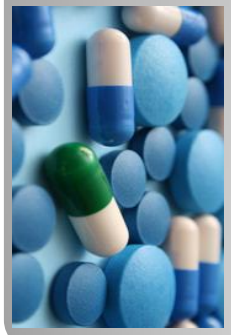
Clinical Importance of Drug-Drug Interactions Involving Antidiabetic Drugs



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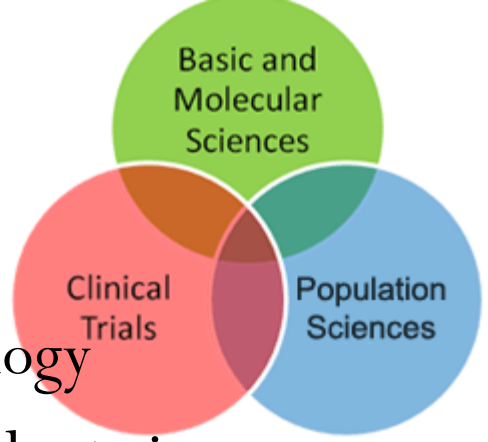
Overview



- Health Service Research:-Pharmacoepidemiology
- Study of the use and effects of medical products in populations
- DDIs are alterations of the activity of one drug (Object drug) caused by the presence of another drug (Precipitant drug)
- Sources of DDIs: Pharmacokinetics (PK) & or Pharmacodynamics (PD) mechanisms
- PK mechanism through CYP enzymes are most abundant.[1]
- ~50% of all drugs used in clinical practice are metabolized by CYP3A4[1]

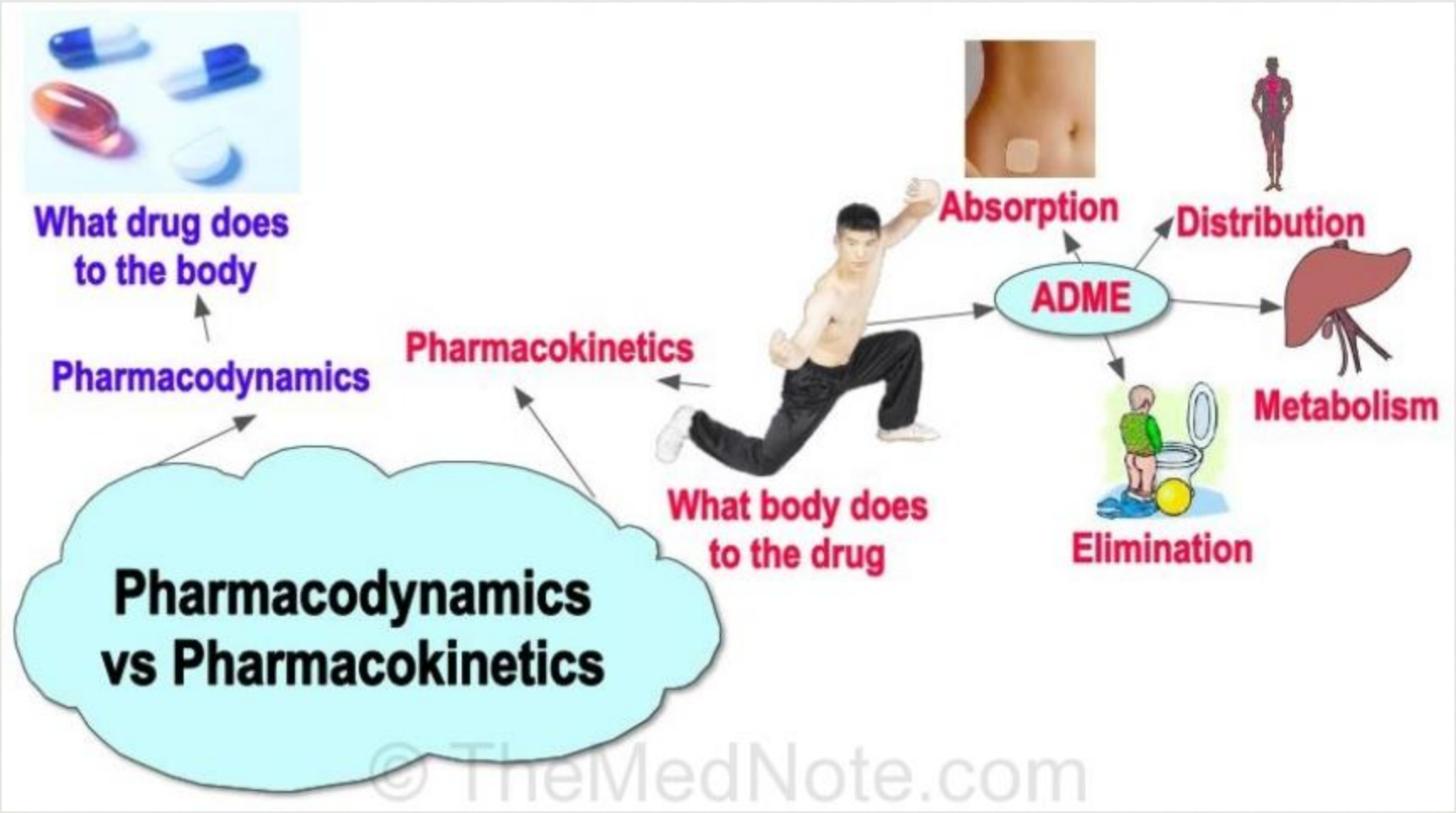
JAMA 2003;289(9):1107-1116[1]

Definition

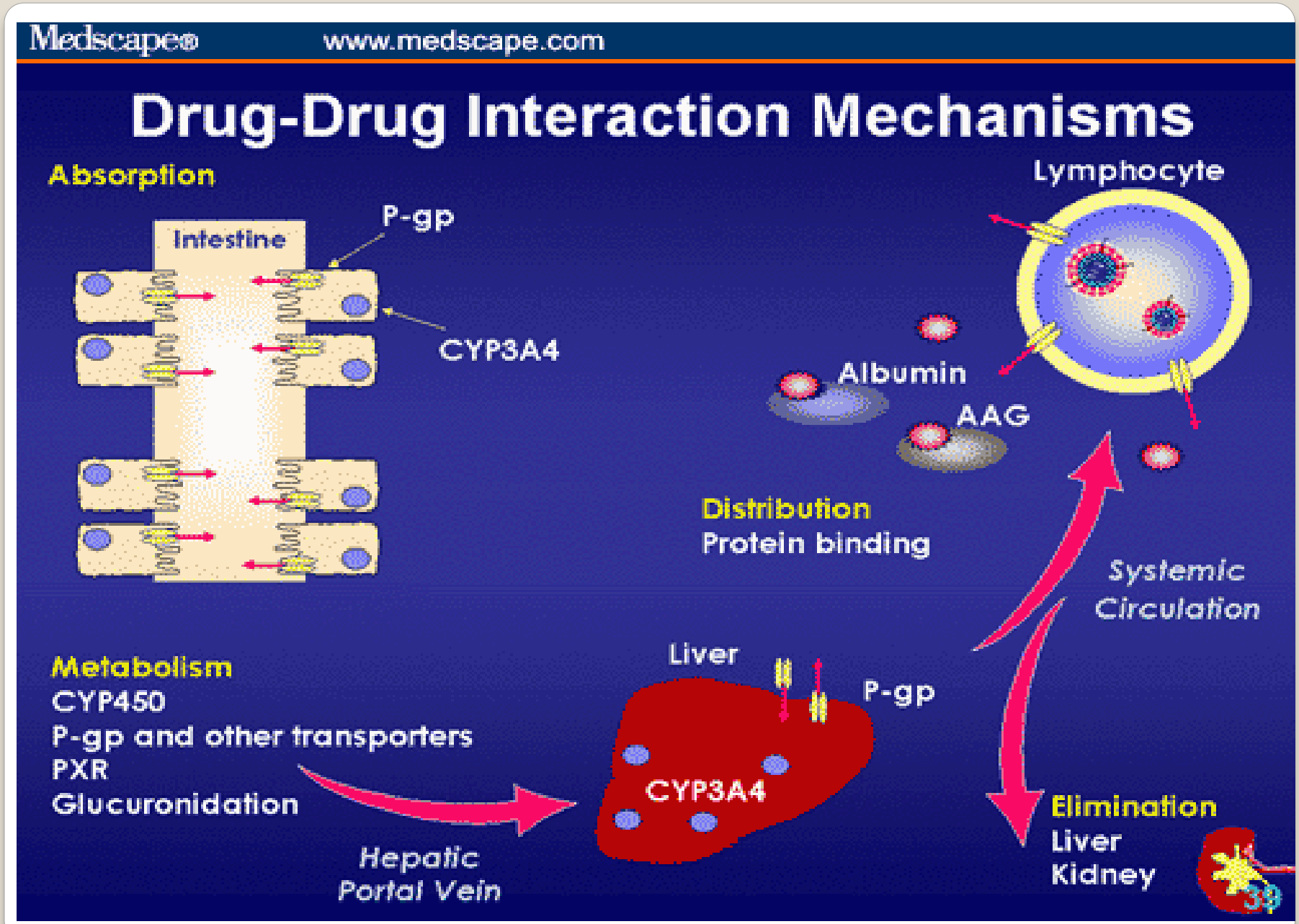
- Precipitant Drug: the drug that causes the interaction

- Object Drug: the drug that is affected by the interaction

Sources of DDIs

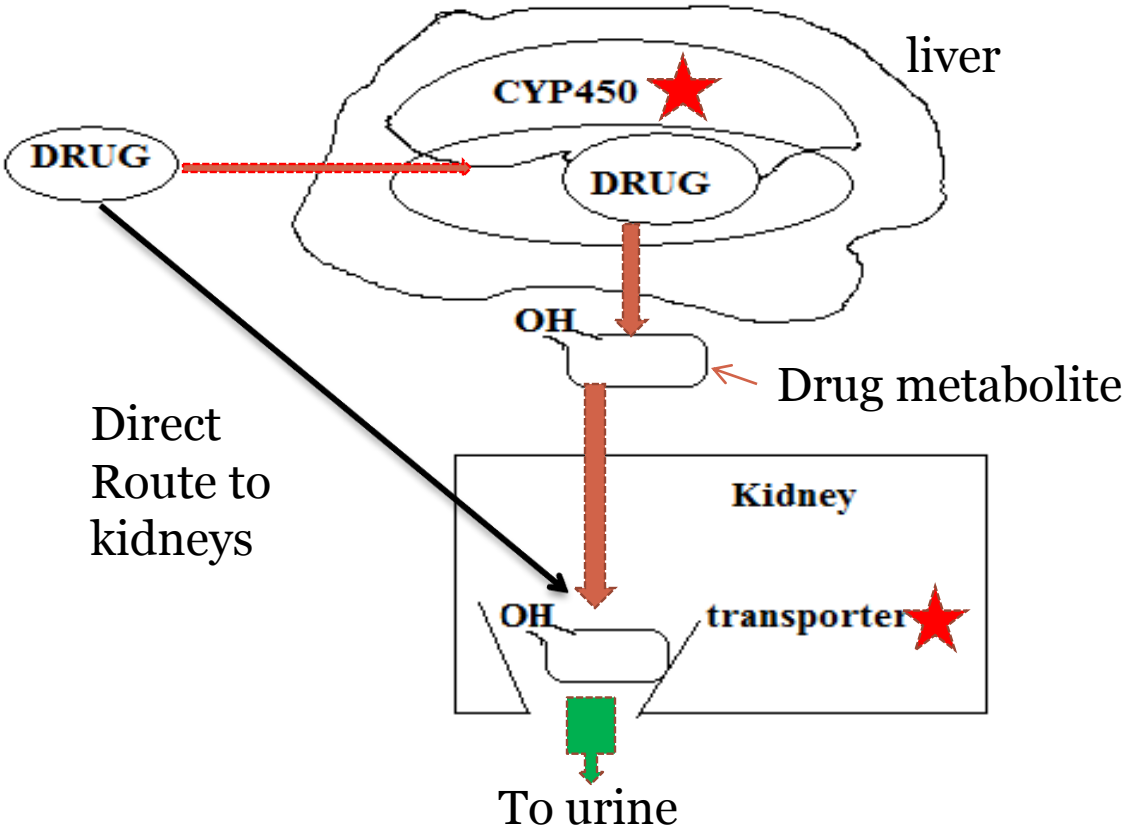


http://www.themednote.com/2011/07/10/pharmacodynamics-vs-pharmacokinetics/#.UB81waN6t8E

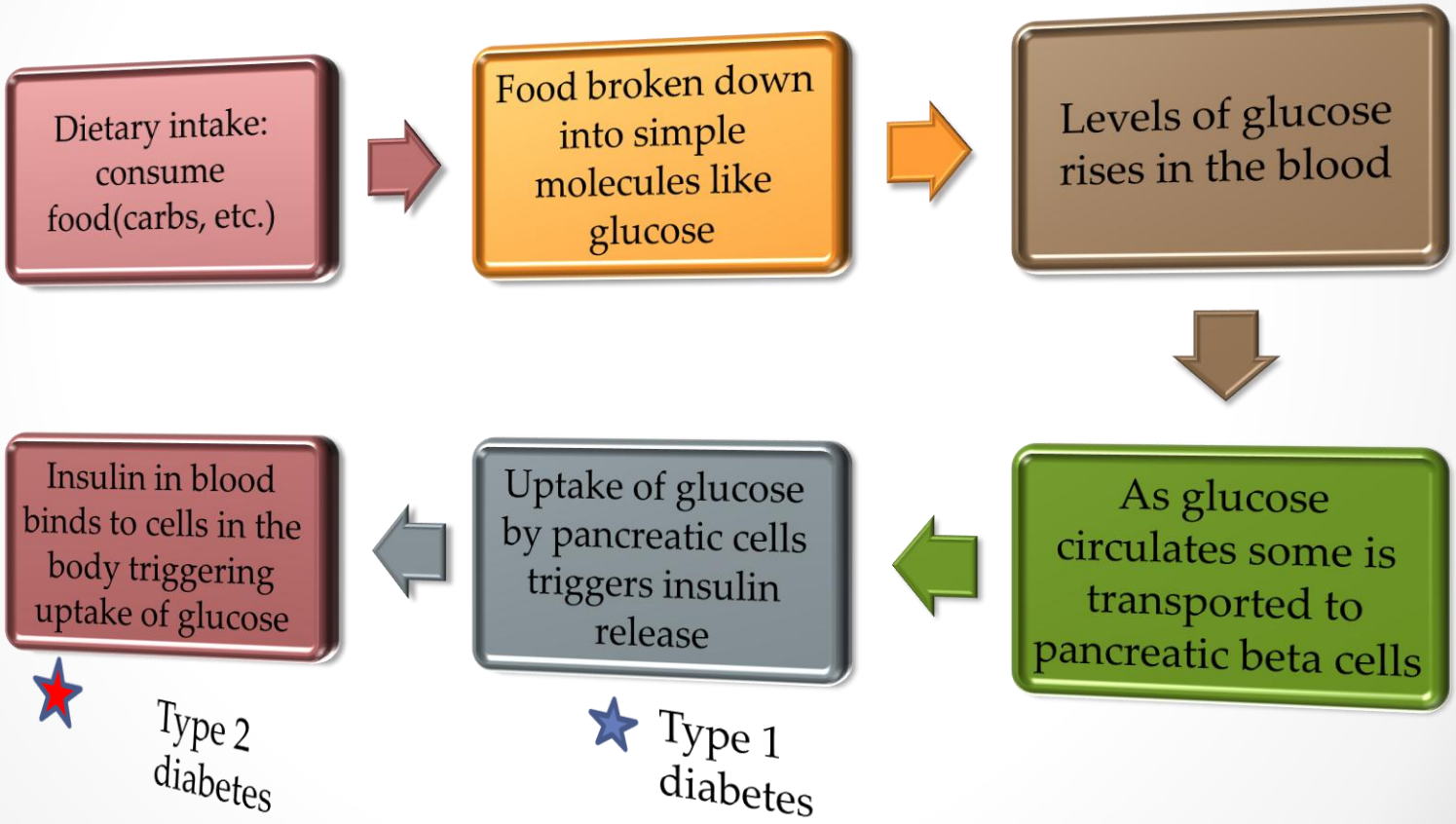


http://www.medscape.org/viewarticle/537501

DDI Focus


liver
CYP450
DRUG
DRUG
OH
Drug metabolite
Direct
Route to
kidneys
Kidney
OH
transporter
To urine

Physiology of Glucose control



Objective

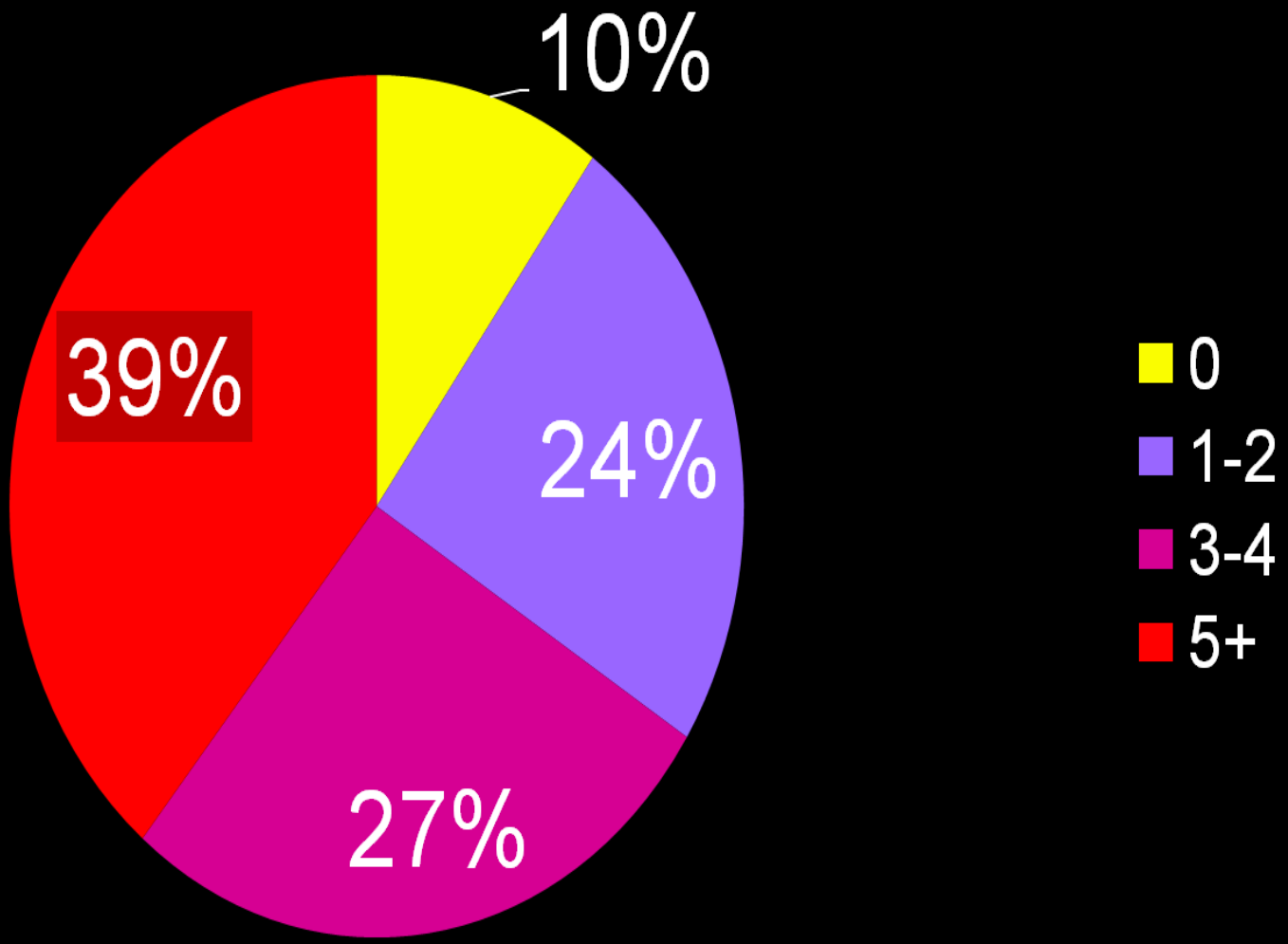
- To develop a series of biologically based hypothesis about clinically important Drug-Drug interactions (DDIs) involving antidiabetic drugs.

SIGNIFICANCE

- DDIs cause at least 13% of adverse drug events(ADEs) in older adults[1] & nearly 3% of all hospital admissions in well established DDIs[2].
- Burden increases with polypharmacy & baby-boomer population
- 70% of respondents from a 2002 public opinion poll indicated that if hospitalized they would be “concerned about receiving two or more medication that interact in a negative way”[3]

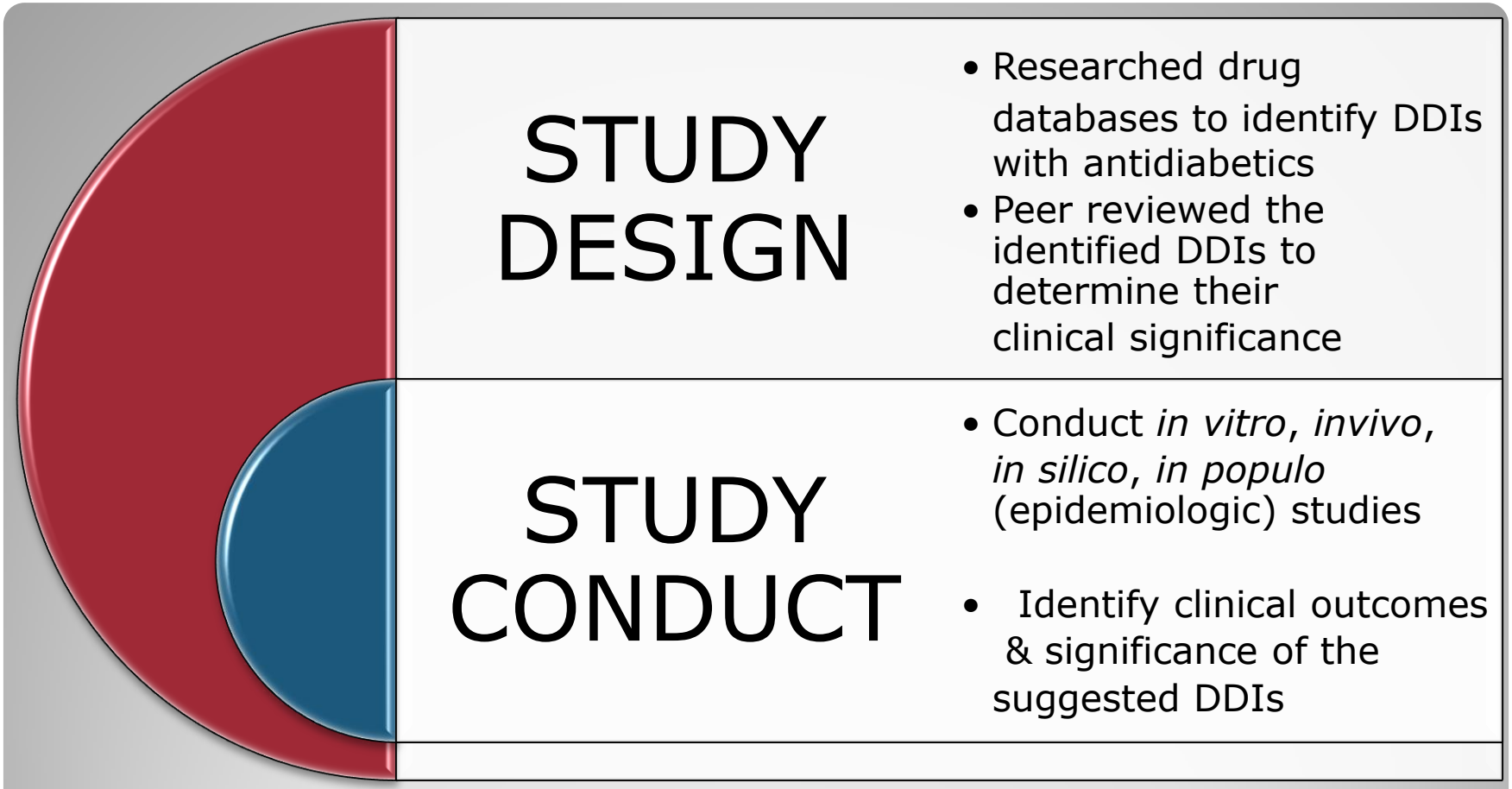
JAMA 2003;289(9):1107-1116[1] Drug Saf 1993;9(1):51-59[2] Clinical pharmacology & therapeutics;2012;Vol91(5):771-3[3]

Rx Medications Used in the Past Month by US Residents age ≥ 65 (2005-08)

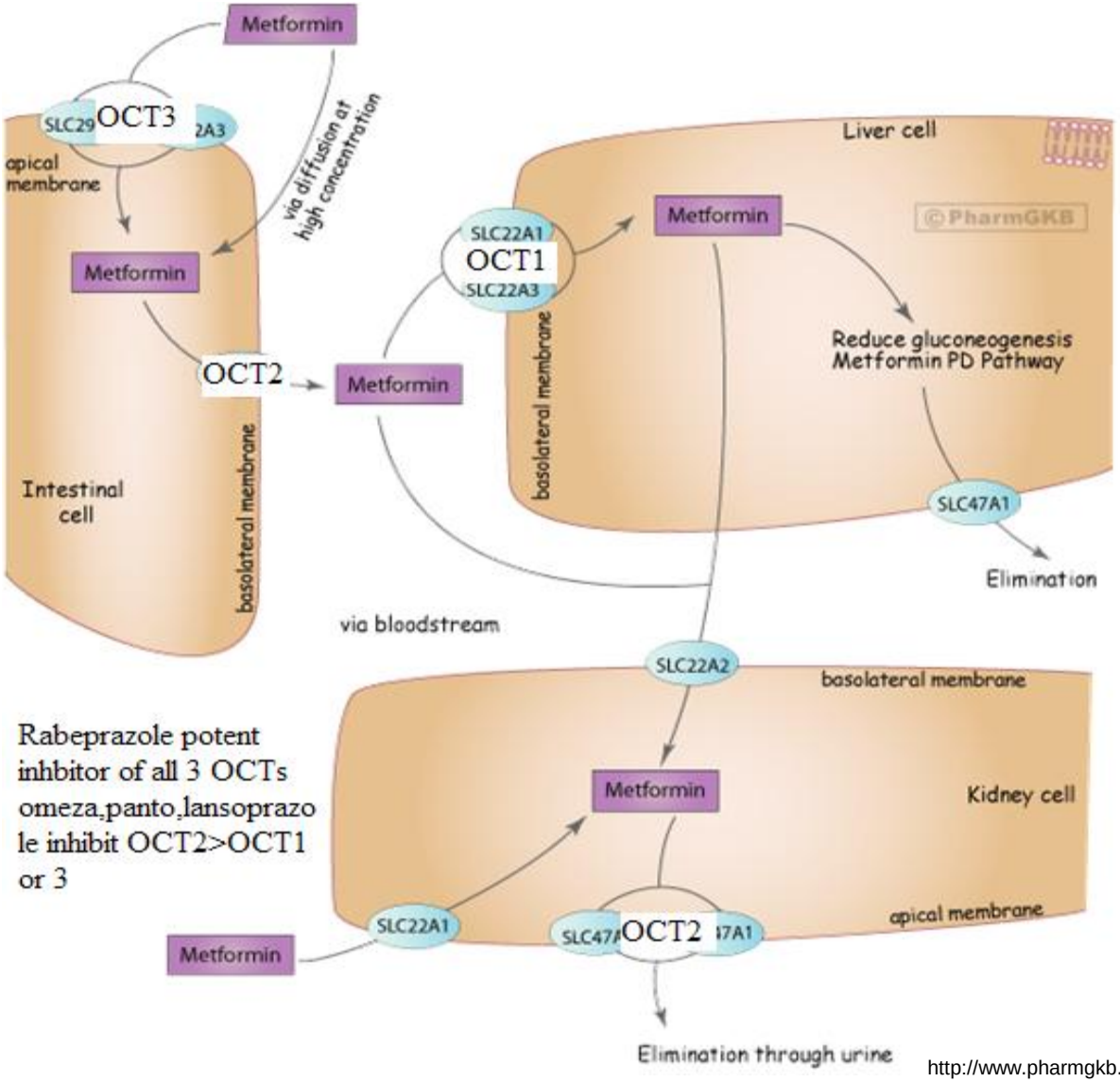


Kit BK et al. Ann Epidemiol 2012;22:112-9.

Methodology



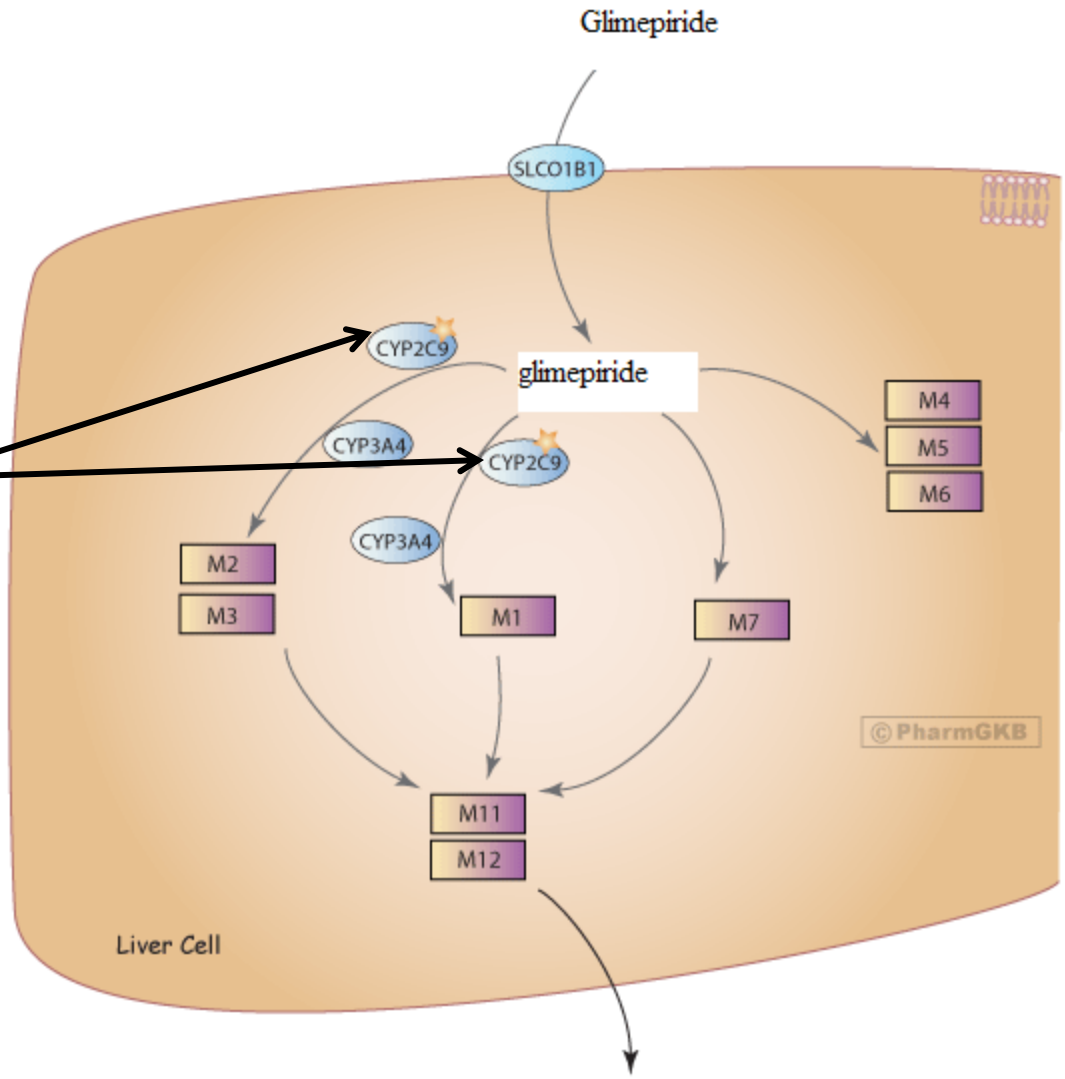
Metformin + PPIs



http://www.pharmgkb.org/pathway/PA165948259

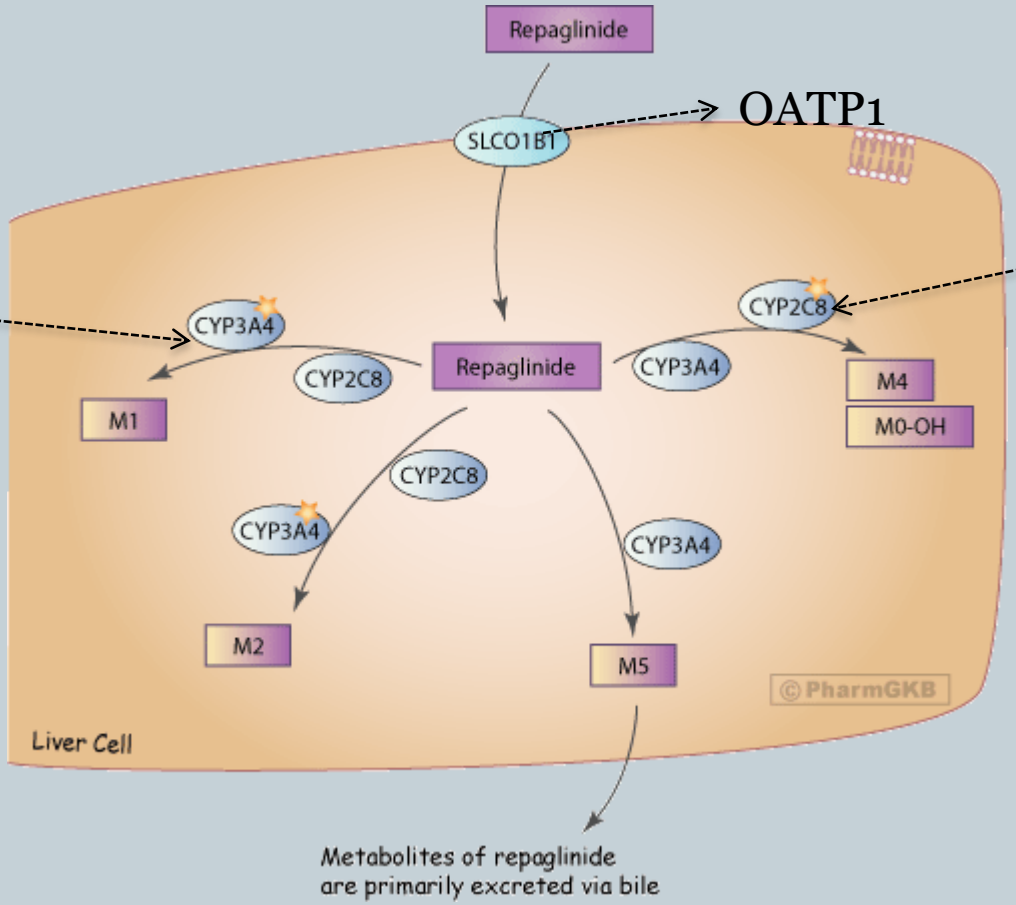
GLIMEPRIDE + STATINS/FIBRATES

Inhibitors:
Fenofibrates
Fluvastatin
Lovastatin
gemfibrozil



http://www.pharmgkb.org/pathway/PA154423659

Repaglinide + statins, fibrates



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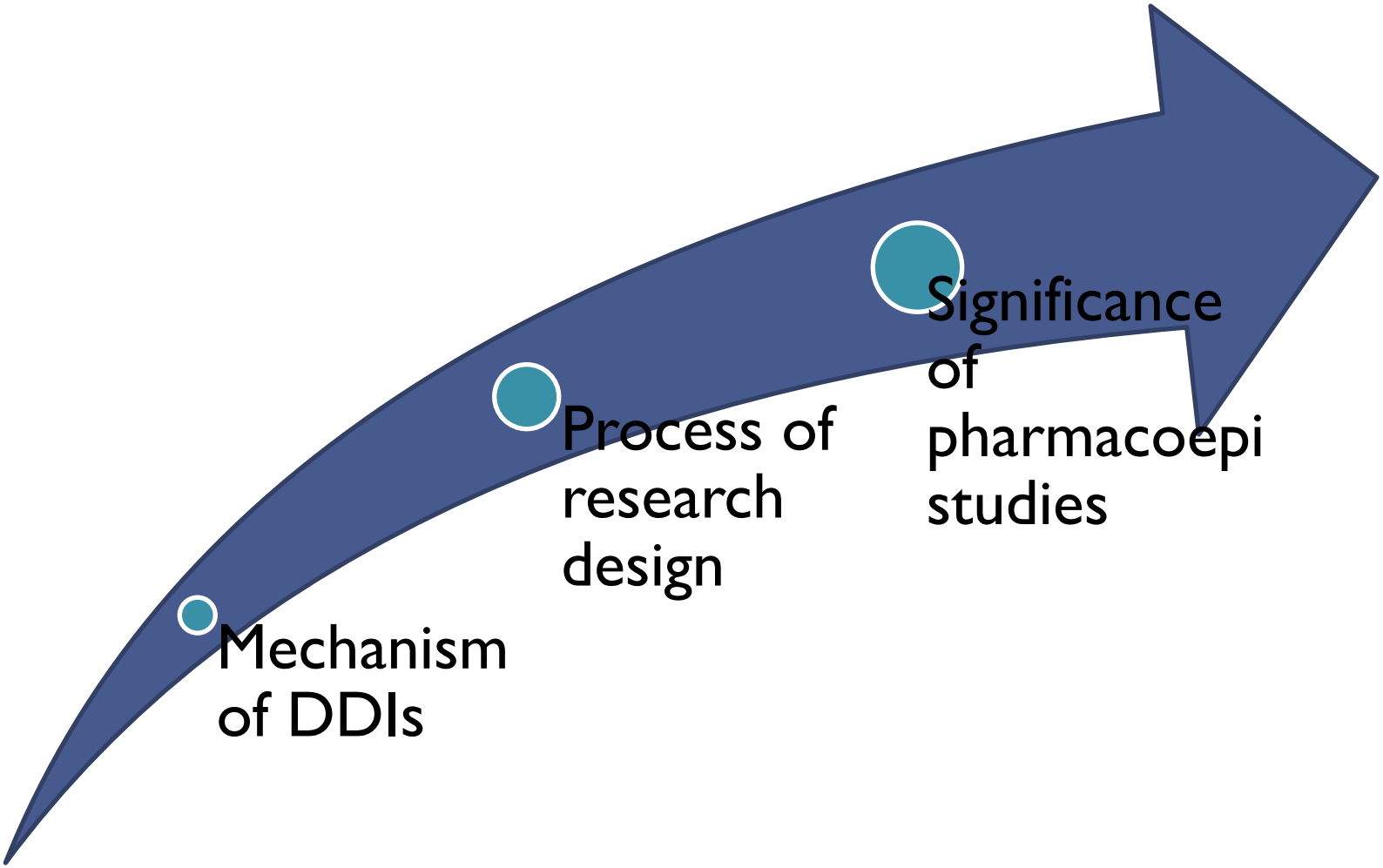
Lesson Learned



Conclusion

- DDIs & ADEs
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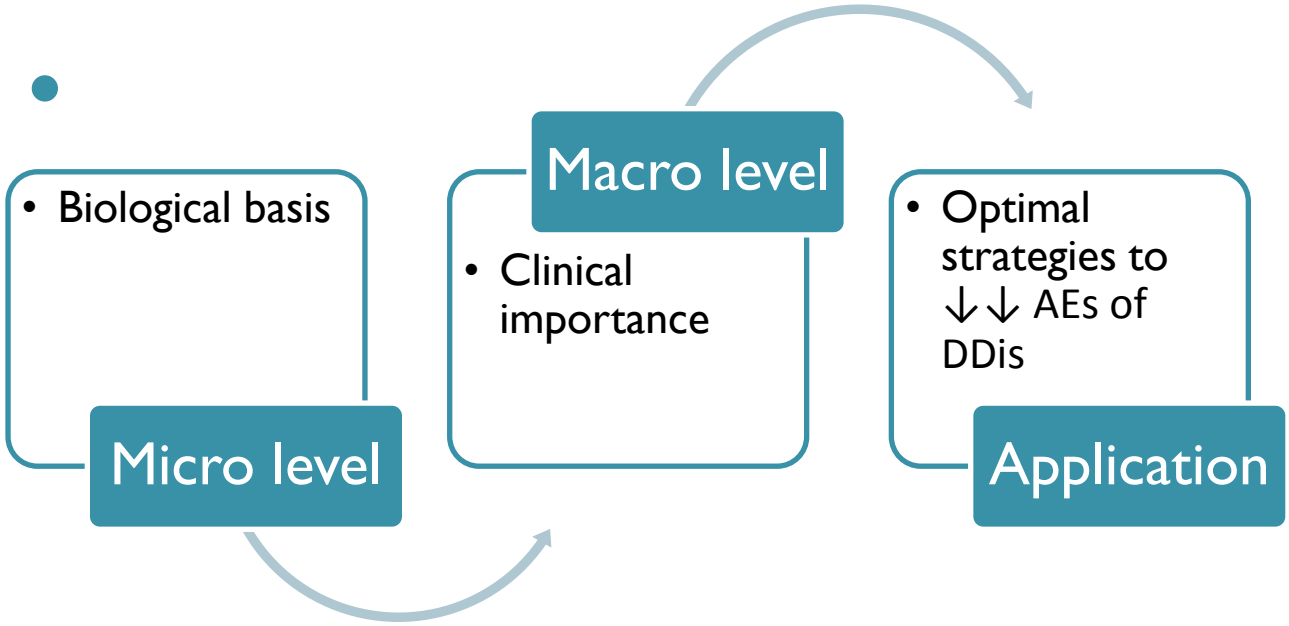

Important Implications for Public health & Clinical care

Acknowledgment

- Sean Hennessy – Mentor & PI
- Charles E. Leonard – Co- Investigator
- Leonard Davis Institute of Health Economics