Differentiating Acute Otitis Media (AOM) from Otitis Media with Effusion (OME) Using Autofluorescence of NADPH in Neutrophils

(Technical Paper)

Medical Deserts and the Inequitable Distribution of Medicine

(STS Research Paper)

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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Introduction

Diagnosis of disease by clinicians is one of the most crucial elements in treating a patient, and it can often be difficult to distinguish between certain diseases. According to a recent study by BMJ Quality and Safety, over 12 million adults in the U.S. are misdiagnosed when visiting a clinician at an outpatient medical center, which equates to about 1 out of 20 adult patients (Bernstein, 2017). Additionally, about 88% of people who go to another doctor for a second opinion leave with a different diagnosis than what they started with (Wallace, 2017). One example of this occurs when diagnosing ear infections. When diagnosing ear infections, fluid may exist in the ear, but clinicians cannot accurately diagnose the patient without knowing if the fluid is infected. Ideally, clinicians will be able to accurately distinguish between Otitis Media with Effusion (OME), where fluid exists in the ear, and Acute Otitis Media (AOM), where the fluid in the ear is infected and requires antibiotic treatment.

To address this problem and assist clinicians in differentiating between OME and AOM, my technical project team is planning on detecting the NADPH in neutrophils existing in the infected fluid of the middle ear using autofluorescence properties. We hope to design a successful proof of concept by experimenting with optics equipment and testing the NADPH autofluorescence spectroscopic response to develop a prototype medical device by modifying the currently existing otoscope and running *in vitro* trials. Through this design project, we hope to make the diagnosis of OME and AOM easier for clinicians to reduce the over-prescription of antibiotics and reduce the number of unnecessary procedures.

However, the technical portion of the project is not enough to overcome the problem of medical misdiagnosis nationwide. This is because there are not only technical problems and

limitations in the medical community but also social impacts that oftentimes are overlooked. For our medical device to reduce the number of misdiagnoses, this device must be equally distributed across the nation. However, medical deserts, which are medically underserved areas that have a lower quality of healthcare, make this close to impossible. Some examples include areas with a lower number of healthcare professionals, poor quality healthcare professionals, highly remote areas, as well as areas with high need of care (Lucas-Gabrielli & Chevillard, 2018).

To ensure proper medical diagnosis occurs nationwide, we need to address this issue and ensure there is equality in medicine. This means that both the technical and social sides of this project must be considered. Although the technical portion may be successful and we may create a prototype for a new medical device, the project is not successful unless we can address the unequal treatment in medical experiences across the world and our device can be fairly distributed and used. In this paper, I will discuss the importance of my technical project along with social inequalities in medicine and how to address them.

Technical Topic

As discussed previously, clinicians have trouble differentiating between OME and AOM when using just a regular otoscope. AOM is an infection of the middle ear, where the tympanic membrane has infected fluid behind it but OME, while it is another middle ear condition, causes the tympanic membrane to have fluid behind it, but the fluid is not infected. These diagnoses are currently unreliable about 27% of the time (Pichichero & Poole, 2001). Additionally, about 2.2 million cases of AOM occur annually among children which amounts to a direct cost of $4 billion per year due to the unnecessary removal of adenoids or tonsils, over-prescriptions of antibiotics, and loss of hearing (Rosenfeld et al., 2016).

The high rate of misdiagnosis between OME and AOM is likely due to the inaccuracy in the current methods of diagnosis. Currently, physicians have two main ways of diagnosing Otitis Media: visual observation and tympanometry. When using visual observation, the clinician will use an otoscope to look into the patient's ear canal to observe the visual properties of the tympanic membrane. The clinician will look for signs of inflammation including redness, swelling, presence of pus behind the tympanic membrane, and vasculature (Pichichero & Poole, 2001; Sridhara & Brietzke, 2012). While this method may inform the clinician that something is wrong with the middle ear, it does not indicate any sign of infection. When using the tympanometry method, the clinician will change the pressure in the ear by creating a vacuum using a pneumatic otoscope and then pump a puff of air into the space to visually observe the rigidity of the tympanic membrane. Using this technique requires clinicians to assume that an infected ear will have little to no tympanic movement caused by the pressure exerted by the fluid behind the membrane (Onusko, 2004; Shanks, 1984). While this model hypothetically makes sense, it's important to remember that in OME there is also fluid behind the ear and this method still does not indicate if the fluid is infected so clinicians cannot accurately distinguish between OME and AOM.

To improve on the existing diagnosis methods, my technical project group plans on differentiating between OME and AOM by determining if the fluid buildup behind the tympanic membrane is infected through autofluorescence. When an infection is detected in the middle ear, an immune response occurs and neutrophils go towards the location of the infection. When neutrophils are active in an immune response, they release high concentrations of NADPH (Segal et al., 2012). NADPH can be excited and detected using autofluorescence with pulsed light at ~360 *nm* and with an emission wavelength of ~450 *nm* (Croce & Bottiroli, 2014). The

advantages of using this technique include both its efficiency and straightforwardness. Unlike other methods, this will allow us to determine if middle ear fluid is infected by using a reaction that takes under a second and requires little image processing as well as no molecular treatment (*Fluorescence Fundamentals - US*, n.d.).

Overall, the development of a new medical device through my technical project will allow clinicians to easily differentiate between OME and AOM by testing for NADPH in the middle ear fluid using autofluorescence. Through the development of this technology, we will be able to reduce the number of misdiagnoses nationwide, reduce the over-prescription of antibiotics to reduce antibiotic resistance in patients, and reduce the number of unnecessary surgeries and procedures.

STS Topic

Beyond the technical implications, it's important to understand the social ramifications relating to my technical project including the inequalities seen in the medical community, especially surrounding medical deserts. Additionally, the creation of new medical devices and technology emphasize these inequalities evident in the unequal distribution of medicine.

As discussed previously, medical deserts are medically underserved areas that have a lower quality of healthcare including lower numbers of healthcare professionals, poor quality healthcare professionals, highly remote areas, as well as areas with high need of care (Lucas-Gabrielli & Chevillard, 2018). They are usually found in low-income and rural communities and are often created along racial lines. These areas cause inequalities in medicine because the citizens in these areas are treated unequally in regards to medical care. For example, medical deserts typically don't receive an equal distribution of medical supplies, they don't have equal

access to medical education for new and improved medical technology, and there are often racial disparities involved in the use of medical instruments.

One of the largest impacts of medical deserts can be felt by the unequal distribution of supplies to these areas. A good example of this is the recent COVID-19 pandemic and how the government chose to distribute emergency supplies. Back in March 2020, when the pandemic was beginning to peak, there was a shortage of supplies, specifically ventilators and personal protective equipment (PPE) in many parts of the country. While there was a shortage nationwide, some cities and states had a surplus of supplies while others, specifically more rural areas, could not get enough supplies to keep up (Tsai, 2020; Wagtendonk, 2020). When comparing the risk of COVID-19 among rural residents by race and ethnicity, it is clear to see that these underserved communities have a much higher risk than those from more affluent communities. In the past decade, more than 125 rural hospitals have closed and those that are still open, are on the edge of making it. Additionally, rural areas have a very small percentage of ICU beds, ventilators, and respiratory treatment compared to other communities (Henning-Smith et al., 2020).

Another large impact of medical deserts is the lack of well-trained healthcare workers and the lack of access to medical education. Similar to the medical supplies, medical professionals are also distributed poorly across the country leaving certain areas with little access to healthcare. Specifically, when studying rural versus urban areas, there are around 68 physicians per 100,000 people in rural areas while there are 84 physicians per 100,000 people in urban areas. The national average is around 80 physicians per 100,000 people in the United States, so we can see how understaffed rural areas are in terms of healthcare professionals (Petterson et al., 2013). Another large issue is the distribution differences between nurse practitioners (NP) and physician assistants (PA) when compared to physicians. Studies have

shown that physicians are more likely to work in urban areas while NPs and PAs are more likely to work in rural areas (*Primary Care Workforce Facts and Stats No. 3*, n.d.). This means that people may have access to some version of healthcare but it's less likely to be treated by a more highly trained physician in rural areas when compared to urban areas. Beyond this, with less highly trained physicians in rural areas, it becomes more difficult for healthcare professionals to continue their education to learn and develop their skills with new medical devices.

Lastly, the impacts of medical deserts can also be seen in the development of medical instruments in which racial disparities are created. One example of this is the racial bias in pulse oximetry measurements. A pulse oximeter is used for estimating blood oxygen levels, but studies show that this device may not be accurate when used on people with darker skin tones. Reports show that at low oxygen saturation levels, or when a patient is hypoxic, the pulse oximeter cannot detect these levels of those patients with dark skin (Sjoding et al., 2020). Beyond medical devices simply being not designed for certain racial groups, racial bias also exists with clinicians treating patients. Racism in the medical field has existed since slaves were originally brought to America and were given the worst health care and had the worst health status. This hasn't changed much over time because even in the 21st century we see clinicians refusing service to patients of certain racial groups based on stereotypes and inferiority mythology (Byrd & Clayton, 2001).

Key Texts

Throughout my STS investigation, reading literature proved crucial in understanding the inequities experienced in healthcare and medical deserts. Unfortunately, there isn't a lot of published research on these topics based in America so I had to also look into reputable blogs

and other resources for more information. Overall, the three following resources were most helpful in completing the STS portion of this prospectus paper.

1. "Race, medicine, and health care in the United States: a historical survey" by W. M. Byrd and L. A. Clayton published in the Journal of the National Medical Association

This resource provided information on the history of the relationship between race and medicine describing the inequitable distribution of medicine during the times of slaves and the problem of how physicians treat patients differently based on race.

2. "Racial Bias in Pulse Oximetry Measurement" published in The New England Journal of Medicine

This journal article brought to my attention one of the first published racial disparities in medicine that has become a worldwide known problem. By researching how the pulse oximeter was designed in a way to discriminate against patients with darker skin tones, I'm able to prevent this from occurring with my project and understand how to design in a more inclusive manner.

3. "Inequality During a Pandemic, Part II: Rationing Life and Saving Gear and Care" by Robert L. Tsai for the Harvard Law Review Blog

I used this blog to further understand the unequal distribution of medical resources during the peak of the COVID-19 pandemic. I chose to focus on the recent pandemic as an example of the inequitable distribution of medicine since it is a very relevant issue and provides a blatant example of inequality and medical deserts.

Next Steps

In addressing the issue of inequality in medicine, we first need to make it a well-defined and clear problem. Through my research, I noticed that most of the resources relating to inequality in medicine and medical deserts were researched and written in other countries. For

example, I found a lot of resources about medical deserts studied throughout Europe, resources on the unequal distribution of medical supplies were studied mostly in developing countries, and the unequal distribution of medical professionals was studied mostly in Australia. Although some of this information can be applied to America, it would be easier to address this issue if there were more studies conducted on this issue in America. I think the first step in making healthcare more equal and accessible across the country would be to simply do more research and have this issue more well-known because, despite the issue existing, nothing can be done about it until the nation is passionate about it.

References

Bernstein, L. (2017, April 4). 20 percent of patients with serious conditions are first misdiagnosed, study says. *Washington Post*. https://www.washingtonpost.com/national/health-science/20-percent-of-patients-with-serious-conditions-are-first-misdiagnosed-study-says/2017/04/03/e386982a-189f-11e7-9887-1a5314b56a08_story.html

Byrd, W. M., & Clayton, L. A. (2001). Race, medicine, and health care in the United States: A historical survey. *Journal of the National Medical Association*, *93*(3 Suppl), 11S-34S.

Croce, A. C., & Bottiroli, G. (2014). Autofluorescence Spectroscopy and Imaging: A Tool for Biomedical Research and Diagnosis. *European Journal of Histochemistry : EJH*, *58*(4), 2461. https://doi.org/10.4081/ejh.2014.2461

Fluorescence Fundamentals—US. (n.d.). Retrieved October 3, 2021, from //www.thermofisher.com/us/en/home/references/molecular-probes-the-handbook/introduction-to-fluorescence-techniques.html

Henning-Smith, C., Tuttle, M., & Kozhimannil, K. B. (2020). Unequal Distribution of COVID-19 Risk among Rural Residents by Race and Ethnicity. *The Journal of Rural Health*, 10.1111/jrh.12463. https://doi.org/10.1111/jrh.12463

Lucas-Gabrielli, V., & Chevillard, G. (2018). ["Medical deserts" and accessibility to care: What are we talking about? *Medecine sciences*, *34*(6–7), 599–603. https://doi.org/10.1051/medsci/20183406022

Onusko, E. M. (2004). Tympanometry. *American Family Physician*, *70*(9), 1713–1720.

Petterson, S., Robert L. Phillips, J., Bazemore, A., & Koinis, G. T. (2013). Unequal Distribution of the U.S. Primary Care Workforce. *American Family Physician*, *87*(11). https://www.aafp.org/afp/2013/0601/od1.html

Pichichero, M. E., & Poole, M. D. (2001). Assessing Diagnostic Accuracy and Tympanocentesis Skills in the Management of Otitis Media. *Archives of Pediatrics & Adolescent Medicine*, *155*(10), 1137–1142. https://doi.org/10.1001/archpedi.155.10.1137

Primary Care Workforce Facts and Stats No. 3. (n.d.). Retrieved October 4, 2021, from http://www.ahrq.gov/research/findings/factsheets/primary/pcwork3/index.html

Rosenfeld, R. M., Shin, J. J., Schwartz, S. R., Coggins, R., Gagnon, L., Hackell, J. M., Hoelting, D., Hunter, L. L., Kummer, A. W., Payne, S. C., Poe, D. S., Veling, M., Vila, P. M., Walsh, S. A., & Corrigan, M. D. (2016). Clinical Practice Guideline: Otitis Media with Effusion (Update). *Otolaryngology–Head and Neck Surgery*, *154*(1_suppl), S1–S41. https://doi.org/10.1177/0194599815623467

Segal, B. H., Grimm, M. J., Khan, A. N. H., Han, W., & Blackwell, T. S. (2012). Regulation of innate immunity by NADPH oxidase. *Free Radical Biology & Medicine*, *53*(1), 72–80. https://doi.org/10.1016/j.freeradbiomed.2012.04.022

Shanks, J. E. (1984). Tympanometry. *Ear and Hearing*, *5*(5), 268–280.

Sjoding, M. W., Dickson, R. P., Iwashyna, T. J., Gay, S. E., & Valley, T. S. (2020). Racial Bias in Pulse Oximetry Measurement. *New England Journal of Medicine*, *383*(25), 2477–2478. https://doi.org/10.1056/NEJMc2029240

Sridhara, S. K., & Brietzke, S. E. (2012). The "Spoke Sign": An Otoscopic Diagnostic Aid for Detecting Otitis Media With Effusion. *Archives of Otolaryngology–Head & Neck Surgery*, *138*(11), 1059–1063. https://doi.org/10.1001/2013.jamaoto.337

Tsai, R. L. (2020, April 13). *Inequality During a Pandemic, Part II: Rationing Life-Saving Gear and Care (Harvard Law Review) | The shortage of ventilators and personal protective equipment (PPE) in parts of the country has raised the most acute equality concerns regarding the*

treatment of people who are gravely ill. Some jurisdictions have more protective and life-saving equipment on hand than others do, but this pre-crisis distribution is a product of many factors beyond existing... https://blog.harvardlawreview.org/inequality-during-a-pandemic-part-ii-rationing-life-saving-gear-and-care/

Wagtendonk, A. van. (2020, March 29). *The government is distributing emergency Covid-19 supplies. But some states are losing out.* Vox. https://www.vox.com/policy-and-politics/2020/3/29/21198704/emergency-covid-19-supplies-fema-states-federal-government

Wallace, A. (2017, April 4). *Study finds more than 20 percent of patients are misdiagnosed*. UPI. https://www.upi.com/Health_News/2017/04/04/Study-finds-more-than-20-percent-of-patients-are-misdiagnosed/7911491312817/