



Pharmacology Red Flags in Cancer

How to Avoid Early Cancer Claims

Kansas City Risk Selectors Meeting

Gaslight Grill, Leawood KS

Thursday, October 12, 2017

Scott Whitmore, RPh, MBA

Agenda

Cancer Treatment Pharmacology

Cancer Drugs

Rule Engines and Relative Mortality

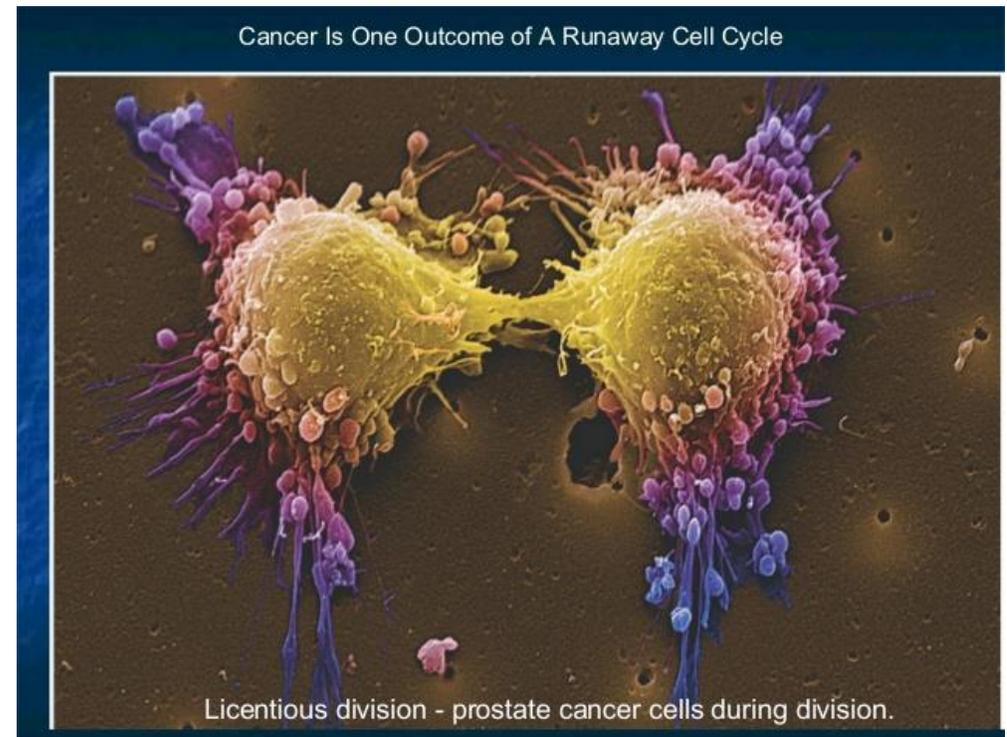
Rx Red Flags for Cancer

New Cancer Therapies



What is cancer?

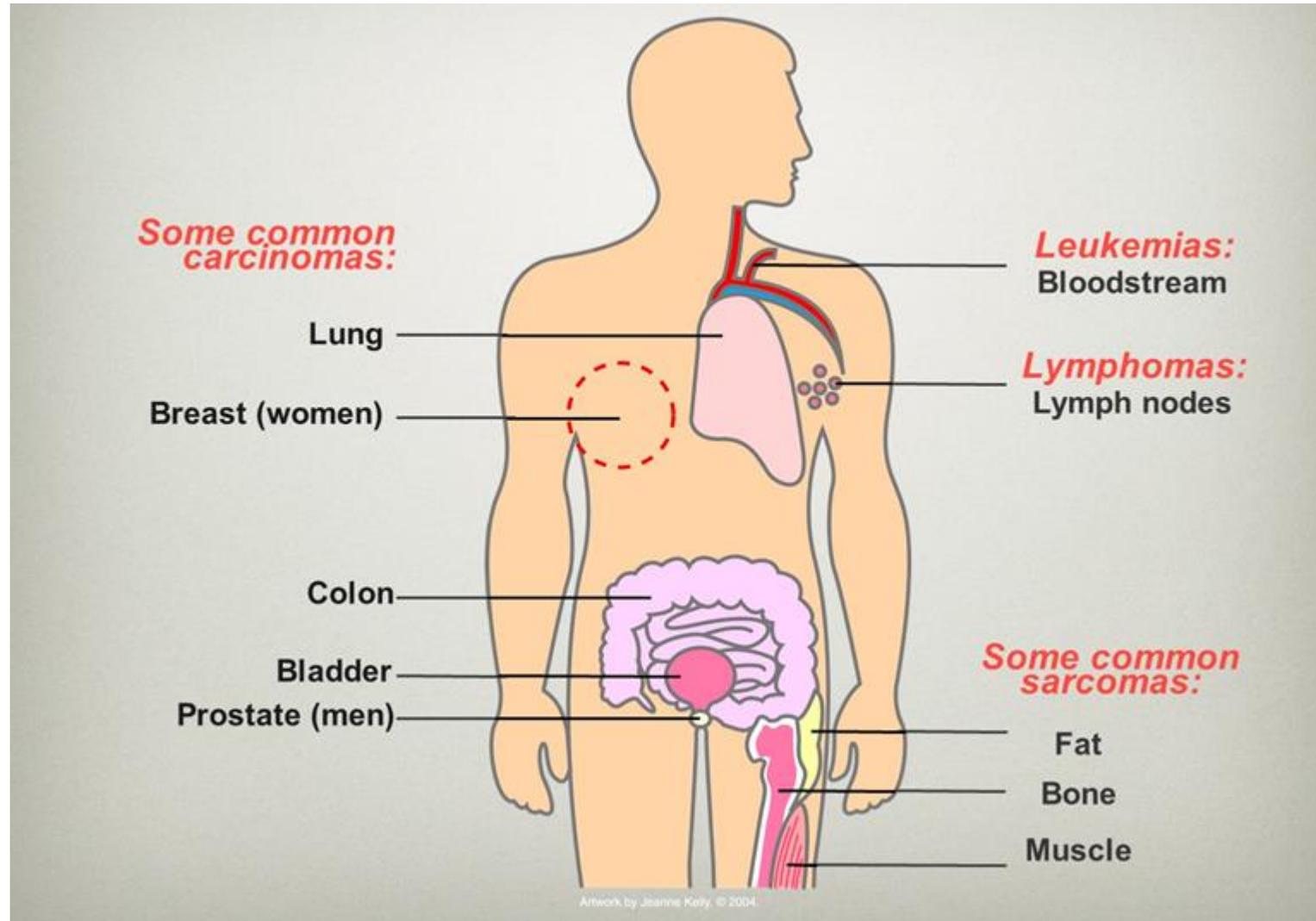
- Uncontrolled growth and spread of abnormal cells
- Neoplasms
- Malignant tumors
- Benign tumors



How do cancer cells differ from normal cells?

Cancer Cells	Normal Cells
Non-differentiated cells	Differentiated cells
Abnormal nuclei	Normal nuclei
Do not undergo apoptosis	Undergo apoptosis
No contact inhibition	Contact inhibition
Disorganized; multilayer	One organized layer
Undergo metastasis and angiogenesis	Localized

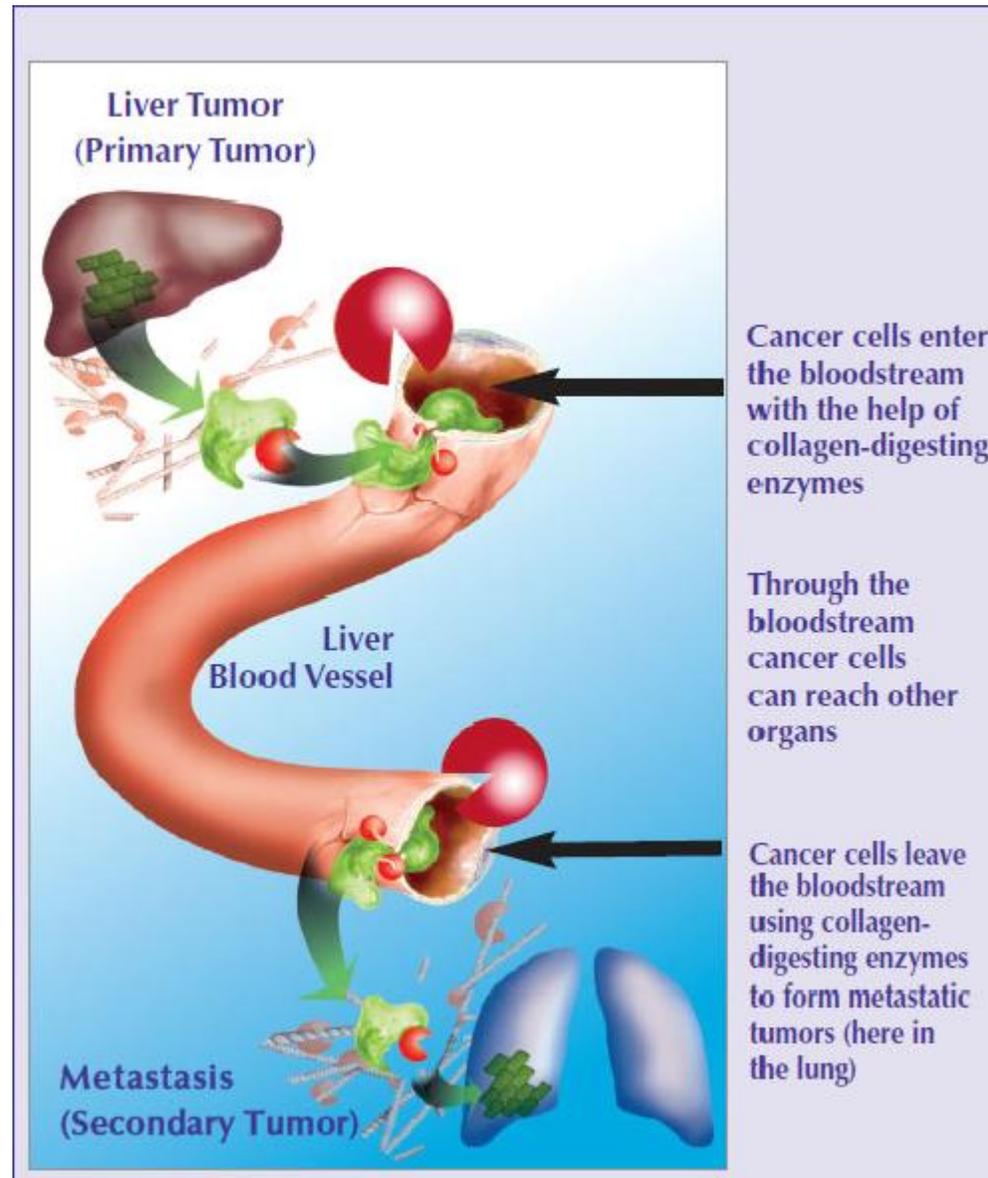
There are about 200 different kinds of cancer.



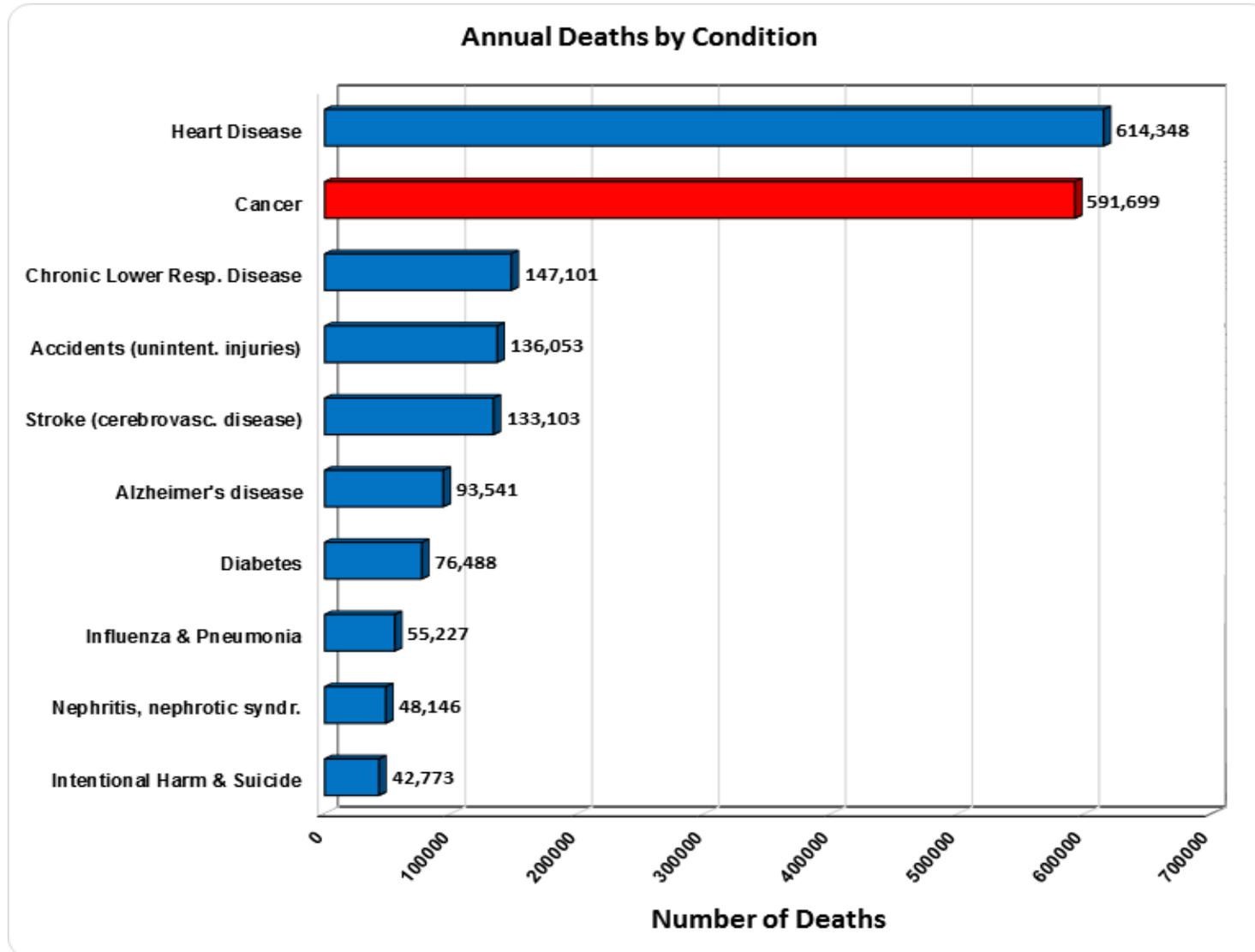
Example of Advanced Metastatic Breast Cancer.



Metastatic cancers are difficult to treat.



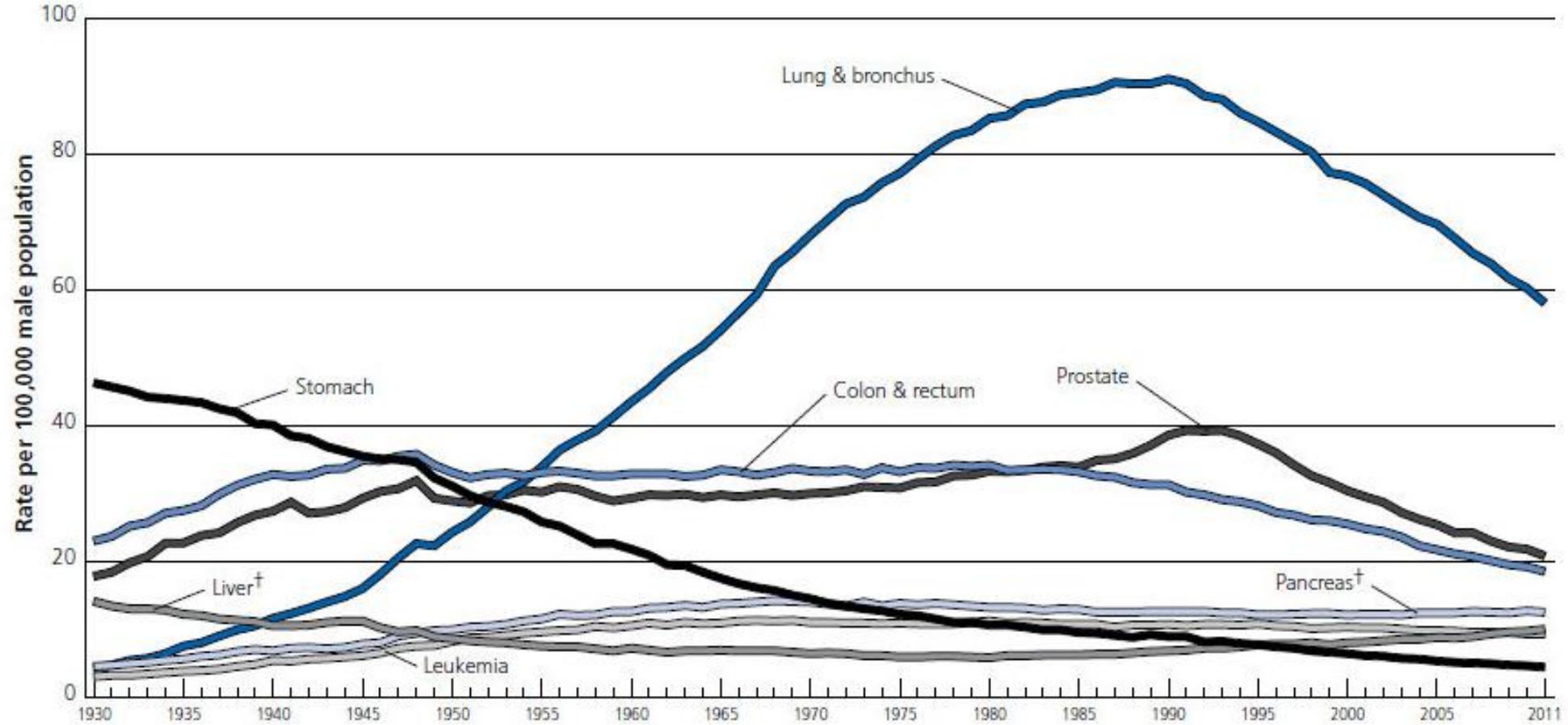
Cancer is the second leading cause of death in the U.S.



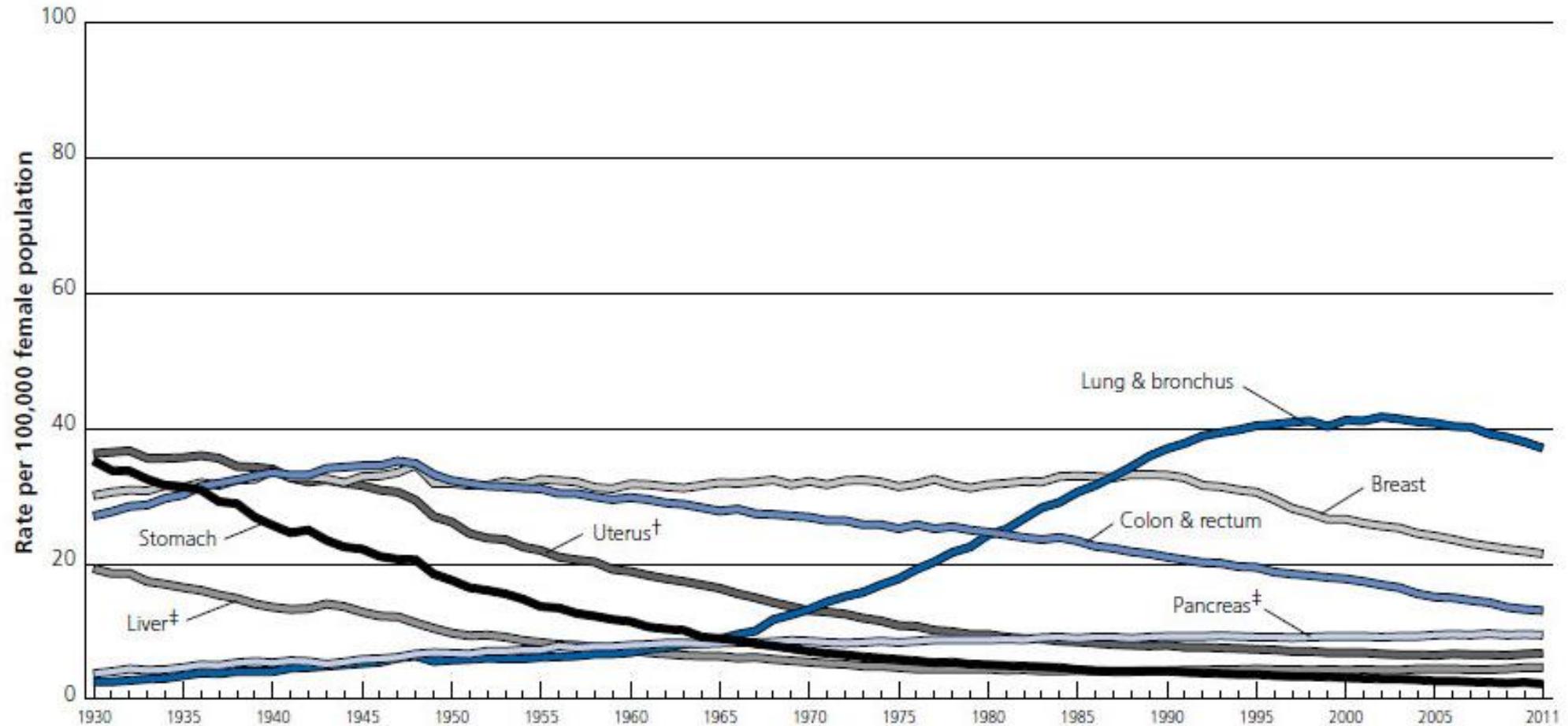
CDC Health, United States, 2015,
Table 19 (Data are for 2014)

Centers for Disease Control and
Prevention, 2015

U.S. Male Trends in Age-Adjusted Cancer Death Rates by Site



U.S. Female Trends in Age-Adjusted Cancer Death Rates by Site



Underwriters are declining based solely on chemotherapy drugs.

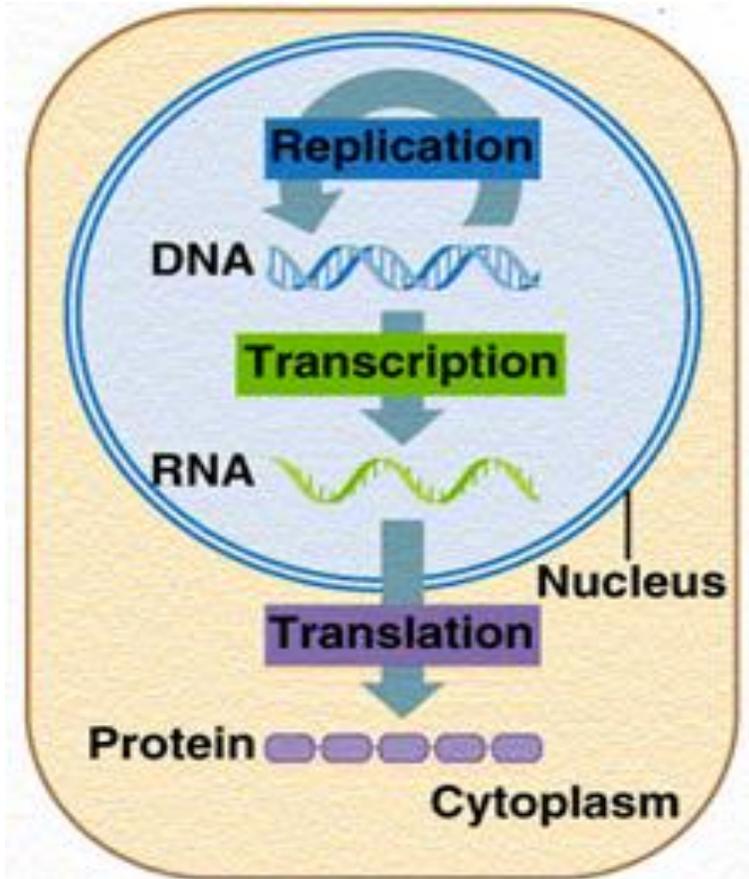
Over 200 cancer drugs

Over a dozen distinct mechanisms of action

Most applicants are declined

Combined relative mortality when chemo on profile: 282%

Most antineoplastic drugs act on the proliferating cycle of the cell.



- Destruction of DNA or inhibition of DNA duplication
- Inhibition of nucleic acid (DNA or RNA) synthesis
- Interfering with the transcription in RNA synthesis
- Inhibition of protein synthesis
- Interfering with hormone balance

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Recall some classic cancer agents...

Alkylating Agents

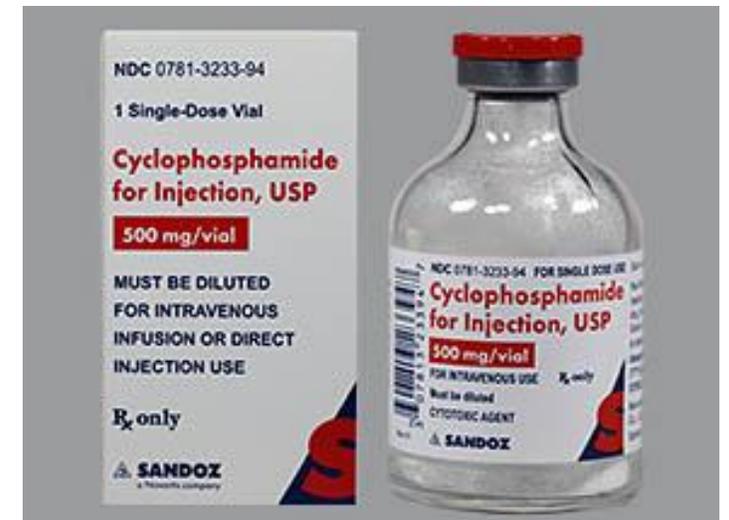
- Alkylates and cross-links DNA thereby inhibiting nucleic acid and protein synthesis

Popular Examples

- Cyclophosphamide, cisplatin, Temodar

Cancer Uses

- Various, testicular, ovarian, bladder
Hodgkin lymphoma, pancreatic CA, etc.



Recall some classic cancer agents...

Antibiotic Oncologics

- Binds and intercalates into DNA inhibiting nucleic acid and protein synthesis
- Triggers DNA cleavage by topoisomerase II

Popular Examples

- doxorubicin, bleomycin

Cancer Uses

- Various, acute lymphocytic leukemia, acute myelogenous leukemia, squamous cell CA, Hodgkin lymphoma



Recall some classic cancer agents...

Hormonal Oncologics

- Selectively binds to estrogen receptors producing estrogenic and anti-estrogenic effects (estrogen receptor modulator)

Popular Examples

- tamoxifen, anastrozole, leuprolide

Cancer Uses

- Various, breast CA (metastatic), prostate CA



Recall some classic cancer agents...

EGFR Antagonists

- Binds to epidermal growth factor receptor inhibiting cell growth and survival

Popular Examples

- Erbitux, Caprelsa

Cancer Uses

- Various, colorectal CA (metastatic), squamous cell head/neck CA, medullary thyroid CA



Recall some classic cancer agents...

Antiangiogenic Agents / mTOR Inhibitors

- Binds and inhibits vascular endothelial growth factor decreasing microvascular growth and metastatic progression

Popular Examples

- Avastin, Afinitor (everolimus), Sutent

Cancer Uses

- Various, Giant cell astrocytoma, renal cell CA, GI stromal tumor, NSC lung CA, etc.



Recall some classic cancer agents...

Kinase Inhibitors

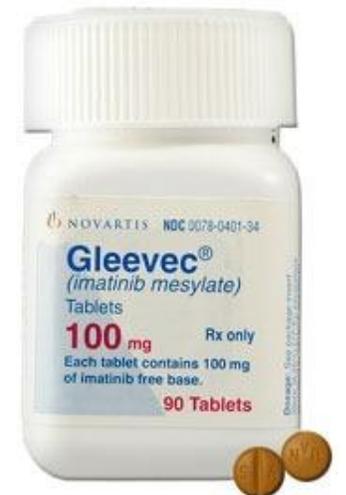
- Inhibits Philadelphia chromosomal tyrosine kinase and myeloid leukemic cell proliferation
- Induces apoptosis

Popular Examples

- “nibs”, Gleevec (imatinib), Nexavar (sorafenib), Sprycel (dasatinib)

Cancer Uses

- Various, Ph-positive chronic myeloid leukemia (CML), hepatocellular and renal cell CA



And many others...

Monoclonal Antibodies

- End in “mab” (i.e. Rituximab)
- Work by attaching a drug to an antibody specific to protein on cancer cells
- New drugs and new indications frequently



***How can underwriters become
armed against clandestine
cancer Rx treatment regimens?***

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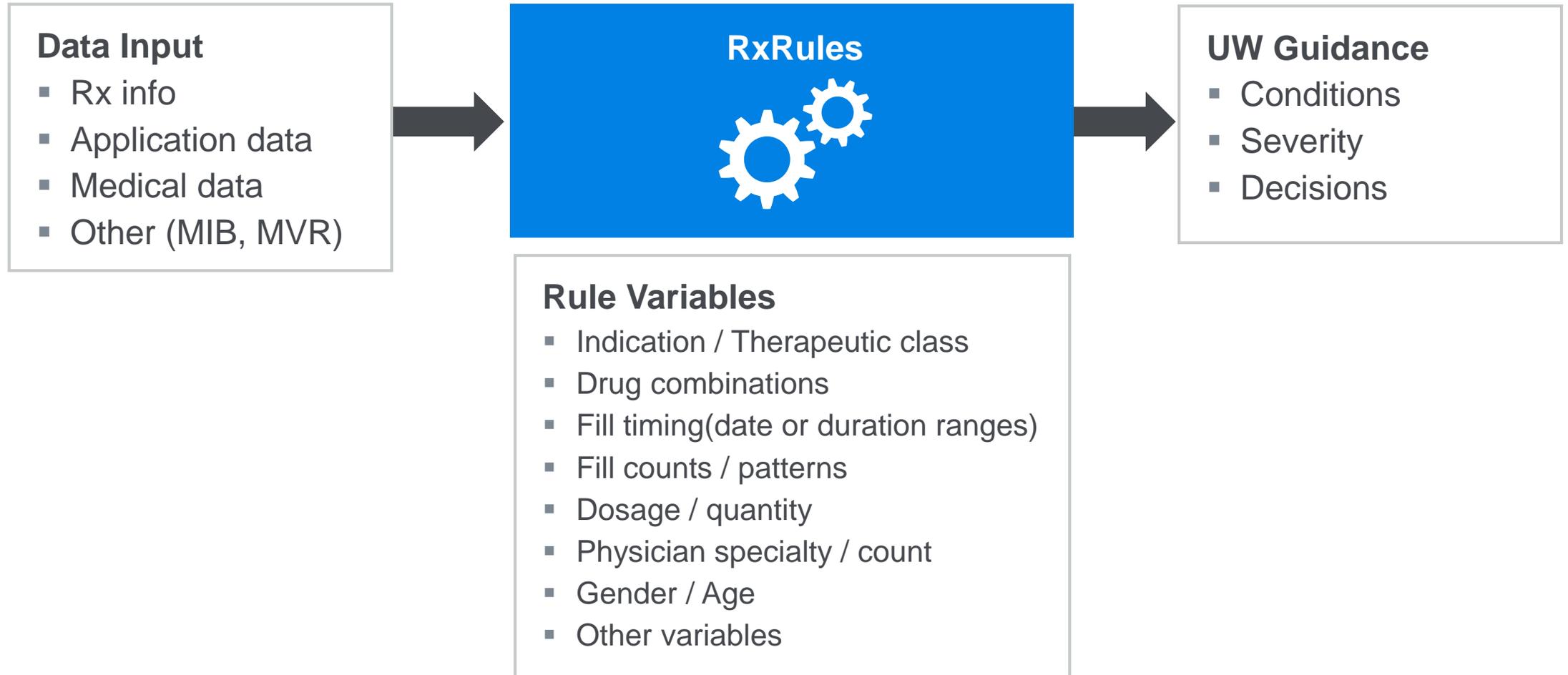
Rule Engines and Relative Mortality

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What is RxRules?



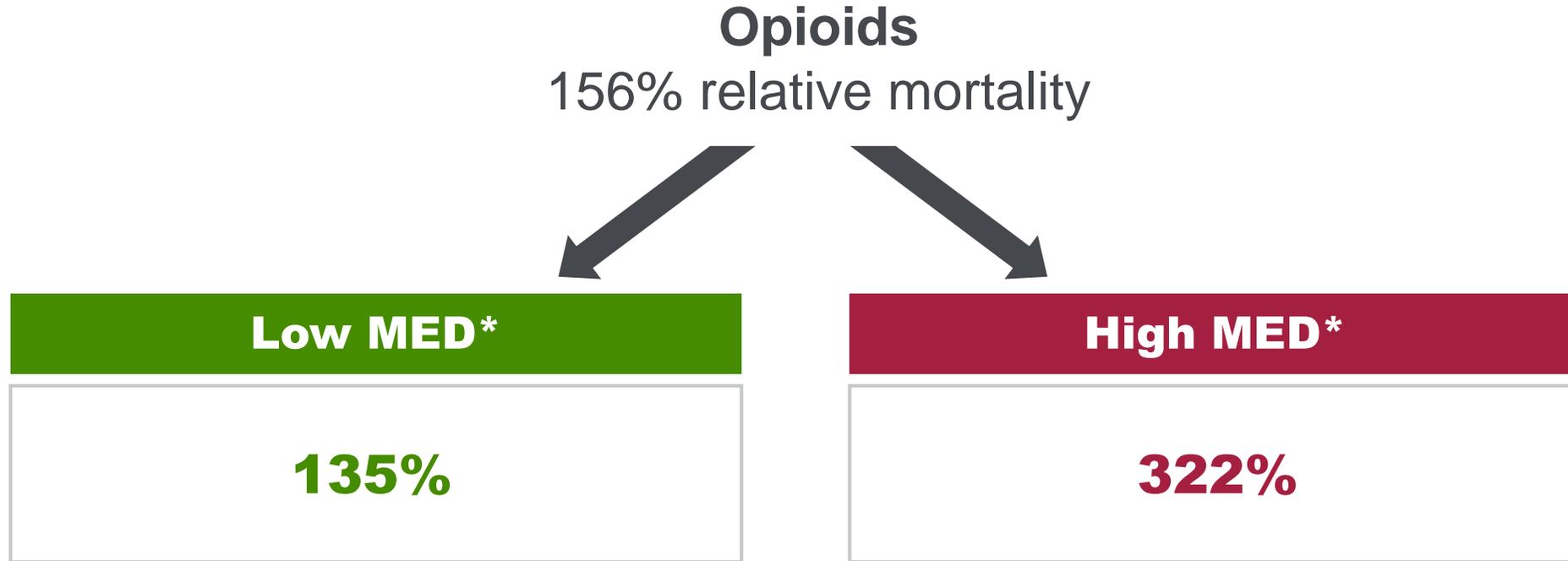
Cancer leads to disease-induced Rx treatments.

Examples:

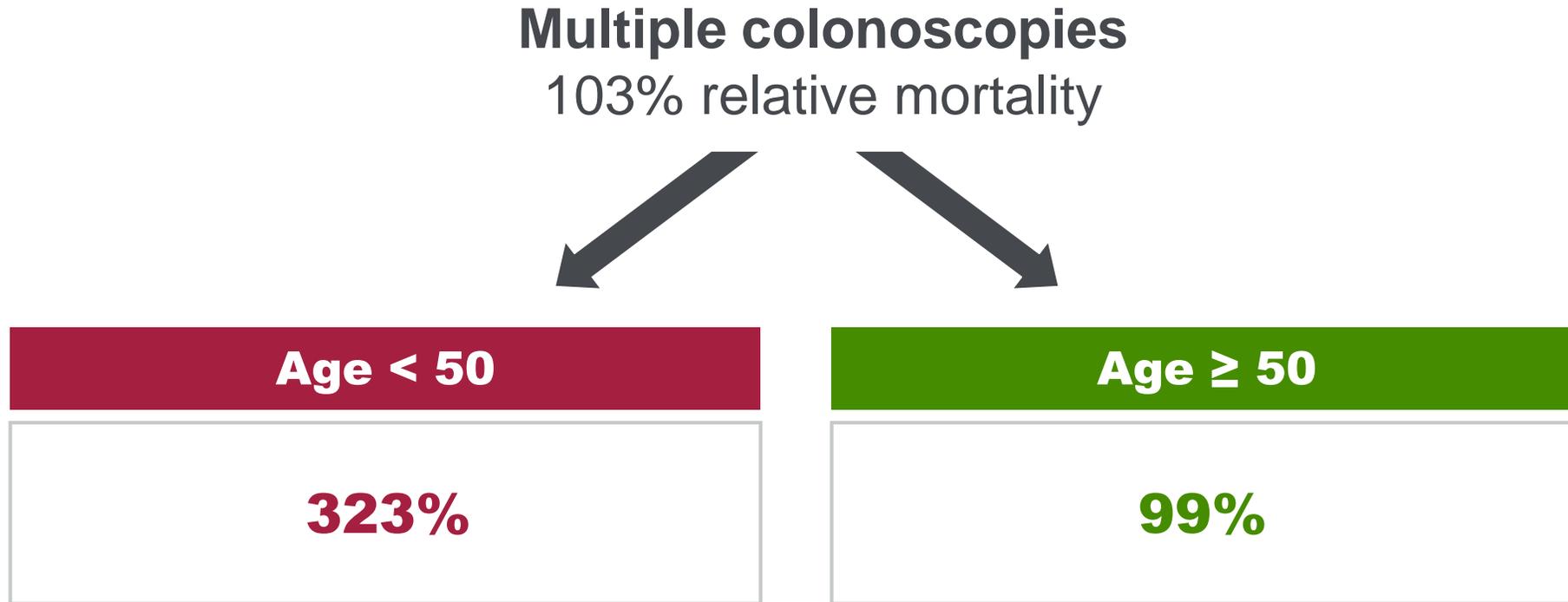
- Opioids treat cancer affiliated pain
- Repeated colonoscopies signal colon cancer
- Patterns of opioid, benzo and a hypnotic common with cancer derived palliative care
- Megace can be used for HIV, Cancer wasting or failure to thrive



Opioid dosage equivalence matters.



Procedure counts combined with applicant age matter.



Certain drug combinations are red flags for palliative care.

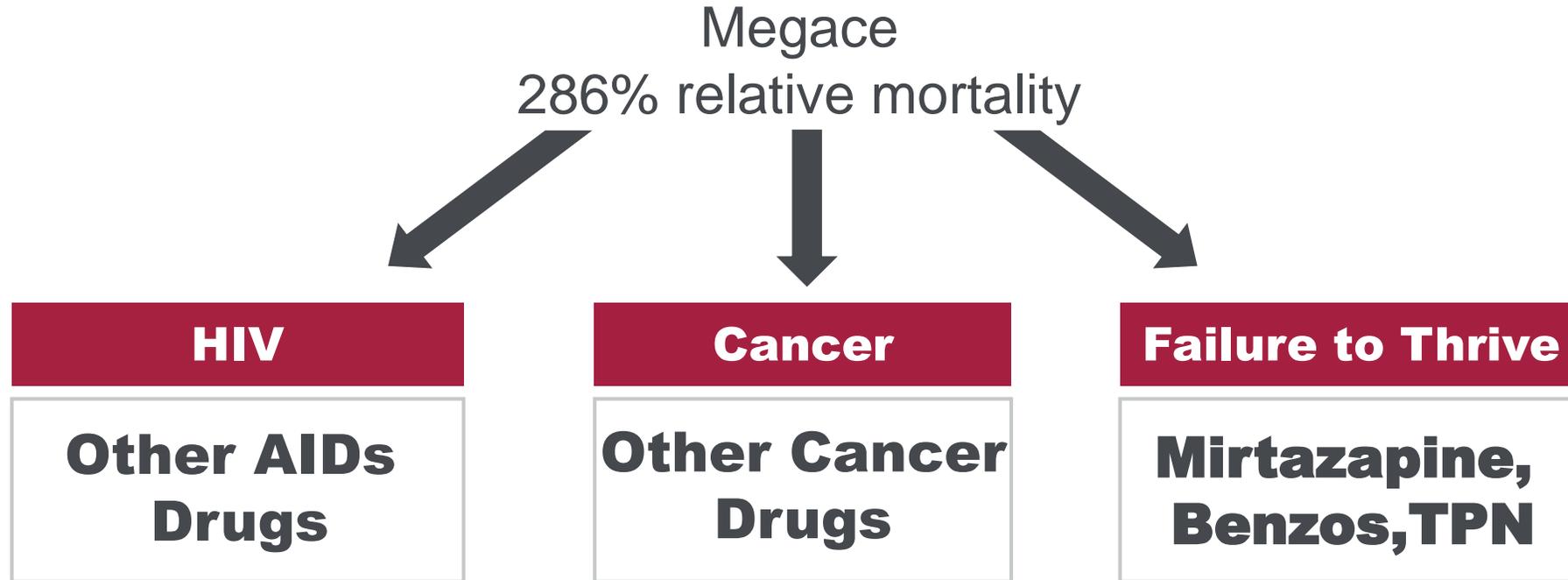
Combined Relative Mortality

- Opioids (158%)
- Benzos (126%)
- Short Acting Hypnotic (115%)

.....
491%



A rules engine can provide severity context for drugs with multiple uses.



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Prescriber type provides key cancer treatment insight.

- Oncologist overall– 229% RM
 - Why an oncologist prescriber?
 - Allopurinol Rx- tumor lysis syndrome vs gout
 - 6-mercaptopurine- ALL vs UC or Crohn's by gastroenterologist
 - Methotrexate (MTX)- various cancers (5-10%) vs RA by rheumatologist
 - Leucovorin – advanced colorectal cancer vs MTX overdose

Beware of drugs used to treat chemotherapy ADRs.

▪ Anti-emetics

- Compazine (prochlorperazine)- look at fill counts, gender and OB-GYN prescribers
- Marinol (dronabinol) - almost always cancer or HIV
- 5-HT3 antagonists (Zofran, Anzemet, etc)- number, frequency and timing of fills, prenatal vitamins, use within 2 weeks of steroid (dexamethasone), OB-GYN or ER
- Neurokinin antagonists (Emend) – surgery or chemo induced N&V, generally after a failed 5-HT3 trial

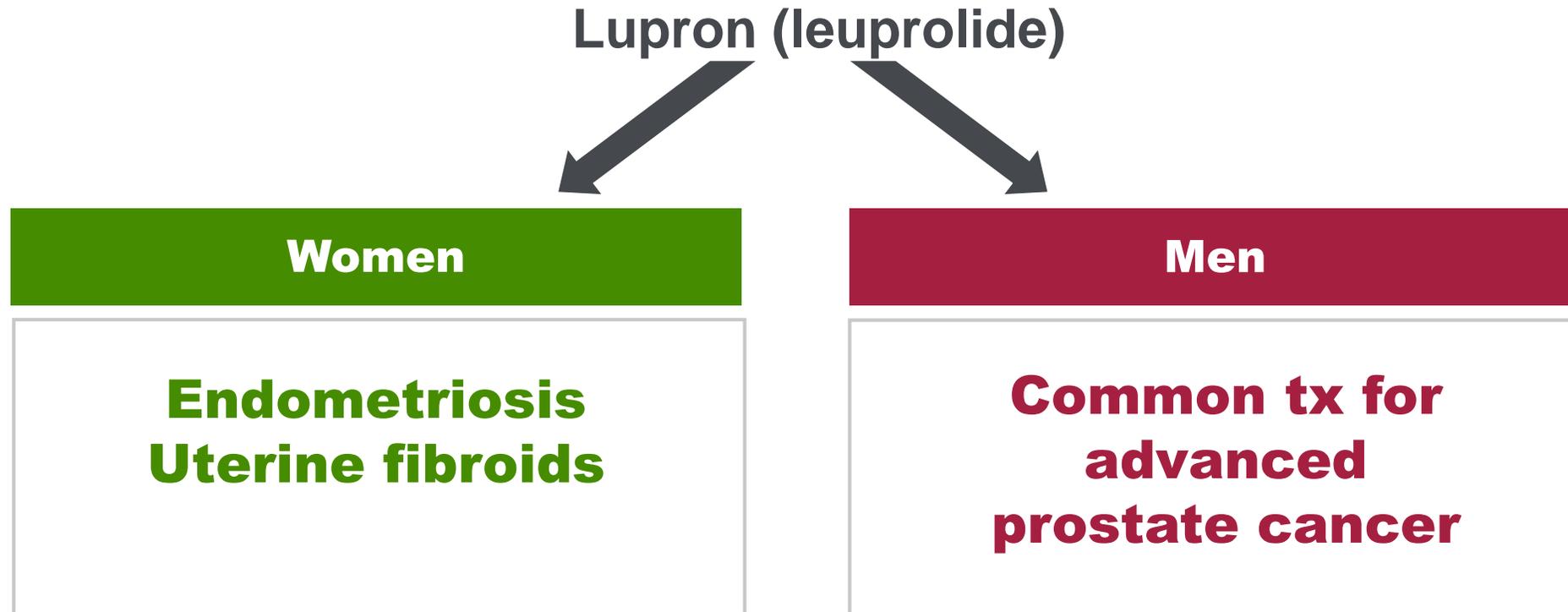
Beware of drugs are used to treat chemotherapy ADRs.

- Hematopoietic Agents

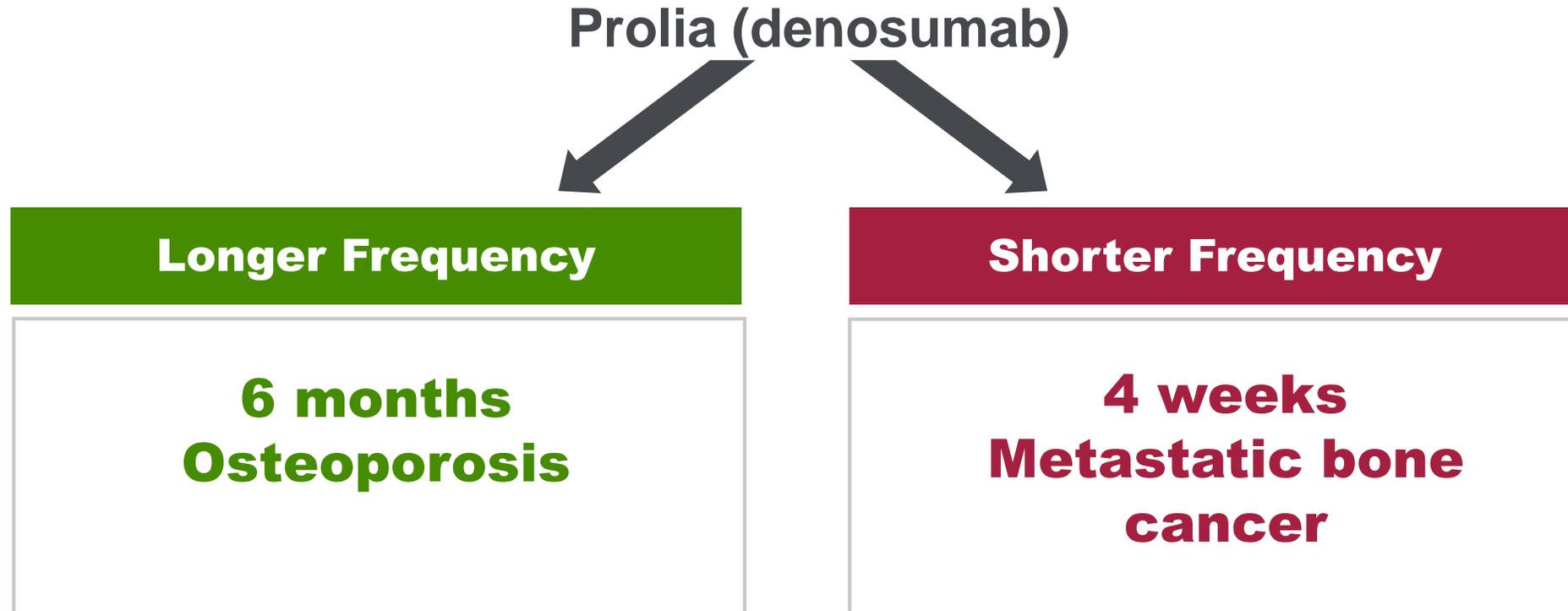
- Neupogen (filgrastim) - treats low white blood cell counts usually second to chemotherapy
- Epogen (not Procrit for CKD) - treats low bone marrow red blood cell production caused by chemotherapy



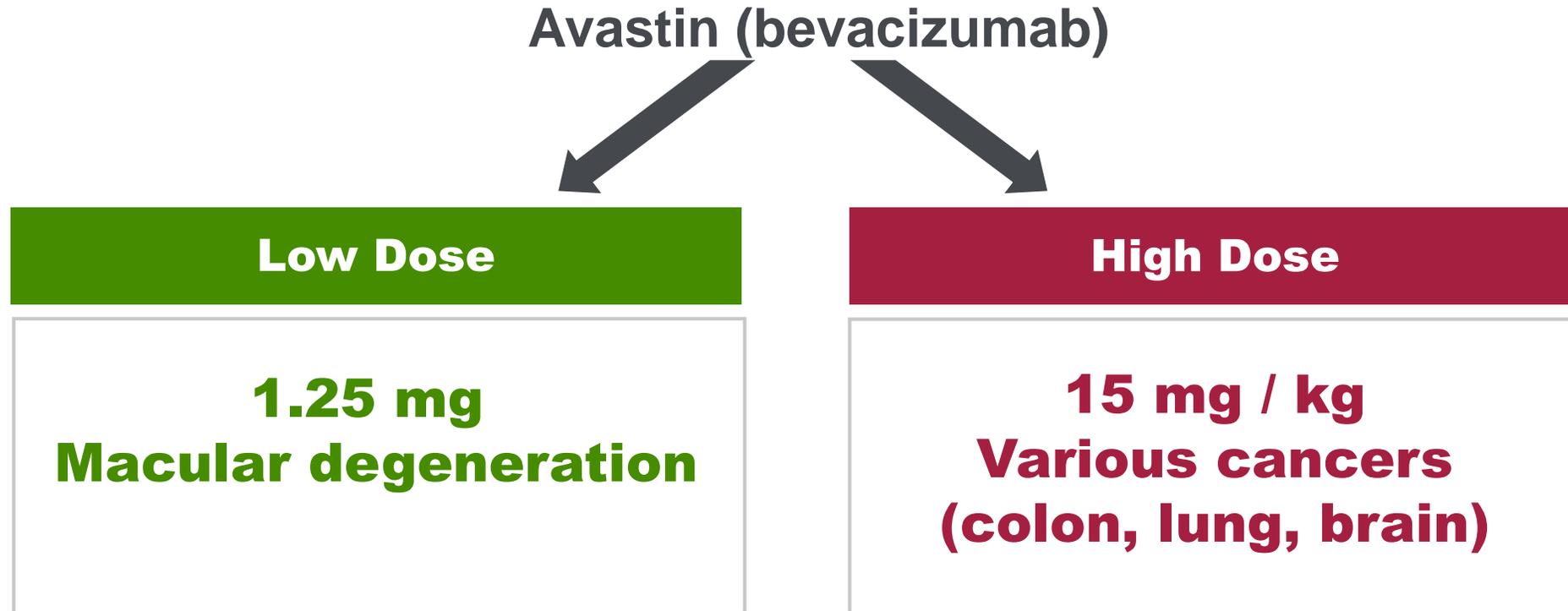
Gender can signal presence of cancer.



Frequency of monoclonal antibody treatment provides insight.



Cancer treatment dose also matters.



Differentiate breast cancer by drug combo, prescriber type, fill timing and duration of treatment.

- Herceptin (trastuzumab)
 - Rule out metastatic gastric cancer as monotherapy
 - Metastatic breast cancer when used with paclitaxel or pertuzumab
- Femara
 - OB-GYN: most likely for ovulation induction
 - All other prescribers: rule out female and male breast cancer
- Maintenance Tx (tamoxifen, Arimidex, Aromasin)
 - Determine treatment start date
 - Clinical guidelines suggest 10 years of therapy
 - Be weary of kinase inhibitor everolimus



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Majority of cancer drugs approved in 2017 are “nib’s” and “mab’s”

Brand Name	Generic Name	Cancer Treatment	Approval Date
Bavencio	avelumab	Merkel cell carcinoma	March 2017
Zejula	niraparib	Ovarian, fallopian tube, peritoneal CA	March 2017
Kisqali	ribciclib	Breast CA	March 2017
Alunbrig	brigatinib	Non-small cell lung CA	April 2017
Imfinzi	durvalumab	Urothelial carcinoma	May 2017
Nerlynx	neratinib	HER2 breast CA	July 2017
IDHIFA	enasidenib	Acute myeloid leukemia	August 2017
Besponsa	Inotuzumab ozogamicin	Acute lymphoblastic leukemia	August 2017

RxRules and drug mapping are updated regularly with new drug info.

- New drug updates provided monthly by MediSpan
- Drugs are coded to naturally flow into similar buckets
- Pharmacy staff conducts quarterly reviews of new therapeutic entities
- Revisited during each of the 80+ RxRules implementations conducted to date
- Clinical expertise by licensed pharmacists, medical directors and underwriters

Summary

- Cancer is the 2nd leading cause of death in U.S.
- Cancer treatment can be difficult to identify and interpret
 - Underwriting expertise is critical
- A rule engine can help
 - Identifies red flags / cancer indicators
 - Interprets multi-indication drugs
 - Manages / captures new drug therapies



Questions?

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