US trends in opioid access among patients with poor prognosis cancer near end-of-life

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February 24, 2022

Dana-Farber
Cancer Institute

The burden of cancer pain

- Cancer pain is common
  - Prevalence >66% among patients with **advanced malignancies**
  - Prevalence >80-90% near end-of-life (EOL)
- Advanced cancer pain is distressing and costly
  - More than half patients experience moderate-to severe pain
  - Degrades physical, emotional, social, & functional wellbeing
- Pain is a major driver of acute care utilization among patients with active or advanced stage cancer

van den Beuken-van Everdingen, *JPSM* 2016; Enzinger JCO 2021
S DeAndrea, *Annals Oncol* 2008; Cleeland NEJM 1994; Caterino JAMA Open 2019

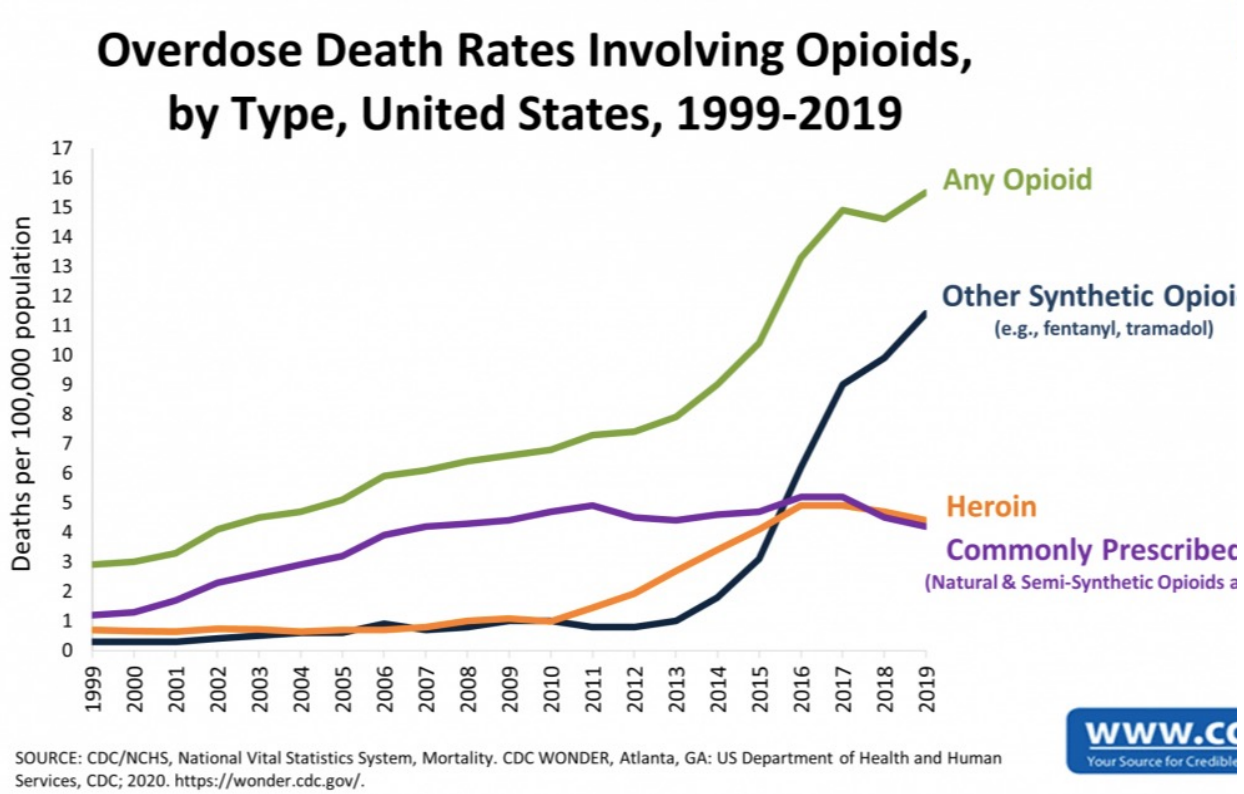
Cancer pain treatment and undertreatment

- Guidelines recommend stepwise approach to treatment
  - Opioids for moderate-to-severe pain
  - Non-controversial for advanced cancer
- 30-40% of patients with cancer pain are undertreated (conservative estimate)
- Racial/ethnic minorities twice as likely to be undertreated
- Undertreatment matters:
  - Less complete/durable pain relief
  - Greater interference with activity, mood, relationships, life enjoyment
- Rates of undertreatment improved modestly from 1990's→2010

Cleeland *NEJM* 1994; S DeAndrea, *Annals Oncol* 2008; Fisch *JCO* 2012

Competing crisis: US epidemic of opioid abuse & overdose

- 1999-2010: Per capita opioid prescribing quadrupled (180→782 MME)



http://www.hhs.gov/opioids; Rudd RA et al, MMWR, 1/1/16

Policy response to opioid crisis

- Policies implemented to restrict inappropriate prescribing
  - Prescription drug monitoring programs
  - Insurance coverage restrictions & state-mandated qty/dose limits
  - 2016 CDC guidelines: avoid/minimize opioids, risk mitigation strategies
- Regulations are having their intended effects
  - Since peak, per-capita opioid prescriptions have fallen 25%
  - Initiation of new opioid therapy has fallen 45%
- Regulations are also having unintended effects
  - Oncologist prescribing is falling at similar rates to generalists
  - State PDMP implementation associated with steeper declines

Zhu W, *NEJM* 2019; Dowell D, JAMA 2016; Guy GP, *MMWR* 2017; Agrawal A. et al JAMA Oncol 2020; Jairam V et al JNCI 2020; Graetz JAMA Oncol 2020

Study motivation

How has the US opioid epidemic impacted opioid access and pain management for patients dying from cancer?

Enzinger AC, Ghosh K, Keating NL, Cutler DM, Landrum MB, Wright AA "US Trends in Opioid Access Among Patients With Poor Prognosis Cancer Near the End of Life" *Journal of Clinical Oncology.* 2021; 39(26):2948-58

Methods: retrospective cohort study

- 20% random sample of Medicare FFS beneficiaries
  - Died 2007-2017
  - Diagnosed with “poor prognosis” cancer
  - Age 66+, continuous FFS & Part D coverage >1yr
- “Poor prognosis cancers” defined by
  - ICD 9/10 codes for leading causes cancer death (ACS & NDVSS)
  - Metastatic codes required for less aggressive cancers
  - Supplemented codes for highly lethal but less common cancers

Methods: key outcomes

- Outpatient opioid Rx fills: NDC codes from CDC
  - Overall & by medication class
  - Long-acting opioids
  - Weak, short-acting (e.g. tramadol, codeine, propoxyphene)
  - Strong, short-acting (oxycodone, morphine, hydrocodone, hydromorphone)

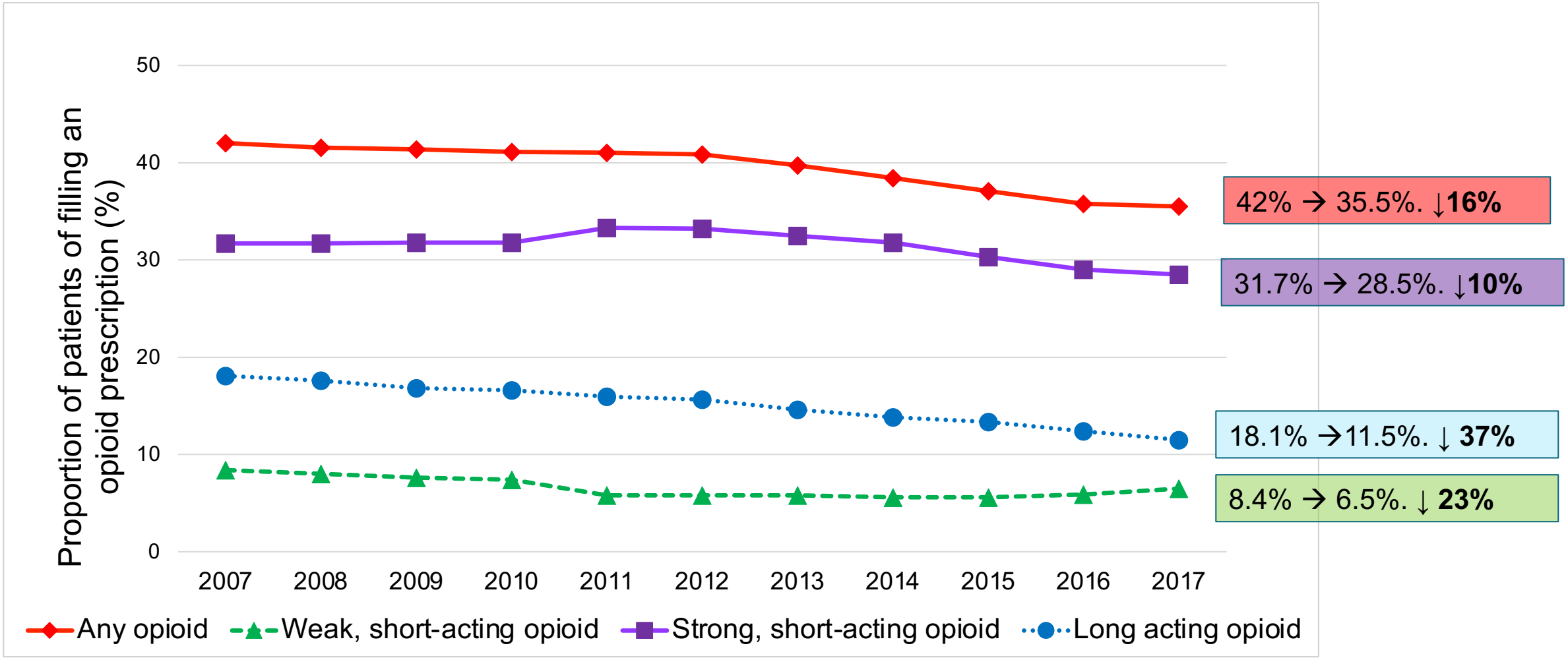
- ED visits for pain explored as a potential consequence of undertreated pain
  - Considered “pain-related” if pain in first four codes (using OCM OP-35)
  - Alternatively defined pain-related w/ malignancy-associated pain code
  - ED visit for nausea/vomiting as a control condition

Methods continued

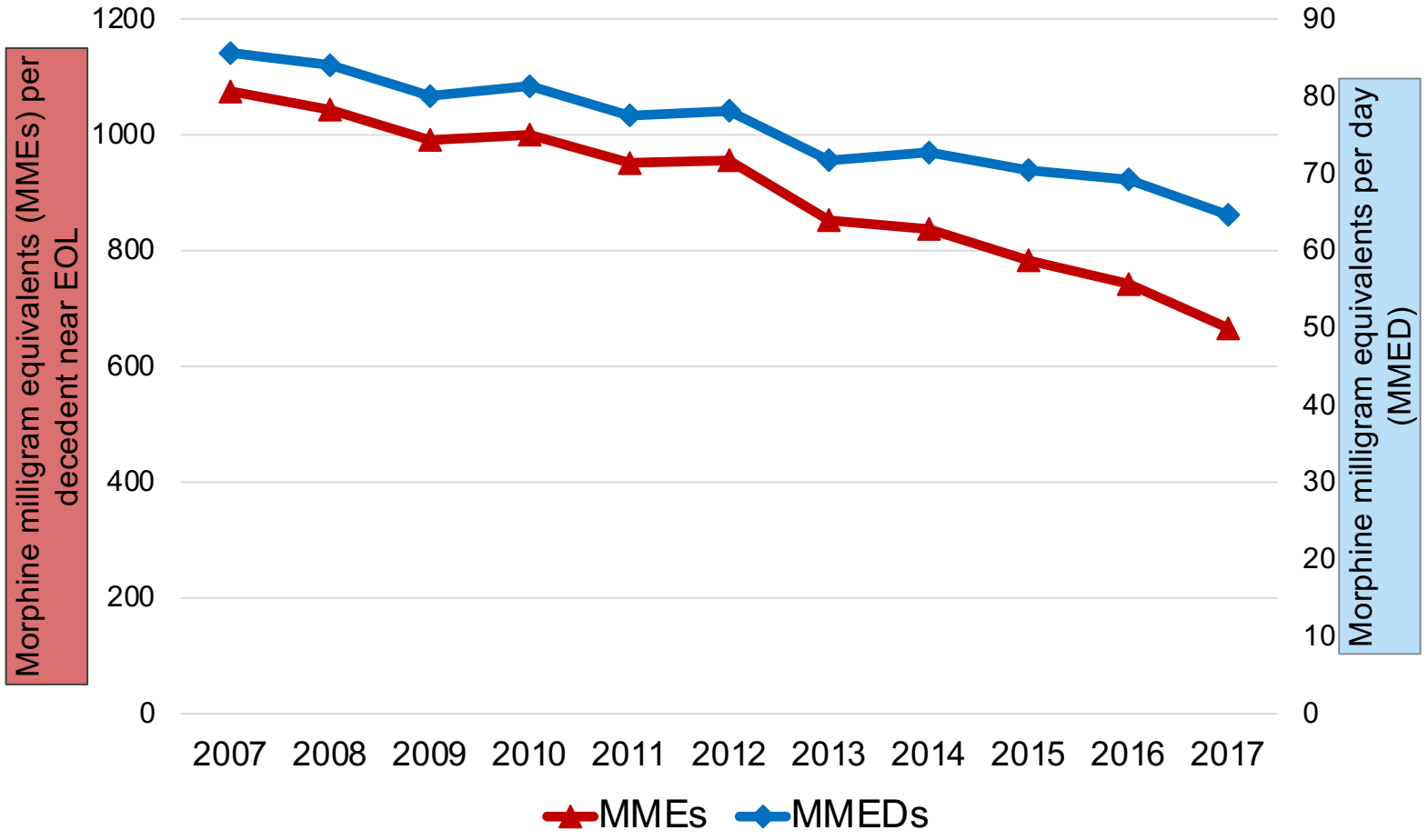
- Key outcomes examined in last 30d before death or hospice
- Metrics of opioid access
  - proportion of patients filling ≥ 1 Rx near EOL (overall and by type)
  - Mean daily dose among opioid users
  - Total dose filled per decedent
  - Prescription-level trends (number of Rx, daily dose/Rx, days supply/Rx)

Characteristic	Total population 270,632	2007 22,003	2012 23,620	2017 27,345
Female	51.8%	54.3%	51.8%	49.7%
Race - White	84.8%	84%	84.5%	85.5%
Black	9.2%	10%	9.3%	8.6%
Other	6%	6%	6.2%	6%
Age - 66-74	39.1%	39.1%	39%	39.6%
75-84	41.1%	43%	40.6%	40.1%
85+	19.8%	17.9%	20.4%	20.3%
Cancer - Lung	34.2%	36.1%	35%	31.3%
GI	26.4%	26.8%	27%	27.8%
GU	11.6%	10.7%	11.1%	11.8%
Heme	9.1%	8.4%	8.4%	11.3%
Breast	6.6%	6.7%	6.6%	7%
Hospice enrollment	61.7%	57.1%	61.1%	66.2%
Hospice LOS	15.3d	14.9d	15.4d	15.2d
Days in a facility near EOL	5d	5.2d	4.8d	5.7d

Proportion of patients filling an opioid Rx near EOL



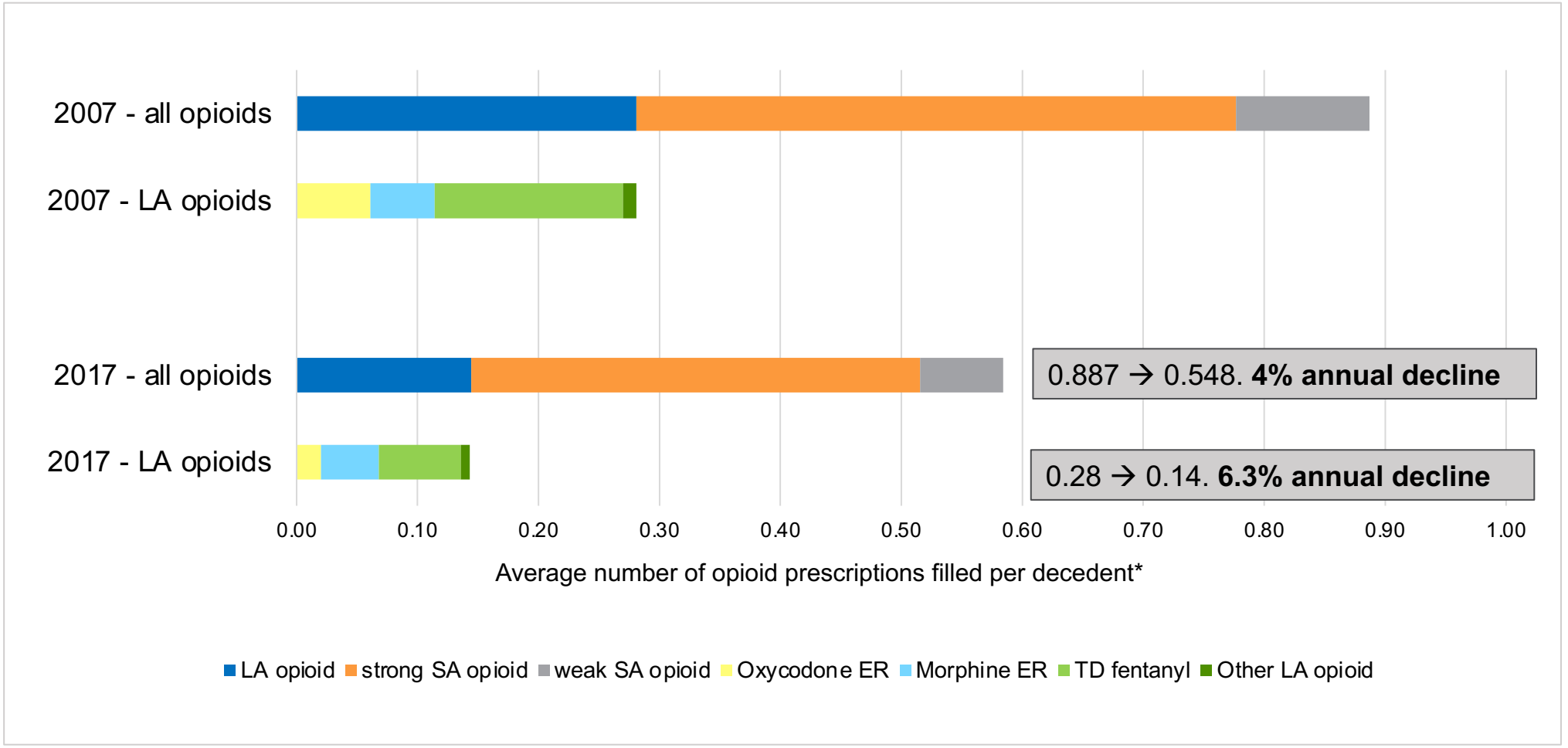
Mean daily dose among users, mean total opioid dose per decedent



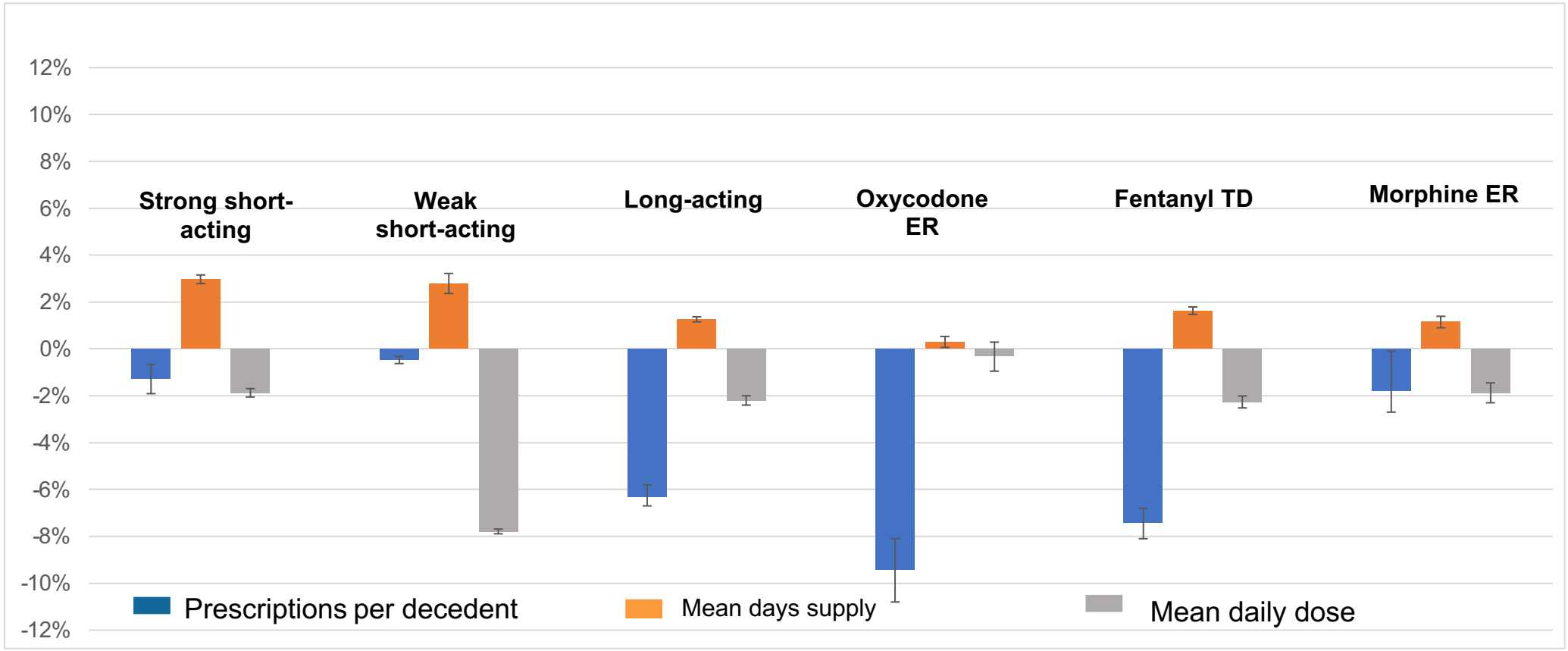
86MMED → 65MMED. ↓**25%**

1079 MME → 666 MME. ↓**38%**

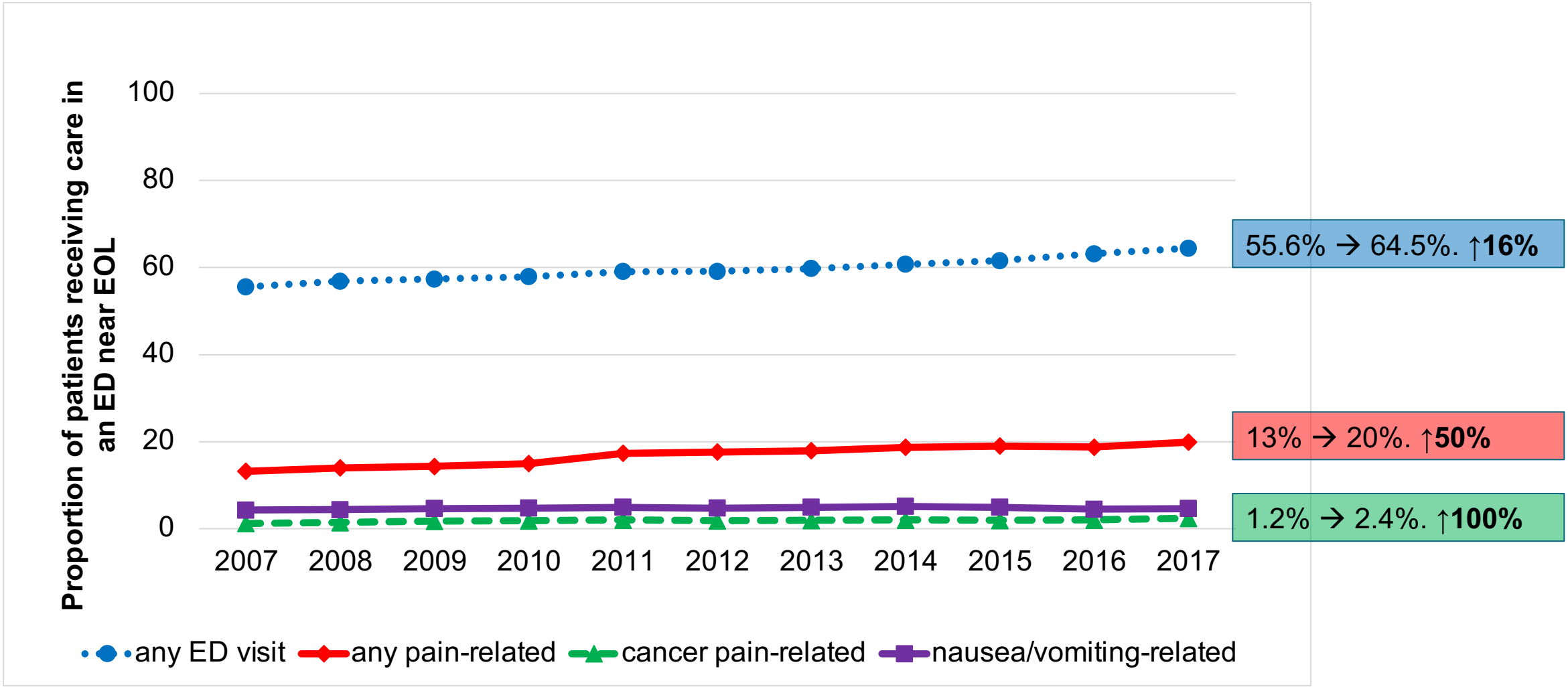
Opioid prescriptions filled per decedent by medication class



Annual changes in the number of opioid prescriptions filled per decedent near EOL, mean days supply, mean daily dose per prescription



Trends in ED visits near EOL



Sensitivity Analyses

- Main findings held in multiple sensitivity analyses
  - Examining last 30, 60, 90d before death/hospice
  - Examining trends separately among hospice and non-hospice decedents
  - Examining trends in last 30d of life, without censoring hospice

Conclusions

- 2007-2017, EOL opioid access fell for patients with poor-prognosis cancers
  - Total opioid supply fell by 38%
  - 15.5% decline in the proportion receiving any opioid
  - Mean daily dose fell by 25%
  - 36.5% decline in proportion receiving LA opioids
- 50% rise in pain-related ED visits raises concern that decreased opioid access may be having a detrimental effect on pain management

THANKS

Alexi A. Wright

Mary Beth Landrum

Nancy L. Keating

Kaushik Ghosh

David Cutler

Funding: AHRQ U19HS024072

Closing the Global Pain Divide: An Equity and Health Imperative.

The Global Palliative Care and Pain Relief Research Hub Webinar Series at Memorial Sloan Kettering Cancer Center; February 24, 2022

Dr. Felicia Marie Knaul

University of Miami Sylvester Comprehensive Cancer Center, Institute for Advanced Study of the Americas & Miller School of Med. And, Tómatelo a Pecho, A.C.

http://www.thelancet.com/commissions/palliative-care

In agonizing, crippling pain from lung cancer, Mr S came to the palliative care service in Calicut, Kerala, from an adjoining district a couple of hours away by bus. His body language revealed the depth of the suffering.

We put Mr S on morphine, among other things. A couple of hours later, he surveyed himself with disbelief. He had neither hoped nor conceived of the possibility that this kind of relief was possible.

Mr S returned the next month. Yet, common tragedy befell patient and caregivers in the form of a stock-out of morphine.

Mr S told us with outward calm, "I shall come again next Wednesday. I will bring a piece of rope with me. If the tablets are still not here, I am going to hang myself from that tree". He pointed to the window. I believed he meant what he said.

Stock-outs are no longer a problem for palliative care in Kerala, but throughout most of the rest of India, and indeed our world, we find near total lack of access to morphine to alleviate pain and suffering.

Dr M R Rajagopal, personal testimony

The Lancet Commission on Global Access to Palliative Care and Pain Relief

Health Systems and Global Health

+

Palliative Care Specialists

- **Co-chaired Knaul & Farmer**
- **33 commissioners**
- **61 co-authors from over 25 countries**

Led by the University of Miami in collaboration with Harvard University

5 Key Messages from the Lancet Commission Report

1. Alleviation of the burden of serious health-related suffering from life-threatening or life-limiting conditions & at end-of-life is a global health and equity imperative.

2. Universal access to an affordable Essential Package of palliative care can alleviate much of the burden of SHS.

3. LMICs can improve the welfare of poor people at modest cost by publicly financing the Essential Package of palliative care & through full integration into Universal Health Coverage.

4. International and balanced collective action is essential to achieving universal coverage of palliative care & pain relief by facilitating effective access to essential medicines, while implementing measures to prevent non-medical use.

5. Better evidence and priority setting tools must be generated to adequately measure the global need for palliative care, implement policies & programs, and monitor progress towards alleviating the burden of pain and other SHS

Update in progress: All 2019 estimates are rounded/approximate

Note: Adjusted down as we are including new estimates for children.

Global burden of Serious Health-Related Suffering: Overall and for Cancer (2019)

26+ million deaths
- **Half of the 55 million global deaths**

8.7+ million deaths from Cancer
- **90% of the 9.7 million cancer deaths worldwide**

And…
- **42+ million people experienced SHS (non-decedents)**
- **7.2 million people experienced SHS (non-decedents) from cancer**

At least 68+ million people worldwide:
80% in LMICs
At least 15.9+ million people worldwide with cancer:
60% in LMICs

Essential Package of PC Services

- Designed to
  - relieve the most common and severe suffering (physical, psychological, social, or spiritual) related to illness or injury,
  - be cost effective in LMICs,
  - help strengthen health systems
  - protect patients and their families from catastrophic health expenditures.
  - Items can and should be provided at any level of care.
- Consists mainly of
  - medicines on the WHO List of Essential Medicines for Palliative Care for adults and for children that are inexpensive and easy to use but that also are effective to relieve the common symptoms of serious chronic, complex, or life-limiting health problems.
  - small, inexpensive equipment,
  - Necessary human resources
- Recommended – in a social welfare program and, for the poorest patients and families, five types of support to satisfy basic needs.
- **Should be made universally accessible by everyone everywhere by 2030 in countries of all levels of income.**

Intervention: essential, most basic package

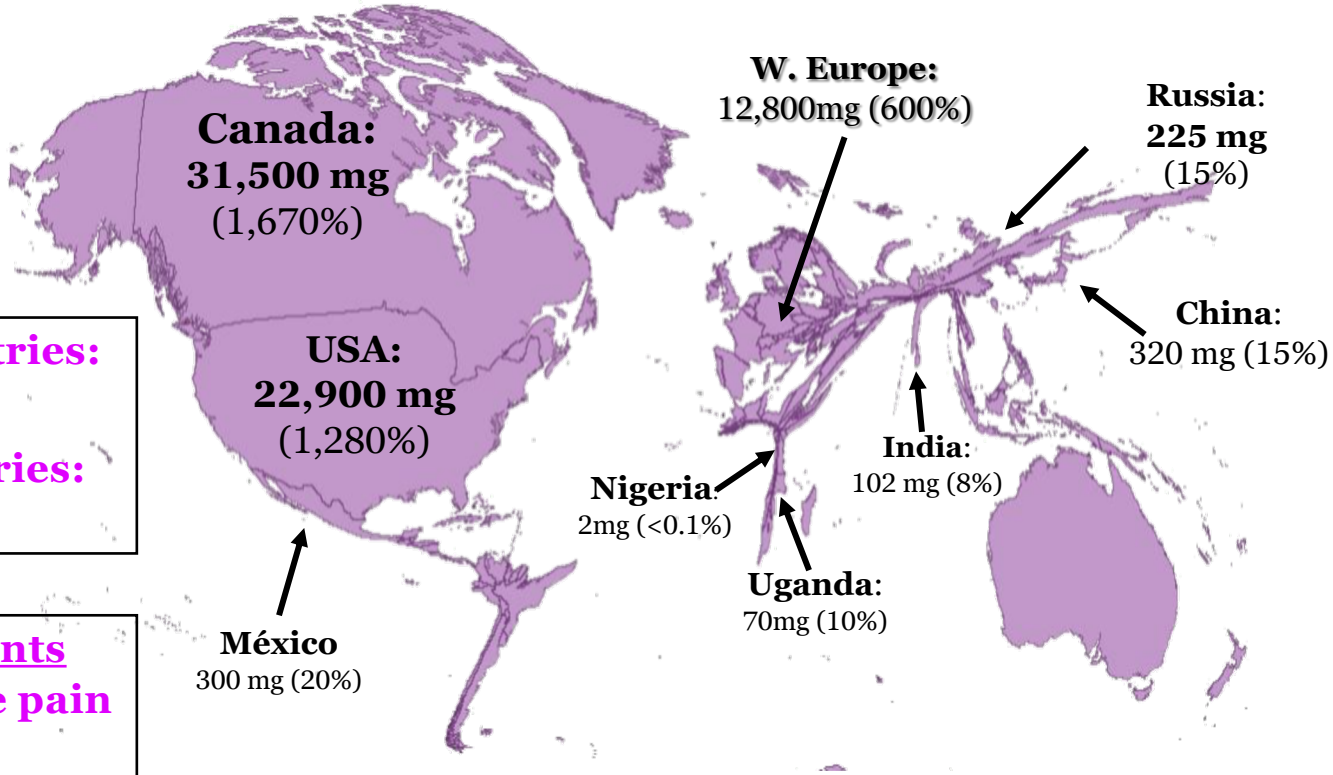
Medicine
Amitriptyline
Bisacodyl (Senna)
Dexamethasone
Diazepam
Diphenhydramine (chlorpheniramine, cyclizine, or dimenhydrinate, oral & injectable)
Fluconazole
Fluoxetine or other SSRI (sertraline and citalopram)
Metoclopramide
Metronidazole
Morphine
Naloxone Parenteral
Omeprazole oral
Ondasetron
Paracetamol oral
Petroleum jelly

Medical Equipment
Pressure Reducing Mattress
Nasogastric drainage or feeding tube
Urinary catheters
Opioid lock box
Flashlight with rechargeable battery
Adult diapers/ Cotton and Plastic
Oxygen
Psychiatrist, psychologist or counsellor
Physical Therapist
Pharmacist
Community Health Workers
Clinical Support Staff
Non-Clinical Support Staff

Morphine: off-patent,
immediate release, oral and injectable

Aligned with Sustainable Development Goals (SDGs): Should be made universally accessible by 2030

The Global Pain Divide: Inequity of access distributed opioid morphine-equivalent (DOME, mg/patient) & % of SHS palliative care need, 2019



50% poorest countries:
<1% of opioids

10% richest countries:
90% of opioids

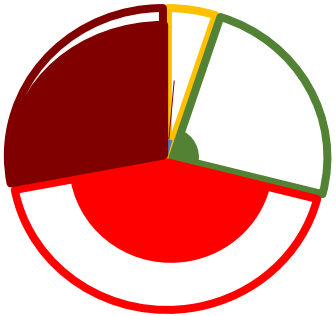
<u>60 million patients</u>
suffer preventable pain every year

Source: Author calculations using INCB (2017-19) and IHME-2019.

Total medical and palliative care unmet need for opioid analgesics (in DOME), 2019

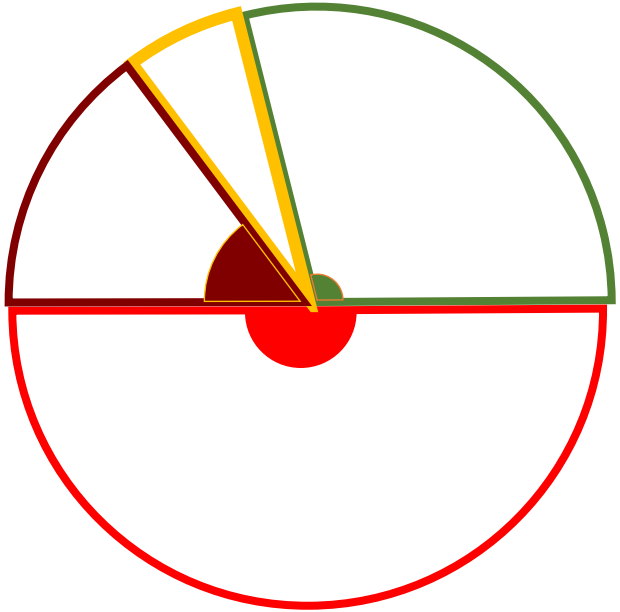
Benchmark: Western Europe High-Income

Palliative Care need



Total need: 85++ tons
Unmet need = 52 tons

Projected total need



Total need: 671++ metric tons
Unmet need: 639 metric tons

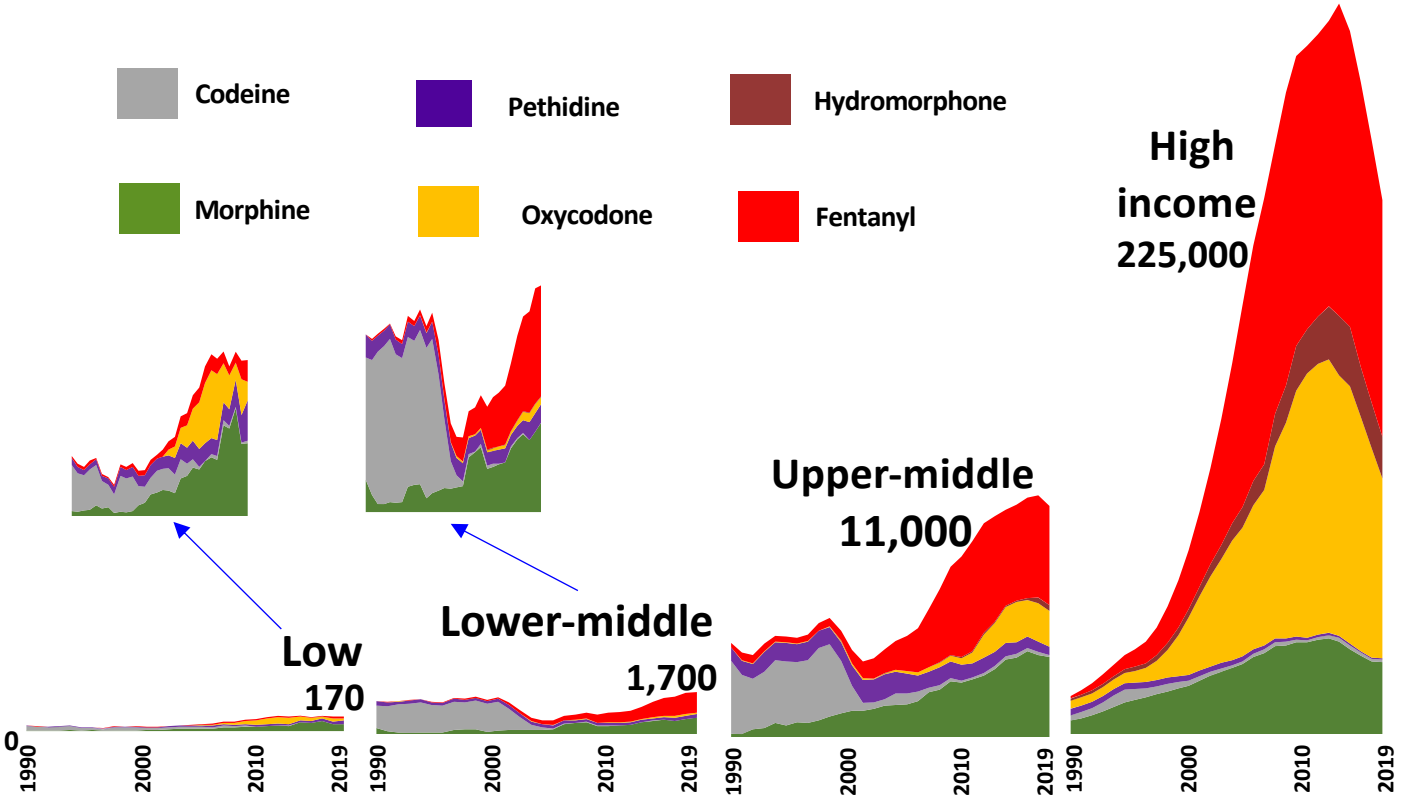
Income regions

- Low
- Lower middle
- Upper middle
- High

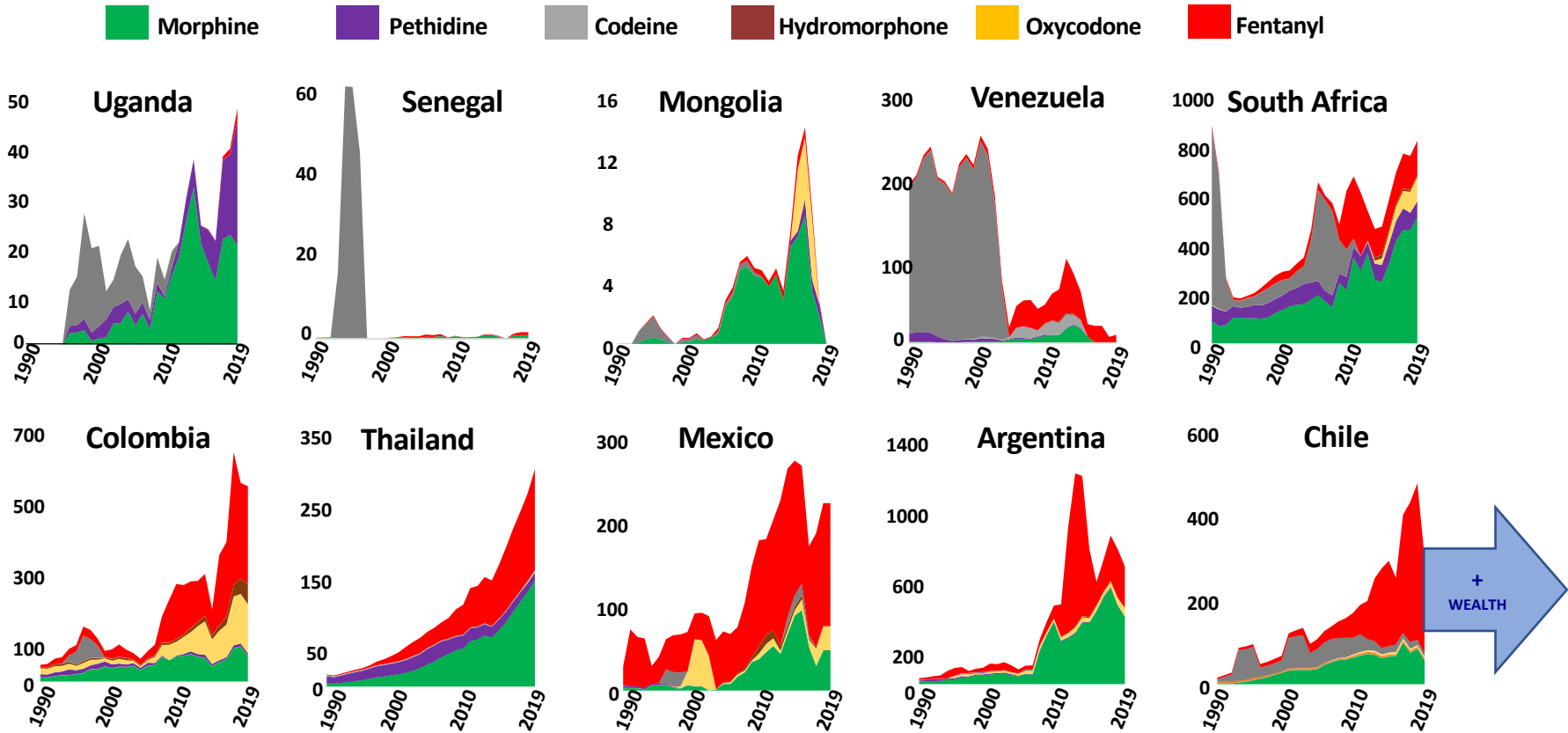
Source: Update based on Knaul, Farmer, Krakauer et al, 2019. http://www.thelancet.com/commissions/palliative-care.

Distributed opioids:

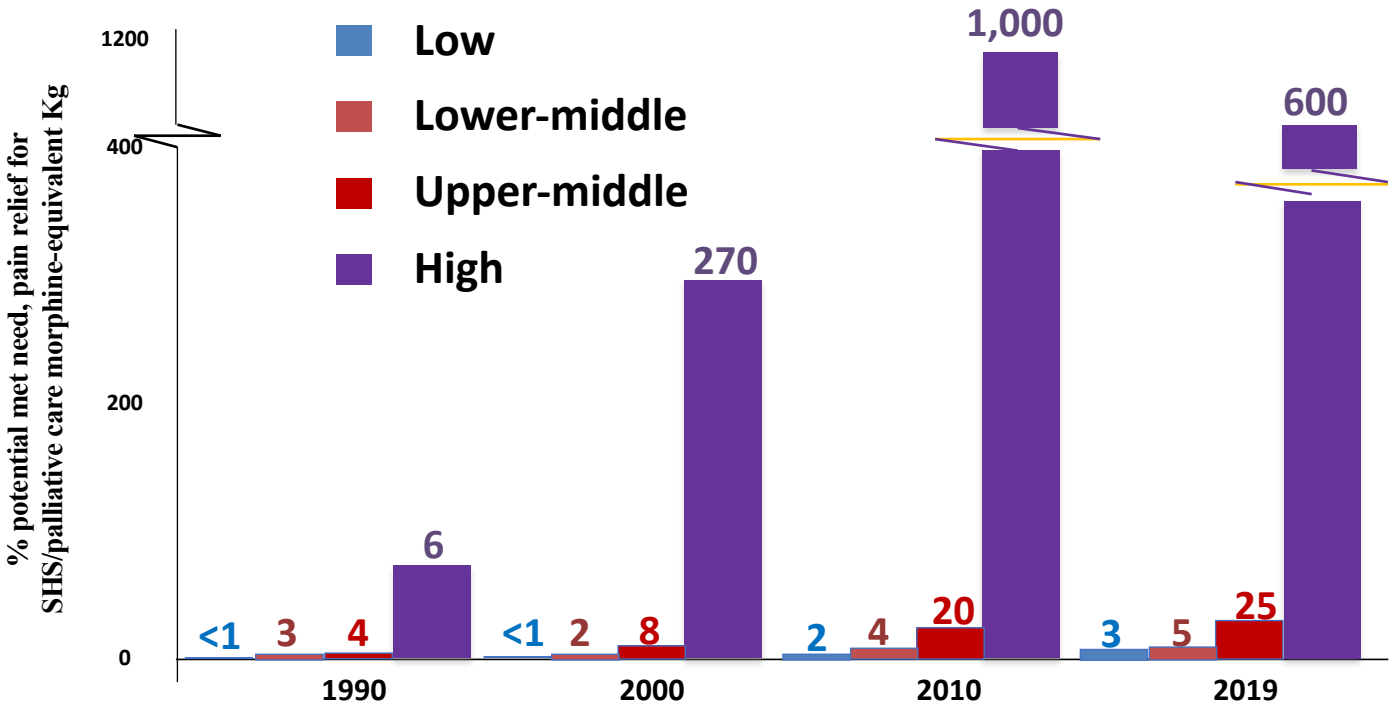
By income region (1990-2019), morphine-equivalent in kgs



Distributed Opioids 1990-2019: Select countries, Morphine Equivalent (Kg)



Potential met need based on morphine equivalent: Income groups (%, 1990 to 2019)



Integrate into UHC by strengthening health systems by function to expand access to PC & PR

Without access to palliative care and pain relief, neither UHC nor SDG3 can be achieved

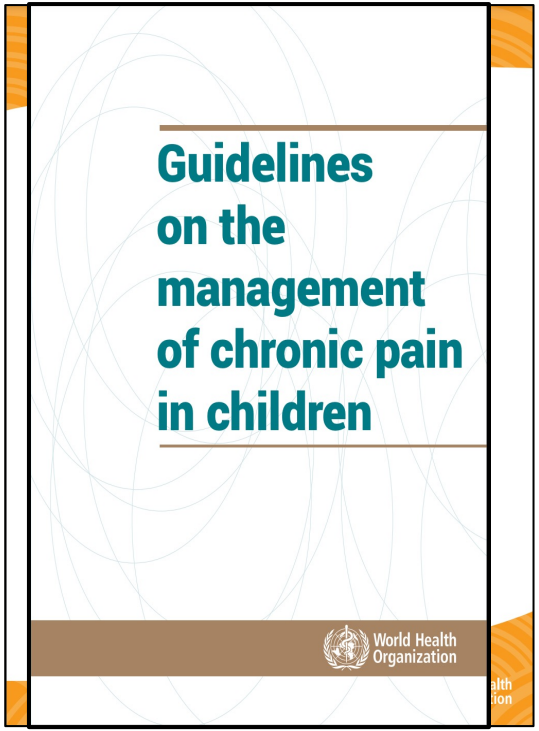
Stewardship	Financing	Delivery	Human Resources
Priority setting: **In national health agenda**	• **Explicit inclusion in national insurance & social security** • **Guarantee public funding with specific budget allocations; start with EP** • Develop pooled purchasing for competitive prices	• **Develop and implement secure opioid supply chain and ensure prescription practices** • Integrate at all levels of care and into disease-specific programmes	• **General competency mandatory component of ALL health professional curricula** • **Establish as a recognized medical & nursing specialty**
Planning: comprehensive guidelines, programmes			
Regulation: integrated guidelines that encompass all providers			
Monitoring and evaluation of performance: Promote civil society involvement			
Intersectoral advocacy: All actors thru MOH			

WHO Opioid Pain Guidelines

- Result of evidence-based extensive expert-group consultations by the WHO
- Endorsed the principle of balanced availability of narcotic drugs for medical and scientific purposes while preventing diversion and abuse

In response to pressure from the U.S., both guidelines were retracted in June 2019. The guidelines for children were updated in Dec 2020

RETRACTED



RETRACTED AND UPDATED

A balanced approach is essential –
adequate attention to medical needs of all patients, and management of risk of non-medical use

- Monitor the supply and marketing of opioids
- Prevent direct marketing of opioid medications to health care providers by pharmaceutical companies
- Ensure that indications for use and prescription of opioid medications follow evidence-based practice

Ensure that teaching & licensing for all health workers – nurses, doctors, social workers and faith counsellors – by mandate, include basic competencies in palliative care & pain relief as a core component of a balanced approach to close the global pain divide.

Toward an economics of hope:

We can close global pain divides

Getting closer to “right”

Advocating for a world free from health-related suffering

Global Palliative Care and Pain Relief Research Hub
February 24, 2022
Katherine Pettus PhD, Advocacy and Partnerships Director, IAHPC
kpettus@iahpc.com
http://www.hospicecare.com

What IS “right”? –The good news

A world free from health related suffering

Patient and community – as opposed to disease & substance – centered

Unpack and expose the wrongs

Institutions

History

Narrative

Identify the headwinds

Human rights based advocacy

Affected populations

Evidence

Patient centered

Distinct from lobbying

Where’s the hope?

Partnership building

Narrative re-framing

Restorative practices

Education

Image used with permission Naumaddic arts Richard Barnes

Lead with beauty

Share stories

Build partnerships

The Global Palliative Care and Pain Relief Research Hub

The Global Pain Divide

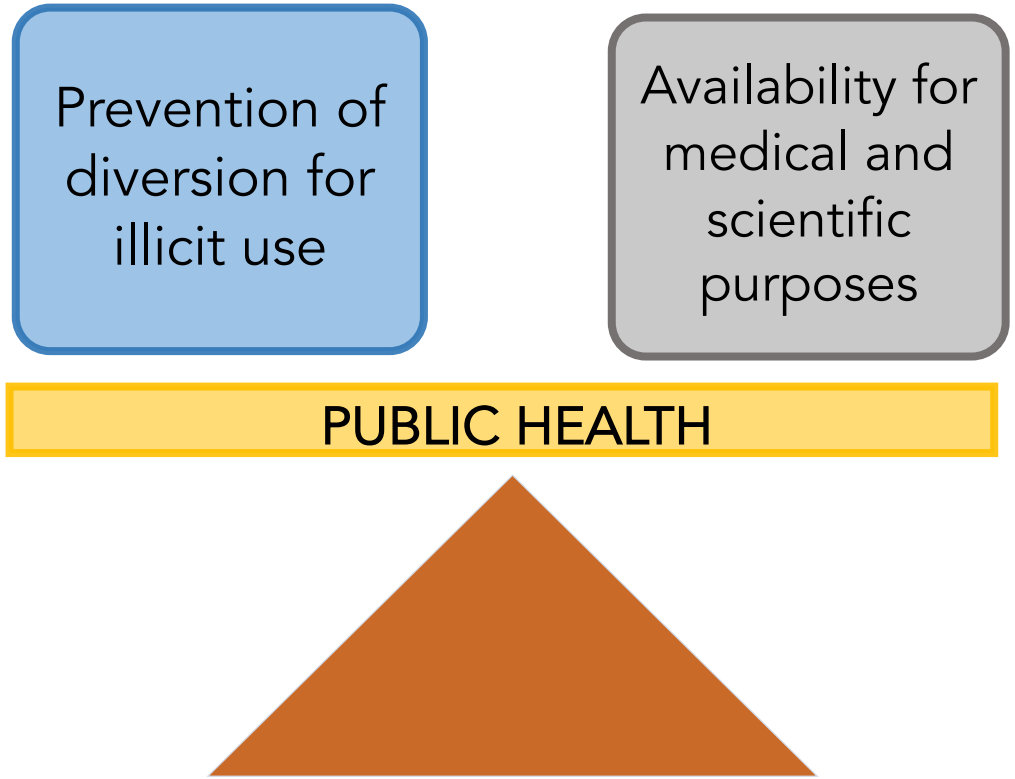
Smriti Rana

Pallium India

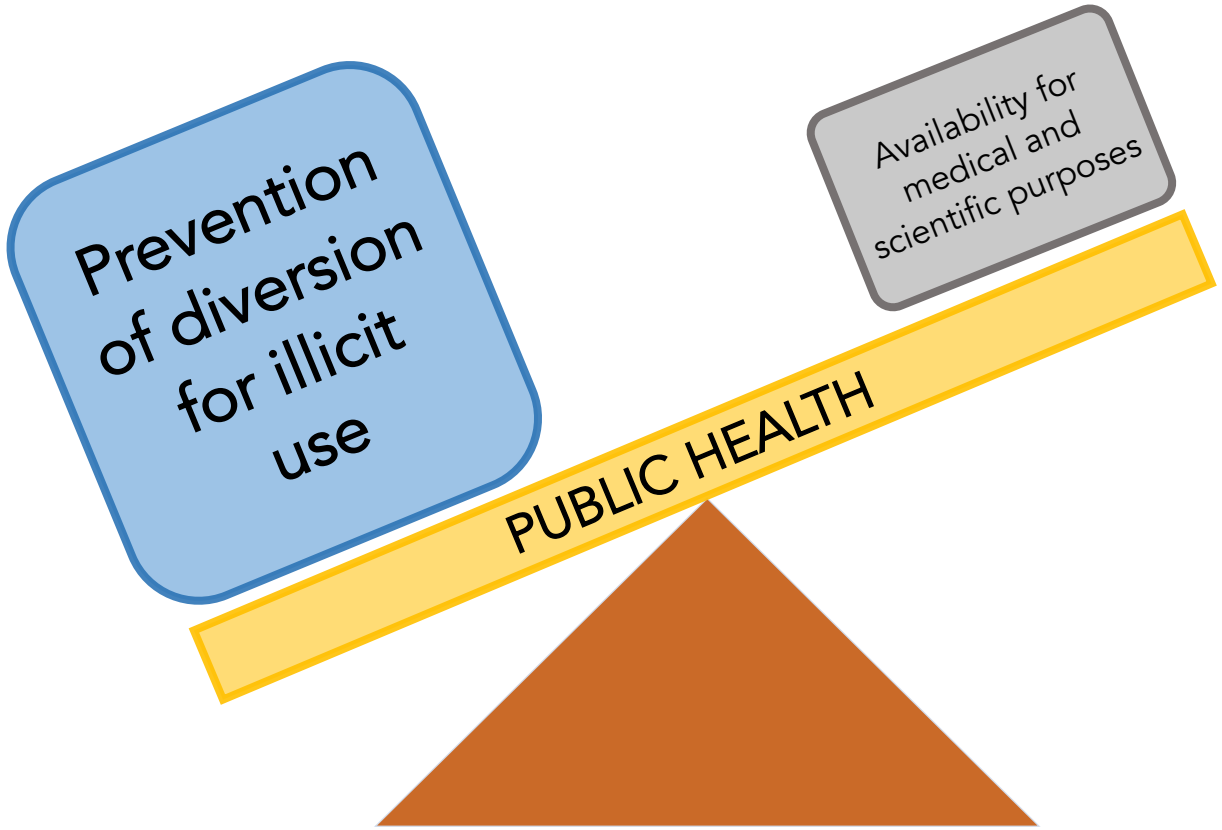
PRESENTED BY

Memorial Sloan Kettering Cancer Center
Sylvester Comprehensive Cancer Center, part of the University of Miami Health System
University of Miami Institute for Advanced Study of the Americas
International Association for Hospice Palliative Care

Principle of Balance



PALLIUM INDIA



PALLIUM INDIA

"IF YOU'RE NOT AT THE TABLE, YOU'RE ON THE MENU."

MICHAEL ENZI

PALLIUM INDIA

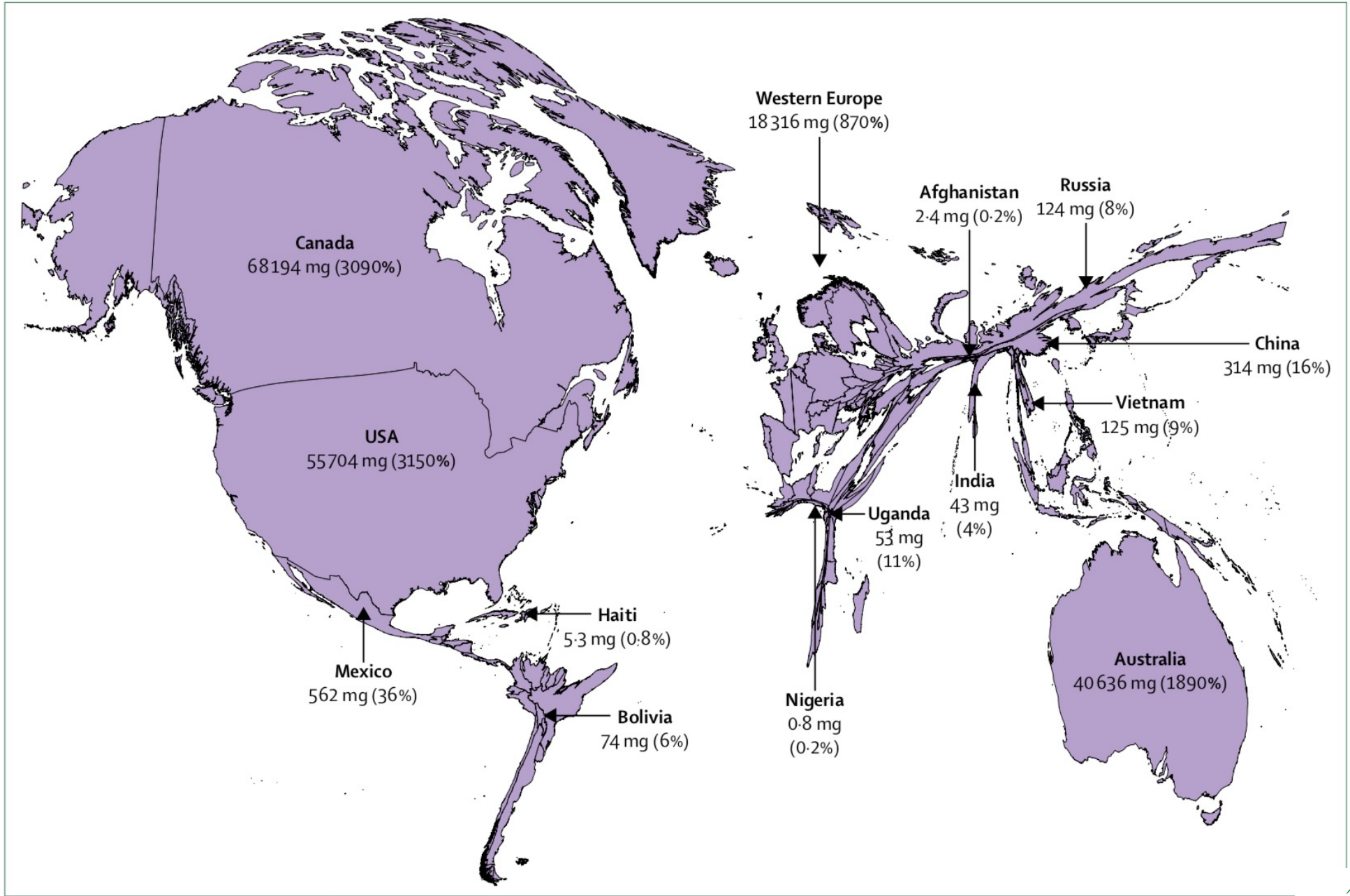


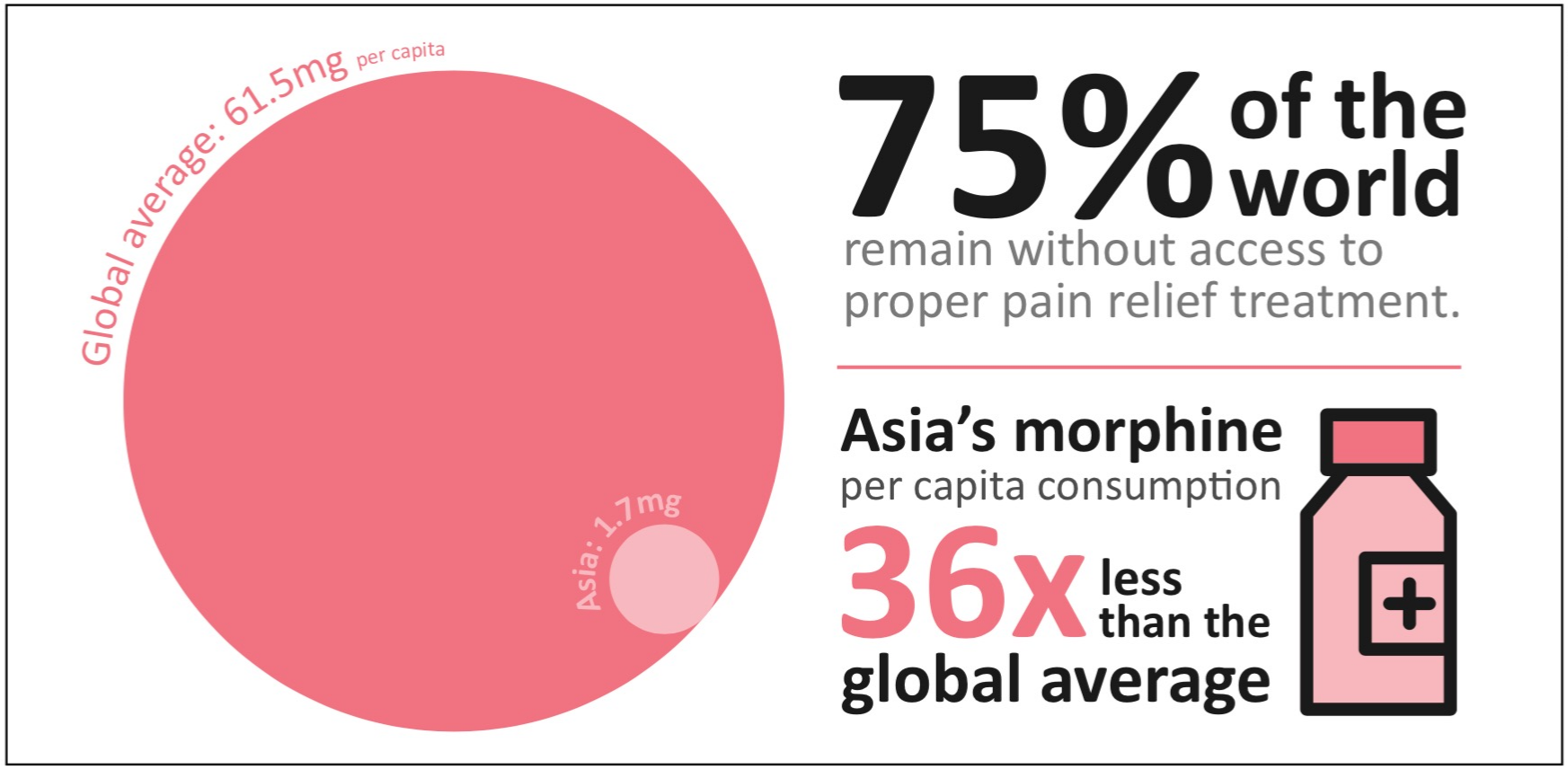
***Figure 1*: Distributed opioid morphine-equivalent (morphine in mg/patient in need of palliative care, average 2010–13), and estimated percentage of n that is met for the health conditions most associated with serious health-related suffering**

Source: International Narcotics Control Board and WHO Global Health Estimates, 2015. See additional online material for methods.

PALLIUM INDIA

CONSUMPTION OF MORPHINE IN INDIA
after the introduction of the Narcotic Drugs &
Psychotropic Substances (NDPS) Act of 1985

PALLIUM INDIA

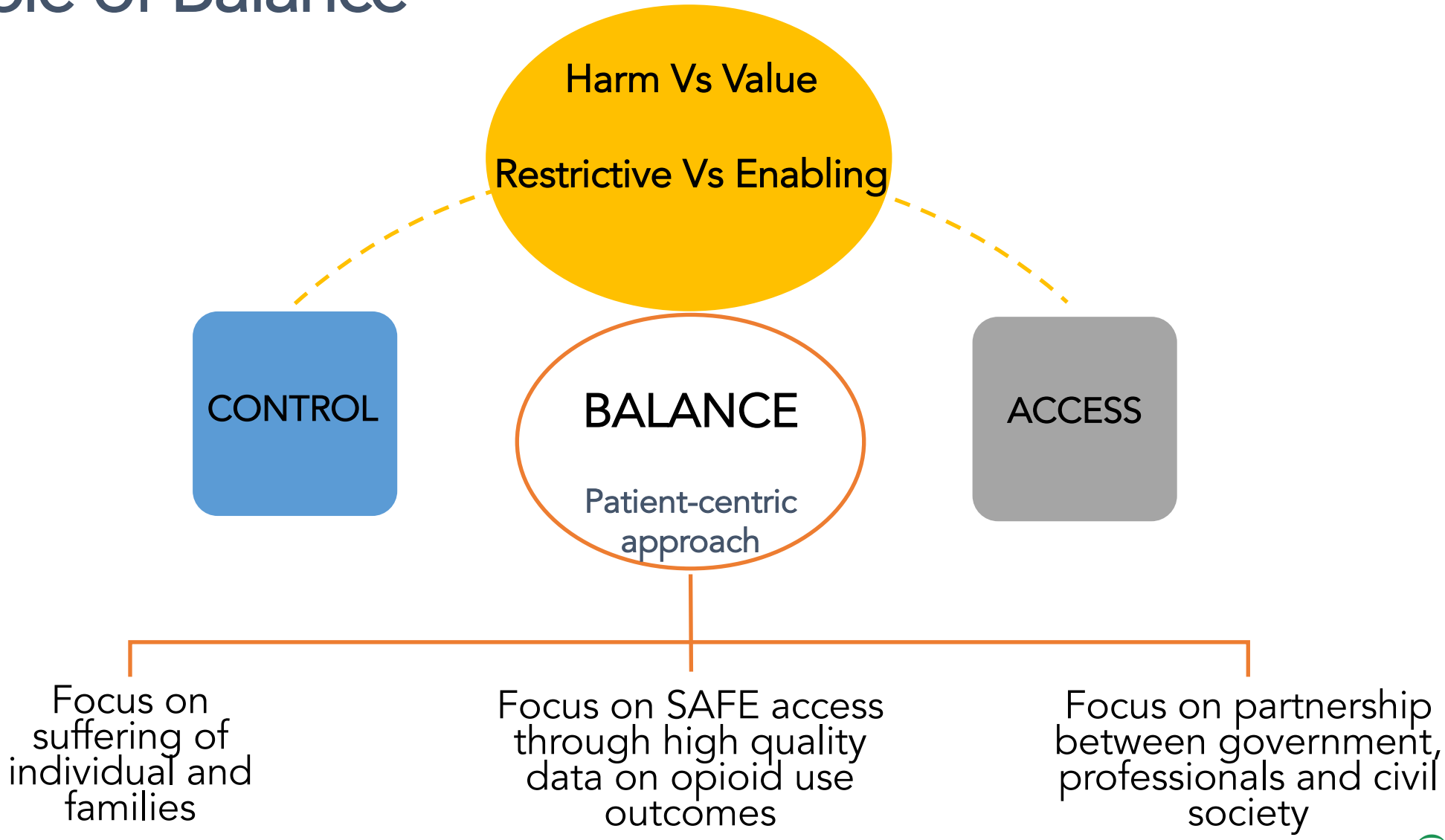


Credit: Juan Fernández Ochoa, IDPC

*International Drug Policy Consortium - **10 Years of Drug Policy in Asia**: How far have we come, 2019*

PALLIUM INDIA

Principle of Balance



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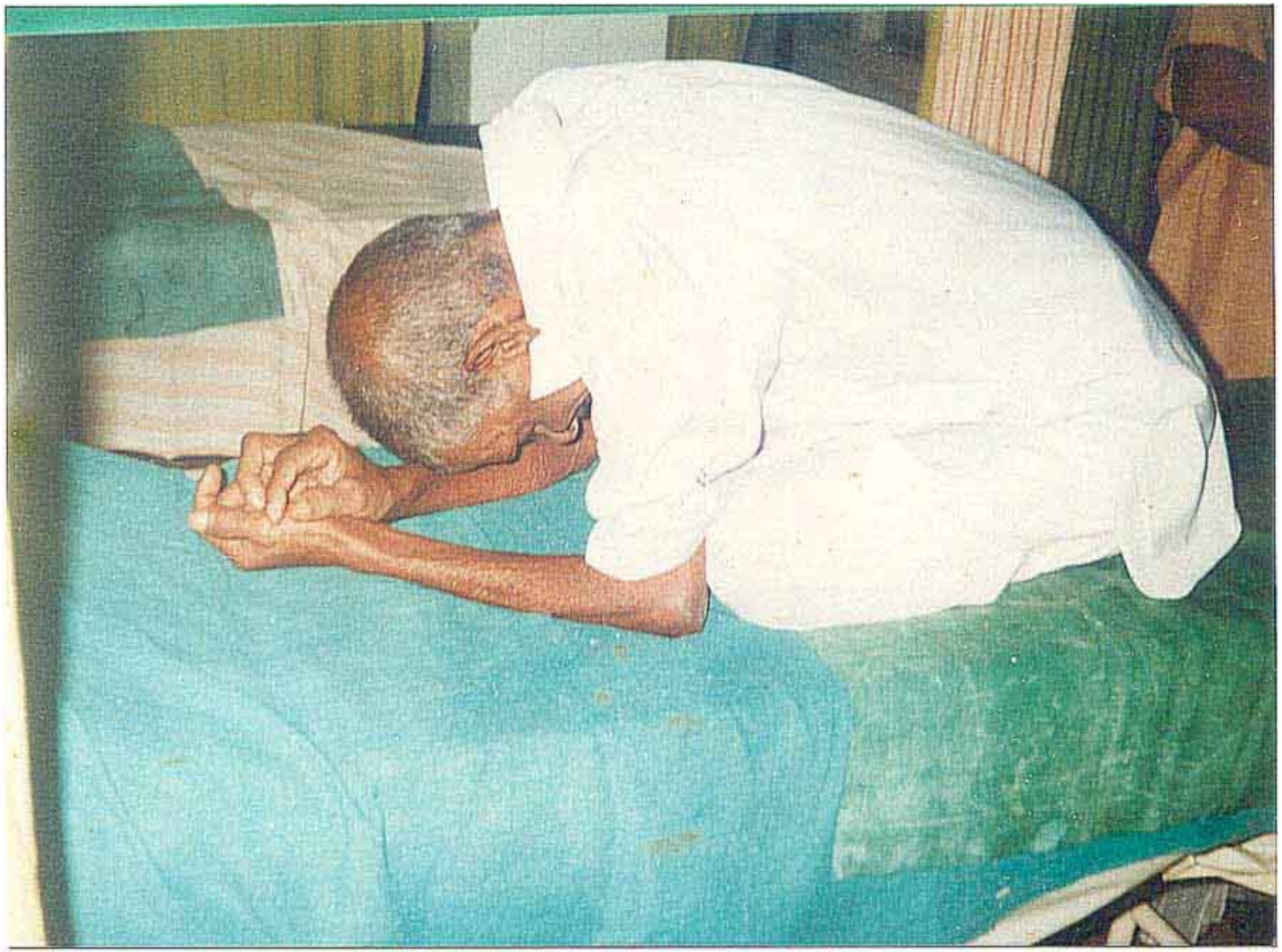

Spent most of 3 weeks in this position, in pain

PALLIUM INDIA

Rs.3/-
(<5 Cents US)
worth of opioid medicines later:

Was able to sit up and have a cup of tea

PALLIUM INDIA