In the next 30 or 35 minutes I'll take you through a topic, how I chose my topics for research and what I've learned from them and that I will share with you. So I started my career at Trippmer Pondicherry and as a medical student I had no interest in research at that time. From Trippmer I moved to the All India Institute of Medical Sciences and there during my residency again I was interested exclusively in patient care. I did get introduced to some very big researchers but still research did not fascinate me. I was not very fascinated by means, medians, P values etc. I did present a paper in my journal club on the impact of transplants in thalassemia by Dr. Lucarelli from Italy and that fascinated me and I thought that I would choose transplant as my career and that motivated me to go to the US. It's a different thing that while being in South India I did not see thalassemia and while being at Ames since hematology was a separate department and we did not rotate through him even though he was in the methodology during our training I did not see thalassemia as well during my residency training. Anyway I moved to the US, I moved to Detroit and thought that I will do transplants as one of my careers and then see where to go. But when I was at Detroit two things happened during my training. The two things were which made a change in my career thought was the first thing was the development of the drug imatinib against CML and this drug brought down the utility of transplants in one of those conditions which was then the most common condition for doing allogenic transplants. The second thing that happened during my stay in the US was the infamous Bezwoda affair and I call this infamous because as a resident and as a fellow in the US the maximum transplants that I did were for advanced breast cancer and this was a plenary session in the year 1999 in ASCO but and interest in transplant was really growing as a career because if advanced breast cancer had become an indication for transplant imagine how much was the future of the transplanters. But this data was re-examined and unfortunately found to be forged and hence I called I called this as an infamous Bezwoda affair. I was then confused what to do
and then one of my teachers there Dr. Ravindranath I asked him Dr. Ravi I wanted to do transplants but now I am unsure and he told me a single statement some year you become an expert of the disease and not of the procedure because then you may try to put everything into that procedure. That single line really made an impact on me. So I decided that I'll just pursue as an oncologist and not as a primary transplanter and I also thought that transplant I would do and it would just be one of the aspects of treatment that I would offer to my patients. I then moved back from the United States back to my alma mater the All-End Institute of Medical Sciences. When I joined as a faculty there just to let you know that my interview was my joining interview the expert was Professor Advani. So once I joined there as faculty I was still not interested in research. My wife told me some year you should write some projects and I said I was not very keen but then you know it's always good to listen to your spouse and I did. But then I thought what projects to write and the person who had made an impact for research during my residency even though I didn't like research was Dr. M. K. Bhan. Just to let you know many of you may know him but those who of you who don't know I probably considered Professor M. K. Bhan as the biggest medical researcher aims as ever produced and perhaps maybe the biggest medical researcher from our country. He's the one who brought out the low or smaller ORS the Rota vaccine and what a thinker he was. He made me think that your own data is more valuable than what you read in the books. So with those thoughts I said let me see what topic to choose and I said we have different stages of disease. One of the problems was that there were too many patients and inadequate infrastructure to handle the load that was another challenge. There was obviously financial unaffordability for several molecules at that time old and now many of them modern molecules. So Dr. Bhan had said these challenges are opportunities if you have a research mindset which I did not have at that time. But I was also told by several people that while you are addressing the challenges simultaneous cutting edge research is also needed. With this thought

process the first disease that we worked on in our group was retinoblastoma and at that time the entire world was working on only intraocular retinoblastoma but at all in the Institute of Medical Sciences at that time almost 35 to 40 percent of the patients were presenting unfortunately with proposed eyes and advanced retinoblastoma and this prompted us to choose advanced retinoblastoma as one of the topics of our research and Dr. Venkad Radha Krishna who is currently the head at Adiara Cancer Institute did this work of using pre-operative chemotherapy
and converting accentations to enucleations in these patients. He also showed the impact of PET CT scan as a major useful parameter to tell which patients will definitely do worse and he was able to show that if there is uptake in the optic nerve virtually every single patient ended up dying. So this paper he published and he also brought out a new staging system as part of his work on MRI findings of advanced retinoblastoma. The lesson was that choose topics which are relevant to your place, your city, your country. You don't have to ape something flamboyant if it is not applicable to your micro environment. Nobody in the western world would have ever thought of doing any research on advanced retinoblastoma because they never saw it. Inadequate infrastructure was another issue. So when I say inadequate infrastructure I don't mean to say that we did not have the facilities. The patients were too many and the beds were few and this probably is a problem at several institutes across the country. As a newly joined faculty member one of obviously at that time things were different we were admitting all neutropenic fever patients for which we didn't have beds and they were we were waiting we didn't know what to do. So the first study we did on this aspect to handle the inadequate infrastructure was to see if we can convert some of the intravenous antibiotics to oral antibiotics and see if that can work in low-risk febrile neutropenia in the outpatient setting so that the beds can be conserved and this seemed to work well. It was safe and it was feasible. Once we took once we were able to solve the low-risk febrile neutropenia problem then the next issue was the AML patients where we were routinely admitting patients for high dose era C and then keeping them for their toxicities and very with a very with a difficult mindset not knowing what to do what will happen. We decided that we will give outpatient consolidation therapy for AML and we found it was safe and feasible not only that we were able to cut down the antimicrobial use with much fewer healthcare resource utilization. Once having solved this problem the next one was the relapse AML. So when I joined we were not treating relapse AMLs but over a period of time we started treating relapse AMLs and then the issue was again that we didn't have beds and we decided to use the ADE regimen as an outpatient approach and again we found that we could do it. The outcomes were similar to those who were in patient and in fact there was no increase in mortality rather there was less nosocomial infections and lesser use of antibiotics. So again it became a cost effective efficient approach. Then one of my current colleagues who was then my DM resident Akash did this work on actually discontinuing antibiotics in low risk febrileutropenia once they became a febrile even though the neutrophils were very low. Again the saved cost less antibiotic use with no compromise on outcomes. We have just concluded a trial which took seven years to complete due to the COVID pandemic of early stoppage of empiric antibiotic therapy in high risk febrileutropenia and we are still to publish the data on this recently completed trial. So the lesson that we learned was that these challenges actually resulted in better outcomes. Less beds were needed, lesser use of antibiotics, lower nosocomial infections and finally lower costs. Coming to financial and affordability of modern molecules. There has been one of the greatest papers very recently published from from the Tata hospital on low dose immunotherapy in head and neck cancer. Again as you can see that much lesser cost was able to provide equivalent outcomes. Likewise I was very fascinated by the metronome. Those of you who know it's an instrument which is played by the musical orchestras as background music which gives intervals

of regular musical sound. The metronomic therapy concept and we did a randomized trial and we were able to show that in non-bone sarcomas the use of metronomic therapy was better than placebo. And this very concept of showing the benefit of metronomic therapy in non-bone sarcomas got extrapolated then to rhabdomyosarcoma as maintenance therapy where in currently it is the standard of care to give a prolonged metronomic regimen for one year in rhabdomyosarcoma. After having published this data one of my other colleagues was able to show that oral metronomic therapy is as effective as pazopanib in advanced soft tissue sarcomas. Again as you can see the survival curves of pazopanib and for oral metronomic therapy is exactly same. Again the lesson learnt is all the existing challenges that we had resulted in something better or equivalent than the so-called standard therapy. So I have talked about different stages of disease inadequate in infrastructure financial unaffordability but then sometimes over a period of time I started doing research not just for these things but also where I had my own passion. My own interest got generated from my own health issue of severe motion sickness and that prompted my interest in anti-ematics. I've also been very fascinated by traditional medicines. My interest in anti-ematics prompted me to do this study on aprepidant as an add-on therapy when high ematogenic chemotherapies and this study was one of the studies which was used for bringing this into the guidelines. Again drug repurposing of olanzapine was another study that I grouped it which was the first evidence of use of this drug in children receiving chemotherapy. Again this resulted in significant improvement in nausea and vomiting with high ematogenic therapy and again this got incorporated into the guidelines. As I said I have been very fascinated by the Indian system of medicine as well. All of us know that whenever we get nauseous we like to take ginger and we did this interesting study with the College of Nursing at All India Institute where we use ginger powder versus placebo as an add-on therapy in cisplatinum based chemotherapy and again it improved nausea and vomiting though it is yet to find mainstream acceptance. I'm now going to switch cares and having told you about how I chose research topics I'll tell you what I have learned from these topics and the and the research that I have done over the period of years. I'll pose a question to all of you and it's an MCQ which is the most important quality needed to be a successful researcher. To be very intelligent, to work very hard, to have a very novel idea and it's not listed here and any of the choices may be right. It is not a neat question or a names entrance question where only one answer is right. Here more than one answer may be right and you may have your own choices but my choice is it is not listed here and I'll tell you why I say so. I'll start by telling you why I say so which projects get favored for funding. Those which are multi-centric, collaborative, improve standard of care and of national importance but I'm going to focus on the first two aspects only.

Multi-centric and collaborative. In India, all of us work as single nuclear families and we need to understand the concept of joint families. So coming to INPOG, Dr. Poona Kure from the Tata Hospital and Anupam Satchtiva initiated the Indian Pediatric Oncology Group in 2008. They said that we'll form a group and they chose neuroblastoma as a disease. So they sold the seeds for this group. It took some time to take off and then a new group was found in 2015 and this new group invited memberships, formed subcommittees, set rules for collaboration, authorship, acknowledgments and set targets for the group in general.

So we formed 25 subgroups. One of the criticisms that time was that if one disease has not matured, how will you succeed in 25 subgroups? And the answer that we gave was

that we don't want 25 to succeed. We want only 10 or 20% of these to succeed. These are just

subgroups created. We just want some of them to succeed. And believe me, this happened in early

2015 and by mid-2015, we had a provisional registration for ALL and a Hodgkin study and one which was in process for AML. By 2016, so many groups became active.

And by 2017, in two years, you can see the number of groups that became active in this oncology group. It increased in 2018 and by 2018, for one of the studies, the recruitment also got completed. And just to let you know, by 2020, more than 12,000 patients had been recruited in various studies. This number went up to 18,000 in July 24.

Why did I spend this time on this collaboration? I have stayed in a nuclear family in New Delhi and I have not had the fortune of being in a joint family. But I've had the fortune of having a joint family in my institute and making it as a joint family with several institutes across the country. So why do I say this is important? When you, so coming to the first quality being very intelligent, even if you are not very intelligent, if you are in a joint family, maybe somebody will be very intelligent and will take care of your lack of being super intelligent. Coming to hard work. Well, you all of us need to work hard. There's no question about that. Nobody says that you don't work and then you achieve success. That doesn't happen.

But when you work hard in a nuclear family, 5 plus 5 is 10. But in a joint family, it's not 5 plus 5. It's multiplicative. It's 5 into 5 and it becomes 25. You have the same cohort of samples that can be used in multiple studies. You have one person doing PCR and he will do the same work for 10 studies. So it's multiplicative game, not additive.

I'll come to another question which we'll try to answer the next part. Do we have to be in an academic center to be a successful researcher? A question which many people say and I'll give you the example of this gentleman, Dr. Kawasaki. Dr. Kawasaki after World War II was working in a hospital which was owned by the blood bank in Japan. And he saw some patients in his practice with some swollen lips and URI and eyes and something. And he said it's a new disease and he was mocked at by the big doctors from the University of Tokyo saying that oh no no it's nothing. It's just the same URI. But he was very confident. He published a paper in 1960s which is supposedly one of the best papers of a descriptive study of what these patients were. Even then he was not acknowledged. But he continued to believe in what he was saying and it took 20 years in 1992 when Kawasaki disease got into the Nelson's textbook of pediatrics. My next question to all of you is do we require big grants to do big research and publish big? So 12 years back in 2012 I was very interested in looking at the impact of micronutrients in pediatric cancers. I sent the study to ICMR and like many of my failed applications this was one of them and I got a single statement that there is no novelty so it's not funded. Then I collaborated with the scientist who was an expert on micronutrients and that scientist had sufficient funds to assist me in the research. And 12 years later the study

got published in a reasonable impact factor of nine impact factor it got published 10 years later.
Well if it was not novel 12 years back it still got published 10 years after that.
While funding is desirable lack of funding does not imply that the planned research cannot be fulfilled. I would say look for alternate lab based strategies or you can always look for
rich collaborators that is what I did. Well we have two points here invention and innovation.
Invention is something totally new. I am not an Einstein but innovation is something that
many of us can do and we don't need big money for that which is kind of repurposing or as you
know there's music being refurbished being brought out. I'll take you back to 1990s in Bangladesh
and a lot of women were dying of postpartum hemorrhage and there was a balloon which was
very expensive and most of the women there obviously could not afford it.
But then this lady Dr. Sai Babakthar while working in the gynecology hospitals used a condom she hooked it to a Foley's catheter and simply used it as a balloon to control postpartum hemorrhage and it got it was really spread worldwide as in the by the WHO as the Sai Babakthar technique for controlling postpartum hemorrhage.
The point that I was trying to make was that you don't always need big money to do big research.
I'll again come back to that question that I posed for you and I have added two more
points in that the most important quality to be a successful researcher. Intelligence,
hard work, novelty of ideas which I said that if you have a group somebody will may give you
a more novel idea as well. Collaboration a very important thing that I talked about big grants but not listed here. Again your choice could be anything maybe it's collaboration
but for me it is still not listed here and this is the last point that I'm going to present before
you. Why I say that the most important quality is still not listed to be a researcher.
Many of you who have done PhD are a very difficult DM or MCH thesis after working for three years
or five years may have sent a paper somewhere and the very same evening it may have come back
by the editor. It's not suitable please choose some other journal and they'll give you a list of
five or ten journals that you can apply to. It may have happened and you would have thought
oh I worked for five years and this editor just rejected me in three hours.
I can tell you that I have submitted when I submit an application for funding my success rate is
less than 20 percent. Many of them say oh you have reasonable funding I said but I submit many more.
I have more rejections than successes and I want to tell you this very interesting motivating letter.
Dear Dr. Marshall I regret that your research paper was not accepted for presentation. The number
of abstracts that we received continues to increase and for this meeting 67 were submitted and we
could only accept 56. In the 11 abstracts in the Australian Gastro-Intrology Society
out of the 11 abstracts that were not accepted for either an oral or a poster

presentation was
the abstract of Dr. Marshall and this very rejected abstract won him the Nobel Prize for
Helicobacter pylori as the causative organism for pepitical disease.
The reason I say is I tell my PhD students that if your first paper gets published in science
or cell good luck very good but I'm not sure if you will be a researcher for times to come.
For those who fail I say research is still awaiting you for being successful. I don't mean to say that
don't publish in your first score please do that's good luck but remember that if you succeed first
time failure will still come and how you accept the failure is more important than how you take the
success. I consider personally having failures more important than getting successes. Some of
the biggest actors Amitabh Bachchan still going strong with Kon Bhanigakarot Pati those of you
who are fond of movies like me I can tell you I'm very fond of Hindi movies. It took seven years
for Amitabh Bachchan to get his first success in 1973. Seven years it again took eight years
for Anil Kapoor to get his first success after coming to the film industry in 1977. So those
who get initial failures tend to go to late. So success is not the absence of failure rather it
is persistence through failures and I will end my talk here with key three lessons for you
what I have learned. Sustainable collaboration having a joint family with a single kitchen
is the key to successful research. Lack of funding does not preclude conducting innovative research.
Research is about sustaining failures and not successes hence the term research.
I want to thank my team this is just a very small part of my team.
My acknowledgments I'm not giving any names because the names are far too many and I was scared
that if I have mentioned some I may miss many my teachers my residents who teach me so much.
I don't know if I teach them but they teach me a lot my PhD students my colleagues my collaborators
my family funding agencies NGOs FARMA industry and above all my institute where I work and where
I stay the all-end institute of medical sciences. Thank you CRST for giving me this opportunity.
Thank you so much for this patient hearing. Thank you so much.