

Review Article

The Translational Physiologist: Strengthening Research to Enhance Quality of Life

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Summary: Translational research and the Translational Physiologist are new concepts but important for optimizing quality of life of citizens. This paper reviews the origins of the concepts, phases, partnerships and critical factors in translational research. Some barriers to proper functioning of the Translational Physiologist in Nigeria and the role the Translational Physiologist in repurposing are discussed. The paper highlights collaboration between the Translational Physiologist and other specialists to attain optimal health and enhanced quality of life of the citizens.

Keywords: *Bench to bedside; Reverse translation; Translational research; Translational Physiologist.*

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INTRODUCTION

Translational physiology is a very recent concept that was suggested by John Hall in 2002 (Hall, 2002) and derives from translational research but with special emphasis on the physiological sciences. It widens the scope of physiology from the traditional areas of integrative and clinical physiology and extends the investigative scope of basic research to community health. It is therefore a model for physiological investigation from molecular and cellular physiology to population physiology and public health (Seals, 2013). Thus, while integrative physiology aims to connect observations from subcellular events to the whole organism, and clinical physiology focuses on specific groups of patients and healthy controls, translational physiology extends the study of physiological functions from the molecular level to populations of humans with application to public health. Integrative and clinical physiology, however, remain foundational parts of translational physiology (Seals, 2013). The aim of translational physiology is to enhance the societal impact of physiology by promoting and strengthening its role in biomedical research (Seals, 2013).

Currently in Nigeria, physiology is taught in the traditional integrative physiology mode with some addition of clinical physiology. Most researchers conduct their business in silos and results of such studies often end up on the shelf without benefit to the general populace. Translational physiology seeks to extend the traditional integrative physiology into the populace and therefore into public health. In other words, translational physiology extends from molecular and cellular levels through organ/system physiology, the organism into population

studies and public health. Translational physiology, therefore, seeks to expand the frontiers of physiology and reorientate the way research in physiology is designed and executed. To establish and promote translational physiology, physiologists must be properly trained and oriented. Such training must inculcate the philosophy and methodologies of translational research (as described below) and public health. Translation physiologists must also inherit and grapple with the challenges and problems associated with translational research in a developing country. More effort should be made at integrating the traditional integrative physiology to population physiology and public health. Translational physiologists will need to embrace and employ the tools and techniques of population studies and public health research like epidemiology, behavioural science and public policy including those that are needed for synthesizing, disseminating and implementing observations made at the clinical research level to the community. The tools include systematic reviews, meta-analyses and medical guidelines development. Since translational physiology derives from translational research, what then is translational research?

Origin and Basic Concepts of Translational Research:

Translational research started in the early 1990s (Curry, 2008). Originally, it was associated with biology-based attempts at finding new drugs for the treatment of cancer (Sugarman and Mckenna, 2003). Later it got associated with other disciplines of medicine like cardiology, neurology, psychiatry and pathology (Cripe *et al*, 2005). Several terminologies have been used to describe translational research. These include "Bridging the chasm", "walking the bridge," "lost in translation," and "Bridging the gap,"

Presently, it is referred to as “from bench to bedside” (Bench 2 Bedside) (Farrel *et al*, 2019). Translational research encourages and promotes multidisciplinary collaboration between Basic Medical Scientists and Clinical Researchers and thus is aimed at converting results from basic research into activities that directly benefit society. It brings together biomedical scientists, physicians, bioengineers, epidemiologists, patent experts, and several other specialists to achieve the purpose of advancing health care. Translational research identifies and supports the adoption of best medical and health practices for the good of the patient or general public. In addition, translational research encourages academic participation in drug research and development. On the other hand, translational science focusses on unraveling the operational principles underlying the translational process (Gillard *et al*, 2019).

Relationships in translational research

Basic Medical Science research is the foundation of medical discovery. Through it, key information about the fundamental molecular, biological and chemical processes of life are obtained. Clinical trials involve testing new methods of diagnosis, prevention, and treatment of illness using human subjects. It aims to determine whether the new procedure or drug is safe and effective. Through clinical trials, new medications, medication combinations, new uses for existing medications and medical devices are evaluated. Translational research serves as the bridge between basic medical research and clinical trials. It transforms scientific ideas and discoveries into new treatments and approaches to medical care with the aim of improving the health of the population. Examples of translational research include drug development, studies of disease mechanisms, including proteomics, genomics, genetics, metabolomics, and animal models.

Observational studies, such as case reports do not qualify as translational research. Quality of life studies or comparative treatment studies involving patient cohorts in which there is no adequate control group have limited translational value due to limitations in study design. Translational research is broader than the term “applied research”. Applied research is any research that may possibly be useful for enhancing health or well-being. It does not necessarily have to have any effort connected with it to take the research to a practical level. An example of applied research is demonstrated in the study of Jaja *et al*, (2002). In Nigeria, the traditional way of carrying children for extended periods and long distances is on the back. In Europe and America, women prefer to carry the child with the aid of a suspender on the chest when they are not pushing the baby around in a pram. The researchers investigated the energy conserving implications of carrying weight on the back or on the chest. Ten (10) healthy females between the ages of 19.0 years and 24.0 years were recruited for the study. The control experiment consisted of the measurement of arterial blood pressure (mm hg), pulse rate (beats/min) and oxygen consumption (l/min) and the calculation of energy expenditure in each subject after walking a distance of 76.5 meters in two (2) minutes (without carrying any load). Experiments were then repeated with a load of 6.4 kg (average weight of a 6-month-old baby) carried on the chest with a suspender or tied to the back respectively after one week interval. Results showed that pulse rate, oxygen

consumption and energy expenditure were significantly higher when weights were borne on the chest than on the back and showed that carrying babies on the chest was more energy demanding and thus less efficient than carrying the baby on the back. The study thus validated the age-old African tradition of carrying babies on the back.

Partnerships in translational research

Translational research involves partnerships. Figure 1 shows the partnerships in translational research. The central operators are the translational researchers that include the translational physiologists, medical doctors and any other interested and qualified researcher. The physiologist serves as the expert on the bench and is responsible for all results obtained from the laboratory. The medical doctor in the team assists in the recruitment of patients from the outpatient clinic or ward of an approved hospital for the study. The translational researchers will also work with other health practitioners that are not members of the team, especially to ensure orderly recruitment of patients or subjects. These practitioners will also ensure that the patients or subjects are properly catered for. The principal investigator (pi) emerges from this group and is responsible for general management of the project throughout its duration.

Another arm of the relationship is the patients or subjects or participants. This group includes the control and the test subjects. Participants must understand the aims of the study and must be accorded with the greatest respect. All participants of a study must sign a consent form and ethical approval must also be obtained from the relevant institutional review board or the experimentation ethics committee of the institution before the study begins. Where necessary, each participant will have to fill out a well-structured questionnaire that will obtain personal information concerning the participant. Information obtained from such questionnaire are held in strict confidence.

Funding is very important for successful research. Thus, translational researchers must seek out and work with donor agencies for adequate funding. Donor or grant awarding agencies, which may be local or foreign, may include the pharmaceutical industry, Tertiary Education Trust Fund (TETFUND), the parent university, philanthropic organizations and individuals. Pharmaceutical companies could be important allies for the provision of research funds especially for clinical trials. They could also be important in manufacture and marketing of the final product.

The research team will also deal with regulatory organizations like the National Agency for Food and Drug Administration and Control (NAFDAC). This agency is responsible for protocol review and authorization of clinical trials before they are conducted in Nigeria. It is also responsible for carrying out inspection of trial sites to monitor the conduct of authorized studies to ensure that the well-being and safety of the participants are protected and that data obtained are credible. The National Health Research Ethics Committee (NHREC) is responsible for accreditation of the Independent Ethics Committee (IEC) and/or Institutional Review Board (IRB) of different institutions that give ethical opinion on study protocols. Researchers will obtain approval of institutional review boards and ethical committees in their institutions before studies can commence.

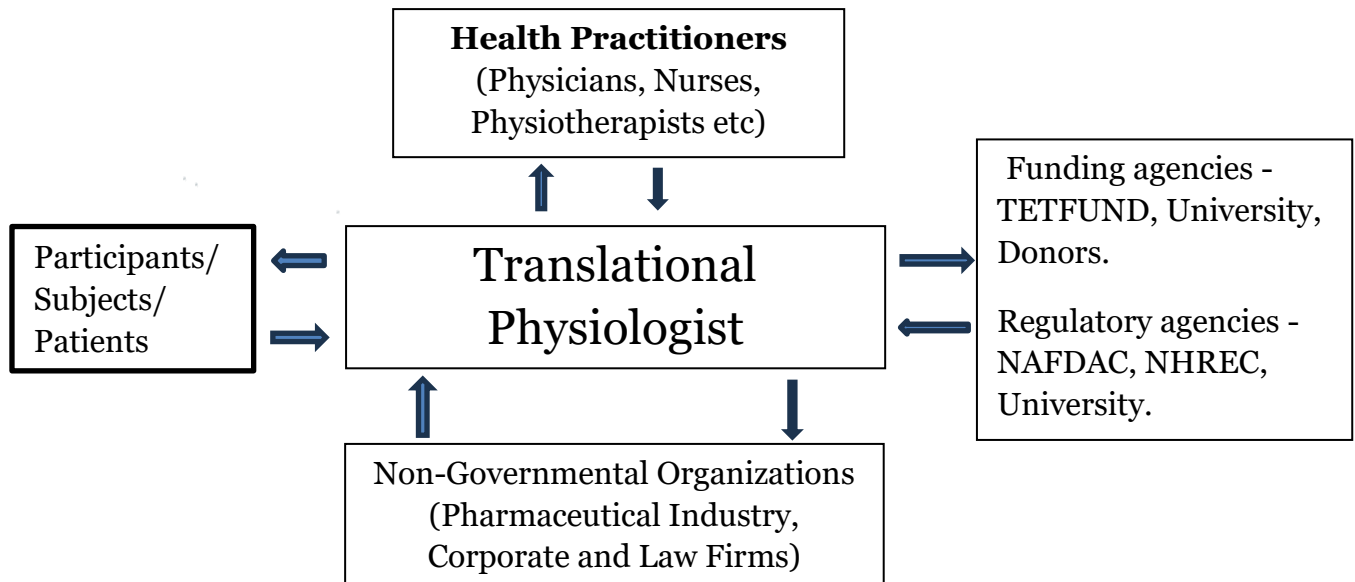


Figure 1.
Partnerships in translational research.

Critical factors in translational research. The following factors are critical in translational research.

Excellence in science. Any person that intends to be part of a translational research team must have a thorough knowledge of the subject. The researcher must also possess adequate and/ or relevant laboratory skills or techniques to deploy for the study. The individual must also have the ability to interpret data. The translational physiologist must possess adequate knowledge and training in experimental design and data analysis. The scientist should be able to conduct research that ensures transparency and reproducibility of his work.

Ability to traverse domains. The translational physiologist should be able to collaborate with others and break down disciplinary boundaries to collectively advance the development of a medical intervention. being a translational scientist requires venturing beyond one's own research discipline or professional domain to gain an understanding of the fundamental knowledge, methodologies, and priorities of all other disciplines and domains involved in a translational research project. an effective translational scientist should be an interpreter of the multiple languages of biomedical, clinical, and public health research for those translational team members caught up in their silos. in other words, a translational researcher or scientist should have expertise in one or more translational domains to be able to contribute novel solutions to complex problems.

Ability to manage interpersonal relationships. Since translation research involves working as a team, it is imperative that all members of the team function in harmony. Any person involved in translation research must be able to manage interpersonal relationships. Courtesy and friendliness towards each other are essential ingredients of teamwork. Even where disagreements arise, effort must be quickly made to amicably settle such. Disharmonious interpersonal relationships and rivalry will impede the success of the study.

Skilled communicator: The translational physiologist/researcher must have the ability to communicate clearly to all stakeholders across diverse social, cultural, economic and scientific backgrounds. This includes colleagues in other fields, patients, grants donors and reviewers. Skilled communication involves that the researcher is able to write and speak in a manner that there is no ambiguity about the researcher's thoughts.

Project management. Although there will be a team leader or principal investigator, each member of the team should have a clear understanding of the objectives and his/her place in contributing to the success of the general plan. The team leader should be able to assign roles and responsibilities to team members and manage progress throughout the project's duration. The timelines, budget and scope of the project must be adhered to and tasks completed within the guidelines.

In complex projects, it may be essential to seek assistance of project managers who would ensure order. This is essential when a team of equal people from different disciplines relate to each other in a horizontal hierarchy. The functions of the project managers would include the preparation of a target product profile, providing work breakdown structures, managing external liaisons, and providing structure to projects, especially in regard to dependencies and bottlenecks, identification of milestones, and other stage markers. other functions would be the provision of templates to ensure timely and adequate recording of data and to organise team meetings. These types of activities may not be suited to the average university researcher but essential in translational research.

Phases of translational research: Translational research is made up of phases labelled phase 1 to phase 3 or t1 – t3. Phase 1 or t1 refers to the development of concepts and discoveries from basic research through early phase clinical trials (bench to bedside) (Homer-vanniasinkam and Tsui, 2012). It requires basic science skills, some clinical skills and appropriate laboratory infrastructure. Phase 2 extends the results or observations obtained in t1 by establishing the

efficacy in humans. In phase 2 or t2, observations from clinical research are extended into medical and community practice (bedside to community). Phase 2 research needs skills in behavioral science and epidemiology research. Phase 3 or t3 of translational research is the implementation and dissemination into the community of phase 2 research results (clinical practice to community or population health) and involves the ability to influence public policy (Woolf, 2008; Homer-vanniasinkam and Tsui, 2012). Application of research results to the community may stimulate further information that can lead to further research, this time from the bedside to the bench referred to as “reverse translation” (Marincola, 2003; Homer-vanniasinkam and Tsui, 2012; Liebman and Marincola, 2012; Van der laan and Boenink, 2012).

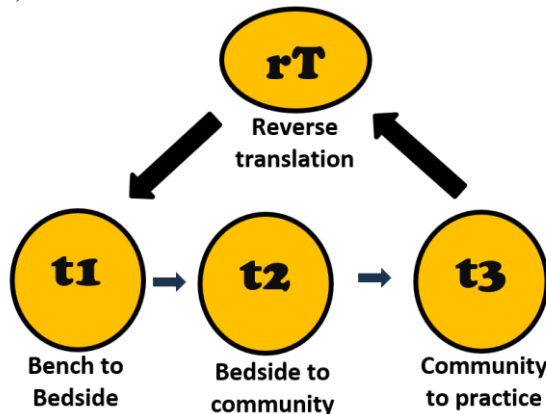


Figure 2
Phases in translational research

Barriers to translational research in Nigeria: There are several barriers, impediments or hurdles to the successful implementation of translational research in Nigeria.

Lack of funds: First and very important is the lack of funds for research. Researchers should be able to attract grants for funding research from public and private sources. The only meaningful source of government funding for research in Nigeria is through the Tertiary Education Trust Fund (TETFUND), funded by the federal government of Nigeria. There is little or no support for research from different state or local governments. Corporate organizations and private individuals are also not providing financial support for research especially with the instability in the Nigerian economy. Researchers are then left with supporting research with personal funds. This cannot provide meaningful financial support for translational research. Research support from international donors is very scanty and when available may not go far enough to support long-term studies in translational research.

Collaborations with international partners are of great benefit to local research capacity building. These partnerships are expected to provide funding, technical assistance, and mentorship, further strengthening local research capabilities (Olatunji *et al*, 2023). The transfer of knowledge, expertise, and technology from international partners to local researchers contributes to the overall growth and advancement of research in the country. The ultimate goal of these collective efforts is to empower local researchers and institutions to conduct impactful research that addresses the specific health challenges of local

populations. by investing in research infrastructure and capacity building, Nigerian research institutions can generate locally relevant evidence, inform health policies, and improve health-care delivery. These efforts are expected to result in better health outcomes for our local populations. International donors and collaborators are few and when available dictate or cater to their own research needs which may not necessarily support translational research direction, efforts and needs in Nigeria.

Research culture and interest: Lack of funds demotivates interest in research (Salami and Kanmode, 2021). Lack of or reduced interest in research further leads to reduced research culture in the universities. Although the functions of the university lecturer are 3-fold, - research, teaching and community service, - the university lecturer focuses more on the latter two than on research due to demotivation.

Lack of collaboration among researchers: Translational research requires collaboration among researchers (Olatunji *et al*, 2023). Working alone or in silos therefore becomes an anathema. Translational research is multidisciplinary and depends on a network of researchers working collaboratively. Basic science largely seeks to acquire knowledge while translational research seeks to improve health. The successful translational physiologist needs to be comfortable in both of these cultures, be fluent in many fields, and thrive on collaboration. Nigerian researchers must therefore embrace collaboration with other researchers in order to improve health care in the country (Salami and Kanmode, 2021).

Prolonged work stoppages: Work stoppages in Nigerian universities contribute to demotivating research. Work stoppages arise from disputes between various university trade unions and the federal or state governments or between the university-based unions and the university management. The length of work stoppages had varied from a few days to a year. In the period of the stoppage, little or no research is done. In some cases, salaries of staff had been withheld and researchers abandoned to their own means. This further contributes to dampening the morale of the researcher. Sometimes, expensive reagents are lost to work stoppages, and this affects research activity and output.

Economic uncertainty. Economic uncertainty in Nigeria has a great impact on research in Nigeria (Salami and Kanmode, 2021). Instability in the foreign exchange regime is detrimental to trade. Over time and sometimes in a frame of a few days the local currency, the naira, loses value in favor of foreign currencies which impacts negatively on the cost of reagents and equipment vital to research. Without a stable foreign exchange regime, it becomes difficult to plan and execute any meaningful research because it is difficult or impossible to buy or import any meaningful research equipment or reagent that is priced in foreign currencies. A stable foreign exchange climate is therefore necessary for meaningful research in Nigeria.

Brain drain: The issue of brain-drain due to frustration arising from one or a combination of factors enumerated above limits capacity for translational research. Brain-drain constitutes a loss of valuable local expertise (Olatunji *et al*,

2023). the exodus of talent from research institutions in Nigeria to more stable areas of the world rob the local institutions the expertise required to innovate and further develop or deepen translational research in our local environment. the weakened research capacity and capability of the institutions effectively impedes the ability of research institutions to contribute meaningfully to solving health challenges in Nigeria. translational research will not have its maximum beneficial impact in Nigeria if skilled researchers continue to migrate to areas of better opportunities outside the country.

Lack of interest by policy makers. Another barrier that had been identified as hindering translational research is the reluctance of policy makers to accept and adopt local research findings into policy. policymakers play a critical role in the translation of research findings into policy but may not be appropriately equipped for the task. The limited capacity of policymakers to use evidence had resulted in delayed adoption of research findings for policy formulation. Local policy makers rely on international organizations for direction and therefore are reluctant to embrace locally produced research findings and turning them into policy (Damba *et al* 2022).

Translational research and repurposing: Nigeria is very rich with a variety of plants and herbs which traditional healers had employed in folklore medicine. These concoctions or decoctions are obtained from plant sources. While some of the mechanisms of action of these traditional medications had been worked out, a lot of the mechanisms of action of others are still not well understood. translational physiology research affords the opportunity of validating and adopting some of the medicines from plant sources into modern treatments of diseases like diabetes mellitus, asthma, cancer, sickle cell disease, alzheimer's and parkinson's disease. Translational physiologists are well suited to identify, characterize and quantify the chemical composition of identified leaves, roots, stems that are needed to treat the various ailments ravaging mankind (Salisu *et al*, 2019; 2022).

Translational physiology research can play a role in drug repurposing or drug repositioning. drug repurposing refers to research efforts at finding new therapeutic uses for currently approved drugs or agents that had previously been withdrawn, or relatively out-dated drugs (Akindele *et al*, 2022). Successes had been recorded in this regard and a few examples include sildenafil which was used in the treatment of angina but is currently used to treat erectile dysfunction. Other examples include the repurposing of aspirin as an analgesic to the treatment of colorectal cancer and topiramate originally used to treat epilepsy and now applied in treatment of obesity (akindele *et al*, 2022).

Antioxidants such as l-arginine have been studied to determine their beneficial effect in the management of sickle cell disease (Jaja *et al*, 2016; Saka *et al*, 2023). Sickle cell disease (SCD), a group of multisystem autosomally recessive inherited hemoglobin disorders, is caused by a point mutation in the gene encoding β chains of hemoglobin. this disease is highly prevalent in Africa, and Nigeria contributes the greatest number of sufferers (Diallo and Tchernia, 2002; Piel *et al*, 2013). Sadeghi *et al*, (2023) carried out a systematic review and meta-analysis assessing

the effect of the use of l-arginine in patients with SCD. The study confirmed that the use of l-arginine could be beneficial in the management of SCD. However, it was recommended that for a firm conclusion and rationale for arginine therapy for these patients, more studies with larger population sample sizes, longer follow-up durations, and well- developed designs were needed. Successful clinical trials, acceptance and adoption of l-arginine for the management of sickle cell disease will be another example of repurposing or repositioning.

CONCLUSION

Translational research and translational physiology are new areas of endeavor and specialization. In order to serve the community adequately, Nigerian universities must recognize the place of translational research in modern day scheme of things. investing in translational research will bring a lot of financial rewards to the university and her staff through patents. On their own part, translational physiologists will contribute to the attainment and preservation of optimal societal function, health and quality of life and solidify the critical role of the subject in the biomedical research enterprise. To achieve these objectives, the translational physiologist must collaborate with other researchers from diverse fields. Collaboration is the driver of translational research and the essence of translational physiology.

REFERENCES

- Akindele A. J., Fatokun A. A., Uzochukwu I. C., Steenkamp V., Agyare C., Familoni O. And James M. O. (2022). Editorial: Translational Research and Drug Repurposing For Non-Communicable Diseases (NcDs). *Front. Pharmacol., Sec. Translational Pharmacology*. 13; 202.
- Cripe, T.P., Thomson B., Boat T.F. And Williams D.A. (2005). Promoting Translational Research in Academic Health Centers: Navigating The "Roadmap." *Acad. Med.* 80:1012-1018.
- Curry Sh (2008). *Translational Science: Past, Present, And Future. Biotechniques For Preclinical Development.* 44(2); I-Viii.
- Damba F.U., Mtshali N.G. And Chimbari M.J. (2022). Barriers And Facilitators Of Translating Health Research Findings Into Policy In Sub-Saharan Africa: A Scoping Review. *Humanities Soc. Sci. Coms.* 9:65.
- Farrell A.T., Panepinto P., Desai A.A., Kassim A.A., Lebensburger J., Walters M.C. *Et Al.* (2019). End Points For Sickle Cell Disease Clinical Trials: Renal And Cardiopulmonary, Cure, And Low-Resource Settings. *Blood Advances.* 3(23): 4002-4020.
- Gilliland C. T., White J., Gee B., Kreeftmeijer-Vegter R., Bietrix F., Ussi A. E. *Et. Al.* (2019). The Fundamental Characteristics Of A Translational Scientist. *Acs Pharmacol. Transl. Sci.,* 2: 213–216.
- Hall Je (2002). The Promise of Translational Physiology. *Am. J. Physiol. (Lung Cell Mol Physiol.)* 283: L235–L236.
- Homer-Vanniasinkam S. and Janice Tsui_J. (2012). The Continuing Challenges of Translational Research: Clinician-Scientists' Perspective. *Cardiol. Res. Pract.* 2012: 246710.
- Jaja S.I., Ogungbemi S.O., Kehinde M.O. And Anigbogu C.N. (2016). *Supplementation With L-Arginine*

- Stabilizes Plasma Arginine And Nitric Oxide Metabolites, Suppresses Elevated Liver Enzymes And Peroxidation In Sickle Cell Anaemia. *Pathophysiol.* 23: 81–85.
- Jaja S.I., Oludemi B. F. And Renner J. K. (2002). The Effect Of Load-Bearing Either On The Back Or On The Chest On Oxygen Consumption And Energy Expenditure. *Niger J. Health And Biomedical Sci.* 1(1): 41-44.
- Liebman M.N. And Marincola F.M. (2012). Expanding The Perspective Of Translational Medicine: The Value Of Observational Data. *J. Translational Med.* 10:61.
- Marincola Fm. (2003). Translational Medicine: A Two-Way Road. *J. Translational Med. Medicine* 1(1):1-2.
- Olatunji G., Emmanuel K., Osaghae O.W., Timilehin I., Aderinto N., Abdulbasit M.O. (2023). Enhancing Clinical and Translational Research In Africa: A Comprehensive Exploration Of Challenges And Opportunities For Advancement. *J. Clin. Translational Res.* 9(5): 357-368
- Piel F.B., Patil A.P., Howes R.E., Nyangiri O.A., Gething P.E., Dewi M., *Et Al.* (2013). Global Epidemiology of Sickle Haemoglobin In Neonates: A Contemporary Geosttistical Model-Based Map And Population Estimates. *Lancet* 381:142–151.
- Sadeghi A., Taherifard E., Ebrahimi N.D., Rafiei E., Hadianfard F. And Taherifard E (2023). Effects Of L-Arginine Supplementation in Patients with Sickle Cell Disease: A Systematic Review And Meta-Analysis Of Clinical Trials. *Health Sci. Rep.* 6: E1167.
- Saka W.A., Anigbogu C.N., Kehinde M.O. And Jaja S.I. (2023). L-Arginine Supplementation Enhanced Expression Of Glucose Transporter (Glut 1) In Sickle Cell Anaemia Subjects In The Steady State. *Cur. Res. Physiol.* 6: 100096.
- Salami A., Kanmod K.K. (2021). Translational Medical Research In Nigeria: Challenges, Prospects And Recommendations For The Future. *Euro. J. Translational Clin. Med.* 4(1):71-78.
- Salisu, T. F., Okpuzor, J. E. And Jaja, S. I. (2019). Identification, Characterization And Quantification Of Chemical Compounds In Selected Edible Wild Leafy Vegetables. *Ife J. Sci.* 21(1): 215–227.
- Salisu T.F., Ottu B.O., Oloyo A.K., Okpuzor J.E. And Jaja S.I. (2022). Assessment Of Wild African Vegetables On Cardiac Functions, Antioxidants And Blood Lipid Profile In A Rat Model Of Myocardial Infarction. *Fuw Trends In Sci. & Tech. J.* 7(1): 070–082.
- Seals Dr (2013). Translational Physiology: From Molecules to Public Health. *J. Physiol.* 591: 3457–3469.
- Tchernia D. And Diallo G. (2002). Sickle Cell Disease in Africa. *Cur. Opinion in Hematol.* 9(2):111-116.
- Van Der Laan A.L. and Boenink M. (2012). Beyond Bench and Bedside: Disentangling The Concept of Translational Research. *Health Care Analysis* 23; 32-49.