

The Power of Persistence: María Amparo Pascual MD MS Founding Director, National Clinical Trials Coordinating Center, Havana

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Throughout the 1980s, Cuban researchers at the country's biotech campus known as the Scientific Pole were making innovative discoveries and began developing unique therapies and vaccines unavailable elsewhere in the world. The pace and level of innovation meant prioritizing the establishment of a dedicated, internationally-certified institute for clinical trials. These and other accomplishments in science and related sectors, coupled with statistics revealing that 53% of all scientists in Cuba are women, prompted *MEDICC Review* to publish a series of interviews with outstanding Cuban women in science, technology and medicine.

In this, the second installment in the series, we spoke with Dr María Amparo Pascual, a biostatistician, researcher and professor, and the driving force behind the design and establishment of Cuba's Clinical Trials Coordinating Center (CENCEC). From 1991 to 2014, Dr Pascual served as founding director of CENCEC. During that time the center implemented internationally-recognized good clinical practices (GCP), launched the National Clinical Trials Coordinating Network to support trials overseen by CENCEC, began conferring master's and doctoral degrees in clinical trials; initiated a quality management system for all trials (receiving ISO 9001 certification in 2008) and created the Cuban Public Registry of Clinical Trials—a bilingual, WHO-accredited Primary Registry, the first in the Americas. In 2013, the BBC recognized Dr Pascual as one of the most influential female scientists in



Latin America for her achievements, including becoming Cuba's first biostatistician and her work at CENCEC.

In 2014, Dr Pascual stepped down as director of CENCEC but didn't slow down or leave the center she helped build, literally from the ground up: she currently serves as management consultant and researcher at CENCEC, as well as director of the Research Ethics Evaluation System Project there. She is also a professor in the Center's clinical trials graduate degree program and of bioethics at the Medical University of Havana. She is finishing her doctoral dissertation on clinical trials in Cuba and the founding and evolution of CENCEC.

MEDICC Review: You're a biostatistician with a remarkable career in science and research. How did you get involved in clinical trials?

María Amparo Pascual: I love biostatistics and I've dedicated my life to science. It's my passion. Early in my career, I worked at the Ministry of Public Health (MINSAP) evaluating how Cuban institutes conduct research and our research methodology: Is it relevant? Is it rigorous? Is it replicable? In the mid 1980s, I began my first foray into clinical trials as head of the Clinical Research Department at the National Institute of Oncology and Radiobiology (INOR). I was a one-woman department, working completely alone; all my time was devoted to researching clinical trials methodology, international protocols and related topics. I was fascinated.

By that time, the research campus known as the Scientific Pole was developing innovative therapies and biopharmaceutical

products, so it became imperative to establish a center for clinical trials [founded in 1981, the Scientific Pole received a billion dollars in investment from the Cuban government and within a decade included 52 institutions dedicated to scientific research and development—Eds.]. A group of Cuban scientists with related experience was convened and I was proposed to direct the new center.

I enjoyed my work immensely at INOR and was very good friends with my colleagues there, so it was difficult for me to decide to make the move. Agustín Lage, INOR's director at the time, convinced me that it was an exciting opportunity and that I was the right person for the job. But he also warned me that such a move wasn't without risk: I would be organizing a clinical trials center from scratch and in an uncertain context. This was during the 1990s, what's known as the Special Period, when resources were scarce and Cuba was in dire economic straits. But I'm a

Sagittarius! I love challenges and exploring beyond my comfort zone, so I decided to take the leap.

MEDICC Review: That was almost 30 years ago. Were there many women scientists in leadership positions at that time in Cuba?

María Amparo Pascual: Back then it was quite rare to have a woman directing a scientific institution. There were a handful, like Dr Concepción Campa, who led the Finlay Vaccine Institute team that developed the VA-MENGOC-BC vaccine for meningitis, and Lidia Tablada, who founded and directed the National Center for Animal Health, but the rest were men. For a man to be named director of an institution was unremarkable. But women have to work doubly hard to reach that level—they're usually responsible for resolving issues related to their children or home for instance, and there's also a certain level of gender bias women have to overcome—especially back then since it was so novel to have a women director. It wasn't easy. But where other people see limitations and difficulties, I see opportunity.

Today it's a different story. I've noticed younger men, in my own family, among my colleagues, assuming much more responsibility at home and for child care, for instance. They're present and actively participating in domestic life. It's also striking how many women are directing institutions or hospitals today. Likewise, we have many women in leadership positions in politics, ministries and the like. Nevertheless, while over 50% of scientists in Cuba are women, we don't represent half the directors of scientific institutes.

MEDICC Review: In your experience, have you noticed a difference in leadership styles between men and women?

María Amparo Pascual: In my opinion, men and women *do* have different styles of leading but I think generalizing can be dangerous, so this doesn't apply to all men or all women, but I've found that women are generally more demanding of themselves. And this translates into being more demanding in their work and with the team they're leading. We see a problem and we want to solve it—I think this is an attitude towards life that not all, but many women have. Like a dog with a bone, we don't let go until we've solved the problem and that leaves an impression on those working with us. Women leaders in my experience tend to be more human as well—when it comes to conflict resolution, for example, or when someone is having personal challenges, they are more likely to offer counsel when it's requested and appropriate.

I also think part of the reason Cuban women scientists make effective leaders is their persistence. Of course, they have to know the subject matter inside and out. In my case, I have to know about clinical trials. I have to know what has been achieved, I have to have experienced it firsthand. A director can't lead and delegate if they haven't done the work themselves. This provides an undeniable authority to their leadership, underscores their persistence and helps others believe in their vision.

Leaders and directors aren't perfect—we're human after all! But the best leaders—regardless of gender—are those who can marshal and allocate resources responsibly, who can walk in other people's shoes and empathize. It helps if they are humble and lead by example. When you lead by example, you will make

mistakes and commit errors, we all do, but when workers see their leader walking the walk and not just talking the talk, as the saying goes, that has an impact. With good, effective leadership, workers feel confident and secure. We have seen cases of worthy, important institutions that are deteriorating due to poor leadership.

MEDICC Review: You mention persistence as an important characteristic of leadership. Can you talk about some examples from your own experience establishing CENCEC?

María Amparo Pascual: Persistence was key since we basically started from scratch. First we had to design a strategic program and learn what we didn't know. To achieve this we visited clinical trial centers and consulted with experts around the world: Italy, Belgium, France, Canada—from that experience, we learned how to design, conduct and evaluate clinical trials according to international protocols; we trained specialists, and organized and equipped the entire institution, from laboratories to work spaces. Although Cuba was in terrible economic shape at the time, the political will was there and resources were made available to establish the center based on standardized norms and best practices.

We began in a cramped office, only 120 square feet. My desk was right beside the bathroom, so anytime anyone used it, they had to squeeze by my desk! We worked in rotating shifts for lack of space. But as the Scientific Pole grew and more products required trials, we moved to an old convent. We had an entire floor, so it was bigger, but it didn't have the proper conditions for the work we were doing and the strategy we were developing. So we persisted, insisting that we needed a larger, more conducive space.

It took three years, but again, the political will was there and we received resources to further develop CENCEC as a center for conducting efficient, high quality clinical trials in accordance with standard protocols. It wasn't an easy task: we had a full staff by this time, and a very robust product pipeline with ongoing and pending trials. Moreover, the decision was made to erect a new building with all the proper conditions, to house both CENCEC and Cuba's regulatory agency, the State Center for Quality Control of Medicines, Equipment and Medical Devices. Luckily, we had the full support of MINSAP and then Minister Dr Roberto Morales, allowing us to inaugurate a new, high-tech and fully equipped center in 2014. By that time, we had a staff of 150 people—the majority women; and I'm proud to say that half of the people who were part of our desk-by-the-bathroom team are still working at CENCEC today.

MEDICC Review: Given the day-to-day challenges in Cuba, including low salaries, how has CENCEC been able to retain scientists and researchers?

María Amparo Pascual: Obviously, everyone needs a minimum salary to maintain themselves and their families and, while salaries are low, it's important to recognize that money isn't the only factor driving why and where people work. Motivations beyond money include having a passion for what you're doing and working in conditions favorable to pursuing that passion, enjoying opportunities for professional advancement, and receiving recognition for your achievements. This helps create a sense of support, appreciation, commitment and pride—especially, in our case, since producing safe, effective biotechnology and

pharmaceutical products is strategically and economically important for Cuba. Our workers receive recognition not only from their colleagues, but also from national leaders and international authorities.

When CENCEC started, it was obligatory for our researchers to pursue higher degrees—they were given one day a week to study, go to school. We instituted an academic development strategy early on and in 2008 initiated master's degrees and doctorates in clinical trials. We were also one of the first scientific centers to link pay to performance, which also helps retain talent. Together, these factors paved the way for one of CENCEC's major achievements: designing, implementing and maintaining a quality management system for all clinical trials. It was launched in 2006 and in 2008 received ISO 9001 certification from the Spanish Standardization and Certification Association.

If I leave any kind of legacy, it's having helped create a team of people who are engaged, who love what they do and come to work every day motivated to do more. Is this because I'm a woman and does it have to do with my managerial style? Could be . . . but retaining workers—in any sector—depends on the individual, on the recognition they receive, and on leadership.

MEDICC Review: And the younger generations? Are they pursuing careers in science?

María Amparo Pascual: Recently a young CENCEC colleague and I were talking about this same issue. I see a new generation of scientists hungry for knowledge, traveling to the provinces to work with our national network of clinical sites, visiting hospitals and colleagues within the network, and studying for higher degrees, all while earning a salary which doesn't resolve their day-to-day problems. And I began to analyze why . . . why do people choose to work here even though they don't earn that much? What motivates them to choose a career in science? As a graduate school professor, I ask young people thinking of going into the sciences: Do you like it? Are you passionate about it? Would you rather be doing science than anything else? When a student is lukewarm, waffling between science and another field, I tell them: Science is not for you. Sometimes here in Cuba we put a fine point on how many scientists we have, how many doctors we have. It's an accomplishment to have so many doctors, so many dentists and health professionals, but these statistics, while laudable, don't tell the whole story. We have to ensure that those who pursue science are passionate about it, that science is what keeps them engaged and excited. If that means we're training fewer scientists, let's train fewer scientists! It's a question of quality not quantity.

MEDICC Review: And would having fewer scientists mean better paid scientists?

María Amparo Pascual: Again, I don't want to generalize but I think many people are so hyper focused on money, they lose sight of other virtues and advantages implicit in a given profession. There are Cubans today who abandon their careers, opting for whatever job will make the most money the fastest. Others look overseas and emigrate. But others stick with science and research, despite low salaries. It's important that leaders transmit what makes a certain career or workplace attractive, highlighting favorable factors for different kinds of work and recognizing that

everybody has other pursuits and passions in their lives that are important. It can't be all work, all the time—that doesn't make for a well-rounded or happy individual.

The salary issue is nothing new: it has been debated and analyzed at all levels and providing solutions and raising salaries is high on the agenda. But it's taking a long time. Meanwhile, day-to-day economic challenges persist for these workers; the situation can cause researchers to lose enthusiasm and motivation. Nevertheless, I don't think raising salaries is enough to resolve all these issues.

Unfortunately, sometimes the discourse here sounds like a parent lecturing a child: "You have to motivate workers to produce more! They have to work harder! Low production is why salaries are low!" That's not the way to motivate people—even if it comes from good intentions. It may have worked 30 years ago, but we're in a different historical moment and need different strategies so people feel committed to their work, so they feel appreciated and compensated for their contribution. This doesn't transcend the salary challenges, but it helps to some degree.

MEDICC Review: The Cuban Public Registry of Clinical Trials lists more than 200 trials underway in different phases. Conducting these trials depends on a national network of clinical sites, specialists and participants. Can you talk about this piece of CENCEC's work?

María Amparo Pascual: A Canadian colleague once told me, "CENCEC is the largest clinical trial center in the world!" I didn't understand what he meant until he said, "It covers the entire nation; few centers have such extensive reach." And it's true: Since the beginning, CENCEC's strategy has incorporated different elements to take advantage of our single, universal health system. In 1993, we established the National Clinical Trials Coordinating Network, including a certification program for clinical sites, ensuring they're applying GCPs; that same year, Cuba conducted its first controlled, randomized and concurrent multicenter clinical trial. More than a hundred independent ethics committees for scientific research were also established across the country; these operate in accordance with WHO guidelines. People working in these clinical trial sites are indispensable to the process. Yet, I see challenges here. What they do isn't directly linked to production, strategy or services and thus while their work is just as important, it's not as tangible or visible. So they generally receive less recognition for their contributions and lower salaries than colleagues working in other parts of the process. How can we raise their spirits and keep them motivated? Higher salaries of course, but we need to forge other solutions as well. This is an area warranting more study.

MEDICC Review: Trials are underway with Cuban biotech products in countries around the world, including the USA. Can you comment on the recent collaboration between our two countries to test and produce one of Cuba's market leaders, CIMAvax-EGF?

María Amparo Pascual: There has been tremendous enthusiasm for this non-small cell lung cancer therapy since Phase IV clinical trials concluded in Cuba in 2015 showing CIMAvax-EGF to be safe and effective. These were highly complex trials, including over 1000 participants across 61 clinical sites. That same year,

the Roswell Park Cancer Institute in Buffalo, New York signed an agreement to start clinical trials of CIMAvax-EGF and several other Cuban biotechnological products in the USA. Just recently, this collaboration has taken a step further, with Cuba's Molecular Immunology Center and Roswell Park joining to manufacture CIMAvax-EGF at the Mariel Special Development Zone west of Havana.

Collaboration like this doesn't happen overnight—the agreement is the result of years of hard work. Once again, persistence is paying off. Fortunately, there has always been interest in bilateral cooperation between US and Cuban scientists and health professionals. I hope that as a result of this persistence, US patients will one day have access to CIMAvax-EGF and other Cuban vaccines and therapies [the embargo and related travel restrictions prohibit US citizens and residents from traveling to Cuba for medical treatment—Eds.]

Remember, this is brand new territory for both countries, but perhaps it's the first step towards closer collaboration in other sectors. Bringing new biotech and pharmaceutical products to market involves high levels of risk and few are willing to be the first to take that risk—particularly in a climate of uncertainty and fear. And there has been a lot of fear manufactured about Cuba, especially recently in the USA. When other entities and companies see that Roswell Park can do it, that fear begins to wane and they begin to think: If they can do it, maybe we can too. I don't want to get ahead of myself, but this agreement could be a bellwether; already we're seeing stronger cooperation in the cultural and environmental sectors, so who knows what doors this might open? I have colleagues at the University of Miami, for

instance, who are very interested in working with us on bioethics but restrictions for legal travel on the US end make it difficult; it would be great to be able to deepen this collaboration in the future.

MEDICC Review: You have so much energy . . . Any plans for retirement?

María Amparo Pascual: When CENCEC's new center was inaugurated in 2014, I asked to be relieved of my position as director so I could finish my doctoral dissertation—or try to finish it! I'm in my 70s, I have a 92-year old aunt I take care of, plus I head CENCEC's ethics committee and am a graduate school professor. I'm no longer the director, but I still work at CENCEC, with a regular desk in the open office work space with the other researchers there. I like being around other scientists and most of them are young, which I like too.

I don't want to admit it, but I'm ancient! Many times I've asked myself: why am I still working?! But I love what I do and think it's in my blood. My mother was a teacher and my father was still working at age 92—he instilled in me the idea that work should be a passion, that you live to work, not the other way around. I'm convinced that our future success depends on passing the baton to younger generations who share this philosophy. We're seeing this right now in politics with our new President who embraces new technologies, employs new methods of communication, and explores different solutions. We have very talented young people, with the knowledge, experience and maturity to assume leadership roles to move Cuban science forward; we need to encourage and support them. 