Notable Grand Rounds
of the
Michael & Marian Ilitch
Department of Surgery

Wayne State University
School of Medicine

Detroit, Michigan, USA

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HOW TO BUILD AN ACADEMIC CAREER
FOCUSED ON RESEARCH

March 16, 2022
About Notable Grand Rounds

These assembled papers are edited transcripts of didactic lectures given by mainly senior residents, but also some distinguished attending and guests, at the Grand Rounds of the Michael and Marian Ilitch Department of Surgery at the Wayne State University School of Medicine.

Every week, approximately 50 faculty attending surgeons and surgical residents meet to conduct postmortems on cases that did not go well. That “Mortality and Morbidity” conference is followed immediately by Grand Rounds.

This collection is not intended as a scholarly journal, but in a significant way it is a peer reviewed publication by virtue of the fact that every presentation is examined in great detail by those 50 or so surgeons.

It serves to honor the presenters for their effort, to potentially serve as first draft for an article for submission to a medical journal, to let residents and potential residents see the high standard achieved by their peers and expected of them, and by no means least, to contribute to better patient care.

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How to Build an Academic Career Focused on Research

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This paper is based on Dr. Levy’s Surgical Grand Rounds presentation on March 16, 2022

Introduction
I have been involved in over 110 research studies, including 23 NIH-funded programs. Research is not the only way forward in a physician’s career, but if it is where your interest lies, there is a way to go about it in order to be successful.

This paper is about how to build an academic career focused on research. It uses my own journey as the exemplar, not to toot my own horn but to inspire young physicians and help them understand how they may start out with an interest in a question and from that build a career in research.

Planting the Seed
Henry David Thoreau said: "Though I don't believe that a plant will spring up where no seed has been, I have great faith in a seed. Convince me that you have a seed, and I am prepared to expect wonders."

My seed began in the surgical realm, with the intestinal fatty acid binding (IFAB) protein, which at one point colleagues and I thought might be a biomarker for any intestinal badness—appendicitis and so on. It did not lead to anything concrete but it did lead me to understand that an intern is allowed to ask questions!

The best way to understand such questions is to search the literature for people who have been researching them for a while, and try to link up with them. The most important things I have learned through this are:

(a) Do not be intimidated by the authors of a publication; rather, reach out to them.

(b) People are generally friendly and want to work with others. Research is not the cutthroat environment I first imagined, with every man and woman for themselves, but a truly collaborative environment where people give opportunities and relish the success of others.

(c) Judge each day not by the harvest you reap, but by the seed you plant.

Hypertension in Romania
My research story proper began in Romania, where I went as one of several residents to help develop an emergency medicine capacity. Figure 1 on the next page shows Romanian colleagues with whom I worked. The group was led by Dr. Raed Arafat, a Palestinian who started the pre-hospital ambulance program depicted in the image and went on to become Romania’s Health Minister.

The day I arrived in the country I was rushed to a soccer field where a man had fallen off the back of his donkey-drawn cart and landed on a sickle, whose curved blade entered the left side of his abdomen and exited on the right side. A wet cloth had been wrapped around his bowels. To me, as a resident physician, this was exciting
from a training perspective. Two chest tubes later and flying in the medevac helicopter, I thought my pathway was set: I wanted to fly around taking care of difficult cases.

But after a month in Romania I became intrigued by another medical issue: Romanians drink a lot of a home-distilled alcohol called Țuică. There’s a finer variant of it called palincă. Both are made from fruits such as grapes and plums and pears. The problem is that poor home distillation techniques lead to methanol contamination. My thoughts of treating bowel eviscerations on soccer fields began to veer instead towards what could be done about methanol contamination in Romanian home-distilled alcohol.

These thoughts led to the first publica-
tion of my career, in the Journal of Toxicology—Clinical Toxicology in 2003.1 We found that 74% of the samples we collected were contaminated with methanol. Fortunately, the alcohol proof is quite high, which balances things out during metabolism.

Even more impressive to me was that the Romanians had adapted a process of treating acute hypertensive heart failure—flash pulmonary edema, in which the patient’s blood pressure is markedly elevated and they cannot breathe. Romanian doctors were treating it with massive doses of nitroglycerin—2 milligrams (2,000 micrograms)—the equivalent of five sublingual nitroglycerin tablets.

I visited remote Roma villages and would see, for example, a woman in her 70s, BP 300/150, pulse oximetry of 80% on room air, who could barely move. Into such patients we would inject those large doses of nitroglycerin, and their blood pressure and pulse oximetry would improve markedly and they would be able at least to walk in no time.

We designed and conducted a 40-person study of this treatment, which we called the Romanian Pulmonary Edema Nitroglycerin Trial (RoPENT). Our paper about it (Figure 2) was not published, but it is a good example of encountering a medical situation and wanting to understand it scientifically to see if it really is doing what you think it is doing. Just because you see something work once or twice before your eyes does not necessarily mean it is always going to work—it takes a randomized controlled trial to determine that.

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Hypertension in Detroit
On moving to Detroit after my residency I was surprised to find that even though the people looked very different, the hypertension problem was the same. In those days we often saw very hypertensive patients with acute heart failure in the emergency room at Detroit Receiving Hospital. (They do not present so often today because physicians and heart failure patients themselves are better at getting their blood pressures under control. However, chronic hypertension remains a major issue.)

Seeing 50 year-old black men and women in resuscitation with sky-high blood pressures and pulmonary edema, I wondered why not try the Romanian approach? This thought led to my first grant, of $24,995 from the Emergency Medicine Foundation, to conduct a study of patients in the resuscitation bay at Detroit Receiving Hospital, administering 2 milligram pushes recurrently of high-dose nitroglycerin by bolus to see how it affected their outcomes.

This study was published in 2007 in the Annals of Emergency Medicine. Getting there was tough—the paper was at first rejected outright, but on appeal (on the grounds that this was something never done before) the editors accepted it. The open-label, non-randomized study compared 29 ED patients to 45 historical controls and found great outcome benefit from the intervention, including decreased endotracheal intubation, decreased use of BiPAP, and decreased ICU admissions.

Ten years later we were able to report that this study actually changed the way medicine was practiced at Detroit Receiving and Sinai Grace Hospitals. Our retrospective analysis found that hundreds of patients treated with high-dose nitroglycerin by bolus infusion had better outcomes, including significant reductions in ICU admissions and hospital length of stay.3

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Fig. 3. Clinical Policy on High-Dose Nitroglycerine


Developing Expertise

This marked the beginning of my career as an expert in hypertensive acute heart failure. My colleagues and I subsequently went on to publish a number of papers in this area, and I’m proud to say that the soon-to-be-published 2022 Clinical Policy Statement in the emergency medicine literature on acute heart failure includes three critical questions, one of which is whether vasodilator therapy with high-dose nitroglycerin is safe and effective. It gives no level A or B recommendations because there are no good randomized control trials, but it does give a level C recommendation that it is safe and effective and may be beneficial in patients with acute heart failure and markedly elevated blood pressure. (See Figure 3 on previous page.)

While it certainly feels good to see one's work come to fruition in that way, more importantly it puts the researcher "on the stage" nationally. If you look to grow a research career, you do not want to publish meaningless papers—you want to publish papers that are going to be impactful. When you do, people start to recognize you as an expert in your content area.

When you write a personal statement (for an NIH grant or just for your biosketch) you declare your content expertise. The way to establish credible content expertise is by doing the research, establishing the literature, and becoming the person (or one of the people) to whom others refer. As a result of my published research I started getting invited into National Heart, Lung, and Blood Institute workshops on heart failure. As well, I became involved in scientific statements from the American Heart Association and in statements on heart failure by the European Society of Cardiology. Then I started getting involved in promoting the idea that emergency medicine—a field that often is referred to as a “jack-of-all-trades and master of none” profession—was a key player in acute heart failure, which previously was seen merely as chronic heart failure gone awry, not as something that warranted specific, dedicated understanding and education concerning its treatment.

We started publishing papers around management of acute heart failure, pointing to what was next for acute heart failure research, and then started getting involved in clinical trials. It is really important to promote the role of the emergency department to enrich patient identification and enrollment, because the research mindset often fails adequately to consider where the patients will come from. From a surgical perspective it is easy to think that the best way to enroll patients would be during floor rounds, but the

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reality is that to catch people in their most acute state and have all the physiologic parameters that will be needed for a study, you must get to them early.

We established a robust infrastructure for emergency medicine at Detroit Receiving and Sinai Grace Hospitals,\(^\text{10}\) with a team of people on call 24 hours a day, seven days a week. We had and still have an effective staff that works well with collaborators and colleagues. One of the key studies we got involved in was called Relax AHF\(^\text{11}\). It was a study of Relaxin (subsequently renamed Serelaxin, a drug under development by Novartis)\(^\text{12}\).

We were able to randomize people with heart failure within 16 hours of presentation, which is important in showing the outcomes of an acute intervention—the earlier you can intervene, the better you can assess the outcome of the intervention. All prior studies had enrolled people in the ICU or on the floor 24 to 48 hours after they presented—when people were already on their pathway to recovery and were unlikely to demonstrate an outcome benefit from the intervention\(^\text{13}\).

It is important to consider what are you trying to accomplish with your research. Outcome benefit was critically important in this case. Whatever you’re trying to change, you should want to know whether your proposed intervention actually changes the outcome. If you don’t do it early enough, oftentimes it won’t.

We started publishing on Serelaxin and establishing not just our clinical expertise but also our understanding of the biochemistry involved. We were eventually appointed to the steering committee in a leadership group for the ultimate definitive trial of 6,500 patients, which was published in the *New England Journal of Medicine* in 2019. The trial was negative, but that is how science moves forward. Authorship—not necessarily as first author—of even a negative study helps to establish expertise.

**The Acorn**

In his *Essays and Poems*, Ralph Waldo Emerson wrote: “The creation of 1,000 forests is in one acorn.” *Figure 4* (next page) shows the growth of my “forest” of publications from 2006 up to 2015. I was focusing then on the areas in green—on heart failure publications and building up an understanding of heart failure. But when I came to Detroit, I found the problem to be a little bit different from most other places. Not only were young black men and women presenting with acute hypertensive heart failure, they were presenting with acute hypertensive heart failure caused entirely by uncontrolled hypertension.

How many patients in Detroit present with completely normal blood pressures? I am not talking about those crashing in the ICU—I mean patients on the floor. How often do we prescribe antihypertensive medications, or at least consult medicine to come in and manage the hypertension? This is such an important and ubiquitous condition here that every physician in Detroit, no matter their specialty, needs to be part of the solution for hypertension management.

My career was advancing and I thought I was on the right trajectory, at least in the heart failure

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\(^\text{10}\) These are two of seven hospitals forming the 2,000-bed Detroit Medical Center. Receiving was the first hospital in the nation to achieve Level 1 trauma status.


world, but what we really were dealing with in our local population was hypertension. It is a life span problem in Detroit. It is not that people here suddenly wake up with elevated blood pressure and everything starts to go bad; rather, there is an age-related upward creep in blood pressure, which leads to vascular insult and injury that then leads to organ damage, which in turn leads to the consequences we see all too often: multi-infarct dementia, chronic kidney disease, early onset heart failure, diastolic dysfunction, etc.

A Fork In the River
The Detroit population essentially is on the early vascular aging trajectory shown in Figure 5 (opposite); hence, so much heart failure in young people. As a researcher with an academic mindset, I could have continued my career fixing the distal problem—acute hypertensive heart failure—or I could instead swim upstream to find the source of the problem of mortality and morbidity from heart disease in Detroit's young. For them to achieve an average life course, things have to change—society has to change, the way everything is done has to change. That became the ethos of my future in research.

Of all patients who come through the ERs at Detroit Receiving Hospital and Sinai Grace Hospital, 87% get discharged home. It may seem to surgeons that their emergency medicine colleagues consult them on every single patient, but I promise you that is not the case. We do discharge a handful of people. But most of the patients who go home are going to be at risk for hypertension, which we are not going to address in the emergency department, yet that visit to the ER may be the only encounter that patient has with any physician all year. It is incumbent on us at least to recognize the role we play in all of this.

Hypertension and Subclinical Target Organ Damage
Thinking about the life course trajectory, it occurred to me that subclinical target organ damage in the heart might be a way to better understand the impact of hypertension on population. With funding from Blue Cross–Blue Shield of Michigan, we took echocardiograms of people in the emergency department to better understand their early onset hypertensive heart disease and subclinical hypertensive cardiomyopathy. We found that almost 90% of patients with blood pressures >160 systolic and no prior history of heart disease already had structural changes in their heart by the time we did echos on them.

It was a little bit unheard of to start doing echos in the emergency department. John Flack, who was chair of Internal Medicine at the time and a big hypertension researcher, became my mentor. Here was an emergency physician, who started out doing acute heart failure trials, migrating in mentorship to the Chair of Internal Medicine because his specialty was hypertension! The important point to note from this is that cross-departmental or even cross-institutional mentorship may be critical to a successful research career. You are not limited in access to people in your university. There are a lot of people in other insti-
tutions who have similar interests and who would be delighted to be contacted, especially if you have fresh ideas and are not afraid to share them.

We designed a trial to reverse subclinical target organ damage. I submitted a proposal to the Robert Wood Johnson Foundation Physician Faculty Scholar Program, a program designed to foster early career development of researchers. We wrote a paper looking at lower blood pressure goals to try to improve subclinical target organ damage.\(^\text{14}\)

**Vitamin D and Subclinical Hypertensive Heart Disease vs. Better Blood Pressure Control**

Dr. Flack was interested in vitamin D, so we started to look at the relationship between vitamin D and subclinical hypertensive heart disease. I got my first National Institutes of Health R01 grant to look at this problem. We were doing cardiac MRIs with vitamin D supplementation in emergency department patients at a time when it was unheard of to take patients from the ER to get cardiac MRIs to look for structural abnormalities in subclinical hypertensive heart disease. That trial (see Figure 6, next page) found no benefit from vitamin D supplementation in this population—again, a negative but important finding.

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because someone like me, who has been there and done that, will be reviewing your grant applications at the NIH, and is going to look for that trajectory of success, that track record of prior work in the area.

I have now been on 25 different NIH study sections and reviewed hundreds of NIH grants. I myself learn a tremendous amount from the process but most importantly I am able to guide young grant writers because I know what their reviewer expects. I am one of those who writes the obnoxious comments that come back with your rejected application! Bear in mind that reviewers do not mean to be jerks, by the 10th grant in their tall stack of grants waiting to be read, it is hard not to be a little bit ornery!

Having decided to establish the literature on hypertension in the ER, we started looking at things like incidence of hypertension visits, and the issue of hypertensive emergencies—the assumption that everybody who comes to the ER with massively elevated blood pressure is in some critically ill state that needs an immediate intervention. We showed that in fact, that is not the case. Such cases are few and far between. Figure 7 (opposite) shows data we culled from national records.

We also started looking at whether lowering blood pressures in patients who come to the ER really did anything for them and whether there was really a benefit in sending to the ER a

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200/100 patient for a dose of Catapres (the answer is “No!”) What was the prognosis for completely asymptomatic patients as they climb that ascending trajectory towards early onset disease, subclinical target organ damage, and ultimately, clinical disease?

A problem with our medical community to some degree, and with our patient population for sure, is that patients tend to wait until there’s a problem. Patient: "I never had a problem before, so why did I have a stroke? How could I have a heart attack?" Doctor: "Well, I looked at your record, and eight years ago you were told you had hypertension and you never did anything about it," or, "We never did anything to support you in your life course to prevent this."

Root Causes
This takes us to back to content expertise: Furthering hypertension management in the emergency department and submitting papers to journals such as the American Journal of Hypertension to get the literature out there to help people understand what we are trying to do is one thing, but all the while, the deeply disturbing graph in Figure 8 (next page) lurks in the background. This graphic has become the single most important focus of my research; indeed, it constitutes the meaning of my career at this point. And it takes us back to consideration of the root cause of a problem.

We often think of unintentional injuries as the big problem in our population, but Figure 8 (next page) shows that age-adjusted mortality from heart disease is the real killer for Wayne County as a whole and the city of Detroit in particular. How can we live in a society in America where you have a community almost twice as likely to die of heart disease than anyone else, when the problem—underlying hypertension—is inherently treatable?

We age-adjust mortality to avoid comparing a community in, say, Florida, which has a large number of older folks, and conclude that its mortality rate is much higher than communities.
elsewhere. Age-adjustment accounts for the relative contribution of each age category to the mortality rate. Always, age-adjustment tends to reduce the raw mortality rate (especially in place such as Florida). But in Detroit, age-adjusted mortality for heart disease drives the rate up.

Why? Because young people are dying long before their time. In Detroit, not only are people dying more often, they are dying younger.

Years of potential life loss (YPLL) is an estimate of the average years a person would have lived if they had not died prematurely—essentially, a measure of premature mortality. It is three times higher in Detroit than in the rest of the state. That is a tragic disparity and a huge problem. We must think more broadly about a life course approach. We know that elevated blood pressure is the strongest modifiable risk factor for cardiovascular disease worldwide. This is not a mystery. We no longer need to prove that lowering blood pressure has beneficial effects. It is proven. In fact, we know we could save 94 million lives over the next 25 years if we got more people's blood pressure controlled, if we reduced sodium in their diets and got blood pressure treatment to at least 70% of the population (Figure 9, p.11).

But we are losing the battle. Figure 10 (p. 11) shows the trend in blood pressure control over the last ~20 years. On the left of the Figure is blood pressure control amongst all people with hypertension; on the right, amongst people on antihypertensive medications. We cannot even reach 50% of control amongst all hypertensives, let alone 60% or so amongst those who are on medications. Even more disturbing is that in the last few years we have begun to see a decline in hypertension control rates. The effective hypertension control rate in the city of Detroit is 18%.

The surgeon in the OR, taking care of a patient with an acute problem, is going to fix it immediately. But remember that at least 60% of Detroit's

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Three Public Health Interventions Could Save 94 Million Lives in 25 Years
Global Impact Assessment Analysis

<table>
<thead>
<tr>
<th>Effect of Hypertension Treatment on Systolic Blood Pressure</th>
<th>Percent of Patients With Hypertension Treated, %</th>
<th>Sodium Intake Reduction, %†</th>
<th>Number (Millions) of Deaths That Could Be Delayed (95% Uncertainty Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mm Hg</td>
<td>50</td>
<td>10</td>
<td>11.3 (10.1–12.5) 17.0 (15.1–18.8) 28.2 (25.2–31.3)</td>
</tr>
<tr>
<td>10 mm Hg</td>
<td>50</td>
<td>30</td>
<td>23.5 (20.7–26.2) 32.1 (27.8–36.0) 55.6 (48.5–62.2)</td>
</tr>
<tr>
<td>10 mm Hg</td>
<td>70</td>
<td>10</td>
<td>17.8 (16.0–19.5) 21.3 (20.5–22.3) 41.2 (37.3–45.2)</td>
</tr>
<tr>
<td>10 mm Hg</td>
<td>70</td>
<td>30</td>
<td>29.0 (26.4–32.8) 38.2 (33.5–42.4) 67.8 (59.9–75.2)</td>
</tr>
<tr>
<td>15 mm Hg</td>
<td>50</td>
<td>10</td>
<td>13.5 (12.1–14.9) 19.0 (18.0–21.4) 34.5 (31.1–38.0)</td>
</tr>
<tr>
<td>15 mm Hg</td>
<td>50</td>
<td>30</td>
<td>25.6 (22.6–28.4) 35.9 (31.4–40.1) 61.5 (54.6–68.5)</td>
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<tr>
<td>15 mm Hg</td>
<td>70</td>
<td>10</td>
<td>23.0 (20.8–25.2) 30.5 (27.8–33.3) 53.5 (48.6–58.5)</td>
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<tr>
<td>15 mm Hg</td>
<td>70</td>
<td>30</td>
<td>34.6 (31.1–38.2) 44.8 (39.9–49.5) 79.5 (71.0–87.7)</td>
</tr>
</tbody>
</table>

*Increasing hypertension coverage alone to 50% could delay 13.4 million (12.2–14.6) deaths if assuming a 10-mm Hg decline and 19.8 million (18.1–21.7) deaths if assuming a 15-mm Hg decline. With 70% coverage, the deaths delayed could be 26.7 million (24.3–29.2) with a 10-mm Hg decline and 39.4 million (35.9–43.0) with a 15-mm Hg decline.
†Reducing salt intake by 10% could delay 15.3 million (12.9–17.7) deaths, and reducing salt intake by 30% could delay 43.4 million (36.9–49.5) deaths globally.

Fig. 9. How To Save 94 Million Lives

JAMA | Original Investigation

Trends in Blood Pressure Control Among US Adults With Hypertension, 1999-2000 to 2017-2018

Paul Muntner, PhD; Shakia T. Hardy, PhD; Lawrence J. Fine, MD; Byron C. Jaeger, PhD; Gregory Wozniak, PhD; Emily B. Levitan, ScD; Lisandro D. Colantonio, MD, PhD

Fig 10. Trends in BP Control
predominantly black population has hypertension, so the patient is going to have other issues.

We have started to design a study of how to improve chronic hypertension amongst the emergency department patients without worrying about target organ damage—how to treat the root cause rather than the end organ manifestations of the complications that develop from untreated hypertension.

We recently completed an NIH-funded study of text message based interventions. The findings were neutral—just texting someone to remind them of their blood pressure or the need to take medications or whatever is not going to get to the root of the problem.

**Going To the Source**
To figure out what the community itself wants we did a project with the Robert Wood Johnson Foundation called the Hypertension Intervention Project ([Figure 11](#)). [Figure 12](#) shows a cohort of peer-to-peer educators we developed during the project—at the end of the study we invited them to a (low sodium!) dinner to talk about the results of the study and to recruit people to be part of a hypertension community advisory board to help us understand the problem as they saw it rather than as I saw it. I could then work on finding ways to get them to try to help fix the problem.

We started incorporating patient experiences not just into our care pathways but into the clinical trials. How do we know what people want and what they’ll be receptive to? It is an important thing to consider, as this quote from our paper argues:

“Patient centeredness is a concept that is increasingly being viewed as essential for clinical research. A core principle involves a comprehensive assessment and integration of patient and caregiver perspectives into trial design. Importantly, this involves more than just soliciting feedback. Patients and caregivers are now considered vital members of the study team, even serving as coinvestigators who may help to conceive, plan, and develop the study: continue to direct the day-to-day conduct of the study: and fully participate in the dissemination of the study results. The Patient-Centered Outcomes Research Institute offers substantial funding to support this approach, but getting started, particularly at institutions that lack a robust community engagement infrastructure, can be daunting. In this Special Communication, successful methods that have been used by researchers to engage patients, caregivers, and the broader health care community in the research process are outlined, and examples of currently funded studies that have fully engaged key stakeholders are described. Although trials are designed to assess efficacy and effectiveness and inform future implementation and dissemination, this Special Communication emphasizes methods to ensure trial results are relevant to and understood by the individuals and groups that they are intended to impact. Critical next steps in this new research approach are also discussed. In doing so, this will inspire future cardiovascular research that evaluates not only traditional end points, such as mortality and readmission, but also emphasizes true patient-centered outcomes, including quality of life, knowledge and satisfaction, caregiver burden, time tradeoffs, and out-of-pocket costs.”

It is also very important to know that while we may think everything in healthcare revolves around us, healthcare is in fact responsible for only about 20% of the total outcomes in patients (see [Figure 13](#), p.14). That is because so much

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19 Source: Buis et al. Text Messaging to Improve Hypertension Medication Adherence in African Americans From Primary Care and Emergency Emergency Department Settings: Results From Two Randomized Feasibility Studies. JMIR Mhealth Uhealth 2017:5:e9.

Improving Blood Pressure Among African Americans With Hypertension Using a Mobile Health Approach (the MI-BP App): Protocol for a Randomized Controlled Trial

Lorraine R Buis¹, PhD; Katee Dawood², BS; Reema Kader³, MLIS; Rachelle Dawood³, BA; Caroline R Richardson⁴, MD; Zora Djuric⁵, PhD; Ananda Sen¹, PhD; Melissa Plegue⁶, MA; David Hutton⁷, PhD; Aaron Brody⁷, MD, MPH; Candace D McNaughton⁸, MD, PhD; Robert Brook⁸, MD; Phillip Levy⁴, MD, MPH

Fig. 11. Blood Pressure Trial Protocol

Fig. 12. Community Blood Pressure Educators
more happens to the patient at home and in other settings than ever happens at the doctor’s office or hospital room or ER bay. We may deliver the best care in the world to our patients, but then there's everything else going on in their lives. If a patient must decide between paying for our prescription or putting food on the table (or buying their kids books for school, or Christmas presents, or whatever) our care may be to little avail.

The Exposome
We tend to throw social determinants around as if they are the most important thing in health care, and they really, really are! But how do we do something about it? We have to start to understand what these things are. Health behaviors are dependent on socioeconomic factors, on the physical environment that a person comes from, and so on. In my experience, surgeons at my institution get that. They do the right thing for the patients we care for in the ER, every single time. “Social admit? No problem. Person can't get the care they need? No problem, we'll take them on our service.” I've always admired that about our Department of Surgery. It is built into the ethos of who they are, and I thank them for that.

But the exposome (Figure 14) is not simply the patient—it is everything that goes into them, goes on around them, and goes on inside them (transcriptomics, proteomics, metabolomics, genomics, and so on21). In their specific external environment, what is a patient doing? Do they smoke, exercise, eat healthy food? Do they have enough water? What is going on around them? Do they live in a polluted area, with tons of PM 2.5 in the air they breathe? Do they live in an area with no recreational facilities? Do they have the social capital in their neighborhood to get (or offer) help if there's a problem?

21 For example, we talk about things like salt-sensitive hypertension, which only manifests with a high sodium diet. Avoiding a high sodium diet avoids the consequences of what is presumed to be a genomic predisposition towards hypertension.
PHOENIX
Understanding the exposome marks a transition in my career right now. We have started developing PHOENIX, the Population Health Outcomes aNd Information Exchange, whose goal is to understand all of these factors so that we can understand the exposome of the person and also aggregate information geospatially, to understand where a community’s greatest risk exists and incorporate other data points to look at the upstream mediators and moderators of the risks that we’re seeing. Figure 15 below shows the PHOENIX model.

When a community has a high rate of stroke, it is not just a high rate of stroke in the community; it is uncontrolled blood pressure and all the social factors that contribute to it. If we want to engineer a solution to that problem, it is not going to be rapid detection of stroke, yet that is what we focus on often in hospital-based healthcare today. The solution really lies upstream. To prevent strokes, we have to treat hypertension; and to treat hypertension, we have to manage the social factors that contribute to it.

PHOENIX is our way of doing this. It originally started with understanding blood pressure and its impact on cardiovascular disease. We knew that at the population level, lowering blood pressure by 1 or 2 or 5 millimeters of mercury has a dramatic impact on health outcomes. It is not the individual going from 136 to 134; it is an entire population going from 140 to 138 or 135. That has a huge impact on health outcomes. But how do you measure a population’s blood pressure? The emergency department takes everyone’s

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blood pressure. By aggregating ED data and integrating it with data on social factors, we would know where to target interventions upstream.

**Figure 16** below shows the result of aggregating health data, social determinants, community event data, and potentially cell phone generated data, aligned geospatially and temporally so that we know where and when, at any given point in time, circumstances exist. We can then track everything, over time, passively, because we have the data feeds. Specifically, Figure 16 shows the deviation in years of average life expectancy in the state of Michigan. The average in Michigan is 77.7 years. In parts of the city of Detroit people are dying 12 to 15 years younger than the national average. Pretty much across the city of Detroit, people are much more likely to die at a much younger age than the state average. That would be unacceptable anywhere, and should be unacceptable especially in America.

Using PHOENIX, we have begun to try to understand what is going on. **Figure 17** (opposite) shows our hypertension surveillance dashboard, reporting (at the time) 552,000 emergency department encounters between Henry Ford and the Detroit Medical Center, aggregated by census tract and mapped out across the city. We're now at almost 2 million encounters mapped out in this way. This approach will not fix the individual person directly, but may do so indirectly through fixing the problem at the population level. It is about how to help everyone overall.

In the tract where the Detroit Medical Center sits, we aggregated data from 4,500 ER visits over 26 months, The mean blood pressure was 137, which is way too high. Forty-five hundred visits from a community with just 2,100 residents amounts to almost two ER visits per person, whose median age is 29 with a blood pressure of 137. If you don't think those are going to be tomorrow's strokes and kidney disease patients
and heart failure patients, you are sorely mistaken, because they will be.

The social factors that exist in that community include $14,000 median household income, 61% of families living below poverty, 96% black, and 35% unemployed, but only 12.5% uninsured, so there are opportunities there. We need to think about how we can reach that population. The area deprivation index (a standardized measure of deprivation and general social context of the population being cared for) is the worst it could possibly be.

We built PHOENIX with funding from the Michigan Health Endowment Fund, which was matched by the Wayne State University School of Medicine, amounting to about a million dollars. Data contributors include the DMC ERs, Loveland Technologies (now ReGrid), the Detroit East Medical Control Authority (DEMCA), EMS, the Wayne County Medical Examiner, the Michigan Poison and Drug Information Center, the Michigan Department of Corrections, the Michigan Department of Health and Human Services, and MIHIN (the Michigan Health Information Network, the state’s health information exchange). Hospital and clinic data for every single patient in Michigan is aggregated and shared with MIHIN, so there is an aggregated record of all health encounters wherever they may have occurred.

We are working to leverage this information not just for Detroit but also beyond. We are working with the Cloud Platform team in Google’s Detroit office to build an infrastructure where we can automatically ingest multiple data streams, put them into a common aggregator called Big Query, and produce a trove of information that will enable us to do really cool things like aggregate Google Maps data on doctors offices, pharmacies, and dentists to try to understand to what extent those factors contribute to a given neighborhood’s health outcomes. (Figure 18, p.19) shows the process model.)

We will then be able to stop thinking purely in terms of census tracts (of which there are 297 in the city of Detroit) and instead conceptualize “social tracts”. Even neighborhoods that are ge-
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...ographically proximate may have very different social factors or built environment factors. For example, bus stations, commerce locations, and physician’s offices may cluster in one location but be rare in a neighboring location. If they are rare, where do people go? If they are sick but have nowhere to go, they are going to call an ambulance and come to the ER. To prevent ER over-utilization we must reach out to those communities. How do we know what communities to go to? By looking at the maps we are generating.

Double Whammy and a Silver Lining

While we were building PHOENIX, all of a sudden COVID struck. People started dying from it, not because COVID was indiscriminately causing death to people in Detroit because of the color of their skin but because the virus was super-imposing physiologic stress on an already stressed physiology in people with not as much physiologic reserve to withstand the virus compared to other populations.

In other words, a disparity condition that already existed—a community where people are dying 12 to 15 years earlier than people in other communities because of uncontrolled hypertension and heart disease—was being exacerbated through an adverse interaction with a virus. What could we do about this? To find out, we needed to get into the communities where the problems were occurring. We needed to find these people before they developed complications with COVID, we needed to get out there and start testing people. We already offered screening, focusing initially on healthcare workers and first responders, at Wayne Health in Detroit and at Access in Dearborn, but we knew we had to get out into the community.

We were fortunate that PHOENIX was already running. (That is an important point about research: It may have no immediate impact but it may lay a foundation for other things later.) PHOENIX was a perfect foundation for action when the pandemic struck. We started creating maps incorporating social vulnerability before...
The Wayne State University Phoenix Data Warehouse and Ingestion Platform in Google Cloud

Fig. 18. PHOENIX Process

Fig. 19. Areas at Risk
Internet bandwidth and the technology for effective telehealth. The COVID death rate was highest in North Central States yet Michigan was one of the worst in terms of uptake of telehealth. Nationally, hypertension management suffered and blood pressures rose. We were setting ourselves up for the next wave of people who would be not only more likely to develop complications but also less likely to be physiologically resilient when the next variant or the next virus arrived.

Our data showed us that the Sinai Grace neighborhood had a high density of COVID cases and a high density of hypertension. We knew early on that mortality risk corresponds to extreme social vulnerability and that if we wanted to reduce mortality we had to get out into communities. Since we were already going into neighborhoods to test for COVID, we began to develop portable population health solutions to the root cause. In other words, we did not just want to treat COVID but also to solve the root causes of disease. We were already doing COVID antibody testing because the community wanted it. If we were going to stick needles in arms to do this, why not simultaneously measure lipids, hemoglobin A1C, basic metabolic profiles, and screen for HIV?

And while we’re at it, why not bring in patient navigators and community health workers to tackle the social factors contributing to poor health? They might find someone COVID positive living in a home with six other people unable to isolate, and if so be in a position to give them resources. A lot of people have food insecurity, so they could offer fresh produce to people in need. Figure 21, also featuring early versions of the Ford vehicles, shows us doing just that in Hamtramck, a small town enclave virtually surrounded by the city of Detroit.

We became a pillar of the state of Michigan’s Racial Disparity Task Force and a centerpiece for how the state is addressing COVID and its impact on black and brown communities. The state of Michigan gave us $4.5 million to purchase new vehicles (on the left in Figure 22) that have medical grade refrigeration built in and power inverters for blood centrifuges and other equipment.

The Healthcare Encounter: A New Paradigm
We have reimagined what healthcare is. Healthcare does not have to mean waiting in a doctor’s office for 40 minutes for a 15 minute encounter when all you really want is your blood pressure to be taken and your bloodwork done. So we started to think of healthcare differently. Could we take healthcare as a whole—not just COVID—to people? Could we bring care to neighborhood locations and make them the destination of the care, particularly preventive care?

We are probably never going to doing surgery in the back of these vehicles. That is not the intent. The point is just to think differently. The pandemic has challenged all of our thinking and has allowed us (hopefully) to think differently about what we want going forward. Part of our response has been to write about it: Our paper published recently in PLOS ONE: “Pandemic response to portable population health” is an example. As part of the formative evaluation we were able to show that our data-driven deployment approach enabled us to get from a base of about 20% of people from vulnerable communities early on, to almost 45% today and rising. Our approach gets us into the neighborhoods to help people with their problems.

We evolved from nasal swab testing to antibody testing to all of the other activities shown in Figure 23. We are now close to 74,000 encounters in the field (see the dashboard at Figure 24) and we have 10 vehicles. We continue to get a lot of funding—already more than $40 million in just 16 months, a mix of philanthropy, state funding, and grant funding—and other valuable support.

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Fig. 20. Mobile Health 1.0

Fig. 21. Mobile Health 2.0

Fig. 22. Mobile Health 3.0
We not only do testing and vaccinations but also provide social services. We have community health workers and navigators on site. We've done more than 2,500 social services in the field. People come to get COVID tested and walk away with a link for food assistance or public benefits or whatever they need. (See Figure 25.)

We continue to evolve the model. We have been doing blood pressure screening (more than 3000—see Figure 26) and I'm proud to say that we recently published in the journal *Hypertension* our concept of using mobile units for mass population screening and hypertension.

We started screening the population not using auscultatory methods but OMRON Hem 907XL IntelliSense Professional Digital Blood Pressure Monitor, determined during the SPRINT trial to be the definitive way to measure blood pressure. At the push of a button, it measures three blood pressures unattended and averages them, resulting in a much more accurate measure of blood pressure. We use it in the field, in our fleet of mobile health vans. This has never been done before. We have found that only 37% of the people we test (young and old) have normal blood pressures, and 57% have hypertension, either untreated or ineffectively treated.

We are now also conducting blood tests. Of 1,100 tests to date, 35% revealed previously undetected high cholesterol (see Figure 27, p.24). 55% of the black population we test has chronic kidney disease and does not even know it. EGFR (a measure of kidney function) is less than 90. We are getting to the point where we can actually enable mass screening out in the community with a vision towards coming up with a meaningful solution for this population health problem. We have written about cardiometabolic risk factor control during times of crisis and beyond.24 This aligns with what the Surgeon General is pushing for (see Figure 28, p.25.)

**Full Circle**

Controlling hypertension is the single most important population health risk we face as a medical community. Taking our data around hypertension and transitioning from controlling COVID as the outreach mechanism to controlling hypertension as the outreach mechanism brought us full circle back to where all of this started; namely, how better to treat the end manifestation of uncontrolled hypertension.

Working with colleagues at NYU, the university of Alabama/Birmingham and several other sites, we successfully submitted a $20 million proposal to the American Heart Association’s Health Equity Research Network grant mechanism, the first of which focused on efforts to prevent hypertension (Figure 29, p.25). Our project within that network is called LEAP HTN, which has the goal to reach people with elevated blood pressure before they develop hypertension, using geospatial analysis to enhance mobile outreach, factor in the known social factors, and give people choices (Figure 30 p.27). By helping an at-risk person on their journey, helping them understand the risk factors they face, we may be able to do something different in terms of changing the outcomes.

Being part of the AHA network encouraged us be even more ambitious. We submitted a proposal to the NIH for a P50 Specialized Center Grant (which is often a career-defining achievement, the equivalent of three RO1s). P50s are awarded for individual or independent investigator research projects, the holy grail for researchers. Three of our projects, collectively known as ACHIEVE GREATER (Addressing Cardiometabolic Health Inequities by Early PreVEntion in the GREAT LakEs Region) and based on the concept of lifespan equality, were funded (see Figure 31, p.27). Life expectancy is the average age of death in a population. Lifespan equality is the variance in the average age of death by

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24 Brook, Levy, and Rajagopalan. Cardiometabolic Risk Factor Control During Times of Crises and Beyond. https://doi.org/10.1161/CIRCOUTCOMES.120.006815
Fig. 23. Tests Offered

<table>
<thead>
<tr>
<th>Service</th>
<th>Start Date</th>
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<tbody>
<tr>
<td>SARS-CoV-2 Nasal Swab Diagnostic Testing</td>
<td>3/20/2020</td>
</tr>
<tr>
<td>SARS-CoV-2 IGG Antibody Testing</td>
<td>4/28/2020</td>
</tr>
<tr>
<td>HIV Testing</td>
<td>5/19/2020</td>
</tr>
<tr>
<td>Hypertension Screening</td>
<td>6/6/2020</td>
</tr>
<tr>
<td>Other Serology Testing (A1c and lipid panel)</td>
<td>9/26/2020</td>
</tr>
<tr>
<td>Linkage to Care for Social and Medical Services</td>
<td>10/1/2020</td>
</tr>
<tr>
<td>COVID-19 Vaccinations</td>
<td>3/15/2021</td>
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Fig. 24. Dashboard

Fig. 25. Social Services Delivered

<table>
<thead>
<tr>
<th>Referral Category</th>
<th>Program Totals</th>
<th>2021 Total</th>
<th>Q1 2021</th>
<th>Q2 2021</th>
<th>Q3 2021</th>
<th>Q4 2021</th>
<th>Number of Follow ups attempted</th>
<th>Number of Followups Completed</th>
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</thead>
<tbody>
<tr>
<td>Number of individuals assisted with social service referrals onsite</td>
<td>2525</td>
<td>1259</td>
<td>662</td>
<td>291</td>
<td>214</td>
<td>92</td>
<td>2018</td>
<td>1211</td>
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<td>Food Assistance</td>
<td>862</td>
<td>436</td>
<td>258</td>
<td>77</td>
<td>68</td>
<td>33</td>
<td>628</td>
<td>371</td>
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<tr>
<td>Public Benefits Assistance</td>
<td>429</td>
<td>193</td>
<td>137</td>
<td>34</td>
<td>15</td>
<td>7</td>
<td>324</td>
<td>170</td>
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<tr>
<td>Unemployment Assistance</td>
<td>359</td>
<td>153</td>
<td>110</td>
<td>33</td>
<td>8</td>
<td>2</td>
<td>289</td>
<td>161</td>
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<tr>
<td>Navigator Services (Health Insurance Navigation)</td>
<td>242</td>
<td>108</td>
<td>52</td>
<td>22</td>
<td>27</td>
<td>7</td>
<td>166</td>
<td>96</td>
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<tr>
<td>Utility Assistance</td>
<td>136</td>
<td>90</td>
<td>10</td>
<td>18</td>
<td>47</td>
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<td>Voter Registration</td>
<td>47</td>
<td>10</td>
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<td>0</td>
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<td>25</td>
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<td>PCP Referral *</td>
<td>116</td>
<td>94</td>
<td>9</td>
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<td>Transportation Assistance</td>
<td>39</td>
<td>10</td>
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<td>0</td>
<td>10</td>
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Fig. 26. BP Screening

<table>
<thead>
<tr>
<th>Categories</th>
<th>Number (%)</th>
<th>BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>3,039</td>
<td>126.9 ± 23.1 / 76.6 ± 14.7</td>
</tr>
<tr>
<td>Normal BP</td>
<td>1136 (37%)</td>
<td>105.5 ± 9.28 / 65.0 ± 8.34</td>
</tr>
<tr>
<td>Systolic BP &lt;120 and diastolic BP &lt;80 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High BP Categories**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated BP</td>
<td>306 (10%)</td>
<td>124.2 ± 2.8 / 70.1 ± 6.44</td>
</tr>
<tr>
<td>Systolic BP 120-129 and diastolic BP &lt;80 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension categories***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP ≥130 and/or diastolic BP ≥100 mm Hg</td>
<td>1597 (53%)</td>
<td>142.7 ± 19.39 / 86.4 ± 12.43</td>
</tr>
<tr>
<td>Stage I</td>
<td>629 (21%)</td>
<td>127.7 ± 8.73 / 80.3 ± 6.84</td>
</tr>
<tr>
<td>Systolic BP 130-139 and/or diastolic BP 100-119 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>968 (32%)</td>
<td>152.4 ± 18.15 / 90.4 ± 13.6</td>
</tr>
</tbody>
</table>
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communities. As we saw earlier, it is a huge consideration and concern in the city of Detroit. To change it, we must think about how to do things differently, and reaching people before they have hypertension is certainly different. Project 1 will reach people with stage 1 hypertension and project 2 will reach those with stage 2 hypertension.

Project 3 will be in collaboration with colleagues in Cleveland who are looking at screening for coronary heart disease by offering free coronary artery calcium screening in the community. They have done three studies in over 60,000 people, but only 5% of the population they reached was black and impoverished. Our focus is to take it to the population that really needs it. Cleveland has very similar problems to Detroit, which is not surprising since Cleveland and Detroit have similar socioeconomic circumstances (see Figure 32, p.28).

A grant reviewer’s comment "Very effective use of graphics and data” is always gratifying and Figure 32 is the kind of graphic they mean. How could anyone argue with the need for action when every single metric is far worse in Detroit, and almost as bad in Cleveland, than it is nationally. This is the compelling data that makes a research proposal successful.

Health care should not be about "profiteering" on the ills of the population; it is recognizing the problems for what they are and proposing creative interventions. Our proposed solution is PAL2—Personalized, Pragmatic, Adaptable Approaches to Lifestyle and Life circumstance. It is critical, as providers, for us to acknowledge life circumstance because we often tell patients "You should do this!” “You need to do more for your blood pressure!” “You need to take your medications!” “You need to stop salt!” “You need to exercise!” Too often, we berate them, without any idea of whether their circumstances will allow them to comply or not.

By incorporating things like life circumstance we can better understand if a change of caregiver will help. Why not let community health workers—folks from the community who are trained and share and understand the circumstances and speak the same language—be the primary caregiver? That has become our fulcrum going forward.

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Fig. 27. Blood Testing
As a physician, I’ve seen firsthand the devastating effects of hypertension. Left uncontrolled, it leads to heart attacks, stroke, kidney disease, and cognitive decline in later life, and it can impact mother and baby during and after pregnancy. In addition, as evidenced from the global COVID-19 outbreak earlier in the year, we’ve seen the broad impact of preventable health conditions on worse outcomes.

Hypertension is unfortunately common, but there are interventions and programs that have been successful in improving control. Our country has many hypertension control champions—doctors, practices, communities, and health systems that have excelled at achieving high rates of hypertension control among their patients. We need to learn from their many years of “blood, sweat, and tears” and apply their principles in new settings.

While hypertension is more prominent among older adults, it is not simply a condition of the elderly. All ages are impacted, and early identification and long-term control can preserve cardiovascular health now and into the future. We know that lifestyle changes, such as being physically active and adopting a healthy diet, can promote hypertension control, yet many communities have significant barriers that prevent people from making these changes. We also know that many people with hypertension require medications to achieve control. Access to high-quality health care, prescription of appropriate medications, and clinical and community support are needed to prevent and treat hypertension, publicize local resources, and establish a plan for care supportive of long-term control.

The Surgeon General’s Call to Action to Control Hypertension summarizes recent data on hypertension control, identifies select goals and strategies, and provides recommendations for areas of focus when resources are limited. While the recent trends don’t look good—we’ve hit a plateau in hypertension control—I believe that with focus and collaboration, we can improve our trajectory.

Join me in taking control of hypertension across our nation. Together, we’ve got this!

Jerome M. Adams, MD, MPH
Vice Admiral, U.S. Public Health Service
Surgeon General
U.S. Department of Health and Human Services

Fig. 28. Surgeon General’s Call for Action

$20M awarded for scientific research to ensure health equity in preventing hypertension

Teams from Beth Israel Deaconess Medical Center, Johns Hopkins University School of Nursing, NYU Grossman School of Medicine, University of Alabama at Birmingham and Wayne State University receive American Heart Association research grants to study high blood pressure prevention in underrepresented populations

Fig. 29. A Major Award
**Conclusion**

A Chinese proverb holds that the best time to plant a tree is 20 years ago, and the second best time is now. Building a research career is a long game but there is no cause to be so intimidated as not to start playing the game. Another Chinese proverb says that a journey of a thousand miles starts with a single step. The hardest thing is taking that step. Once you realize your interest in research, take that step—reach out, make that phone call or text message, or ask your attending or your senior resident: "What do you think of this?"

I hope that knowing what it looks like to achieve success in the academic world will encourage, not daunt, the budding researcher. The single most visible sign of success is NIH funding, and the surest way to NIH funding is through publication. I routinely publish on average 20 to 40 publications a year, by no means always as lead author. The number of your publications is an indicator not only of your research success, but of your recognition as a content expert in the area.

It is important to recognize that research is a team game. There have been no independent investigators in any investigation I have ever been involved in. You have to work with people and the number of collaborators you have and different journals that you publish in is a measure of the breadth and depth of your research. As you get broader and deeper you will be invited to things such as NHLBI Centers, and ultimately you will be appointed to such posts as vice chair of chest pain guidelines or something that really represents all of your hard work over your career. It is publish or perish, but you can enjoy the journey!

Love and work are to people what water and sunshine are to plants. I love the work that I do. I've never been happier in my career than now, and I would not be where I am today had I not chosen a path of research. It is not that I could not do the work in emergency medicine (as taxing, draining, and mentally challenging as it is).
Fig. 30. LEAP-HTN

Fig. 31. ACHIEVE GREATER
### Fig. 32. Detroit and Cleveland vs. the National Average

<table>
<thead>
<tr>
<th></th>
<th>Detroit</th>
<th>Cleveland</th>
<th>Nat’l Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children in poverty (%)</td>
<td>52.2</td>
<td>50.9</td>
<td>20.4</td>
</tr>
<tr>
<td>Income inequity score</td>
<td>-39.6</td>
<td>-39.6</td>
<td>-1.1</td>
</tr>
<tr>
<td>Racial segregation score</td>
<td>40.3</td>
<td>32.5</td>
<td>10.9</td>
</tr>
<tr>
<td>Unemployment (%)</td>
<td>18.6</td>
<td>9.0</td>
<td>6.8</td>
</tr>
<tr>
<td>3rd Grade reading proficiency (%)</td>
<td>19.2</td>
<td>22.8</td>
<td>46.2</td>
</tr>
<tr>
<td>Violent Crime (per 100,000)</td>
<td>1900.4</td>
<td>1439.3</td>
<td>436.1</td>
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<tr>
<td>Air pollution (PM2.5)</td>
<td>9.7</td>
<td>9.6</td>
<td>8.5</td>
</tr>
<tr>
<td>Housing w/ Lead Risk (%)</td>
<td>44.2</td>
<td>47.6</td>
<td>17.6</td>
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<tr>
<td>Limited access to healthy food (%)</td>
<td>48.3</td>
<td>46.6</td>
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<tr>
<td>Smoking (% adults)</td>
<td>28.9</td>
<td>27.8</td>
<td>16.7</td>
</tr>
<tr>
<td>Physical inactivity (%)</td>
<td>37.6</td>
<td>36.9</td>
<td>23.9</td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>43.6</td>
<td>42.7</td>
<td>30.4</td>
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