

Personal View

Overcoming Challenges of Cancer Treatment Programmes in Developing Countries: A Sustainable Breast Cancer Initiative in Ethiopia

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ABSTRACT:

The incidence of breast cancer is rising in many developing countries. Here we describe a programme to improve the support infrastructure for the management of patients with breast cancer in Addis Ababa, Ethiopia. Tamoxifen, a cheap, oral, yet effective, anti-cancer agent was made available freely to encourage staff and patients to follow well-defined, but achievable, protocols of care. Mammography, improved histopathological review, tissue hormone receptor assays, agreed treatment algorithms with a cycle of continuous audit of over 250 patients and cross-departmental patient management groups led to a considerable improvement in the management of breast cancer patients in a single institution. Aspects of this programme are now being extended to other regional hospitals in Ethiopia. Fairly limited investments in programmes for cancer can stimulate considerable improvements in the overall approach to malignant disease by encouraging a positive approach, even in very low resource environments. Reeler, A. V. *et al.* (2008). *Clinical Oncology* 20, 191–198

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The Rising Incidence of Cancer in the Developing World

The rise in disability due to chronic disease is now inevitable in a world in health transition. Infection as a major cause of suffering and death is giving way to new epidemics of non-communicable disorders, such as cardiovascular disease, diabetes and cancer [1]. Different countries are in different stages of this transition depending on their age structure and economy. Some countries are faced with a double burden with increasing infection problems compounded by surging cancer rates. This is fuelled in part by the globalisation of unhealthy lifestyles [2] and partly by the fact that the world population is ageing with a predicted average longevity of 73 years by the year 2020 compared with 66 years in 1997. It has been estimated that there will be a greater than 100% increase in the population aged over 65 years in more than 30 countries [3]. Ageing alone will dramatically increase the cancer burden everywhere. By the year 2020, there will be 20 million new cancer patients each year. Seventy per cent of them will live in countries that between them will have less than 5% of the resources for cancer control [4]. It is not widely appreciated that cancer actually kills more people in developing countries than AIDS/HIV, tuberculosis and malaria put together [5].

Advances in Understanding the Causes of Cancer and its Treatment

Over the last decade there has been an explosion in our understanding of cancer at a molecular level and we are now poised to see some very significant advances in prevention, screening and treatment. Massive technological change is likely in surgery, radiotherapy and chemotherapy, leading to increased cure rates, but at a price [6]. The completion of the human genome project will almost certainly bring sophisticated genetic risk assessment methods requiring careful integration into existing screening programmes [7]. Preventive strategies could considerably reduce the global disease burden at low cost. And palliative care to relieve pain and suffering should be a basic right of all cancer patients. The next 25 years will be a time of unprecedented change in the way in which we will control cancer.

However, the optimal organisation of prevention, detection and treatment services are universal problems in all economic environments. Clearly, successful implementation will be easier in high resource settings. Developing strategies to improve cancer care in poor countries requires considerable imagination and effort. It is not just about donating drugs, but more about creating local knowledge,

capacity and structures for policy, prevention, early detection and effective treatment and follow-up.

Cancer in Developing Countries

Prevention

Several pilot projects have been set up with ministries of health around the world. The epidemiological and economic spectra of these pilot studies differ considerably. International agencies, unilateral aid providers, educational organisations, professional bodies, charities and the health-care industry are all approaching the same problem in different ways. The central plank of most cancer strategies is the World Health Organization cancer priority ladder (Table 1). This provides internationally agreed priorities for developing effective cancer control. It needs to be carefully adapted to local circumstances [8]. Tobacco control is a ubiquitous problem, but the methods used to achieve long-term control will differ. Furthermore, careful political consideration across a range of government departments will be necessary, especially in those countries where tobacco is a major source of employment and taxation. Infection control is an achievable target, but is geographically very specific. Hepatitis B, for example, is fortunately rare in many developing countries and so universal vaccination strategies to reduce the incidence of hepatoma would be inappropriate. Encouraging healthy eating and discouraging food manufacturing practices that increase fat and lower fibre content are cheap interventions that will reduce the burden of cardiovascular disease as well as cancer [9].

Treatment

In spite of the effectiveness of prevention, a curable cancer programme is an essential tool of political persuasion. Many have been critical of the large sums spent on cancer patients by tertiary care facilities in poorer countries. But the effective organisation of services into a hub and spoke

Table 1 – The World Health Organization cancer priority ladder

Tobacco control
Infection control
Curable cancer programme
Effective pain control
Early detection
Sample cancer registry
Referral guidelines
Clinical care guidelines
Nurse education
National cancer network
Clinical evaluation unit
Platform technology for region
Clinical research
Basic research
International aid programme

model similar to that currently being enacted in the UK [10] could focus care where it can be most effective.

Ensuring the availability of basic cancer surgery, radiotherapy and chemotherapy for potentially curable cancers provides the first step in setting up a comprehensive cancer service. Agreed referral and clinical care guidelines that can subsequently be audited are an essential component. Furthermore, this provides a cadre of interested professionals who can be encouraged to take a more holistic view of the cancer problem in their country. Such programmes encourage the local ownership of comprehensive cancer control from prevention through to palliative care by those involved in resource allocation. Cancer registries can cost less than £7000 (\$10 000) per year to run and can provide an excellent database for time trends and measuring the impact of specific initiatives.

These developments must also embrace the private sector. Increasingly, the emergent middle class in poorer economies are turning to the private sector for healthcare. If specialist services are not available, then there is no choice but to travel abroad, often at considerable expense, especially when compared with average earnings in many countries. Encouraging private sector involvement locally not only makes economic sense for future consumers, but also provides for a technological trickle down effect.

Given the universal shortage of doctors in developing countries, it is necessary to educate and rely on the other cadres of health professionals. Specialist nurse education is a major priority. The use of nurses in chemotherapy delivery areas and radiographers in the planning and delivery of radiotherapy can be enhanced by introducing basic clinical decision-making skills following pre-set guidelines. Psychosocial and information needs are best handled by those working closest to the patient and their family. Developing the role of the nurse is a high priority in most resource-constrained settings.

Evaluation, audit, education and clinical research are all interrelated. Good research can be done anywhere provided the problem addressed is carefully chosen. Unfortunately there is a great tendency for physicians in developing countries to wish to emulate colleagues in the developed world. In doing so, unrealistic high technology projects are attempted, which are doomed unless part of a pre-agreed international programme. Realistic assessment of research strategies with proper peer review is essential [11].

A Holistic Approach to Breast Cancer in Ethiopia

Recent symposia at American Society of Clinical Oncology, European Cancer Organization, International Union against Cancer and the Global Health Council have done much to stimulate awareness of the growing cancer burden in developing countries. However, there are still very few examples of cancer initiatives in developing countries that address the full range of needs from prevention, early detection to treatment and palliative care. One rather unique example is described here — a pilot programme on

breast cancer at Tikur Anbessa Hospital in Addis Ababa, Ethiopia.

Ethiopia is the oldest independent country in Africa. It is a very poor country, where half of the population of 71 million people lives on less than 50 cents/day. Eighty-five per cent of the population works in agriculture. There are multiple ethnic groups — Christians account for about 35%, Muslims for 45% and Animists for about 12%. The largest ethnic groups are the Oromo, Amhara and Tigre [12]. Access to healthcare is very limited, particularly in rural areas and Ethiopia has very high maternal mortality of 850 (500–1200) per 100 000 [13].

Breast cancer is the second most frequent occurring cancer among women, the most prominent being cancer of the cervix. Current breast cancer rates in Ethiopia are low, although there is probably very substantive underreporting as rural women seek help from traditional healers before seeking help from the government system. Many are never diagnosed and are therefore never reported. There is little awareness of breast cancer among healthcare professionals, particularly in the rural areas. In addition, Ethiopia has many competing public health challenges, including high maternal mortality and a rising HIV/AIDS incidence. In spite of these challenges, the Ministry of Health does put a great deal of emphasis on chronic disease management, including cancer control. However, given the very limited resources of the Ministry of Health and the many competing priorities, cancer control has not received significant funding, until now.

In 2005, AstraZeneca initiated the sponsorship of a comprehensive programme on breast cancer in Tikur Anbessa University Hospital, Addis Ababa, Ethiopia. Project funds have ranged from US\$200 000 to US\$500 000 per year,

with a total commitment for the 6 year programme of about US\$1 700 000. Drug donations of tamoxifen and anastrozole for the past 3 years have so far amounted to an additional US\$124 000. This targeted investment combined with careful planning and close collaboration with local health personnel has resulted in effective capacity building at Tikur Anbessa Hospital, including purchases of important diagnostic equipment, training programmes and the establishment of new patient management systems. The programme aims to create a centre of reference for breast cancer treatment in Ethiopia and, in doing so, validate a model for how to build capacity for breast cancer treatment in a developing country setting. Tikur Anbessa Hospital was selected as the main site of the project given that it, at the time of the start of the project, had the only oncologist in the country. It also had the only radiotherapy unit in Ethiopia. In addition, starting the project in the main university hospital of Ethiopia would probably have a greater effect on medical policies and education than if another hospital was selected. The project was implemented as a partnership between Tikur Anbessa Hospital, Axios International, Hammersmith Hospital, London and AstraZeneca. The Ministry of Health, other Ethiopian university hospitals and private hospitals in Addis Ababa have collaborated and participated in workshops to develop guidelines or reporting forms.

At the start of the project there was very limited diagnostic and treatment capacity at Tikur Anbessa Hospital. In the past 2.5 years the project has turned Tikur Anbessa Hospital into the first treatment centre for breast cancer in Ethiopia and it has had a significant systemic effect (see Table 2). The clinical guidelines (See Figs. 1–5) were developed as one of the first initiatives and they have now

Table 2 – Improvements in systemic response to breast cancer

January 2005	October 2007
No data on breast cancer patients	Monthly reports on the number of breast cancer patients diagnosed and followed up
No guidelines for the clinical treatment of breast cancer	Guidelines developed, printed and distributed to all five teaching hospitals
No standardised pathology reporting	Standardised pathology reporting form
No pain management guidelines	Guidelines developed but access to morphine for palliative care still restricted
No mammography	New mammography installed and 13 staff trained – 97 tests conducted year to date (YTD)
No estrogen receptor/progesterone receptor (ER/PR) testing in any hospital in Ethiopia	ER/PR tests available and six staff trained – 40 tests conducted YTD
Existing ultrasound broken	Ultrasound machine installed and two staff trained – 54 tests conducted since June 2007
No data on average time per breast cancer patient between diagnosis and surgery	This has decreased from 2–3 months in 2006 to 1–2 months in 2007
No access to anastrozole	Tamoxifen available free of charge in March 2006*: 262 patients have benefited so far. Anastrozole available free of charge in Ethiopia in July 2007: seven patients have benefited so far
Frequent stock outs of consumables, reagents and drugs	Training and reporting tools for pharmacy and radiology

*Tamoxifen has been available in Ethiopia since 1999, but only for patients who could afford to pay.

been distributed to all five university hospitals in Ethiopia. In addition, the project has initiated and established a multi-disciplinary approach to breast cancer management in Tikur Anbessa Hospital. Clinical guidelines were agreed at the start for the following six situations (Figs. 1–5):

- locoregional and systemic treatment;
- systemic adjuvant treatment: hormone receptor-positive disease;
- systemic adjuvant treatment: hormone receptor-negative disease;
- management of recurrent disease;
- follow-up for asymptomatic patients and for patients with recurrence.

Specialists from oncology, radiology, pathology and surgery meet every month to discuss specific patients with cancer and this cross-disciplinary approach has significantly heightened the quality of treatment and care for the patients, including reducing the waiting time from surgery to radiotherapy to less than 2 months compared with more than 1 year before the start of the project.

The Referral System

One of the most significant challenges of a breast cancer project that focuses on one hospital only is to have a meaningful effect on the health system of the country. It is not within the scope of this project to purchase the diagnostic equipment that was acquired for Tikur Anbessa

Hospital for all of the other university hospitals in Ethiopia. However, even with a limited budget it is possible to have a broader effect in a country, beyond the hospital that is the site of the project. To do so the project needs to focus on the 'software side' of breast cancer treatment, such as the development of guidelines and standardised reporting with the appropriate involvement of the Ministry of Health and the other referral hospitals.

A recent assessment (refer to Table 3) of the other university and regional hospitals in Ethiopia revealed that although they all had mammography and ultrasound and carried out fine needle aspirations, none of the hospitals, apart from Tikur Anbessa Hospital, had clinical or palliative care guidelines, standardised pathology reporting, ER/PR testing, nor a trained oncologist or cross-departmental management groups to oversee the clinical treatment of each patient. Access to appropriate drugs was extremely limited, with only one hospital outside Tikur Anbessa having access to tamoxifen. Patients from Gondar Hospital, which is 750 km from Addis Ababa, had to travel to Addis Ababa to buy tamoxifen themselves and bring it back to Gondar Hospital.

All of the guidelines and reporting forms developed in this project have been printed and distributed to all of the above hospitals. There is also a close collaboration with the medical faculty of the university to ensure that training curricula benefit from the updated guidelines on clinical management, palliative care and pathology reporting.

The assessment also concluded that Gondar Hospital could benefit from the donations of anastrozole and

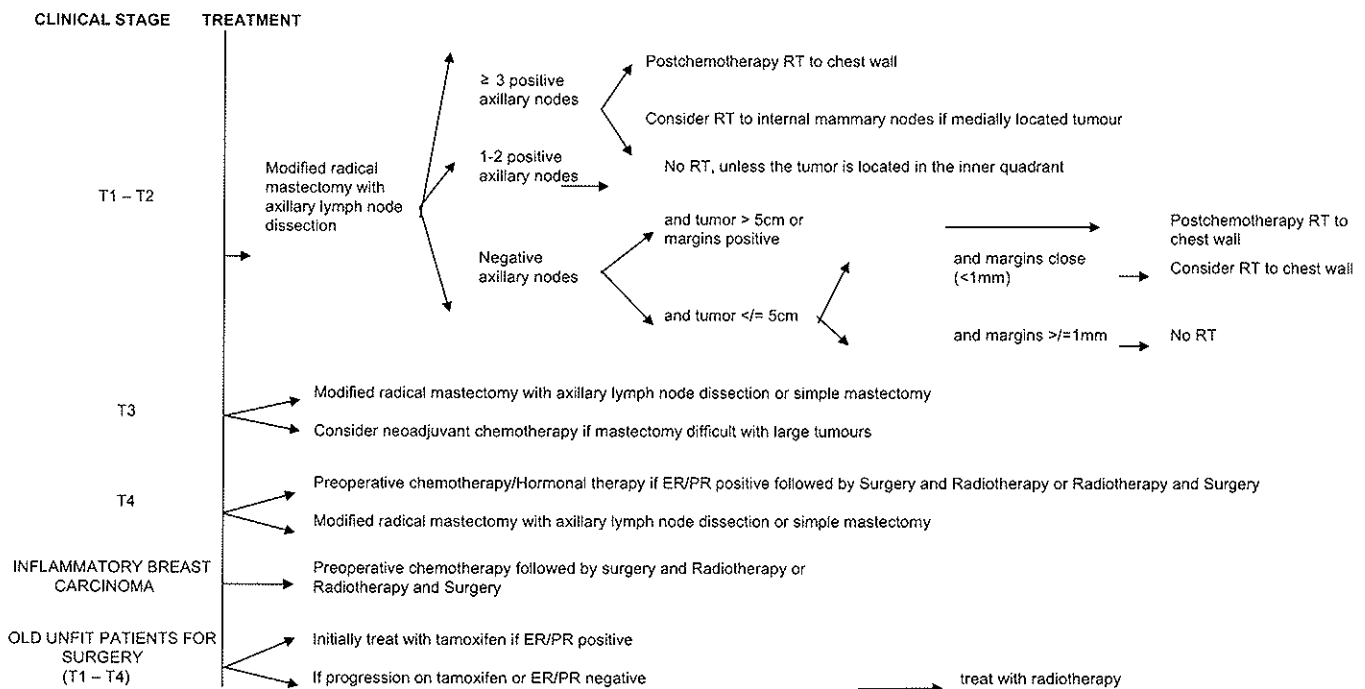


Fig. 1 – Locoregional and systemic treatment.

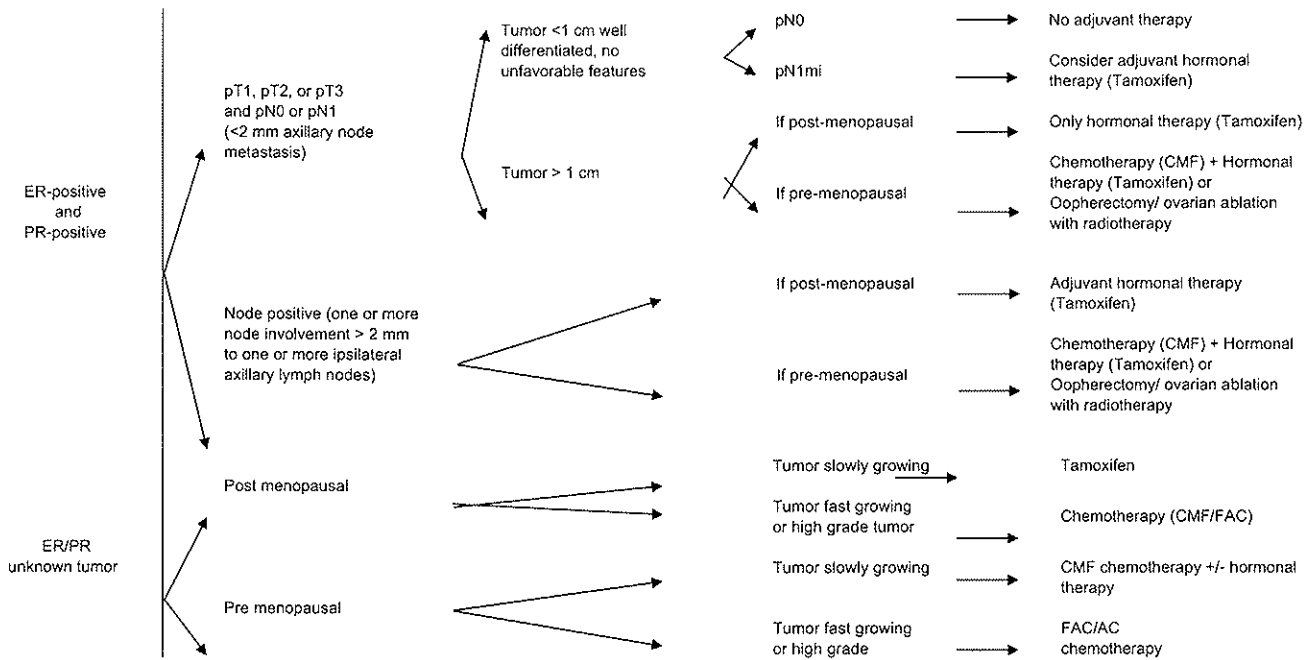


Fig. 2 – Systemic adjuvant treatment: hormone receptor-positive disease.

tamoxifen by AstraZeneca. Patients diagnosed at Tikur Anbessa Hospital, but originating in the Gondar region, will have the possibility of being followed up and receive their breast cancer drugs at Gondar Hospital. In total, 262 patients, 254 women and eight men, have benefited from the donation of tamoxifen. Anastrozole only became available in July 2007, but already seven patients were on anastrozole. Figure 6 illustrates the rate of diagnosis of new patients and their follow-up.

One hundred and seventy-eight of these patients were from Addis Ababa and the rest were from the surrounding regions. However, so far all of these patients have had to travel to Tikur Anbessa to receive their drugs from the main hospital there and although follow-up rates are good, the travel is a heavy burden on poor patients.

The project is now trying to lighten the burden on the patients by enabling Gondar Hospital to dispense anastrozole and tamoxifen. One of the oncologists from Tikur Anbessa will travel periodically to Gondar Hospital and see follow-up patients while at the same time training local doctors from the hospital in breast cancer treatment and care. This way the expertise that is currently concentrated

in Tikur Anbessa Hospital will be shared with other hospitals.

Public Awareness and Patient Support

The Ethiopian Cancer Association has existed for a number of years, but has not been very active. Its president is also the main oncologist at Tikur Anbessa Hospital and he is naturally very busy. The AstraZeneca funding has made it possible to hire a dedicated manager for the Ethiopian Cancer Association, who started working this year. Initial activities have focused on building the organisational and management structure. However, activities are now starting with regard to awareness and fundraising for breast cancer and it is expected that activities and, therefore, public awareness will increase in the coming years.

Policy Support for the Ministry of Health

The pilot project has aimed at a close collaboration with the Ministry of Health from the start. The ministry has sent

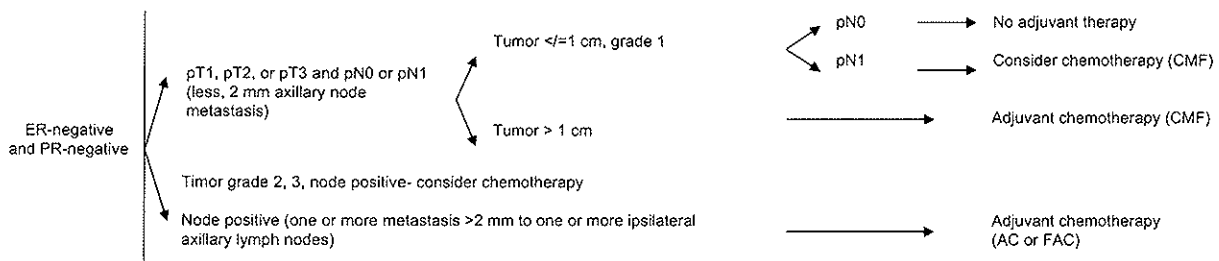


Fig. 3 – Systemic adjuvant treatment: hormone receptor-negative disease.

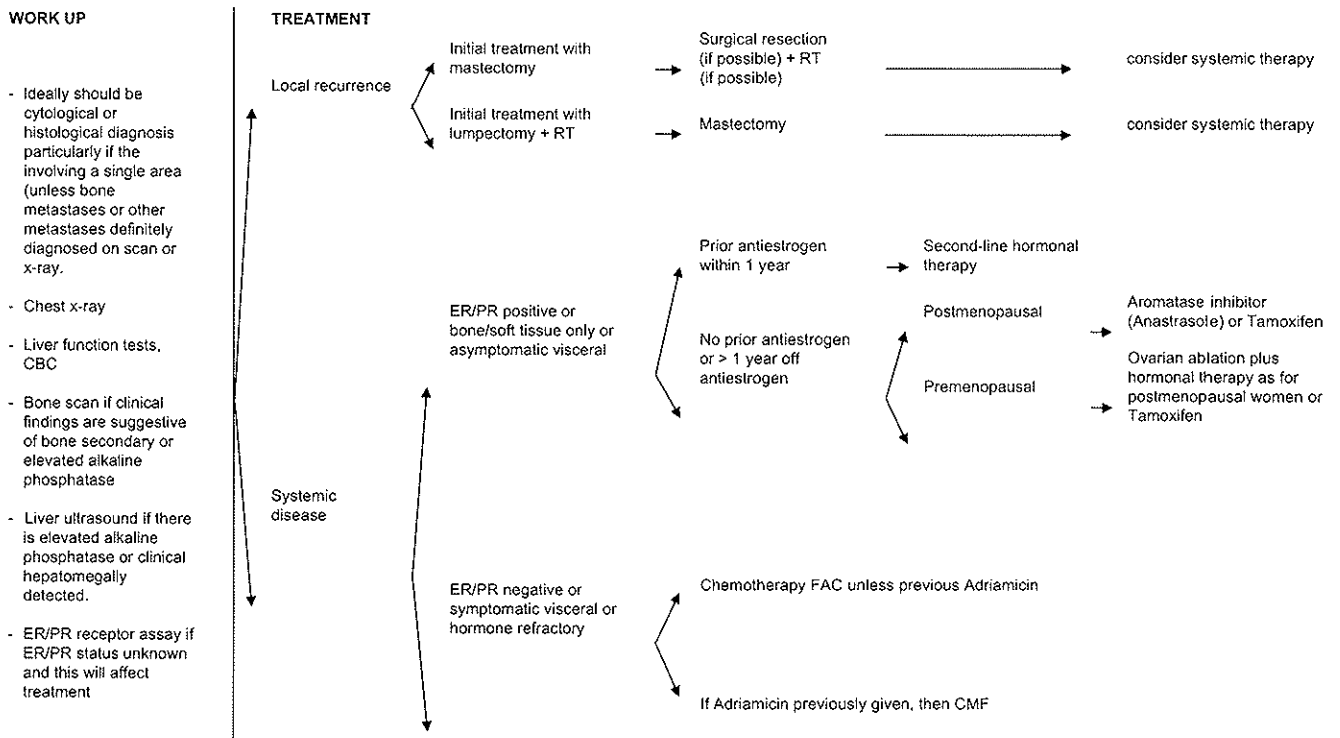


Fig. 4 – Management of recurrent disease.

representatives to all workshops to develop guidelines or pathology reporting forms and project leaders are active in the ministry's planning group for chronic diseases. Recently, the Ministry of Health decided that among many competing priorities for chronic disease prevention and

management, cancer registries would be given priority. The pilot project aims to assist the Ministry of Health in establishing a pilot for cancer registries in Addis Ababa, including both public and private hospitals from the city. This pilot would enable the ministry to get initial

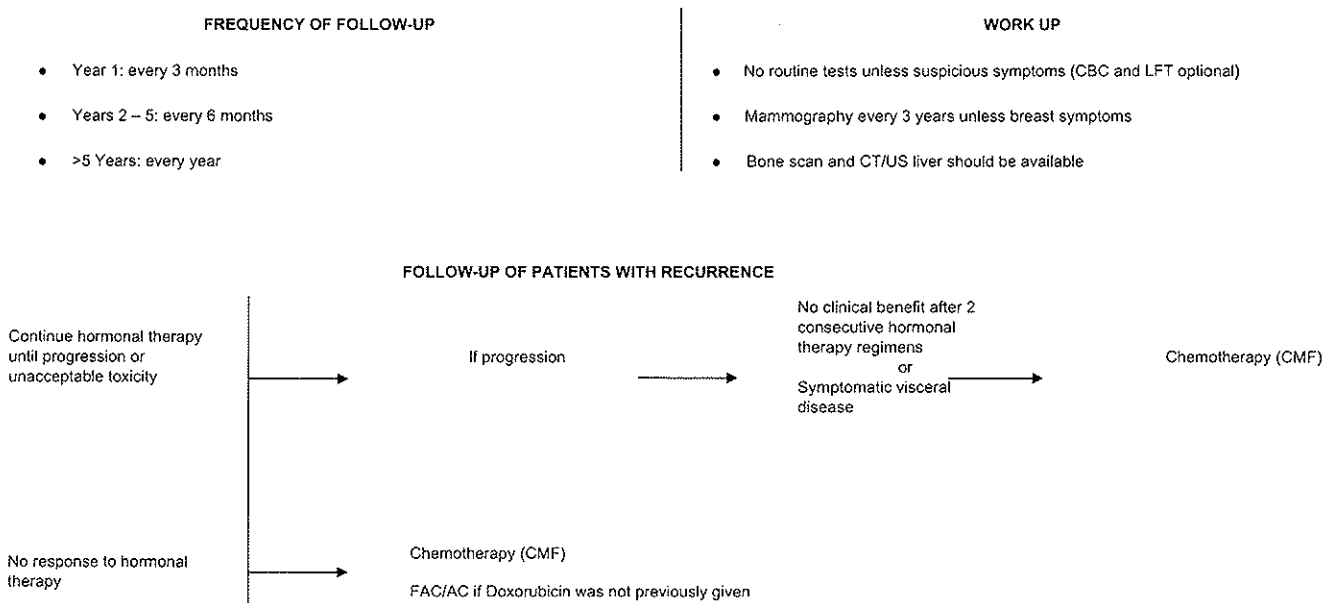


Fig. 5 – Follow-up of asymptomatic patients.

Table 3 – Capacity assessment of Ethiopian university hospitals

Diagnostic and treatment capacity	Tikur Anbessa	Jimma	Awassa	Shashe-mene	Gondar	Mekele
Clinical guidelines	Yes	No	No	No	No	No
Standardised pathology reporting	Yes	No	No	No	No	No
Palliative care guidelines	Yes	No	No	No	No	No
Noivadex available	Yes	No	No	No	Yes	No
Arimidex available	Yes	No	No	No	No	No
Patient clinical management group in hospital	Yes	No	No	No	No	No
Number of oncologists	2	No	No	No	No	No
Availability of mammography	Yes	No	No	No	No	No
ER/PR tests available	Yes	No	No	No	No	No
Availability of ultrasound	Yes	Yes	Yes	Yes	Yes	Yes

experiences with cancer registries that could then be used later to widen the registries to become national registries.

The Broader Impact

The most interesting aspect of the pilot programme in Tikur Anbessa Hospital is how a project with limited budget in a single site can actually have a much broader systemic impact in a country. By focusing the project on developing guidelines, collaborating with the Ministry of Health and other health institutions in the development of these guidelines and by supporting the Ethiopian Cancer Association, this focused breast cancer project is actually having a much larger impact than Tikur Anbessa Hospital alone. We hope that the approach and lessons learned from this project may help other pilot programmes increase their reach and impact on cancer prevention and treatment in the developing world.

Conclusion and Challenges

Some of the main challenges in this project are applicable to other projects aiming at improving the treatment of cancers in developing countries. Perhaps the most important one is the lack of information about the

epidemiology and aetiology of cancers in Ethiopia. As mentioned above, there are no cancer registries in Ethiopia and it is therefore extremely difficult for health planners to design appropriate prevention and treatment programmes and to allocate scarce resources [14].

Human resources are a serious obstacle in improving cancer treatment in Ethiopia and other developing countries. There are only two trained oncologists in Ethiopia at present and no specialised cancer nurses, which is far from enough to cover the needs of the country. This is a general problem in developing countries where there are very few specialised doctors in general and it will certainly become an increasingly serious problem as the incidence of chronic diseases continues to rise in these countries.

The registration and importation of new drugs, for instance anastrozole, have been difficult and very time-consuming. Drug registration is often a very lengthy process in developing countries and often the project has to apply for exemptions in order to get life-saving drugs into the country. Similarly, custom release procedures can be very slow and delay patients from benefiting from new diagnostic equipment or drugs.

Another serious challenge is the restricted access to morphine as a 'specially controlled substance'. Morphine is classified as such in most developing countries, based on

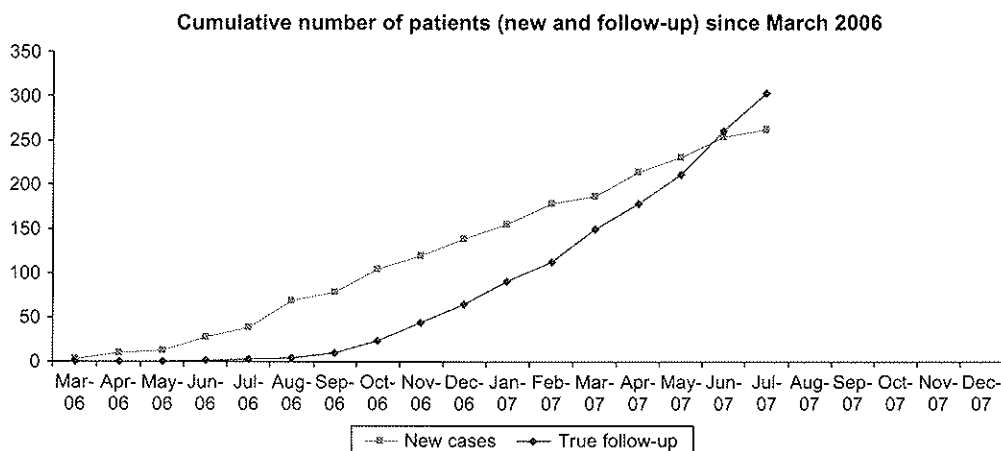


Fig. 6 – Cumulative patient numbers since project inception.

recommendations from the International Narcotics Control Board. This board is monitoring the United Nations' drug control conventions, which aim to prevent illicit drug trafficking. This international classification of morphine has proven to be a major obstacle for palliative care for terminally ill patients, including cancer patients. The World Health Organization has highlighted this as a major problem in cancer treatment and care in developing countries, but progress on this issue in Ethiopia and other developing countries has been slow.

In many developing countries there is no 'culture' of maintenance and sustainability. In Tikur Anbessa, as in other countries, there were no dedicated budgets for maintenance and improvements. The project has tried to assist the hospital in developing a business plan for the future that will ensure that machines will be maintained and that some of the real costs of running the equipment will be provided for. However, this is a difficult task, as many public hospitals, such as Tikur Anbessa, have little control over their own budgets, which are funded by the Ministry of Finance. Public hospitals also need to maintain a balance between providing for poor patients who cannot pay and raising standards to attract private patients who could generate some income for the hospital. However, the sustainability plan for Tikur Anbessa Hospital has been approved and will hopefully be put into effect next year.

The key lesson from this initiative is that obstacles to quality prevention, early detection and treatment of cancer in the developing world can be overcome with the types of innovative partnership and targeted funding seen in this project. A limited pilot can have a much broader impact as a learning tool for the rest of the health system and for surrounding countries. The model of the Ethiopia breast cancer project and its related partnerships should be replicated and scaled up to other developing countries.

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