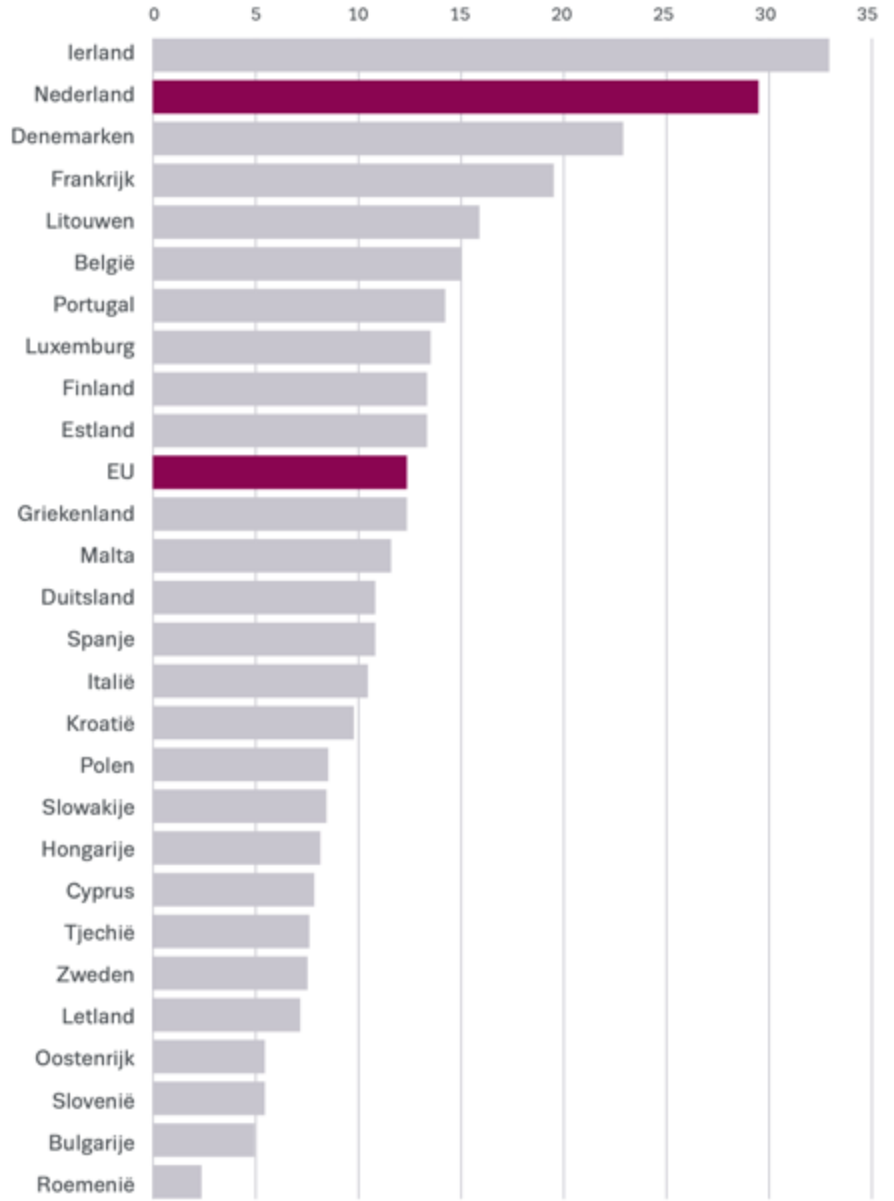
Interacties Voeding & Medicatie

Afbeelding 1. Dagelijkse consumptie van 5 porties of meer groente & fruit, 2019 [2]
(% van de bevolking van 15 jaar en ouder)



Model van Boullata & Hudson (2012)

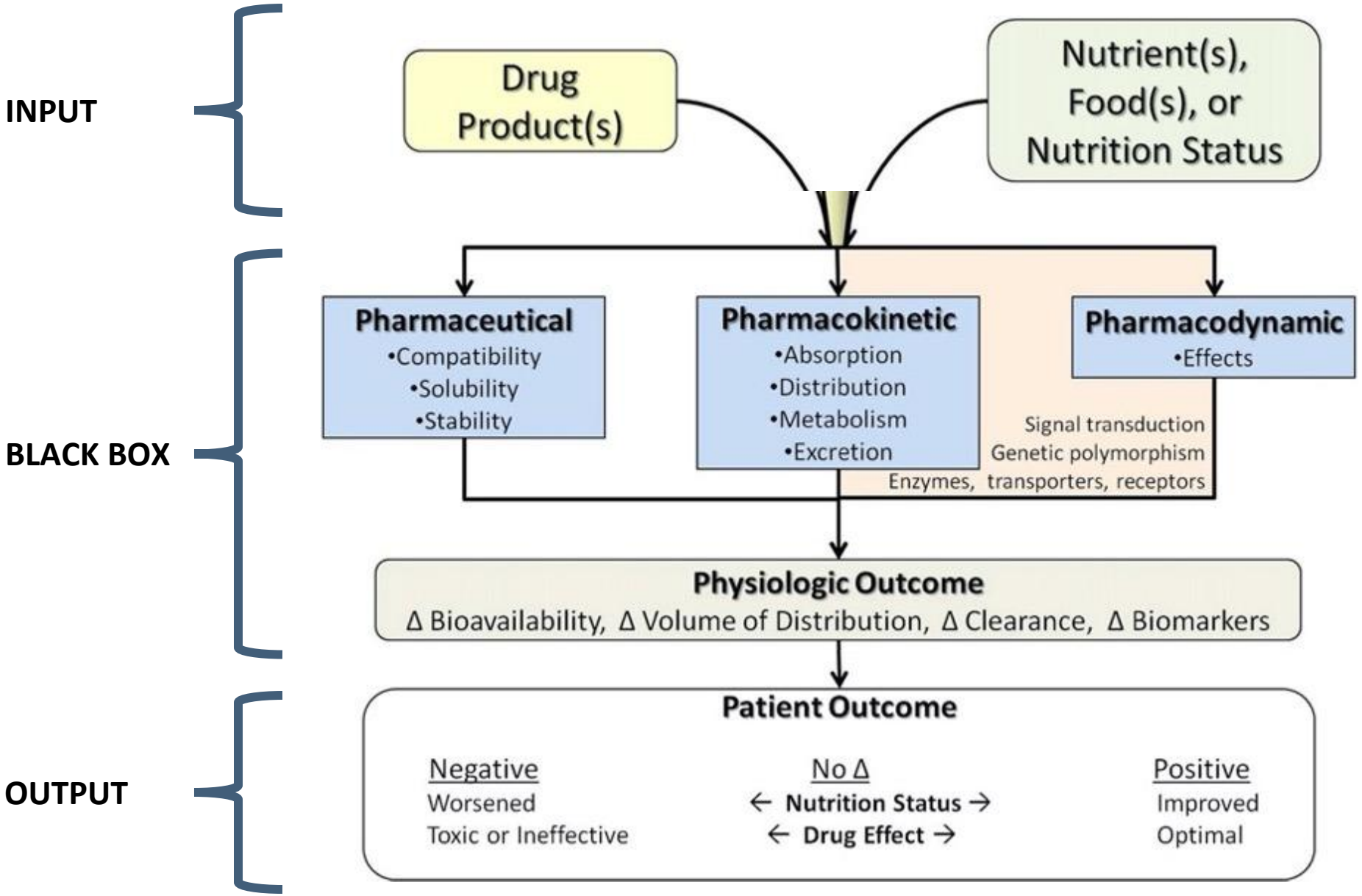


Fig. 1. Working model of drug-nutrient interactions [Boullata and Hudson 2012]

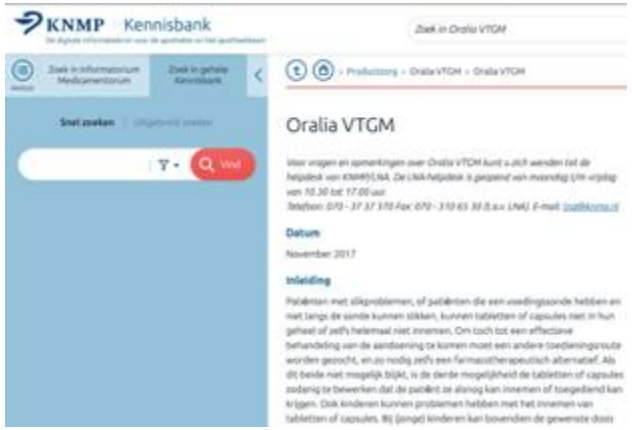
Inname

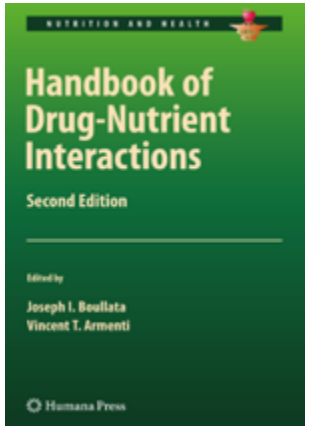
- Complexering
- Verandering viscositeit
- Denaturatie eiwitten
- Beïnvloeding stabiliteit

>> Opname geneesmiddel / voedingsmiddel ⬆️ of ⬇️

Rond toediening

- Wel of niet vermalen / mengen?
- Let op toedieningsvormen Bijv. XR, OROS, SR, MGA
- Let op bij sondevoeding en TPV





In de Maag

- Vol of leeg
- Type maaltijd
- Oplosbaarheden
- Maaglediging
- Zuurgraad

Beïnvloeding

Biologische Beschikbaarheid

Eerder in ontwikkeltraject invloed voeding onderzoeken op biologische beschikbaarheid van orale medicijnen

(Vette) maaltijd verhoogt biologische beschikbaarheid van orale oncolytica

De opname van orale oncolytica in het bloed neemt fors toe door ze in te nemen bij een (vette) maaltijd, wijst onderzoek uit. Meer aandacht voor de interactie tussen voedsel en orale oncolytica kan dus leiden tot (kosten)effectiever gebruik van deze middelen. Dat vergt echter wel aanvullend onderzoek.

In een niet eens zo heel grijs verleden betekende chemotherapie wegens kanker voor de patiënt per definitie een behandeling per infuus. Anno 2012 is een groeiend aantal oncologische medicijnen oraal te gebruiken. Dat heeft een aantal voordelen. Zo bespaart het de patiënt de regelmatige gang naar het ziekenhuis. En doordat de patiënt

P-gp remmers en inductoren

Inhibitors and inducers of P-glycoprotein (P-gp) drug efflux pump (P-gp multidrug resistance transporter)

Inhibitors of P-gp	
Amiodarone	Lapatinib
Abrocitinib	Ledipasvir
Azithromycin (systemic)	Levoketoconazole
Cannabidiol and cannabidiol-containing coformulations	Neratinib
Capmatinib	Ombitasvir-paritaprevir-ritonavir (Technivie)*
Carvedilol	Osimertinib
Clarithromycin	Propafenone
Cobicistat and cobicistat-containing coformulations	Quinidine
Cyclosporine (systemic)	Quinine
Daclatasvir	Ranolazine
Diosmin (a plant flavonoid sold as dietary supplement)	Ritonavir and ritonavir-containing coformulations*
Dronedarone	Rolapitant
Elagolix	Simeprevir
Elagolix-estradiol-norethindrone	Tamoxifen¶
Eliglustat	Tepotinib
Elexacaftor-tezacaftor-ivacaftor	Tezacaftor-ivacaftor
Erythromycin (systemic)	Ticagrelor¶
Flibanserin	Tucatinib
Fostamatinib	Velpatasvir
Glecaprevir-pibrentasvir	Vemurafenib
Itraconazole	Verapamil
Ivacaftor	Voclosporin
Ketoconazole (systemic)	

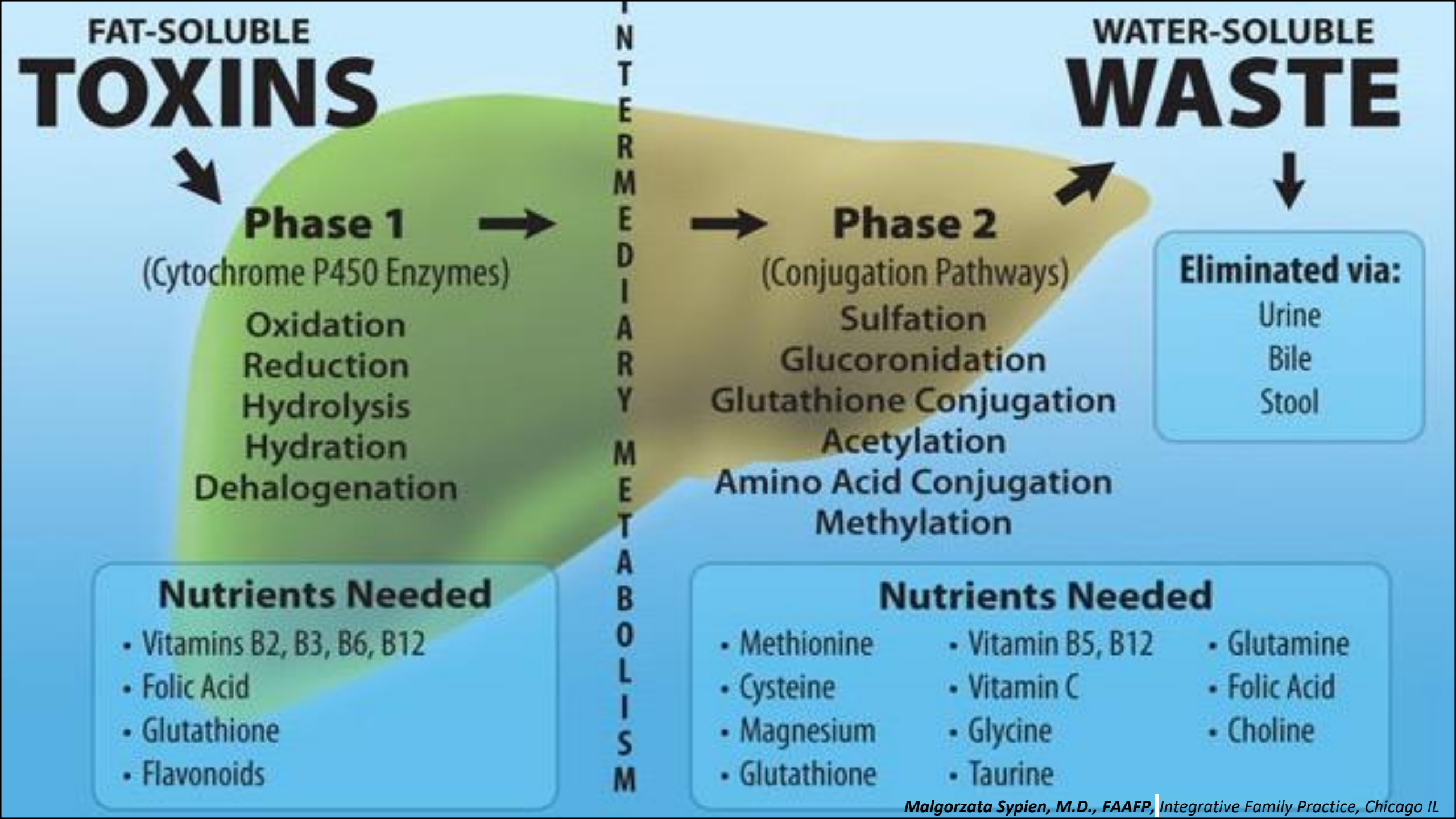
Inducers of P-gp
Apalutamide
Carbamazepine
Fosphenytoin
Lorlatinib
Phenytoin
Rifampin (rifampicin)
St. John's wort

Tabel 1: Voorbeelden van P-gp substraten (Uit: Martinez et al., 2008)

Anticancer drugs	**Opioids**
Doxorubicin	Loperamide
Docetaxel	Morphine
Vincristine*	Cardiac drugs
Vinblastine*	Digoxin
Etoposide*	Diltiazem*
Mitoxantrone	Verapamil*
Actinomycin D	Talinolol*
Steroid hormones	**Immunosuppressants**
Aldosterone	Cyclosporine*
Cortisol*	Tacrolimus*
Dexamethasone*	**Miscellaneous**
Methylprednisolone	Ivermectin
Antimicrobial agents	Amitriptyline
Erythromycin*	Terfenadine*
Ketoconazole	Ondansetron
Itraconazole*	Domperidone
Tetracycline	Moxidectin
Doxycycline	Phenothiazines
Levofloxacin	Salamectin
Sparfloxacin	Vecuronium

* Zijn ook substraat van CYP3A

UpToDate 21 febr 2022



Malgorzata Sypien, M.D., FAAFP, *Integrative Family Practice, Chicago IL*

CYP3A4 in de Darmen

How Grapefruit Juice Potentiates Drug Bioavailability

Grapefruit juice enhances the effect of some commonly used medications by increasing their bioavailability via the selective down-regulation of a specific subfamily of the cytochrome P450 enzyme system in the small intestine.

Nutrition Reviews, Volume 55, Issue 11, November 1997, Pages 398–400,

Inducers

Drug Interactions Flockhart Table ™

1A2	2B6	2C8	2C9	2C19	2D6	2E1
beta-naphthoflavone	artemisinin	rifampin	carbamazepine	carbamazepine	dexamethasone	ethanol
broccoli	carbamazepine		dabrafenib	efavirenz	oritavancin	isoniazid
brussel sprouts	dabrafenib		enzalutamide	enzalutamide	rifampin	
carbamazepine	efavirenz		enzalutamide	enzalutamide		
char-grilled meat	letermovir		letermovir	letermovir		
insulin	nevirapine		nevirapine	norethindrone		
methylcholanthrene	perampanel		phenobarbital	prednisone		
modafinil	phenobarbital		rifampin	rifampicin		
nafcillin	phenytoin		secobarbital	ritonavir		
omeprazole	rifampin		st. john's wort	st. john's wort		
rifampin	roflumilast					
rucaparib						
teriflunomide						
tobacco						

Table 1. Drug–nutrient interactions

Pathway	Effects	Herb/Nutrient	Common Victim Drugs
CYP3A4, UGTs, P-glycoprotein	Induction	Hyperforin: St. John's wort	Cyclosporine, tacrolimus, digoxin, nonnucleoside reverse transcriptase inhibitors, protease inhibitors, etoposide, paclitaxel, vinblastine, vincristine, vindesine
CYP3A4, CYP2D6	Inhibition (MB)	Berberine, hydrastine: goldenseal	Midazolam (CYP3A4 probe), cyclosporine, amitriptyline, clozapine, codeine, desipramine, donepezil, flecainide, fluoxetine, meperidine, methadone, tramadol
CYP3A4	Inhibition	Furanocoumarins: grapefruit juice, Seville orange juice	Benzodiazepines (triazolam, midazolam, diazepam, alprazolam), ritonavir, sertraline, cyclosporine, buspirone, levothyroxine, oxycodone
CYP2E1	Inhibition	Allyl sulfides, isothiocyanates: garlic, watercress	Acetaminophen, chlorzoxazone
CYP1A2, CYP2E1	Inhibition	Sulfur-containing glucosinolates: cruciferous vegetables	Acetaminophen, chlorzoxazone, haloperidol, theophylline
GSTs, UGTs	Induction	Cruciferous vegetables	Acetaminophen
CYP2C19	Induction	Ginkgo biloba	Omeprazole
CYP2C9, CYP2C19, CYP3A4, OATPs	Inhibition	Silymarins: milk thistle	Losartan, omeprazole, midazolam, warfarin, simvastatin, felodipine, rosuvastatin, nifedipine
CYP3A4, CYP2C9	Inhibition	Ginseng	Warfarin
CYP3A4	Inhibition	Echinacea	Midazolam, estrone 3-sulfate
CYP3A4, CYP2D6, P-glycoprotein, UGTs	Inhibition	Piperaceae: black pepper	Phenytoin, rifampicin, propranolol, theophylline, nevirapine
GSTs, CYP3A4 P-glycoprotein	Induction Inhibition	Ginger	Midazolam, digoxin
CYP3A4, P-glycoprotein	Induction	Vitamin D	Midazolam, digoxin
CYP3A4, CYP1A2	Inhibition	Resveratrol	Cisapride, cyclosporine, testosterone

Abbreviations: CYP = cytochrome P450; GSTs = glutathione S-transferases; OATPs = organic anion transporting polypeptides; UGTs = uridine diphosphate glucuronosyltransferases.

https://www.kidneynews.org

Vruchtensappen

journal homepage: www.jfda-online.com

Review Article

Food-drug interactions precipitated by fruit juices other than grapefruit juice: An update review

Meng Chen [a], Shu-yi Zhou [b], Erlinda Fabriaga [b], Pian-hong Zhang [c], Quan Zhou [a,*]

Table 1 – Significant drug interactions precipitated by fruit juices based on RCTs.

Juices	Object drugs	PK/PD effects
Apple juice	Fexofenadine [13–16], aliskiren [18], atenolol [19]	Great decrease (↓) in drug bioavailability and potential lower (↓) efficacy
Orange juice	Aliskiren [18], atenolol [25], celiprolol [27], montelukast [28], alendronate [35], clofazimine [36]	Great decrease (↓) in drug bioavailability and potential lower (↓) efficacy
	Fluoroquinolones [31–34]	Great decrease (↓) in drug bioavailability, potential higher (↑) risk of therapeutic failures and subsequent bacterial resistance
	Ferrous fumarate [29]	Substantially enhanced (↑) iron absortption and its anti anemia efficacy
	Aluminum-containing antacid [30]	Greatly enhanced (↑) aluminum absorption and increased (↑) aluminum toxicity
Seville orange juice	Felodipine [40]	Significant increase (↑) in AUC of felodipine and decrease (↓) in the dehydrofelodipine-felodipine AUC ratio (an index of CYP3A4 activity)
Pomelo juice	Cyclosporine [42]	Significant increase (↑) in AUC and C_{max}, and potential higher (↑) risk of supratherapeutic concentrations of cyclosporine
	Sildenafil [43]	Significantly reduced (↓) bioavailability and potential reduced (↓) efficacy
Grape juice	Cyclosporine [44]	Significantly decreased (↓) bioavailability and potential higher (↑) risk of subtherapeutic concentrations of cyclosporine
	Phenacetin [45]	Marked reduction (↓) in AUC and C_{max}, and a delay in time to peak concentration
Lemon juice	^{99m}Tc-tetrafosmin [47]	Enhanced (↑) hepatobiliary excretion and improved (↑) myocardial SPECT image quality
Pomegranate juice	Intravenous iron during hemodialysis [51]	Attenuation (↓) in oxidative stress and inflammation induced by intravenous iron
Cranberry juice	Triple therapy medications for H. pylori [55]	Higher (↑) eradication rate of H. pylori eradication in females
Blueberry juice	Etanercept [56]	Significantly improved (↑) efficacy and reduced (↓) side effects of etanercept
Lime juice	Antimalarials (artemether and camoquine) [57]	Improved (↑) antimalarial efficacy
Wheat grass juice	Chemotherapy (fluorouracil, adriamycin and cytoxan) [59]	Significantly reduced (↓) side effects of chemotherapy

Notes: PK, pharmacokinetics; PD, pharmacodynamics; CYP, cytochrome P450; SPECT, single photon emission computed tomography; C_{max}, peak serum concentration; AUC, area under the serum concentration–time curve.

BBQ & roken

> Gastroenterology. 1999 Jul;117(1):89-98. doi: 10.1016/s0016-5085(99)70554-8.

Effects of a chargrilled meat diet on expression of CYP3A, CYP1A, and P-glycoprotein levels in healthy volunteers

Conclusions: Ingestion of chargrilled meat results in induction of CYP1A enzymes but not CYP3A4 or P-glycoprotein. This observation, combined with the correlation between adduct levels and CYP1A expression, supports an adaptive role for CYP1A but not CYP3A4 or P-glycoprotein.

Roken, BBQ en bv. broccoli, koolsoorten, spruitjes (kruisbloemigen)

>> Inductie CYP1A2 >> snellere werking CYP1A2

>> Snellere afbraak van geneesmiddelen die substraat zijn

Vb. caffeine, bep. antidepressiva/antipsychotica, melatonine, e.a. hormonen

Farmacodynamiek

- Coumarines met vitamine K-rijke voeding (bv boerenkool, spinazie, broccoli)

  > 150 µg/d → meer stollingsfact → INR ↓ max. 100 µg/d vit.K suppletie & afwisselen

- Alcohol met benzo's, opiaten, antidepressiva & antipsychotica → versterking effect
- Alcohol met NSAID's → meer kans maagirritatie
- Magnesiumsuppletie met benzo's → versterking spierrelaxatie
- Melatonine en 5-HTP met slaapmedicatie → versterking sedatief effect

Voedingsstatus

- Veel bijwerkingen impact op voedingspatroon /-intake
- Gastro-intestinale bijwerkingen: min. 25% vd GNM!
- Afname eetlust: oncolytica, antibiotica, immuuntherapie etc.
- Toename eetlust: antipsychotica, antidepressiva, anticonceptie, carbamazepine, corticosteroïden, lithium, valproïnezuur

Lareb
Nederlands Bijwerkingen Centrum
Netherlands Pharmacovigilance Centre

Invloed op Reuk en Smaak

- Smaak GNM
- Lokale schade aan cellen of zenuwen
- Psychisch (aversie, associaties uit verleden)
- Effecten op beleving en beloning
- Door veranderde speekselproductie

Speeksel

- **Toename:** zure producten, kauwen, clozapine, parasympathicomimetica zoals pilocarpine, rivastigmine, pyridostigmine
- **Afname**: vb. ACE-remmers, lithium, diuretica, opiaten, anticholinergica

Mondgezondheid

- Tandvleeshyperplasie (ciclosporine, tamoxifen, fenytoïne, calciumantagonisten)
- Toxisch effect mondslijmvlies (mn oncolytica)
- Brandend gevoel (ACE-remmers)
- Candida infecties (antibiotica, cortico’s, cytostatica, immuunsuppressiva)
- Aften, erosies (bv NSAID’s, kaliumzouten, sublinguale tabl, ACE-remmers, calciumantagonisten)
- Verkleuring gebit (antibiotica)

Samenvatting

- Verschillende mechanismen
- Complex, o.a. door polyfarmacie, comorbiditeiten, individuele aspecten
- Relatief weinig (gedegen) onderzoek
- Informatie verspreid, geen complete database
- **Wees alert bij wijzigingen in medicatie, voeding, gezondheidsstatus**

Aandachtspunten suppletie

1. Opname en Biologische Beschikbaarheid
2. Formulering: juiste verhoudingen, doseringen, cofactoren etc.
3. Geen onnodige toevoegingen & toxinen
4. Certificering producent, analyse certificaten opvraagbaar
5. Herkomst grondstoffen, bij voorkeur “natuurlijk”

Opname & BB

1. Opname gereed of omzetting nodig? (vb. vit B12)
2. Chelatie: organisch versus anorganisch gebonden
3. Interacties: bevordering of remming opname
4. Toedieningsvorm
5. Gezondheidsfactoren: bv. Microbioom, pH, genetica, orgaanfuncties
6. Natuurlijke versus synthetische middelen

TOP 10 LITERATUURBRONNEN INTERACTIES

- TRC Natural Medicines
- MSKCC.org
- Medline Plus
- Drugbank.com
- FDA
- Drugs.com
- NPN Factsheets - supplementinfo
- CBG-meb.nl
- Orthokennis / Natura Foundation
- NIH (National Institute of Health)

TIPS INFORMATIEBRONNEN INTERACTIES & SUPPLETIE

- https://naturalmedicines.therapeuticresearch.com/databases.aspx
- https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs
- https://medlineplus.gov/druginformation.html
- https://go.drugbank.com/drug-interaction-checker
- https://pubmed.ncbi.nlm.nih.gov
- https://www.drugs.com/drug_interactions.html
- https://www.medicijngebruik.nl
- https://www.geneesmiddeleninformatiebank.nl
- https://www.naturafoundation.nl/kenniscentrum / https://www.orthokennis.nl/zoeken/interacties / https://www.sohf.nl/indicaties
- https://www.webmd.com/interaction-checker/default.htm

Take Home Messages

- IA’s veelvoorkomend, vaak complex, niet altijd klinisch relevant
- Veel farmacokinetisch >> klasse-effecten
- Wees alert op drastische wijzigingen in eetpatroon / eetlust, dieten (Ramadan, int. fasting), bijwerkingen i.r.t. eetpatroon
- Raadpleeg meerdere bronnen (tegenstrijdige info)
- Let op risicogroepen en polifarmacie : ouderen, kinderen, HIV, diabetes, kanker, alcoholisten, zwangeren, genotypen (bv. slow metabolisers)