agents, including the rocket fuel hydrazine and the burning of wood fuel in the home. These examples illustrate how far this classification is from defining the detailed real-world risks. Rocket-testing workers can be exposed to hydrazine, but most of us will never come upon it. And the risk from your wood-burning stove clearly depends in a complicated way on the wood, the stove, and how much you use it.

The remaining doubt on shift working is largely because clear evidence in humans is very hard to obtain. There is good evidence, IARC conclude, that interfering with rhythms of light and dark in experimental animals can increase the probability of cancer, and indeed on how these changes occur. But do things work in the same way in humans? There are inconsistencies in the evidence. It is not ethical or feasible to carry out long-term experiments in humans, so instead researchers observe people, and record their working patterns and cancer diagnoses. Unavoidably, there are many possible biases in such studies. Perhaps the people studied are not typical, or their work records were inaccurate. Also, people who work shifts differ from those who do not in many ways, and perhaps these other differences are the real cause of any increase in cancer risk.

The IARC assessment, "probably carcinogenic in humans", has not changed since they last considered shift working in 2007. They have certainly considered much new evidence; all but one of their references describe work published since 2007. But the new evidence from human studies still has unavoidable inconsistencies and potential biases. Future research might make things clearer, but that will not be easy.

Should you be concerned by this classification if you work night shifts? IARC have left open the possibility that shift working has no effect at all on cancer risk. If it has, the evidence on the size of any risk is not clear. If the risks were really substantial, the research results in humans could well have been clearer and more consistent. My feeling is that this should not be a major worry for night shift workers.

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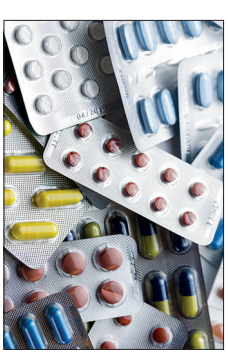
1 IARC Monographs Vol 124 group. Carcinogenicity of night shift work. *Lancet Oncol* 2019; published online July 4. http://dx.doi.org/10.1016/S1470-2045(19)30455-3.

2 IARC. IARC Monographs Meeting 124: night shift work (4–11 June 2019). Questions and answers. https://www.iarc.fr/wp-content/uploads/2019/07/QA_Monographs_Volume124.pdf (accessed July 12, 2019).

Improving affordability of new Essential Cancer Medicines



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Effective cancer care requires investment in health infrastructure, a trained health workforce, and quality-assured, affordable medicines within a sustainable supply chain. To this end, in a major move to increase access to cancer medicines in low-income and middle-income countries (LMICs), WHO has added ten new cancer therapies to its 21st Model List of Essential Medicines.[1] When WHO labels medicines as essential, it means that they have proven their utility and should be available and affordable to all. Therefore, these medicines should be included in national essential medicines lists, which would enable governments to use scarce resources to select medicines more effectively.

Including cancer medicines in the WHO Essential Medicines List is the crucial first step. Effective national policies incorporating legal and regulatory frameworks that promote access are needed to make cancer diagnosis and treatment widely available.[2] Cancer medicines often come at a high price, creating challenges even for high income countries (HICs), while their availability in LMICs is limited or non-existent. The new WHO Essential Medicines List should prompt governments and other stakeholders to take action to decrease the price of medicines in order to make them accessible.

The situation of lenalidomide in South Africa is a case in point. Lenalidomide is an essential medicine for the treatment of multiple myeloma. Until 2016, South African patients had access to generic lenalidomide manufactured in India under a section 21 legal authorisation that allows the sale and use of unregistered products. The generic lenalidomide was priced at US$2289 per patient per year. This authorisation was withdrawn when Celgene registered its patented product in the country and priced it at

$51 000 per patient per year. The medicine is now no longer available in the public sector, which cares for 84% of the population. Patients in the private sector are also struggling to pay the 20% co-payment. In India, however, where the patent application for lenalidomide was rejected, the generic versions are available for $2000 per patient per year.[3] Another example is afatinib, which is a first-line tyrosine kinase inhibitor used to treat lung cancer, the leading cause of death from cancer in men in LMICs and the second leading cause after breast cancer in women.[4] Afatinib, now listed in the Essential Medicines List as equivalent to erlotinib, is not widely available in LMICs, and when this medicine is available, its price is a major challenge to access. For example, in Pakistan, where afatinib costs over $1000 per month of treatment,[5] many patients cannot afford it.

Studies on the cost of production of cancer medicines show that substantial reduction in price is possible. Using a validated algorithm[6] for estimating the cost of production, accounting for tax and a 10% profit margin, it is estimated that lenalidomide could cost $2·55 per month, afatinib could cost $8·85 per month, and abiraterone $60·97 per month.

The drive to lower the price for medicines is always met by concern about the loss of revenue to finance the research and development sector. Yet the global sales figures for medicines that have been on the market in HICs further provide evidence that this concern is unwarranted. For instance, cumulative sales incomes of cancer medicines in 2017 for trastuzumab and rituximab were $88·18 billion and $93·74 billion, respectively. WHO studied sales revenue from 99 cancer medicines approved by the FDA from 1989 to 2017, illustrating that the average financial return on investment was $14·50 for every $1 of spending. A third of the cancer medicines studied had already reached blockbuster status with over $1 billion annual sales income.[7] Most of these sales take place in HICs. Therefore, making these new medicines affordable in LMICs is not likely to impair future research and development.

Countries could take some of the following measures to improve access to cancer medicines, including new paediatric cancer drugs: pooling their procurement at the regional or subregional level to create economies of scale and increase their negotiating power, encouraging sustainable supply of low-cost generics[8] and the uptake of biosimilars, and using flexibility in trade-related aspects of intellectual property rights (TRIPS) agreements to lift a patent monopoly when needed to access generics. Pharmaceutical companies should also engage in public health oriented voluntary licensing of products through the Medicines Patent Pool. There is ample evidence that the abovementioned options work in other fields, notably in the area of HIV and hepatitis C virus.[9,10]

Countries will continue to need the support of WHO in expanding cancer care and treatment. WHO's pivotal report on cancer medicines pricing necessitates that the organisation steps up its attention on cancer care and translates these efforts into forceful strategies.

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1 WHO. World Health Organization model list of essential medicines: 21st list 2019. Geneva: World Health Organization, 2019. https://apps.who.int/iris/handle/10665/325771 (accessed July 9, 2019).

2 Perehudoff SK, Alexandrov NV, Hogerzeil HV. The right to health as the basis for universal health coverage: A cross-national analysis of national medicines policies of 71 countries. *PLoS One* 2019; **14:** e0215577.

3 Tomlinson C, Moyo H, Zizvi Z, Waterhouse C, Meyer S, Low M. Exploring patent barriers to cancer treatment and access in South Africa: 24 medicine case studies. October 2017. https://www.canceralliance.co.za/wp-content/uploads/2018/02/Exploring-Patent-Barriers-to-Cancer-Treatment-Access-in-SA-24-Medicine-Case-Studies-October-2017-update-January-2018.pdf (accessed July 9, 2019).

4 Bray F, Ferlay J, Soerjomataram I, Siegel R, Torre L, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; **68:** 394–424.

5 Medicines Patent Pool. Exploring the expansion of the medicines patent pool's mandate to patented essential medicines: a feasibility study of the public health needs and potential impact. May 24, 2018. https://medicinespatentpool.org/resource-post/exploring-the-expansion-of-the-medicines-patent-pools-mandate-to-patented-essential-medicines (accessed July 9, 2019).

6 Hill AM, Barber MJ, Gotham D. Estimated costs of production and potential prices for the WHO Essential Medicines List. *BMJ Glob Health* 2018; **3:** e000571.

7 WHO. Pricing of cancer medicines and its impacts. Geneva: World Health Organization, 2018. https://apps.who.int/iris/bitstream/handle/10665/277190/9789241515115-eng.pdf?sequence=1&isAllowed=y (accessed July 9, 2019).

8 Wirtz VJ, Hogerzeil HV, Gray AL, et al. Essential medicines for universal health coverage. *Lancet* 2017; **389:** 403–76.
9 't Hoen E, Veraldi J, Toebes B, Hogerzeil HV. Medicine procurement and the use of flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights, 2001–2016. *Bull World Health Organ* 2018; **96:** 185–93.
10 Medicines Patent Pool. Products licensed for HIV, hepatitis C, and tuberculosis. https://medicinespatentpool.org/what-we-do/global-licence-overview/licences-in-the-mpp/ (accessed July 1, 2019).

The growing burden of cancer in the Gaza Strip

Globally, more than 18 million new cases of cancer were diagnosed in 2018, and almost 10 million deaths were registered.[1] In the occupied Palestinian territory (the West Bank and Gaza Strip), cancer is the second most common cause of death exceeded only by heart disease.[2] Most cases are diagnosed at a late stage, leading to difficulties in symptom control and treatment options, and compromising quality of life and survival.[3]

As of April, 2019, 5 163 667 people live in the occupied Palestinian territory, according to UN estimates. Two million people are living in the Gaza Strip, which is a narrow, overcrowded strip of land located southwest of the West Bank, measuring 362 km² and with a population density of 5525 people per km². 75% of the population live below the poverty line and unemployment was 52% in 2018 (an increase of 8% from 2017) according to the Palestinian Central Bureau of Statistics.[4]

There are only two oncology departments in the Gaza Strip, one at Ranteesy Hospital and another at the European Gaza Hospital. Cancer therapy generally includes surgical treatment, chemotherapy, and radiotherapy or combination therapy, in addition to auxiliary services, such as radio-diagnostics, laboratory services, and nuclear medicine.[5] However, medical facilities in the Gaza Strip suffer chronic shortages of many essential medicines, due in part to the complex and ongoing sociopolitical and economic crises faced by the Ministry of Health, as well as political instability and lack of funding.[6] On average, 30–40% of essential chemotherapy drugs are out of stock at any one time in Gaza.[7] The unavailability of systemic treatment affects 7415 (60%) of 12 359 patients. Missing just one chemotherapy dose or cycle can dramatically decrease the effectiveness of the treatment and increase the risk of drug resistance in patients.[8]

Surgery is the main cancer intervention in Gaza. It is sometimes the first and often the last modality used to treat cancer in Gaza, usually due to the absence of other options. More than 85% of surgical treatment of cancer is done without adjuvant or neoadjuvant chemotherapy, owing to the shortage of these drugs. Radiotherapy is still unavailable throughout the Gaza Strip. Radioisotopes and radioactive substances used for diagnosis and radiotherapy services, which are crucial, for example, for biopsying axillary lymph nodes and therefore assessing the spread of breast cancer, are banned from entering the Gaza Strip.

The high number of patients with cancer in oncology wards and the delay in receiving adequate cancer treatment force the medical staff to look for other options, such as referring patients for treatment outside Gaza in other countries.[9] This option has several drawbacks. More than 60% of patients are prohibited from entering these countries by governments. For the remaining 40% of patients, even if they do manage to travel, their treatment is a substantial financial burden on health authorities, as well as the patients themselves and their families. There is also a substantial social and psychological burden. Further, referrals are usually delayed during travelling, which leads to deterioration of the patient's condition, and sometimes death.

A lack of epidemiological studies and reliable data motivated us to do a retrospective assessment of the cancer burden in the low-income, isolated territory (the Gaza Strip) within the occupied Palestinian territory. We calculated the total number of new annual cancer cases during the past 8 years (2011–2018). Annual cancer incidence, strategic treatment intervention, and mortality were also calculated.

We found 12 359 new cancer cases in the Gaza Strip between 2011 and 2018. Of the five governorates of the Gaza Strip, Gaza City had the most cancer cases (5685 [46·0%] of 12 359), followed by Khanyounis (2101 [17·0%]), Deir al-Balah (1644 [13·3%]), north Gaza (1508 [12·2%]), and Rafah (1421 [11·5%]). The