

UNIVERSITY OF ILORIN



ONE HUNDRED AND FORTY-THIRD (143RD) INAUGURAL LECTURE

**“TOWARDS BETTER PREVENTION / CONTROL
OF HYPERTENSION AND DIABETES”**

BY

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DR. EMMANUEL OBI OKORO,
Professor of Medicine
University of Ilorin

**This lecture is dedicated with love &
gratitude to my mother.**



**MAMA IFIANA OKORO (nee UTUETU)
Passed on 14th November, 2013
Celebrated /interred on 14th February 2014
(St. Valentine's Day)**

Courtesies

The Vice Chancellor Sir,
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My Lords Spiritual and Temporal
Distinguished Invited Guests
Gentlemen of the Print and Electronic Media
Friends and Relations
Great Unilorites!
Ladies and Gentlemen.

Preamble

An inaugural lecture is a media /social event used by a University to celebrate the scholarly achievements of a professor.

This deepens public understanding of how University work improves human condition.

More importantly, it allows Professors to give a public account of how their research has expanded what is possible.

Sometimes, this event transforms into a platform for the system to hear from itself through the perspective of ONE in a frank manner that can galvanise redemptive action.

Today's presentation has some of these elements and more.

For ease of presentation, one intends to follow this outline: courtesies, preamble, introduction, my contribution, recommendations, conclusion and acknowledgements

Introduction

Nigerians die unnecessarily from hypertension (HBP) and type 2 diabetes (DM2), even when on treatment. Some argue (Enwere *et al* 2006) that non-adherence to therapy because of high treatment cost and widespread poverty contribute to this observation.

But, needless medicines, tests and hospital visits can escalate treatment costs (Okoro *et al* 2001; Okoro & Davies 2001, Okoro EO *et al* 2002, Okoro EO *et al* 2002, 2005, Okoro & Oyejola BA 2004, Arije A *et al* 2007, Unadike BC *et al* 2008, Okoro EO *et al* 2009, Ajayi EA *et al* 2010).

This means better utilization of resources can lower cost and improve quality. Surprisingly, Nigerians generally contribute more to treatment costs than those living overseas.

For example, in Germany, with an average GDP per Capita of about \$ US 42,230 almost everyone has social health coverage with no household paying more than 10% of health care cost. This is not so in Nigeria, where the GDP per capita is only \$ US 2,450, and social health coverage remains below 10% and users pay 70-90% of total treatment cost at point of use [see Okoro EO *et al* 2005, 2009, data.worldbank.org].

HIDDEN WEALTH IN OUR POVERTY PYRAMID

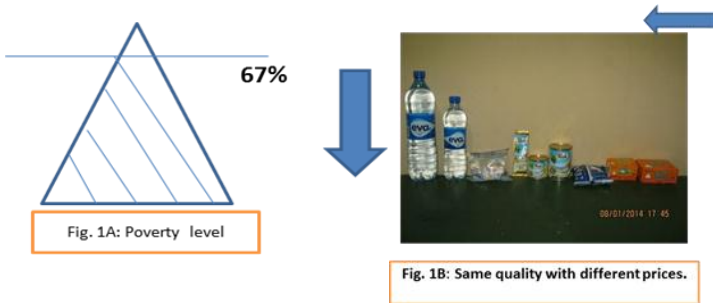


Fig 1A & B : Depicting poverty level in Nigeria and same quality brands at different prices.

Nevertheless, Nigeria is a huge market of over 170 million people who are predominantly poor (Fig 1 A) with unmet health needs. The real challenge is how to deliver quality care for common conditions like HBP and DM2 at lower costs within the purchasing power of majority at the bottom of the poverty pyramid.

Already, imaginative entrepreneurs are creatively turning poor people into paying customers; by making needed products / services available at prices within their purchasing power without compromising quality through size reduction/packaging (Fig 1 B). Our (Okoro EO *et al* 2005, Okoro EO *et al* 2007, Mokuolu OA, Okoro EO *et al* 2007, Okoro EO *et al* 2009) Research & Development (R & D) experience suggests that ordinary people are willing to pay more for health care innovations that deliver superior and affordable services .

The focus of this presentation is about my research contributions in finding new ways of delivering better care at a lower cost.

Specifically:

Evolve initiatives to prevent HBP/DM in at risk individuals develop affordable care that saves Nigerian lives better and prevents costly hospitalisations from complications in those already afflicted.

Mr Chairman sir, my contributions.

BUT FIRST, A BRIEF BACKGROUND TO MY CONTRIBUTIONS

Data (Ekere AC *et al* 2005, Unachukwu CN *et al* 2008, Adedapo ADA *et al* 2012) from many different regions of the country now indicate that HBP and DM2 diabetes as part of non-communicable diseases(NCDs) may have overtaken infections (communicable diseases) as a leading cause of hospitalizations and untimely deaths in Nigerians. Specifically, the ever rising incidence of HBP and DM2 is now approaching epidemic proportions with some reports (Okoro & Oyejola 2004, Ogeh SO *et al* 2012) indicating that 60-70% of those with DM2 have elevated BP , while another 20-35% in the background population also have HBP.

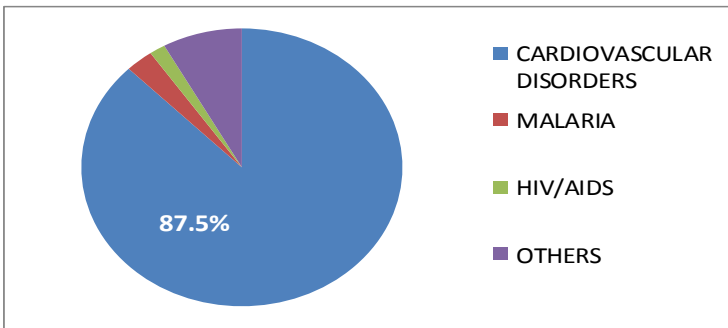


Fig. 2: Autopsy data showing main drivers of untimely deaths (Source : Obiora & Amakiri 2012)

Autopsy reports (Izegbu *et al* 2007 , Mbakwem AC *et al* 2009, Obiora & Amakiri 2012) now increasingly show that HBP with or without DM2 has emerged as the leading driver of untimely deaths in Nigerians, 18 years and older , ahead of MALARIA, HIV/AIDS and RTA (Fig.2). These observations are consistent with an epidemiologic transition to Western type disease pattern.

Not only that, the age of onset of these conditions is becoming lower with each generation to the extent that some teenagers now manifest them , unlike in previous decades, when HBP and DM 2 were predominantly afflictions of late middle age and elderly Nigerians (Williams AO *et al* 1975 , Osuntokun BO *et al* 1979, Mbakwem AC *et al* 2009, Ogah SO *et al* 2012 Fasanmade OO *et al* 2013).

BUT WHAT IS HYPERTENSION?

The driving force generated by the pumping action of the heart that moves blood around the body is called blood pressure. This increases with age and can become a health hazard causing untimely death and complications if the increase is persistent . This sustained elevation of BP is termed HYPERTENSION.

WHAT IS DIABETES?

This condition is characterised by persistent elevation of blood sugar. There are mainly two types of diabetes.

Type 1 results from lack of insulin production and predominantly afflicts the young who require daily insulin injection for life. On the other hand, over 95% (Okoro & Oyejola 2004) of Nigerians with diabetes suffer from type 2 variant which results from inability of the body to utilise insulin. With time however, the body fails to produce insulin from exhaustion. This is a progressive disease that predominantly manifests in middle age/elderly , but this is changing as illustrated earlier.

Untreated, DM2 is crippling and can lead to blindness, kidney failure, amputation, stroke, etc and untimely death. When

DM2 and HBP manifest simultaneously in the same person, this risk is amplified, a situation akin to turning a smouldering fire into a raging inferno by adding petrol.

HYPERTENSION AND TYPE 2 DIABETES: TWO FACES OF THE SAME COIN

Unfortunately, majority (70%) of Nigerians with DM2 also have elevated BP, just as many with HBP exhibit abnormal glucose metabolism, a silent forerunner of overt DM (Okoro & Oyejola 2004, Ogbu & Neboh 2009). Significantly, our work (Okoro *et al* 2000, Okoro EO *et al* 2002, Ologe, Okoro & Oyejola 2005) indicate a genetic origin for this overlap , thereby suggesting a common disease mechanism for both conditions (Bernard & Cheung –Chao 2012).

But despite this hereditary nature, not everyone with inherited risk develops HBP and DM2 at the same age in later life, even if at all.

This shows that factors beyond heredity may be involved in disease manifestation. Therefore, if known such factors could be manipulated to delay or even prevent disease onset. This insight came from our experience in cancer prevention which needs to be quickly disposed of.

PREVENTING DEADLY ADULT LIVER DISEASES THROUGH CHILDHOOD INTERVENTION.

Liver cancer/cirrhosis are deadly adult conditions in Nigerians with a short survival time because of lack of effective therapy. It is caused mainly by childhood hepatitis B infection acquired from infected mothers or other infants. The situation is however improving as fewer Nigerians are being afflicted (Holcombe & Babayo 1991, Odusanya OO *et al* 2005) following strong recommendation **.... for the in cooperation of this [hepatitis B vaccine] into the current [then] EPI (expanded programme on immunisation) as there is strong evidence of early infection in life **.

This was part of my submission to the West African College of Physicians (WACP) for specialist certification (Okoro EO 1988). It is a matter of record that 13 years later, routine childhood immunisation with Hepatitis B vaccine has become an entrenched public health intervention for preventing adult deaths from hepatitis B-related LIVER CANCER / CIRRHOSIS. Nevertheless, not all Nigerian children are protected because of poor immunisation coverage (Odusanya OO *et al* 2005, WHO report 2012 see www.who.int/mediacentre/fact.sheets/fs378/en, CDC Morbidity & Mortality Weekly Report (MMWR 2013) and non-sustainability of the programme without subsidy from foreign entities. This means the survival of Nigerian children depends on the benevolence of overseas charities (Fig. 3).

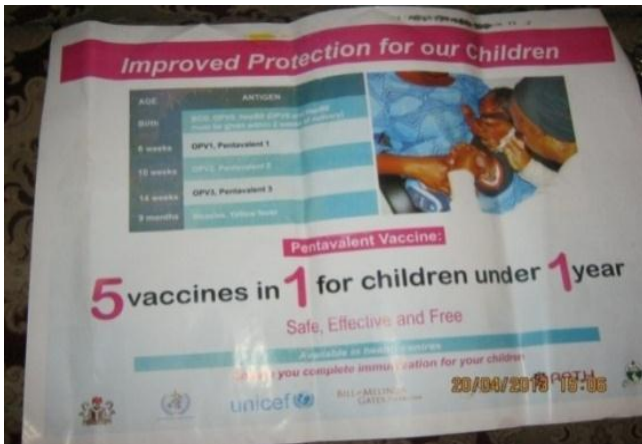


Fig 3: showing financial sponsors of childhood immunisation programme in Nigeria.

This is not something normally associated with truly independent nations. But, Nigerians generally have strong attachment to their children whom they see as precious gifts from God as reflected in names such as Omokowa, Nwakaego,

Omoboriowo, etc. And gladly pay more for affordable services which improve their children’s health and survival (see Emmanuel Ogoigbe 2013 , Mokuolu OA. Okoro EO *et al* 2007). This is something designers of critical public health programmes may wish to take more advantage of to make them self-sustaining, just as traditional healers do when people consult them with more expensive items like live goats, chickens, red clothes, spirit, cash, *Nzu*, etc.

SOME INSIGHTS ON BLOOD PRESSURE BEHAVIOUR IN NIGERIAN GROUPS

Fig. 4

Distribution of mean systolic and diastolic blood pressure by age in boys and girls from Tudum Wada (urban o-o), Zaria City (Hausa traditional settlement area of indigenous population x-x) and Zaria Kewaye (rural ●-●)

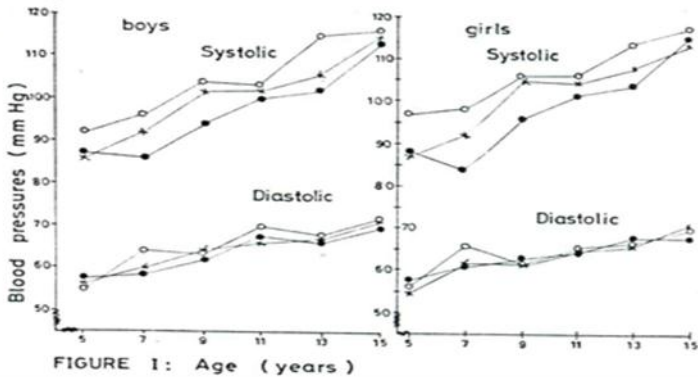


Fig 4: Showing BP rise by neighbourhood and age (source: Hamidu LJ, Okoro, EO, Ali MA 2000).

The studies (Hamidu LJ, Okoro, EO, Ali MA 2000, and Okoro EO *et al* 2013) show that the rise of BP with age is more in affluent urban neighbourhoods than in rural and less affluent city areas. And this BP divergence by place of residence is apparent even in subjects as young 5-6 years (Fig.4). Intriguingly, areas with comparatively slower rise in

BP were the same ones where the observed life styles were predominantly traditional. Interestingly, teenagers whose biologic parents have HBP and or DM2 also exhibit higher BP readings compared to their counterparts without such family history (Okoro EO *et al* 2002). Together, our research indicates that heredity and place of residence are crucial determinants of the magnitude of BP rise with age.

But age-related rise in BP is not inevitable, as populations living on low –salt diets, rarely develop elevated BP, if anything, their BP can fall with age (Akinkugbe OO 1972). Unfortunately, black people are generally more sensitive to the pressor effect of dietary salt (Azinge EC *et al* 2011, Wei W *et al* 2012).

This means Nigerians genetically prone to developing HBP are likely to do so faster, if their diet is persistently high in dietary salt. Incidentally, not everyone with this trait may be aware of their status, thus, are less likely to take preventive measures until it is sometimes too late.

In this regard, our research (see Okoro EO *et al* 1998a, 1998b, 2002a for details) have the potential in identifying such individuals. Specifically, the studies showed that 14% of variations in SBP were due to differences in taste sensitivity to dietary salt in the entire study population. And this increased to 47%, 49% respectively in those with a parent having HBP, DM2 compared to 7% in those whose parents had NORMAL BP, even though the three groups were of comparative body sizes (BMI). What this means is that teenage offspring of people with hypertension & type 2 diabetes with higher blood pressure levels can be identified from a pool of undifferentiated young people well before clinical disease manifest.

In other words, genetically susceptible individuals are identifiable in early childhood through their reduced sensitivity to salt taste which can make them more likely to consume more salt because they taste it less (Okoro EO *et al* 2002 , Azinge EC *et al* 2011). And as higher BP levels in childhood can predict future HBP/DM2 (Fuentes RM *et al* 2002), our

research has the potential for early identification of those at risk at a time when preventive measures are more effective. Therefore, a low salt diet beginning in early childhood in those with inherited risk identified through their diminished salt taste can become an integral part of their lifestyle established from early childhood as in **TRAIN A CHILD IN THE WAY S/HE SHOULD GO AND WHEN S/HE IS OLD, HE WILL NOT DEPART FROM IT (Proverbs 22:6).**

THE ROLE OF BODY SIZE/SHAPE ON BLOOD PRESSURE LEVEL AND GLUCOSE METABOLISM

Fleshy individuals considered overweight are generally perceived as being at risk of developing HBP and DM2. Some experts (Odugbemi TO *et al* 2012, Amira *et al* 2011) believe such body types as avoidable and result from eating too much and not exercising enough. But this view overlooks compelling evidence (Stunkard A J *et al* 1986, Sorensen TI *et al* 1988) from studies involving identical twins separated at birth and raised in different environments which clearly demonstrate that adult body shape/ size are largely genetically determined.

ROLE OF BODY SIZE /PREFERENCE IN VARIATIONS OF BLOOD PRESSURE

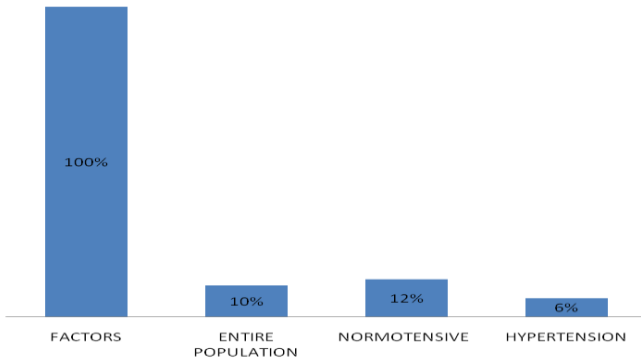


Fig. 5: Showing negligible contribution of body dimensions to BP variations.

Interestingly, our community based studies (Okoro EO *et al* 2013, 2011) did not reveal any evidence linking body weight (BMI) or shape (WC) or both in any major way to the variations of BP observed even amongst those with HBP (Fig. 5). Not only that , despite having the strongest correlation ($p=0.4$) with BP , the influence of increasing age on the effects of body weight (BMI) or shape (WC) on BP was trivial; with a unit expansion in waistline (WC) increasing Systolic BP by 0.35mmHg in under 50s compared to BMI which increased BP by 1.1mmHg in older subjects .

ROLE OF BODY SIZE IN GLUCOSE METABOLISM

This same observation appears true for blood sugar levels {RBS} as neither body size nor shape accounted for more than 1 % of the observed variations in RBS (Okoro EO *et al* 2013, 2011, 2008).

Significantly, the prevalence of impaired glucose handling - a marker of overt type 2 diabetes in the three communities studied was only 0.3% compared to 2.3 % and 2.5 % reported in similar Nigerian Cities at the time(see Okoro EO *et al* 2013, 2002a for detail). This can mean that, neither body size (BMI) nor waist circumference (WC) usually regarded as risk indicators for the development and worsening of HBP / DM2 were as evocative of this risk in the communities in question as described in non-African groups (Okoro EO *et al* 2013, Dowling HJ *et al* 1995). This is also consistent with our findings in some adolescent groups where higher BP was determined more by a positive family history of HBP or DM3 than by body dimensions (Okoro EO *et al* 2002) .

Furthermore, excess weight ($BMI > 25Kg/m^2$) though over-represented in those with HBP/DM2, this was evident in only 38.1 % of subjects compared to 26.1% in those with normal BP (Okoro EO *et al* 2013). In other words, being slim or of normal weight does not always protect against HBP/DM2,

just as being overweight does not by itself always connotes susceptibility to these conditions (Akintunde AAA *et al* 2010, Ajayi EA *et al* 2010 Ekore RI *et al* 2009, Okosun IS *et al* 1998) . Therefore , our pre-occupation with body size as a control strategy may be diverting attention/ resources from more important factors operating in our modern life that are eroding the protection our ancestors enjoyed against these conditions, as new evidence (see details in Kuller LH 2009, Danei G *et al* 2011, Finucane MM *et al* 2011) is also indicating that the role of excess weight in the genesis and progression of HBP and DM2 may have been exaggerated.

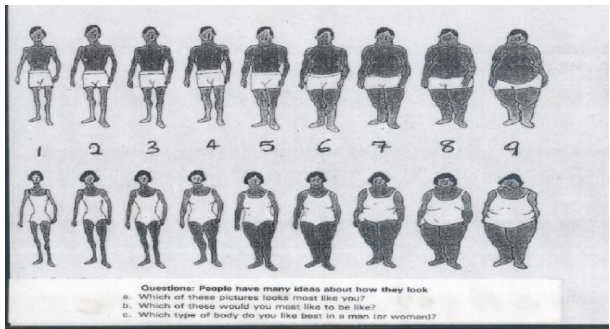


Fig. 6: showing increasing body dimensions (source: Okoro EO *et al* 2008, 2013).

Surprisingly, most subjects regardless of BP categorisation preferred bigger body size/shapes with visible fat (PBF >5) (Fig 6) consistent with other reports (Oloruntoba-Oju, Taiwo 2008. Casmir Igbokwe , 2008, Hesse-Biber SH *et al* 2004) indicating that bigger body size is favourably viewed as a sign of health and wealth in many indigenous cultures across Nigeria e.g. Ogori, Efik, Ijaw where young women still undergo a fattening process to improve appearance as part of marriage rites. Not only that , many Nigerian men are known to have names of endearment for voluptuous women with

large bottom (so called *ikebe super, orobokibo*, etc ,see www.Nigeriansjnamerica.com as at 19/3/2012).

Intriguingly, this preference for bigger body types is also evident (Miller KJ *et al* 2000; Becker DN *et al* 1999) in black communities overseas where citizens are constantly bombarded with information linking excess weight to adverse health consequences. This could indicate a possible racial/ethnic angle to this preference. To be sure our research (Okoro EO *et al* 2008, 2011, 2013) reveals a collective standard of visual beauty in some Nigerian communities that value a body type considered overweight by Western standard. And this desire seems a powerful one capable of driving a unique weight control behaviour inimical to weight loss even in people with hypertension and type 2 diabetes constantly indoctrinated (Okoro EO *et al* 2001, Okoro & Oyejola 2005) to lose weight as part of standard therapy.

Even so, it has since become evident (Gonclaves FM *et al* 2007, Sanchez AM *et al* 2000, Danaei G *et al* 2011, Finucane MM *et al* 2011, Okoro EO *et al* 2013) that at almost every weight level and body shape type , black people of African descent tend to accumulate less visceral fat. This means bigger WC/ BMI may not carry the same risk for HBP / DM2 as extensively described in Caucasians and other non-African groups. Specifically, our work could indicate that 90-95% of the factors that determine who gets HBP or abnormal sugar level has nothing to do with body size or shape. This heterogeneity of HBP and DM2 in terms of disease pathogenesis can mean that risk factors are not the same in all groups and every one. Consequently, preventive measures that work for one group may not necessarily apply to another. Specifically, without recalibration for local realities shown in our data, adopting programmes designed to fit into foreign models of HBP/DM2 control are less likely to deliver the desired health outcome, if weight loss remains the over-riding focus. Therefore, uunderstanding risks specific to individuals and groups can lead to better prevention especially as it appears that the genes that

now put many Nigerians at risk of developing HBP/DM2 are the same evolutionary adaptations that enabled our ancestors to survive extreme scarcity of food and salt (Okoro EO *et al* 2013, Coutler DM *et al* 2005).

Given these considerations, the question is this:

ARE HYPERTENSION AND DIABETES PREVENTABLE?

YES, both conditions are preventable.

For example, several local studies (Okoro EO *et al* 2008, 2011, 2013, Lucille L *et al* 1990, 1994, Okosun IS *et al* 1998, 2000) show that HBP and DM2 are increasingly occurring in younger Nigerians of normal weight or, at lower body weight levels compared to their counterparts overseas of different race and ethnicity . This and other unique characteristics of HBP and DM2 in communities also exhibiting a collective standard of visual beauty that desire bigger body types, means that weight control measures widely advocated in other jurisdictions may be problematic.

Incidentally, our community studies (Okoro EO *et al* 2013, Hamidu, Okoro & Ali 2000) in Kaduna and Kwara States showed that in groups where local cuisines and other life styles were predominantly traditional , the rise in BP with age was less pronounced and the prevalence of abnormal glucose metabolism- a forerunner of DM2 - was even less so .

Our traditional staples such as *amala*, *egusi* , *efo* which are almost vegetarian are known to contain micronutrients capable of moderating the genetic expression of inherited risks , in a way that can prevent or delay the clinical onset of HBP and DM2. Unfortunately, ignorance limits vulnerable people from turning abundant food items we have into nutritious / palatable meals.

For example, despite evidence (Iya N *et al* 2006) showing that having HBP/DM2 is not considered a barrier to healthy diets others in the background population are eating , a lucrative market for selling plantain flour, honey, wheat, imported food items, etc to those with DM2 as substitutes

for cassava, yam, sweet potato, coco-yam, etc, presumed to worsen diabetes control is flourishing . But restricting food choices can escalate treatment cost, jeopardise diabetes control and undermine quality of life.

INDIVIDUALS WITH CONTROLLED DIABETES CAN EAT DIETARY SUGAR JUST LIKE EVERYONE ELSE

Nevertheless, Nigerians are constantly indoctrinated to abstain from eating dietary sugar/ sweet food items for fear of jeopardising diabetes control.

But this is reasonable if DM were a disease that results from eating too much sugar, which is not the case.

Surprisingly, the notion of glycaemic index (GI) where food items are classified on the basis of their ability to rapidly or slowly elevate ambient blood glucose in a way that can aid or overwhelm the residual glucose handling mechanism is consistent with this practice . However, GI is a laboratory phenomenon as most balanced / healthy diets are a combination of many food items which complement each other.

Given the impact a restrictive/ bland dietary regime can have on quality of life, it seem important to attempt to answer the question:

DOES DIETARY INTAKE OF SUGAR AS PART OF A REGULAR MEAL HAVE ANY ADVERSE EFFECTS ON DIABETES CONTROL?

In attempting to answer this question our experimental design allowed subjects with controlled DM to take their tea or beverage with any amount of sugar that suits their taste having previously established that taste sensitivity to sugar vary with individuals, age, geographic region and ethnicity in Nigerians (Okoro EO *et al* 1998, 2000, 2002).

The protocol facilitated the generalization of our (Okoro EO *et al* 2007, 2011) results which showed that taking moderate amounts of sugar as part of regular diet did not aggravate diabetes when the disease is controlled. Significantly,

more evidence has since emerged showing that eating sweet fruits is not only nutritionally good in diabetes, but also helps to achieve better control (Christensen AS *et al* 2013). Notably, eating dietary sugar and sweet fruits in moderation is no longer considered inimical to best practice in diabetes care in many jurisdictions (ADA 2013).

DIET AND LIFESTYLE RECOMMENDATIONS.

In the light of our research findings and current understanding, eating right can overcome our genetic predisposition to HBP and DM2 even without becoming slim by European standards (Okoro EO *et al* 2013, Reis *et al* 2011).

Of note, in the past when HBP and DM2 were less prevalent, Nigerian families lived predominantly on almost vegetarian diets with pieces of animal products shared at the end of each meal as a reward for children finishing their food. Animal products e.g. eggs were widely considered delicacies and only liberally eaten as treats during festivities of Christmas, Eid, etc.

Unfortunately, the influence of globalization is changing our nutritional pattern and eating habits to those capable of accelerating the onset of HBP/DM2 (Odegaard AO *et al* 2012). This means susceptible individuals can prevent or delay the development of these conditions which in practical terms means embracing more of our local cuisines. For example, using local spices/ herbs we have in abundance instead of salt as condiment can result in better control of HBP/DM2 (McCunne & Johns 2002, Oselebe HO *et al* 2012) because of their micronutrients which can minimise the genetic expression of inherited risk in a way that substantially starves off the clinical onset of HBP and DM2 and undermine their capacity to compromise health and life expectancy. This effect is amplified where activities of daily living involve being physically active (Reis JP *et al* 2011, Jarent & Frank 2012, Matheson EM *et al* 2012) as observed in Okelele, Idi-Ape

and Pakata, Zaria Kewaye, Zaria City, Kongo where BP levels and RBS were comparatively lower. In other words, by eating more of our traditional staples and being up and about can avert HBP and DM2 even in overweight individuals that are genetically susceptible.

The earlier these habits are internalised the greater the chances of success. And school health programme remain a veritable platform to accomplish this, hence our invitation to primary and secondary schools.

BACKGROUND TO MY CONTRIBUTIONS IN THERAPEUTICS

The pattern of morbidity/mortality in Nigerians with DM2 as reported by experts (gbera AO *et al* 2007, Unachukwu CN *et al* 2008, Ajayi & Ajayi 2009) is so different from that observed in rich countries (Karter AJ *et al* 2002) but are nonetheless, avertable if effective therapy is accessible to all in need. Unfortunately, high treatment cost limit access to those in need.

Mr. Chairman, ladies and gentlemen, my contributions in this regards.

TREATING ACUTE DIABETIC HYPERGLYCAEMIC EMERGENCIES IN RESOURCE POOR SETTINGS

Diabetes ketoacidosis (DKA) and hyper-osmolar non-ketotic hyperglycaemia (HONK) are rapidly changing metabolic acute emergencies that can complicate DM and frequently kill Nigerians.

Standard treatment protocol (Goguen & Gilbert 2013) recommends ICU admission and access to a chemistry laboratory with the capacity to promptly do an array of tests round the clock. Even where these are available, people still succumb to these emergencies, though survivability appears to be improving (Ezeani IU *et al* 2013). However, fatality rates remain high where basic facilities are inadequate and those in needs are unable to pay for such intensive testing,

even when available. These challenges resulted in a clinical case management system that required mainly a hand-held glucometer (about N10,000 in cost) and utilisation of available tests users can afford without reference to the central laboratory or ICU admission against expert recommendations at the time (Umpierrez & Kitabachi 2003). Surprisingly, a review of the performance of this intervention strategy revealed (Okoro EO *et al* 2007) that almost half of the patients in the series were at some point in our care and this raised disturbing questions about the effectiveness of the educational component of our treatment programme, given their preventive nature.. Even so, the results showed that attention to local realities and judicious resource utilisation can sometimes deliver better and comparative outcome at a more affordable cost (Ogbera AO *et al* 2009, Unachukwu EN *et al* 2008, Eregie & Unadike 2010, Chijioke A *et al* 2010, Obiako & Ogunniyi 2012).

BLOCKADE OF VASCULAR 5HT₂ RECEPTOR CANNOT BE A NOVEL MECHANISM FOR ANTIHYPERTENSIVE THERAPY

BACKGROUND: Janssen Pharmaceutical, a global giant in the development / marketing of medicines used in treating mental illnesses, *serendipitously observed* that ketanserin effectively lowered BP. At the dose range this happens, ketanserin potently blocked 5HT₂ receptors in the vascular smooth muscles (VSM) involved in BP regulation. This led to the announcement that blockade of vascular 5HT₂ receptors was a novel pharmacologic strategy for anti hypertensive therapy. The problem, with this proposition was that ketanserin also had other actions similar to the way established hypertension medicines such as prazosin (MINIPRESS) lowered BP albeit, at higher doses. Not long after, a report (as detailed in Okoro EO 1993) emerged showing that ketanserin was equally effective in 5 patients with autonomic neuropathy, a situation where receptor mechanisms were inoperative. This clearly

indicated that blockade of vascular 5HT₂ or and α_1 receptors were unlikely to be the major mechanism by which this drug lowered BP.

Therefore, as at December 1988, the way this molecule worked to lower BP remained a mystery and this was deeply troubling given its clinical implications. One was immediately assigned a project aimed at unraveling the mode of action of this intriguing compound soon after my arrival in Sydney, Australia to train in advance Clinical Medicine and Experimental/Clinical Pharmacology and Hypertension with Professor GS Stokes in the Hypertension unit of Department of Clinical Pharmacology, Royal North Shore Hospital of Sydney and the Wellcome laboratory of Sydney University. This was a frightening proposition especially for me without a prior degree in experimental science. Surprisingly after many false starts and long hours the results published in Okoro EO *et al* 1995a, 1995b, 1996, 1997a, 1997b, 1997c, 1999, Okoro EO 1999 emerged.

INTERACTION BETWEEN 5HT₂ RECEPTORS & VOC/ OTHER BENEFITS

The project was most prophetic in its conclusion that 5HT₂ receptor was linked with voltage –operated calcium channels (VOC), contrary to the prevailing wisdom at the time, that Ca²⁺ uptake into VSM by neurotransmitter receptors followed an ionic channel distinct from that activated by depolarization with K⁺ .i.e VOC. Thirteen (13) years later, with more sophisticated tools Dr. Sarah Lummis *et al* at University of Cambridge, England and California Institute of Technology, USA reported their outstanding results (see NATURE 2005, 438 (7065), 248-252) which confirmed our prediction) using rather *primitive* tools that neurotransmitters in essence open ion channels in response to binding with the appropriate receptors.

Curiously, when this position was first canvassed in our Tuesday research meeting at the *Wellcome*™ laboratory,

there was such disbelief on everyone's face, you could almost think one had just killed Jesus Christ, especially coming from the only black face in the room. However, the experimental results showed that hypothesis was not so *weird* after all.

The project probably contributed in saving the global drug industry from making huge investments in R & D activity in pursuing the hypothesis that blockade of 5HT₂ receptor was a mechanism for antihypertensive therapy which our experimental data clearly indicated was unlikely.

DEVELOPING AN APPROPRIATE THERAPY FOR HYPERTENSION IN DIABETES

The starting point of this work was our (Okoro & Oyejola 2004) observations that barely 11% of treated patients with DM₂ had their BP controlled to desired levels even with majority on expensive BP medications e.g. ACEIs when cheaper ones like thiazides were available. This prescription pattern though intriguing was consistent with expert recommendations at the time that thiazides ought to be avoided because of their perceived potential to precipitate / aggravate diabetes and induce electrolytes derangement (Opadijo & Omotoso 1996, Opadijo OG 1997).

These considerations made prescribing thiazides with concomitant K supplementation or in co-formulation with K sparing drug standard practice in minimising presumed excessive urinary loss of K. This therapeutic approach though scientifically grounded escalated treatment cost and amplified the risk of medicine-related injuries. Paradoxically and contrary to expectations, the data (Okoro & Oyejola 2004) showed that majority on thiazides achieved better BP control when compared to their counterparts on more expensive medicine types and this also occurred at comparable level of diabetes control.

This prompted extensive study of the literature which indicated that even in doses as high as 50 or 100mg,

thiazides lowered BP in Nigerian groups without metabolic consequences of clinical relevance (see details Okoro EO *et al* 2001, Okoro & Oyejola 2005, Olowoyeye, Dosunmu ,Okoro, Omotoso 1988).

Unfortunately, most of the evidence for these conclusions originated from experiments in groups without diabetes, thereby making it inappropriate to apply such findings in diabetes.

Consequently, it was crucial to answer the question as to whether or not thiazides were safe and effective in diabetes. The theoretical background and peculiarities of our practice area which formed the basis of our experimental design, protocol and methods are extensively detailed elsewhere (Okoro EO *et al* 2001,2002,2005). Our results showed that 12.5-25 mg HCTZ was well- tolerated with sustained fall in systolic BP at the end of 52 weeks without any clinically relevant changes in diabetic control, serum K⁺ or creatinine. Of note ,however, was a perceptible rise in SBP at the end of six (6) months which indicated a second drug that works differently to lower BP may be required over time to maintain BP at the same level in some subjects . Incidentally, our preliminary findings (Okoro EO *et al* 2001) were published ahead of ALLHAT (2002) ; the largest US government commissioned study to find cost –effective drug treatment from available options for HBP in US Citizens with DM2 and reached the similar conclusion as ours , but only after spending millions of dollars across many US universities. This case showed that research does not always need to be expensive nor originate from technologically advanced nations to have the desired health impact . More importantly, a local manufacturer now produces low dose thiazide as a stand - alone medicine (JURETIC) and the research has also inspired another local manufacturer , details later.

Interestingly, when first presented at a scientific meeting of diabetes experts at University of Lagos, the work met with such hostility that one contributor accused this

presenter of dangerous medicine and misleading trainees . Pleasantly, prescription of thiazides in DM is increasing and many scholars are now advocating their widespread use in diabetes (Opadijo & Omotoso 1996, Opadijo OG 1997, Busari & Opadijo 2007) after initially condemning thiazides as causing diabetes. In any case, low dose- thiazide is now standard initial therapy for hypertension in type 2 diabetes globally. For decades, doctors were trained with the notion that thiazides are contra-indicated in DM2 but, our experience shows that popular practice can be deceptive and reinforce the need to safeguard the academic culture where ideas/wisdoms, no matter how sacrosanct can be challenged if they are not delivering as expected .

CONTROL OF HYPERTENSION IN DIABETES

This work notwithstanding , published evidence (Isezuo A *et al* 2003, Adigun *et al* 2003, Arije A *et al* 2007, Unadike BC *et al* 2008, Ajay EAi *et al* 2010) continue to show widespread preference for ACEIs/ARBs and other more expensive BP medicines . Where this preference exists higher rates of uncontrolled BP are recorded. The implication of this is that majority of treated Nigerians are not attaining lower BP targets that can optimally prevent untimely deaths and reduce the incidence of diabetes related complications simply because the therapeutic focus is on medicine types rather than optimal BP reduction. In other words , higher treatment costs are incurred without the expected health benefits simply because of drug combinations inappropriate for Nigerians as black Africans when those that work best for them are widely available and cheaper (Okoro & Oyejola 2004, Okoro EO *et al* 2001, 2003, 2005, 2009 , Adigun *et al* 2003, Unadike BC *et al* 2008, Ajayi EA *et al* 2010 , Ogah OS *et al* 2012). Furthermore , the evidence of superiority of ACEIs and ARBs over thiazides in lowering BP is lacking (Zheng Y *et al* 2011, Mancina G 2006, Casas JP *et al* 2005, ACCORD study group 2010). Therapeutically, similar cardiovascular outcomes

are seen with different drug regimens as long as equivalent decreases in BP were achieved (ALLHAT 2002 , UKPDS 1998).

Significantly, Nigerians generally respond less to ACEIs/ARBs, Beta blockers, etc, and often require higher doses than in Caucasians even though such differences are quickly abolished when thiazides are added (Ajayi AA *et al* 1989, ALLHAT (2002), Casas JP *et al* 2005, BLOOD PRESSURE LOWERING TREATMENT TRIALISTS' COLLABORATION (2005), Mancia G 2006, ACCORD study group 2010. This means that at a daily price of N180, Varsalta (-an ARB) can pay for almost 180 days' supply of a low-dose thiazide at N1 daily that delivers similar cardiovascular outcome (Ajayi & Oyewo 1998 , Okoro EO *et al* 2001, 2004,2005, 2009 , ALLHAT 2002, Adigun AQ *et al* 2003). Not surprisingly, many ARB and ACEIs are now available in our market as co-formulation with a thiazide ; at doses which on their own independently and effectively lower BP in many Nigerians including those with type 2 diabetes(Okoro EO *et al* 2001, 2002, 2005 , Olowoyeye JO *et al* 1988). This has implication for value-for-money as the health benefits of reducing BP in DM2 is tied more to the extent of BP reduction rather than drug type used in achieving it. This is an important therapeutic issue as lowering BP is more effective in saving lives than normalising blood sugar to pre-diabetes level which in itself can be fatal (ALLHAT 2002, UKPDS 1998).

More importantly, most of the interventions widely promoted as best practice in our jurisdiction (Fig.7) in hypertension and type 2 diabetes therapy /control e.g. weight reduction, cholesterol lowering (usually with drugs), Aspirin use, preference for ACEIs/ARBs originate from R & D in Europe and American and are often at variance with what work best for the genetic variants of hypertension and type 2 diabetes that commonly afflicts Nigerians and other black people of African ancestry.

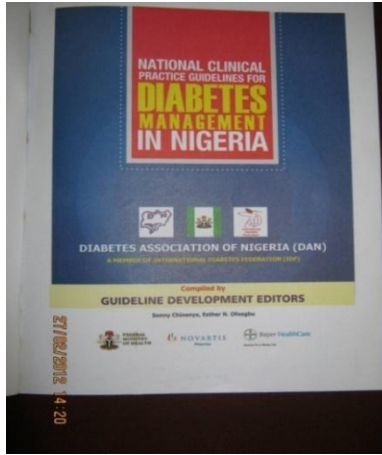


Fig 7 :Showing endorsed national treatment guideline.

For example, in many Western countries, lowering cholesterol (usually with drugs) is standard therapy for preventing untimely deaths and recurrence of other atherosclerotic events in people with DM 2 /HBP especially in those 40 years or younger (ADA 2013). To be sure elevated cholesterol is frequently present in Nigerians with DM2. Indeed, one recent report (Ogbera & Azenobor 2013) indicated that this occurs in over 80 % of cases. Incidentally, atherosclerosis as a histological finding is not rare in Nigerians (Williams *AO et al* 1975, Erete *IE et al* 2012) and this can be accelerated by elevated BP which frequently accompanies diabetes in our compatriots(Okoro & Oyejola 2004).

Given this background, it seems commendable that a panel of diabetes experts and Market Authorization Holders (MAHs) of lipid altering medicines e.g. statins have come together to advocate lowering of blood cholesterol as an effective intervention to improve treatment outcome in Nigerians with HBP/DM2 as endorsed by the relevant authorities in 2012 for nation-wide implementation (Fig. 7). The problem with this however, is that autopsy data (Fig. 8) indicate otherwise and show that genetic factors related to

race/ethnicity and geographic locations rather than cholesterol level underlie atherosclerotic complications in hypertension and type 2 diabetes.

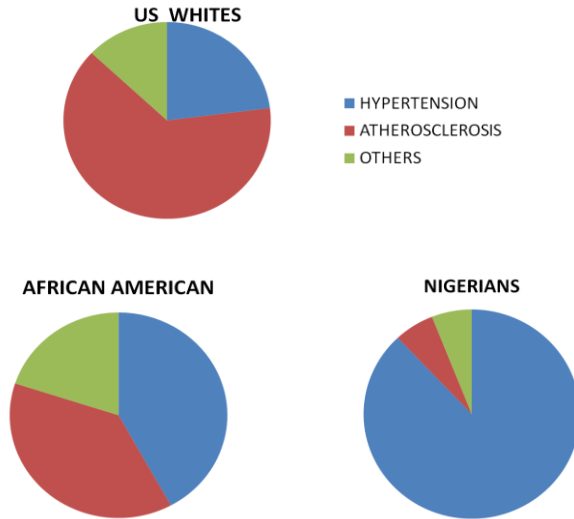


Fig. 8: Showing frequency of atherosclerotic disorders by race/ethnicity constructed with data from Rotimi O *et al* 2004, Onwuanyi A *et al* 1998

Specifically, uncontrolled BP, not atherosclerotic disorders e.g. heart attack remain the dominant cause of sudden death even in African –Americans unlike in their Caucasian compatriots with whom they share a common environment as home, thus, signalling that an African ancestry, even a faded one (Sinha M *et al* 2006, Karter 2003), can confer some protection against occlusive atherosclerosis and show that Nigerians are less prone to the adverse cardiovascular consequences of elevated cholesterol and atherosclerosis.

Even so, several academic hospitals have reported (Sani MU *et al* 2006, Oyati AL *et al* 2005 , Kolo PM *et al* 2013) seeing more clinical cases of atherosclerotic heart diseases

in Nigerians than in previous decades . Put in context, however , such increase still represents less than 1% of all heart diseases treated in one such centre (Kolo PM *et al* 2009).

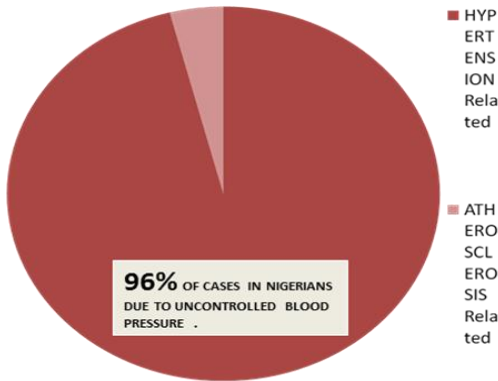


Fig. 9: constructed with data from Obiora CC & Amakiri CNT 2012.

Fig. 9: Showing the contribution of occlusive atherosclerosis to sudden deaths in Nigerians (Source: Obiora & Amakiri 2012).

This latter is consistent with more recent (Obiora CC & Amakiri CNT 2012) autopsy findings (Fig .9) in Nigerians dying from fatal Stroke and Heart disorders which also extend earlier research (Williams AO *et al* 1975, Rotimi O *et al* 2004, Falase AO *et al* 1975, 2001, Mukadas & Misbau 2009) showing that cardiovascular deaths / morbidities in our compatriots with DM2 result mainly from UNCONTROLLED BLOOD PRESSURE and not from *ATHEROSCLEROSIS AND ELEVATED CHOLESTEROL* .

For these reasons, it is extremely difficult to justify lowering of cholesterol as a high priority intervention in saving the lives of majority (> 94 %) of Nigerians with HBP/ DM2 (fig 9) at no risk of atherosclerotic events as is increasingly becoming the practice (Enwere OO *et al* 2010,

Ajayi EA et al 2010, Chinenye & Ofoegbu 2011, Ogbera & Azenabor 2013). Nor is it the imperative advertised to prescribers and patient groups , where lowering cholesterol with these medicine types are now directly promoted to healthy individuals as a weight reduction therapy (Fig. 10); with one fatality already recorded in using statins this way.

PROMOTIONAL ACTIVITY ON HOSPITAL GROUND



Fig. 10A and B: showing direct promotion of cholesterol - lowering medicines to patients in hospital.

Aggressive marketing of this kind (Fig 10 a & B) can do more harm by diverting scarce patient's resources from life-saving therapies that are also low cost and more affordable. This is more so as HBP/DM2 disproportionately afflict the poor and the daily cost of lowering blood cholesterol with drugs can pay for initial BP control in some patients with DM2 for over 180 days at present price level (Okoro EO *et al* 2001, 2004, 2005, 2009, ALLHAT 2002, UKPDS 1998). This is an important point as our payment system requires over 90% of users of health services to pay treatment cost at point of care regardless of need and means.

Given these considerations, most fair minded people will agree that we need medicines that are not only safe and

effective, but also AFFORDABLE and can deliver the HIGHEST VALUE- FOR - MONEY.

Doing so can be challenging , but it is also an opportunity for innovative MAHs to earn more , given the large size of our health market and the emerging diseases pattern in which HBP and DM2 predominate.

Surprisingly, a shorter version of this submission presented to World Health Organization Centres' meeting of over 130 national medicine regulatory agencies /consumer protection agencies in Rome, Italy, on Saturday, 28 September 2013 formed the major thrust of the Director's report to WHO- an organ of UN (see UR 63 October 2013 www.who-umc-org). And is now the basis of a proposed international research conference and global debate involving academics, drug companies, regulators and professionals and health care providers being put together by WHO in Sweden later in the year. This presenter has been invited to speak and join other experts in debating the issue of risks and how this should affect medicine use across ethnic/ racial/national boundaries. Hopefully, a global consensus would emerge on the best way forward in using existing medicines to deliver better care and in the development of new ones that can satisfy the needs of health systems and key stakeholders.

The point here is that most of our interventions widely promoted as best practice in HBP/ DM2 care (Fig 9, Ajayi EA *et al* 2010, Enwere OO *et al* 2010) are in reality derived from research conducted in populations with genetic variants of these conditions that have therapeutic needs diferent from those that commonly afflict Nigerians. This means treatment that delivers the best outcome is not necessarily the same for everyone because of racial and genetic differences. Understanding risks specific to individuals and groups can deliver better care. The challenge ,therefore, for research scientists and health systems is to determine through research which therapy from existing options works best for the population it serves.

In other words, advocating a therapeutic policy of one –size- fits all (Fig .9) can divert scarce resources from life saving therapies that are cheaper. It has to be restated that delivering effective remedies at lower cost can expand access to quality care for ordinary people. This way, so called poor people can be turned into paying customers; a strategy beneficial to the sustainability of health systems and the bottom line of Key stakeholders.

IMPROVING HEALTH SERVICES THROUGH RESEARCH AND INNOVATION

Not only that , available data at the time showed that service delivery was problematic with many public tertiary hospitals operating below set quality threshold with long waiting time and extreme inconvenience, being a common experience of ordinary people even when accessing basic health care (Okoro EO *et al* 2005, see [www. Servenigeria.com](http://www.Servenigeria.com) visited last 7-1-2014).

But understanding such service gaps and local health priorities better (Okoro EO *et al* 2005, Okoro & Oyejola 2005c , Okoro EO *et al* 2001, 2005b , Okoro EO , Adejumo AO *et al* 2002) can be an inspiration to deliver superior care. Specifically, our research showed that the cost structure of DM /HBP care was such that medications alone accounted for over 60% of treatment cost patients bear followed by transportation cost at 21% (Okoro EO, Adewara AA *et al* 2005). But not all drug prescriptions and hospital visits are justifiable on the basis of the best evidence at the time (ALLHAT 2002, UKPDS, Okoro E O , Adejumo A O *et al* 2002, Okoro & Oyejola 2004, Okoro E O *et al* 2010). Further, the high telephone density among those with diabetes means quality care can be delivered without the need for patients to leave their homes on every single occasion (Okoro EO, Sholagberu HO *et al* 2010).

Therefore, by adopting a strategy of judicious medication use (Okoro EO (TG 1) 2005, Okoro EO *et al* 2007, Okoro EO *et al* 2009, Mokuolu AO, Okoro EO *et al* 2007)

better therapies were deployed and our capacity to detect other medicines related problems also improved.

For example, the home-grown system devised detected an upsurge in pentazocine consumption (Fig 11).

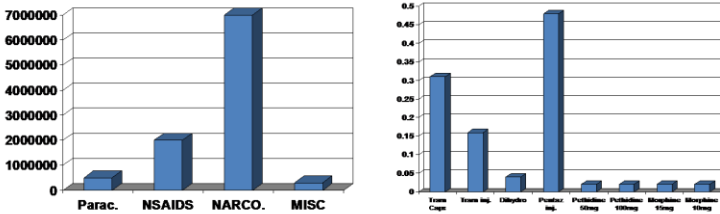


Fig. 11: Showing upsurge in narcotics and pentazocine consumption.

As no clinical indication could be found for the increase and pentazocine availability was unrestricted because international narcotics legislation considered it less addictive at the time in 2005-2006, measures were introduced to control its use as a schedule substance.

Unfortunately, despite these efforts and those of NAFDAC and Federal Ministry of Health at the time prompted by these observations, the empty vials, syringe / needles and empty bottles of spirit (alcohol) in the public toilet of a popular local hotel (Fig 12) could signal that pentazocine may have become a recreational drug of abuse especially in those with Sick Cell disease (Mudrick C *et al* 2011, Makanjuola & Olatunji 2008)



Fig. 12: Showing empty vials of pentazocine injection, needles/syringe and whisky bottle in a hotel toilet in 2012.

Overall, however, the strategy resulted in progressive increase in patronage and a concomitant rise in internal revenue (IGR) which contributed to the hospital's capacity to pay salaries/allowances as at when due at the time despite persistent financial *short fall* from owner government during the period (Okoro EO 2005).

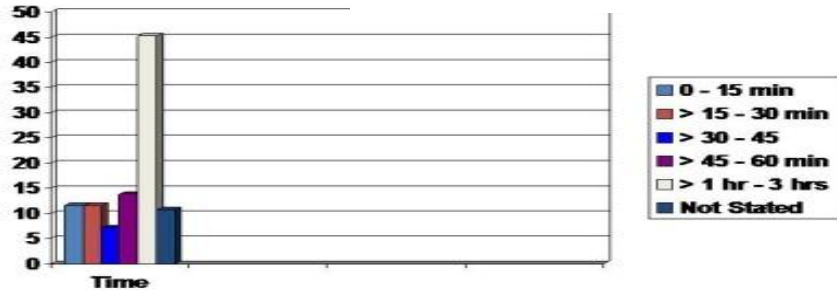
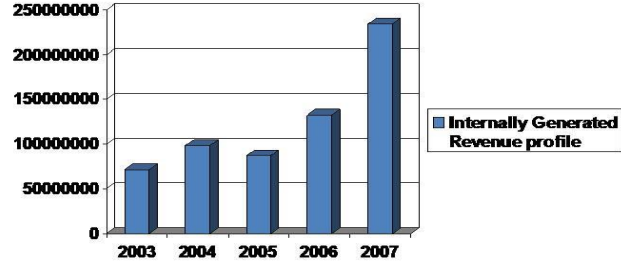
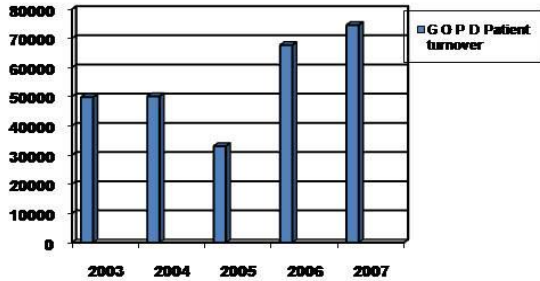


Fig. 13: showing increasing patients turnover and revenue and distribution of waiting time

Unfortunately, despite these modest gains, TIMELY CARE and SERVICE QUALITY fell short of users' expectations. Specifically, the performance indicators for quality service revealed that implemented innovations delivered some but, not all desired outcomes (Fig 13) Nevertheless, the lessons learnt from this initial failure were crucial in testing the hypothesis as to whether or not better quality is possible at an affordable price for basic health conditions like HBP/DM in public hospitals.

It was the expectation of the UK Government which funded the trialing that our ideas at the minimum , would deliver the following:

Provide 70% of total hospital patients convenient services relevant to basic health care in one location within 1.5 hours of arrival at the service points of Antenatal Care (ANC) or General Out Patient Department (GOPD) .

Make it possible for at least 95% of patients paying total health care at the point of service to be able to do so without asking for fee waiver.

And MDG –related health services that included care of HBP, DM, pulmonary tuberculosis, HIV/AIDS, uncomplicated malaria and malaria prevention, diarrhoeal diseases, malnutrition in children, adults as well as routine antenatal care would be available at the service outlets concerned.

Much more were delivered at the time as many of the legacies of these modest R & D efforts remained over 5 years after. For example, treatment guideline based on local research (see Okoro EO *et al* 2002, Okoro & Oyejola 2004 and Okoro E O *et al* 2009) for HBP/DM2 and other common conditions was introduced to reduce treatment variability and optimised resource utilisation with cost savings.

Quality standards with performance targets were set and monitored at ANC and GOPD (Fig 14)

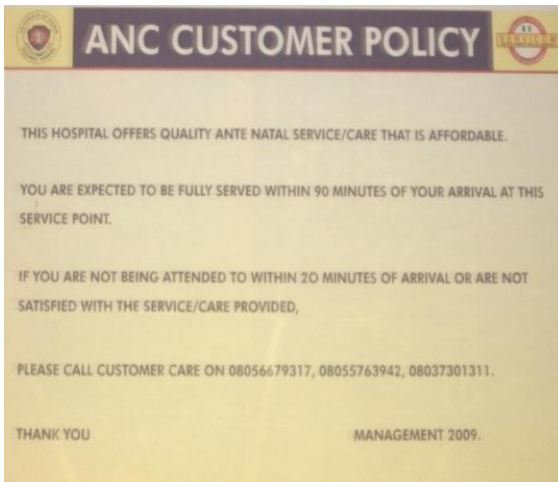


Fig. 14: Showing advertised quality standards

And a *RECEPTION/CUSTOMER COMPLAINT / CARE COUNTER* was created to empower patients, paying customers, to demand for better service (Fig 15).



Fig. 15: showing reception/customer complaint / care counter

And an officer with background in frontline service in the Aviation industry was engaged as Customer complaints/care officer and reported daily to this presenter as pioneer NODAL OFFICER responsible for service quality .



Fig.16: Showing stake holders forum in session

A STAKEHOLDERS FORUM of patients, suppliers, journalists, representatives of market women, youth, religious groups, traditional rulers, professionals, government representatives , hospital authorities, professionals ,etc, was created to brainstorm for solutions to service gaps captured in user's complaints. Meeting was quarterly and the platform also functioned as a review board for appeals from decisions originating from the grievance resolution mechanism of customer service office. The system had a reward mechanism tied to performance based on previous research (OkoroEO, Adejumo AO *et al* 2002).



Fig. 17: Showing specially trained staff motivated to achieve set objectives and targets.

Specifically, nurses/ midwives, record clerks, pharmacists, technologists, community/ research nurse achieved the objective of serving citizens better with resources available.



Fig. 18: showing those at the top with independent evaluation teams from the UK Govt and the Presidency: SUCCESS HAS MANY FACES

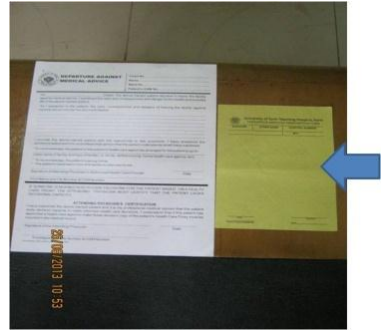


Fig 19: Showing a one- stop ante-natal facility developed and yellow prescription paper for better narcotics control.

Incidentally, many of the infra-structure spinoffs of these R & D efforts remained available for public use over 5 years after handover.

The facilities remain a monument to the uncommon foresight of Drs (now professors) Kuranga/ Mokuolu administration in supporting the ideas that produced them and the magnanimity of the UK government in funding their trialing through the PSRF programme.

The following individuals are hereby acknowledged for their contributions during implementation:

Professor Ben Oyejola (Statistics); Dr P Aboyeji ,now Professor (O & G) and Professor Bayo Lawal (Sociology/Arts /Education). Above all, I remain indebted to the * *small people** down the hierarchy who gave their all including working at weekends/ public holidays to meet tight schedules at no extra cost.

These examples illustrate the capacity of academic units to deliver better services through simple innovations and home –grown solutions.

But beyond that, the enormous creativity inherent in Nigeria’s university system can be unified around the common objective of delivering the highest quality of HBP/DM2 care with available resources in accordance with local priorities ,

if the determination to make this happen exists. To be sure , we have shown (Okoro EO *et al* 2007, Mokuolu AO , Okoro E O *et al* 2007) that optimum care is possible at an affordable price , if effective strategies are devised to minimize the wasteful use of medications and tests particularly for conditions like hypertension and type 2 diabetes that can be effectively treated with largely history and physical examination (Okoro EO *et al* 2002, Rheeder P *et al* 2002, Okoro EO *et al* 2009) .

THE ROLE OF PHARMACUETICAL INDUSTRY IN HEALTH CARE

We are not unique in this as other Nigerian scholars have also published evidence (see recent review by Ogah OS *et al* 2012, Adigun AQ *et al* 2003, Arije A *et al* 2007, Okoro EO *et al* 2001, 2005, William AO *et al* 1975, Erete IE *et al* 2012, Isezuo S *et al* 2003, Rotimi O *et al* 2004) showing that the genetic variants of hypertension and type 2 diabetes in our population require optimal BP control for the best cardiovascular outcome rather than a strategy of lowering cholesterol and modulating atherosclerosis as a universal treatment priority in reducing cardiovascular mortality in Nigerians with HBP/DM2 .

In other words, BP medicines like thiazides (N1 daily), CCB (N10) as against N180 daily for ARBs, statin (N180 daily) or aspirin (N5 daily) represent better value for money in preserving the health and extending the lives of Nigerians with HBP/DM2 compared to their non- African counterparts (ALLHAT 2002, UKPDS 1998 Okoro EO *et al* 2009). This means the health value of a medicine is determined more by its ability to meet the therapeutic needs of the condition being treated rather than by its expensiveness.

Consequently, prescribing expensive therapies when cheaper ones as effective and safe are available can accelerate the emergence of adverse cardiovascular events by diverting scarce resources from life-saving remedies that are

low-cost (Ajayi AA *et al* 1989, Okoro EO *et al* 2004, Unadike BC *et al* 2008, Okoro EO *et al* 2009, Ajayi EA *et al* 2013). While such a strategy can boost sales, it is likely to be at the expense of quality and affordable care (Okoro & Davies 2002). Nevertheless, it is my perspective from experience elsewhere (Stokes GS, Brooks P, Johnson H, Monaghan JC, Okoro EO, Kelly D 1990, 1992, 1994, Okoro EO *et al* 1995, 1997, 1999.) that a robust partnership between academia and the Pharmaceutical industry (PI) will benefit health systems and key stake holders more when effective medicines are used.

Even in jurisdictions where the nexus between university research and public good is not always apparent, it was surprising that our modest contributions (Okoro & Oyejola 2004, Okoro EO *et al* 2001, 2005) could be considered important enough by May & Baker (M&B) Nigeria in developing this product Thiapril™ (see Fig. 20) for treating high- risk hypertension including type 2 diabetes, which others are now actively adopting.



Fig. 20: Showing locally manufactured medicines based on research on low dose thiazide

This example demonstrates that mutually beneficial partnership between scholars and PI that delivers better care is also possible locally. However, such partnership can become problematic if treatment guidelines evolve from a joint panel of scholars–professionals and MAHs whose products are involved, because of conflict of interests. It is even worse if financial sponsorship of the process is by the same commercial entities and key drug treatments recommended are inconsistent with the evidence of what works best for Nigerians with hypertension/type 2 diabetes (Okoro & Davies 2001, 2003). When doctors' prescription decisions are influenced in such powerful ways by * *opinion leaders/experts* * as inadvertently endorsed by Health Authorities probably on face value, this can undermine the delivery of effective health care that represents the best value-for-money based on evidence.

This can be devastating to public health, if more than two thirds of prescriptions fail to lower BP to desired targets simply because prescribed medicines are the wrong ones for their race / ethnicity. The consequence can be that an intervention like BP reduction capable of cutting deaths by more than 50% may end up achieving only 10 %, while at the same time costing more.

In the absence of evidence of health benefits, universal aspirin and statins prescriptions not only escalate treatment cost but can result in fatalities. Therefore, high quality local studies are needed to address this issue as the evidence (see Jennings & Touyz 2013, Okoro EO *et al* 2013, Murray CJ *et al* 2003) is lucid on the heterogeneity of hypertension/type 2 diabetes and treatment that delivers the best outcome is not the same in every racial/ethnic groups.

Unfortunately, when University hospitals operate more as general/specialist hospital / Federal Medical Centres concerned with routine general/specialist practice rather than as academic centres with a mandate of constantly finding new ways through research to deliver the best care possible

with resources available, this can undermine their capacity to function as R & D centers regardless of whether equipped or not with state-of-the-art medical technology to international standard as in the FGN/VAMED project.

Of note, health systems that consistently deliver superior health care are those constantly driven by new ideas-based on research and not necessarily those with the most money or that deploy sophisticated medical technology (Rheeder P *et al* 2002, Gaziano TA *et al* 2005, and Ndinjock R *et al* 2011) .

To be sure, Nigerian university system has a rich tradition of high quality scholarship dedicated to finding home grown solutions for superior health care services to the extent that National Universities Commission (NUC) is able to proclaim that “..*We train for...our needs* “.

For example, in the early eighties , this presenter along with other trainee specialists were mentored by our supervisor , then a Senior Lecturer , Dr John Olubunmi Olowoyeye to develop a new therapy for life-threatening hypertension suitable to our situation which is now a global standard (Olowoyeye JO, Okoro EO , Omotoso ABO 1986, Kotchen TA 2012).

Sadly, there is little in the diabetes treatment guideline for Nigeria referred to earlier (Fig. 9) that suggests this is still the case. And this could signal that there are issues with the capacity of some of our training programs in adequately preparing future specialist –scholars to serve the best health interest of Nigeria and its people, as trainee specialists themselves are now openly voicing (see PUNCH OCTOBER 2013).

In addition, the impression need not be given that our scholarship can support a marketing policy of importing excess medicines developed specifically for treating the genetic variants of HBP and DM2 predominantly seen in Europe and America and then sell them at a prohibitive cost to unsuspecting Nigerians by promoting the notion that lowering cholesterol generally prevents Nigerians from dying from atherosclerotic heart attack and stroke , when this is not the case.

In this regard, there is some evidence (Okoro & Davies 2001, 2003) that inappropriate BP medicines are sometimes promoted as ideal for profit motive and personal gains.

Instructively, many countries in Africa with less resources, fewer professionals per capita, lower government spending in public health services are delivering better health outcomes (see Guardian Newspaper of Monday, 4 November 2013), thereby, showing that allocating more resources alone is never enough to serve citizens better. Our scholarship need to respond to the radical needs of our health system that is making it under perform .

Specifically, this lecture has drawn attention to the fact that Nigerians with type 2 diabetes and elevated BP receiving care in many academic centres may not always be treated in accordance with the best evidence of what is most effective for them at the lowest possible cost. Therefore, it seems so vital to ensure that when citizens pay to access health care they receive services designed to improve their conditions, not those intended to exploit or even harm them. Consequently, academics have a responsibility to ensure their skills/competence are not inadvertently made available to third parties intent on turning our communities into experimental grounds for medicines developed for the health benefits of other jurisdictions (see University of Ilorin Act 1979).

This raises two issues:

First, it means quality control processes in patient care that should ensure consumers are optimally protected against substandard care and exploitation is not always fully operative. Second, it shows that the capacity of some academic units to design and deliver effective treatment that meets the therapeutic needs and peculiarities of our variants of hypertension and type 2 diabetes is suspect.

RECOMMENDATIONS

Consequently, the following recommendations are made:

First, regulatory bodies with oversight function for medical training need to go beyond assessing compliance with training requirements and pay closer attention to quality of patient care which drives doctors' education.

Second, consumers need to stick to the same professionals and avoid using drugs and tests recommended for friends and relations with the same conditions because of treatment variability and the different therapeutic needs of people with HBP/DM2 .

Third, consumers protection agencies, regulatory authorities, civil societies, media, religious groups/organizations and well-meaning Nigerians need to come together to raise public consciousness on the responsibility providers have for delivering quality / affordable care.

CONCLUSION

Even so:

My research has contributed to the evolution of a superior treatment for hypertension in type 2 diabetes that is low cost and now a global standard.

The work has also inspired the production by M & B Nigeria of a unique medicine for treating high –risk hypertension.

More importantly, implementation of ideas from my research as funded by the UK government has demonstrated that with internal efficiency and effective quality control processes in patient care, we can deliver world –class care for common conditions that included HBP/DM2 at affordable prices citizens can pay for .

Co-incidentally, similar principles and objectives as previously reported (Okoro EO *et al* 2001, 2005a 2005b, 2005c, 2009) are now driving reforms in UK public health system (NHIS) since 2010 to make it more responsive to UK

citizens' needs and also resemble key elements in US Affordable Care Act 2012 aka Obamacare.

ACKNOWLEDGEMENTS

Mr VC Sir, beyond money, research remains the most valuable tool for improving health systems.

While we always seem to have enough to work with when the motive of our scholarship is to use our talents to serve humanity better, using primitive tools to do so can involve plenty of pain. Luckily, many individuals were helpful in lightening this burden.

But time constraint would not permit me to mention everyone by name, even if I wanted to. This anonymity can only deepen my gratitude to all of you my friends. Still, one cannot but remember J.O. Olowoyeye, FRCPC, FWACP, a humanist and a monument to Medicine.

This great son of Nigeria from the then Ondo State (now Ekiti State) was truly a mentor at the postgraduate professional level. Regrettably, this very good human person was left with little choice than to leave the system.

That was the era and I hope not anymore, where powerful elements within gave the impression that other peoples' academic success or failure are decided regardless of merit and quality of contributions. But, here I am today standing before you good people and by the grace of my CREATOR having reached the peak of my career as a Professor of Medicine.

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