Information Session

for Member States and Non-State Actors in Official Relations

World Health Organization

Technical Report on Pricing of cancer medicines and its impacts

25 April 2019

ACCESS TO MEDICINES, VACCINES AND PHARMACEUTICALS

WHA Resolution 70.12

Operative paragraph 2.9

To prepare a **comprehensive technical report** to the Executive Board at its 144th session that examines **pricing approaches**, including **transparency**, and their **impact on availability and affordability** of medicines for the prevention and treatment of cancer, including any evidence of the **benefits or unintended negative consequences**, as well as **incentives for investment in research and development** on cancer and innovation of these measures, as well as the **relationship between inputs throughout the value chain and price setting, financing gaps for research** and development on cancer, and **options** that might enhance the affordability and accessibility of these medicines.

Information Session Overview

1. Approach and scope of the report
2. Findings
3. Options
4. Questions

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Report structure

Report was structured into 5 Chapters

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Introduction

- Prevention and treatment of cancer
- Purpose of this report
- Scope and methods

Benefits and risks of cancer medicines

- Evidence of benefits and risks of newer cancer medicines
- Opinion of the EML Cancer Medicines Working Group

Pricing approaches for cancer medicines

- Objectives of national pricing policy and pricing approaches
- Industry's pricing approaches
- Payers' pricing approaches

Impacts of pricing approaches or lack thereof

- Impacts on price, availability and affordability
- Impacts on R&D, price and pricing transparency
- Unintended negative consequences

Options that might enhance affordability & accessibility

- Six areas of potential options

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Chapter 1

Context, scope and methods

High prices of and growing expenditure on cancer medicines have challenged cancer care

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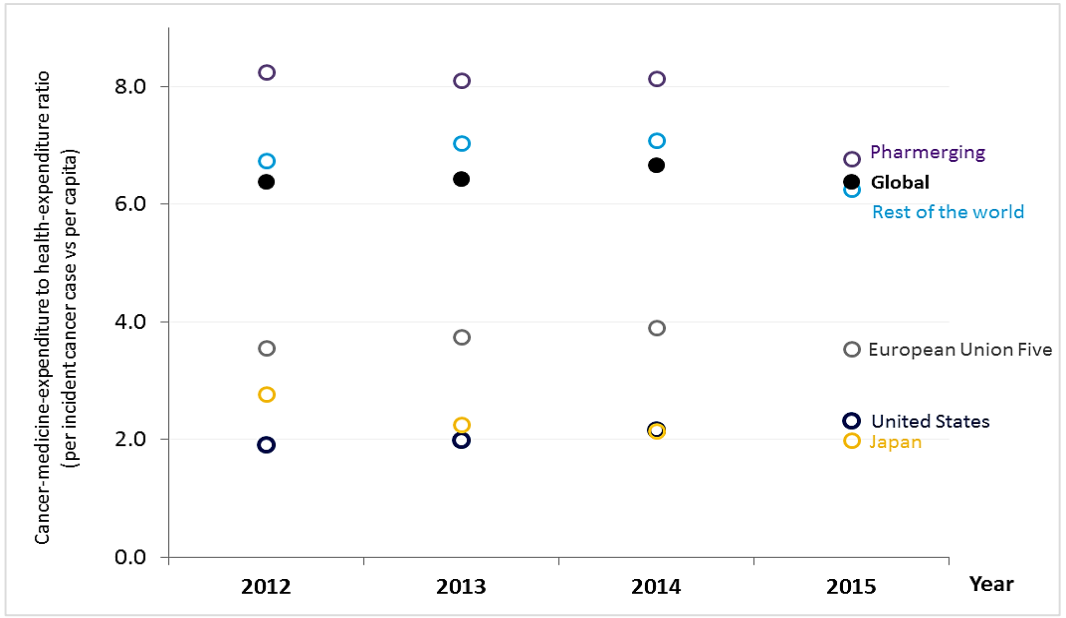
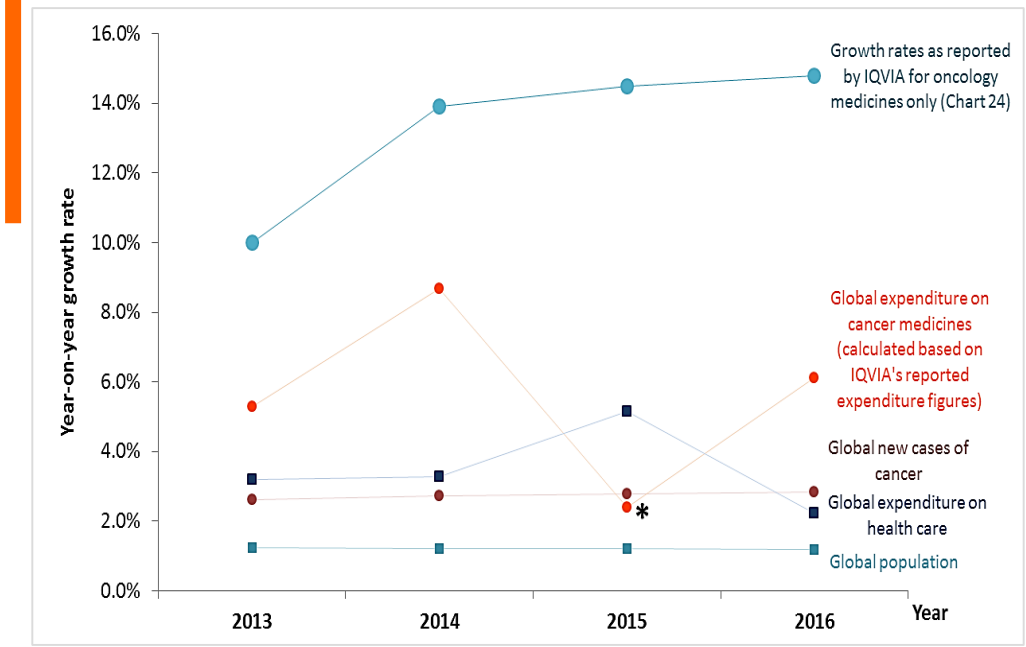
Pages 3-4

- **Spending on cancer medicines (2017)** = US$133 billion (compare to US$ 90.9 billion in 2012)

Expenditure on cancer medicines grew at rates (5.3–8.7% per year) **higher than** the growth rates of people newly diagnosed with cancer (2.6–2.8% per year)





Per-capita expenditure on cancer medicines has been about **2- to 8-fold above** the overall per-capita health expenditure

Existing approaches on managing medicine prices have not resulted in acceptable outcomes

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Multiple reviews at international and national levels

- UN High-Level Panel on Access to Medicines, OECD, EU Commission, US The President's Cancer Panel, UK National Audit Office, Australia's Community Affairs References Committee

Common themes from these reviews

- seeking better alignment of prices and the costs associated with the use of cancer medicines with their health benefits in clinical practice compared to alternative medicines
- enforcing greater transparency on the prices of cancer medicines and the costs of research, development and production
- correcting the imbalance on the negotiating powers between payers and manufacturers
- enhancing the use of generic and biosimilar cancer medicines with a view to enhancing competition
- ensuring appropriate application of patent law and rights for market exclusivity to avoid over-compensating innovators and becoming barriers to access

Improving patient access to cancer care

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Page 5

- **Access to cancer medicines is linked to systemic factors**
  - financial resources, insurance coverage, availability and skill set of the health workforce, health care infrastructure and physical access to health services
- **Strategies to improve access to cancer medicines should be holistic**
  - Across all surgical, pharmacological, radiological and social interventions
  - Across prevention, treatment, rehabilitation and palliation
- **Strategies should consider the entire health care sector**
  - Benefits of improving access to cancer medicines are not achieved at the expense of essential health care products and services for other disease areas.

Approach and scope of the technical report are aligned with the operative paragraph

Pages 6-8

Approach

- Consult two informal advisory groups of experts
- Review policy documents, publicly available literature and other grey literature
- Collate documented examples and case studies
- Perform quantitative and qualitative analyses

Scope

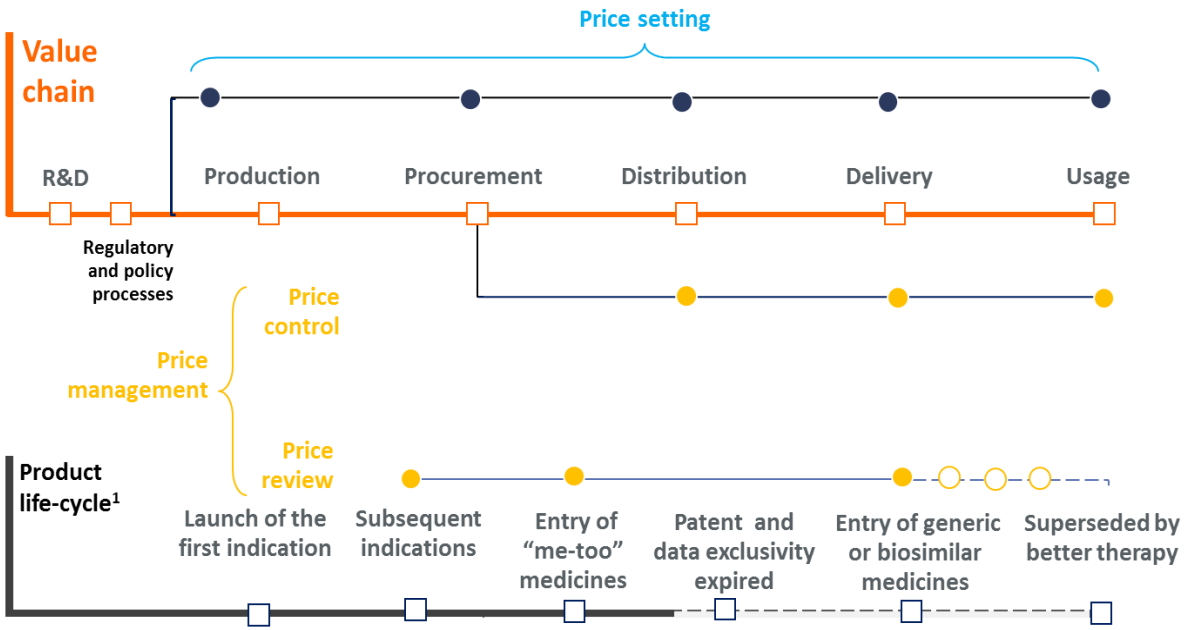
- Pricing approaches
  - Value chain: R&D to usage
  - Product life cycle: market launch to entry of generic/biosimilar products
- Impacts
  - Price
  - Availability
  - Affordability
  - R&D incentives and gaps
  - Price transparency
  - Unintended consequences
- Options

Key terms defined for the purpose of the report

Pages 7

Cancer medicines: Medicines for the prevention and treatment of both solid tumours and haematological cancers in both adult and paediatric settings

Value chain and product life-cycle



Availability: Medicines in national formulary

Affordability

- health system: Proportion of spending on cancer medicines compared to existing expenditure on medicines or other health products and services
- individual patients: Number of days' wages needed to pay for the cost of treatment

Transparency: Disclosure and dissemination of information to relevant parties to ensure accountability. e.g. price transparency refers to disclosure of the net transaction prices between the sellers & the payers/buyers

Unintended consequences: Unplanned outcomes arising from planned actions that have deviated from the original intent.

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Chapter 2

Benefits and risks of cancer medicines

Some cancer medicines lead to substantial improvements in patient health outcomes

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Page 10

- **Much progresses since the advent of chemotherapy in 1940s**
  - Better disease characterization
  - Introduction of targeted therapies and immunotherapies
- **Cancer medicines have contributed to site-specific improvements in survival for specific cancers**
  - Together with the significant contribution from prevention, early diagnosis, and improvements in pathology, imaging, radiotherapy and surgical interventions
- **Some cancer medicines improve health outcomes substantially**

An increasing number of clinicians question the benefits of some newer cancer medicines

Pages 11-13

- **Concerns over insufficient evidence of benefits on clinical outcomes**
  - Inadequate evidence base
    - Only one-third of cancer medicines approved by US Food and Drug Administration (2008–2012) and European Medicines Agency (2009–2013) had established evidence of prolonged survival at the time of approval
  - Modest survival gains
    - Among cancer medicines approved on the basis of extended survival, overall survival was extended for a median 2.7 months (range: 1.0 month to 5.8 months)
- **Concerns about safety profile**
  - Greater risk of 'toxic death' (OR=1.4) and treatment discontinuation (OR=1.33) for newer targeted drugs than control

European Society for Medical Oncology (ESMO)'s work on defining the magnitude of clinical benefits

Page 13-14

- **Using the ESMO's Magnitude of Clinical Benefit Scale as a screening tool**
  - To identify candidate medicines that might be potentially suitable for inclusion in WHO Essential Medicines List (EML)
  - Medicines that receive an ESMO score equal to 4, 5 or A-B could be eligible to become EML candidates if clinical benefits meet or exceed the 4-6 month survival interval

- **Need to comprehensively evaluate all evidence**
  - cumulating results across clinical trials and evaluating their consistency, to identify potential limitations of validity and generalizability at global level.

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Chapter 3

Pricing approaches by industry and payers

National pricing policy and pricing approaches generally specify both health system-related and economic goals

Page 16

Health system-related goals

- Ensure timely and equitable patient access to affordable medicines
- Improve prescribing and dispensing practices
- Promote ethical practices among medicine suppliers and health professionals
- Ensure system transparency with clear lines of accountability

Objectives
of pricing policy and pricing approaches

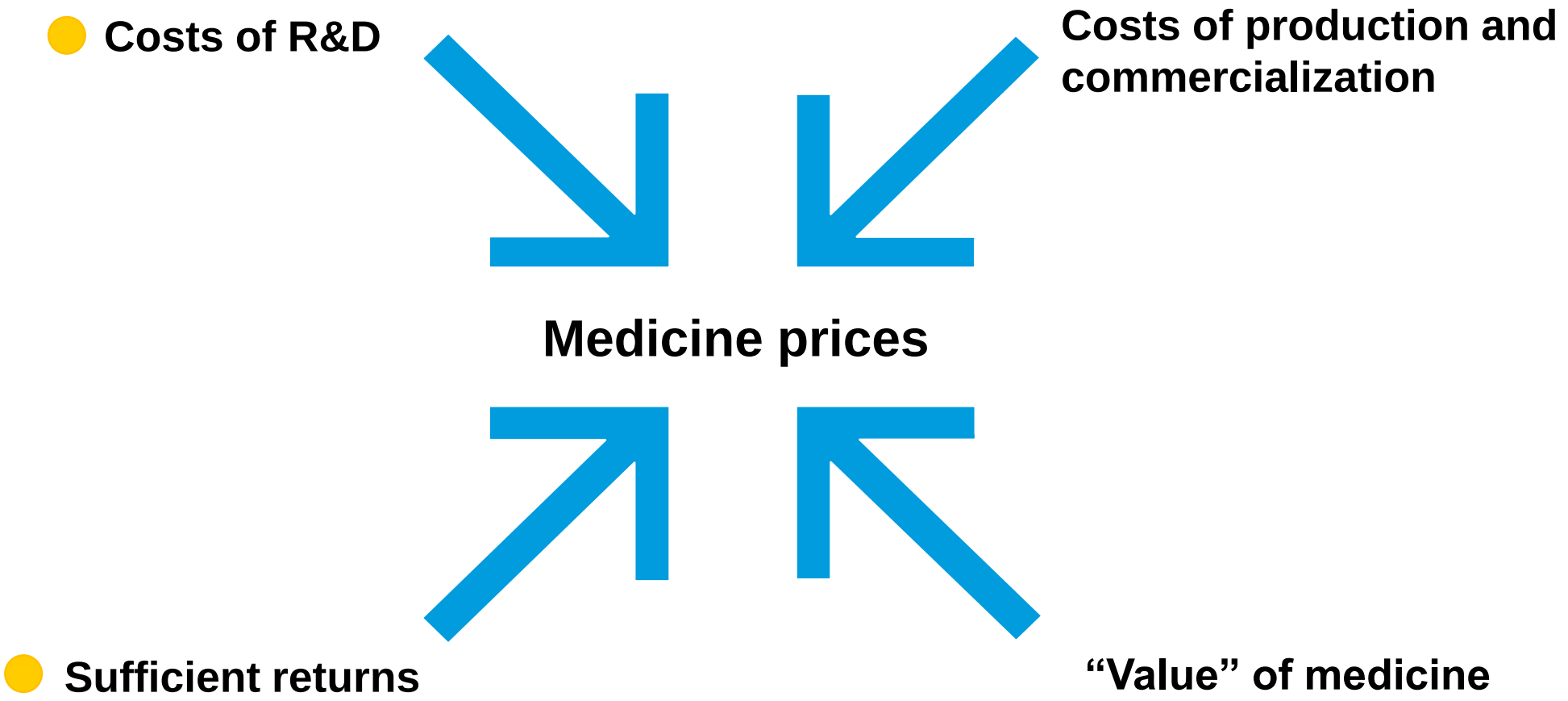
Economic goals

- Achieve prices of medicines that are financially sustainable
- Promote efficiency
- Enhance competition
- Promote innovation
- Support the development of a responsible and commercially-viable pharmaceutical industry

Industry’s pricing approaches

Four broad determinants of medicine prices from the industry perspective have been described

Pages 17-31



Analysis on R&D costs and return

Pages 23-26

Study objective

- To systematically compare sales incomes of cancer drugs with the R&D costs

Rationale

- High costs and high risks of R&D have been presented to justify high medicine prices
- Estimated R&D costs are highly variable and non transparent: US$100-150 million to US$4-6 billion
  - Needs to cover for the risks of failure
  - Needs to cover for the costs of capital
  - Different (and non-transparent) methodologies

Method (1)

Pages 23-26

Design

- Observational study: Reported sales income of individual cancer medicines compared to the estimated overall R&D costs reported in the literature
- Scope: Medicines approved by US FDA (1989-2017) for any cancer-related indications
- Sales income to the end of 2017: Net of rebates and discounts but not expenses & taxes

Data

- Sources: Sales data from originator companies' consolidated financial reports; risk-adjusted R&D cost from Prasad and Mailankody (2017)
- Missing data: growth rates, other sources, or estimated from known reported values if required
- Exclusion: Medicines with missing data for than half or more of the years since approval

Method (2)

Pages 23-26

Analysis

- Standardization: All data expressed in 2017 US dollars with adjustments for inflation
- Descriptive statistics: Average and cumulative sales incomes, and return-on-investment (ROI)

Uncertainty & assumptions

- Non-cancer indications: No adjustment for data if not disaggregated
- Three sensitivity analyses
  - **Indication extension**: Incorporated costs of up to 5 post-approval Phase I-III trials
  - **Excluded medicines**: Incorporated R&D costs with accrual of $0 revenue
  - **Higher than average R&D costs**: 2 x base-case R&D cost estimates ($1.6b ; $438m-$5.6b)

Sales incomes greatly exceeded R&D costs

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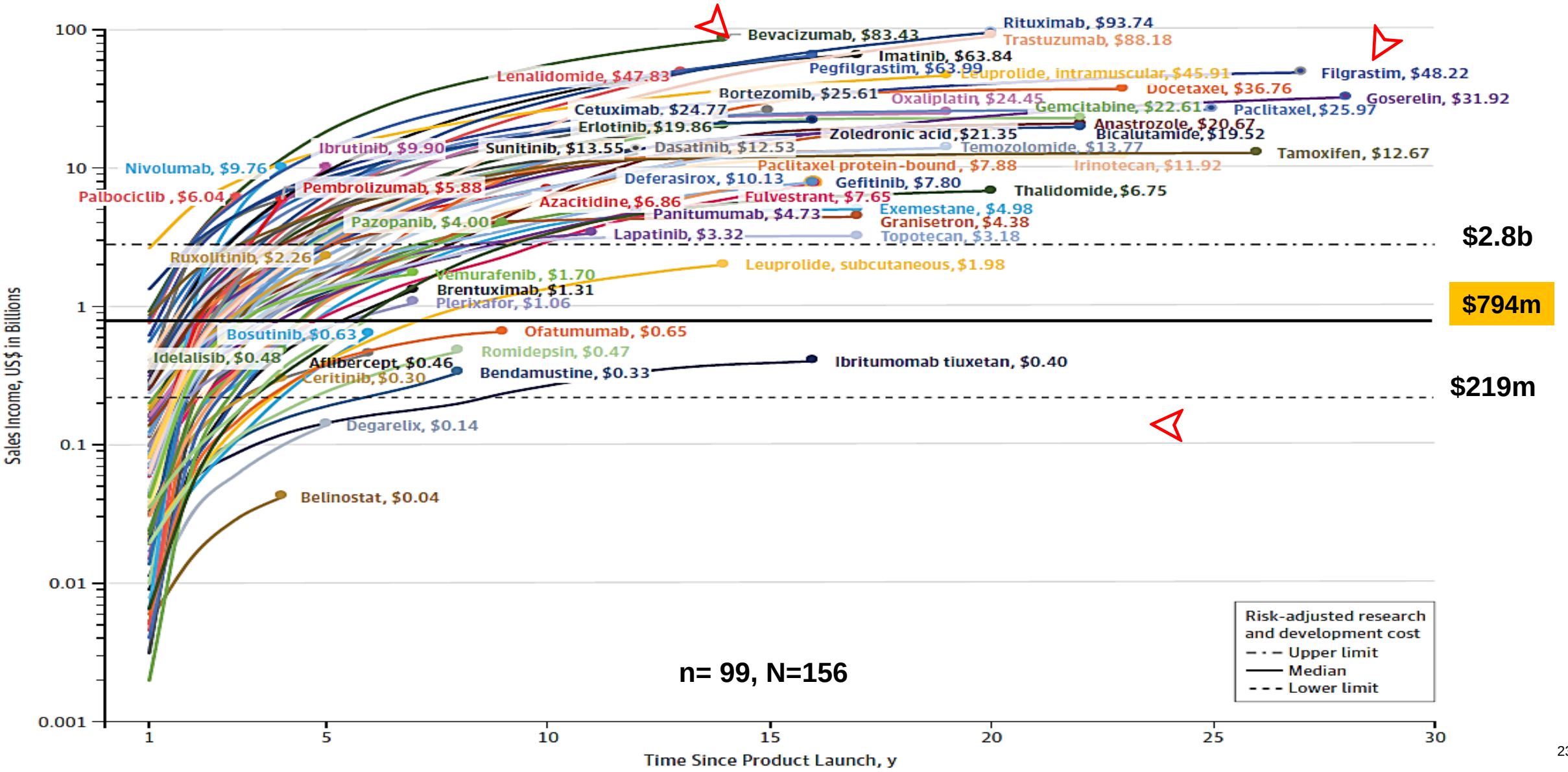


Cancer drugs, through their high prices, have generated substantial financial returns

Pages 23-26

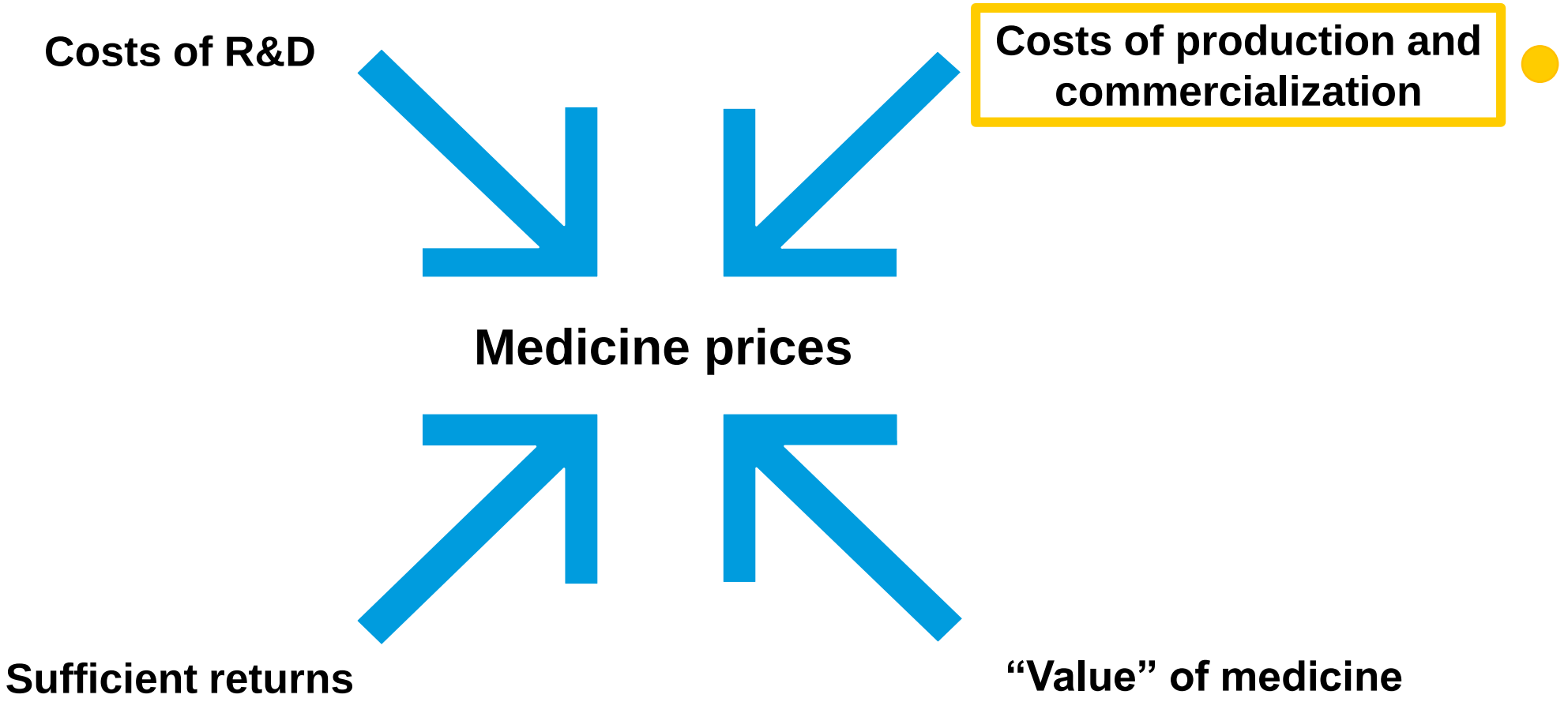
Sales income by 2017

- Average income per year since approval: $3 million to $5.9 billion
- % ‘blockbuster’ drugs: 33.3%
- Number with total income ≥$50 billion: 5

Revenue Return on investment

- Base case: $14.50 ($3.30-$55.10)
- Time to cover max R&D costs (2.8b) 5 years (2-10 years)
- Risk-adjusted R&D costs x 2: $6.70 ($1.20-$27.10)
- Costs but no accrual of revenue for excluded medicines: $8.80 ($1.70-$34.40)

Four broad determinants of medicine prices from the industry perspective have been described



Summary of evidence on costs of production

Pages 18-20

- **Marginal production cost is low**
  - Commercial production of sofosbuvir: 0.9%-1.5% of price
  - Tyrosine kinase inhibitors: 0.2%-2.9% of the treatment prices

- **Marginal production costs are likely to remain low over a wide range of quantities**

Costs of sales and expenses are high in proportion

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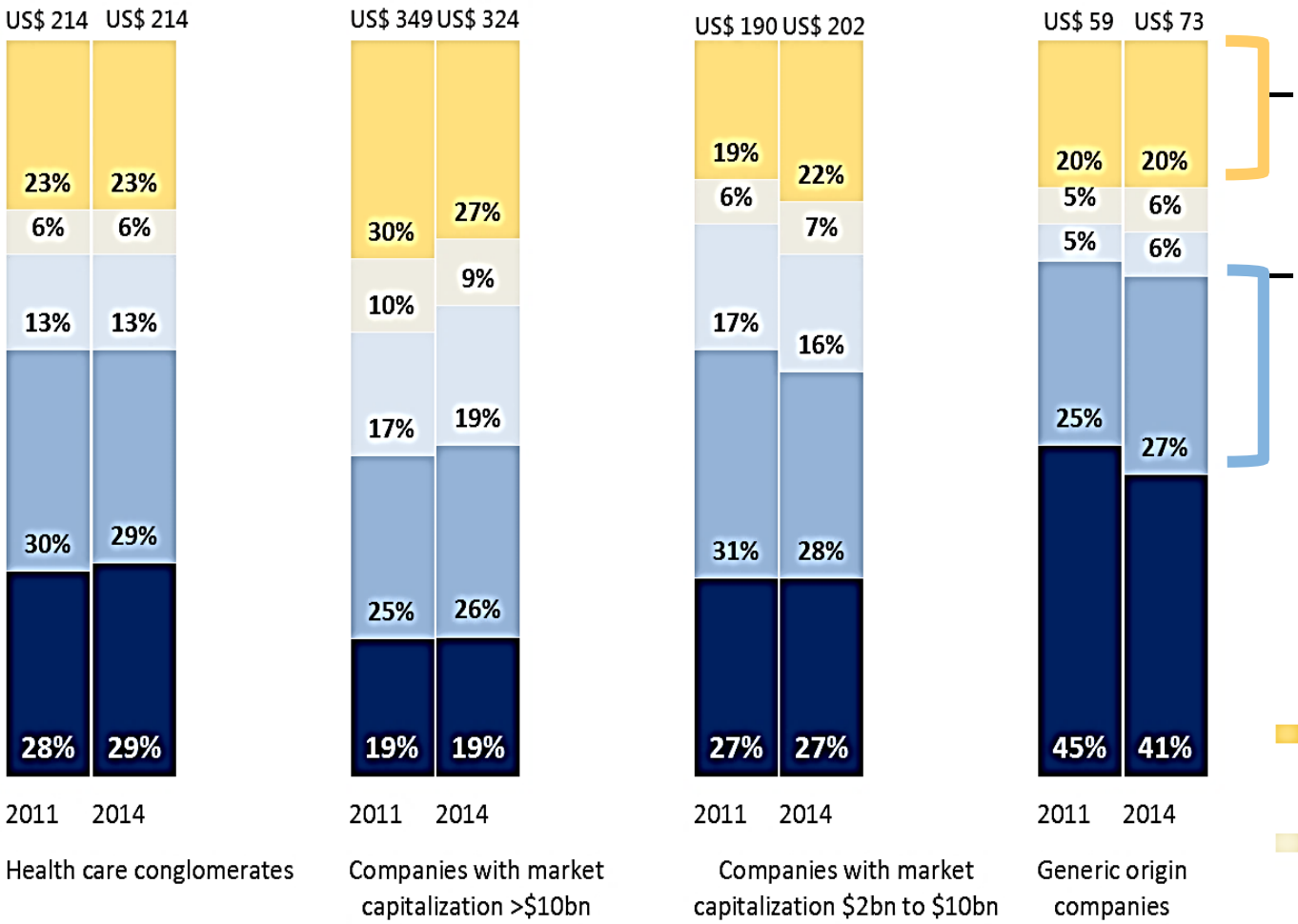
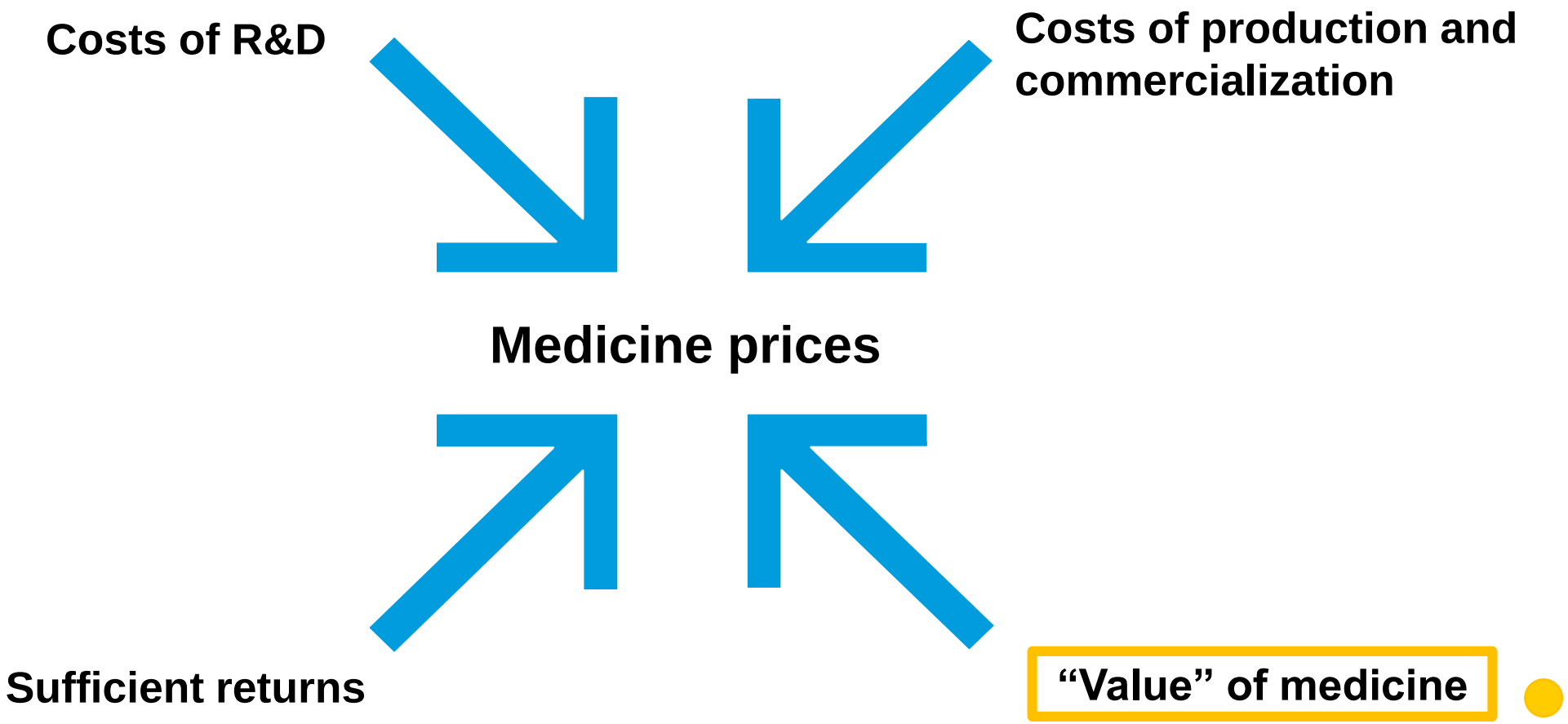
Pages 18-20



- Earnings before interest and tax range: 20%-30%
- Costs of marketing and promotional activities account for a large proportion of the expenses

Earnings before interest and tax (EBIT)
Depreciation and amortization
Research and development
Selling, general and administrative expenses
Cost of goods

Four broad determinants of medicine prices from the industry perspective have been described



Value based pricing has been proposed and used as a method of pricing new medicines

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Pages 20-23

Some sources of uncertainties from value-based pricing

Different technical approaches

in undertaking "value" assessments

Incomplete evidence

to inform judgements about "value" at the time of decision-making

Artificially high "value"

of a new medicine relative to an inefficient current practice, even though the absolute magnitude of benefits is low

Different conceptualizations and perceptions

of value

Emphasis on setting prices according to income expectations

- Evidence of price increases without evidence of increased value (e.g. better efficacy or safety)
- Extensive planning activities for pricing of medicines many years before the value of medicines has become known i.e. the clinical evidence from the pivotal Phase III trials

Payers’ pricing approaches

Payers' Pricing approaches

Pages 32-48

Setting prices

Cost based: factors of production

What to include and how?

Tender and negotiation: best price

Market dynamics?

Reference pricing: benchmarking

To what?

Value based: (Anticipated) outcomes and preferences

What to include and how?

Other related measures

Maximum ceiling price, managed entry agreements, Taxes

Managing prices

Regulation of mark-ups / remuneration: structure

To whom and at what level?

Regulate price increase: Frequency and magnitude

Restriction

Revise prices: changing market conditions or therapeutic landscape

When and how?

Cost-based pricing is infrequently used

Pages 32-33

- **Practical challenges in obtaining reliable cost information**
  - Difficulties to allocate costs specific to a medicine for setting of prices
  - Much more widely to determine prices downstream in the value chain (i.e. ex-pharmacy and consumer prices) because the cost of goods is easier to determine
- **Potential impacts on innovation and supply**
  - Potential weak incentives for innovation because prices are not linked to the magnitude of benefits/harms
  - Potential perverse incentives for inefficient R&D and production in order to attract higher profit margins
  - Monopolist may exit market, potentially causing medicine shortages

Many countries have adopted elements of value-based pricing

Pages 34-35

- **In theory, value-based pricing is more likely to encourage innovation**
  - Linking price to value: value-based approaches are more likely to encourage companies to innovate and produce medicines with attributes that society and governments value most
- **In practice, there remains considerable challenge in assessing, measuring and translating the value of a medicine to a price**
  - No universally accepted view on what dimensions of value should be considered for the purpose of determining medicine prices
  - Different effect sizes for different cancers (e.g. erlotinib for NSCLC vs pancreatic cancer)
  - Subjective valuation e.g. innovativeness
  - Strong technical capability, system capacity and a supportive politico-legal environment are required for implementing HTA to determine value and price of medicine

Reference pricing has been widely applied

Pages 35-37

External reference pricing

- Differences in method and purpose vastly different size and range of reference countries
- Figure 3.9 on page 37
  - Countries with higher GDP per capita often seek price references from countries with comparable national incomes
  - Lower-income countries appear to have relied on prices information from countries with a wide range of national incomes, reflecting different timing of product launch and large price variability

Internal Reference pricing

- To regulate the prices of ‘equivalent’ medicines: expired patent and end of market-exclusivity period end, or therapeutic equivalents

Managed entry agreements (MEAs) have been commonly used for newer cancer medicines

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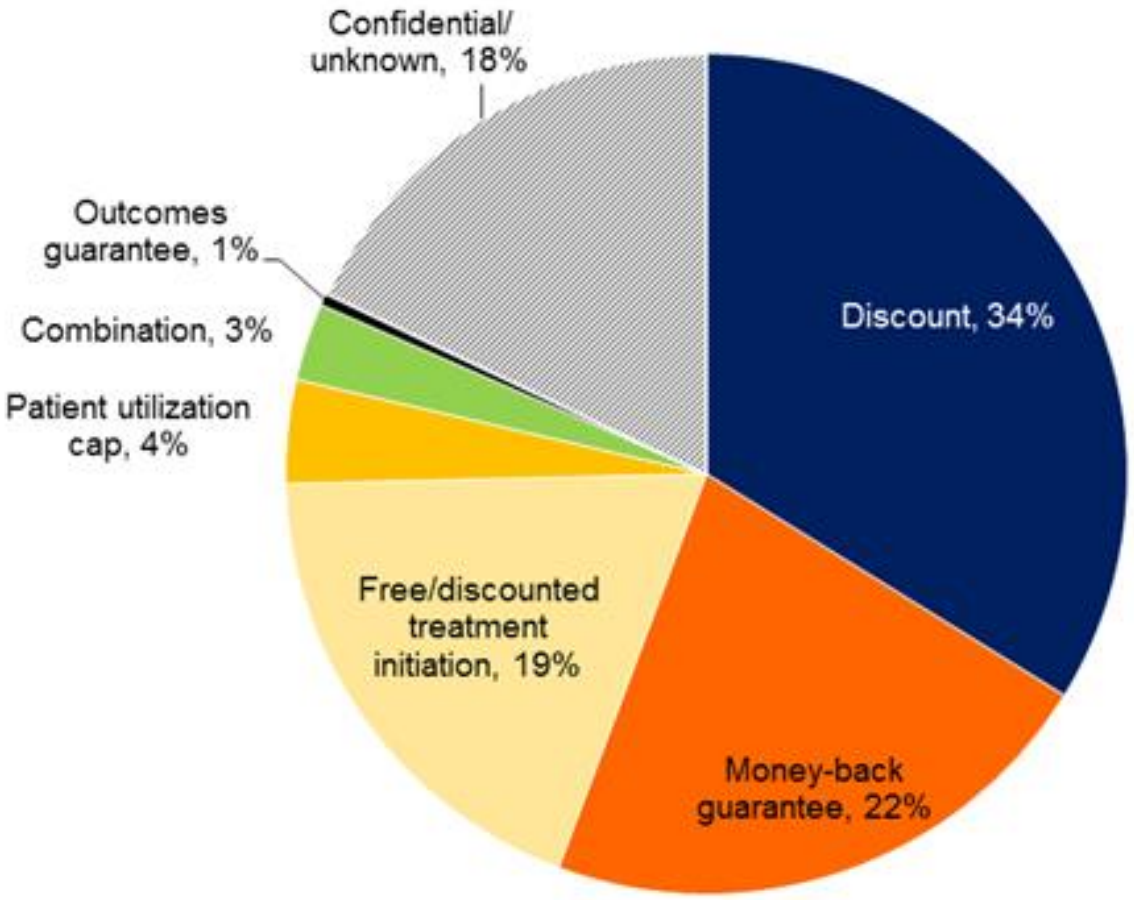
Pages 40-41

- **Intended to share the risks**
  - Financial risks
  - Uncertainties relating to performance
- **Implementing MEA could be complex, and the design would need to be operationally manageable**
  - Strong information infrastructure to ensure data quality
  - Capture changing clinical practice
  - Acceptable distribution of risks
  - Transaction and administrative costs

Types of MEA applied for cancer medicines in European countries



Country authorities have routinely monitored prices and used measures to achieve system efficiencies

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Pages 39-48

- **To control prices throughout the supply chain and at various time points throughout the product life cycle**
  - Regulating mark-ups
  - Reassessing prices upon changing market conditions
    - Entry of generic and biosimilar products,
    - Changes in indications of individual medicine (i.e. market size)
- **To achieve greater system efficiencies with an indirect effect on prices**
  - Requiring clinicians to obtain approval from the payer before prescribing or dispensing
  - Policies to encourage prescribing of generic or biologically similar products
  - Reduction or exemption of taxes on medicines
  - Pooled procurement

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Chapter 4

Impacts of pricing approaches or lack thereof

Impacts

I. Price
II. Availability
III. Affordability
IV. R&D
V. Transparency of pricing and prices
VI. Unintended negative consequences

Impacts on price

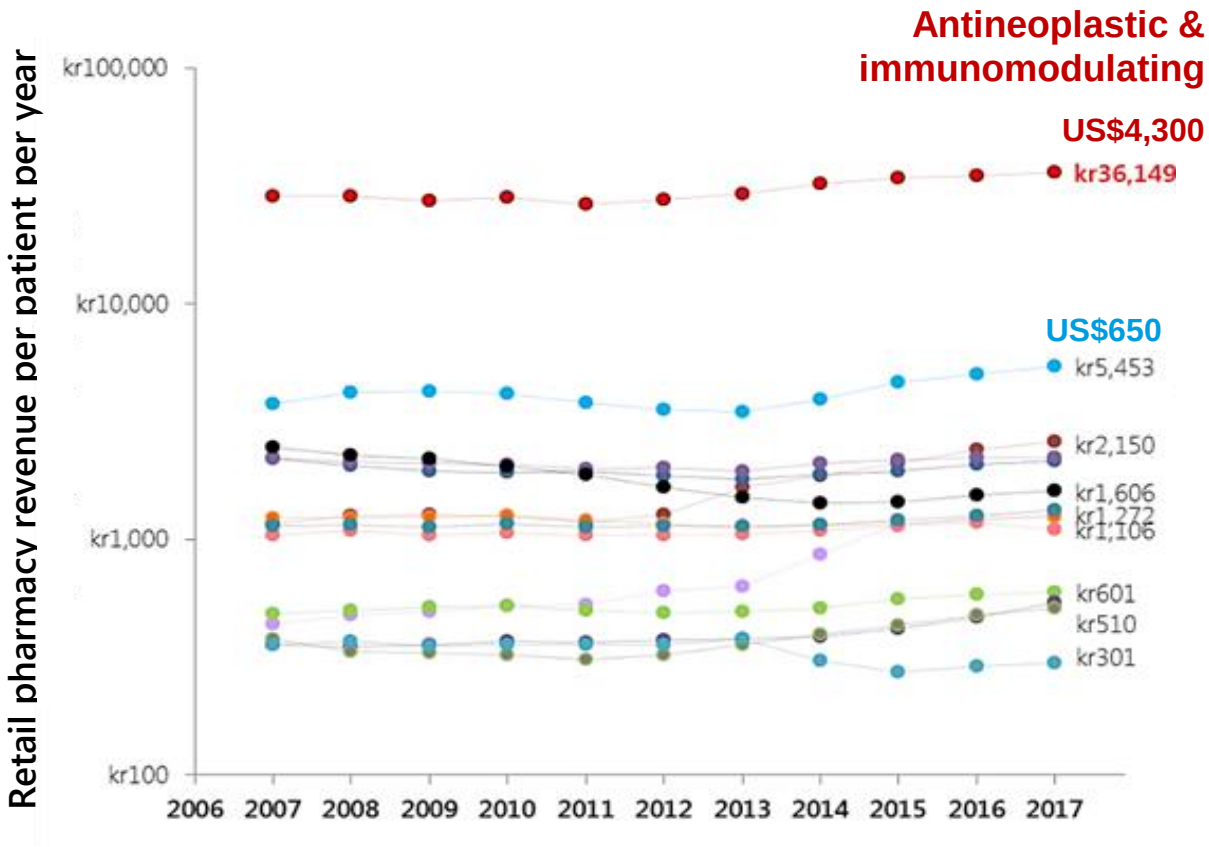
Prices and costs of many cancer medicines are high in absolute and relative terms

Pages 53-55

- Annual costs of cancer medicines introduced in the past decades are often **at least in the tens of thousands of US dollars per patient**

- Comparative evidence shows that **prices and costs of cancer medicines are higher** than the prices and costs of medicines used in other therapeutic areas

Comparative expenditure on cancer medicine in Norway



Considerable variability in the prices of cancer medicines within a country and across regions

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Pages 55-57

- **Not commensurate with the demand or country's purchasing power**
  - Four studies included in the report
  - e.g. Procurement prices of EML cancer medicines were generally higher in African countries compared to Latin American countries, despite having comparable levels of income
- **Implications**
  - Procurement practices may not be the most efficient, as lower prices could have been achieved.
  - Impair countries' coverage of essential cancer medicines when prices are higher than their ability to fund and provide the medicines.
  - Inequitable access resulted from regional differences in medicine prices within a country because only some patients having access to the medicines at lower prices

Could a lack of consistent price regulation lead to uncontrolled medicine prices?

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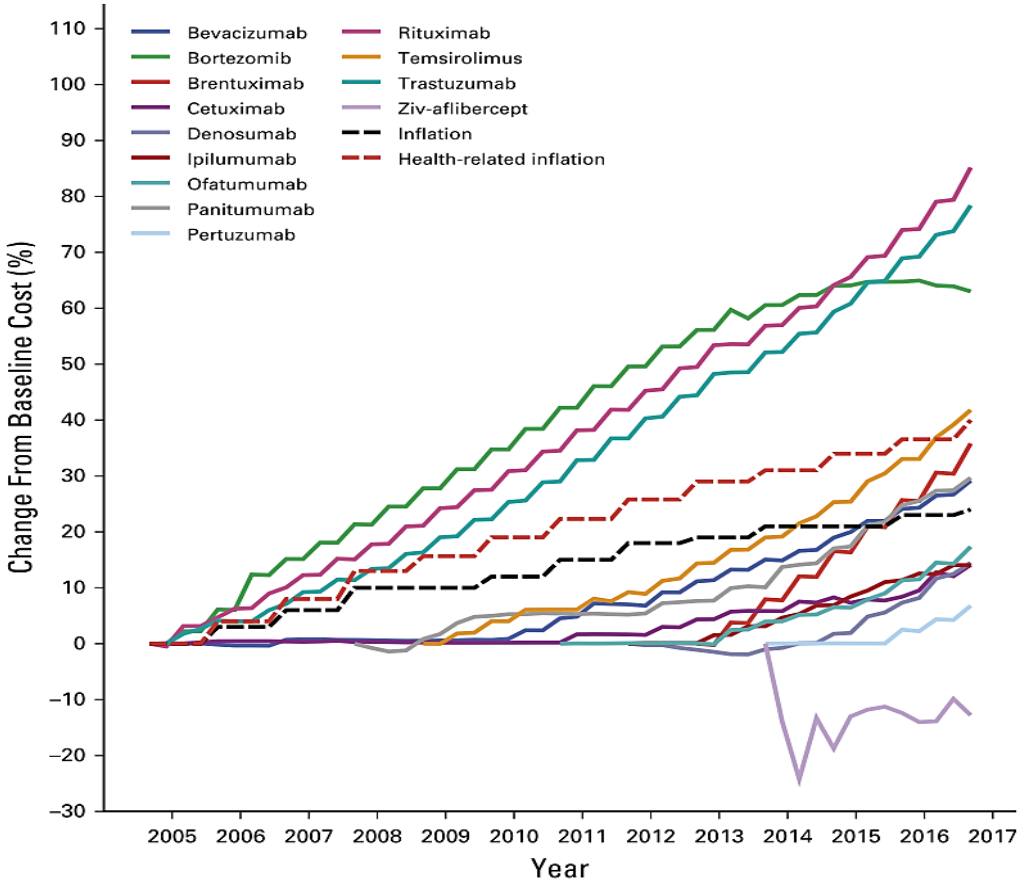
Pages 58-59

- **A lack of uniform pricing policies may result in ineffective control of medicine prices and cost-shifting activities**

- **Implications of uncontrolled and significant increase in price**
  - Inequitable patient access
  - Firms engaged in wasteful non-price competition (e.g. advertising, sales promotion, preferential contractual arrangements)
  - Distort international price expectation

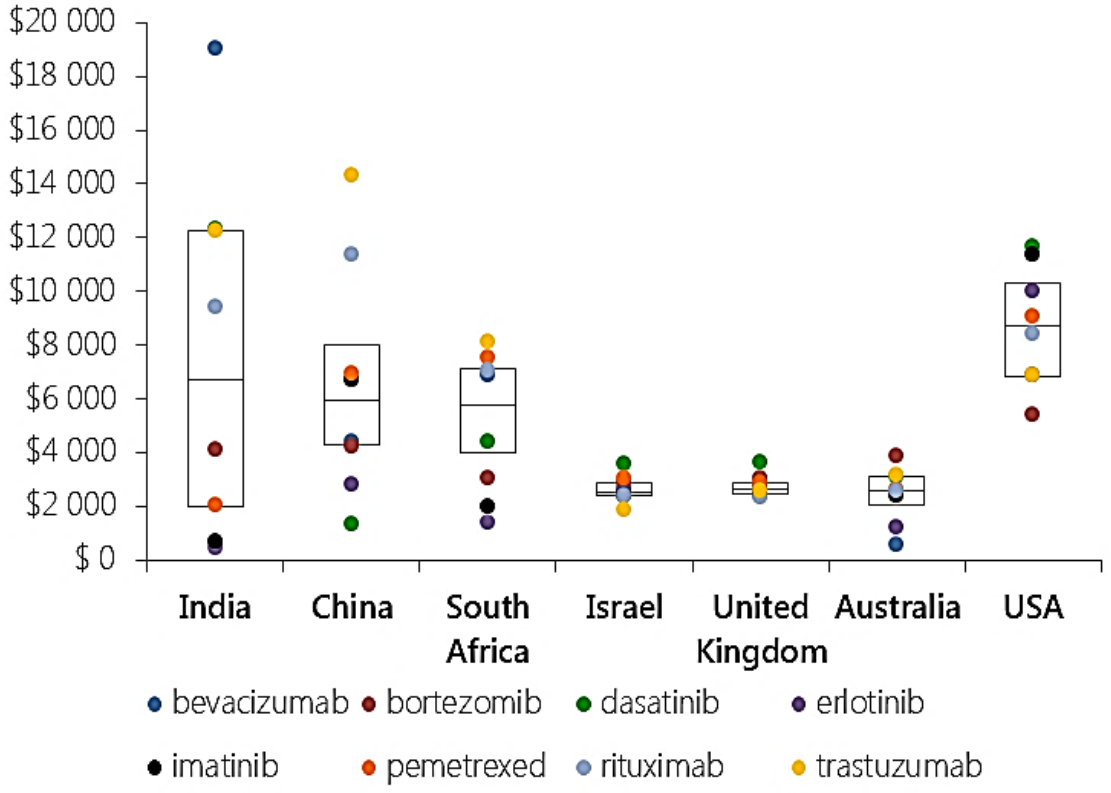


Average cumulative percentage change from baseline mean monthly cost in the USA, in real terms = **+19.1%**

A higher degree of pricing regulation may result in lower medicine prices and costs

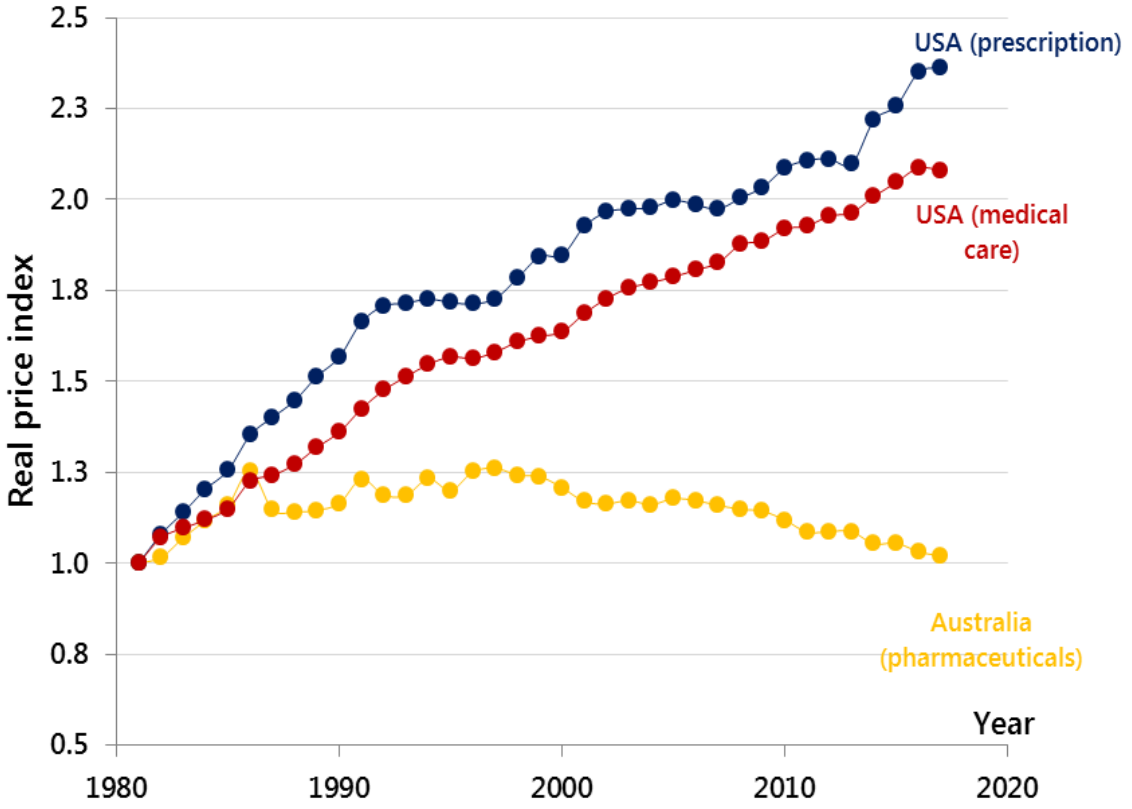
Pages 59-61

Monthly costs in 2016 US$ (purchasing power parity)



Source: Goldstein et al 2016

Change in price level for pharmaceuticals relative to the change in price level for all goods and services



Source: Author's calculation based on data published by governments

Market competition could result in lower medicine prices and expenditure savings

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Pages 64-67

- **Price reductions with entry of generic medicines/therapeutic equivalents**
  - Price of generics are significantly lower than originator brands (e.g. imatinib Latvia, cancer meds in India)
  - Generic entry would, on average, result in 20%-30% lower price than the originator brand in the first year, with cumulative price reductions of up to 80%
- **Lower prices have translated into expenditure savings**
  - E.g. in India, generic paclitaxel, docetaxel, gemcitabine, oxaliplatin and irinotecan have generated an estimated savings of about ₹ 47 billion (US$ 843 million) in 2012
- **Market and policy factors could influence the effectiveness of competition**
  - Existing price or non-price policies, number of competiting comparnies/products/indications and market size; regulatory requirements and processes,
  - Robust competition policy to curb anti-competitive behaviours (e.g. pseudogenerics, tacit or actual collusion, ‘product hopping’, non-value-add activities

Impacts on availability

Availability of cancer medicines (or lack thereof) should be understood within context

Page 68

- **Different country and healthcare contexts**
  - e.g. System capacity and epidemiology
  - This means:
    - some cancer medicines may not be as necessary or even useful (e.g. in the absence of companion diagnostic tests for genetic profiling, or technical skills and labour for safe prescribing and administration).
    - some cancer medicines may confer only marginal benefits and cause more harms to patients in the absence of appropriate supportive care
- **Data often only represented the availability at one point in time**
  - i.e. cross-sectional data
  - This means that it might not indicate the persistence of (non-)availability

Two global surveys in 2014 and 2016 showed variations in the availability of cancer medicines

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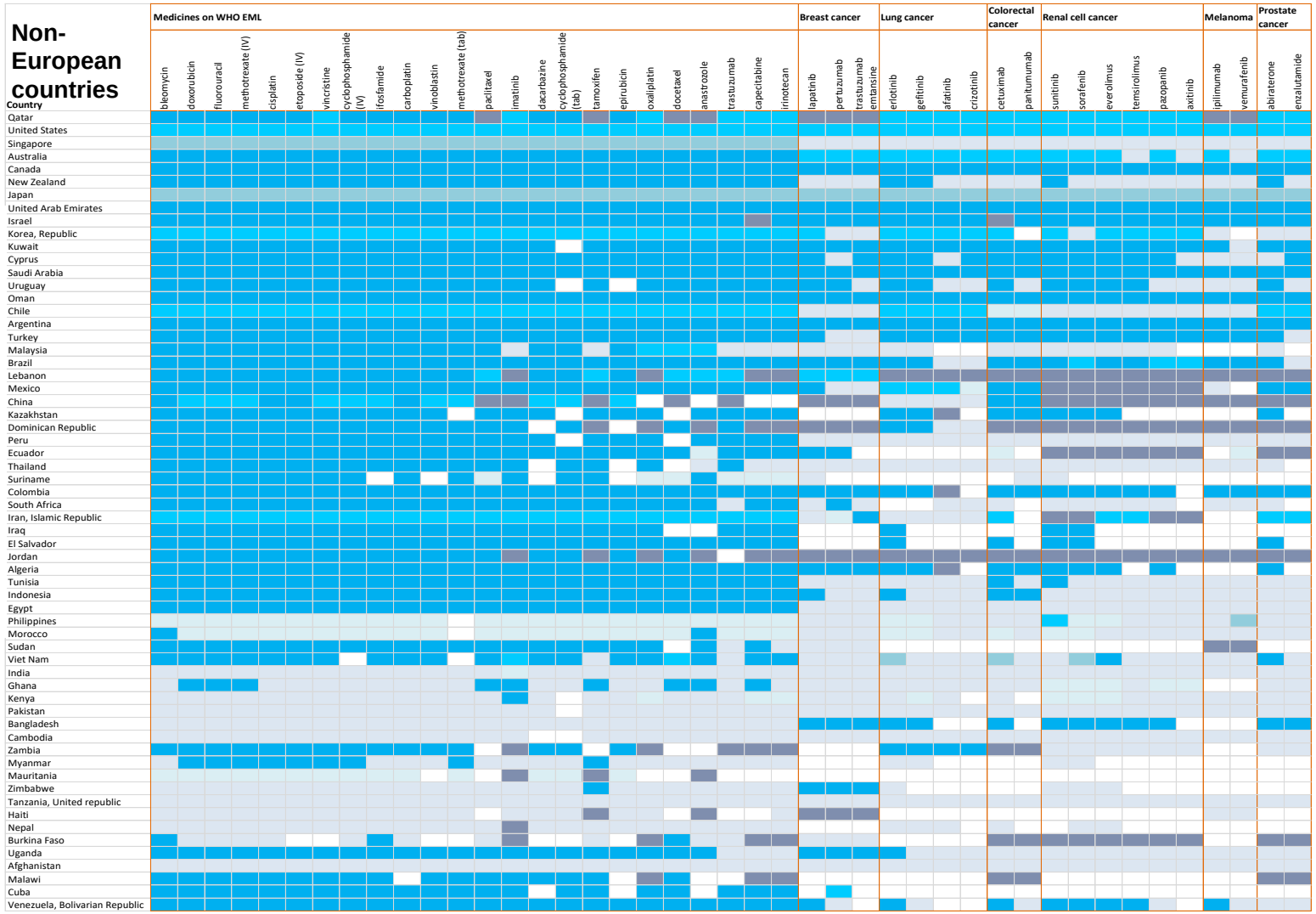
Page 69



- In general, countries with lower income had **lower availability** of cancer medicines, or **availability only with higher patient out-of-pocket costs**

- Available and free
- Available and at <25% cost to patients
- Available and at 50–100% cost to patients
- Available and at 25–50% cost to patients
- Available and at full cost to patients
- Not available
- Missing data

Same observations in European countries for cancer medicines

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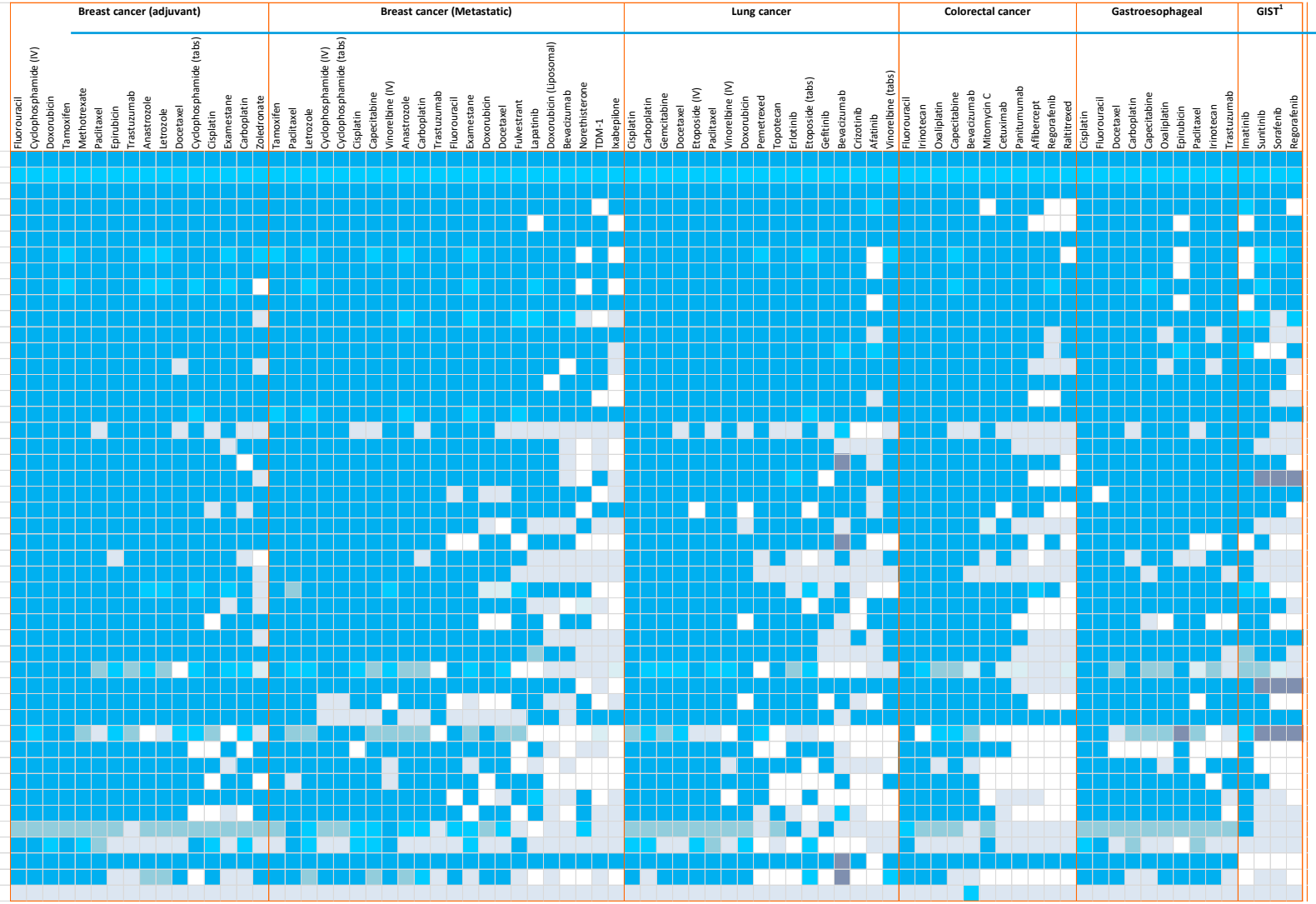
Page 70

European countries



- Breast cancer (adjuvant)
- Breast cancer (metastatic)
- Lung cancer
- Colorectal cancer
- Gastroesophageal
- GIST

- Available and free
- Available and at <25% cost to patients
- Available and at 50–100% cost to patients
- Available and at 25–50% cost to patients
- Available and at full cost to patients
- Not available
- Missing data

Country-specific studies have also found similar observations

Page 72

- **2017 Study in Pakistan (Punjab)**
  - Potential inequity in access in this region
    - Higher availability of higher-priced originator than lowest-priced generics: 52.5% vs 28.1%
    - Higher availability in private sector than public sector: 71.9% for originator brands and 20.0% for lowest-price generics vs 31.4% for originator brands and 11.7% lowest-price generics
- **2013 study in 76 non-high-income countries**
  - Lower availability of EML cancer medicines in lower-income countries
    - Low-income countries (median =11 medicines) vs lower-middle-income (18 medicines) vs upper-middle-income (26 medicines) countries
  - Considerable variation in availability
    - Among countries belonging to the same income grouping
    - Among countries in the same WHO region

Have high costs of cancer medicines restricted patient access?

Pages 72-73

- **Applying eligibility criteria could ensure efficient & high-quality use of medicines**
  - Eligibility criteria by indications, patient characteristics, qualifications of the physician, context of use, pre-authorization
- **BUT cost-containment measures undertaken due to the high costs of cancer medicines, irrespective of population needs, have resulted in reduced, delayed and even cancelled treatment**
  - Studies documented the impacts of restricted access to rituximab, imatinib, sofosbuvir in various countries

Judicious selection and rational application of access requirements can deliver better health outcomes

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Pages 74-75

- **A policy of trying to fund the same number of cancer medicines as are available in other countries will not result in substantive health improvements, but will result in significantly higher costs.**

- **Countries should instead consider their specific health care context, including factors such as population need and available funds.**
  - Narrative evidence review of access to cancer medicines in New Zealand, Australia and the USA
  - Lower availability and 'slower' access of cancer medicines in New Zealand and Australia than the USA has **not** had a negative impact on patient access to medicines that deliver good clinical value
    - Access to cancer medicines, while important, is only **one part of the spectrum of cancer care** required for improving the health outcomes of cancer patients

Impacts on affordability

A three-step analysis to assess affordability

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Page 76

1. If countries were to spend 1% to 5% of their total annual health expenditure on cancer medicines with a view to providing universal coverage to these medicines, what would be the per-person "budget" for cancer medicines per year?

2. How would the size of this per-person budget for cancer medicines compare to the costs of common treatment regimens for various cancers?

3. In the absence of insurance coverage, what would be the duration of time that an individual would need to work in order to obtain sufficient income, from earning the average population wage, to pay for a course of treatment fully out of pocket?

Treatment would not be affordable for individual patients without financial support from governments

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Pages 75-79

Per-person annual "budget“ for universal coverage

Income	Low	Lower-middle	Upper-middle	High
1%–5% total HE	**$800–$3 800** ($ 600; $ 5 100)	**$ 1 600–$ 8 000** ($ 1 100; $ 12 900)	**$3 100 – $15 600** ($ 1 900; $ 22 600)	**$8 100 – $40 600** ($ 4 700; $ 73 100)

Numbers in parenthesis are adjusted for purchasing power.

Estimated annual costs of Tx

	India	South Africa	Australia	USA
Breast cancer (adjuvant AC-TH)	**$ 18 500** ($ 67 900)	**$ 33 900** ($ 74 400)	**$ 41 800** ($ 37 000)	**$ 71 700** ($ 71 700)

Time equivalent based on average annual wages (not disposable income)

~ 10 years

1.7 years

- Estimated costs of cancer treatment frequently **exceed** the estimated per-patient annual "budgets" **even if** countries were to spend 1% to 5% of their total annual health expenditure on cancer medicines

Impacts on R&D

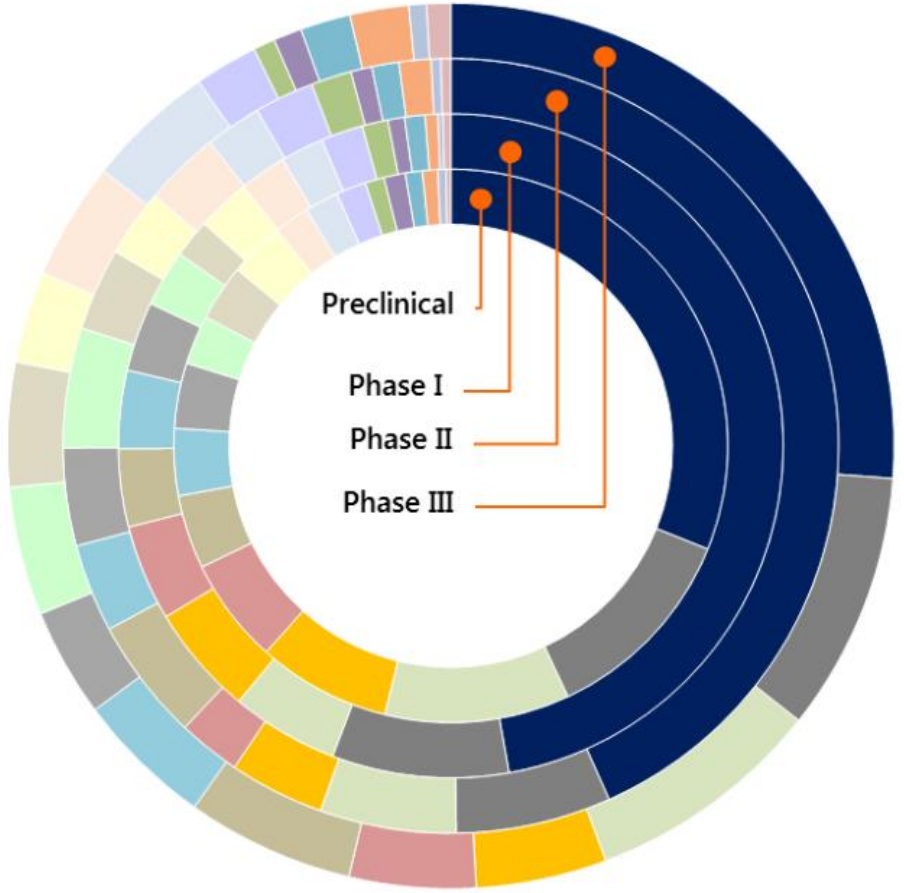
Excessive financial returns from cancer medicines have distorted R&D and will stifle future innovation

World Health Organization

Pages 80-82

Oncology

- **High number of clinical trials on cancer medicines**
  - Almost twice as many clinical trials on cancer medicines as in the next four highest therapeutic categories
- **Experts have noted significant inefficiencies**
  - Duplication and the pursuit of marginal therapeutic indications
  - Some failed investments could have been prevented given the lack of compelling prior evidence



Incentives for investing in R&D of cancer medicines

World Health Organization

Pages 83-87

- **Public sector has made a wide range of contributions to the R&D of medicines generally, including cancer medicines**
  - Various incentives: Direct research funding, research infrastructure, cancer registries, medical research workforces, tax credits or reductions
  - A lack of consolidated information on the true extent of public sector contribution
- **Some stakeholders have questioned whether companies can legitimately claim to recover the full costs of R&D by setting high prices for medicines.**
  - Need to clarify whether the public has been "paying twice", or should be paying twice, for medicines developed with at least partial support from public resources.
  - Clarify the relationship in joint research ventures between the government, industry and universities when pursuing

Determining research priorities and gaps requires both technical assessments and value judgments

World Health Organization

Pages 87-89

- **What ought to be the level of R&D investment?**
  - Objective benchmarks: prevalence, mortality, DALYs
  - Society's preference and prejudices against certain cancers
- **Observed trends reported in the literature**
  - Type of cancers
    - Highest proportions of funding: haematological, breast and prostate cancers
    - Possible "underinvestment": liver, thyroid, lung, oesophagus, stomach and bladder
  - Type of interventions
    - More research funding for drug therapies than radiotherapy and surgical interventions
- **Higher funding levels in leukaemia and breast cancer areas may be in line with social expectation, and hence, be justified**

Impacts on transparency

Confidential agreements on rebates and discounts have obstructed market transparency

World Health Organization

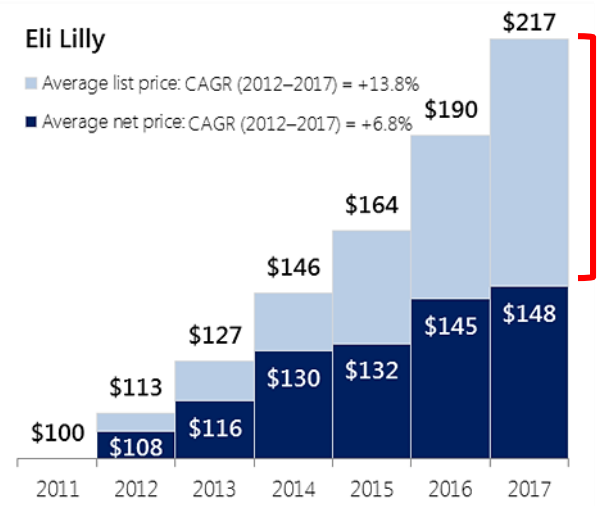
Pages 90-92

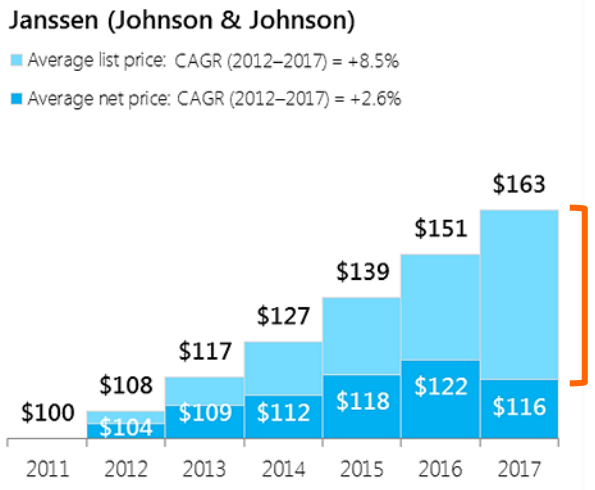
- **Use of discounts and rebates may signal competition**

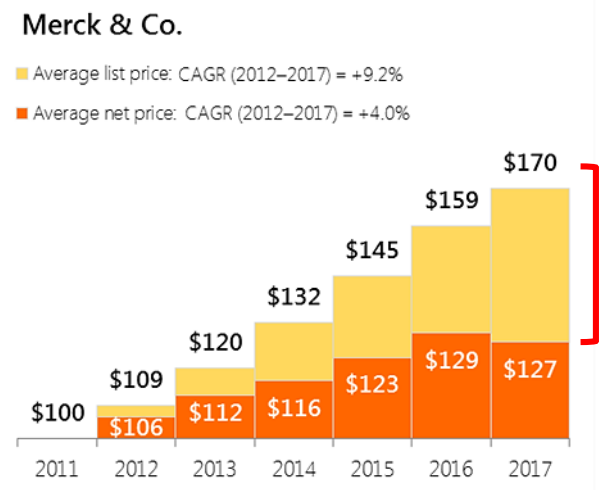
  BUT

- **<u>Confidential</u> rebates and discounts have impaired information about the level of price competition**
  - Masking actual increases in medicine price
  - Preventing potential competitors from understanding pricing strategy
  - Keeping list prices high to impair the effectiveness of external reference pricing.

Growing differences in list prices and net transaction prices (in the USA)







Lack of price transparency is inconsistent with the notion of good governance & may impair market efficiency

World Health Organization

Pages 90-92

- **Principles of good governance demand, inter alia, transparent process and outcomes**
  - Non-disclosure compromises clear lines of accountability: Tax payers (well-informed stakeholders) would not be in a position to participate in decision making and judge if the responsible authorities have acted in the best interest of tax-payers or not.
- **Informational asymmetry is a known condition for causing market failure**
  - Pricing transparency would enhance efficiency by promoting price competition (all other things equal)
  - Imbalance of power in transaction
    - Pharmaceutical companies have more information during price negotiation, than the party negotiating on behalf of health care authorities
    - Purchasing parties reportedly felt “pressurised” into accepting the offers and conditions proposed by pharmaceutical companies in the absence of full information.

Theoretical arguments on the effects of price transparency are inconclusive

Pages 92-93

Would price transparency can lead to adverse outcomes?

YES

- In the absence of transparency, companies would be “more likely to set low prices in developing countries and high prices in developed countries”.
- Companies would “elect not to sell to buyers in low-price markets”
- Uniform pricing might “facilitate collusion among sellers” and make “cartels easier to enforce”

NO or Do not know

- No evidence: prices of medicines are highly dispersed and poorly correlated with the country’s ability to pay.
- Companies seem to have already chosen not to launch or delayed the launch of medicines in countries with lower capacity to pay, irrespective of price disclosure
- There are known cases of collusion and there is an assumption that regulators are ineffective in identifying large-scale illegal business practices.

Lack of evidence of the effectiveness of confidential agreements in lowering prices and improving access

Page 94

- **By default, there is a lack of evidence on the effectiveness of confidential agreements**
  - Small survey showing contrasting views about the benefits of confidential agreements
  - Contrasting perceptions could not simultaneously be correct, considering that none of the respondents had information about the prices in other health systems

- **No information about the prices and access that would be otherwise achieved in the absence of confidential provision**
  - Potential trade-offs need to be better understood
    - Administrative burden of negotiating and executing the agreements.
    - Widespread adoption of confidential agreements might have perpetuated the imbalance of information and negotiating powers between payers and manufacturers

Improving price transparency should be encouraged on the grounds of good governance

Pages 94-95

- **Limited evidence on the effectiveness of transparency measures**
  - WHO's V3P
    - Favourable outcomes have been achieved through greater price transparency, such as better contract negotiations, and price reduction resulting in savings in some countries (e.g. Countries in the WHO Western Pacific Region, and Indonesia, Lebanon
  - Brazil's Banco de Preços em Saúde that mandated publication of purchasing prices
    - no consistent pattern of decreasing prices within the two Brazilian states during the five-year period

- **Further research is needed to monitor the impact of improving price transparency.**

Unintended negative consequences

Reported three areas of potential unintended negative consequences

<u>Possible</u> negative policy outcomes that have deviated from the original policy intent

"unintended" or objectionable consequences as they contravene the law

1

Indication expansion in cancer medicines initially designated with orphan drug status

2

Shortage of cancer medicines due to low prices

3

Inefficient, unethical and illegal conducts

Current policies for rare disease medicines may have led companies to pursue an indication for rare cancer first and then expand to other more common cancers

Pages 95-97

Policy incentives to stimulate the R&D of medicines for rare disease, including rare cancer

- Rationale: "there is **no reasonable expectation** that the cost of developing and making available in the US a drug for such disease or condition will be recovered from the sale in the US"
- Incentives: Longer market exclusivity, research grants, tax credits, protocol assistance, regulatory fee reductions, shorter clinical trial, shorter approval time
- Valuing 'rarity' in pricing decisions: high prices despite having modest efficacy at best

Possible unintended consequence

- High return: "> 9% of orphan drugs had revenue greater than US$ 1 billion per year"
- Indication expansion: 26% of 374 medicines initially approved as an orphan drug from 1983 to 2016 expanded their label to other indication(s)
- "Practice of salami slicing" resulting in "artificial rare disease": Total patient populations greater than the 'rare' threshold
- Diversion of resources: away from other previously unaddressed or under-addressed rare diseases

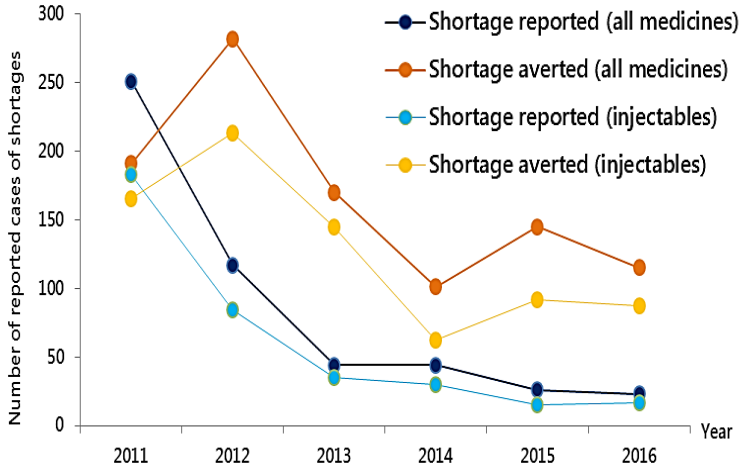
Have low prices caused shortage of cancer medicines?

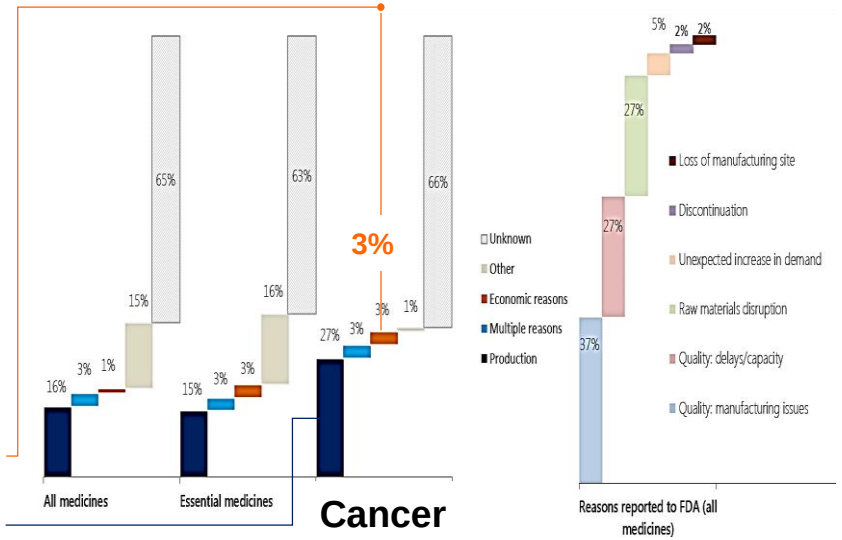
Pages 98-99

- **Cases of supply disruption, but overall number of shortages has decreased in recent years**
  - No data on persistence of shortage
- **Low market attractiveness are possible contributing factors**
  - low prices and small market sizes

BUT

- **Shortages are probably due to problems related to not meeting the quality standards for injections**





Payers should give equal importance to reducing high prices as well as raising unsustainable low prices

High prices and profits from cancer medicines may encourage companies or individuals to take risks and engage in unethical, even illegal business practices

World Health Organization

Pages 100-101

Emergence of substandard or falsified (SF) medicines	Higher risk of exposure to SF bevacizumab for individuals in counties where patients have greater ability to afford more expensive treatment or higher reimbursement Higher risk to SF medicines during shortages of essential cancer medicines because patients needed to source medicines from unauthorized channels
Anti-competitive business practices	Antitrust cases: withholding the supply of five cancer medicines where there were no alternatives
Deceptive marketing activities	Promoting off-label use and paying "illegal remuneration" to doctors to induce the utilization
Imposing wastage	Pack sizes or dosages that would result in wastage: significant unused portion in the dosage presentation; discontinuation of lower strength dosages for dose titration.

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Chapter 5

Options that might enhance affordability and accessibility

Options that might enhance the affordability and accessibility of cancer medicines

Table in Executive Summary (pages xiv-xvi)
Pages 103-112

1. Strengthening pricing policies at the national and regional levels
2. Improving efficiency of expenditure on mediciness
3. Improving transparency of pricing approaches and prices
4. Promoting collaboration cross-sector & cross-border information-sharing, regulation & procurement
5. Managing demand-side factors influencing medicines utilization
6. Realigning incentives for research and development

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