

Colorectal cancer in Mexico: should a middle income country invest in screening or in treatment?

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Published online: 10 December 2009

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Abstract Mexico, like many other middle-income countries, is experiencing a demographic and epidemiological transition resulting in an older population suffering from chronic diseases. At the present time, cancer is the second cause of death in the country. Until recently, cervical carcinoma was the most frequent type of cancer in the country, however, the incidence of breast, prostate and colon cancers is growing. The demand for health care and health expenditure represented by cancer treatment challenges the limited resources the country has, particularly as patients seek treatment in advanced stages of the disease. Interestingly enough, these types of cancers could be detected in the early stages with rather simple screening procedures. The purpose of this paper is to describe the Mexican health system, and the impact of its fragmentation on access to medicines. Focusing on colorectal cancer (CRC), we describe its epidemiology, screening procedures and the inequities in health care access for these patients.

Keywords Cancer · Mexico · Health systems · Middle income countries · Colorectal cancer

JEL Classification I11 · I12 · I18

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Country profile

The Mexican health-care system is, organisationally, different from other OECD countries. The fragmented health system is characterised by the presence of several public purchasers that are vertically integrated with providers, and serve different parts of the population with little inter-connection. In addition, there is a very large, and mostly unregulated, private sector [1]. The country's health expenditure is one of the lowest among the OECD countries (6.6% GDP 2006). Mexico does not have a single, national scheme providing health care coverage as a whole. Access to health care, insurance coverage and health outcomes vary across regions, and are characterised by a relatively low level of public spending with a high burden of out-of-pocket expenditure [2].

The Mexican health-care system

Approximately half the population enjoys social insurance coverage for health care, including pharmaceuticals. The other half of the population relies on federal and state-funded services, with the exception of a minority which has private health insurance. Social insurance is compulsory for all salaried workers in the formal labour market. The socially insured population receives health care at the Instituto Mexicano del Seguro Social (IMSS, Mexican Institute of Social Services) and at the Instituto de Seguridad y Servicios Sociales de los Trabajadores Del Estado (ISSSTE, Institute of Security and Social Services for Government Workers). The IMSS and ISSSTE beneficiaries and their dependents are covered for most health-care services, including most prescription pharmaceuticals included in their respective formularies, and receive health

care at no out-of-pocket cost, as long as using providers employed by the IMSS or ISSSTE.

The uninsured population obtain health-care services through the Ministry of Health (MoH) or state health services facilities¹, subject to an evaluation of socio-economic status; however, patients must pay out-of-pocket for any drugs. Recent reforms have established a public health insurance scheme, the Seguro Popular de Salud, or Popular Health Insurance, covering drug costs for patients enrolled in the programme based on a catalogue of 249 essential interventions and 17 interventions (mostly high-specialty) relating to catastrophic expenditures [3]. Private insurance in Mexico is very limited. At present, only 3% of the population, mostly high-income individuals, has private insurance with employer-subsidised group plans accounting for half of private health insurance coverage.

The public sector, whether state (MoH) or social security (IMSS, ISSSTE), provides health services at all levels of care in their own facilities (23,269 medical facilities). The private hospital sector provides around one-third of all hospital beds in the country (4,103 hospitals with 3,082 private) [4, 5]. Nearly half of the private hospital facilities are concentrated in Mexico City, while richer states have a greater availability of private sector facilities than poorer states [1, 5]. Private sector hospitals in Mexico are quite diverse: small physician-owned clinics with fewer than five beds account for 27% of private hospital beds [6]. Over half of private hospitals do not have X-ray units; about one-third do not have a full-time doctor [1]. Only 3% of private hospital beds are in hospitals with more than 50 beds. These hospitals provide high-tech and highly specialised care.

The country is undergoing demographic and epidemiological transition,² with mortality and morbidity patterns in most states having increasing chronic and lifestyle-related illnesses,³ ultimately placing greater pressure on health care systems.⁴ Furthermore, the social security sector is facing pressures from within as a result of increasing pension payments for its own workers.

¹ Mexico's health system is decentralised, each state has its own secretariat of health and provides only for their region. This paper will use generically the MoH, but this will also cover state services.

² Mexico's current population is approximately 109 million people, and by 2025, almost 10% of the Mexican population is estimated to be over 65; this percentage is expected to double by 2050.

³ However, in states with lower levels of socio-economic development and in rural areas, a considerable epidemiological backlog remains.

⁴ The burden of chronic diseases has increased, and cancer is the second cause of mortality after cardiovascular diseases.

Pharmaceutical expenditure

Mexico has witnessed growth rates in health expenditure surpassing general rates of inflation, primarily due to pharmaceutical costs. Although the country has the lowest per capita income among most OECD countries, pharmaceutical expenditure is much higher than total health spending, with one of the highest percentages of GDP [5]. However, yearly PPP average expenditure is only \$138.00 USD (€ 95) compared to \$792.00 USD (€ 535) in the US [7]. Drug prices in Mexico are about 80% of American prices; nevertheless, when prices are adjusted for income, differences in pharmaceutical prices are more than five times the income-adjusted level [5]. Furthermore, about 90% of the pharmaceutical expenditure comes from private agents [8].

A large proportion of individuals without access to social security (IMSS, ISSSTE) protection belong to the poorest segments of the population, and a high share of households in lower-income quintiles face catastrophic and poverty-creating health-care expenditures.

Expenditure and resource allocation

A consequence of half the population without health insurance coverage is a large discrepancy in total disposable income devoted to health care [9]. The social security (IMSS, ISSSTE) agencies, the MoH and the Mexican states health authorities are obliged to purchase their pharmaceuticals from two sets of positive lists: the Cuadro Básico, or Basic Formulary, and the Catálogo de Insumos, or Catalogue of Inputs [5].

Approval of a new drug for the formulary is made by the Inter Institutional Commission. All requests for formulary inclusion must follow a bylaw stipulating three criteria: drugs must have marketing authorisation, meet all safety and clinical tests, and be cost-effective. With regards to the last criterion, the applicant must submit with the request all pharmaco-economic tests pertaining to the drug. The bylaw is currently being revised to make the cost-effectiveness criterion, which has been in place for only 2 years, more explicit and to clarify its implementation [5].

Public purchasers procure pharmaceuticals for dispensation in publicly owned and operated pharmacies. Except for drugs with patents, all medicines purchased by public-sector institutions must follow a set of regulations (i.e. public biddings).

The IMSS is the most important pharmaceutical buyer, purchasing 883 different pharmaceuticals in 2005, of which 99 (11%) were patented. Private hospitals drug purchases work through negotiations with both distributors and manufacturers. Typically, hospitals buy the latest drugs

directly from producers, and the purchasing institution can enter into direct negotiations with the producer [5].

Most public pharmaceutical expenditures are made by the IMSS and ISSSTE. Public pharmaceutical expenditure as a proportion of total pharma expenditure was 8.2% in 2002, 10.4% in 2003 and 11.6% in 2004 [10].

Budgetary constraints have limited both the quantity and quality of care to the poor, leading to significant implicit rationing throughout the system; for example, availability of most drugs in the MoH is extremely poor. There is also wide variability in quality across and within both the public and private sectors.

Of all drugs released globally between 1995 and 2001, most new products had been marketed in Mexico within 4 years of the first global launch, and 73% were available within 5 years [11]. The launching of new drugs is slower than in most developed countries (where a majority of new drugs are launched within 3 years), but similar to OECD countries such as Spain and Austria, while better than countries such as Portugal. To some extent, manufacturer's decisions regarding product launch (and pricing) in Mexico are likely to be affected by Mexico's proximity to the US who provides the largest market for pharmaceuticals globally and at highest prices. The US is the largest single exporter of drugs to the Mexican pharmaceutical market, supplying about one-quarter of total imports [12].

Costly treatments are only available in specialised hospitals, which are mainly located in highly populated urban areas. For cancer patients, new drugs are sometimes available at some hospitals of the social security system. For private patients and patients receiving health care at the State health system (including the Instituto Nacional de Cancerología, INCan), most new drugs are available, but with out-of-pocket payments.

Physicians have access to new drugs, often through phase three clinical trials required by the regulatory authorities before a registration is granted or phase four trials. Although therapeutic-diagnostic guides are distributed to physicians, enforcement is neither regulated nor sanctioned.

Cancer registries and data sources

The fragmentation of the institutional arrangements, combined with provider decentralisation, contributes to poor quality of statistical data available in Mexico [3]. In the absence of a National Cancer Registration System, the Registro Histopatológico de las Neoplasias de México (RHNM) is the primary information source. The most recent information available [13] reported 150,000 total new cancer cases [14]. Most patients were seen at the IMSS (36.3%), followed by private hospitals (26.7%), Secretariat

of Health hospitals (22.8%), and armed forces and PEMEX (Mexican oil company)⁵ (14.2%). Of these new cases, cervical and breast cancers were most frequent in women, and prostate and lung cancers in men. According to De la Garza [15] during 2008, 28,883 women, 26,846 men and 1,630 children died from malignant diseases.

Screening

In 1994, the MoH established the National Programme for the Prevention and Control of Cervical Cancer. After 10 years of a massive campaign promoting pap smears for Mexican women and also an increase in the number of clinics, reports show more than 6.5 million women have been screened for cervical cancer [15, 16].

At the beginning of the present Government Administration, a National Health Programme 2007–2012 was developed, in order to achieve its targets by the year 2030 [17]. This Program has five different goals (improve population health, decrease inequities, provide quality health care, health promotion), ten approaches that will give administrative viability and sustainability, through 74 lines of action [17].

An important line of action is the National Programme for Cancer Control (PNCC), which includes five central themes:

1. Prevention and early detection of cancer
2. Development of oncology diagnosis and treatment guidelines for the ten most frequent neoplasms in Mexico
3. Implementation of palliative care
4. Improvement of medical infrastructure and medical services administration
5. Enforcement of the control of tobacco consumption

Total expenditure for women programs in 2005 was 38 110.80 million Pesos (€ 8.9 millions), representing 8.5% of total health expenditure and 0.5% of GDP [18]. The programs were financed with public funds (64.5%), and only 35.5% were funded out-of-pocket. In contrast, total health expenditure has greater private than public funding (56.5 vs. 43.5%). Screening programmes and treatment for cervical cancer represent 4.5% of total health expenditure [18]. During 2000–2005, a decrease in cancer mortality was reported (15.7/1,000,000 women), as a result of an improvement in cervical screening programmes now covering 70% of women aged 25 years and older [19–21].

⁵ The type of cancers diagnosed have changed during the last decade, the incidence of cervical carcinoma has decreased and breast, prostate and colon cancer incidences have increased.

Currently, previously uninsured Mexican women have free access to cervical cancer treatment, including surgery, radiation therapy and chemotherapy via the social protection plan insurance programme [22].

Breast cancer is a serious threat to the health of women globally, and an unrecognised priority in middle-income countries. In Mexico, mortality has increased by 27% in 5 years, accounting for more deaths than cervical cancer since 2006, and is the second cause of death for women aged 30–54. Incidence data is under-reported; 6,000 new cases were detected in 1990, and a projected increase to over 16,500 per year by 2020. Most cases are self-detected and only 10% of all cases are detected in Stage I. All Mexican women have access to free treatment either with the social insurance (IMSS, ISSSTE), or through the Popular Health Insurance⁶. Despite these entitlements, services are lacking and early detection, particularly mammography, is very limited. As of 2006, only 22% of women aged 40–69 reported having a mammogram. Barriers exist on both the demand and the supply side [23].

The 2005 expenditure on breast-cancer detection programmes was 2.5% of total health expenditure during a 5-year period (2000–2005); the percentage of women 40 to 69 years undergoing a screening procedure (mostly mammography) increased from 12.6 to 21.6%. In 2003, there were 100,000 mammograms performed in Mexico; in 2007, the number increased to 228,000. Public clinics and hospitals around the country use more than 500 units of mammography equipment. The government is interested in having a cancer centre in most of the 32 states by 2012 [15].

Although prostate cancer incidence is increasing in the country, there is no a national screening programme. Only 0.9% of total health expenditure was invested in prostate cancer [24].

Country infrastructure for cancer treatment

Health-care supply is low in Mexico by OECD standards. In virtually all dimensions for which health data are available, Mexico lies well below the average. In 2006 the doctor-to-population ratio was 1.9; scanners CT 3.6 per million population, and radiation therapy equipment 1.3 per million population (Fig. 1) [5].

The system is profoundly unequal in terms of its financing and health outcome. Differences in resource

⁶ The Popular Insurance Scheme provides health coverage through voluntary public insurance for persons not covered by social security (IMSS, ISSSTE). It currently provides coverage for 266 medical operations listed in the Universal Health Service Catalogue. A trust was created to fund treatments which can cause catastrophic expenditures, including childhood cancers, breast and cervical cancer.

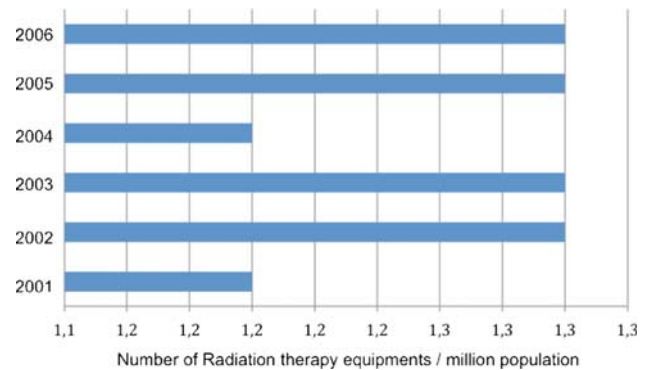


Fig. 1 Radiation therapy equipment/million population

availability and quality also exist across institutions. Large disparities in the health care facilities are present in Mexico City, the northern and the southern states.

Most of the states have social security and private hospitals, [25] however, cancer care for the uninsured is irregular. Poverty and geographical barriers (i.e. remote areas) create difficulties in obtaining cancer care, mostly among the Mexican Indian natives, and in the southern states. Financial restraints result in inequity in treatment access as cancer patients may not be diagnosed, and may be improperly staged or treated. In an effort to decrease the care gap, a national cancer network has been implemented by the MoH and State governments with 26 centres improving access to evidence-based cancer treatments nationally.

Mexico's fragmented health system also influences cancer care expenditure. Out-of-pocket payments are standard for the poorest uninsured population seen by the MoH. Although medical care, including surgical and radiation therapy, is subsidised, pharmaceutical costs are high. Financial restrictions make new chemotherapeutic agents unavailable for the uninsured and occasionally for social security (IMSS, ISSSTE) patients.

Although no accurate data are available, public cancer treatment may be delayed for as long as 6 months due to bureaucracy and work overload in the IMSS and ISSSTE, while lack of knowledge in primary health care may delay treatment for the uninsured. The waiting time for treatment at the INCan is 2 months, mostly because overloaded diagnostic procedures (chest X-ray, CT scans, PET scans) delay proper staging. Waiting time for surgery is 5 weeks, radiation therapy as long as 2 months, and chemotherapy 2 weeks.⁷ Privately diagnosis, staging and treatment procedures can be carried out within a week. It is important to mention that advanced disease is frequent at time of

⁷ However, often these patients are treated by general physicians for several months before their referral to the Institute.

diagnosis in the public (MoH) and social security (IMSS, ISSSTE) settings.

No uniform care is available, thus patients may receive frontline or very poor treatment. This variation is further contributed by the absence of national treatment guidelines, the fragmented health system and economic factors.

All cancer centres and tertiary care hospitals have skilled surgeons and standard radiation therapy procedures, however, access to chemotherapy and mainly novel agents may be limited. Recent IMSS budget constraints have made access to new drugs difficult. In contrast, ISSSTE patients have access to novel drugs. Private patients have private insurance or have personal wealth, enabling them to pay out-of-pocket. In the public (MoH) setting, payments are out-of-pocket unless a clinical trial is available. Although most novel cancer treatments are licensed in Mexico, only wealthy or insured private patients, those receiving treatment at the ISSSTE, or patients enrolled in clinical trials may have access to the new targeted therapies.

Cancer care facilities

There are several large cancer centres in Mexico City: INCan, Centro Hospitalario 20 de Noviembre, Instituto Nacional de Pediatría, Hospital Infantil de México, Hospital de Pediatría IMSS, Hospital de Oncología IMSS, Hospital General de México SSA, Hospital Juarez SSA. There are also a number of private hospitals equipped with modern radiotherapy and medical oncology facilities. Although insufficient linear accelerators are available, there are a large number of old cobalt units in many cancer centres [15].

The Instituto Nacional de Cancerología

The State Health services range from primary health-care facilities to highly specialized National Institutes of Health (INSalud). A high percentage of the population (57.9%) [25], receive different types of medical attention at state facilities.

The INSalud is a government organisation consisting of 12 institutions with different areas of specialisation. Its purposes, in addition to medical treatment, are research and medical education. The INCan is the largest cancer centre nationally located centrally, operates under the INSalud umbrella, and provides specialised cancer care to the uninsured population. At INCan, an average of 4,000 new patients are seen annually, mostly those living in Mexico City and nearby states. The hospital is fully equipped for diagnosis and provides oncologic treatment with radiation

therapy, surgery and chemotherapy. The medical staff consist of highly trained oncologists (radiology, surgical oncology, medical oncology, gynaecology, endoscopy, immunology, infectious diseases, etc.). In addition, a cancer centre network consisting of 26 hospitals distributed nationally provides cancer care to uninsured patients living in the rest of the country with the majority of physicians receiving training at INCan.

Colorectal cancer

According to 1998–2002 cancer registry data [26], CRC represents 3.8% of new cancer cases, a 36% increase during this period [27]. Furthermore, CRC mortality has also increased over the same period.

The CRC incidence is higher in the northern states, which, despite higher income, have poorer diet (low fibre, higher meat consumption and harmful fats) and lifestyle placing them at risk for CRC development. In contrast, the southern state population has lower income, impacting meat and fibre consumption [28]. Furthermore, incidence varies among hospitals and their subsequent populations (Table 1) [29].

Currently, more than 80% of patients are treated in tertiary cancer centres with advanced tumours (Stages III and IV) [30]. Although the reported mortality in Mexico is less than 5/100,000 inhabitants, the lowest worldwide [31], there is clear disagreement between tumour stage at diagnosis, scarcity of resources and reported mortality particularly due to the poor state of cancer data collection.

Late diagnosis of the CRC patients may be attributed to referral bias and the absence of screening programmes, and may contribute to the low survival of these patients [32].

There is no national CRC screening programme, however, local initiatives are implemented in some states or by particular health providers. Although a national programme is needed, it is important to acknowledge that socio-cultural and economic factors associated with CRC screening could affect its success [33]: lack of information about CRC, machismo, embarrassment, diagnosis and test costs, and low participation in CRC screening have all been reported by Mexican communities living in the US [31, 33–35].

CRC at the INCan

CRC patients seen at INCan increased more than 60% in a five-year period. In a recent publication, Rizo-Rios et al., reported 789 new cases of CRC seen at the INCan in a 5 year period (2000–2004) [36]. The male/female ratio was similar, and an age related increasing evidence was noted

Table 1 Incidence of CRC in four hospitals in Mexico City. (Modified from [29])

Hospital	Population attended	1978 [%]	2003 [%]	<i>p</i>
Hospital general	Poor uninsured	15	36	<0.001
Hospital 20 de Noviembre	Middle class government employees	20	51	<0.01
Instituto Nacional de CMNSZ	Middle class uninsured	26	39	<0.106
Hospital Español	Upper middle class, European	37	39	ns

(average age of diagnosis 62 years in men and 65 years in women).

CRC treatment (non-pharmaceutical)

In Mexico, no treatment guidelines for CRC exist, however, surgical procedures are carried out according to American guidelines found at the National Comprehensive Cancer Network (NCCN).

Precise clinical staging often requires a diagnostic colonoscopy and frequently a risk benefit assessment is used to decide surgical treatment (nutritional aspects, cardiovascular risk, presence of distant metastasis, colonoscopy results and possible benefits of surgical resection). Wide surgical resection of the involved bowel segment and regional lymphatic drainage are standard surgical procedures [37].

Operative treatment of rectal cancer includes en bloc resection of the rectum as an intact unit with its lympho-vascular drainage contained within the fascia propria of the mesorectum using sharp dissection techniques (Total Mesorectal Excision). Preservation of the anal sphincters and avoidance of a permanent colostomy is preferred in rectal cancer if eradication of the cancer with adequate margins is also achieved. A temporarily diverting colostomy may be necessary depending on intra-operative findings. Transanal local excision of rectal cancer may be appropriate and curative for selected patients with small, early-stage and accessible tumours that exhibit favourable histological features. Palliative treatment for unresectable rectal cancers includes fulguration, laser photocoagulation, radiation therapy and endostenting [37].

Due to surgical complexity, most CRC surgeries are performed in large hospital facilities by trained surgeons (gastroenterologist, oncologist and occasionally general surgeons). At INCAN, surgical procedures are performed according to the NCCN Clinical Practice Guidelines in Oncology.

Radiation therapy and chemotherapy are used for advanced disease in conjunction with surgical resection (according with NCCN Clinical Practice Guidelines in Oncology). While radiation therapy has little role in management of colon cancer, it is an important treatment

modality for rectal cancer. Bulky rectal cancers may be treated pre-operatively to improve resectability. For Stage-II (invasion through the muscularis propria of the rectal wall) or Stage-III rectal cancer (metastases to regional lymph nodes), radiation therapy is a useful pre-operative or postoperative adjunct and is also used in combination with chemotherapy.

Pharmaceutical CRC treatment

Chemotherapy is essential to provide a chance of cure for patients with more advanced disease, with 5-fluorouracil plus leucovorin (5-FU/LV) forming the basis of standard treatment. Recently, new agents have become available with a subsequent increase in life expectancy for patients with Stage-IV disease from 5 to >20 months.⁸ Treatment facilities, use and adherence to clinical management guidelines and access to new, effective agents may be dramatically different within the country. Treatment costs are particularly expensive for Stage III/IV.

In the public setting there is no uniform formula for CRC treatment. Government employees (ISSSTE) are able to access all types of CRC treatment, however, none of these new agents are available for the IMSS CRC patients. Out-of-pocket payments for pharmaceuticals at the Secretariat of Health hospitals, including INCAN, limit the possibility to access to novel drugs. These treatments may only be available if patients are enrolled in pharmaceutical industry-financed clinical trials as there is no reimbursement for the public sector. Private insurance may pay for these new drugs, however, only a small percentage of the population has access to private insurance.

Post-treatment surveillance

There are no national guidelines for post-curative treatment surveillance. Postoperative surveillance varies according to health provider type with private practice physicians often

⁸ Oral versions of traditional 5-fluorouracil therapy (Capecitabine, UFT), additional cytotoxic chemotherapy (Irinotecan, Oxaliplatin), and new targeted biological treatments (Cetuximab, Bevacizumab).

having closer follow-up, yet no specific protocol is followed. For patients in the social security (IMSS, ISSSTE) system, different follow-up protocols may be implemented according to workload. At INCan, patients with resected stage II or III CRC have:

- Clinical evaluations every 3 to 6 months for the first 3 years, every 6 months during years 4 and 5, and yearly thereafter
- Serum carcinoembryonic antigen levels every 3 months for at least the first 3 years after primary resection
- Colonoscopy once a year, if normal, 3 years later, and if normal, at subsequent 5-year intervals
- Proctosigmoidoscopy: every 6 months for 5 years in patients with low anterior resection
- Yearly CT scans of the chest and abdomen for 3 years

Conclusion

Colorectal cancer is one of the most common forms of cancer, affecting large subsets of the population in developed nations and, increasingly, in low-middle-income countries. Due to a combination of changes in population age structure and vast transformations in lifestyle behaviour, an increasing proportion of individuals are at increased risk of developing what is considered mostly to be an avoidable disease.

Despite evidence on the effectiveness of some screening procedures, their use remains low in Mexico. Social-cultural factors may play a role in the under-utilisation of cancer screening in addition to low levels of education, income and limited government interest. Consequently, patients often seek medical care at advanced stages of the disease.

If preventive programmes remain unchanged, the increasing demands for curative health care may cause great financial and management challenges to the health care system in Mexico.

Conflict of interest statement The authors do not report any conflict of interest associated with this paper.

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