

# Making an Impact in Public Health through Philanthrocapitalism: The PaCT Project and ImPaCT Commercial Ventures

By  
**TODD G. REID**

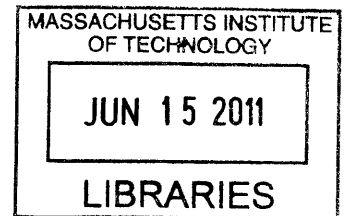
Sc.D. Nutrition Epidemiology  
Harvard University, School of Public Health, 2010

SUBMITTED TO THE MIT SLOAN SCHOOL OF MANAGEMENT IN PARTIAL FULFILLMENT  
OF THE REQUIREMENTS FOR THE DEGREE OF  
MASTER OF BUSINESS ADMINISTRATION  
AT THE  
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

JUNE 2011

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# **Making an Impact in Public Health through Philanthrocapitalism: The PaCT Project and ImPaCT Commercial Ventures**

By

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**Submitted to the MIT Sloan School of Management  
on May 6, 2011 in partial fulfillment of the  
requirements for the Degree of  
Master of Business Administration**

## ABSTRACT

Large-scale epidemiologic longitudinal cohort studies are a distinct area of epidemiology and public health. To conduct such studies, it often requires exorbitant resources.

African collaborators and a team of Harvard scientists have initiated what is groundbreaking to the field of epidemiology and will be the largest investigations into lifestyle ever conducted in history: **The Africa/Harvard School of Public Health Partnership for Cohort Research and Training (PaCT)**, a four-nation, large scale longitudinal cohort study comprising 500,000 study participants in Uganda, South Africa, Tanzania, and Nigeria, investigating lifestyle factors and their relation to chronic diseases( i.e., cancer, heart diseases, mental illness, diabetes, etc.).

This cohort study will be paired with an innovative philanthropic venture capital firm, ImPaCT Commercial Ventures. This business entity will be responsible for the commercialization of the intellectual property (IP) generated from the cohort study, decades-long collection of behavioral and genetic “Big Data” (primarily collected through mobile phones) from the study’s 500,000 study participants. A select group of corporations will have semi-exclusive rights to the intellectual property to create and refine innovative products (goods and services) that help prevent chronic diseases and other public health threats in Africa, and they will also serve as limited partners in the ImPaCT Commercial Fund. This venture Fund will support a portfolio of entrepreneurial start-up ventures that also develop innovation around chronic disease prevention. ImPaCT will profit from this commercialization of IP and by equity ownership in the start-up ventures. ImPaCT, structured as a “Benefit” Corporation, will earmark some of its profit to help sustain the resource-intensive and expensive longitudinal cohort study.

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## I. Introduction

**Large-scale epidemiologic longitudinal cohort studies** are a distinct area of epidemiology and public health. To conduct such studies, it often requires exorbitant resources. Teams of specifically skilled epidemiologists and statisticians manage the studies and hundreds of thousands of people are recruited and followed over time for the collection of scientifically sound data on individuals' lifestyle and behaviors as the participants develop diseases. These behaviors are then analyzed to assess their associations with disease outcomes.

**Venture Capital (VC)** is a distinct business model and is a subset of private equity, targeted financial investment to help nurture the expansion of companies, new product development, and restructuring of a company's operations, management, and ownership. VCs provide financial investment to early-stage, high-potential startup companies. The Venture Capital Fund is a financial group that amasses relatively large sums of money and invests this capital in promising startup companies and makes a profit by owning equity in the companies in which it invests.

This body of work serves as a blueprint for how the two methods can be compatible and, when combined, synergistically the sum is greater than the parts, helping to better and more rapidly translate public health research into practice.

## II. Overview of the PaCT research project

Overshadowed by a burden of chronic diseases similar to that seen in high-income countries, a menacing epidemic of heart disease, cancer, mental illness, diabetes, and obesity is growing in Africa. World Health Organization projections for Africa show chronic diseases outstripping infectious diseases in the coming years and causing 46% of deaths by 2030 if nothing is done.

In conjunction with African colleagues, a team at the Harvard School of Public Health has begun an ambitious project to start cohort studies that include 500,000 participants across Nigeria, South Africa, Tanzania, and Uganda. Researchers have spent the last four years laying the groundwork for what we are convinced is groundbreaking in the field of epidemiology and will be the largest investigation into lifestyle ever conducted in history: **The Africa/HSPH Partnership for Cohort research and Training (PaCT)**. The scientific team has met with the ministers of health in the four PaCT nations, have

developed a superb team of African collaborators, and created staff centers in each country where pilot studies are already underway. National samples of schoolteachers will form cohorts in South Africa and Tanzania, while Nigeria will recruit physicians and nurses. Complimenting these more educated groups will be participants from peri-urban and rural locations in Uganda. With this varied group of participants, some of the social, economic, ethnic, and lifestyle diversity in Africa will be captured.

Innovative technology will be used to keep costs down. Cell phones—widely used across all of Africa—will be used to retrieve data and conduct follow-up surveys with participants. A comprehensive biologic bank will be created to enable cutting edge genetic molecular studies. As has been the case with cohort studies in the United States, PaCT will provide a fertile training ground in innovative research, create viable career paths for African scientists, help spur innovation and entrepreneurship, and foster collaboration between African countries as well as with more developed ones.

### **III. Background and Significance**

#### *What are Cohort Studies and Why They are Useful*

Longitudinal cohort studies track changes in risk factors over time and provide information on the burden of disease. These studies enroll tens of thousands of people who are asked questions about what they eat, how much they exercise and smoke, and their family and reproductive histories. These prospective studies can be used to investigate, simultaneously, multiple complex diseases and their risk factors over an individual's lifetime. Participants of the studies are enrolled then followed and tracked for decades to collect additional information and data.

Harvard has been a world leader in designing and analyzing cohort studies, the results of which inform health policy and the design of important prevention programs, and have proven to be crucial in the understanding of the etiology, course, and outcome of some chronic diseases in the US and in other populations. For example, one of Harvard's cohorts, the Nurses' Health Study, which has studied 121,700 nurses for 33 years, has added critical knowledge about the heart-clogging effects of trans-fat, common in processed foods. Those findings instructed food labeling and restaurant laws across the world. Additionally, cohort studies are an incomparable resource for the teaching and training of public health researchers and practitioners. As such, cohort studies are considered long-term investments in public health, as the payoff for them comes over time – expanding often across decades.

#### *Why Cohort Studies are Important for Africa*

HIV/AIDS has been a major health burden in sub-Saharan Africa. Indeed, much of the

public health efforts in sub-Saharan Africa have focused almost exclusively on it and other communicable diseases like TB and malaria, until recently. Many developing countries continue to experience high burden of infectious diseases and injury while simultaneously experiencing an epidemiologic transition where disease patterns are shifting more toward diseases more chronic in nature. This is the case in sub-Saharan Africa. Africa, home to nearly one billion people, however, has no similar large epidemiologic studies investigating the burden of chronic diseases. And the argument that sub-Saharan Africa lacks the sufficient resources to respond to this problem has been established; cohort studies will help better access the magnitude of the problem as well as determine the specific patterns of non-communicable chronic diseases (NCDs) in the African context.<sup>1</sup>

It is important to study these diseases in Africa as scientific findings from Europe and the US may not be applicable. Characteristics and behaviors of the population such as diet, history, and other cultural practices are location specific. Moreover, although cohort methodology has been developed in North America and Europe, high-income countries, in turn, may also gain from knowledge derived from such studies conducted in Africa. The obesity epidemic in the West, for example, is in advanced stages, but we have yet to apply our knowledge to creating interventions that can have a substantial impact.<sup>2</sup>

Africa's genetic diversity and the fact that higher prevalence of diseases such as HIV and TB coexist with NCDs are additional important reasons why cohort studies need to investigate NCDs in Africa. East Africa is the cradle of early human evolution, therefore genetic diversity in Africa is greater and investigating gene-environment interaction helps elucidates mechanisms of disease<sup>3</sup>. When Africa's extended range of cultural practices and wide-ranging historical circumstances are coupled with this genetic diversity, enormous opportunities for scientific discovery can exist<sup>4</sup>.

In order to address this impending global health crisis and manage the burden of non-communicable chronic disease, five recommended cost-effective interventions have been proposed to be affordable in almost all countries (see figure 1).<sup>5</sup> These include Tobacco control, Reduced consumption of dietary salt, increased physical activity and healthier dietary habits to prevent obesity, and reduced alcohol consumption.

Table. Estimated costs of five priority interventions for non-communicable diseases (NCDs) in three countries<sup>16</sup>

Interventions		Cost per person per year (US\$)		
		China	India	Russia
1. Tobacco use	Accelerated implementation of the WHO Framework Convention on Tobacco Control <sup>9</sup>	0.14	0.16	0.49
2. Dietary salt	Mass-media campaigns and voluntary action by food industry to reduce consumption <sup>9</sup>	0.05	0.06	0.16
3. Obesity, unhealthy diet, and physical inactivity	Mass-media campaigns, food taxes, subsidies, labelling, and marketing restrictions <sup>16</sup>	0.43	0.35	1.18
4. Harmful alcohol intake	Tax increases, advertising bans, and restricted access <sup>13</sup>	0.07	0.05	0.52
5. Cardiovascular risk reduction	Combination of drugs for individuals at high risk of NCDs <sup>10</sup>	1.02	0.90	1.73
Total cost per person*	..	1.72	1.52	4.08

Figure 1. Cost-effective Interventions for NCDs

Lancet

### *Economic Development in Africa*

It is a fact that future global economic growth will increasingly come from emerging markets. A series of reports from *Mckinsey & Company* on Africa's economic development posit that emerging markets on the African continent will be no exception. Now more than ever, sub-Saharan Africa offers a more robust platform for profitable new investments<sup>6,7</sup>. In order to remain relevant and stay strategic, businesses are looking for new markets in which to invest and Africa's changing demographics will have significant implications for productivity and demand. Having historically been associated with civil unrest, poor governance and infrastructure, weak institutions, and other difficulties, sub-Saharan Africa will be a major contributor to global successes<sup>7</sup>.

Before the economic crisis, sub-Saharan Africa experienced rapid growth, with an average annual growth rate of 6 percent between 2002 and 2008. The region is proving more resistant to the global economic downturn than most other parts of the world. It is projected to grow by 3.8 and 4.5 percent in 2010 and 2011, and this growth is faster than Europe, Latin America, and Central Asia. Africa's collective GDP, at \$1.6 trillion in 2008, is roughly equal to that of Brazil or Russia and the continent is among the most rapidly growing economic regions in the world<sup>7</sup>.

The following series of milestones and figures represent the flourishing economic development in sub-Saharan Africa<sup>6</sup>:

Botswana, Cape Verde, Ghana, Kenya, Mauritius, Mozambique, Namibia, Seychelles, Zambia, **Nigeria**, **South Africa**, **Tanzania**, and **Uganda** are all now considered frontier



emerging economies with increasingly developed markets.

From 2000 through 2008, real GDP rose by 4.9 percent a year, more than twice the pace of growth experienced during the previous decade. Banking, construction, telecommunications, private-investment, and retailing are all thriving, and privatized state-owned enterprises have opened up more trade, lowered corporate taxes, and have provided critical social and physical infrastructure.

Africa is also gaining increased access to international capital. The annual flow of foreign direct investment into Africa is, relative to GDP, almost as large as the flow into China, increasing from \$9 billion in 2000 to \$62 billion in 2008. Since 1990, sub-Saharan Africa has almost tripled its level of exports and diversified its trade and investment partners. While the combined share of its exports to the United States and the European Union decreased from 73 percent to 49 percent, Chinese imports alone from sub-Saharan Africa increased 200-fold from \$64 million to over \$13 billion.

Because of Africa's abundance of natural resources, as expected the continent's resource sectors have drawn the most foreign capital. Impressive amounts have also flowed into tourism, textiles, construction, banking, and telecommunications, and these cash flows have occurred in many countries on the continent.

Currently, 59 million African households have \$5000 or more in income. Above this amount, individuals begin to spend roughly half of their earnings on nonfood items. If progress continues as expected, the number of these households could reach 106 million by 2014. Africa already has more middle-class households (defined as those with annual incomes of at least \$20,000) than India. This rising consumption will create more demand for local goods and services and help spark rounds of increasing growth domestically.

Southern and eastern Africa are now connected to the global Internet mainframe thanks to a recent \$600 million private investment in high-capacity fiber-optic cable, increasing considerably the continent's capacity for connectivity.

Africa's economic growth is widespread across sectors <sup>7</sup>:

### **Natural Resources**

In addition to being a major supplier of natural resources, sub-Saharan Africa is also the region with the greatest potential for new discoveries. The region should benefit from higher prices, in addition to higher volumes, once global growth resumes.

### **Food and Production**

In sub-Saharan Africa, demand for food is expected to reach \$100 billion by 2015, double the levels in 2000. Sub-Saharan Africa has many success stories with products regularly being exported to European and other Western countries, such as organic

coffee in Tanzania, the production of cassava chips in Ghana, and cut flowers in Kenya, as well as aquaculture in Malawi. Expanding markets such as dairy production in east sub-Saharan Africa could also be scaled up for faster growth.

### **Mobile Phones**

Africa has become the fastest-growing region in the global cellular market in the world, growing from fewer than 2 million mobile phones in 1998 to more than 400 million today, twice the rate of Asia. More than 65 percent of the population now lives within reach of a wireless voice network. Moreover, mobile phones have become the single-largest platform that can be used to deliver government services to the poor. While great progress has been made in improving access to the information and with communications infrastructure in many countries, more efforts are needed to help exploit the potential of these successes to transform other sectors.

### *Links between the Economy and Chronic Disease*

Almost 20 percent of the world's population is estimated to inhabit sub-Saharan Africa by 2050. In 1980, only 28% percent of African's lived in cities and today some 400 million are city dwellers. In twenty years, that share is projected to increase by 100 million more, and Africa's top 18 cities will have combined spending power of \$1.3 trillion.

As urbanization boosts productivity, workers move more from agrarian labor into urban jobs (demand and investment). Companies achieve greater economies of scale by spreading their fixed costs over a larger customer base. This growth acceleration has started to improve conditions for Africa's people by reducing the poverty rate. However, Africa still faces serious challenges including disease, poor education, and high infant mortality (all constant drivers of poverty).

While urbanization and the growing young population will have significant implications for productivity, growth, and demand, ironically, along with this prosperity comes a more sedentary lifestyle, increased pollution, consumption of processed food, and stress—the precise factors that are driving the explosive rates of NCDs on the continent.

### **NCDs and the Threat to Productivity**

The spread of non-communicable diseases threatens this economic productivity in sub-Saharan Africa and also presents a global crisis. Indeed, this increased burden of NCDs in low- and middle-income countries contributes considerably to poverty and becomes a major barrier to their development. NCDs disproportionately affect the poor— thus, further deepening inequalities<sup>8</sup>. Moreover, the poor are more likely to live in settings where legislation, policies, and regulations are inadequate to address and manage NCDs – or where they simply do not exist. Additionally, reduced access to comprehensive services for prevention and treatment of NCDs arise because of financial reasons and

weak health systems.

NCDs also cause poverty. Because they are more chronic, they lead to continued expenditures that trap poor households in cycles of illness, debt, and stress, perpetuating health and economic inequalities. And the effects are far-reaching; NCDs diminish household earnings and a family's ability to provide for and educate children <sup>9</sup>.

Household costs of NCDs have a substantial macroeconomic effect. The loss of productivity reduces a society's effective labor force and, in turn, reduces overall economic output. For every 10% rise in NCD related mortality, a resultant 0.5% reduction in yearly economic growth is estimated <sup>10</sup>. In short, NCD's create poverty traps. On the basis of this evidence, the World Economic Forum now ranks NCDs as one of the top global threats to economic development.

### *The Venture Capital Model*

Venture capital (VC) is financial capital provided to early-stage, high-potential, high risk startup companies. A venture capital Fund makes money by owning equity in the companies in which it invests. These companies typically are novel technology or business models in high technology industries, such as biotechnology, IT, software, etc. Venture capital investment typically occurs after the seed funding round as growth funding or a "Series A" round. This is performed in the interest of generating a return through an eventual realization event, such as an IPO or trade sale of the company.

Venture capital is attractive for new companies with limited operating history because they are too small to raise capital in public markets and the companies have not reached the point where they can secure bank loans or complete a debt offering. The venture capitalists are expected to bring managerial and technical expertise as well as capital to their investments. In exchange for this financial support from the VC, considerable control over companies' ownership and the decisions that a company has to make becomes under the control of the VC.

Venture capital is also associated with job creation (accounting for 21% of US GDP) and the knowledge economy, and it is used as a proxy measure of innovation within an economic sector or geography. Some 11% of private sector jobs come from venture backed companies, according to the National Venture Capital Association. Of the approximately two million businesses created in the USA, only about 700 secure venture capital funding <sup>11,12</sup>.

As VCs typically reject 98% of opportunities pitched to the firm for support, startup companies that wish to secure venture capital require a handful of exceptionally rare qualities. They typically have innovative technology, potential for rapid growth, a well-developed business model, and an impressive management team.

VC investments are illiquid and require three to seven years to harvest. Venture capitalists are expected to carry out detailed due diligence prior to investment. Venture capitalists typically assist at four stages in the company's development: idea generation, start-up, ramp up, and exit. Venture capitalists also are expected to nurture the companies in which they invest, in order to increase the likelihood of reaching an IPO stage when valuations are favorable<sup>13</sup>.

This need for high returns makes venture funding an expensive capital source for companies, and most suitable for businesses having large up-front capital requirements which cannot be financed by cheaper alternatives such as debt. Because the value of intangible assets such as software and other intellectual property is not so easily established, this helps explain, to a large extent, why venture capital is most prevalent in fast-growing technology and in the life sciences or biotechnology fields.

### Rounds of Funding

Six stages of financing in Venture Capital exist that roughly correspond to the stages of a young company's development:

- Seed Money: Low level financing needed to prove and test a new idea
- Start-up: Funding needed for expenses associated with marketing and product development
- First-Round ("Series A" round): Early sales and manufacturing funds
- Second-Round: Working capital for early-stage companies that are selling product, but not yet turning a profit
- Third-Round (Mezzanine financing): Expansion money for a newly profitable company
- Fourth-Round (bridge financing): Intended to finance the "going public" process

### The Venture Capital Fund

A venture capital fund is a pooled investment vehicle (often an LP or LLC company structure) that primarily invests the financial capital of third-party investors in enterprises that are too risky for the standard capital markets or bank loans. Venture capital firms typically comprise small teams with technology backgrounds (scientists, researchers) or those with business training or deep industry experience and, as general partners of the Venture Capital Firm, they manage and oversee the VC Fund.

To protect investment in high-risk, young companies, most venture capital investments are done in this pool format, where several investors combine their investments into one large fund that invests in many different startup companies. By investing in this pool format, the investors are spreading out their risk, as opposed to taking chances and putting all of their money into a few select start-up firms.

Venture capital firms are typically structured as partnerships, the general partners of

which serve as the managers of the firm and will serve as investment advisors to the venture capital funds raised. Venture capital firms in the United States may also be structured as limited liability companies, in which case the firm's managers are known as managing members. Investors in venture capital funds are known as limited partners (See Figure 2). This constituency comprises both high net worth individuals and institutions with large amounts of available capital, such as state and private pension funds, university financial endowments, foundations, insurance companies, and pooled investment vehicles, called fund of fund <sup>14</sup>.

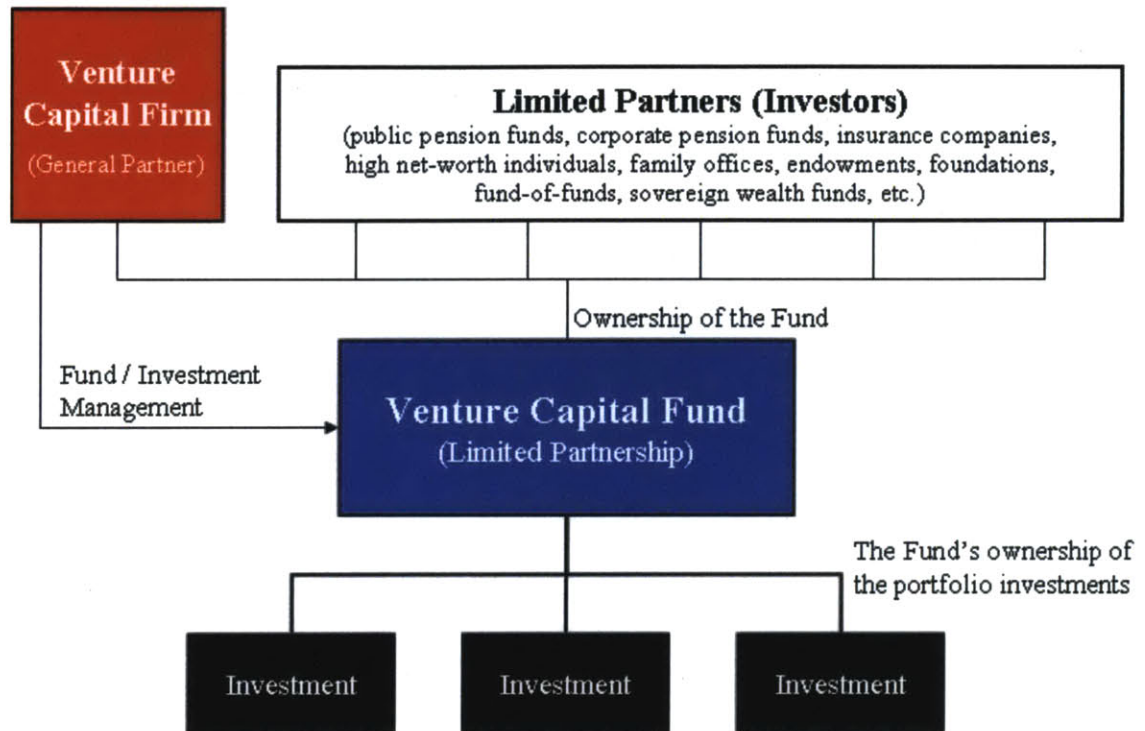


Figure 2. Organizational Representation of a VC Firm and Fund

### Structure of the Funds

Most venture capital funds have a fixed life of 10 years, with the possibility of a few years of extension that for some private companies continuing to seek liquidity. The investing cycle for most funds is generally three to five years. After this, the focus of the fund shifts toward managing and making follow-on investments in an existing portfolio. This model was pioneered by successful funds in Silicon Valley through the 1980s to invest in technological trends broadly but only during their period of ascendance, and to minimize exposure to management and marketing risks.

It can take anywhere from a month to several years for venture capitalists to raise money from limited partners for their fund. When all of the money has been raised, the fund is said to be closed and the 10 year lifetime begins. Some funds have partial closes

when one half (or some other amount) of the fund has been raised. "Vintage year" generally refers to the year in which the fund was closed and may serve as a means to stratify VC funds for comparison <sup>14</sup>.

## Compensation

Venture capitalists are compensated through a combination of management fees and carried interest (often referred to as a "two and 20" arrangement):

- Management fees – an annual payment made by the investors in the fund to the fund's manager to pay for the private equity firm's investment operations. In a typical venture capital fund, the general partners receive an annual management fee equal to up to 2% of the committed capital.
- Carried interest – a share of the profits of the fund (typically 20%) is paid to the private equity fund's management company as a performance incentive. The remaining 80% of the profits are paid to the fund's investors. Strong limited partner interest in top-tier venture firms has led more favorable terms to the venture partnership where certain groups are able to command carried interest of 25-30% on their funds <sup>14</sup>.

## Venture Philanthropy

Venture philanthropy, also known as "**philanthrocapitalism**", takes concepts and techniques from venture capital finance and high technology business management and applies them to achieving philanthropic goals. This hybrid model combines the policies and practices of long-term investment and venture capital models of the for-profit sector with the principles and public benefit mission of the non-profit sector.

Some distinguishing characteristics of Venture philanthropy that make it different from the traditional VC model include:

- Focus on capacity building, instead of programs or general operating expenses.
- Shared risk or higher involvement by donors with their grantees. Some donors, for example, will take positions on the boards of the non-profits they fund.

There are three models for engaging in venture philanthropy. The first is traditional foundations practicing high-engagement grantmaking. The second is organizations which are funded by individuals, but all engagement is done by professional staff. Good examples of this type of venture philanthropy are the Robin Hood Foundation in New York City and Tipping Point Community in the San Francisco Bay Area. The third is the partnership model, in which partner investors both donate the financial capital and engage with the grantees. Most of these are pass-through funds (i.e. they do not have an endowment, but rather grant out all the money they are given annually). Examples of this model are the Silicon Valley Social Venture Fund in San Jose, California and Full Circle Fund in San Francisco, California <sup>15</sup>.

Some other examples of venture philanthropy foundations include Social Venture Partners, The Children's Investment Fund Foundation (CIFF), New Schools Venture Fund, Grassroots Business Fund, Acumen Fund, and New Profit Inc <sup>15</sup> .

### The Need for Venture Capital in Africa

There is a growing need for venture capital and private equity to help invigorate the development of the private sector on the continent. Small and medium enterprises are the driving force of most economies in Africa. To help Africans adapt to global standards and realize their potential economic impact, innovative and creative entrepreneurial approaches are vital.

In Africa, given the current climate, the challenges of small and medium enterprises are largely shaped by economic factors (e.g. poverty), social factors (e.g. urbanization, public health, HIV/AIDS), political factors (e.g. level of democracy, corruption), and ecological factors (e.g. drought, resource scarcity, pollution). As such, these enterprises face social, ethical and environmental challenges, opportunities, and dilemmas that are very different from their European and US counterparts.

Although labor costs may be low, this is often offset by the costs of transportation, raw materials, utilities, and other inputs. As such, it becomes difficult to compete in export markets. Moreover, many small/medium African companies lack access to the reliable financial data necessary for the scrutiny of a company's performance and prospects of the company. Capital remains too expensive for the entrepreneurs hoping to launch an enterprise.

Small/Medium enterprises contribute around two thirds of national income and provide the foundation for a stable middle class in many countries, becoming agents for poverty reduction. And many argue that there needs to be more emphasis on 'Wealth Creation' as opposed to 'Poverty Reduction'. This shift places economic activity on trade, the ability to secure well-paid jobs, and income generation as opposed to a focus on aid, food, medicine and peace-keeping in Africa <sup>16</sup>.

Indeed, entrepreneurs have the potential to be regarded as powerful agents of wealth creation; currently they make up 4% of the population with 16% of the population following as 'entrepreneurial imitators.' These individuals and areas have enormous potential for productive growth. Empowering them to do business through private investment should be a clear priority <sup>16</sup>.

Undoubtedly, Venture Capital Funds have the capacity to play an important role in Africa's economic development and make a transformative impact in Africa and help support the continent's aspiring entrepreneurs.

## **IV. Executive Summary of PaCT Business Plan - ImPaCT Commercial Ventures**

### Value Proposition

Our strategy is to create partnerships with a few corporations, foundations, and/or philanthropists whose interests are aligned with the ethos and objectives of PaCT research.

Our customers are the large corporations and small entrepreneurial start-ups whose development of innovative products (goods and services), geared toward chronic disease and public health prevention, can be enhanced and benefits from the use and access of very large data sets of information on the behavioral and disease patterns of hundreds of thousands of Africans across four nations collected longitudinally over cell phones.

The limited partners of ImPaCT Commercial Ventures will serve as agents for the acquisition of additional corporate customers of PaCT Intellectual property (IP). The most competitive and innovative companies today create platforms around their goods and services and generate a host of strategic partnerships with companies whose own products become aligned to these platforms. The limited partners help derive value; since they will have semi-exclusive rights to PaCT/ImPACT IP, their strategic partners could also benefit from access to the IP. These strategically aligned companies become targeted customers of ImPaCT ventures.

ImPaCT Commercial Ventures essentially has three distinct products that define the Intellectual Property of PaCT/ImPACT:

- 1) "Passive" behavioral data collected from cell phones
- 2) "Active" question-response data entered by study participants of the large cohort in response to surveys and questionnaires (recorded through cell phones and/or on paper)
- 3) Smaller "sub-study" designs (and related data) where a subset of the 500,000 study population becomes a part of "innovation intervention groups" designed to test innovation created from the Fund's portfolio of start-up ventures.

Data from large data sets like PaCT are valuable because they allow companies (large corporations as well as young start-up companies) to create goods and services that make a greater impact on a larger segment of the population. Market testing is labor intensive. Forming groups of people to collect information on products over given time intervals also requires intense resources. By providing corporations and start-up ventures access to an already well-defined population of people, their innovations can



not only be tested and refined more rapidly but also ultimately make a greater impact.

## Market Brief

US companies like Google and Intel are good examples of US-based corporations that would make good partners with ImPaCT Commercial Ventures. African telecommunication companies like GLO and Econet would make ideal partners. In the partnership, we will focus on chronic disease and public health prevention, can also engage in the commercialization of IP generated from the cohort, as well as leverage the IP from the cohort study to define and refine innovation from our grantees, the supported entrepreneurial start-ups that comprise the ImPaCT Commercial Venture Fund portfolio. In essence, the leveraging of the large cohort study allows us to establish our own unique segment of the market.

## Team

Our team of epidemiologists (both in US and in Africa) and computer science/social media experts will help make up the general partners of the fund who would manage the business entity and its Fund, with general partners owning 20% of the company. It is important for this group of general partners to understand the epidemiology and other technical aspects of the PaCT cohort study. After all, the business entity can not optimally operate without a high performing scientifically sound cohort study following 500,000 participants. As such, limited partners would be the investors and own the remaining own 80%.

## The Investment Opportunity

ImPaCT Venture's competitive advantages will come from its alignment with PaCT, the large longitudinal epidemiological cohort study of 500,000 study participants in four African nations. To our knowledge, no other venture capital firm or Fund has access to such a large, organized, and well-defined population of committed participants. And this alignment with the cohort study confers unique advantages in a myriad of ways. First, the 500,000 study population provides a market-testing environment and "intervention environment" for innovation and the commercialization of PaCT intellectual property. This ensures higher return on investment given the potential for a highly refined product. Second, the study population serves as a bellwether for innovation needed for products and services for chronic diseases prevention. This facilitates higher return on investment in products that can be specifically designed with the population in mind. Third, after innovation generated from the ventures in the ImPaCT portfolio have gone to market, additional information about related products -- and the platforms that can and should be created around them -- can come from the cohort, as PaCT study participants are consumers too and vigorously engage in the market. This allows further refinement of products and the creation of much needed supported products. Fourth, the cohort study allows ImPaCT venture to focus both on patient capital, or long-term capital where the investor makes a financial investment with no expectation

of a quick profit (a longer time horizon for return of capital), as well as on high potential entrepreneurial start-up ventures wanting to create innovation for social good (in this case, chronic disease and public health prevention) and also commercialize PaCT intellectual property from PaCT and extend it to a few highly selective corporations.

## **V. ImPaCT Commercial Ventures Business Plan**

### **1. Market Analysis and Competition**

#### Market Strategy

Our strategy is to create partnerships with a few corporations, foundations, and/or philanthropists whose interests are aligned with the ethos and objectives of PaCT research. Ideally, the goal is to target one or two US-based corporate sponsors/investors and two or three African investors. This group of individuals would make up the limited partners of **ImPaCT Commercial Ventures** and become part owners. These partners would have semi-exclusivity to PaCT intellectual property (IP); a select group of strategically aligned businesses of these corporate partners would then pay for the commercialized Intellectual property of ImPaCT.

ImPaCT would create a group of entrepreneurs-in-residents (EIR) from several sources, including MIT-Media Lab's Entrepreneurship Program that helps students cross-registered from MIT Sloan School of Management, Harvard's Business School and Kennedy School of Government, and other academic programs who form teams to translate promising ideas at the Media Lab from compelling prototypes towards real-world products or services—i.e., translating ideas into impact.

ImPaCT would also tap Harvard Business School's newly formed *Innovation Lab* that will serve as an incubator across the university to foster creativity and entrepreneurship for undergraduates and graduates students. Harvard's Office of technology development (OTD), the new Technology and Entrepreneur Center at Harvard (TECH), and the MIT Entrepreneurial center will all serve as excellent resources for ImPaCT.

Another important resource is the MIT Entrepreneurial Programming and Research on Mobiles (EPRM) initiative that is a part of the Program for Developmental Entrepreneurship and aims to foster mobile phone-related research and entrepreneurship in Africa. All of these resources can be used as important portals for the ImPaCT Commercial Fund.

#### Initial Target Market

US companies like Google and Intel are good examples of US-based corporations that would make good partners. African companies and partners such as Strive Masiyiwa, the Zimbabwean businessman who is CEO and Chairman of the South African international

telecommunications group Econet Wireless and Mike Adenuga (Nigeria), chairman of the large telecommunications company Globacom limited (GLO) are examples of potential targets on the continent for partnerships. These partners would then also have representation on the Board of Directors of ImPACT as would a few of the African Principal investigators of the PaCT research project. University endowment funds, too, should be considered for investment.

#### Customer Needs and Current Solutions

***Our customers are the large corporations and small entrepreneurial start-ups whose development of innovative products (goods and services), geared toward chronic disease and public health prevention, can be enhanced and benefit from the use and access of very large data sets of information that represents the behavioral and disease patterns of hundreds of thousands of Africans across four nations collected longitudinally over cell phones.***

Data from large data sets like PaCT are valuable because they allow companies (large corporations as well as young start-up companies) to create products (goods and services) that make a greater impact on a larger segment of the population. Market testing is labor intensive. Forming groups of people to collect information on products over given time intervals also requires intense resources. By providing corporations and start-up ventures access to an already well-defined population of people, their innovations can not only be tested and refined more rapidly but also ultimately make a greater impact. If innovation is tested in, say, 100,000 people who are already constantly followed and tracked in the PaCT cohort already, additional important lifestyle factors and behaviors can simultaneously be examined **together** to understand customer needs and the likelihood of how an individual will adopt our customer's innovation. Additionally, it now becomes possible to better understand what other personal factors and characteristics (behavioral and genetic) are important for a given products function.

#### The Value Chain

The limited partners of ImPaCT Commercial Ventures will serve as agents for the acquisition of additional corporate customers of PaCT Intellectual property. The most competitive and innovative companies today create platforms around their goods and services and generate a host of strategic partnerships with companies whose own products become aligned to these platforms. The limited partners help derive value; since they will have semi-exclusive rights to PaCT/ImPACT IP, their strategic partners could also benefit from access to the IP. These strategically aligned companies become targeted customers of ImPaCT ventures.

The supported entrepreneurial start-ups in the Commercial Fund, too, derive value. Because they also have access to the PaCT/ImPaCT IP, their innovation is more likely to gain traction in the greater population of consumers, of which the cohort study

participants are a subset.

## Segmentation

Currently, **philanthrocapitalism** is segmented into three general areas. The first is traditional foundations practicing high-engagement grantmaking. The second is organizations which are funded by individuals, with engagement done by professional staff. The third is a partnership model in which partner investors both donate the financial capital and engage with the grantees.

It is the third model after which we will pattern the ImPaCT Commercial Venture Fund. However, here again, we offer several layers of value propositions and distinguish ourselves from the other models given that we will 1) focus on chronic disease and public health prevention and 2) can also engage in the commercialization of IP generated from the cohort, as well as 3) leverage the IP from the cohort to define and refine innovation from our grantees, the supported entrepreneurial start-ups that comprise the ImPaCT Commercial Venture Fund portfolio.

## Marketing Communication and Penetration

### **Crowd Funding**

With software techniques created in the MIT-Media lab that use social media to harness the potential of human networking and build proper incentives into viral collaborations, we are developing an online “**What is your Social ImPaCT**” campaign for crowd funding (or crowd financing or crowd sourced capital). Crowd Funding raises capital for new projects or enterprises by appealing to large numbers of ordinary people for small donations. Our online “**ImPaCT**” campaign will invite online users to make small donations while providing them with incentives to invite their friends – and friends of friends at all levels downstream of them -- to do the same. The innovative software will track the downstream recruitment activity of donors’ friends, who have also given small donations, and the tally of these downstream donations will register as the “**Social Impact**” of a given user. This allows a given user to donate a small amount of money but at the same time see a large amount generated, by using the built-in techniques of the online platform that track all of the donation activity generated downstream of the original user encouraging his/her friends to also donate. This campaign, using unique software for a social network environment, will be used to bring awareness to the PaCT project and other deserving public health related research projects and causes, while raising funds for PaCT and ImPaCT Commercial Ventures.

### **Road Shows**

We also have a series of “Road Shows” scheduled at the Harvard Clubs of New York, Washington DC, and Silicon Valley. These are presentations targeted at an audience of potential investors/supporters of the project. Below is an advertisement for a presentation in Boston Massachusetts (figure 3 below).



# HARVARD CLUB of BOSTON

## ANNOUNCEMENT



*The Harvard Club of Boston and Harvard School of Public Health present:*

**DR. HANS – OLOV ADAMI, DR. MICHELLE D. HOLMES, AND DR. TODD G. REID: "THE CHANGING FACE OF AFRICAN HEALTH – THE COMING TSUNAMI OF "MODERN" DISEASES"**

**Monday, March 7, 2011 – Main Clubhouse  
5:30 pm to 7:30 pm Reception and Presentation**

*A chronic disease tsunami is coming to Africa. Aid to Africa has traditionally focused on infections such as malaria, TB, and HIV. But such efforts will soon be overshadowed by the swirling sea of emerging modern diseases similar to those seen in high-income countries, such as heart disease, mental illness, cancer, diabetes, and obesity.*

*The Africa/HSPH Partnership for Cohort Research and Training (PaCT) discuss their plans to help spur a renaissance of innovation on the continent through research, entrepreneurship, and venture capital. Scientists and researchers at the Harvard School of Public Health and those in Africa are collaborating to conduct groundbreaking research and thwart the epidemiologic transition from infectious diseases to chronic ailments.*

*renaissance of innovation on the continent through research, entrepreneurship, and venture capital. Scientists and researchers at the Harvard School of Public Health and those in Africa are collaborating to conduct groundbreaking research and thwart the epidemiologic transition from infectious diseases to chronic ailments.*

*By 2030, according to the World Health Organization, three of the top four causes of death in low-income countries will be heart disease, stroke, and chronic lung disease. PaCT researchers are asking hundreds of thousands of people in Nigeria, Uganda, Tanzania, and South Africa about what they eat, how much they exercise and smoke, and their family and reproductive histories, correlating their answers with information from biological samples. The United States and Western Europe have benefited from similar studies for decades. However, Africa, home to nearly one billion people, has no similar large epidemiologic studies that look at chronic diseases.*

*Dr. Adami, Holmes, and Reid will also discuss their innovative use of technology. For example, with cell phones—widely used across all of Africa—they can retrieve data and conduct follow-up surveys with participants. They plan to develop comprehensive biobank to enable cutting edge molecular studies. The large number of participants will allow the study of gene and environment interactions. Finally, PaCT will provide a fertile training ground in innovative research and create viable career paths for African scientists and entrepreneurs, fostering additional collaboration among countries in Africa, Europe, and North America, and providing new business models and opportunities for the conduct of large scale global health projects.*

*Price per person: \$30 (plus Club charge and tax) includes hors d'oeuvres and presentation. Charges will apply for cancellations received after Thursday, March 3, 2011.*

*For reservations, please [click here](#).*

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Interactive communications by [MembersFirst, Inc.](#)

## **2. Business Model Innovation and Optimization**

ImPaCT Commercial ventures will be structured as a B-Corporation or “Benefit Corporation”. This company structure is the latest innovation among the subset of companies with a social as well as financial mission. These philanthropic firms aim to not only benefit stockholders and clients, but also the greater community.

For a company to obtain B certification, it must receive a passing grade on a long scorecard that covers employment and environmental practices, purchasing policies, and is required to establish whether its goods and/or services are beneficial to society, all while adopting a legal language that states that its directors will honor these practices. The charter of incorporation for this company structure legally requires the company to adhere to socially-beneficial practices. Thirty-one states have now enacted legislation that permits companies to write stakeholder consideration into their official charters.

Like 5013c non-profit organizations, B-Corporations have a mission that needs to benefit the “greater good” of the community, society, or world. However, B-corporations are allowed to evolve and can use some of its funds for initiatives not directly related to the mission but indirectly related to issues important to the board of directors. Non-profits do not pay taxes and can’t use its funds for anything other than the mission for which it is formed. Although B-corporations are currently required to pay taxes, there is a movement to allow these new company structures to receive significant tax breaks.

The B-corporation, ImPaCT Commercial Ventures will manage large philanthropic donations to PaCT research and provide an investment instrument through VC.

### **Competitive Strategy**

In this space of philanthrocapitalism, none focus solely on the provision of goods and services around public health. However, there are a limited number of firms that include healthcare and public health in their portfolio of supported start-ups. One noteworthy successful example of this is the Acumen Fund. This non-profit global venture fund uses entrepreneurial approaches to solve global poverty and concentrates its investment in Health, Housing, Energy, and Agriculture. The Fund supports health-related ventures that include **A to Z textiles Mills** for long-lasting anti-malaria bednets, **Insta Products** that supply micronutrient-rich breakfast in Kenya, **Dart** (insecticide-treated wall lining for homes around the world) and **Sproxil**, providing mobile technology to combat counterfeit medicine.

The Acumen Fund was incorporated in 2001 with seed capital from Cisco Systems (\$2 Million), the Rockefeller Foundation (\$5 Million) and three individual philanthropists (\$1.5M). The Fund has since expanded to include partners like Bill and Melinda Gates Foundation, Skoll Foundation, and Goggle.org. The Fund’s portfolios consist of start-ups in Kenya, Tanzania, South Africa, India, Pakistan and currently support over 25

enterprises and with commitments that range from 300,000 to \$2,000,000 in equity or debt with a 5-7 year payback or exit <sup>17,18</sup>.

ImPaCT Venture’s competitive advantages will come from its alignment with PaCT, the large longitudinal epidemiological cohort study of 500,000 study participants in four African nations. To our knowledge, no other venture capital firm or Fund has access to such a large, organized, and well-defined population of committed participants. And this alignment with the cohort study confers unique advantages in a myriad of ways. First, the 500,000 study population provides a market-testing environment and “intervention environment” for innovation and the commercialization of PaCT intellectual property. Entrepreneurial start-ups can use subsets of the cohort population to refine their innovative goods and/or services so that they ultimately serve the population better when released to market.

Second, the study population serves as a bellwether for innovation needed for products and services for chronic diseases prevention. Data collected from the 500,000 study participants will indicate what needs that should be prioritized. This will subsequently inform decisions around which innovations from the portfolio of supported start-ups are likely to gain traction in the population at large.

Third, after innovation generated from the ventures in the ImPaCT portfolio have gone to market, additional information about related products -- and the platforms that can and should be created around them -- can be extracted from the cohort, as PaCT study participants are consumers too and vigorously engage in the market.

Fourth, the cohort study allows ImPaCT venture to focus both on patient capital, or long-term capital where the investor makes a financial investment with no expectation of a quick profit (a longer time horizon for return of capital), as well as traditional capital gains from high potential entrepreneurial start-up venture wanting to create innovation for social good (in this case, chronic disease prevention) and also commercialize PaCT intellectual property from PaCT and give to a few highly selective corporations.

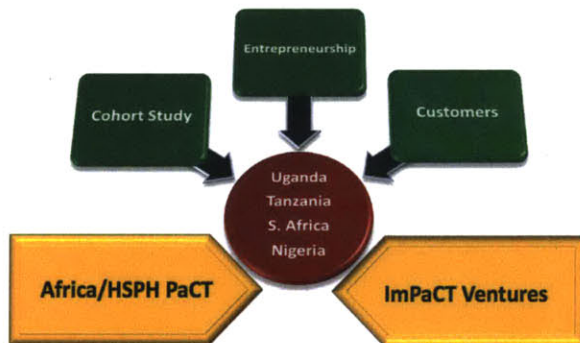


Figure 4. The Four Forces of a PACT/ImPaCT alignment:  
1) Study Participants, 2) Entrepreneurs, 3) Customers, and 4) The PaCT Country specific markets

### **3. Technology and Product**

#### Product Description

ImPaCT Commercial Ventures essentially has three distinct products that define the Intellectual Property of PaCT/ImPaCT:

- 4) "Passive" behavioral data collected from Cell Phones
- 5) "Active" question-response data entered by study participants of the large cohort in response to surveys and questionnaires (through cell phones and/or by paper)
- 6) Smaller "sub-study" designs (and related data) where a subset of the 500,000 study population becomes a part of "innovation intervention" groups designed to test innovation from the Fund's portfolio of start-up ventures.

What makes it unique?

These data, both passive and active, will be collected longitudinally and linked to large volumes of additional aggregated data about the study population including genetic information that will allow an unparalleled investigation into gene-environment interactions.

How does it work?

Active data is collected when a participant enters responses to PaCT research-related questions through the use of cell phones and/or paper questionnaires. The passive data will be collected using techniques developed by Dr. Sandy Pentland of the MIT Media Lab called "Reality Mining". Reality Mining defines the collection of machine-sensed environmental data pertaining to human social behavior. This new paradigm of data mining makes possible the modeling of conversation context, proximity sensing, and temporospatial location throughout large communities of individuals. Mobile phones (and similarly innocuous devices) can be used for data collection without the user having to actively enter data, opening social network analysis to new methods of empirical stochastic modeling and provides insight into the dynamics of both individual and group behavior. By leveraging recent advances in machine learning, these techniques can create generative models that can be used to predict what a single user will do next, as well as model behavior of large organizations. Such data is invaluable to the creation and refinement of innovative goods and services that help manage and fight chronic disease and other public health challenges.



#### **4. Financial Summary**

Scaling to 100% cohort capacity of 500,000 study participants will require, on average, \$10 Million/year to organize, operate, and maintain. Cost to scale to 20% enrollment of cohort will require, on average, \$2 million annually. This supports enrollment, follow-up, and the creation of a questionnaire instrument. When scaling to include a bio-bank and related development such as the collection of bio-specimens, the 20% enrollment costs increases to \$10-15 million annually. In essence, to scale to 100% capacity, the cost of the project is estimated to be 100 million dollars, and this would cover operational and maintenance costs for 10 years.

Another \$10-\$15,000,000 is required to create the ImPaCT Commercial Venture Fund to support entrepreneurship and start-ups. With this fund, we'd make disciplined investments averaging from \$200,000 to \$2 million to start-ups that yield both financial and social returns.

50% of the generated profit from equity in the start-up ventures and the commercialization of PaCT/ImPaCT IP will be dedicated back toward supporting the operational costs of the cohort study. Over a fifteen-year period, we estimate to invest over \$100 million to 70 ventures and license our Intellectual property to 10 -15 corporations for continuous revenue generation.

#### **Ownership**

Our team of epidemiologists (both in US and abroad) will help make up the general partners of the fund who would manage the business entity and the Fund, with general partners owning 20% of the company. We feel that it is important for this group of general partners to understand the epidemiology and other technical aspects of the PaCT cohort study. After-all, the business entity can not optimally operate without a high performing scientifically sound cohort study following 500,000 participants. Limited partners would be the investors and the remaining own 80%. See figure 5 below for organization of Venture.

## A Financially Sustainable PaCT: ImPaCT Venture Fund



Raise seed capital (\$10 to \$15M) from a few (n= 3-4) highly selective **Partners** ( Foundations, Corporations, Philanthropists); More partners enter in subsequent rounds of fundraising.



### The Partners



Align **Venture Fund** with PaCT research project to 1) spur innovation and development and 2) create an investment instrument that helps sustain the research project and offer returns to investors



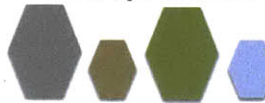
### ImPaCT Venture Fund



**Entrepreneurs** seek capital from The ImPaCT Venture Fund to create scalable start-up companies (some high tech, some low-) around innovation (i.e., high-tech - mobile phone apps/wireless medical devices to prevent chronic disease; low-tech – services, mobile clinics for monitoring. ImPaCT makes money from equity in start-ups; some of the profit becomes steady stream of support for PaCT study.



### Entrepreneurs



### The Strategic Advantage

I. Entrepreneurs (and a few partnered corporations) can test their innovations in **PaCT** study population & II. entrepreneurs supported by ImPaCT have access to IP from cohort (data collected by cell phones over decades), increasing likelihood start-ups will be successful in local market and, thus, increase return on ImPaCT's investment in start-ups.

Figure 5. ImPaCT Commercial Venture

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### SPECIFIC AIMS

Chronic non-communicable diseases (NCDs) that typically affect older people are growing rapidly in Africa. They include cardiovascular disease, diabetes mellitus (DM), mental illness and breast and cervix cancer. Prevention efforts should be based on research in Africans, and virtually no such research exists. Our goal is to establish a large-scale prospective cohort, the Africa/Harvard School of Public Health (HSPH) Partnership for Cohort Research and Training (PaCT) —as a sound scientific basis for prevention of NCDs there.

Regarding these four chronic diseases, we seek to:

- Better quantify their magnitude
- Discover risk factors for NCDs in Africa, and how they interact with the African genome
- Train a new generation of public health researchers and practitioners.

We will follow the classic cohort model exemplified by the British doctors' study and the U.S. Nurses' Health Study. Our ultimate goal is to develop a cohort comprising 500,000 individuals for long-term follow-up, coming from five institutions in four sub-Saharan countries. *The immediate purpose of this program project is to begin by enrolling 100,000 individuals over a five-year period.*

We believe three factors unique to Africa significantly impact its increasing NCD burden. **These inadequately studied factors are: stress, Westernization, and chronic infection.** We will study the impact of these crosscutting themes on the four disease areas mentioned.

Our first theme is stress related to economic deprivation and discrimination. These stressors likely have far-reaching consequences for other lifestyle factors, and ultimately for NCD risk.

Our second theme is Westernization of lifestyle closely tied to the epidemiologic transition.<sup>1</sup> This revolution is taking place at different stages in the countries involved in our proposed project resulting in dramatic changes in reproduction, diet, physical activity and anthropometry, and in particular the transition from starvation to overweight. Also seen is a breakdown of traditional social networks, the consequences of which may be mitigated somewhat through the spread of cell phones.

Our third theme is chronic infections, chiefly malaria, and their possible interaction with lifestyle factors in the etiology of chronic diseases. This is an entirely unexplored area in etiologic research.

We propose four projects here that will cover the bulk of Africa's emerging chronic diseases.

**In Project 1** (cardiovascular disease and stroke), we will investigate the incidence of stroke and myocardial infarction (MI). We will study the contribution of stress, as well as Westernization of lifestyle. We will also explore the idea that HIV infection increases the risk of stroke and MI.

**In Project 2** (diabetes mellitus), we will investigate the incidence of DM. We will look at the impact of stress. We will further dissect the web of psychological factors, eating patterns, obesity, physical activity, change to sedentary lifestyle, shift to western diet, and the combined role of all these factors as contributors to DM. We will ask whether malaria infection increases risk of DM.

**In Project 3** (mental health), we will initiate the first-ever large-scale prospective study of the burden and causes of mental illness in Africa. As in other Projects, stress is a focus. We will study its impact on depression, anxiety, and substance abuse. We will analyze the effect of Westernization on mental health. We will examine whether cell phones have mitigated the negative effects of urbanization.

**In Project 4** (breast and cervix cancer), we will investigate how stress and oppression correlate to later diagnostic stage and suboptimal treatment. We will examine two distinctly African phenomena as breast cancer risks. The first is having many births, starting very early. The second involves Africa's unusual patterns of anthropometry, stemming from starvation, followed by a surplus of western diet. We will also analyze recurrent malaria infection as a breast cancer risk.

## RESEARCH STRATEGY

### 1. Significance

There is a rising, but not yet fully recognized epidemic of non-communicable diseases (NCDs) in sub-Saharan Africa. This includes cardiovascular disease, diabetes and obesity, mental illness, and cancer.<sup>2</sup> Historically, research has focused on maternal and child health and infections. Much less research has been conducted on NCDs.<sup>3</sup> However, as in other developing regions, the people of Africa suffer doubly from infectious diseases and NCDs. NCDs are already a significant burden on the world's poor.<sup>4</sup> The epidemiologic transition from predominantly infectious to non-communicable diseases is already well underway in many low- and middle-income countries. In 2004, NCDs caused one quarter of all deaths in sub-Saharan Africa. By 2030, NCDs will cause 46% of all deaths.<sup>2</sup> Global burden-of-disease studies suggest that the age-standardized death rates of NCDs are now higher in at least four sub-Saharan countries than in high-income countries.<sup>2</sup>

Because medical care is sparse in many African countries, it will be impossible during the foreseeable future to tackle the oncoming tsunami of NCDs with optimal diagnosis and treatment. The only way to reduce suffering and premature deaths is prevention. This program project intends to limit the oncoming disaster by combining approaches never previously pursued in this part of the world.

Through a large longitudinal cohort study representing East, West, and Southern Africa, we intend to:

- provide more adequate measures of the disease burden;
- study existing and novel NCD risk factors and identify targets for interventions; and
- train a new generation of public health professionals to implement emerging knowledge.

Capacity-building is central to improving public health and fostering economic development in Africa. Our cohort study will build capacity in numerous ways. First, the study is led by five African principal investigators (PIs), one at each site. Their role as Site PI will increase their visibility to public health, give them experience with complex cutting-edge epidemiologic research, provide sustained opportunities for academic interaction with Harvard, and foster cross-country collaboration within Africa. Also, we will locate the biologic bank in Africa, and do all laboratory work at African institutions.

Finally, our study design itself will build long-term capacity. A cohort study produces more scientific information as time goes by, as opposed to other study designs, like cross-sectional, case-control, or randomized trials. Our study, and its increasing base of scientific information, will offer sustainable opportunities for research that will and help reverse the brain drain that is a concern in Africa.

This study enrolling 100,000 participants is not only an order of magnitude larger than any previous study of NCDs on the African continent, but it is the opening to a really large cohort study. If we prove feasibility, it will greatly help our efforts to raise funds for our ultimate target of 500,000 participants.

If we move forward, PaCT will be part of the Global Cohort Integration that began in October 2010. This initiative would enroll over 1.5 million cohort participants from India (Barshi Cohort), Mexico (ESMaestra), Sweden (LifeGene), and Africa (PaCT). We have initiated efforts to harmonize IT and biobank procedures, diagnostic algorithms, questionnaires, and pilot studies. Our collaboration will ultimately take advantage of global diversity in genetic and environmental disease determinants.

### 2. Innovation

There is an astounding disparity among nations in etiologic and cohort research. Indeed, using the populations of the US and Africa (with about 1 billion inhabitants), we found that Africa has 0.1% as many cohort enrollees as the US.<sup>3</sup> In the US, it would seem inconceivable that population-based preventive measures would be based chiefly on research conducted in low-income counties on a different continent. Likewise, rational strategies for disease prevention in Africa need to be based on research relevant to that continent. However, no such evidence exists currently, despite the fact that NCDs cause a large disease burden, and that 80% of deaths from NCDs worldwide occur in low- and middle-income countries. Until now, there has been no large-scale attempt to remedy this gloomy situation. Of course, extraordinarily important work has been carried out at demographic surveillance sites integrated through the INDEPTH network. Smaller cohort and cross-sectional studies have been important. We see an urgent need, however, for large-scale, modern longitudinal cohorts with repeated measures of exposures and outcome, based in sub-Saharan Africa, focusing on NCDs.

Launching such a study, as we hope to do, could potentially bring about a dramatic change and indeed create a footprint relevant for the entire continent.

This cohort will permit the study of countless other diseases. We are already entering largely new scientific territory by addressing mental health. Future plans include studies of injuries, accidents, and domestic violence, whilst a separate R01 is devoted to late reproductive sequelae in older women.

Cell phones offer entirely new opportunities for cost-effective, large-scale longitudinal studies. To the best of our knowledge, PaCT is the first study to rely strongly on cell phones for enrollment, retention, and follow-up. A major part of our innovation is research on cell phones use in scientific studies in Africa. We will do so in close collaboration with Dr. Nathan Eagle, a leader in this field.<sup>5</sup> This technology will develop exponentially in coming decades, and it offer hardly predictable opportunities.

### 3. Approach

**a. Background.** Concerns about the oncoming tsunami of chronic diseases in Africa led to discussions in the Department of Epidemiology at the Harvard School of Public Health beginning in the spring of 2007. The emerging Africa/HSPH Partnership for Cohort research and Training (PaCT) has now become a School-wide initiative. Five of nine departments in the school now participate (Epidemiology, Nutrition, Environmental Health, Health Policy and Management, and Global Health and Population). PaCT has been supported since 2008 by the HSPH Dean's Office; this support will end in June 2011.

Through a cascade of activities ranging from weekly teleconferences among all participants to seven visits to sub-Saharan Africa with exploration of potential sites, we have now accomplished the following concrete goals: (1) we have achieved representation among the sub-Saharan countries from East, West, and South so as to maximize genetic diversity (an important future study aim highly prioritized by our African collaborators), and also cultural diversity, (2) we have identified centers of excellence and dedicated colleagues, (3) we have evaluated approaches for enrollment and follow-up (see below under "study population"), (4) we have developed a collaborative structure led by professional facilitators (VISIONS, Inc.) during all-collaborator meetings in Cape Town in June 2009, in Dar es Salaam in June 2010, and in Greece in October 2010, (5) we have met and ascertained support from Ministers of Health in all four countries, namely South Africa, Uganda, Tanzania, and Nigeria (in South Africa, also the Minister of Science and Technology), from university presidents and all relevant deans, and (6) we have initiated pilot projects in all five sites.

Validity of cross-sectional studies can be jeopardized by selection bias, reverse causality, and other limitations. While a case-control design might be feasible in Africa for genetic-association studies of chronic diseases, it cannot study environmental factors or gene-environment interactions. But a cohort study is free from selection and recall bias, and offers unlimited opportunities to study new hypotheses over time. Hence, most of our analyses take advantage of the prospective design by analyzing incident disease after enrollment. However, we believe that for some diseases, we can generate valid information quickly from cross-sectional data collected at baseline. This pertains particularly to understanding some determinants of DM and mental health (Projects 2 and 3).

**b. Cross-cutting themes. Stress:** Stress is defined as any situation where internal and/or external demands are appraised as taxing or exceeding the adaptive or coping resources of an individual or group.<sup>6</sup> We propose to measure it with the Perceived Stress Scale (PSS), the most widely used to measure stress.<sup>7</sup> The PSS has been used in many African settings.<sup>8</sup> Further details of how we will measure stress, post traumatic stress, an social support can be found in Project 3, Mental Health.

**Westernization:** Africa's transition in this era to the western lifestyle is a natural experiment unprecedented in history. It has many dimensions. We will study it based on assessment of: (1) diet through a food-frequency questionnaire, as well as information on dietary pattern and food supplies throughout life; (2) physical activity during work and leisure time during different periods of life, using both existing and new instruments that need to undergo validation in parallel; (3) reproductive history, and (4) anthropometric measures combining current height, weight, and waist-hip circumference with information from pictograms representing childhood (age 7), adolescence (age 16), and each decade of life.

**Infections:** After considerable discussion, the investigators agreed that for most of the specific aims, links between HIV/AIDS and NCDs cannot be studied with adequate power and validity in this cohort. Here is why.

Few active teachers and health professionals have AIDS; and both financial and ethical barriers preclude HIV testing in the entire cohort. So instead, we will use this opportunity to study recurrent malaria infection, reassured in this matter by recent studies showing a high correlation ( $R=0.7$ ) between self-report and laboratory analysis of memory B cells.<sup>9, 10</sup>

**c. Study population.** Ideally, to be most useful, especially regarding disease burden, a cohort study should be based on a representative sample of the entire population. However the need for a representative sample must be balanced with the need for a sample that will produce a valid study. Study validity requires efficient enrollment; willingness to provide biologic samples; accurate recall of lifestyle, other exposures, and medical history; and finally accurate ascertainment of disease outcomes. Recruiting this kind of population is an enormous challenge in countries with sparse healthcare resources and barriers like illiteracy, gender inequity, and reliance on traditional healers. To reach a reasonable compromise between representativeness and internal validity, we have relied on decisions made by our local investigators in Africa. They have decided that the cohort study will be based on a national sample of teachers in South Africa and Tanzania, on health professionals (chiefly nurses and midwives) in Nigeria, and on enrollment in two different communities (one semi-urban, and one rural) in Uganda. We will recruit 20,000 participants at each of the five sites, for a total of 100,000 participants. We are reassured by the news of substantial socioeconomic and lifestyle heterogeneity among both teachers and health professionals. So our approach follows the model of the classic British doctors' study, which began in 1950, and the U.S. Nurses' Health Study, which began in 1976. In these and many other cohort studies, the non-representative population sample was used for etiologic investigations based on the same arguments as outlined above. We are convinced, however, that PaCT will be much more diverse than the British and American studies mentioned.

**d. Recruitment.** Recruitment of participants will vary a lot across the five institutions, due to differences in infrastructure and source population. In South Africa and Tanzania, the nationwide teachers unions are already deeply involved in the planning process, and remarkably committed to participating in the study. Hence, through their union rosters, and through interaction with principals in the various schools, we expect to reach efficiently the entire source population of teachers in the areas selected.

In Nigeria, in January 2009, we met leading representatives both from the Nurses/Midwives Association and the Doctors Association. Because both groups enthusiastically support us, we will have ready access to their rosters of members. As with teachers in South Africa and Tanzania, we will maximize diversity by sampling members distributed throughout the country.

Although computer literacy is rising quickly, currently it's estimated at 30%. So self-administered paper questionnaires will be important. We will use them for health professionals in Nigeria, as well as for teachers in South Africa and Tanzania. We will, however, offer computer-based questionnaires for those with adequate skills. A substantially different approach needs to be taken at the two sites in Uganda, namely Kasangati and Bushenyi. There we will face problems of illiteracy, migrations, and geographical remoteness. The only realistic way to get complete and valid information, considering the different languages and dialects, is through personal interviews. So we will train a cadre of such interviewers. The pilot studies will help us fine-tune and optimize the interviewing method. We are seriously contemplating using cell phones in Uganda, and if we do so, trained interviewers could be located centrally at the universities in Kampala and Mbarara. They would be aided in the villages by local research assistants who would set up the cell phone interviews. (See Table 1 on following page for protocols by site.)

**e. Pilot studies.** After extensive preparatory work (visits to individual sites, three all-collaborator meetings, weekly telephone conferences, and thorough IRB review) pilot studies have now begun at all five sites. Table 1 summarizes their features. Briefly, the pilot study will enroll a total sample of about 2200 individuals and follow them for 6 months. This pilot phase is unique in its scope, size, and strict coordination across institutions. We envision that a series of publications will come from these pilot studies. What we learn from these pilot studies will guide the next and larger phase of this initiative—for which we are now seeking support from the NIA. We expect to learn much about efficient enrollment, retention, and follow-up. Results will become available from all sites in the early fall of 2011.

**Table 1: Summary Table of PaCT Pilot Study Protocols by Site**

	<b>Tanzania</b>	<b>South Africa</b>	<b>Kampala, Uganda</b>	<b>Mbarara, Uganda</b>	<b>Nigeria</b>
<b>PI</b>	Marina Njelekela Co-PI: Kaushik Ramaiya	Jimmy Volmink	David Guwattude	Francis Bajunirwe	Clement Adebamowo
<b>Institution</b>	Muhimbili Univeristy	Stellenbosch University	Makerere University	Mbarara University	Institute of Human Virology - Nigeria
<b>Population</b>	Primary school teachers in 3 districts	Teachers in Cape Metropolitan area	Residents of Kasangati Parish (semi-urban)	Residents of Bushenyi District (rural)	Nurses in 2 hospitals
<b>Outcomes</b>	1. Percent enrolled and retention at 6 months 2. Prevalence of NCDs & risk factors 3. Incident NCDs in 6 months	1. Percent enrolled and retention at 6 months 2. Prevalence of NCDs & risk factors 3. chronic kidney disease 4. Incident NCDs in 6 months	1. Percent enrolled and retention at 6 months 2. Prevalence of NCDs & risk factors 3. Incident NCDs in 6 months 4. Patterns of health seeking	1. Percent enrolled and retention at 6 months 2. Prevalence of NCDs & risk factors 3. Incident NCDs in 6 months	1. Percent enrolled, retention at 6 months 2. Prevalence of NCDs & risk factors 3. Incident NCDs in 6 months
<b>Sample size</b>	400	1000	200	300	300
<b>Recruitment</b>	Random sampling 2 methods compared: Paper forms via Educ. dept distribution system <b>Vs. Teachers Union</b>	Random sample of Education Dept. employment register, Invitation via principal	Random sampling of households Sensitize community leaders Reimburse for time at each visit (~\$3)	Random sampling in 4 villages. Gain support from local village council	All nurses or random sample, invitation from hospital administrator
<b>Inclusion criteria</b>	Age 20-60 years Currently employed National health insurance	Teachers in Cape Metropolitan area Speak English/Afrikaans	Age 18-65 years Residents of parish Speak English/Luganda	Age 18-65 years Speak Nyankole	Age 18-65 years Currently employed
<b>Exclusion criteria</b>	Retired teachers, or retiring in next 12 months	Retired or retiring in next 12 months	Pregnant women Psychiatric illness, too ill, unable to provide consent	Residents of other villages	Retiring in next 6 months
<b>Follow-up</b>	6 months	6 months	6 months	6 months	6 months
<b>Biologics</b>	No	Yes	No	Yes	No
<b>First interaction</b>	Mailed questionnaire Form for anthropometrics & bp filled by clinic nurse Focus groups in Dar only	Questionnaire through school Clinical exam + biological samples at schools	Face-to-face interview by research assistant	Face-to-face interview by research assistant Biologic sample collection	Face-to-face interview by research assistant
<b>Second interaction</b>	Follow-up paper questionnaire Follow-up questionnaire measures incident NCD outcomes + FFQ	Option to follow-up through mail, e-mail or cell phone Follow-up questionnaire measures incident NCD outcomes + FFQ	Household, face-to-face interview Follow-up questionnaire measures incident NCD outcomes + FFQ	By cell phone Follow-up questionnaire measures incident NCD outcomes + FFQ	By cell phone Follow-up questionnaire measures incident NCD outcomes + FFQ

**f. Baseline measurements.** At enrollment time, we will use a uniform questionnaire instrument at all five sites. This instrument is now under development, and we will refine it after the pilot studies. For example, extensive work has gone into developing a food frequency questionnaire that accommodates the wide range of dietary patterns across sub-Saharan Africa. Professor Walter Willett (Chair, Department of Nutrition, Harvard School of Public Health) has played a crucial role in this work. The baseline measurement will also cover a large range of lifestyle factors including, but not limited to, measures of stress, socioeconomic circumstances, education, reproductive factors (among women), physical activity, smoking and alcohol use, healthcare utilization, and anthropometric measures, just to mention a few.

Because a full-scale biobank cannot be funded now, we intend to take blood samples from a random sample of 1,000 participants (5%) at each site, thereby generating a bank of 5,000 blood samples. This biobank, although small, will allow cross-sectional comparisons between the participating institutions and countries. It will also permit more formal case-cohort analyses (in Project 3, Mental Health, when additional samples are taken from individuals with incident disease during the follow-up period). Procedures for the biobanking process are described under Core C, Biological Bank.

**g. Retention and Follow-up.** Retention of men and women in cohort studies is crucial and always a challenge. This is true even for the renowned health professionals cohort studies at Harvard. Only through great effort (including up to six reminders) has retention there remained high over several decades. In the African setting, retention problems may be even worse.

Follow-up will be at least annually. As a cohort study of this size has never been done in Africa, we will explore innovative methods of follow-up. Sub-Saharan African is the fastest growing mobile phone market in the world; household penetration rates often exceed 75%, even in remote regions. Our African collaborators anticipate most participants in this study will have access to their own mobile phone. We believe this presents a significant opportunity to radically improve follow-up and retention of what will be the largest cohort study in Africa. We are developing a platform that enables inexpensive and automated follow-up via interactive text or voice-based surveys.

We plan to try many ways of using cell phones. We will keep in touch by making repeated calls, giving cell phone air-time as rewards, and using the public media. We rely here on the cell phone research in sub-Saharan countries led by Nathan Eagle. He has overall responsibility for the cell phone aspect of PaCT.



Although pilot studies will provide more solid evidence, we are already confident that a high level of retention can be gained in these ways.

A more difficult problem will be to ascertain and validate all the outcomes of primary interest. This will require continuous development work, validation studies, retrieval of hospital records, results from verbal autopsies, and interviews with relatives, as well as other new approaches. Again, we are confident that use of cell phones will help this.

The Global Cohort Integration initiative aims to harmonize the use of algorithms for disease classification in resource-sparse settings. As the specific project proposals explain in more detail, we will use existing validated instruments to assess, for example, stress and mood disturbances.

**h. Samples.** Biological samples will be stored by Core C, the Biobank, during the course of the project and analyzed as-needed for studies initiated by the Projects. Cohort studies increase in value over time, as we have learned at HSPH, becoming fully mature only after 10 years or more. We have every intention to apply for additional funding at the end of the P01 to extend and expand this cohort. However, should the collaboration and the cohort disband, samples would be returned to the collection sites. While the grant is active, Core C will manage samples and Core A and the leadership team will discuss and manage any specimen storage quality control issues.

**i. Timeline.** Our team has discussed extensively the best way to optimize follow-up time--and to maximize the cumulative incidence of disease outcomes--within the constraints of a five-year grant. Based on our discussions, we propose the following timeline:

**Year 1:** Preparatory work, including hiring and training of personnel, development of questionnaire (including translation to and back-translation from the relevant languages), establishment of IT infrastructure, preparation of the biobank, and definition of source population.

**Years 2 & 3:** Enrollment of 20,000 cohort participants per site, for a total of 100,000.

**Year 4 & first 6 months of Year 5:** Follow-up, ascertainment and validation of outcomes, optimization of procedures for retention and compliance, and analyses of cross-sectional data.

**Last 6 months:** Cleaning databases, analyzing data, and preparing manuscripts based on the follow-up data.

**4. Integration.** Integration has been a key goal of PaCT ever since our first round trip to the African countries in January, 2008. We have used the work of the facilitators from VISIONS, Inc. at three subsequent all-collaborator meetings to solidify this goal. Our work on pilot studies and weekly teleconferences has further strengthened it. We have indeed reached a stage where everyone agrees to common standards, centralized data management (see Core B) and biobanking procedures (see Core C). Teaching initiatives (although outside the scope of this program project) will further ratchet up the sense of team work and collegiality. We have seen increasingly concrete plans to develop distance-learning, web-based approaches, and integration through personal contacts both from the African countries to Harvard, and vice versa. All participating institutions have declared their strong support for the Harvard School of Public Health to play a powerful coordinating role in this complicated initiative (see Core A).

**5. Communication.** Core A will work with the HSPH Public Relations office to develop a media strategy for the overall project in the U.S., and to ensure that local communications strategies are developed for each participating site/country. Local communications will be discussed at annual meetings and regular PaCT calls. Thus we will clarify the aims and value of the project locally and globally, and raise awareness of NCDs in developing nations.

**To conclude.** We believe that this first-ever large longitudinal cohort study of chronic disease across four countries and five sites has the potential to become ground-breaking. In sub-Saharan Africa, our study is revolutionary in terms of design, size, and scope. It also provides a powerful infrastructure for capacity-building and for training a new generation of health professionals. African economic growth may not be sustainable unless chronic non-communicable diseases are brought under control. We have seen huge and successful investments in the prevention and treatment of infectious disease in Africa. Now is the time to build on that success, and go after the chronic non-communicable diseases with a large-scale longitudinal cohort study.

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