

Falls and Pharmacology

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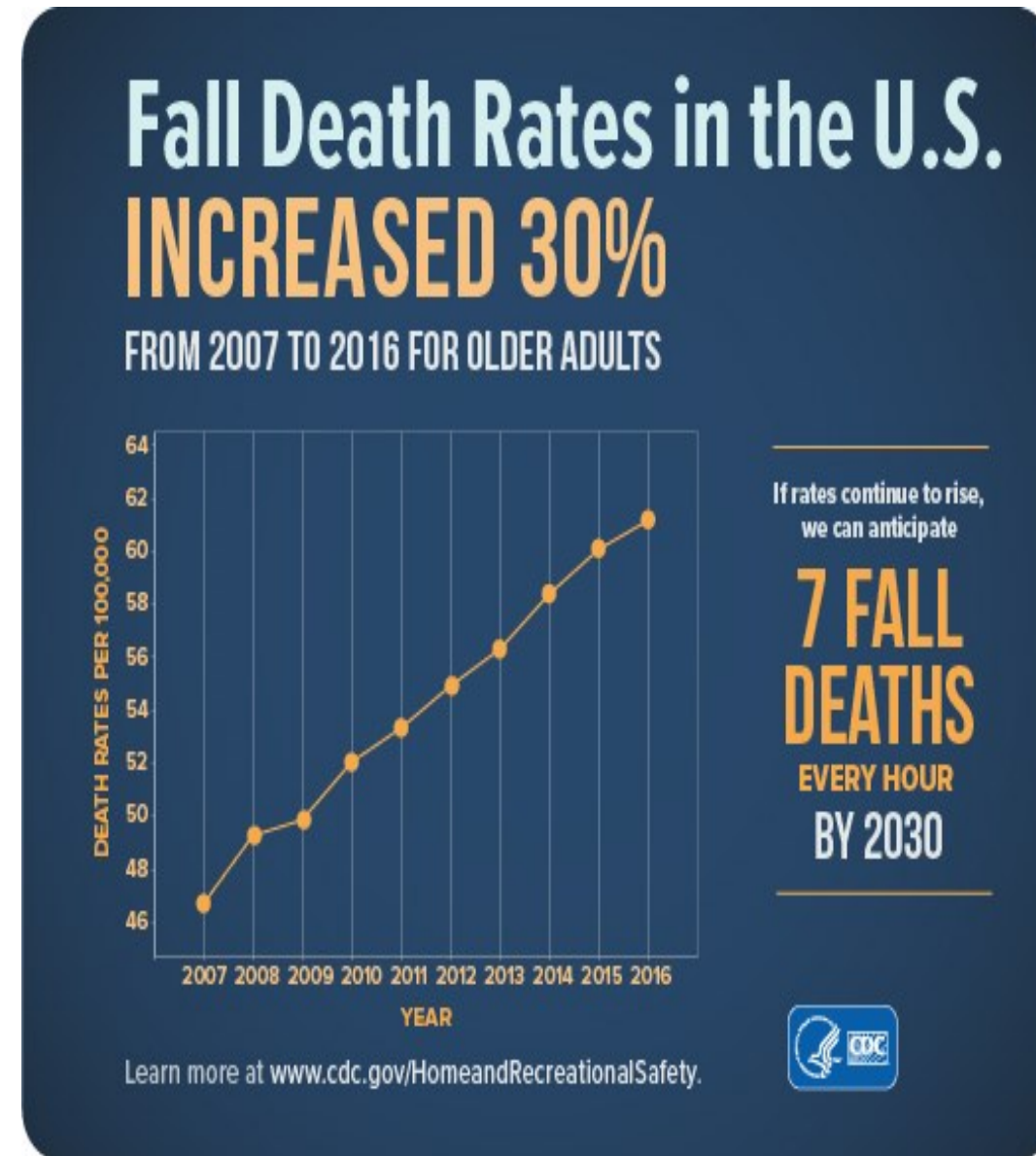
Advanced Physiotherapy
Practitioner

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Risk of falls in general population

- Female
- Low BMI
- Age > 80
- Previous falls
- Difficulty rising from sitting
- Anxiety
- Depression
- Reduced leg muscle strength
- Impaired balance
- Impaired postural reflexes
- Impaired vision
- Impaired cognition
- **Use of sedatives**



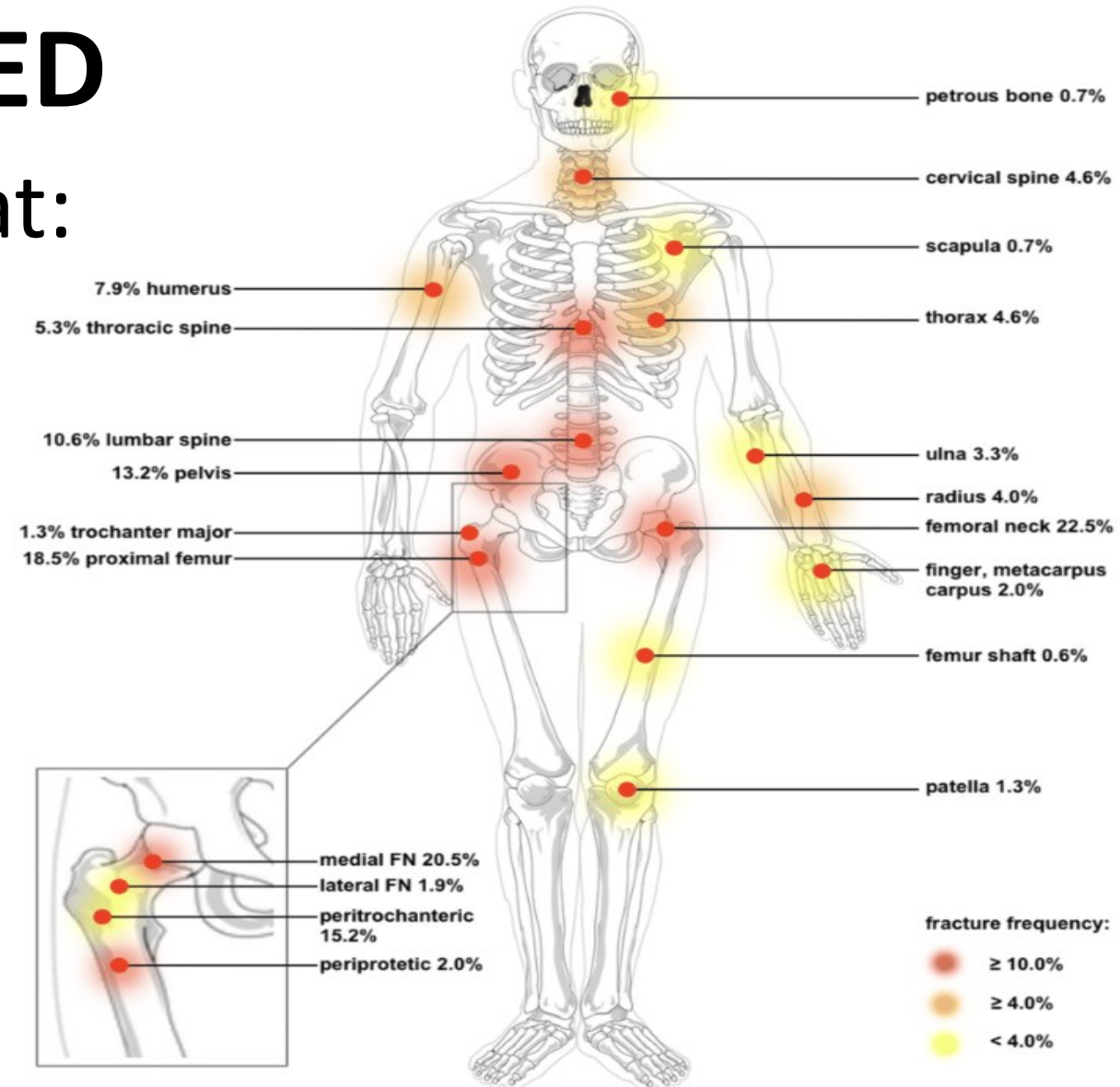
Falls related fractures

Retrospective study of ED

Over 10% of fractures occur at:

- Femoral neck
- Proximal femur
- Thoracic spine
- Lumbar spine
- Pelvis

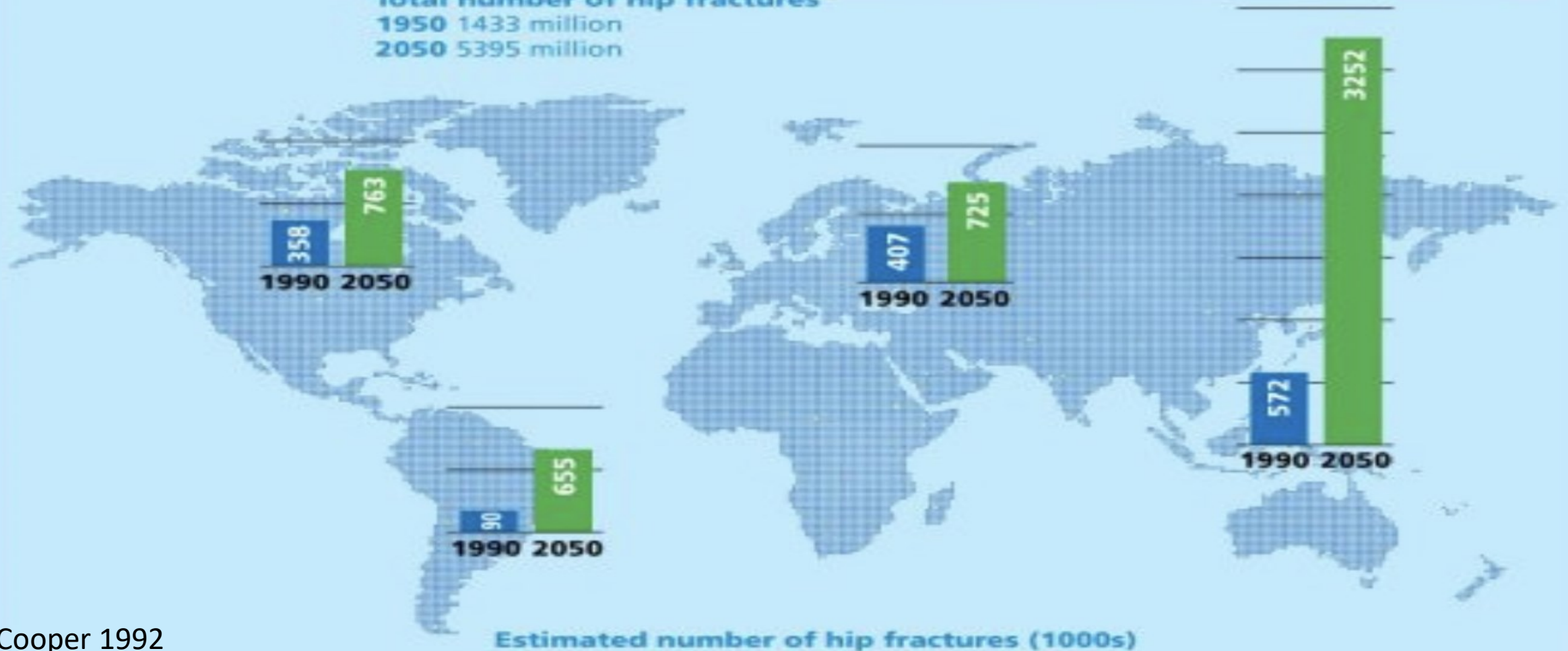
Muhlenfeld 2021



Incidence of fractures

Projected Number of Osteoporosis Fractures Worldwide

Total number of hip fractures
1950 1433 million
2050 5395 million



Post THA & TKA falls risk factors:

Systematic Review & Meta-analysis

- 12 studies of 1,292,689 subjects

- 1. Medications**

2. Psychiatric diseases

3. Living alone

4. Prior TKA

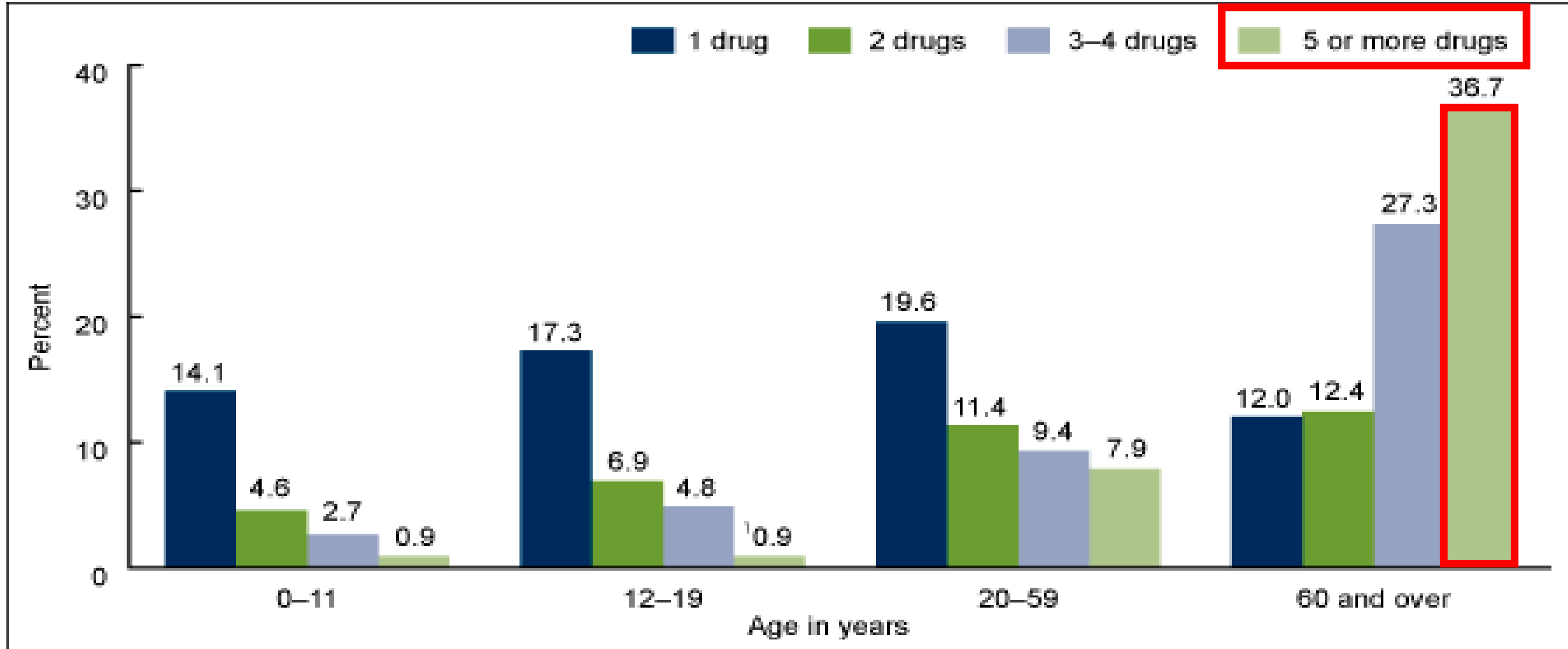
5. Falls history

6. Female

Lo 2019



Polypharmacy and age



¹Estimate is unstable; the relative standard error is greater than 30%.
SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey.

A drug by any other name



Chemical name

- Identifies the chemical elements found in the drug
- Used by researchers

Generic Name

- The universally accepted name of a drug
- Often have a common suffix i.e. Lidocaine, Procaine
- Used by Physicians, Pharmacists

Brand “Trade” name

- Name trademarked by drug manufacturer
- Used by the public

Chemical name	Generic name	Trade name
Acetoamino-phenol	Paracetamol	Tylenol
Acetylsalicylic acid	Aspirin	Disprin
1-1 dimethylbiguanide	Metformin	Glucophage
Aminopenicillin	Ampicillin	Roscillin

Mechanism of drug action

Receptors

A site on the cell with which an agonist binds to bring about change

1. Affinity

- The ability of a drug to bind to a receptor

2. Efficacy

- Ability of a drug to produce a response after binding to the receptor



Mechanism of drug action

Agonist

- A drug that produces a physiological effect on the receptor to which it binds
- i.e. Morphine activates opioid receptors to produce analgesia

Antagonist

- Binds to a receptor to block activation
- i.e. Naloxone blocks opioid receptors without giving analgesia

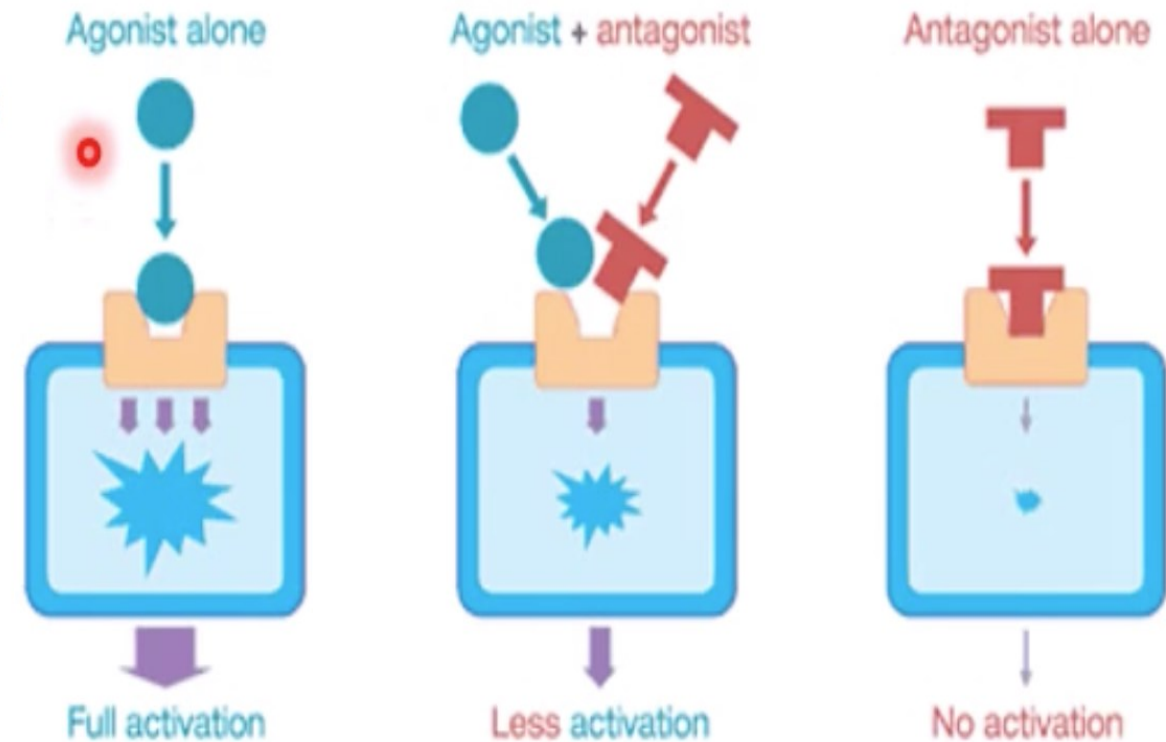
Agonists and Antagonists

Agonists

Drugs that occupy receptors and activate them.

Antagonists

Drugs that occupy receptors but do not activate them. Antagonists block receptor activation by agonists.



Adverse drug reactions



- **Side effects**
 - Predictable, common & occur in many people
- **Toxic effects**
 - Seen at higher doses of drug
- **Intolerance**
 - Exaggerated responses in specific individuals
- **Iatrogenic diseases**
 - Persistence of toxic effects when drug stopped
- **Dependence**
 - Can range from psychological to physical addiction
- **Teratogenicity**
 - Ability of drug to cause fetal abnormalities
- **Carcinogenicity**
 - Ability of a drug to cause cancer

The “big 3”

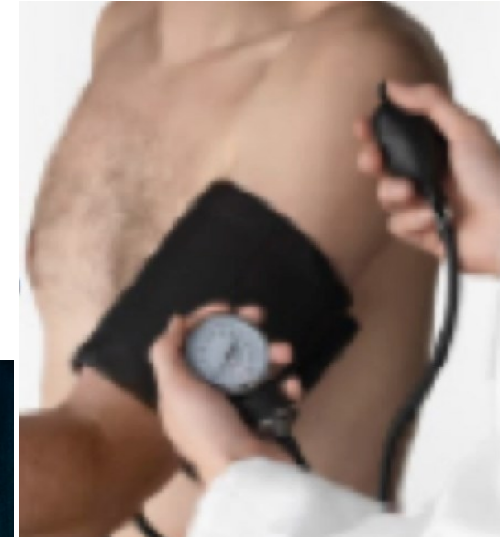
The three most common
comorbidities in
Physiotherapy

1. Hypertension

2. Arthritis

3. Depression

Boissonault 1999



Pharmacology for Physiotherapists



Systems approach

1. Introduction to pharmacology
2. Cardio-vascular & renal systems
3. CNS & ANS systems
4. Musculoskeletal system
5. Hematology system
6. GI & respiratory systems
7. Endocrine system
8. Immune system
9. Complimentary & recreational drugs
10. Reference & cheat sheets



Pharmacology for Physiotherapists

Cardiovascular system

Renal system



Cardiovascular medications

Diseases

- Hypertension
- Angina pectoris
- Arrhythmias
- Heart failure
- Shock
- Cerebral ischemia
- Peripheral vascular disease
- Coagulation
- Hyper-lipidemia



Hypertension CP Guidelines

(Am Soc Hypertension 2014)

Blood Pressure $\geq 140/90$ in Adults Aged >18 years
 (For age ≥ 80 years, pressure $\geq 150/90$ or $\geq 140/90$ if high risk [diabetes, kidney disease])

Start Lifestyle Changes
 (Lose weight, reduce dietary salt and alcohol, stop smoking)

Drug Therapy
 (Consider a delay in uncomplicated Stage 1 patients)*

Start Drug Therapy
 (In all patients)

Stage 1
 140-159/90-99

Stage 2
 $\geq 160/100$

Special Cases

Black Patients

non-Black Patients

All Patients

- Kidney disease
- Diabetes
- Coronary disease
- Stroke history
- Heart failure
 [see table of recommended drugs for these conditions]

Age <60 Years

Age ≥ 60 Years

CCB or Thiazide

ACE-i or ARB

CCB or Thiazide

Start With 2 Drugs
 CCB or Thiazide + ACE-i or ARB

If Needed, Add ...

If Needed, Add ...

If Needed, Add ...

If Needed ...

ACE-i or ARB
 OR
 combine CCB+Thiazide

CCB or Thiazide

ACE-i or ARB

CCB+Thiazide+ACE-i (or ARB)

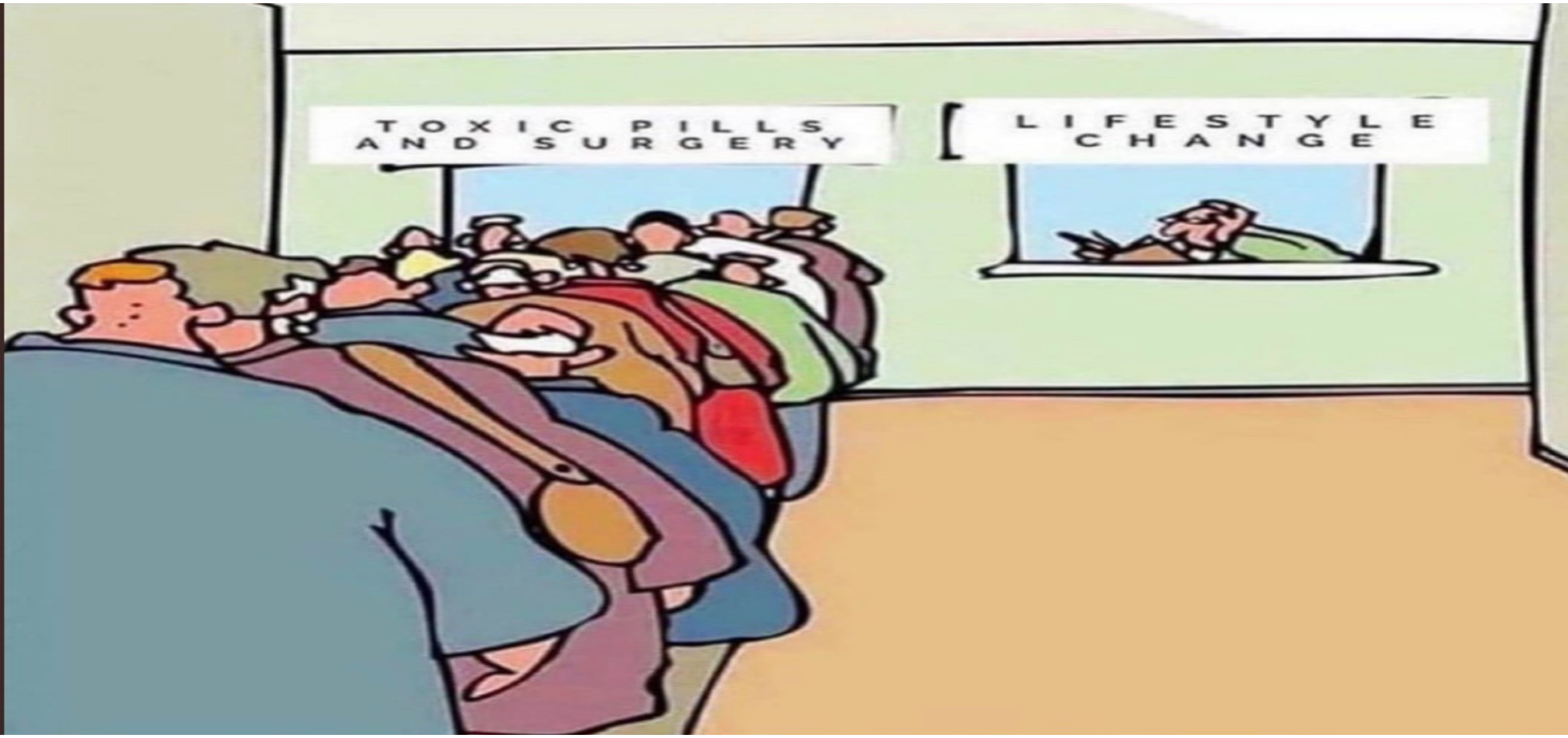
CCB+Thiazide+ACE-i (or ARB)

If Needed, add other drugs e.g. spironolactone; centrally acting agents; β -blockers

If Needed, Refer to a Hypertension Specialist

* In stage 1 patients without other cardiovascular risk factors or abnormal findings, some months of regularly monitored lifestyle management without drugs can be considered.

Reality



Hypertension

Survey of 1812 US Physiotherapists

- 75% reported > 25% of case load had hypertension
- 69% see a new patient with HT > once / week
- 30% see a new patient with HT daily
- 14.8% measured BP on first assessment



Diuretics

- Increase formation & excretion of urine
- Direct effect on BP by reducing blood volume
- Often first line meds in hypertension

Thiazide diuretics:

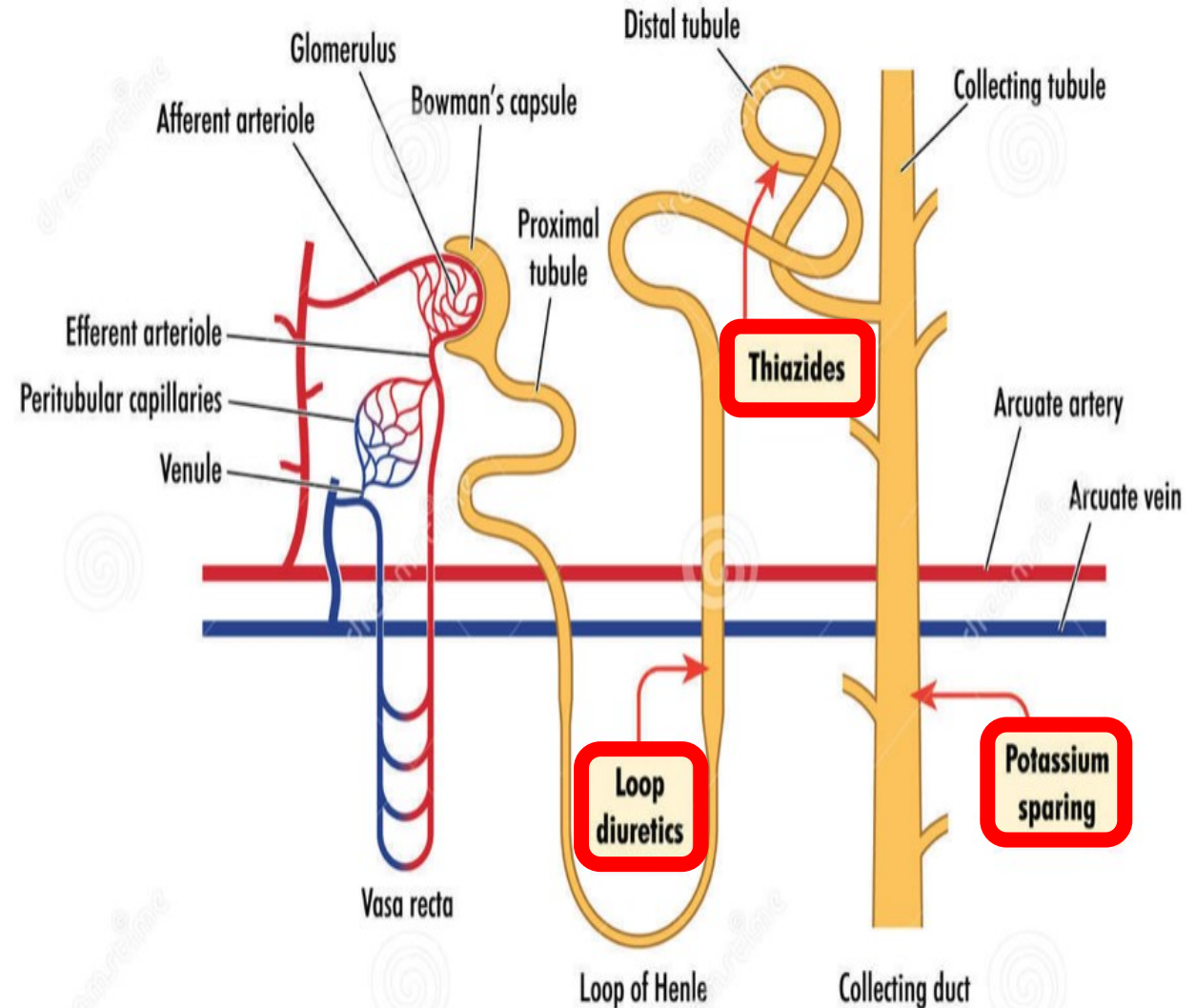
- Reducing edema & blood volume in patients with normal renal function

Loop diuretics:

- Used in CHF

Potassium sparing diuretics:

- Used in CHF with other diuretics



Adverse Effects Diuretics

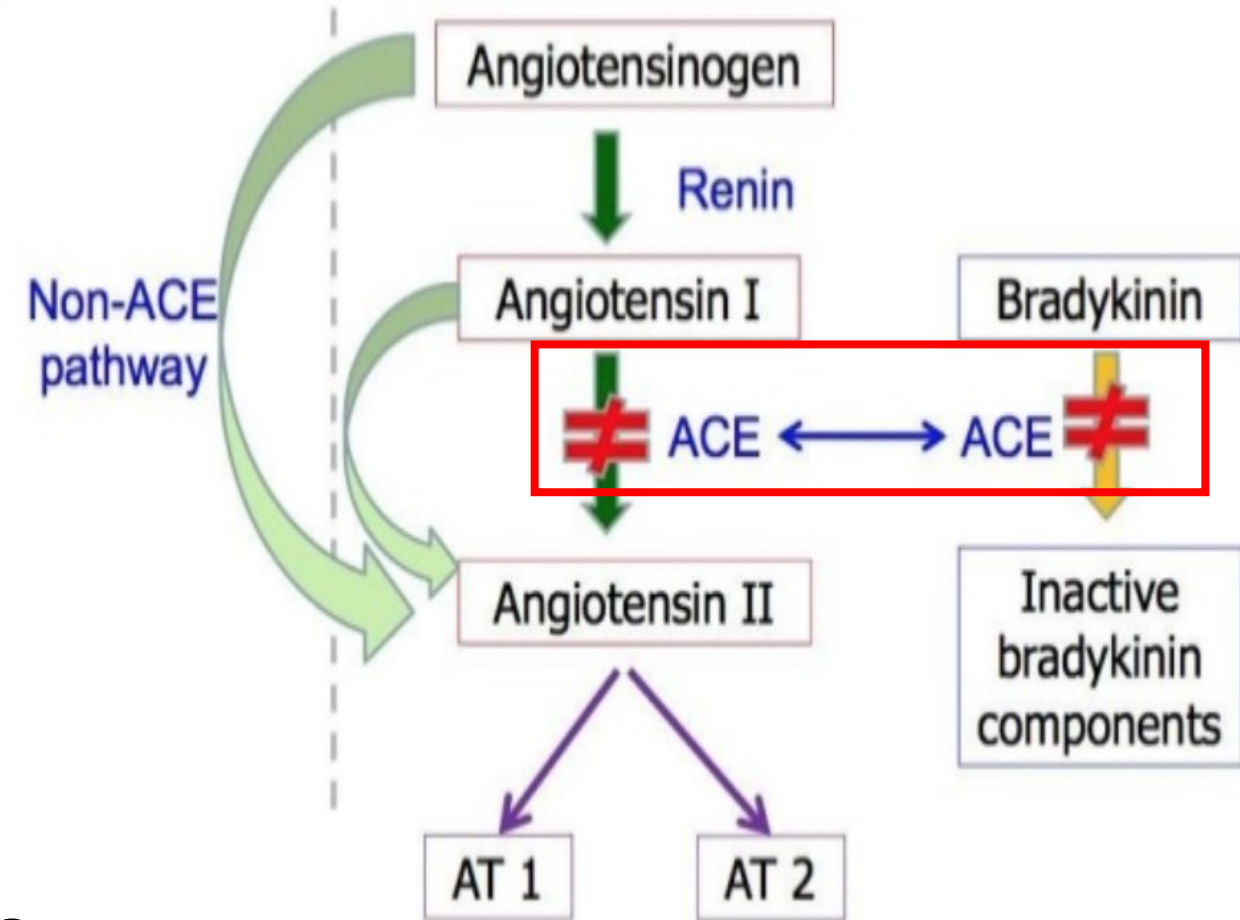
- Weakness
- Dizziness
- Fatigue
- Muscle cramps
- Headache
- Dehydration
- Arrhythmia
- Metabolic alkalosis
- Hypokalemia
- Hypo-magnesia
- Erectile dysfunction
- Hyperglycemia
- Pancreatitis
- Hyperlipidemia
- Hypokalemia
- Hyperuricemia
- Dose-related hearing loss
- Nervousness
- Rash
- Breast tenderness
- Erectile dysfunction
- Increased hair growth in females
- Decreased libido
- GI upset

Angiotensin Converting Enzyme (ACE)

Angiotensin II powerful vasoconstrictor

Medications

- (ACE) Inhibitors
- Angiotensin II receptor blockers
- Calcium channel blockers



≠ : Steps inhibited by ACE inhibitors

(ACE) Inhibitors

Generic name	Trade name
Benazepril	Lotensin
Captopril	Capoten
Cilazapril	Inhibace
Enalapril	Vasotec
Fosinopril	Monopril
Lisinopril	Prinivil, Zestril
Quinipril	Accupril
Ramipril	Altace

Adverse effects:

- **Cough**
- Acute renal failure
- Proteinuria
- Taste alteration
- Edema
- Rash
- Hyponatremia
- Contraindicated in pregnancy

Adrenergic receptors



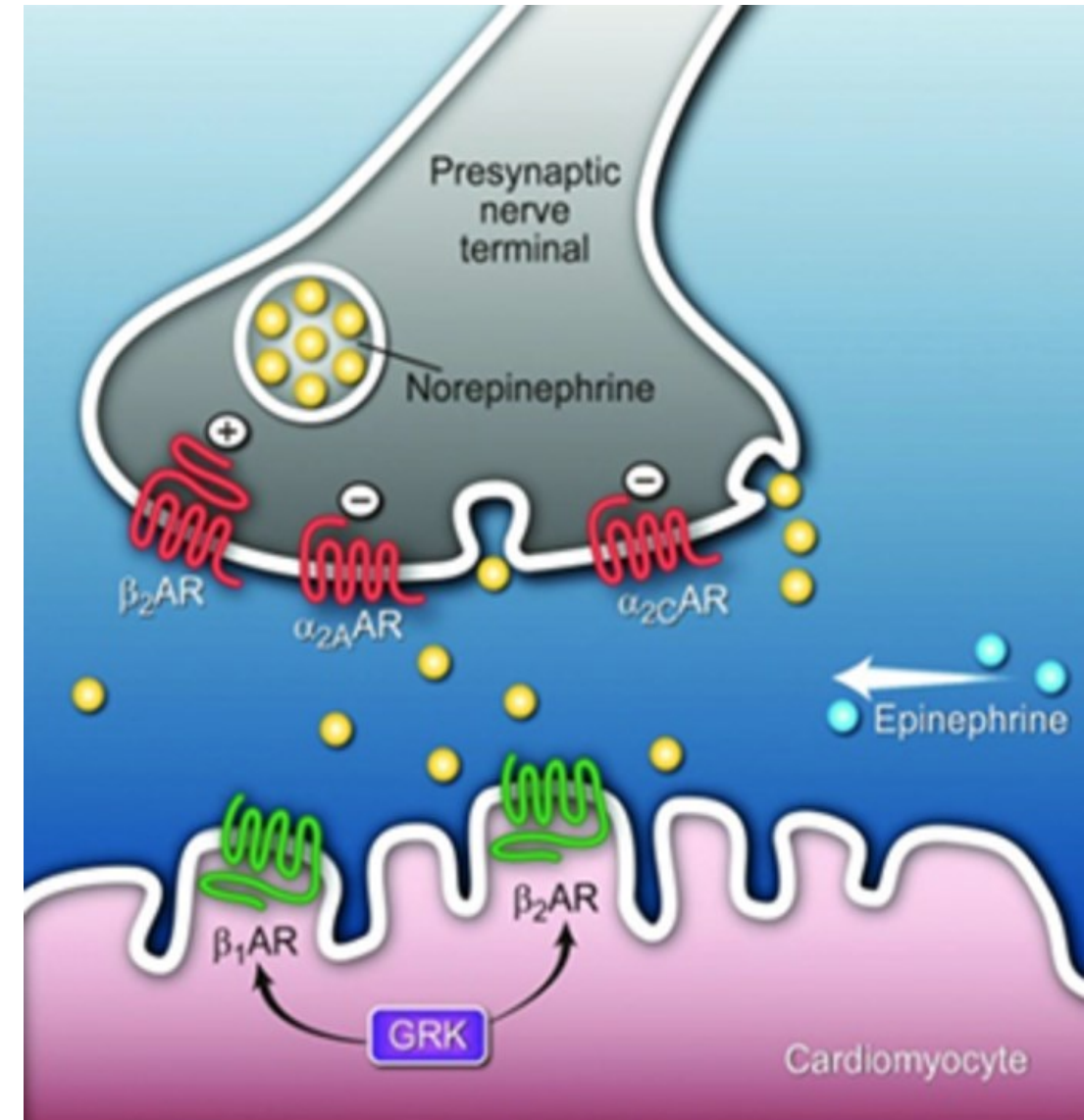
Adrenergic Receptor	Location	Action
Alpha 1	Smooth muscles of arteries & veins	Increase cardiac contraction
Alpha - 2	Sympathetic nerve varicosities	Inhibition of norepinephrine release
	CNS	Inhibition of sympathetic output
Beta - 1	Sino-arterial node	Increased HR
	Atrial & ventricular muscle	Increased conduction velocity & contractibility
	Atrio-ventricular node & Purkinje fibers	Increased conduction velocity
Beta - 2	Smooth muscle of arteries & veins	Relaxation

Beta blockers

Reduce:

- Cardiac output
 - Cardiac rate
 - Force of contraction
- Sympathetic tone
- Myocardial O₂ demand

Generic name	Trade name
Atenolol	Noten
Bisoprolol	Bicor
Carvedilol	Dialtrend, Dilasig
Labetalol	Presolol, Trandate
Metoprolol	Betaloc, Minax, Toprol
Nebivolol	Nebilet
Oxprenolol	Corbeton
Pidolol	Barbloc
Propranolol	Deralin, Inderal



Beta blockers

Indications:

- Angina pectoris
- Atrial fibrillation
- Congestive heart failure
- Essential tremor
- Hypertension
- Migraine prophylaxis
- Mitral valve prolapse

Adverse effects:

- Hypotension
- Lethargy
- Depression
- Bradycardia
- GI upset
- Congestive heart failure

Angina pectoris

3 Sub-types:

1. Stable

- Predictable
- With exertion/stress

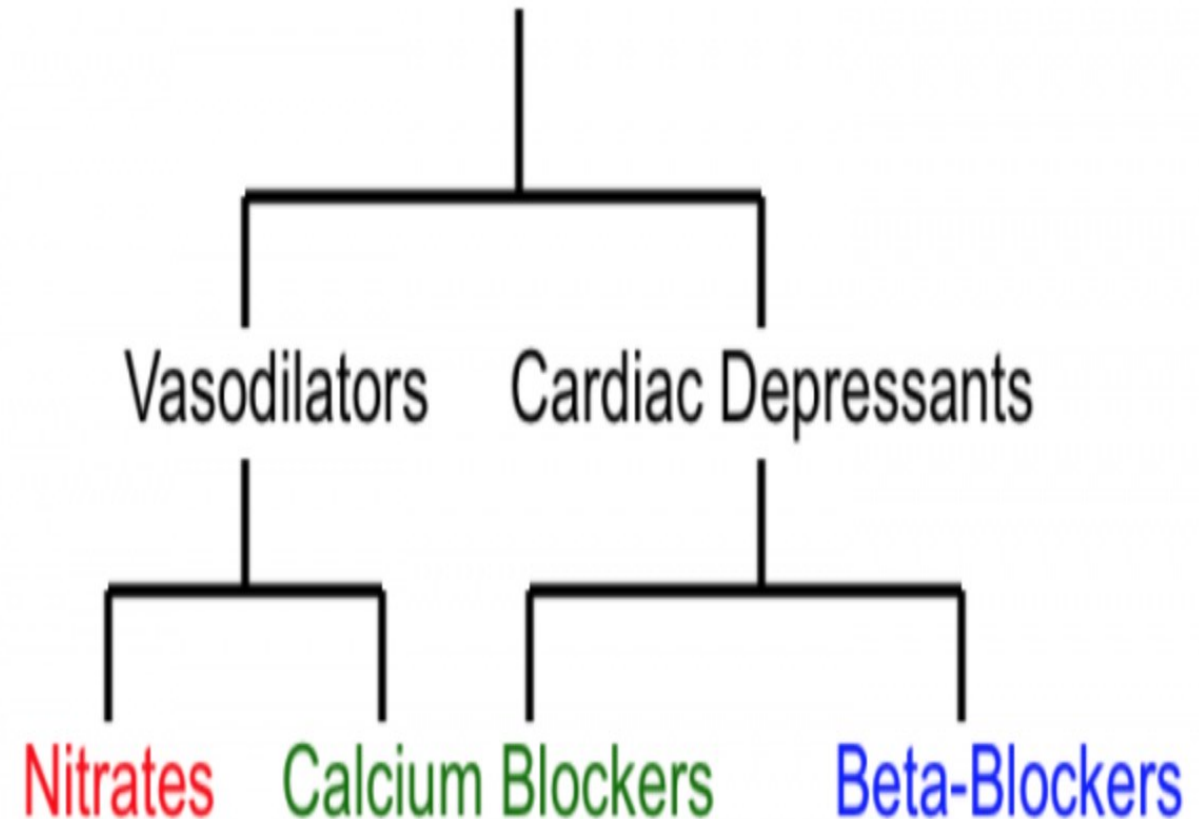
2. Unstable

- Unpredictable
- Severe pain longer lasting

3. Variant

- Occurs at night or rest

Most Common Drugs Used in Treating Angina Pectoris



Organic nitrates

Produce general & cardiac vasodilation

- Nitroglycerin
- Isosorbide dinitrate
- Isosorbide mononitrate

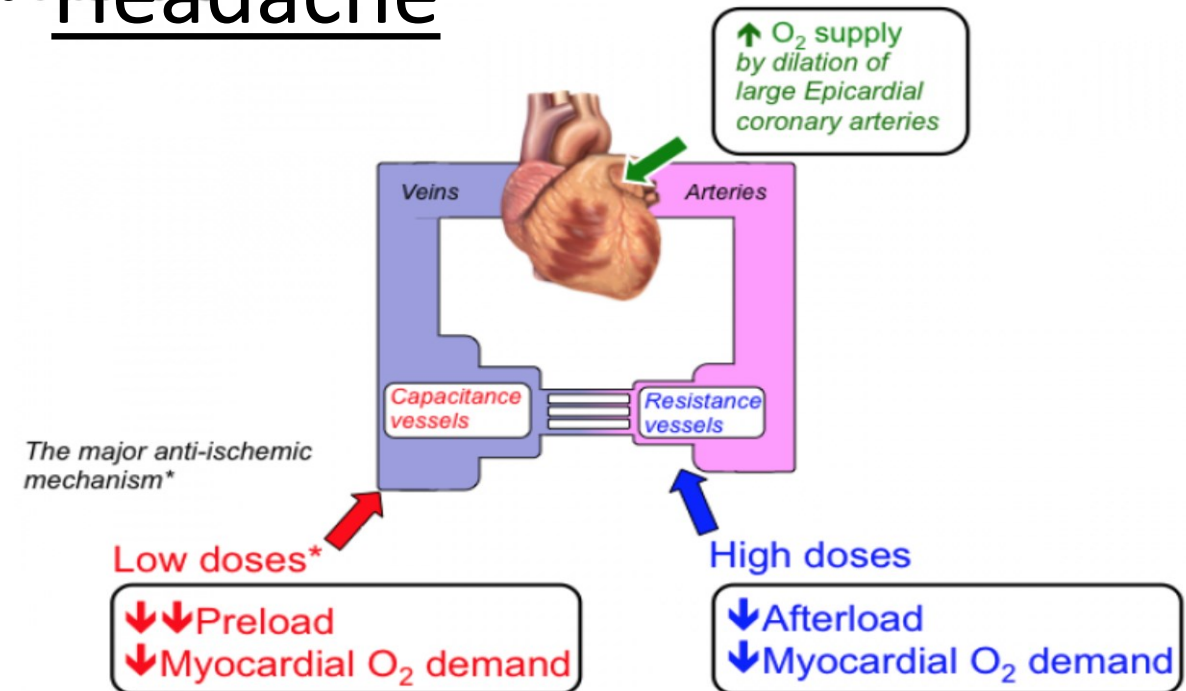
Decrease:

- Amount of blood returning to heart (cardiac pre-load)
- Pressure to pump blood out (vascular resistance)

Adverse effects:

- Nausea
- Dizziness
- Headache

- Orthostatic hypotension



Cardiac Arrhythmia

An abnormality of the rate, rhythm, conduction or site of origin of the cardiac impulse

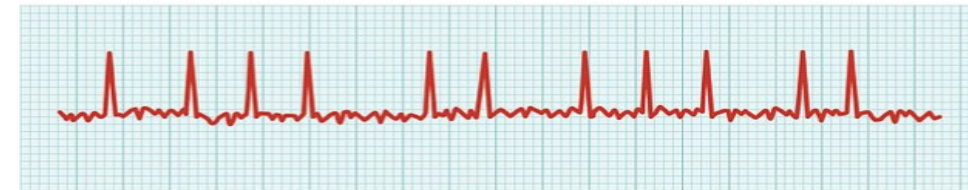
- Result in impaired cardiac pumping ability
- Classified by location of origination in the heart

Associated with:

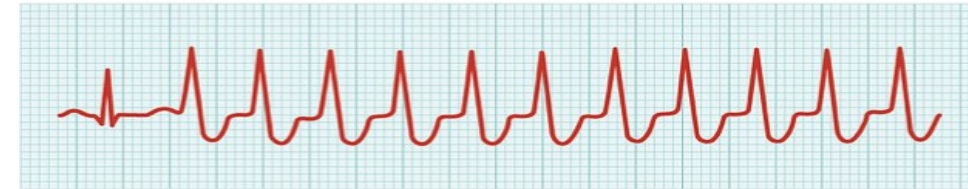
- CVAs
- Cardiac failure
- 80% of cardiac deaths



Second-degree (partial) block



Atrial fibrillation



Ventricular tachycardia



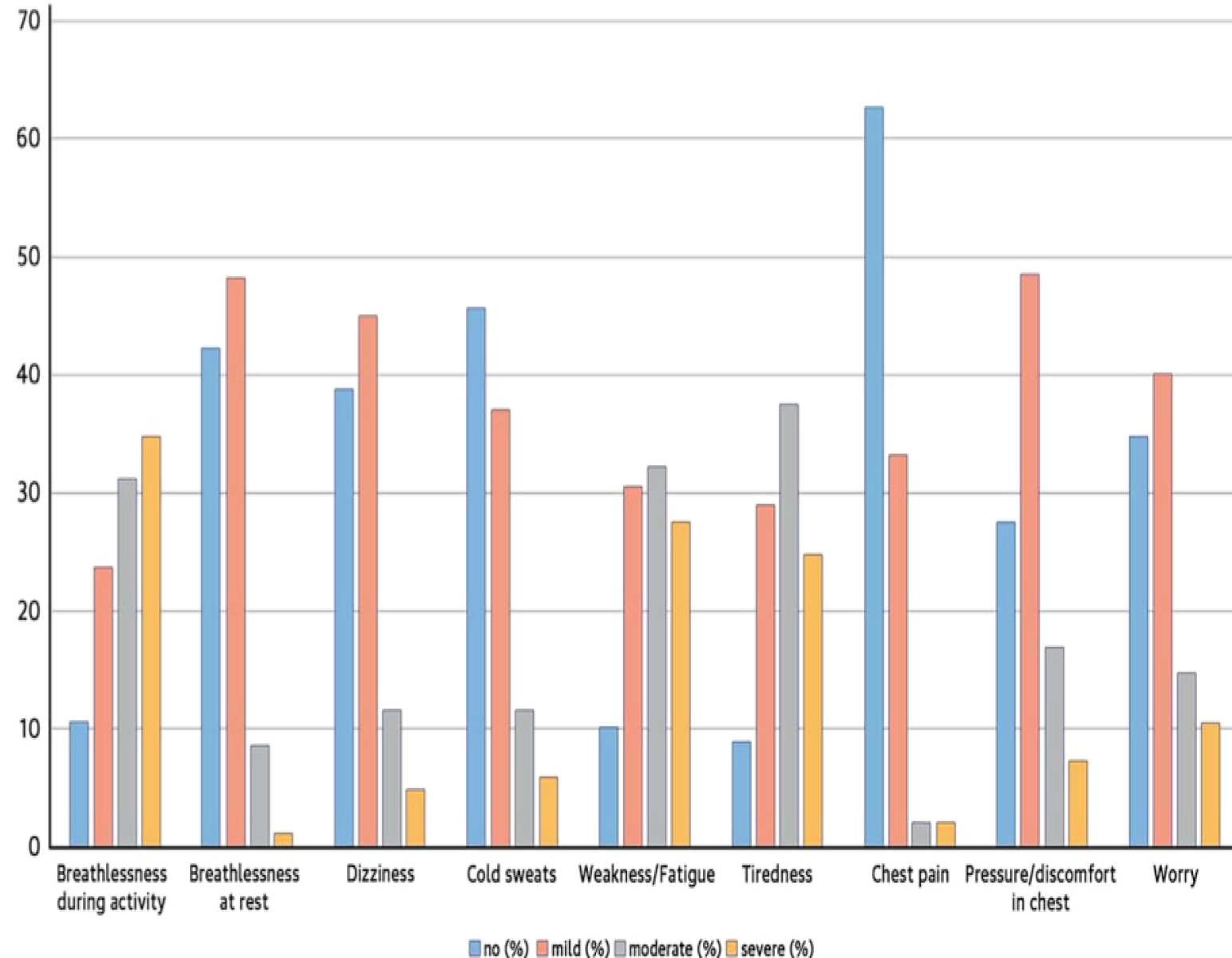
Ventricular fibrillation



Cardiac Arrhythmia

Symptoms of Arrhythmia

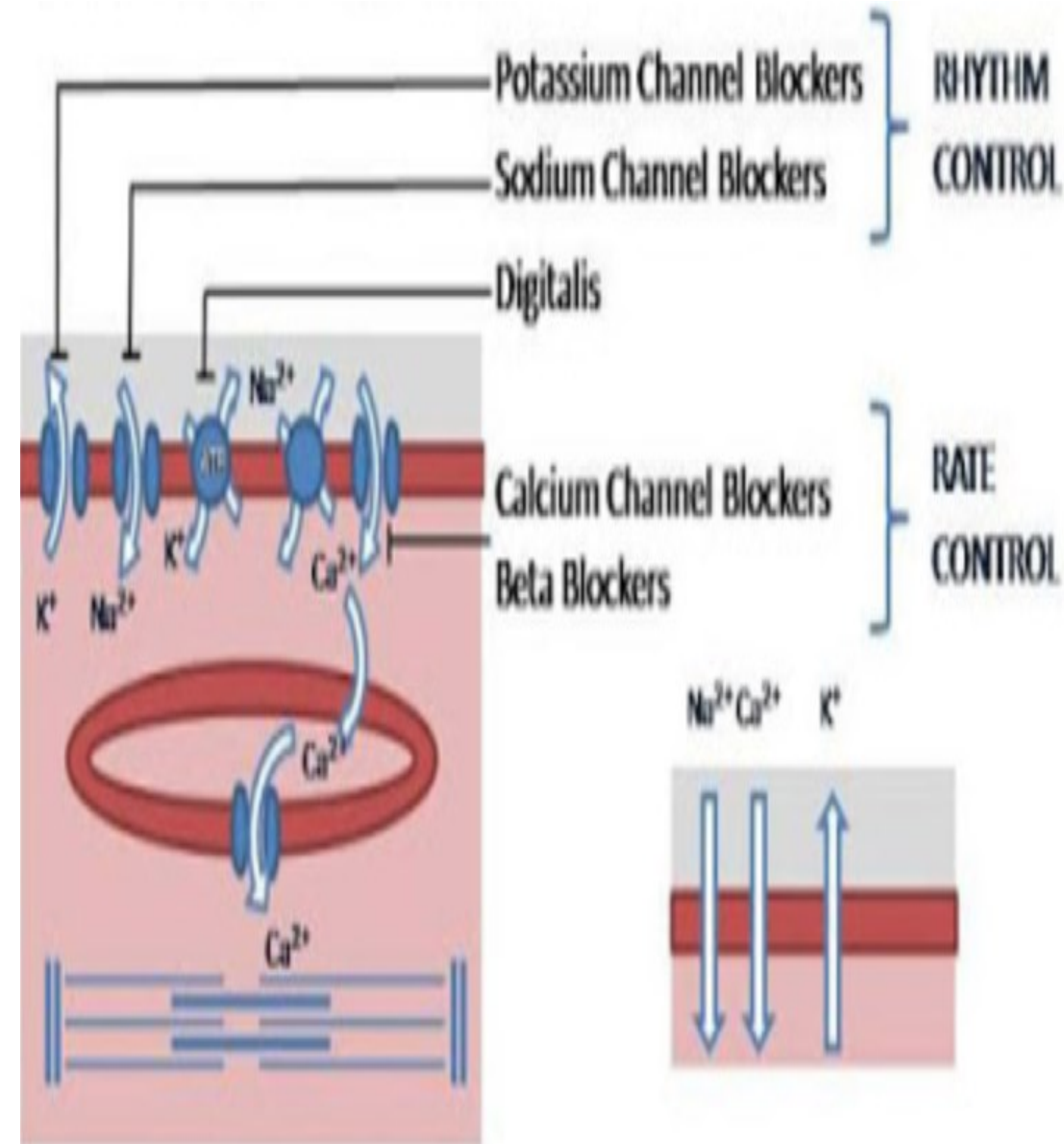
- Fatigue
- Dizziness
- Lightheadedness
- Shortness of breath
- Syncope
- Palpitations
- Angina



Antiarrhythmic medications

Adverse effects:

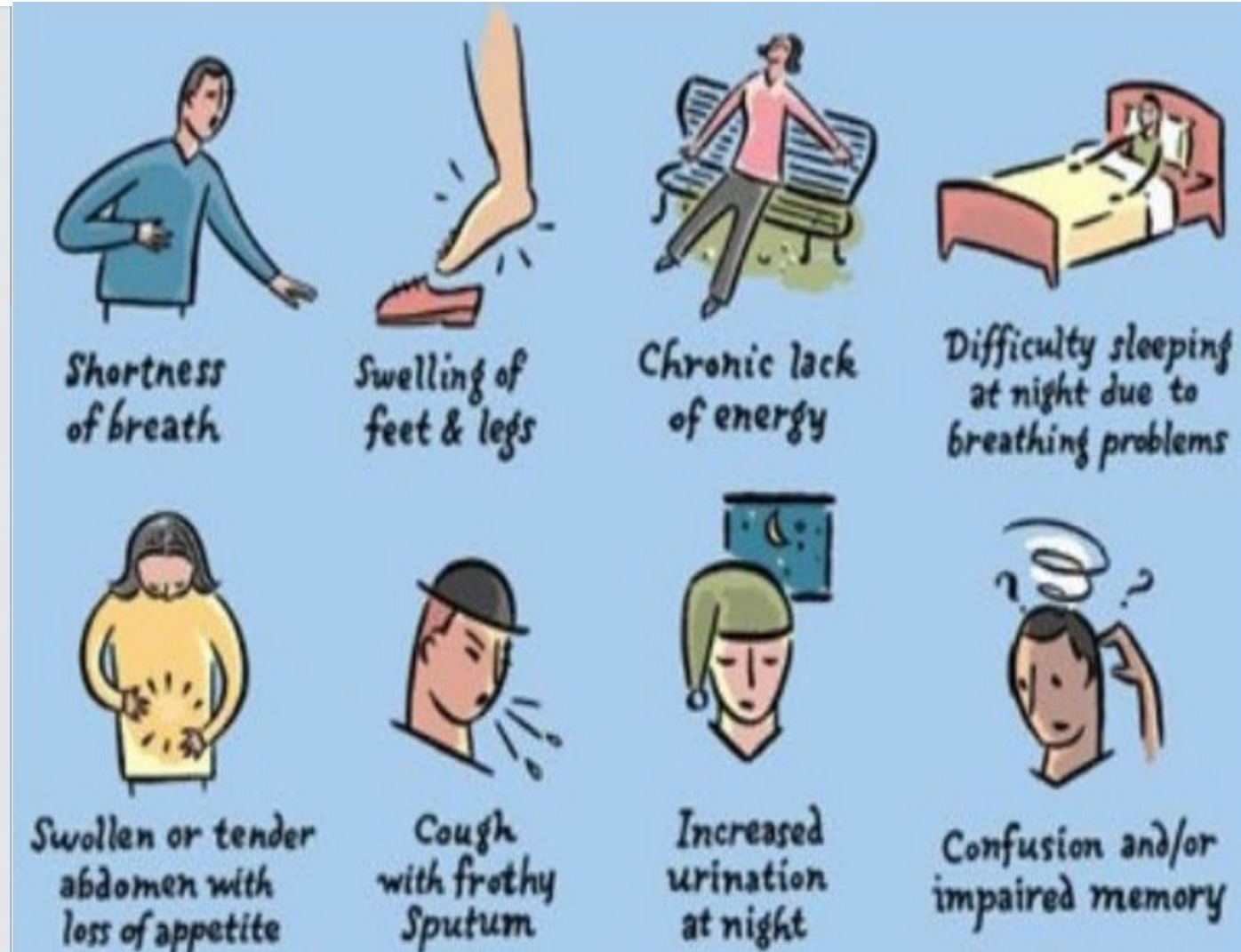
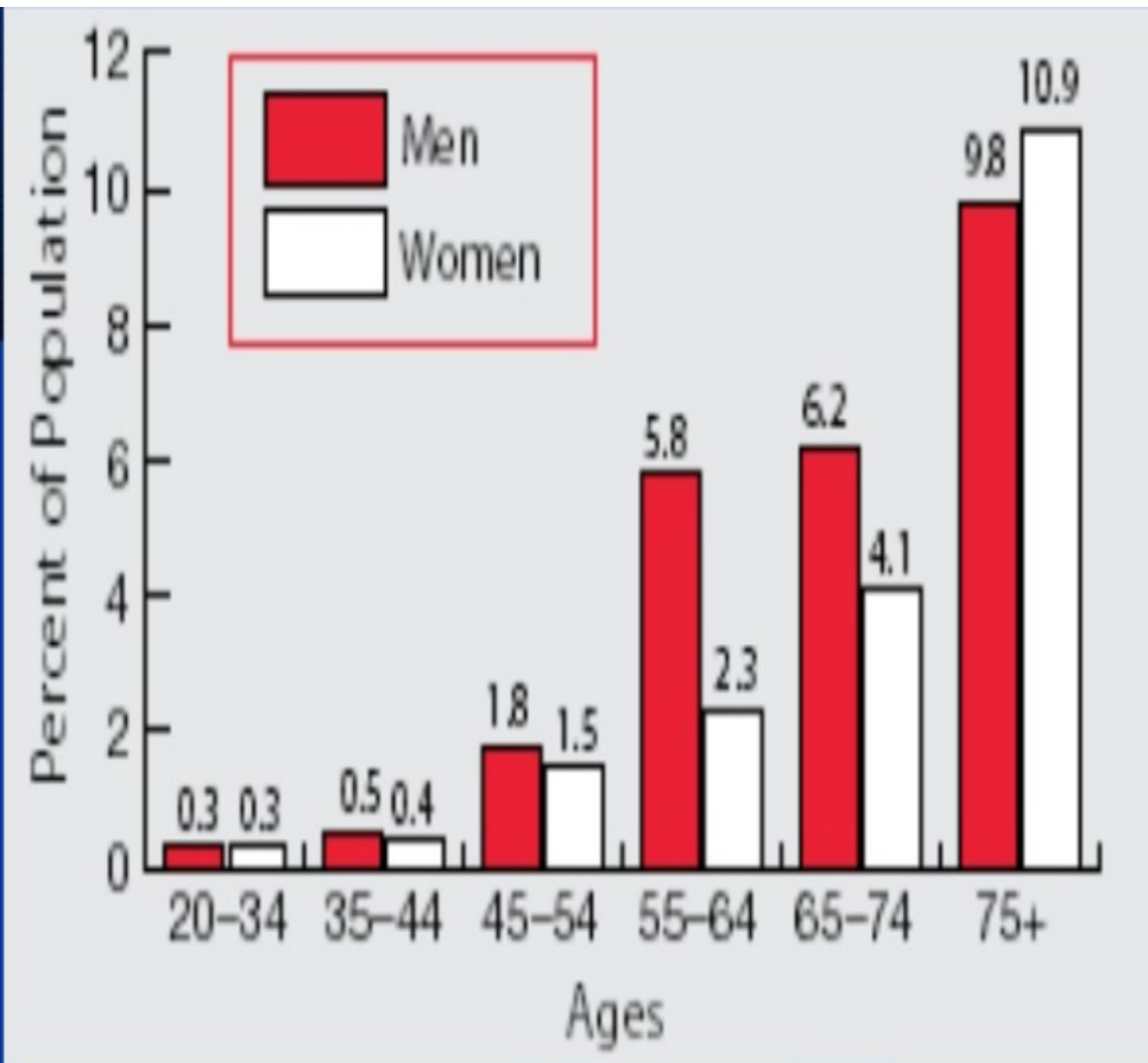
- Dizziness
- Peripheral vasodilation
- Broncho restriction
- Headaches
- Bradycardia
- Tendency to increase rhythm disturbances
 - (helps one kind but aggravates other rhythm disturbances)



Congestive heart failure

Prevalence USA

Signs & Symptoms



Congestive heart failure drugs



Agents that increase myocardial contraction force

- Digitalis

Agents that decrease cardiac workload

- ACE inhibitors
- Angiotensin II receptor blockers
- Beta adrenergic blockers
- Diuretics
- Vasodilators

Signs & symptoms of digitalis toxicity

Cardiac

- Sinus bradycardia
- Ventricular arrhythmias
- Atrio-ventricular block
- Atrial arrhythmias

Non-Cardiac

- Visual disturbances
- Fatigue
- Weakness
- Confusion
- Psychosis
- Anorexia
- GI upset

Hyperlipidemia

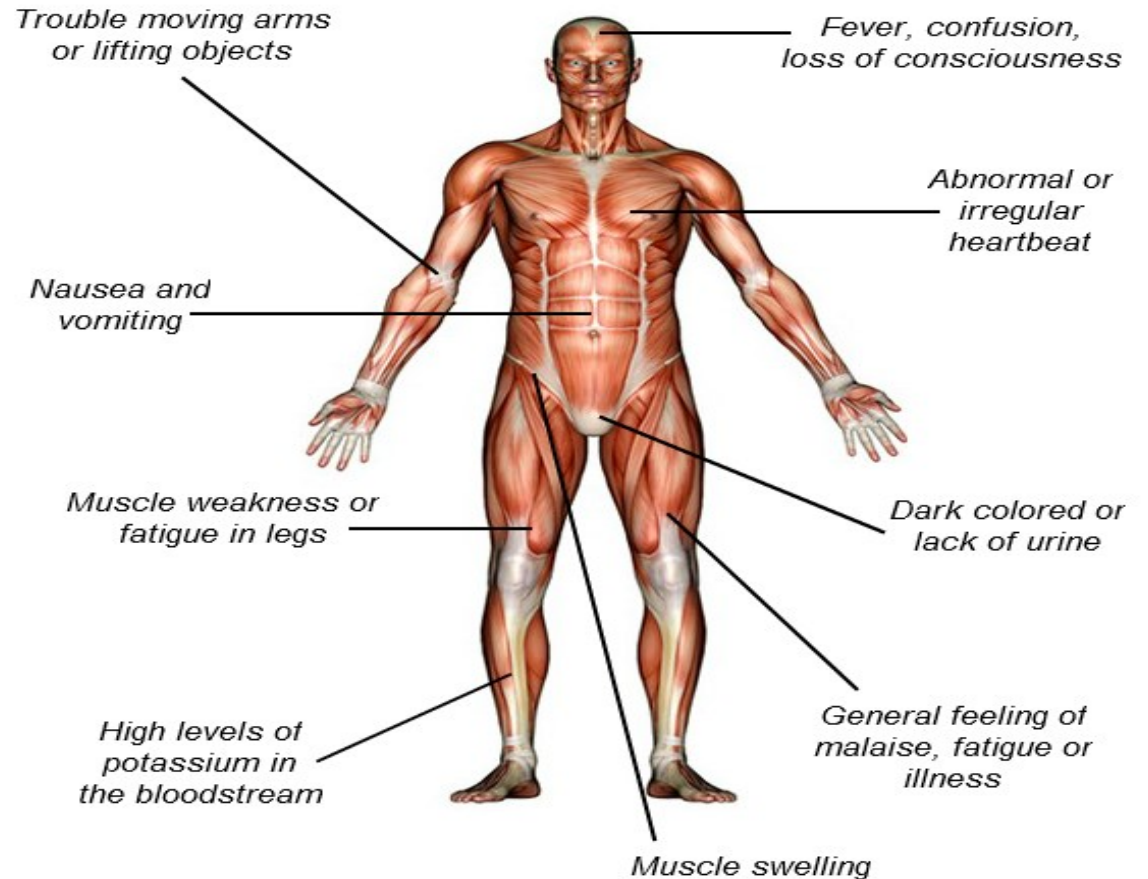
Over 22% of North Americans over the age of 45+ are taking cholesterol lowering statin drugs.

Side effects include:

- Muscle pain and damage
- Neurological side effects
- Liver/kidney damage
- Digestive problems
- Rash or flushing
- Increased blood sugar or type 2 diabetes
- Sexual dysfunction

What is rhabdomyolysis?

Exercise is great for the body. Too much of it, though, can have long lasting, harmful effects on the human body. Rhabdomyolysis is a condition that breaks down overworked muscles and releases the fibers into the bloodstream, causing many complications.



Clotting disorders

Antiplatelets

- Inhibit platelet aggregation & platelet-inducing clotting
- Used primarily to prevent arterial thrombus formation

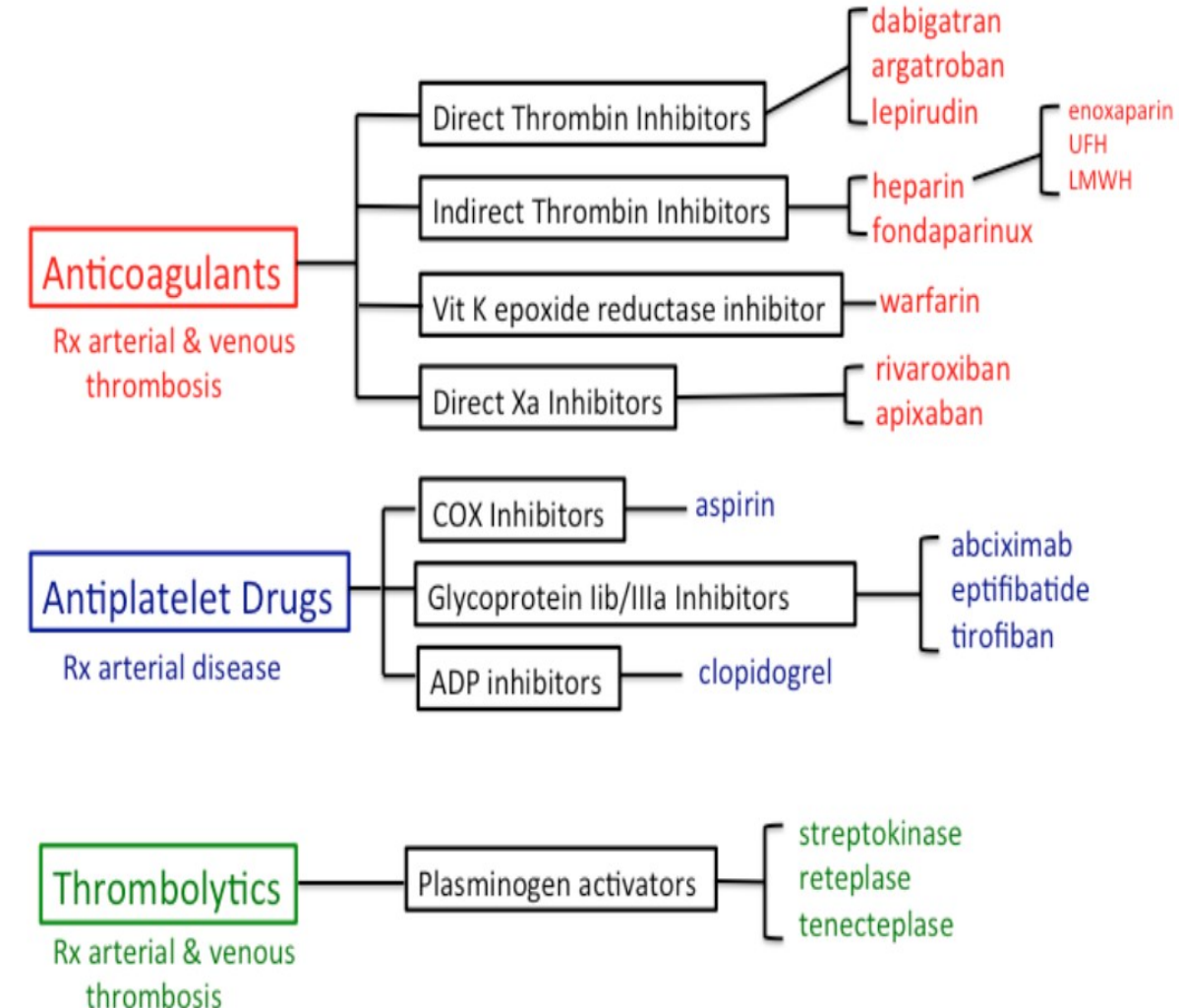
Anticoagulants

- Inhibit synthesis & function of clotting factors
- Used primarily to prevent and treat venous thromboembolism

Thrombolytics

- Facilitate clot dissolution
- Used to reopen occluded vessels in arterial & venous thrombosis

Drugs Used to Treat Clotting Disorders



Clotting disorders

Anti-coagulant medications		
Class	Generic name	Trade name
Anti-platelets	ASA	Aspirin
	Clodogrel	Plavix
	Ticlopidine	Ticlid
	Abciximab	ReoPro
	Eptifibatide	Integrilin
	Tirofiban	Aggrastat
	Dipyridamole	Persantine
	Anistreplase	Eminase
	Streptokinase	Streptase
	Urokinase	Abbokinase

Ciccone 2007

Adverse

Effects:

- Dizziness
- Nausea
- Bleeding
- Headache
- GI upset
- GERD
- Vomiting
- Gastric ulceration
- Skin rashes
- Neutropenia
- Thrombocytopenia
- Palpitations

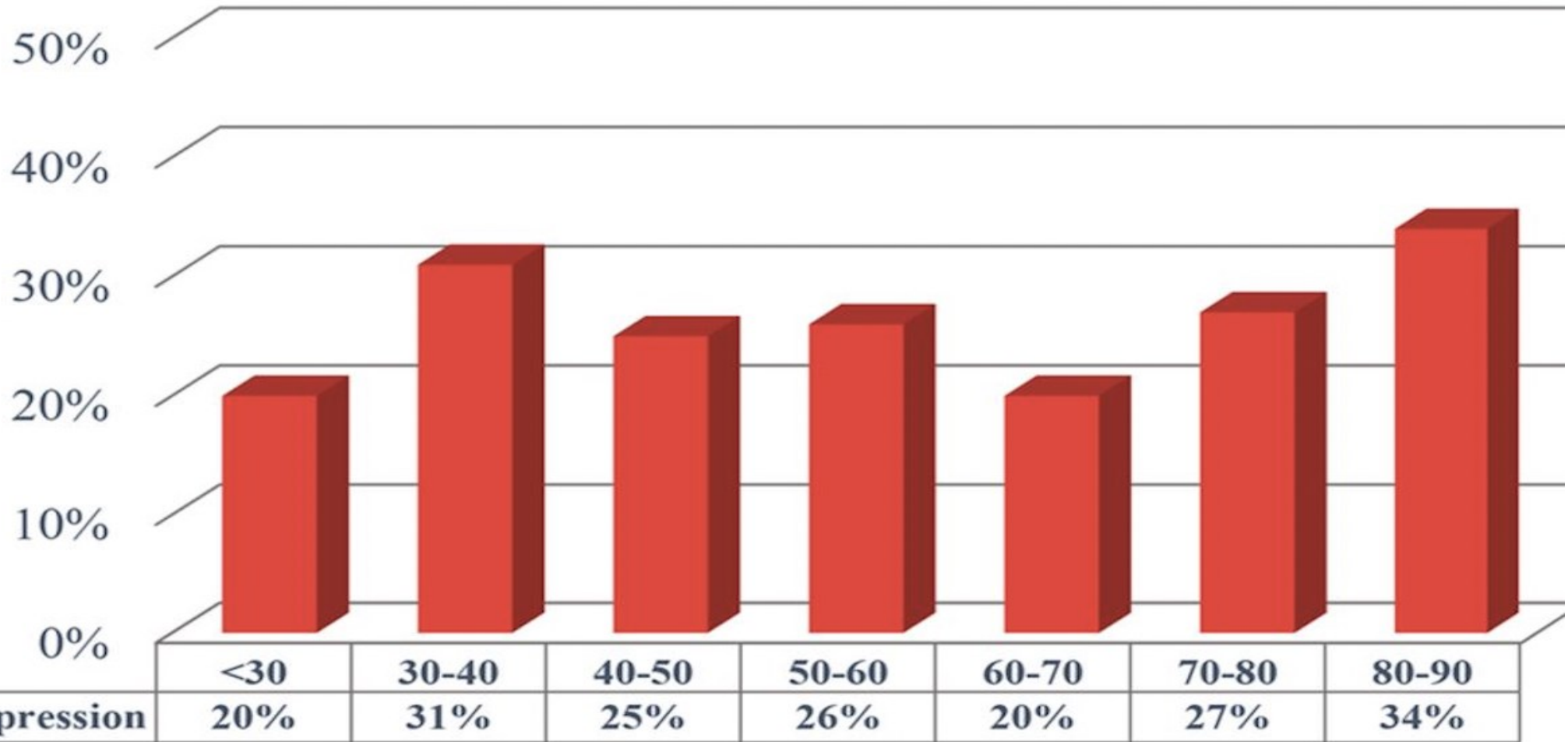
Pharmacology for Physiotherapists

Central & Autonomic Nervous Systems



Depression

Prevalence of depression(%) **B**



Depression Screening



Two Questions to ask:

1. Over the past 2 weeks have you ever felt down, depressed or hopeless?
2. Over the past 2 weeks, have you felt little pleasure or interest in doing things?

Sensitivity 96%

Specificity 57%

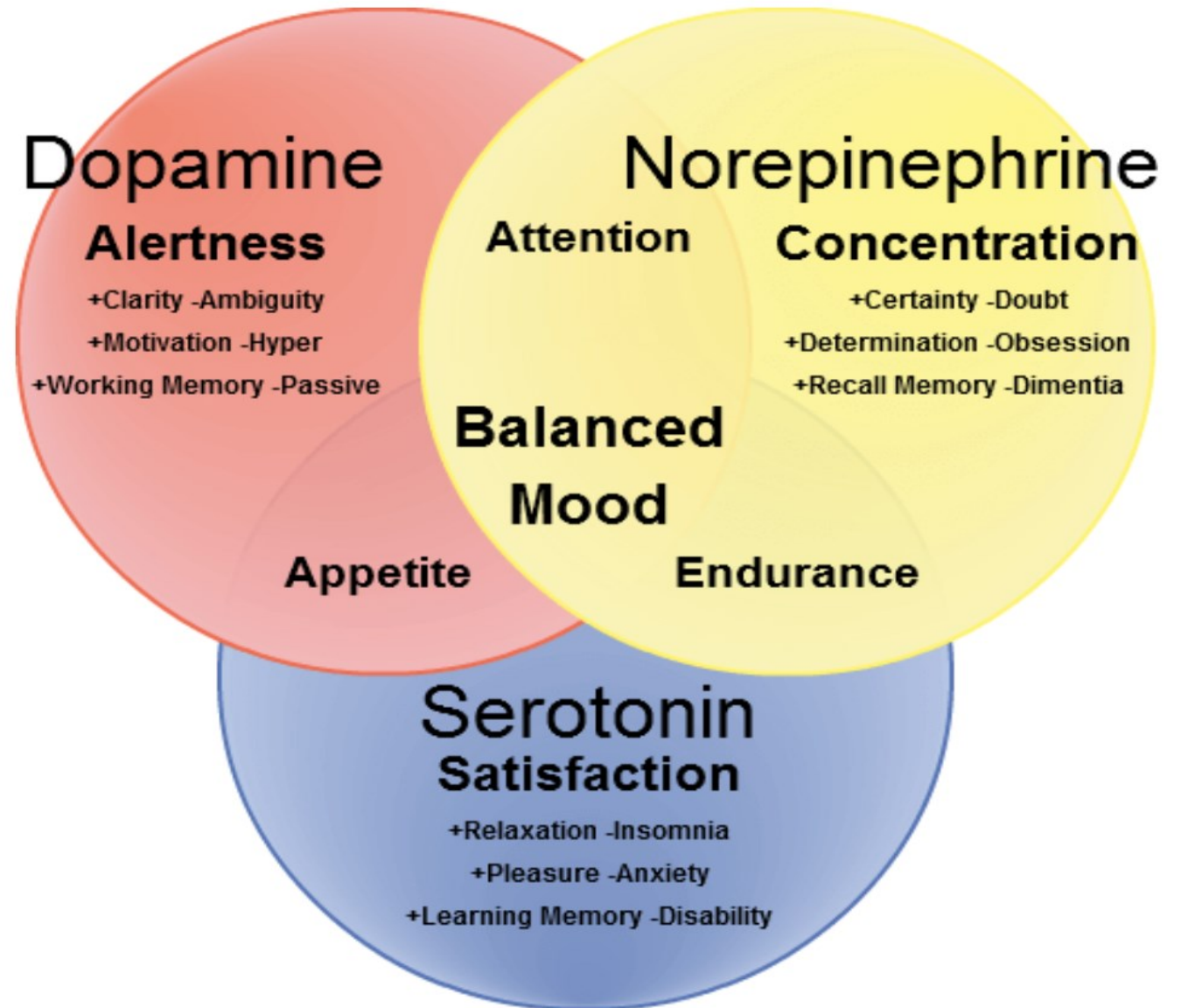
Other questions:

- How are things at work?
- How are things at home?
- We all have stress in our lives.
- Has your stress level increased lately?
- How are you handling it?

Depression

Currently considered to be related to disturbance in CNS neurotransmitters:

- Serotonin
- Norepinephrine
- Dopamine



Presenting complaints



- Apathy
- Malaise
- Vague abdominal pains
- “Stressed out”
- Sleep problems
- Sexual dysfunction
- Lack of libido
- GI complaints (constipation, diarrhea)
- Chronic pain
- Joint pains
- Headaches
- Fatigue

Antidepressants



Tricyclics

- Work by blocking re-uptake of amine neurotransmitters

MOA inhibitors

- Reduce enzyme that removes amine neurotransmitters

Adverse responses

- Sedation
- Seizures
- Confusion
- Orthostatic hypotension
- Tremors
- Cardiac arrhythmias
- Constipation
- Anticholinergic effects
- Weight gain
- Loss of libido
- Urinary retention

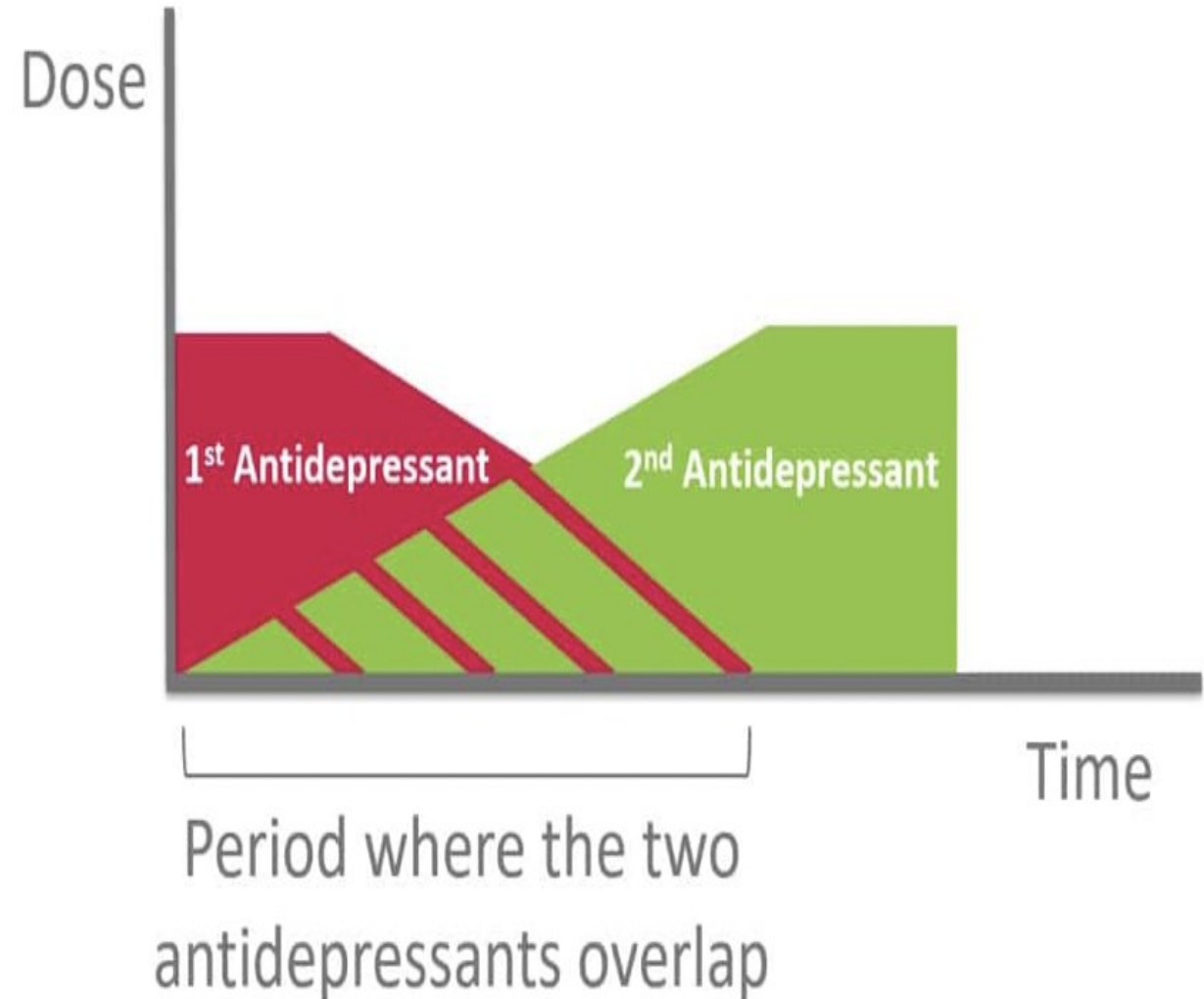
Antidepressants “Second generation”

Work by blocking reuptake of monoamines

Much fewer adverse effects than tricyclics & MOA inhibitors

Adverse effects:

- Seizures
- Insomnia
- Agitation
- Anxiety
- Tremors



Pharmacology for Physiotherapists

Musculoskeletal system



Oral analgesics

Salicylates

- ASA
- Aspirin
- Bufferin
- Excedrin

Acetaminophen

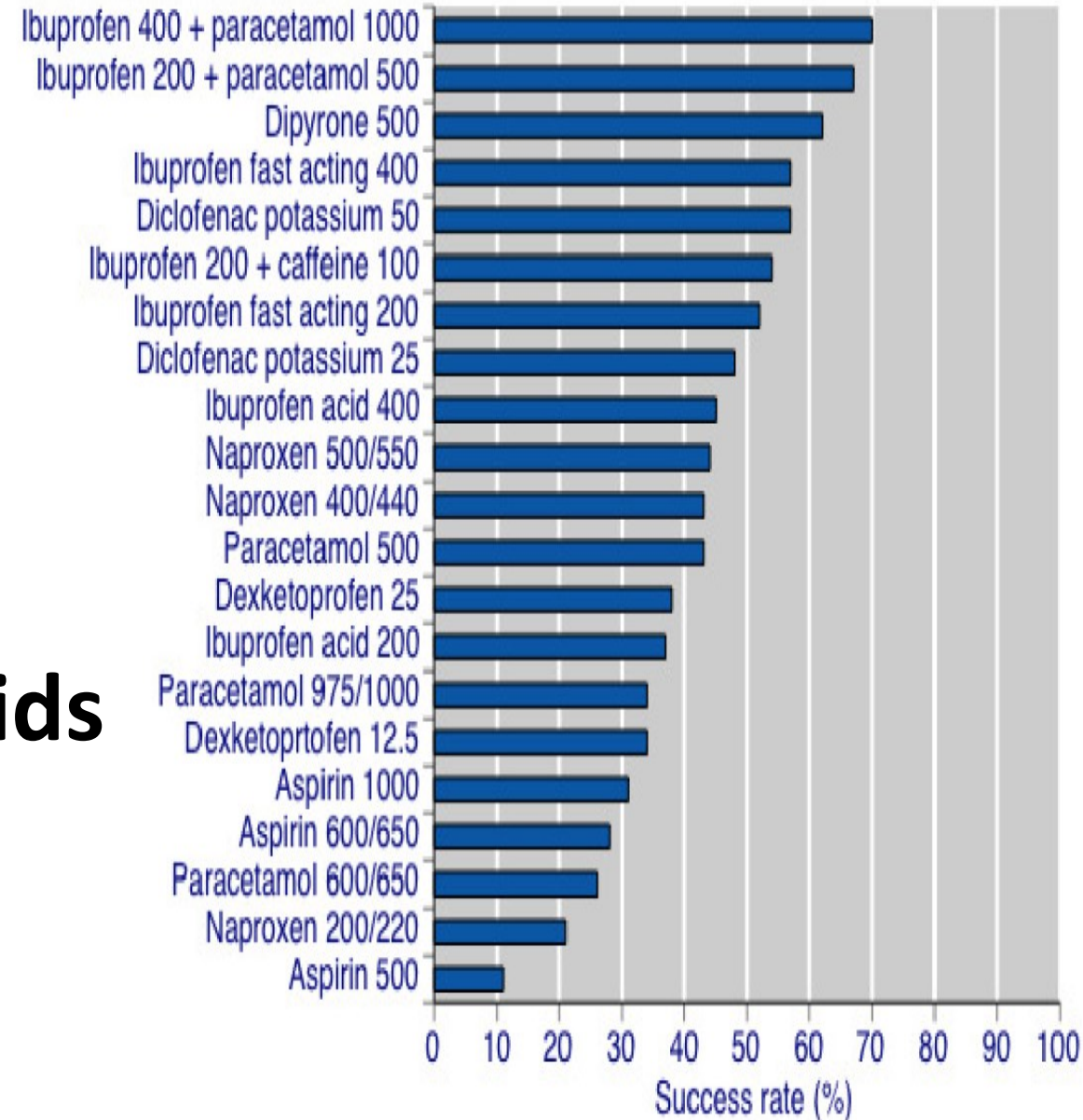
- Paracetamol
- Tylenol

NSAIDs

Ibuprophen
Naproxen

Gabapentanoids

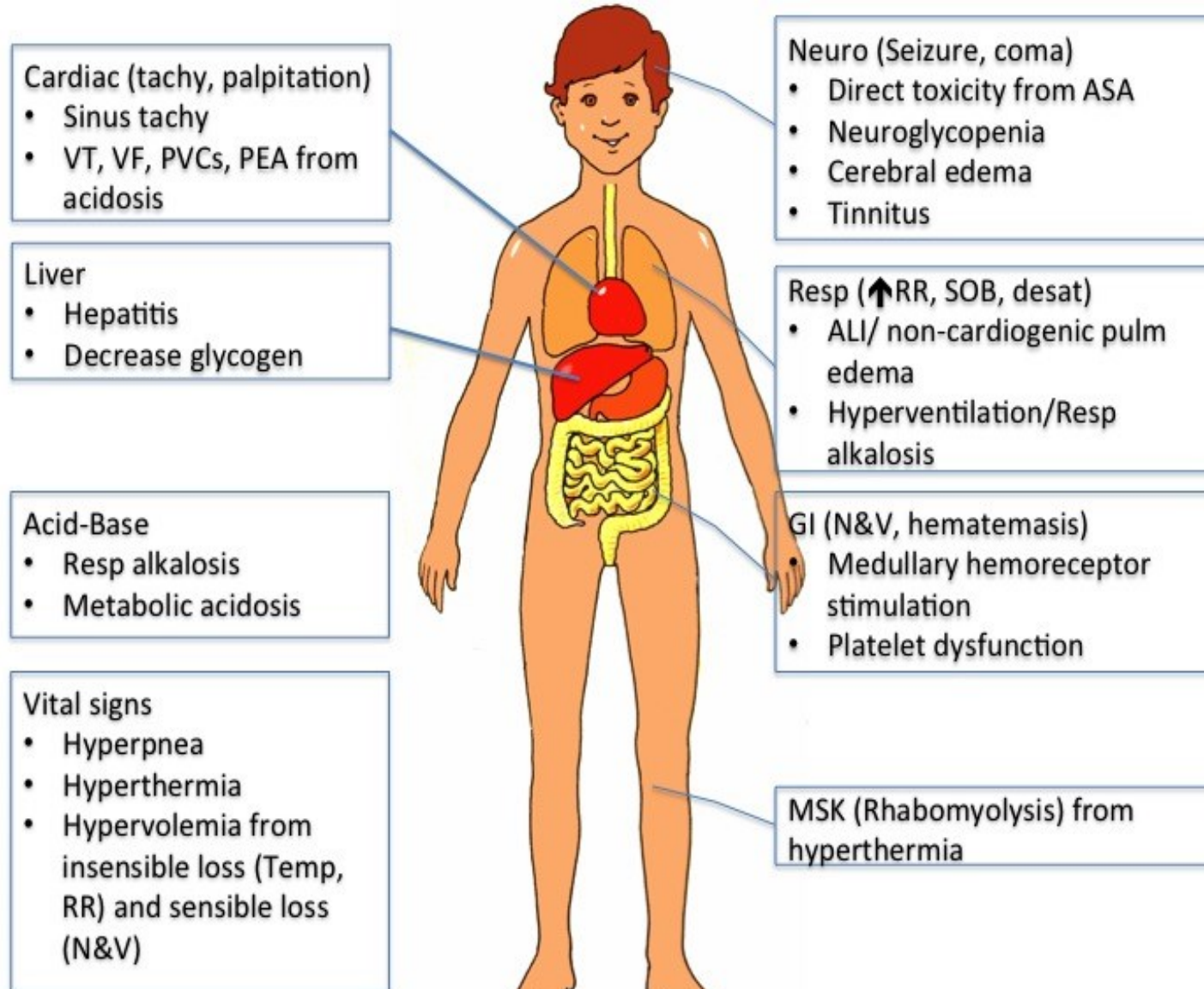
Neurontin
Lyrica



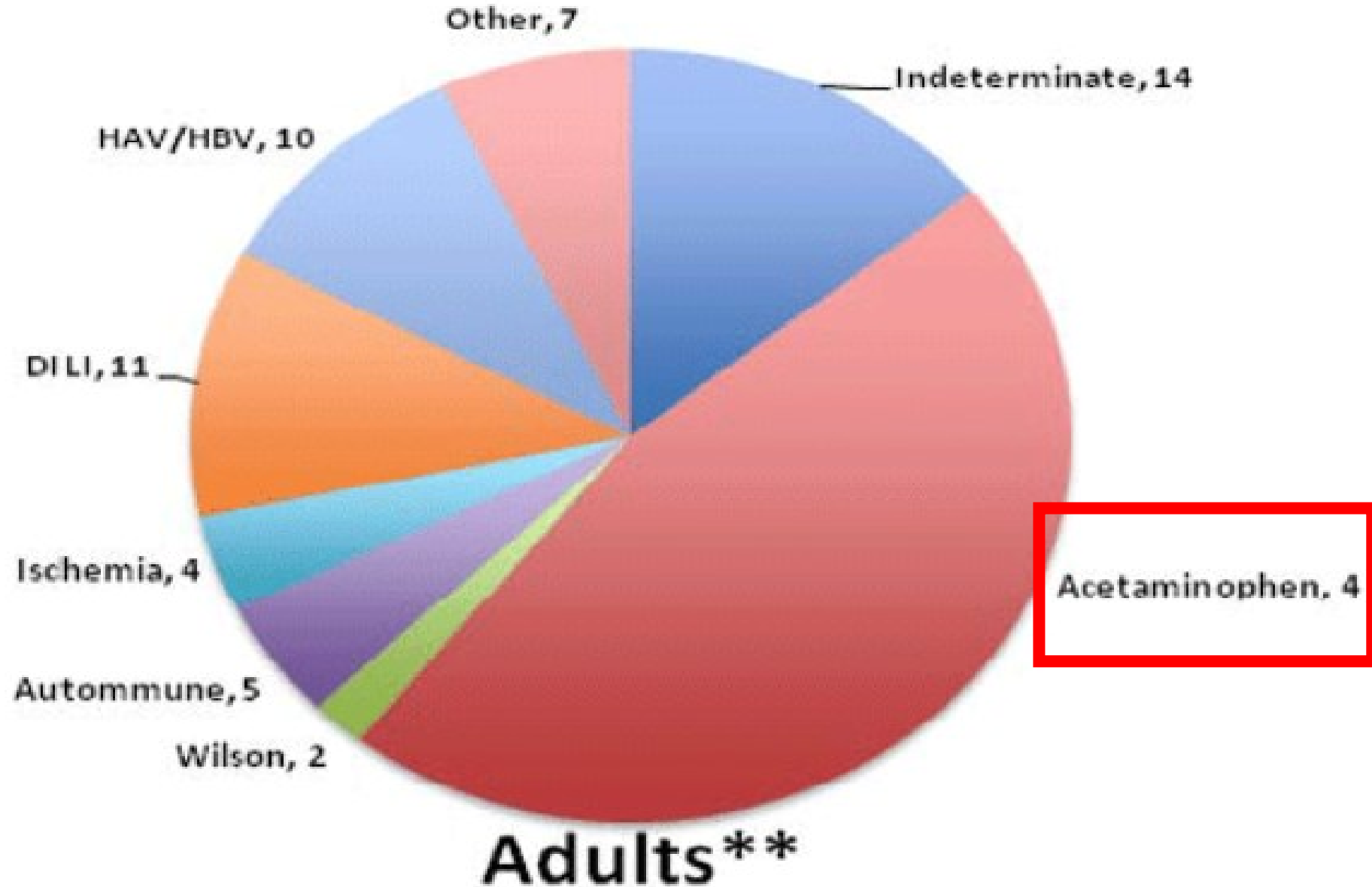
Salicylate overdose

Symptoms

- Restlessness
- Irritability
- Excessive & unorganized talking
- Fear & nervousness
- Deafness
- Confusion
- Excited mood
- Hallucinations
- Drowsiness
- Diploplia
- Seizures
- Burning in throat
- Vomiting
- Decreased urination



Tylenol hepatotoxicity



Gabapentinoids

Gabapentin (Neurontin)

Pregabalin (Lyrica)

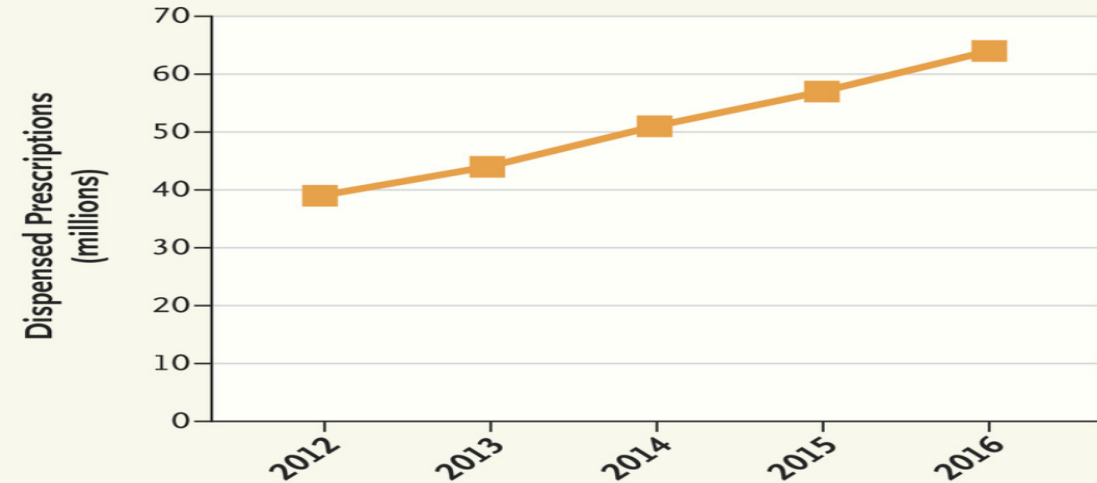
- Anticonvulsant
- Analgesic

Used in treatment of:

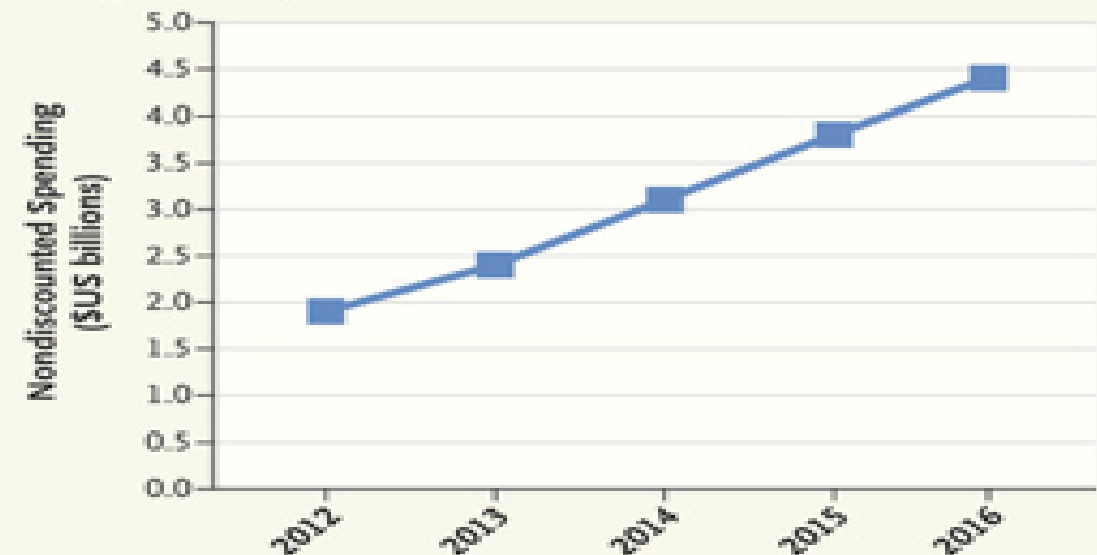
- Neuropathic pain
- Fibromyalgia
- Restless leg syndrome

Among top 15 drugs globally in terms of revenue

A Gabapentin Prescriptions



B Pregabalin (Lyrica) Spending



Gabapentinoids

Adverse effects:

- Seizures (on withdrawal)
- Risk of suicidal behaviours
- Head/body injuries
- Road traffic incidents

Molero 2019

Accidental opioid overdose increases when opioids are co-prescribed with gabapentin



60% Increase in odds of accidental opioid-related death when opioids are co-prescribed with moderate and high dose gabapentin compared to opioid use alone.

2x The risk of accidental opioid overdose nearly doubled with a co-prescription of very high dose gabapentin and opioids.

46% Of all gabapentin users were co-prescribed an opioid in 2013, making the risk of overdose particularly concerning as these drugs are often used together.

Gomes 2017

Opioid analgesics

Natural opium alkaloids

- Opium
- Morphine

Semi-synthetic opioids

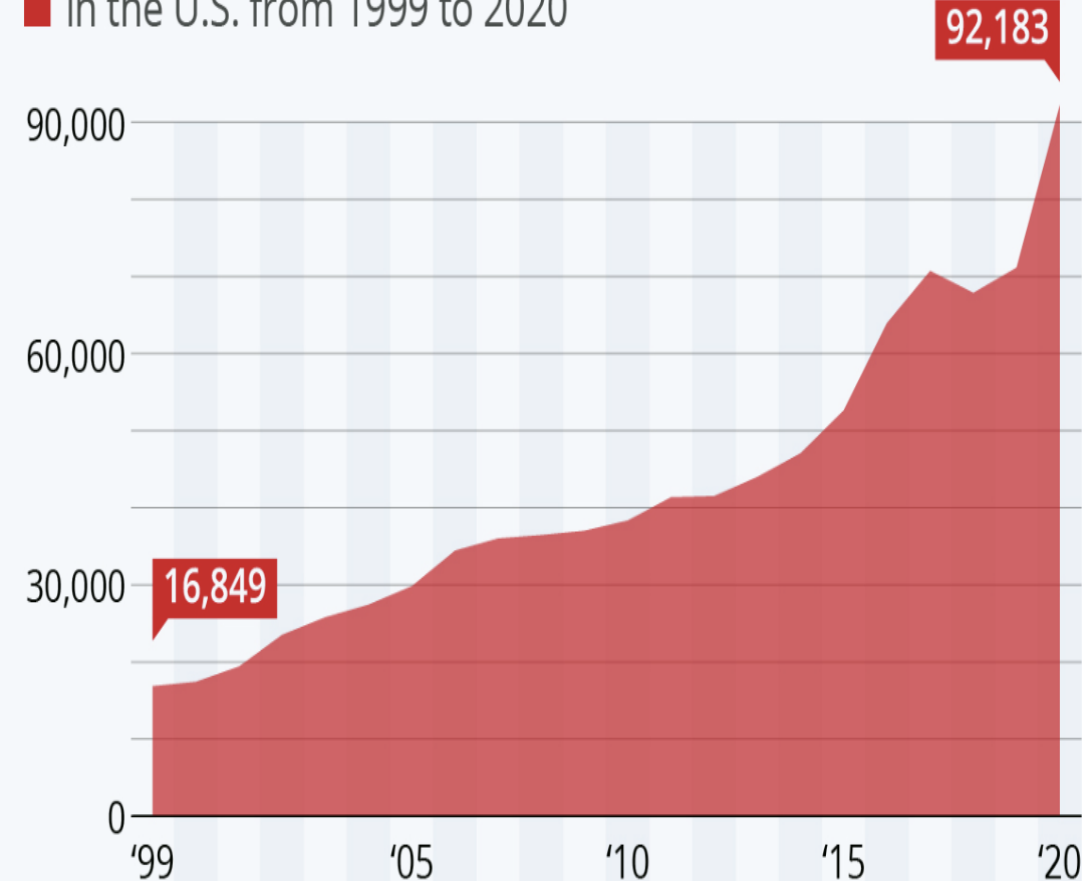
- Heroin
- Oxycodone
- Hydrocodone

Synthetic opioids

- Pethidine
- Fentanyl
- Methadone
- Tramadol

Historic Spike In U.S. Drug Overdose Deaths

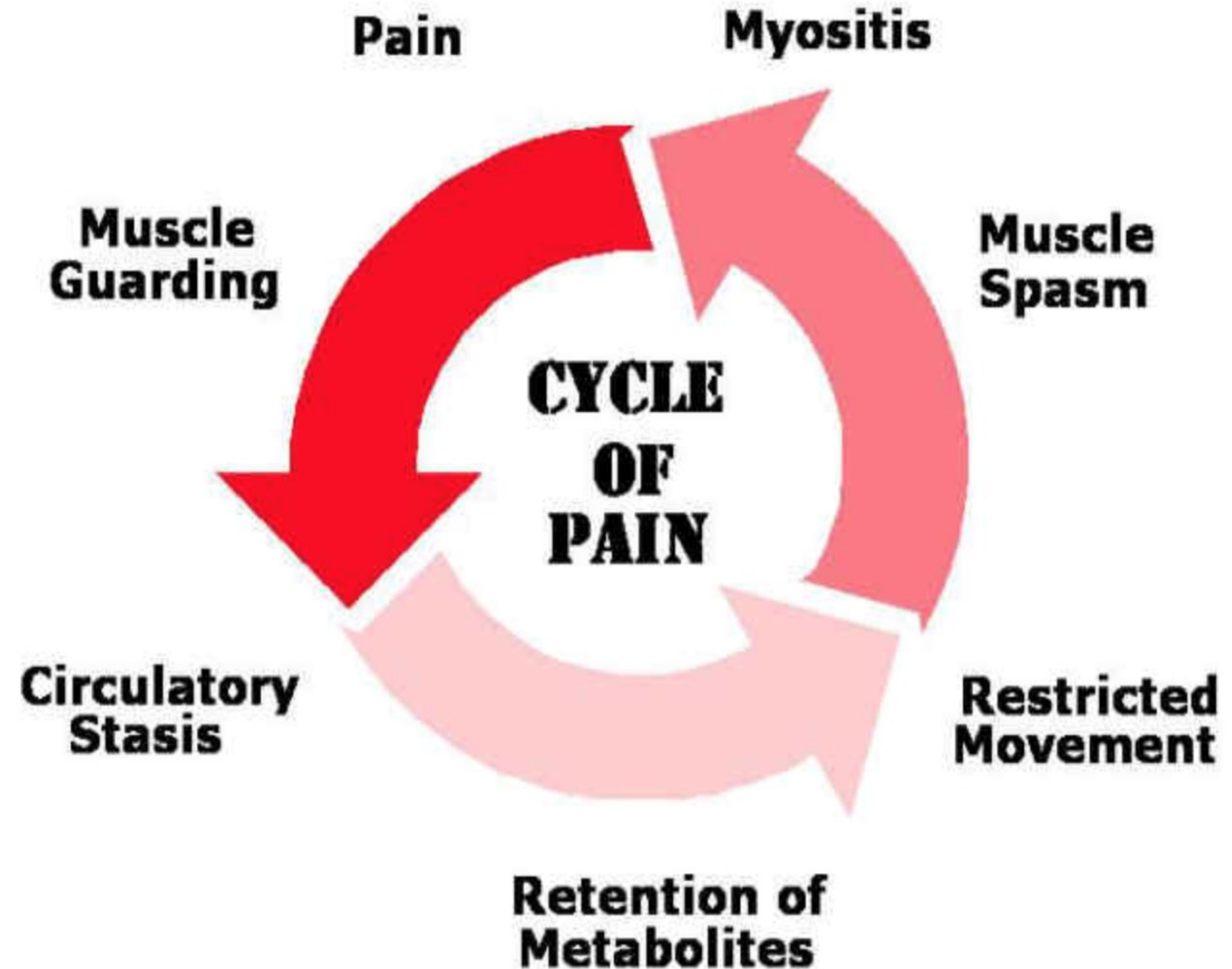
Number of drug overdose deaths in the U.S. from 1999 to 2020*



Increased muscle tone

Secondary to:

- Acute MSK injury
 - Cervical injury from MVC
- Visceral disease
 - Appendicitis
- Inflammatory response
 - Rheumatoid disease
- Psychological factors
 - Fear
- Electrolyte imbalance
 - Cramps



Muscle relaxants

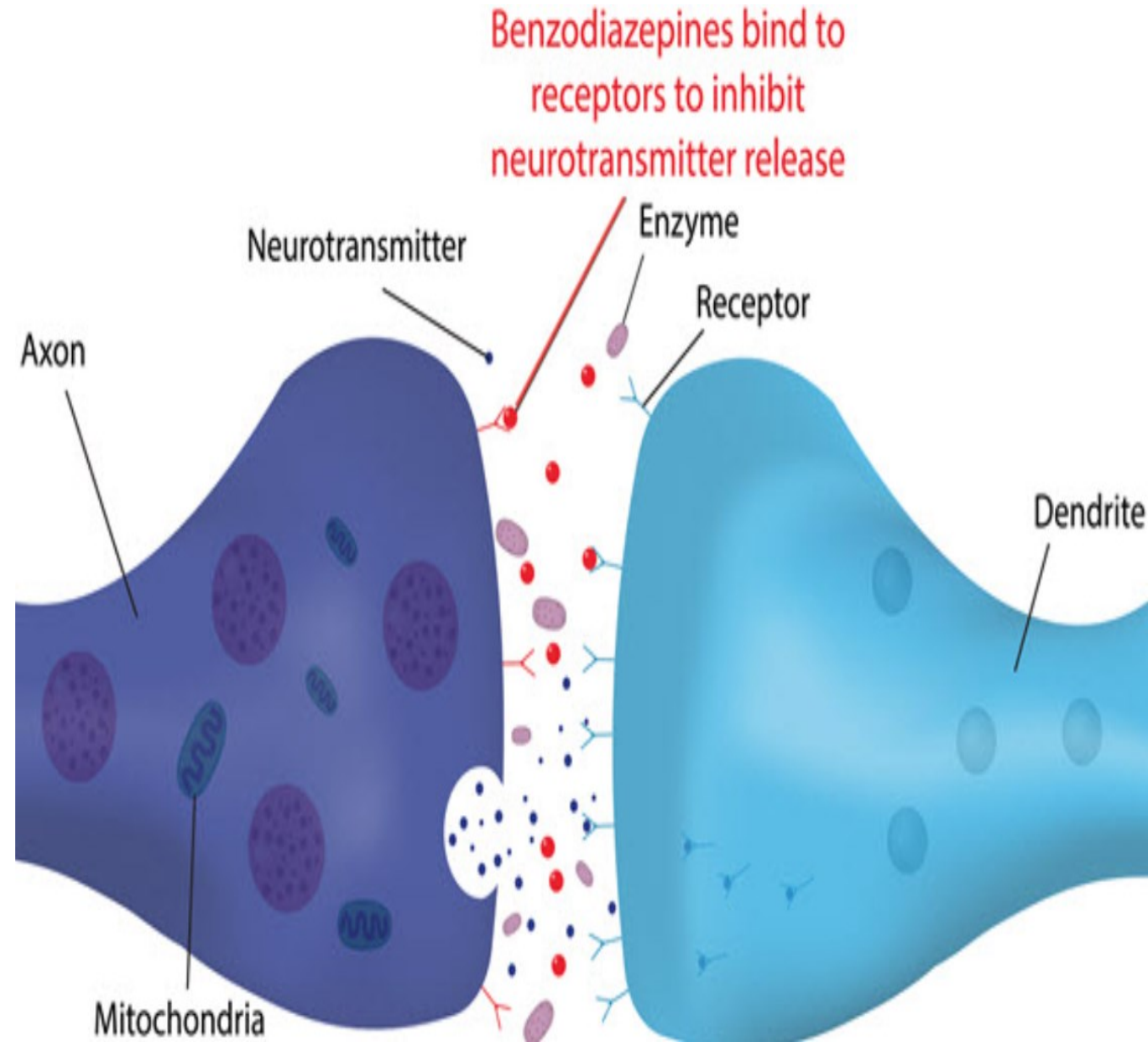
Centrally acting

Benzodiazepames

- Depress spinal polysynaptic reflexes
- Primarily used in outpatient setting

Examples:

- Diazepam
- Baclophen
- Mephenesin



Muscle relaxants

Generic name	Trade name	Adverse effects
Baclophen	Baclophen	<u>Drowsiness</u> <u>Confusion</u>
Datrolene Sodium	Dantrium	<u>Generalized muscle weakness</u> <u>Hepatotoxicity</u>
Diazepam	Valium Xanax	<u>Sedation</u>
Gabapentin Pre-agabalin	Neurontin Lyrica	<u>Sedation</u>
Trizanine	Halcion	<u>Sedation</u> <u>Dizziness</u> Dry mouth

Osteoporosis incidence

Primary osteoporosis

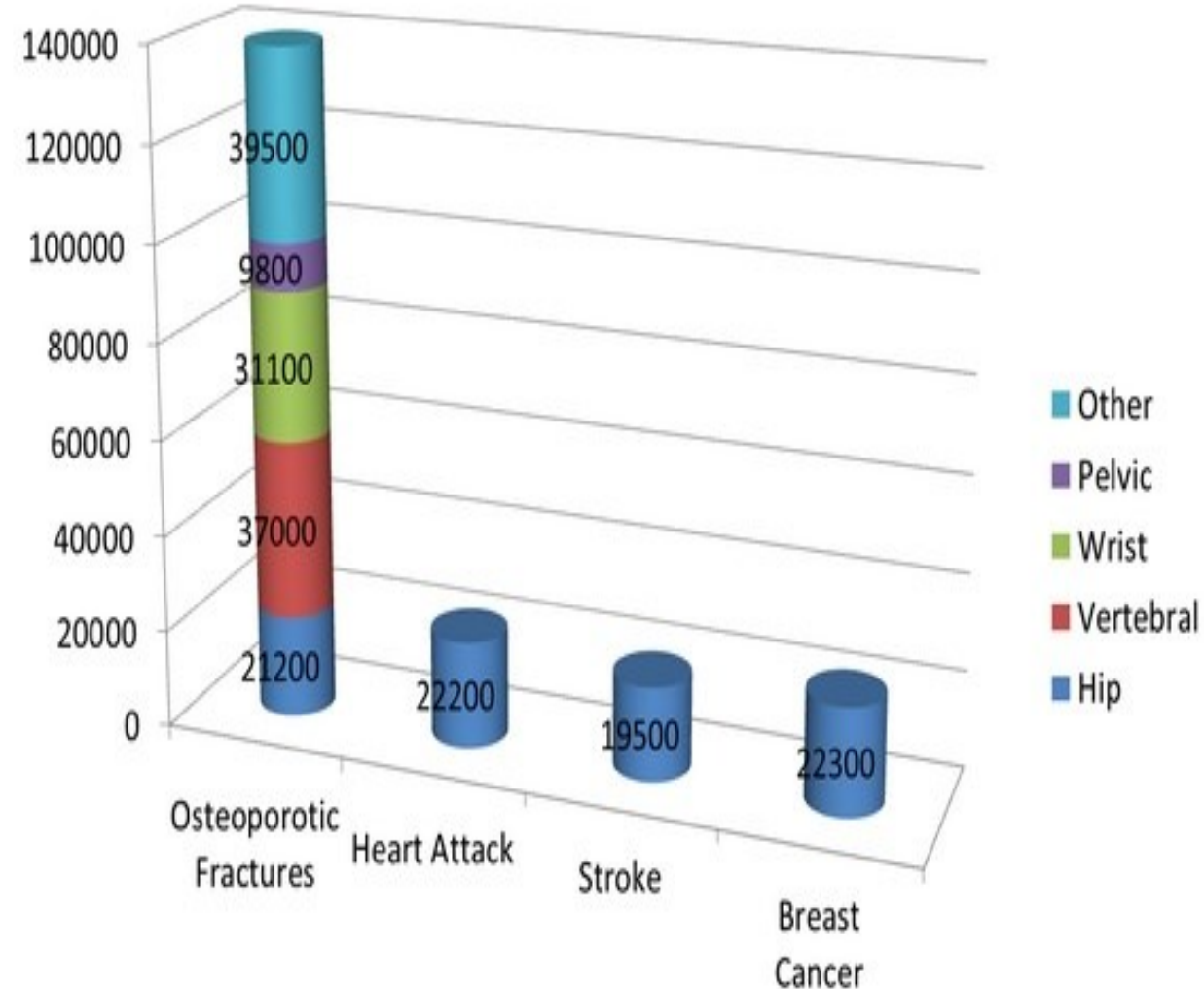
- Age-related disorder
- Reduced density of bone mass
- Increased risk of fracture
- Age and estrogen related

Secondary osteoporosis

Other causes:

- Hyperparathyroidism
- Malabsorption
- Multiple myeloma

Annual Incidence of Common Diseases



Medications contributing to osteoporosis



Anticoagulants

Long-term high dose heparin

- Increase osteoclast activity
- Decreased osteoblast activity

Long-term oral anticoagulants

- i.e. Warfarin
- Antagonist to Vitamin K

Antiepileptic drugs

- i.e Phenytoin
- Converts Vitamin D into metabolites

Loop diuretics

- i.e. Furosemide
- Decrease serum calcium

Gonadal-releasing hormone agonists

- i.e. Goselin, Leuprolide, Nafarelin

Glucocorticosteroids

- i.e Prednisone
- Alter calcium absorption & elimination leading to secondary hyperparathyroidism
- Inhibitory effect on sex hormone production
- Direct inhibition of osteoblast function

Medication treatment of osteoporosis



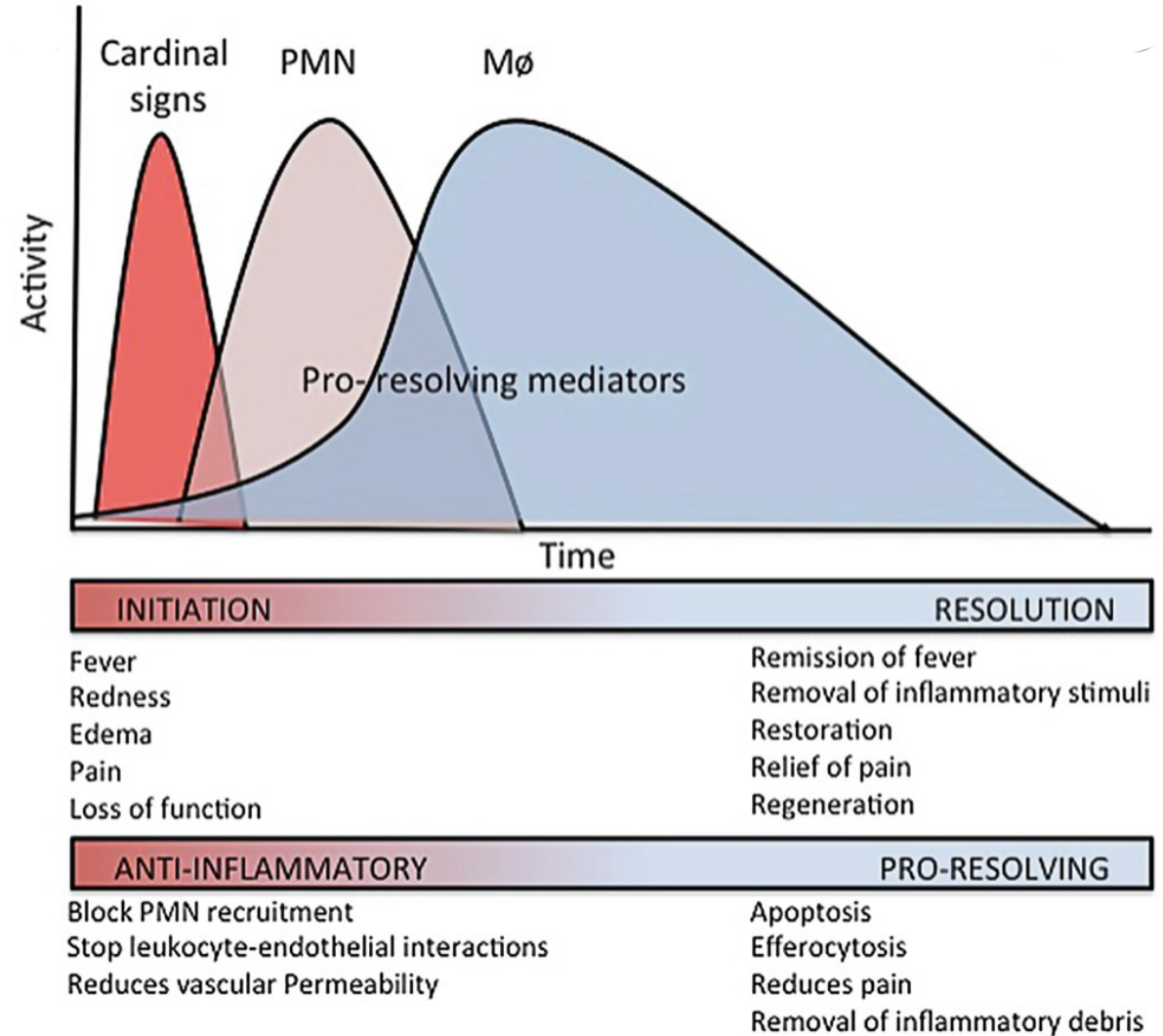
Class	Medications	Adverse effects
Calcium supplements	Tums, Citracal, Neo-calglucon	<u>Confusion, Hyperkalemia</u> , Constipation Headaches, Nausea
Vitamin D	Vitamin D supplements	<u>Fatigue</u> , Headache, Thirst, Anorexia, Metallic taste, GI disturbances
Bio-phosphates	Fosphomax Aredia	<u>GI disturbances</u> Reflux, Fever
Calcitronin	Cibacalcin Calcimar	<u>Stomach pain</u> , Redness, swelling at injection site, GI disturbance, Redness hands & feet
Estrogen	Raloxifen Evistra	<u>Cardiovascular disease</u> Certain cancers

Acute inflammation

- The body's response to injury
- Signals the immune system to heal and repair tissue

Triggers for acute inflammation

- Infections
- Trauma
- Physical & chemical agents
- Tissue necrosis
- Foreign bodies
- Immune reactions



A positive and protective physiological response

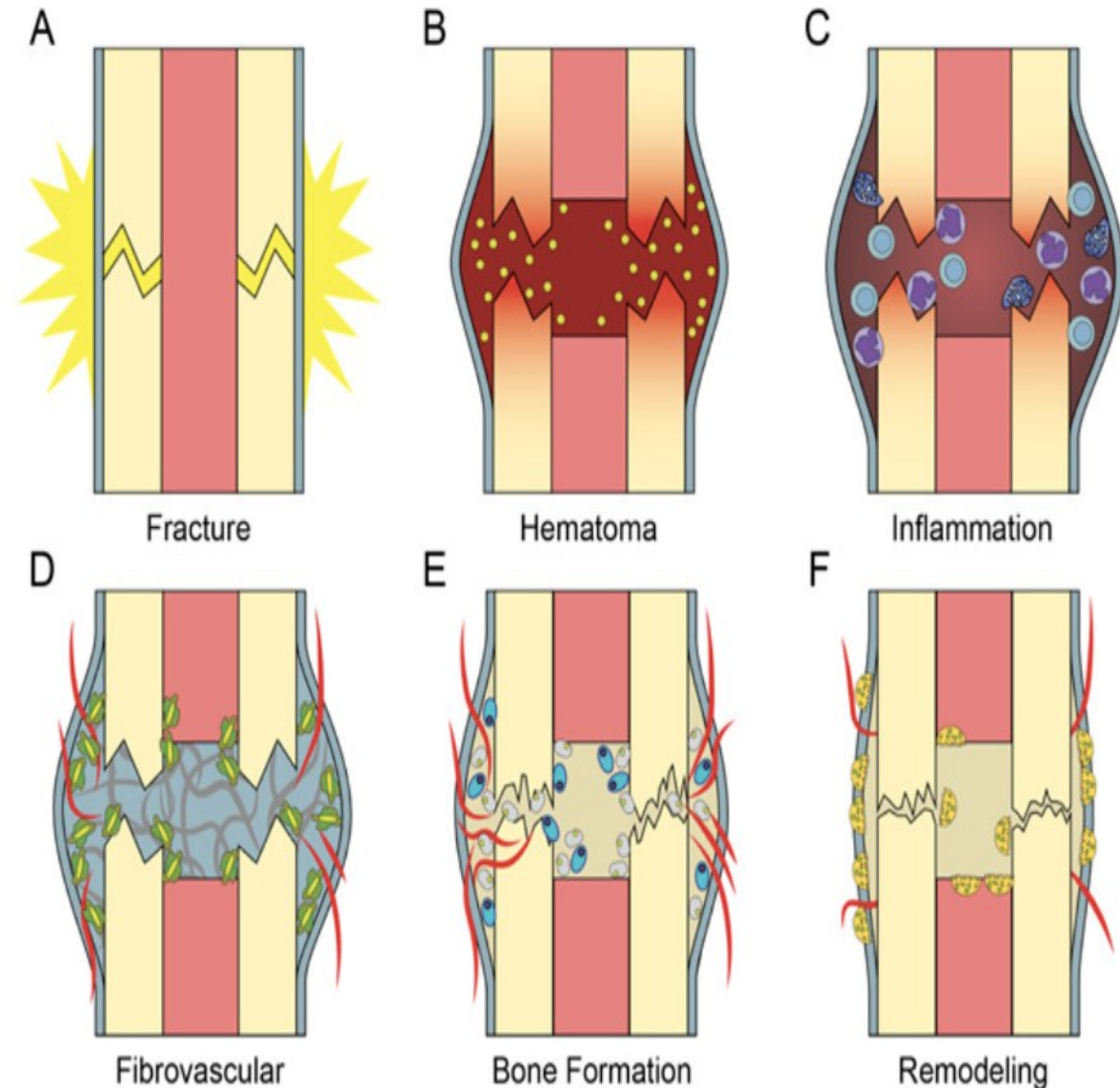
NSAIDs & bone healing

Meta analysis of 16 studies

Post fracture NSAIDs

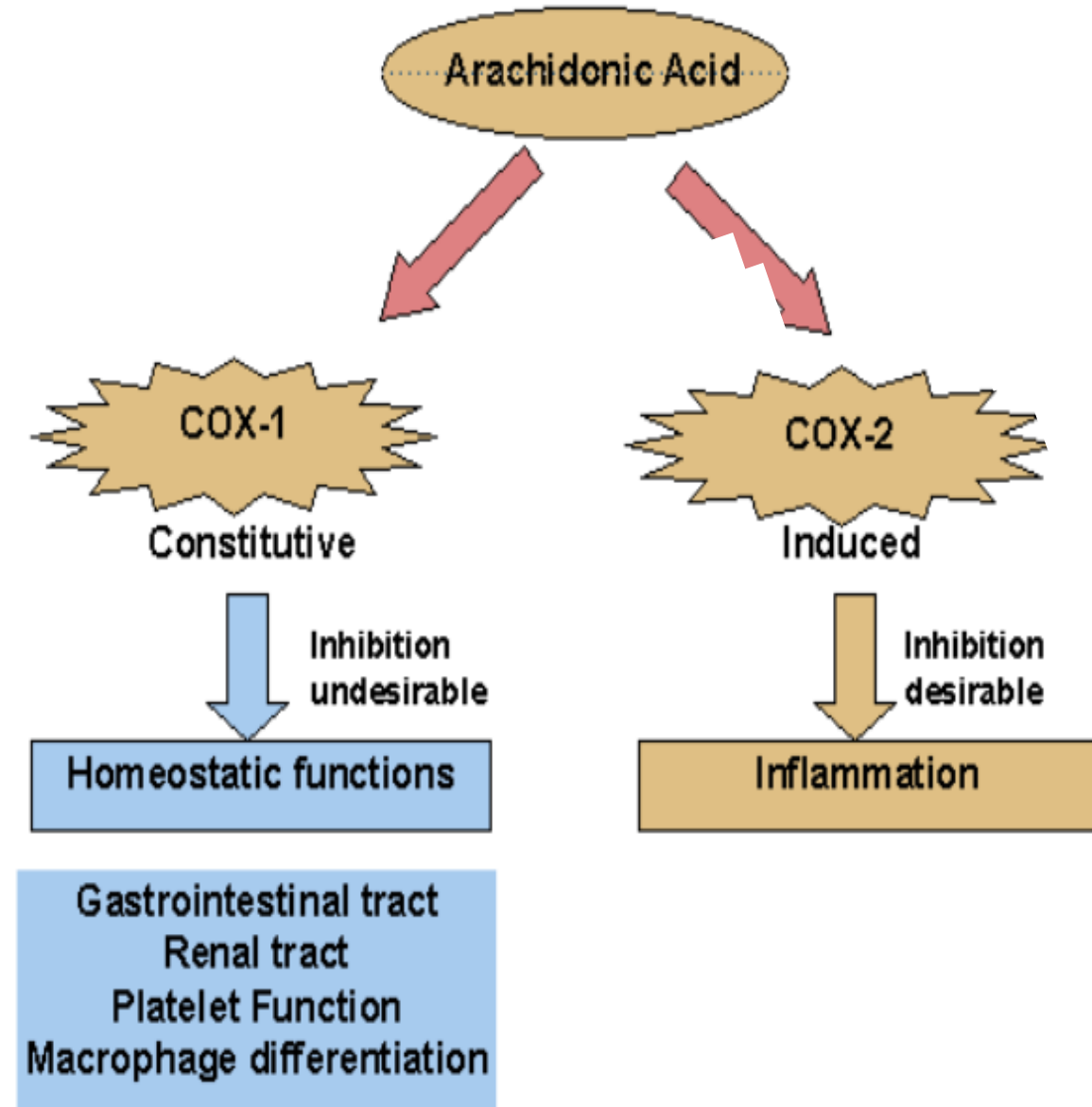
- Delayed union
- Non-union
- pseudarthrosis

“NSAID exposure increased delayed union or non-union odds ratio 2.07”

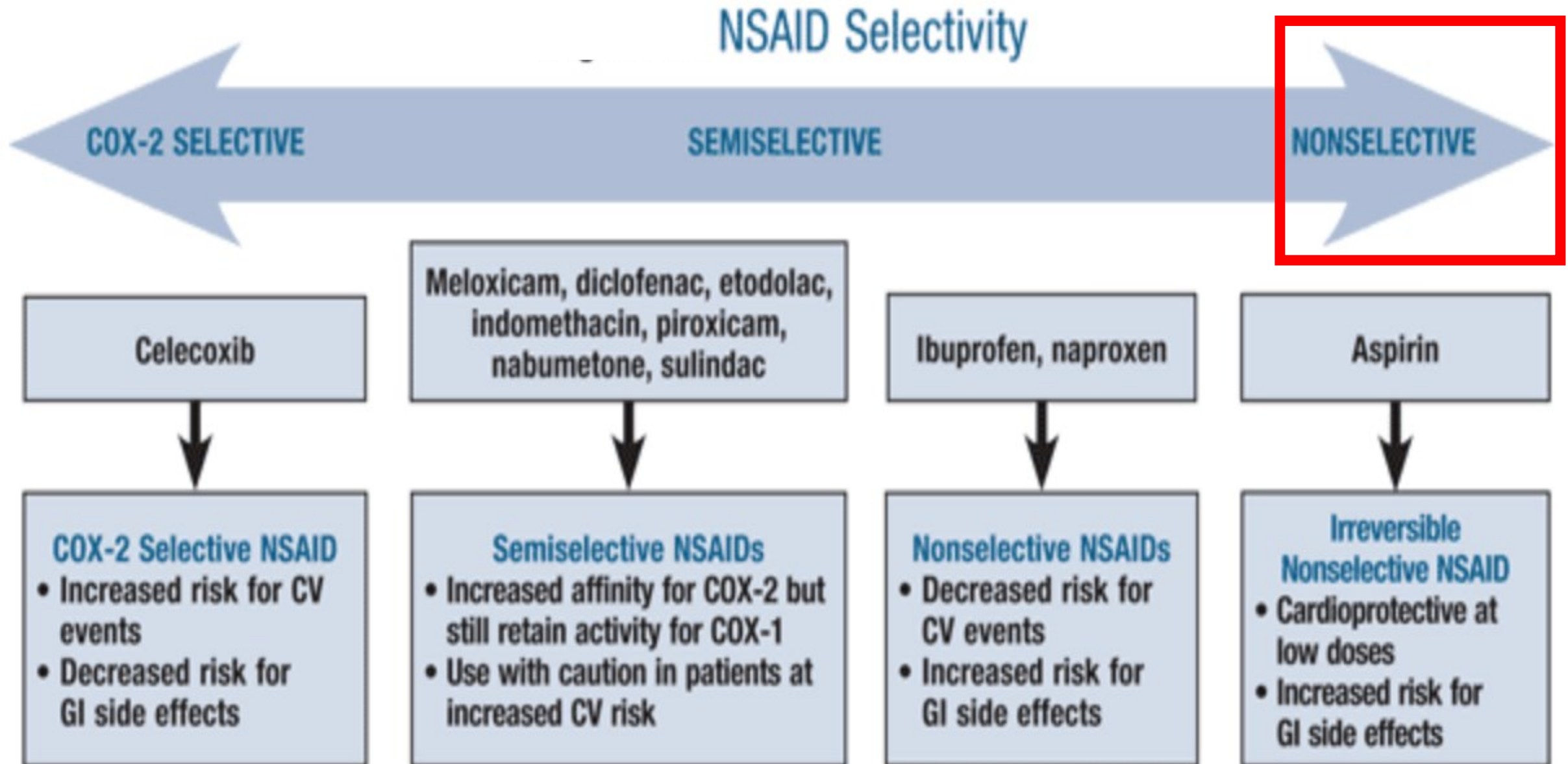


Role of prostaglandins

- COX 1 responsible for mediating normal cell activity (i.e. help protect stomach lining from gastric acid secretions)
- COX 2 produced by injured cells mediate pain and inflammatory response



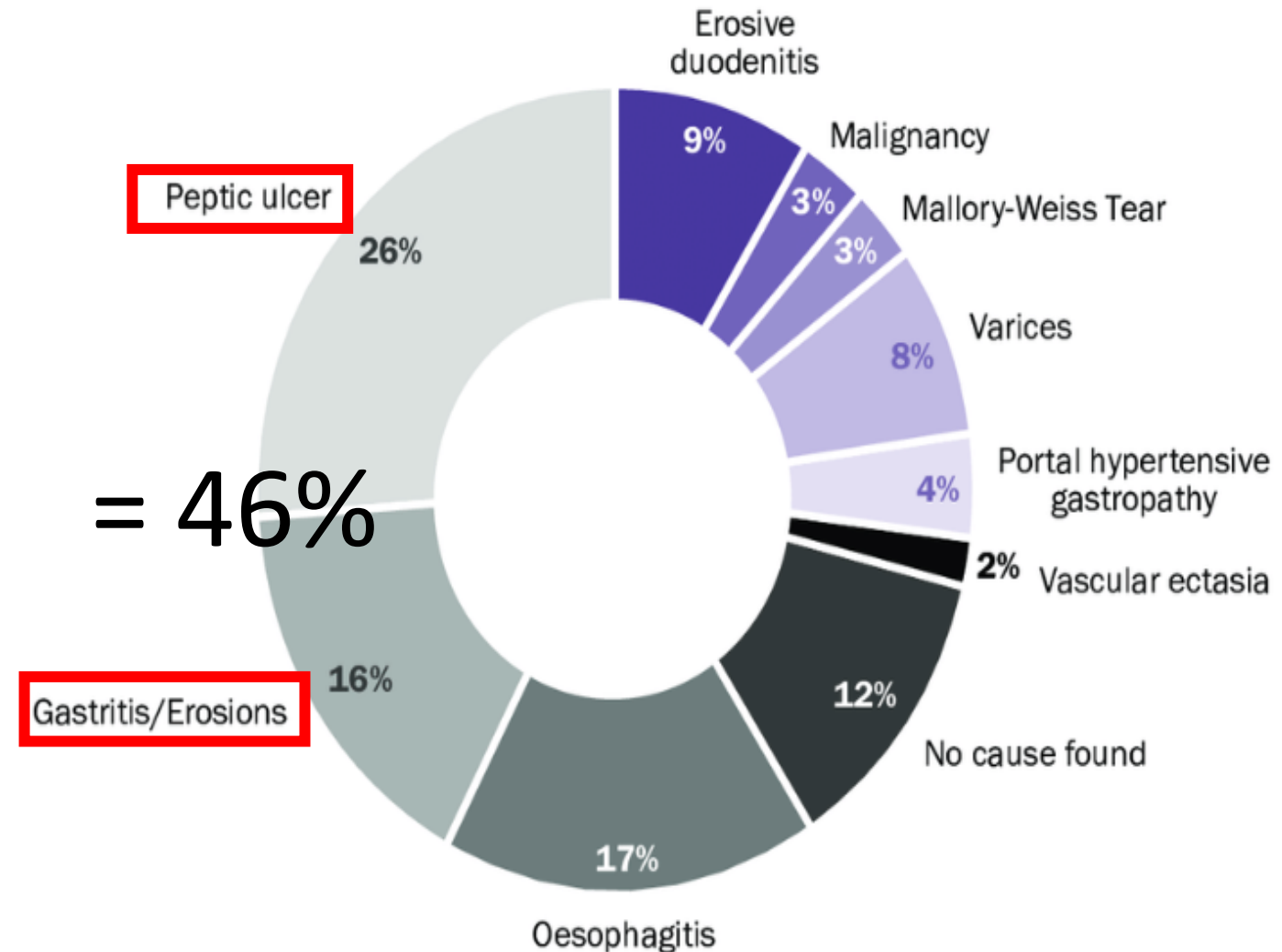
Non-Steroidal Anti-Inflammatory Drugs



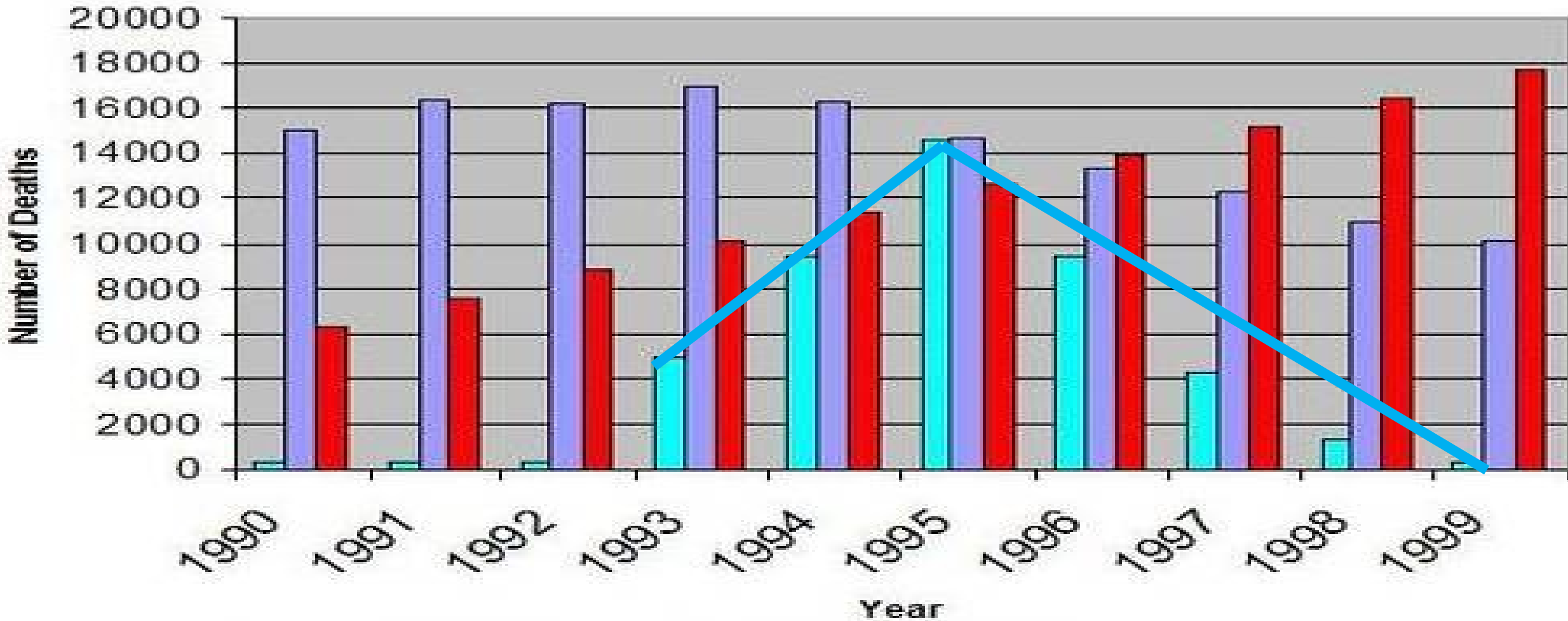
Signs & Symptoms of Acute GI bleed

- Coffee ground vomit
- Bloody diarrhea
- Stool colour may vary between:
 - Bright red blood
 - Black tarry

Causes of death from Acute GI bleed in UK



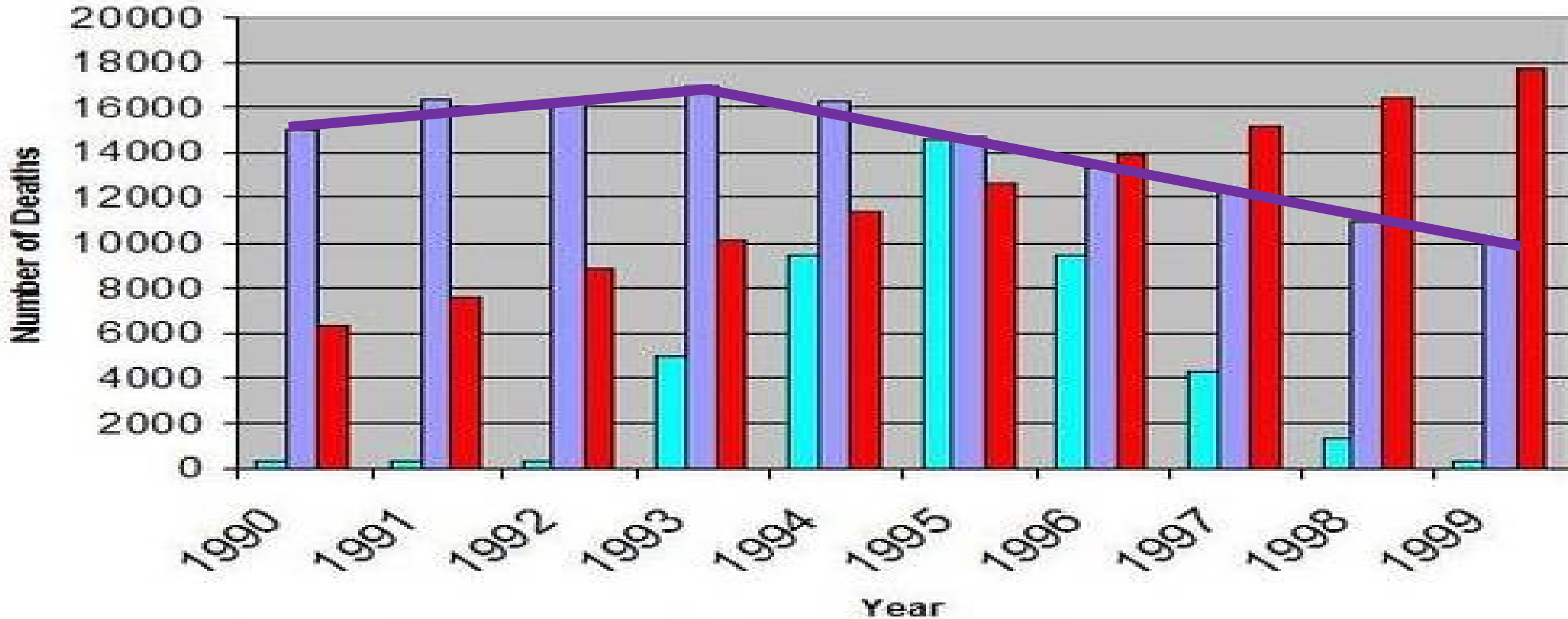
Deaths from war



Deyo 1999



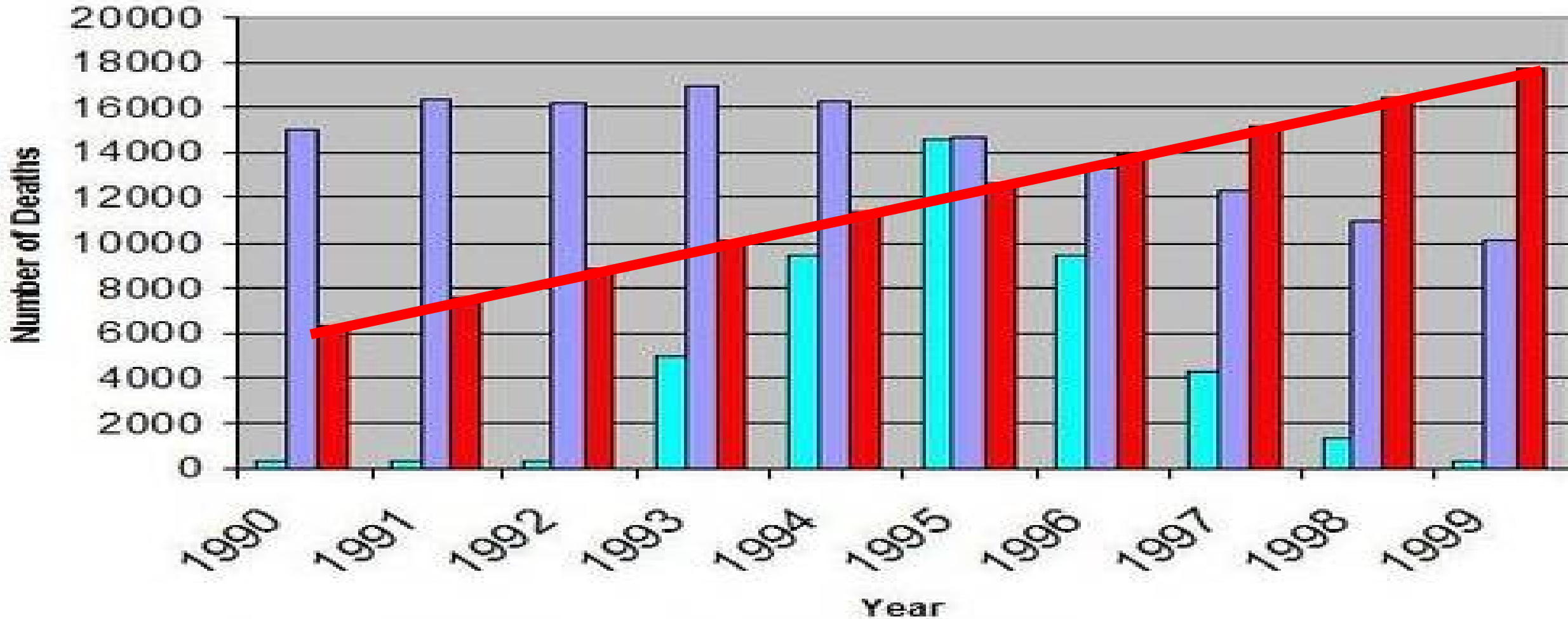
Deaths from guns



Deyo 1999



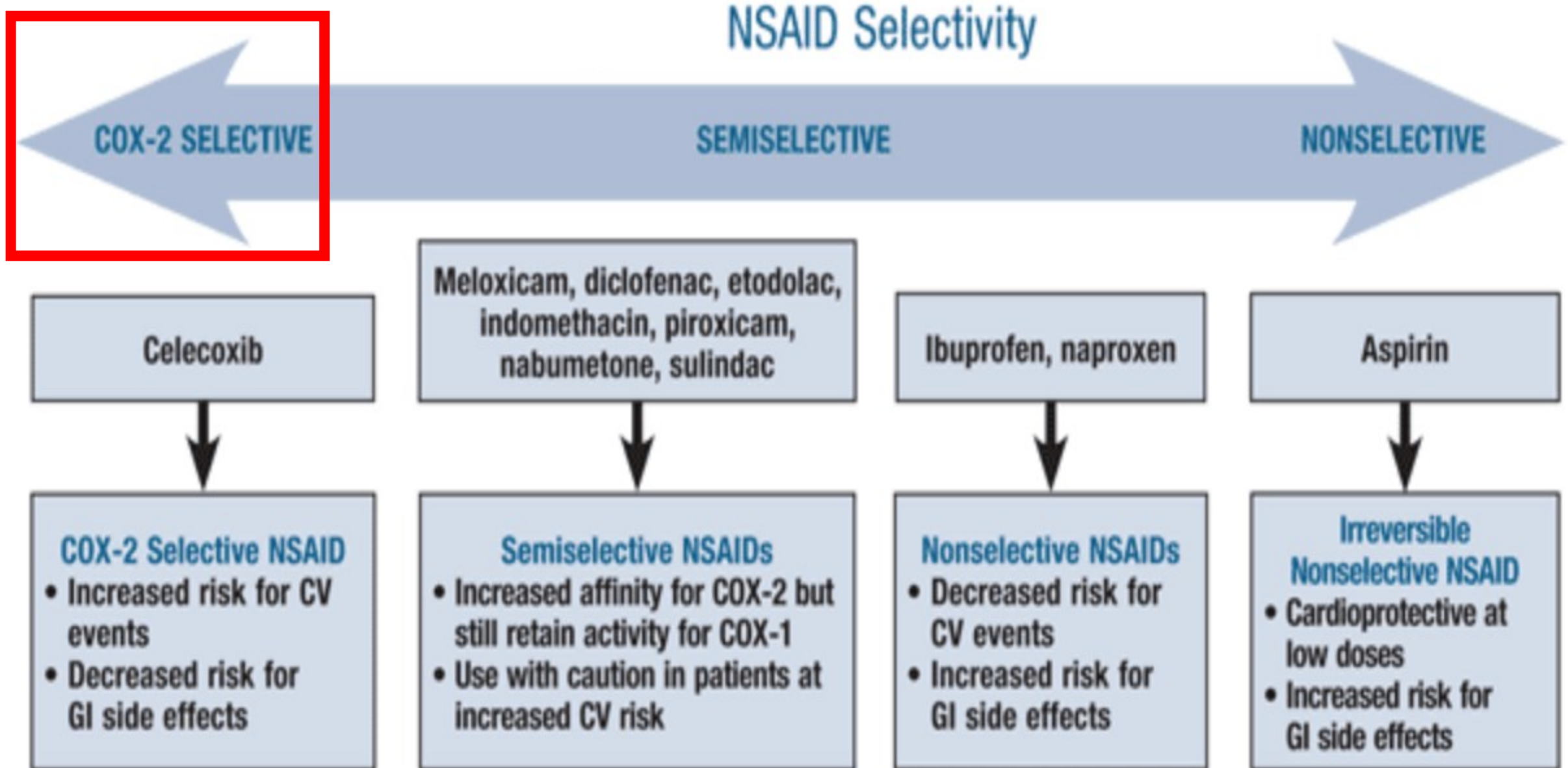
Deaths from NSAIDs



Deyo 1999



Non-Steroidal Anti-Inflammatory Drugs

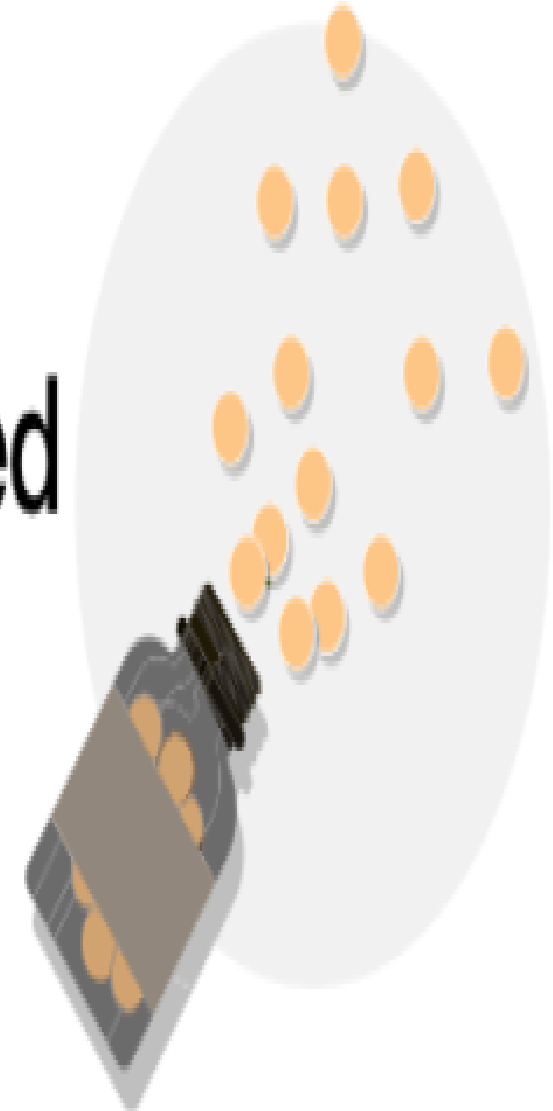


Deaths from NSAIDs

- Most popular selective COX2 inhibitor Vioxx
- Estimated 88,000 heart attacks linked to Vioxx

79 of 4,000

Vioxx users suffered
heart problems
or died



The bottom line

Diuretics: 7% increased risk

Anti-inflammatory drugs: 21% increased risk

Blood pressure medication: 24% increased risk

Sleeping pills (benzodiazepines): 47-57% increased risk

Antipsychotics: 59% increased risk

Antidepressants: 68% increased risk

Opioid painkillers: 68% increased risk

Psychotropic drugs & falls

Medication group	Overall risk	Common medications	Risk effect
Sedating anti-depressants	Very high risk	Amitriptiline Nortriptyline	Drowsiness Slow reaction Orthostatic hypotention
Sedatives	High risk	Lorazepam Nitrazepam	Drowsiness Impaired balance
MOA inhibitors	High risk	Phenelzine Morclobemide	Severe orthostatic hypotention
Anti-psychotics	High risk	Haloperidol Olanzapine	Reflex and balance impairment
SSRI uptake inhibitors	Moderate risk	Fluoextine Duloetine	Bradycardia Impaired sleep

Cardio-vascular drugs & falls

Medication group	Overall risk	Common medications	Effect
Alpha receptor inhibitors	High risk	Doxazosin Tamsulosin	Severe orthostatic hypotension
Centrally acting Alpha-2 receptor blockers	High risk	Clonidine Moxoline	Severe orthostatic hypotension Sedation
Thiazide diuretics	High risk	Bendroflumethiazide Metolazone	Weakness Hyponatremia Hypotension
ACE inhibitors	High risk	Ramipril Lisinopril	
Loop diuretics	Moderate risk	Furosemide bumetanide	Dehydration Hypotension
Calcium channel blockers	Moderate risk	Digoxin Flecainide	Bradycardia Arrhythmia

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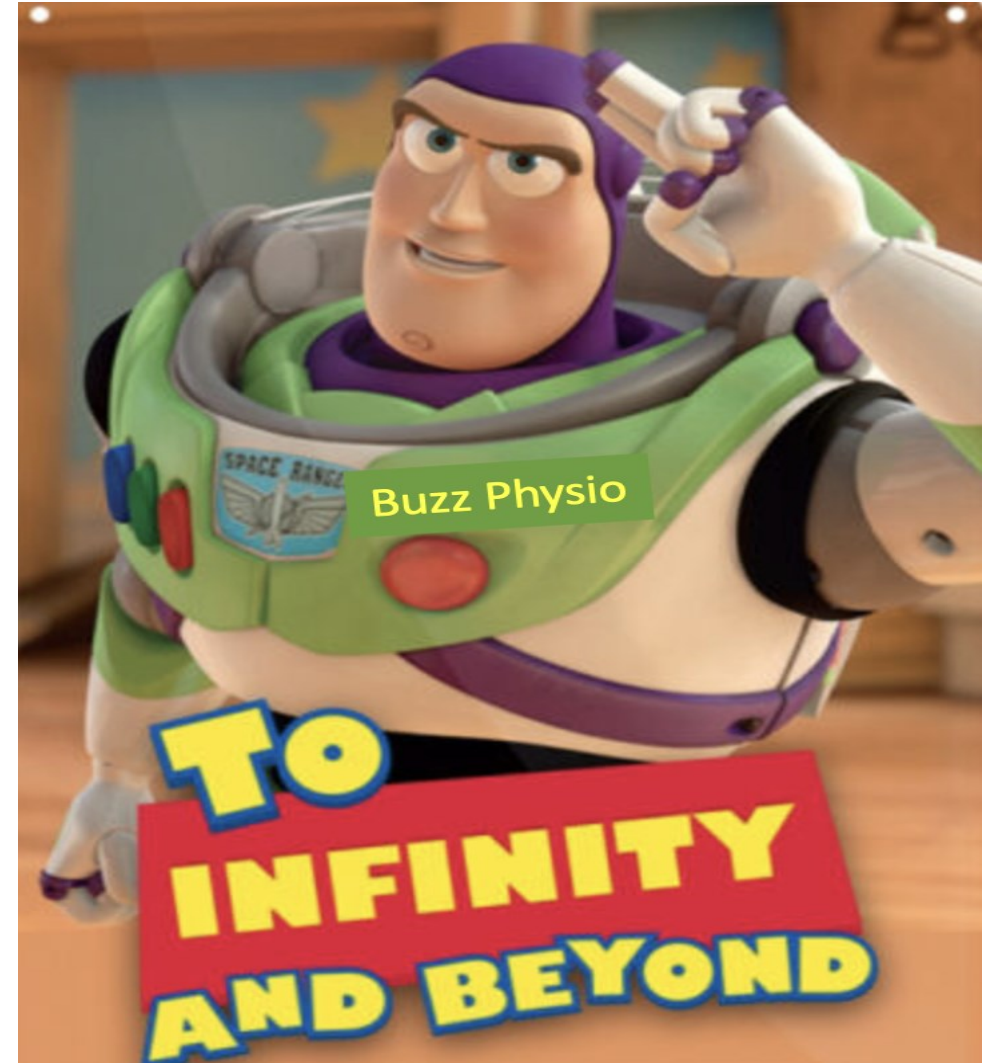
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