prototypes were created and used for subject testing.

The cost of a production-grade prototype was projected to be $33.70 **(Fig 14).** These numbers were derived from "tear-down" analyses of cost of components in similar production-grade wearable devices such as Fitbit. These cost savings would occur as a result of component miniaturization and economies of scale that result from mass manufacturing. The production grade cost of Orbis is well under the original cost specification of $50 for Orbis, allowing for a significant revenue margin based on our product pricing.

Business Analysis

Three end-user segments were modeled for Orbis: substance abuse treatment (SAT) facilities such as addiction and rehabilitation centers, emergency departments (EDs), and primary care physicians (PCPs). Based on internal market size projections, Orbis could reach an estimated 247,946 facilities. In addition, based on survey results, Orbis could save up to 65 minutes per patient and $200,000 per facility, based on the average hourly wage of a physician.

Orbis customers will purchase the wearable device on a per-unit basis, with bulk discounts available for larger customers, and will purchase the software on a subscription basis. Two reasonable potential distribution channels for Orbis were assessed (**Fig 16**). The first is to sell directly to end customer (SAT facilities, EDs, and PCPs), as described above. The second distribution option is partnerships with anti-opioid manufacturers. Collaboration with these pharmaceutical companies would enable Orbis to leverage partners' existing commercialization infrastructure, marketing expertise, provider and patient networks, trained salesforce, and distribution channels. Under this model, Orbis would initially be sold through a "push" marketing strategy, whereby pharma salespeople distribute Orbis devices as part of their promotional package.

Pricing for Orbis will be separated into software and hardware components. The hardware component, including biosensor wristband and charger, will be sold between $900 and $1,500 based on the purchaser. This price is at a discount to comparable research-grade devices such as the Empatica E4 ($1690), and at a premium to less accurate retail fitness trackers such as the Fitbit Charge ($129.95). Additionally, selling Orbis at $900 to hospitals will appeal to purchasing committees, as devices less than $1,000 require less purchase oversight. Devices were expected to be replaced on a biannual basis. The pricing for software was benchmarked to the cost of typical

EMR/EHR software, at approximately a tenth of the cost per patient, ranging from $50-200/month based on the number of patients.

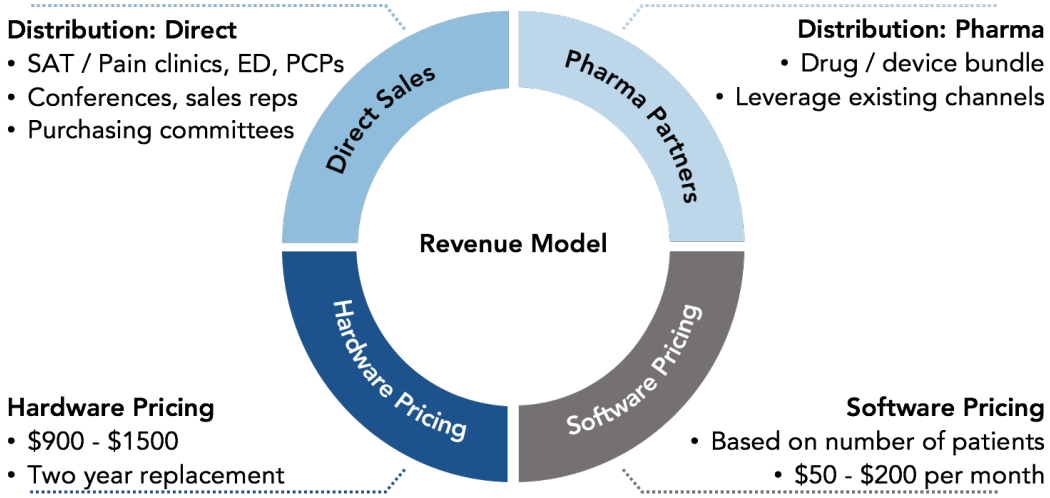

Figure 16. Distribution channels for Orbis.

To expand production of Orbis, we would contract with raw materials suppliers, a printed circuit board manufacturer, a wristband manufacturer, and hire or contract labor for assembly. Depending on the amount of labor outsourced, some factory space may be necessary. In addition to hardware development, we would also need to hire or outsource software developers and marketing consulting services. Projected margins were based on a percentage-of-revenue weight average of software-as-a-service companies and medical device manufacturers (**Fig 17**).

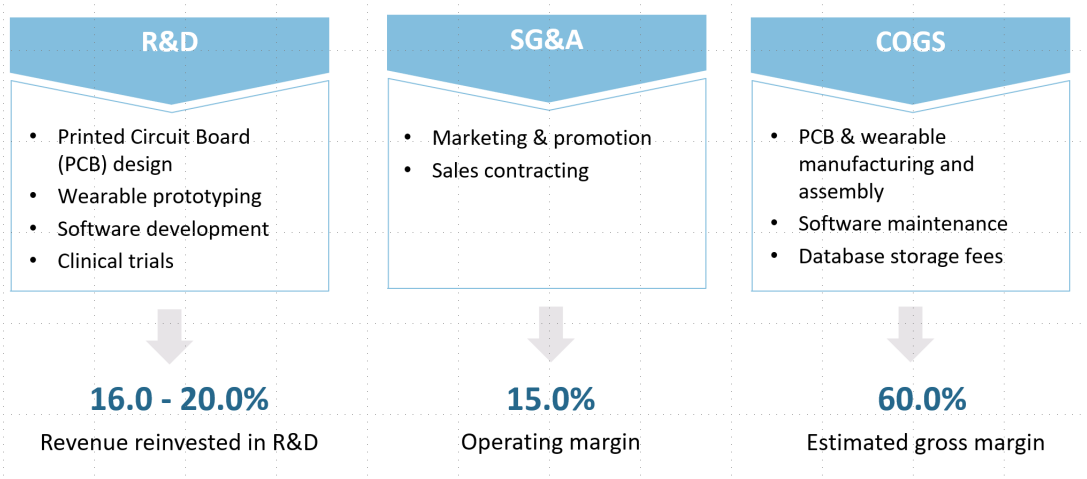

Figure 17. Cost model for Orbis.

As a first-to-market product, Orbis is optimized for a clinical setting to aid clinicians and patients. There are no existing devices suited to COWS score diagnosis. However, a number of health-focused wearables and research-grade devices could enter the market over time (**Fig 18**).

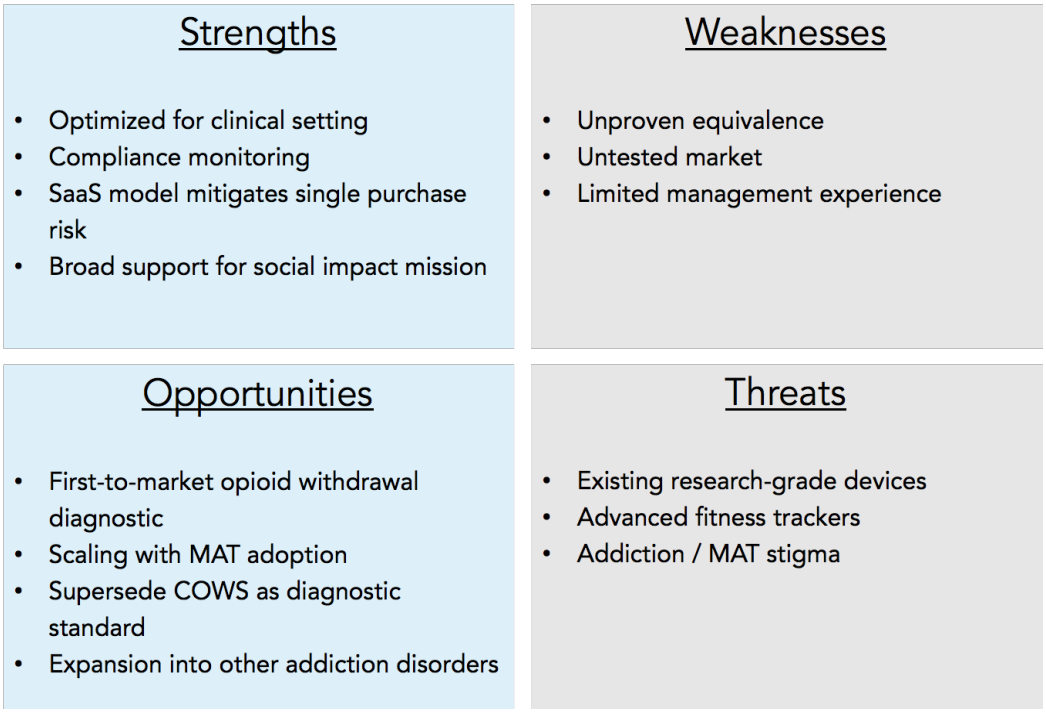

Figure 18. Analysis of Orbis's strengths, opportunities, threats, and weaknesses as a commercial product.

Although Orbis will initially target an in-patient use case, there are opportunities for horizontal expansion (**Fig 19**). Following product optimization with clinicians, there will be a market for outpatient users aiming to monitor their own addiction with oversight from their physician. In addition, Orbis has the potential to supersede the COWS score as the clinical standard for opioid withdrawal diagnosis because it objectively and continuously monitors the major symptoms associated with withdrawal. Ultimately, Orbis could expand to assessing withdrawal from substances other than opioids, providing wide-reaching technology-enabled addiction management.

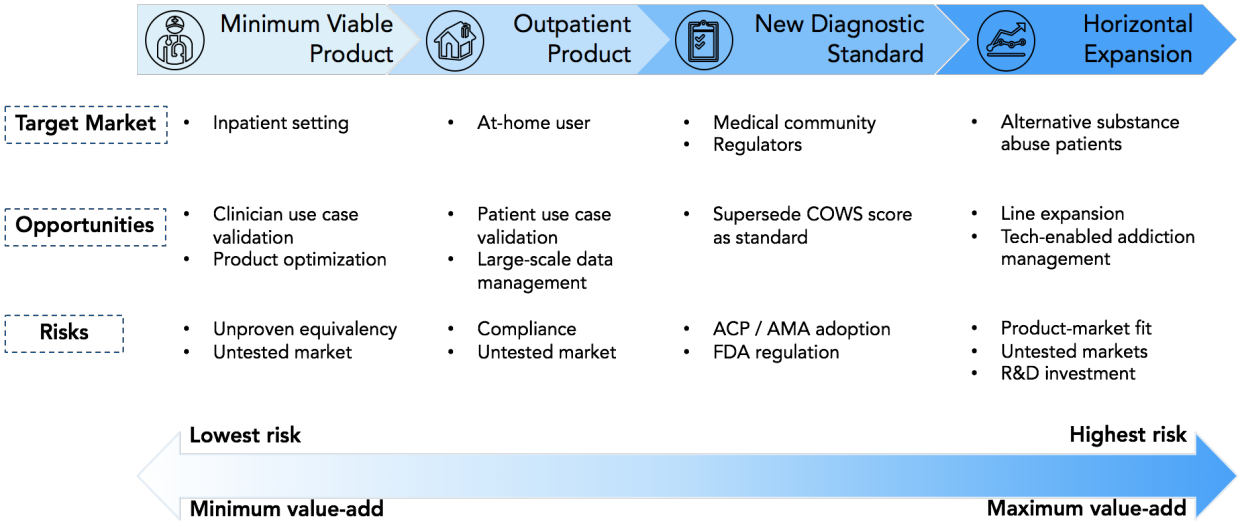

Figure 19. Product roadmap and horizontal expansion.

Conclusions and Summary

Orbis' accurate, continuous monitoring of the COWS score has the capability to help over 2 million Americans access MAT. With robust hardware and software, Orbis is a proof-of-concept device that meets the need for clinicians struggling to address an increasing number of patients and fights the stigma surrounding the treatment of addiction with medication. Accurately translating three biosensors to the COWS score, Orbis shows the utility of objectively monitoring physiological symptoms of withdrawal to improve patient outcomes, increasing physician confidence in treatment decisions and reducing the time-consuming nature of the COWS score.

Although we would need larger studies in the affected population to prove this, we believe that Orbis might lead to improved accuracy and consistency in withdrawal diagnosis, given the subjective nature of the COWS assessment. The reasoning is this: a COWS score that is "off" from a clinician's opinion by +/- 2 points, but is consistent in measurement methodology, is better for a patient than a COWS score that is highly variable between clinicians for the same patient (e.g. different clinicians giving the same tremor a 2 or a 4). We believe that patients would prefer a more objective measurement of their physiological symptoms of withdrawal and would trust a

device to output four out of 11 COWS parameters. However, a clinical-grade Orbis prototype would require a printed circuit board, wireless connectivity, internal battery, and sleeker wearable design. This next-generation prototype would be used in clinical testing to prove efficacy in assessing patients with OUD.

Meeting key specifications in application design, durability, portability, connectivity, and most importantly, accuracy, Orbis is an important step in proving the concept of an integrated biosensor system for withdrawal diagnosis and eventually, addiction management. Orbis has the potential to improve patient outcomes, increase access to MAT, and decrease the burden of the opioid crisis on health care providers and society in general.

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Appendix 3

Cash Flow Model	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028
Revenue	-	101,791	229,734	424,623	838,777	1,660,479	2,513,591	4,340,250	7,642,060	13,921,223	26,037,052
Cost of manufacturing	-	50,000	91,893	169,849	335,511	664,191	1,005,436	1,736,100	3,056,824	5,568,489	10,414,821
Gross profit	-	51,791	137,840	254,774	503,266	996,287	1,508,155	2,604,150	4,585,236	8,352,734	15,622,231
Research and development	30,000	55,000	45,947	76,432	134,204	232,467	351,903	607,635	1,069,888	1,948,971	3,645,187
SG&A	5,000	10,000	149,327	284,498	578,756	1,178,940	1,784,650	3,081,578	5,425,863	9,884,069	18,486,307
Total operating expenses	35,000	65,000	195,274	360,930	712,960	1,411,407	2,136,552	3,689,213	6,495,751	11,833,040	22,131,494
Opearating profit (EBITA)	(35,000)	(13,209)	34,460	63,694	125,817	249,072	377,039	651,038	1,146,309	2,088,184	3,905,558
Gross margin	-	50.9%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%	60.0%
Operating margin	-	(13.0%)	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
R&D as a % of revenue	-	54.0%	20.0%	18.0%	16.0%	14.0%	14.0%	14.0%	14.0%	14.0%	14.0%
SG&A as a % of revenue	-	9.8%	65.0%	67.0%	69.0%	71.0%	71.0%	71.0%	71.0%	71.0%	71.0%

Notes
Margins were calculated as a weighted average of benchmarks (industry averages) for the software and medical equipment and device manufacturing industries, for privately-owned companies of 0-5 years of age. The average was weighted based on percent of revenue derived from Orbis software versus hardware. Source for industry data was IndustriUS CFO. R&D as a percentage of revenue were calculated using Athena health (a healthcare SaaS company) as a comparable.

Appendix 3

Revenue Model	2018A	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028
SAT Facility Penetration Rate	**0.0%**	**0.0%**	**0.0%**	**0.1%**	**0.2%**	**0.3%**	**0.4%**	**0.8%**	**1.5%**	**3.1%**	**6.1%**
ER Penetration Rate	**0.0%**	**0.0%**	**0.2%**	**0.3%**	**0.5%**	**0.9%**	**1.7%**	**3.1%**	**5.6%**	**10.3%**	**18.9%**
PCP Penetration Rate	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.1%**	**0.2%**	**0.3%**	**0.4%**	**0.5%**	**0.6%**	**0.7%**
Total customers											
SAT	-	2	5	10	20	40	49	101	205	418	852
ER	-	1	8	14	25	46	85	156	286	523	959
PCP	-	24	48	97	197	399	811	987	1,202	1,457	1,760
Total customers	-	27	60	121	242	486	945	1,244	1,693	2,398	3,570
Revenue per customer											
SAT	$0	$55,023	$87,039	$176,866	$360,399	$734,384	$716,082	$1,829,585	$3,728,137	$7,596,806	$15,479,973
ER	$0	$11,480	$81,654	$123,857	$226,884	$415,614	$761,333	$1,394,633	$2,554,731	$4,679,833	$8,572,658
PCP	$0	$35,288	$61,041	$123,901	$251,493	$510,481	$1,036,175	$1,116,032	$1,359,193	$1,644,585	$1,984,421
Total revenue	$0	$101,791	$229,734	$424,623	$838,777	$1,660,479	$2,513,591	$4,340,250	$7,642,060	$13,921,223	$26,037,052

Market Size	2018A	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028
SAT Facility Growth Rate	**6.4%**	**4.2%**	**2.8%**	**1.9%**	**1.9%**	**1.9%**	**1.9%**	**1.9%**	**1.9%**	**1.9%**	**1.9%**
ER Growth Rate	**0.1%**	**0.1%**	**0.1%**	**0.1%**	**0.1%**	**0.1%**	**0.1%**	**0.1%**	**0.1%**	**0.1%**	**0.1%**
PCP Growth Rate	**1.5%**	**1.5%**	**1.5%**	**1.5%**	**1.5%**	**1.5%**	**1.5%**	**1.5%**	**1.5%**	**1.0%**	**0.7%**
Total facilities											
SAT	11,136	11,608	11,936	12,161	12,391	12,624	12,862	13,104	13,351	13,603	13,860
ER	5,030	5,035	5,040	5,045	5,050	5,055	5,060	5,065	5,070	5,075	5,081
PCP	231,798	235,252	238,757	242,315	245,925	249,589	253,308	257,083	260,913	263,505	265,250
Total facilities	247,964	251,895	255,734	259,521	263,366	267,269	271,231	275,252	279,335	282,183	284,190
Revenue per customer											
SAT	$263,923,200	$275,115,359	$282,893,214	$288,225,044	$293,657,366	$299,192,073	$304,831,096	$310,576,400	$316,429,989	$322,393,904	$328,470,223
ER	$57,342,285	$57,399,627	$57,457,027	$57,514,484	$57,571,998	$57,629,570	$57,687,200	$57,744,887	$57,802,632	$57,860,435	$57,918,295
PCP	$347,697,128	$352,877,815	$358,135,695	$363,471,917	$368,887,648	$374,384,074	$379,962,397	$385,623,837	$391,369,632	$395,257,237	$397,874,718
Total attainable revenue	$668,962,613	$685,392,801	$698,485,936	$709,211,445	$720,117,013	$731,205,718	$742,480,693	$753,945,124	$765,602,253	$775,511,575	$784,263,237

Growth											
SAT											
Base	6.4%	4.2%	2.8%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%
Down	4.2%	2.8%	1.9%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%
Up	9.5%	6.4%	4.2%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%
ER											
Base	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Down	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Up	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%
PCP											
Base	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.0%	0.7%
Down	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	0.7%	0.4%
Up	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	1.5%	1.0%
Penetration											
SAT											
Base	0.0%	0.0%	0.0%	0.1%	0.2%	0.3%	0.4%	0.8%	1.5%	3.1%	6.1%
Down	0.0%	0.0%	0.0%	0.1%	0.1%	0.2%	0.3%	0.5%	1.0%	2.0%	4.1%
Up	0.0%	0.0%	0.1%	0.1%	0.2%	0.5%	0.6%	1.2%	2.3%	4.6%	9.2%
ER											
Base	0.0%	0.0%	0.2%	0.3%	0.5%	0.9%	1.7%	3.1%	5.6%	10.3%	18.9%
Down	0.0%	0.0%	0.1%	0.2%	0.3%	0.6%	1.1%	2.1%	3.8%	6.9%	12.6%
Up	0.0%	0.0%	0.2%	0.4%	0.8%	1.4%	2.5%	4.6%	8.5%	15.5%	28.3%
PCP											
Base	0.0%	0.0%	0.0%	0.0%	0.1%	0.2%	0.3%	0.4%	0.5%	0.6%	0.7%
Down	0.0%	0.0%	0.0%	0.0%	0.1%	0.1%	0.2%	0.3%	0.3%	0.4%	0.4%
Up	0.0%	0.0%	0.0%	0.1%	0.1%	0.2%	0.5%	0.6%	0.7%	0.8%	1.0%

BASE

Growth Model Scenario	
Case (1=Base, 2=Down, 3=Up)	1

Penetration Model Scenario	
Case (1=Base, 2=Down, 3=Up)	1

Usage Per Customer	ER	SAT	PCP
Average devices per customer	10	25	1
Revenue per device	$900	$900	$900
Revenue Per Customer	$9,000	$22,500	$900

Facility Type	# Patients/Yr	# Facilities	Rev/month	Rev/yr	Total Rev
SAT	52	10,470	100	1,200	12,564,000
ER	4,524	5,025	200	2,400	12,060,000
PCP	23	209,000	50	600	125,400,000

Pricing (monthly)	# Patients
$ 50.00	< 50
$ 100.00	50-100
$ 150.00	100-500
$ 200.00	>500