Title: Better value chemotherapy; Scientific Win-Win approaches

(Win-Win Scientific approaches to increase affordability of Cancer Chemotherapy care)

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Disclosure of interests: None.
Allow me to introduce myself:

Prof. Dr. Ahmed Elzawawy, Port Said, Egypt.
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- President of ICEDOC & ICEDOC’s Experts in Cancer without Borders (International Campaign for Establishment and Development of Oncology Centres www.icedoc.net)


- Past President of AORTIC (African Organization for Research and Training in Cancer) & Advisor, Oxford Cancer Solutions (OCS), Oxford, UK & Afrox AFROX, UK (Co-Founder is: Prof. David Kerr)

& Member in The ASCO’s Resource Stratified Advisory Group.

& - An Editorial Advisory Board member and Commissioner Editor for Oncology, Cambridge Scholars Publishing, UK.
Locally in Egypt:

Professor of Clinical Oncology, Suez Canal University & Chairman of Alsoliman Radiation and Clinical Oncology Center, Port Said, Egypt.

& Senior Consultant and supervisor of Medical and Radiation Oncology departments, Ismailia Teaching Oncology Hospital, Senior consultant of Oncology Insurance Hospital, Port Said, Egypt.

( worldcooperation@gmail.com)
What I present today is not only on my behalf (Ahmed Elzawawy) but, it represents the Win-Win Initiative of Harvard Global Health Catalyst. Hence, it is Hand in Hand with:

Prof. Wil Ngwa, Director of Harvard Global Health Catalyst GHC & Prof. Paul Nugyen; Co-chairs of Harvard Global Health Catalyst GHC & Prof. David Kerr, (Oxford University, UK and Win-Win), Prof. Eduardo Cazap (Argentina, SLACOM and Win-Win), Pof. Twalib Ngoma, (Tanzania and Win-Win), Prof. Riccardo Audisio (Sweden and Win-Win), Prof. Nicholas Abinya (Kenya and Win-Win) & Prof. Luca Incrocci (Netherlands & Win-Win) & Coordinators of Harvard GHC programs: Dr. Credit Omoruyi & Dr, Lydia Asana & Dr. Neeharika Sinha.

Once again, The Win-Win will continue and succeed only with the contribution of many!

The Win-Win belongs to all!

Ahmed Elzawawy
In this Keynote presentation I stress on exploring some positive and constructive points to increase affordability of better value cancer chemotherapy care in the world starting from LMICs and Africa. Our Scope is international and global. This could be realized by different stakeholders. But, You, dear colleagues everywhere are the doers and you are fundamental to realize remarkable improvement. It needless to repeat here detailed data and charts that -you all know- about the tragic lack of access to Cancer care in the world and particularly in Africa.
Needless to say that:

- It can be estimated that, at present, 60% to 70% of Cancer patients in the world have no access to any chemotherapy at all. The percentage is higher for radiotherapy. The picture is more tragic in Africa. In Africa only 5% of Cancer patients have access to Radiotherapy !. No any Radiotherapy services in 29 countries (Total 53 countries)
- The pharmaceutical companies are developing increasingly expensive novels cancer drugs.
- Despite of all organizations, publications, commissions, conferences, nice talks and declarations there with no indication that the rapidly increasing expenses will be lessened in the future, The overall disease-free survival rates are not increasing in a measure commensurate with the rising curve of expenses of cancer treatment.
- The major markets for the pharmaceutical industry and Radiotherapy are in the USA, Western Europe and Japan.
- If there are ways to broaden markets remarkably in the underserved regions in the world, then it will be beneficial to all stakeholders.
• Less than 5% of cancer patients in Low and Middle Income Countries (LMCs), that include the majority of the world’s population, could afford the novel anticancer drugs. This proportion is likely to decrease by the year 2020 with the rise of expenses of the novel drugs.

• We are confronted with a more tragic situation and hard challenges in Africa that require international and regional innovative efforts and collaboration in which the Use of Information and Communication Technologies (ICTs) could remarkably assist.
• If we continue in the same curve of skyrocketing increase of cost of cancer therapy—without commensuration of outcome to patients—then all stakeholders would lose. *There would be increasing difficulties to access to cancer care in LMICs. Even in some of the most affluent countries, the whole system and some markets could collapse.*

• So, *We call for exploring Win-Win Scientifics approaches. All would gain!*
In a WHO survey in 167 countries, it was found that nearly half of the countries had a plan, but accessibly and affordability of the actual treatment remained low in developing countries. Moreover, there are pitfalls in designing National Cancer Control Plans by copying phrases and texts of WHO plans without tailoring every country plan to its real conditions and challenges and that the successful plan is the one that achieve all its goals by full implantation in the real local conditions.

• Today in 2018, after 5 years of the 7 years plans, there is no sign of any remarkable progress toward achievement of this very needed objective. (I can guess that many of you are saying …No….No! )
If the World’s movement continues in the same way of reports, conferences, commissions, task forces, that end with reporting the tragic situation and data, with calls and plans of actions to improve the picture by 2020 or 2025, **but without focused and globally coordinated scientific works to explore unlimited approaches to resource sparing and cost effective care and with practical tactics that consider the incentives and interests of all stakeholders and mobilisation of every possible resources**; financial and human resources and allies in win-win scenarios that cope with the real world, then **it is expected that the problem will tragically escalate in the upcoming 10 years particularly in LMICs and more severely in Africa.**

[www.ecancer4all.com](http://www.ecancer4all.com) (Harvard Global Health Win-Win)


In an article published in 2015 the contributors from different affiliations and including the IAEA replied a critical question about “Have we made a progress regarding global access to radiotherapy services in the past decade?”. They emphasized that it remains a deficit of more than 7,000 radiotherapy machines in the world and the gap between the required and the supply is rising particularly in LMICs in the last 10 years.

In December 2007, The Win-Win Scientific initiative was proposed by Ahmed Elzawawy as an initiative of ICEDOC’s Experts in Cancer Without Borders

- It aims at the increase of affordability of better value cancer care in the world via exploring scientific approaches.

- All the stakeholders—particularly cancer patients and their families—could win! As it considers the interests and incentives of all stakeholders in the real world, hence, it includes the progress of science, flourishing the business of pharmaceutical companies and Manufacturers Of radiotherapy machines and medical devices without ruining a country or individuals economies.

http://www.icedoc.org/winwin.htm
& http://www.icedoc.net/winwin.htm
The notion of The Win-Win is growing. Hence, in 29 April, 2016, it joined Harvard Global Health Catalyst GHC ( Director: Prof. Wil Ngwa), Dana Farber/ Harvard Cancer Center and became one its activities. Hence, it becomes:

“Harvard Global Health Catalyst GHC Win-Win Initiative”.

This would assure progress, continuity and broad partnership. Moreover, the Corps of the Win-Win volunteers has started its formation from particularly younger colleagues plus older experts Ambassadors of the Initiative.

(www.ecancer4all.com & www.icedoc.net/winwin.htm)
We are professional consultants and we are volunteer catalysts (and not a funding body). So, as facilitators, we are encouraging all to do, to connect and networking with each other and to collaborate or partnership. The initiative is opened for partnership with experts, industries, organizations and all constructive ideas that serve its cause. We are NOT competing or replacing any organization or society, but a forum for all. The Win-Win initiative is a notion. It is not one more organization, but a dynamic movement and initiative. It is a hand in hand cooperation.

The Win-Win belongs to all!
• It is not a fanaticism to the term win-win!

Without this approach, we would have many aborted wishes, good theories and regulations that don’t achieve their full goals. This is because in the real world, the interests of all stakeholders’ including among all-oncologists, pharmaceuticals companies, and the communities should be well understood and not be attacked. Otherwise, they will become parts of the problem and not only a key player or contributor in solution.
The 2 Wings of the Win-Win are:

The first wing is “Exploration of scientific approaches for resource sparing and how to increase affordability of better value cancer care”.


You’ll find in this open access references many examples we cited about resource sparing cancer drugs systemic therapy & radiotherapy. www.icedoc.net/winwin.htm
There are so many to say, to do and to explore in the fields of resource saving clinical oncology care and without compromising the outcome on patients.

Please refer to examples of our publications since 2007 and working meetings during ASCO conferences and ESMO ECC http://www.icedoc.net/winwin.htm

The second wing of the win-win initiative:

This wing regards catalyst action and professional advice to increase enormously the rate of establishment of services of clinical oncology in the world starting with the most difficult challenges in Africa. Despite that our scope is the world, but we start with the most lacking services and difficulties in Africa. It is message for Stakeholders and Manufactures of cancer care requirements; drugs and machines, if we succeed together in Africa, you’ll succeed enormously everywhere. We don’t claim that we as win-win catalyst and volunteer advisers - will have the credit but the stakeholders –International and National- and the locals doers of any project are the real heroes.

This Wing was proposed in November, 2015 and declared in 29 April, 2016 during the Harvard Catalyst Summit @ Harvard Medical School.
• It is also a Myth to think that there are no local resources in African and LMICs countries. But, if there is a well-presented project of profitable radiotherapy service then it would be feasible to mobilize local resources to fund.

• Moreover, a well-studied project with good business model customized to the local conditions and that could function in a community could be funded by public or private –public partnership or get loans from banks or local stakeholders. Also, we ask Diaspora to invest and to gain in Win-Win Projects! (For example: In 2014, The remittance from diaspora to sub-Saharan Africa was 67.1 billion $ more than total foreign aid!)
The Notion of better value healthcare:

After 40 years of uncertainties and the money spent in quality studies there is insufficient evidence about whether or how the quality of care has actually improved. Robert Brook, a pioneer quality expert, declared in 2010:

“The end of the quality movement and long live improving value!”

Welcome to the third and The fourth health care revolutions!

The third revolution in health care implies the use of knowledge and informatics for getting better outcomes centered around the customers i.e. the patients. Hence, it implies the use of the new term” Value”.

In 2013, Sir Muir Gray and David Kerr stated that ”Value” will be the eminent term for the upcoming years. It will not extinct the previous terms but it will embrace them

- The Third Healthcare Revolution has begun and it is significant as the First and Second Revolutions.

The Fourth Industrial Revolution has already started its implementation and thoughts for more progress:

- Robotic and Artificial Intelligence.
- Nanotechnology
- Quantum Computing.
The Third Industrial Revolution is transforming every service and industry and its drivers are knowledge, the World Wide Web, and citizens. *This Revolution, driven by citizens, information technology and knowledge, is already underway to create new health services that:*

1) have the patient at their centre; 2) are safer and more effective; 3) produce greater value from the resources invested. These could be summarized as “How to get affordable, evidence based, better value cancer care to patients in the world” The win-win initiative [www.icedoc.net](http://www.icedoc.net)
- **Value** is defined as outcomes relative to costs.
- It encompasses cost-effectiveness and efficiency.
- In the last 50 years, terms like effectiveness, efficiency, cost effectiveness, quality, and safety were the dominant words in fields of health care.
• In this presentation we focus on the exploration of examples of the published and ongoing scientific researches and approaches that could lead to resource sparing and better value chemotherapy care of cancer.

• Most of the examples are concentrated on breast cancer as a model that could be expanded to other cancers in the world. Breast cancer is the world’s most frequently diagnosed cancer among women.
The win-win initiative implies that we don’t copy protocols or guidelines if they don’t fit the local patients and conditions, but to tailor your approaches and protocols in scientifically evidence-based ways in your community and to consider how to get better value health care according to real conditions among your patients in your community.

ICTs could be of high value in exchanging experiences and consultations that could be in turn beneficial to patients in Africa, LMICs and in parts to rich countries as well. For example, [www.ecancer4all.com](http://www.ecancer4all.com) launched by Harvard Global Health Catalyst. (feel free to visit and to communicate)
Cancer drugs: Evidence-based better value chemotherapy care.

Examples of approaches:
- Decreasing hospitalizations for chemotherapy
- Off-label drug use—but surely with scientific base— for higher value treatments
- Controlling drug utilization
- Strategic use of generics
- Drug trials
- Improving and increasing staff training
Scientific researches with contribution of Africa and Africans could:

- decrease the total time spent conducting clinical trials and may reduce its costs,
- enrich the scientific quality with more ethnic and perhaps genetic variability.
- Locally, a) it could be a source of income for investigators, b) increase access to drugs and investigations, c) build capacity for researches and d) most importantly, improve the care of patients.
- I say it frankly: Consider investing in Africa and not just assist by showing pity! It should be a win-win!

The prices of cancer drugs per se constitutes from 10 to less than 30% of the total cancer care. In France, in the contribution of drug costs was less than 20%, such as hospitalization. In the US, price of drugs constituted around 15% and hospital care constituted 40% of the total cost.

Ideally, Value-based pricing of drugs or approval based on incremental cost-effectiveness (ICER), expressed per QALY gained, in relation to average national income would be promising methods for setting limits on the cost of new treatments.
Fewer hospitalizations for chemotherapy:
- By using protocols of intravenous infusion of chemotherapy that require fewer hospitalizations. There is a need to develop more of such protocols, based on scientific pharmacological and clinical information studies and innovative researches.
- Selecting the less toxic pathway regimens - without compromising the total outcome - can result in fewer or less severe adverse reactions, therefore reducing the number of unplanned hospital visits.
- The oral route for administration of chemotherapy could lower the cost of patient’s transportation, administration of drugs by infusion, hospitalizations and the subsequent costs of adverse effects of hospitalizations. Moreover, it may improve the quality of life (3).

More pharmacological and clinical researches for devolving oral forms are warranted. Hence, most known cancers could have regimes of treatment that are totally or partially administrated via oral route. The pros and cons of oral route administration of chemotherapy should be carefully studied in each community in a scientific and realistic ways.
Oral Taxane: Not inferior effectiveness and less side effects

Ongoing developments for other routes of administration of chemotherapy.

- The subcutaneous administration of trastuzumab (herceptin). The ready to use formulation may also significantly reduce pharmacy time as no medicine preparation time is required.

*Adjuvant Subcutaneous Trastuzumab for HER2-Positive Early Breast Cancer: Subgroup Analyses of Safety and Active Medical Conditions by Body Weight in the SafeHer Phase III Study*. The Oncologist October 2018 vol. 23 no. 10 1137-1143)
- The subcutaneous administration of Rituximab in patients with CD20+ non-Hodgkin's lymphoma (NHL) and Chronic Lymphocytic Leukaemia (CLL).

- Another new exciting example of mode of administration is the Transdermal Estradiol in Prostate Ca.
A new nebulizer device for treating lung cancer with the chemotherapy drug cisplatin could deliver small doses and result in quicker responses without the potential for renal damage of the current intravenous method of administration.

Scottish researchers devise inhaler treatment for lung cancer. A spotlight on academic drug innovations (2011) [http://www.esmo.org/no_cache/view-news.html?tx_ttnews%5Btt_news%5D=1261&tx_ttnews%5BbackPid%5D=585&cHash=dd05d3155e](http://www.esmo.org/no_cache/view-news.html?tx_ttnews%5Btt_news%5D=1261&tx_ttnews%5BbackPid%5D=585&cHash=dd05d3155e)
Pharmacokinetic studies for lowering drug dose (and therefore the cost) by changing the infusion regimen:

The phase I/II trials of prolonged infusion of low dose gemcitabine are one example. The usual dose of 1,000 to 1,250 mg/m² for one patient might then be enough for 4 to 5 patients with comparable results in responding to solid cancers such as non–small-cell lung cancer and breast, pancreatic, and bladder cancers.

- Zoledronic Acid (Zometa) 4mg every 12 weeks (instead of 4 weeks) in bone mets.

-Once again: ESMO 2018: Shorter-course trastuzumab could be an option in HER2 positive early breast cancers

Generic equivalents for off-patent drugs, the newer expensive drugs biosimilars (in the real world!): we stressed on not taking the proposal of using cheaper generics off patent cancer or biosimilars drugs as a magic stick and as an ideal solution for more cost effective treatment, without assuring the flow of production and the affordability of generics drugs of good quality.

Particularly in developing countries, the quality, bioequivalence and bioavailability of generics drugs should be assured by regulations or developing a transparent system for international testing.

A generic of good quality or an “original” essential drug would be more cost effective than generics of less quality, even if the later is of fewer prices. Also, the use of first line treatment of tested good quality drugs could reduce the needs for second and third lines treatment that are usually more expensive. Besides, the risk on patients, results of clinical trials and researches in Low and Middle Income Countries (LMICs) would be doubtful if they are done with drugs with questionable quality.
We stress also on that **Generic and biosimilars drugs could be of much more value if there are global regulatory consistency and trust in good quality and flow of drugs.**

We suggested an international body or experts or programs that would assure the quality, bioequivalence and costs of generics cancer drugs particularly in LMICs.. Hence, better value of these drugs would be achieved.

- Edurdo Cazap et al, Global Acceptance of Biosimilars: Importance of Regulatory Consistency, Education, and Trust. The Oncologist October 2018 vol. 23 no. 10 1188-1198
• **Interrupted courses**

Potential research questions include the interrupted courses of Aromatase inhibitors (AI) that probably would be also effective as continuous therapy after prior Tamoxifen and/or AI treatment of breast cancer. The hypothesis is that AI interrupted courses perhaps could enhance response of residual resistant cells.

This area is still in need for more researches.

Repurposing off-patent drugs and creating new combinations of old drugs.

One example is the metronomic use of prolonged low oral doses of cancer drugs. In a phase II trial, low-dose (6 mg per day) oral estradiol achieved the same response as conventional high-dose (30 mg per day) estradiol in approximately 30% of patients with fewer adverse events in postmenopausal women with aromatase inhibitor–resistant, hormone receptor–positive advanced breast cancer.

• **Reduction of use of expensive supportive care drugs** (e.g. Growth factors, expensive anti-emetic) unless there is strong evidence of value according to the assessment for each patient
Estradiol as Potential Treatment for Subset of Triple-Negative Breast Cancers:

• A second form of the estrogen receptor, known as estrogen receptor β, is expressed in approximately 25% of triple-negative breast cancer tumors.

• When estradiol binds with estrogen receptor β in triple-negative breast cancer, it stimulates the expression of a group of proteins called cystatins, which exhibit tumor-suppressing effects on neighboring and distant cancer cells.

http://www.ascopost.com/News/59358?email=81d9054aeab066d936caf8d9140230a9cd6152f4df0ff794a00781eff4aebdad&utm_medium=Email&utm_campaign=TAP%20EN
Genomic studies- that unfortunately lacking in Africa- could guide to more understanding and appropriate treatment.

An example: in recent studies it is shown that **TNBC frequency was higher for African American (AA) and Ghanian (Gh) patients (41% and 54%, respectively)** compared with White American (WA) and Ethiopian (Eth) patients (23% and 15%, respectively; \( P < .001 \))

**Frequency of ALDH1 positivity was higher for AA and Gh patients (32% and 36%, respectively) compared with WA and Eth patients (23% and 17%, respectively; \( P = .007 \)).** Significant differences were observed for distribution of androgen receptor positivity: 71%, 55%, 42%, and 50% for the WA, AA, Gh, and Eth patients, respectively (\( P = .008 \)).

One of the exciting scientific explorations is the repurposed single or new combinations of older drugs. Researchers performed the 300,000 experiments to test 5,000 different combinations of 100 approved cancer drugs in each of 60 cell lines developed by the National Cancer Institute NCI. The new repository of data would be made available to the public on NCI’s Development Therapeutics Program’s website in hopes that it will provide investigators insight into potential drug combinations to target or avoid.

The NCI hopes to accelerate the advancement of novel therapeutic combinations that demonstrate minimum side effects and maximum promise. If confirmed, this will form a basis for future clinical trials on such combinations.


-High-Value Cancer Care Keeps Costs Down? Yes, It's Possible!


-Harold Sox Ethan Basch and Donald Berwick Strategies to Achieve High-Value Oncology Care—A Beginning

AFRICA OXFORD HARVARD CANCER RESEARCH CONSORTIUM

- AFROX-H Trials Network
  (under construction. It will be launched very soon)
Immunotherapy offers hope to certain cancer patients not responding to chemo
Plans on the way for multi-center clinical trials as part of the Harvard win-win.

Harvard-UMASS-Heidelberg-Rwanda-Cameroon-Nigeria (Kenya?)
Would love to include Kenya if interested
Award Winning Approach: Combining 1 fraction of radiotherapy with immunotherapy leads to elimination of metastatic disease

Ngwa et al. Nature Rev Cancer 2018

SRB = Smart Biomaterial or drone
• Some of the points that we are Proposing for colleagues in Kenya:

a) increased access for patients and oncologists to tele-medicine, and training via ecancer4all.

b) Chemoquant: IBM has agreed to include this as part of our www.ecancer4all.com in 2019 with Kenya as one of the countries. You can learn more about Chemoquant here http://gheg-journal.co.uk/2018/02/chemoquant-improving-access-cancer-treatment-africa/ So ICT approach is a major offering for Kenya.


( one of the leaders-partners in Harvard GHC Win-Win is our brother Prof. Nicholas Abinya, Kenya)
Opportunities:

• One fraction means the time it takes to treat one patient currently with 35 fractions of prostate cancer could be used to treat over 30 patients = a scientific approach to increase access to patients. Same for other cancers.

• The immunotherapy tested is anti-CD40 which currently is generic and would cost less than one fraction of radiotherapy for each patient.

• Multi-center clinical trial will validate this with and without the use of tiny drones delivered to precisely target the cancer and boost the abscopal effect to eliminate metastasis.

• Cost of treatment estimated at $200 dollars could transform cancer treatment.

• Want to partner with Kenya for multi-center clinical trial, which is being planned to start late 2019.

(Wil Ngwa, 2018)
Please feel free to refer to some of our relevant publications and presentations in this link and the following examples

1- http://www.icedoc.org/winwin.htm


10-Elzawawy AM: Could African and Low- and Middle-Income Countries Contribute Scientifically to Global Cancer Care? JGO – Journal of Global Oncology Volume 1, Issue 2, December 2015 http://jgo.ascopubs.org/content/1/2/49

11-Elzawawy A. Breast Cancer as a Model to Improve Outcome of Cancer Care in Low- and Middle-Income Countries World Journal of Surgery: Volume 39, Issue 3 (2015), Page 693-694


13- Taking up Africa cancer challenge . Bulletin of World Health Organization April 2018 (in this WHO article our Win-Win notions are stated ) www.who.int/bulletin/volumes/96/4/18-020418/en/
- **Books:**
  - W Ngwa, P Nguyen. *Global Oncology* IOP Publishing 2017

  ……and more!

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The web [www.ecancer4all.com](http://www.ecancer4all.com) (ecancer4all of Harvard GHC win-win is the World’s Premier comprehensive cancer center in the cloud).
Remember that we are not working only to lessen the burden on the parents who have cancer but also to lessen potential deterioration of the socio-economic status of the kids and their future.

All of them are our kids in the world!
Finally

The future starts from NOW!

Let us together- hand in hand - starts the future NOW!

(On behalf of All the team of Harvard Global Health Catalyst Win-Win Initiative)

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Thank you...