



Interventies gericht op verbetering van geneesmiddelgebruik

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Disclosure slide

(potentiële) belangenverstrengeling	
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijven:
<ul style="list-style-type: none">• Sponsoring of onderzoeksgeld• Honorarium of andere (financiële) vergoeding• Aandeelhouder• Andere relatie, namelijk ...	<ul style="list-style-type: none">• Aardex, AstraZeneca, Chiesi, Novartis, Pfizer, Trudell Medical• AstraZeneca, Chiesi, GSK, Novartis, Teva, Vertex <p>Alles ongerelateerd aan deze presentatie en betaald aan UMCG</p>





Hoe doen we het in Nederland?

Adherence Rates and Associations with Nonadherence
in Patients with Rheumatoid Arthritis Using Disease
Modifying Antirheumatic Drugs

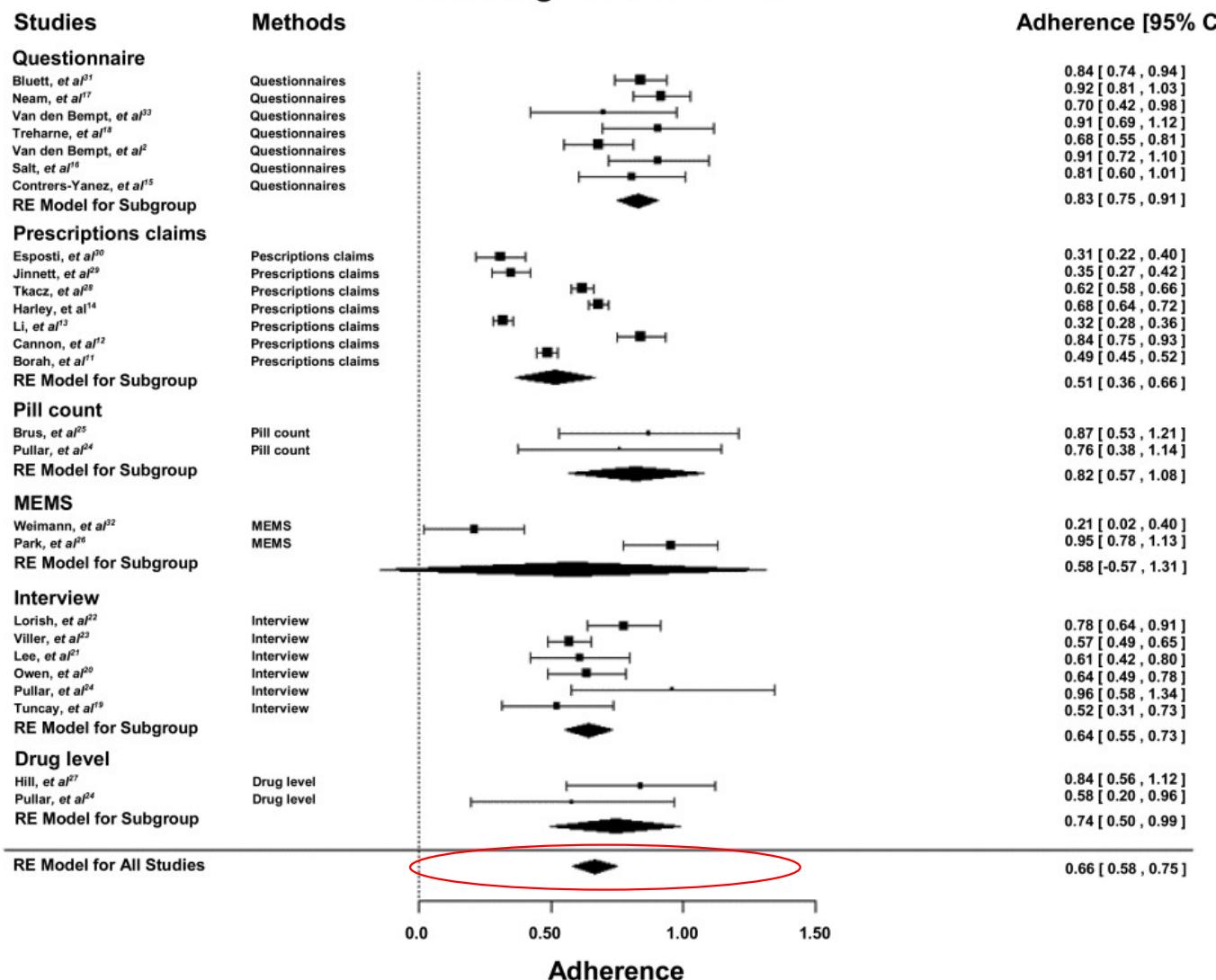
BART J.F. van den BEMT, FRANK H.J. van den HOOGEN, BART BENRAAD, YECHIEL A. HEKSTER,
PIET L.C.M. van RIEL, and WIM van LANKVELD

- N=228 gebruikers van DMARDs...
- 68% via Compliance Questionnaire Rheumatology (CQR)
- 60% op Medication Adherence Report Scale (MARS)
- Duur ziekte, bijwerkingen en lager geloof in noodzaak medicatie (licht) geassocieerd met slechte therapietrouw



En internationaal?

Percentage of adherence

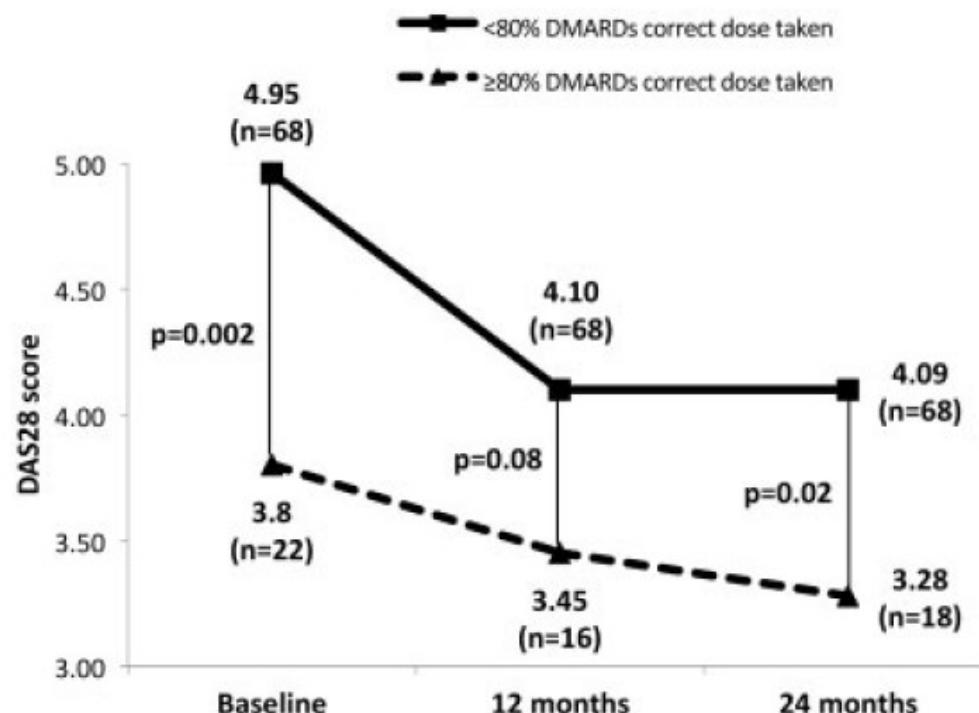
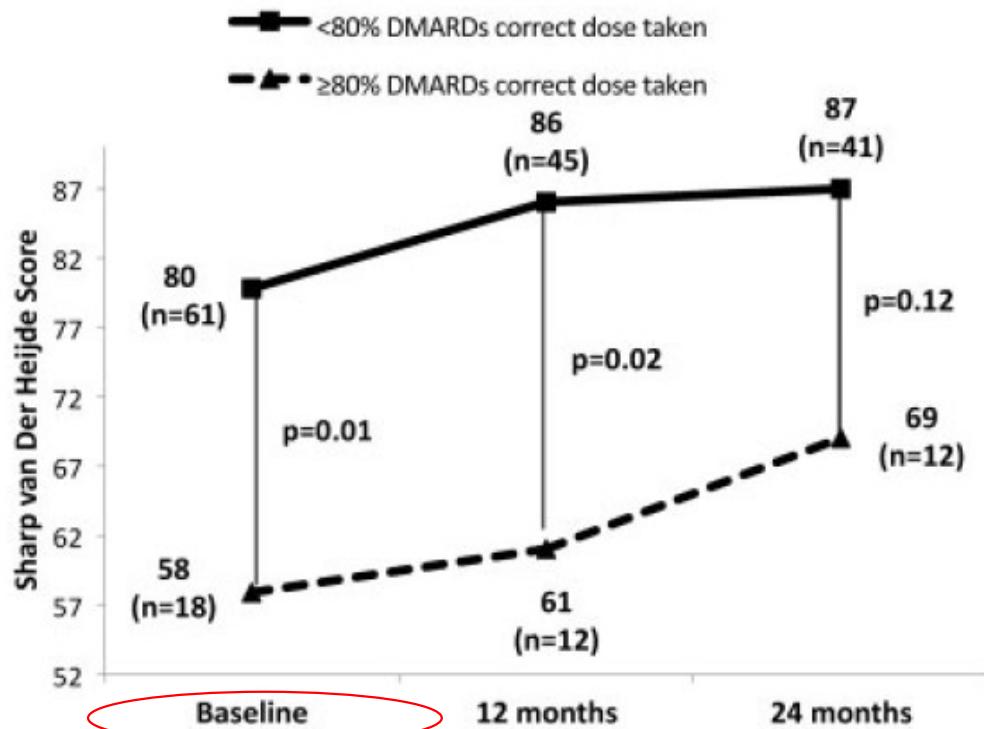


- N=26
- Overall: 66%
- Questionnaire: 83%
- MEMS: 58%



...heeft dat consequenties?

- N=107, 2 jaar follow-up met MEMS
- Therapietrouw DMARDs: 64%; en prednison: 70%
- 21% meer dan 80% genomen: betere uitkomsten!





Stappenplan voor optimale therapietrouw

Identificeer, karakteriseer, intervenieer

- Wie?: Vind therapie-ontrouwe populatie ...hoe?
- Waarom?: Identificatie van “phenotype” therapie-ontrouw
- Wat?: Interventies op maat



Patient reported?: MARS en CQR-5/19

Item

Item 1: "I forget to take my inhalation medication"

Item 2: "I change the dosage of my inhalation medication"

Item 3: "I stop taking my inhalation medication for a while"

Item 4: "I decide to skip one of my inhalation medication dosages"

Item 5: "I use my inhalation medication less than is prescribed"

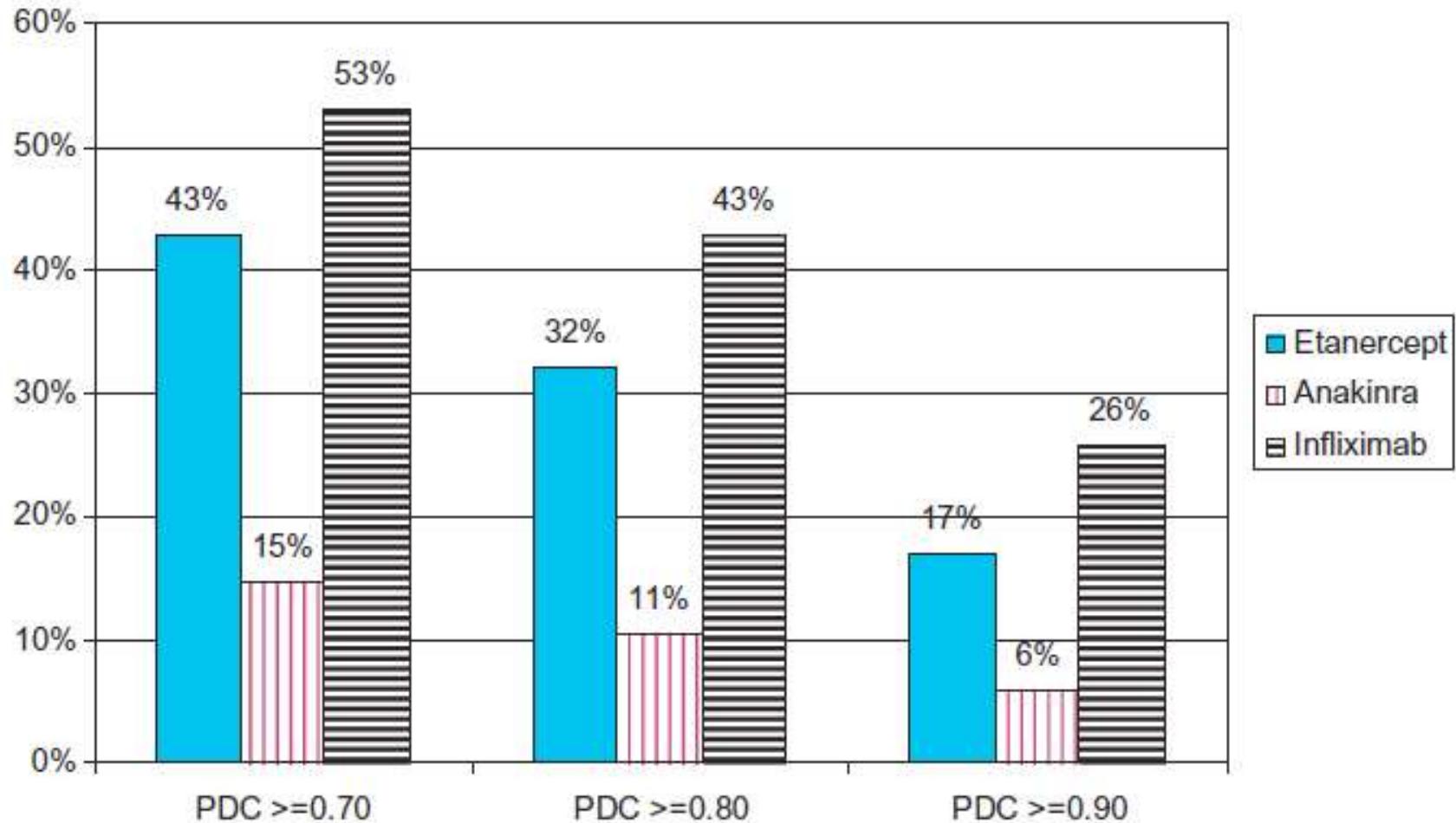
Sum score MARS-5^a (range = 5-25).

^aThe MARS-5 sum score was calculated by summing scores from each individual question

Questions	
Q1	If the rheumatologist tells me to take the medicines, I do so
Q2*	I take my anti-rheumatic medicines because I then have fewer problems
Q3*	I definitely don't dare to miss my anti-rheumatic medications
Q4	If I can help myself with alternative therapies, I prefer that to what my rheumatologist prescribes
Q5*	My medicines are always stored in the same place and that's why I don't forget them
Q6*	I take my medicines because I have complete confidence in my rheumatologist
Q7	The most important reason to take my anti-rheumatic medicines is that I can still do what I want to do
Q8	I don't like to take medicine. If I can do without them, I will
Q9	When I am on vacation, it sometimes happens that I don't take my medicines
Q10	I take my anti-rheumatic drugs, for otherwise what's the point of consulting a rheumatologist?
Q11	I don't expect miracles from my anti-rheumatic medicines
Q12	If you can't stand the medicines you might say: "throw it away, no matter what"
Q13	If I don't take my anti-rheumatic medicines regularly, the inflammation returns
Q14	If I don't take my anti-rheumatic medicines, my body warns me
Q15	My health goes above everything else and if I have to take medicines to keep well, I will
Q16	I use a dose organizer for my medications
Q17*	What the doctor tells me, I hang on to
Q18	If I don't take my anti-rheumatic medicines, I have more complaints
Q19	It happens every now and then, I go out for the weekend and then I don't take my medicines

- +: snel, goedkoop & helpt in “phenotyping“ therapietrouw
- : self-report kan overschatting geven, sociaal wenselijk antwoord

Op basis apotheek/claims data?

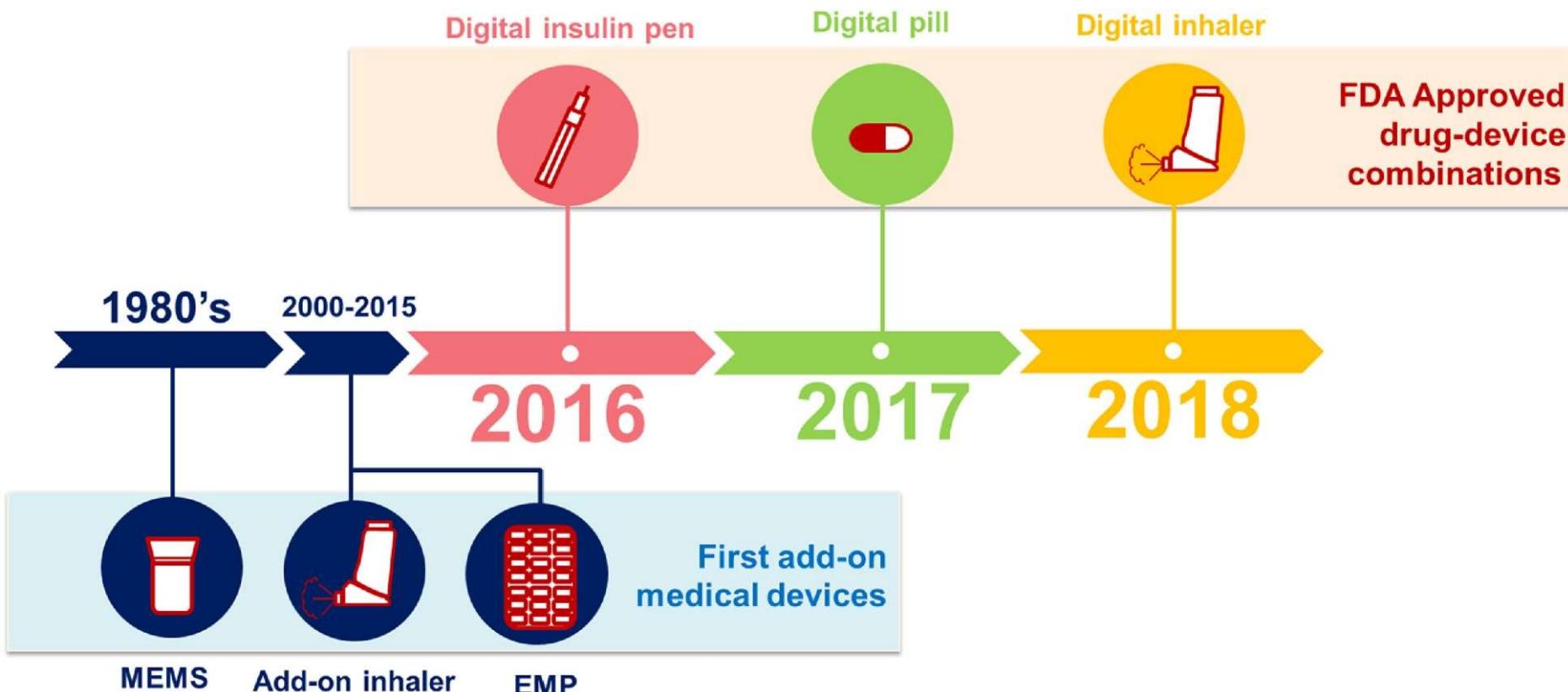


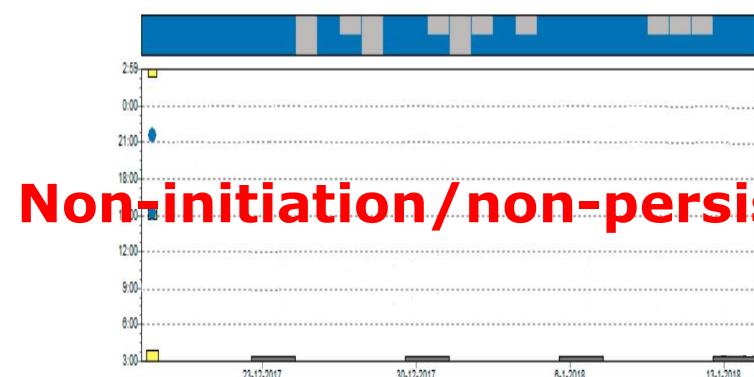
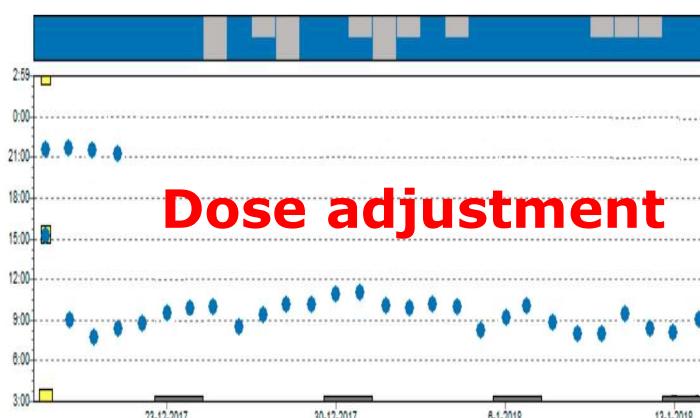
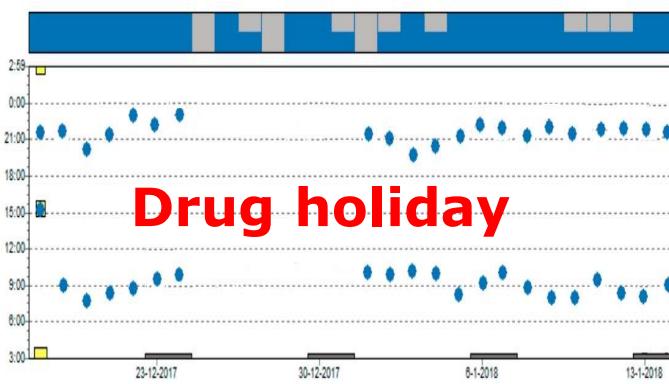
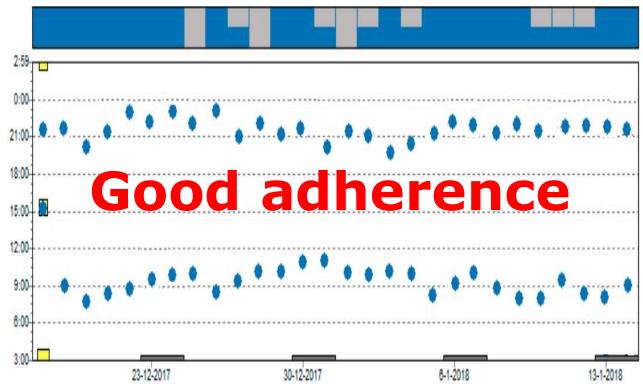
+: objectief, goedkoop, lange termijn

-: afhalen=gebruiken?, herhaalservices?, compleet/details?



Electronische monitoring







Digitale potjes, pillen en blisters

- Smart bottle
- Smart blister
- Smart pill



+: objectief, gouden standaard, veel detail, app connected
-: kosten, openen=innemen?, “big brother is watching...”?



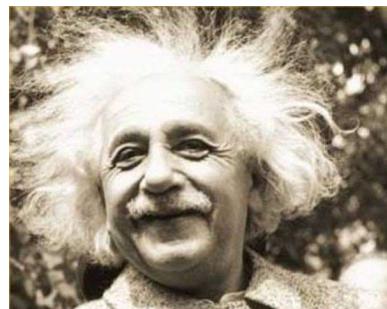
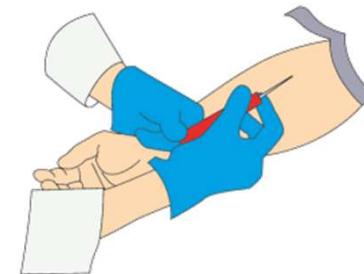
Slimme naaldencontainer of injecties





Bioanalytisch bepalen

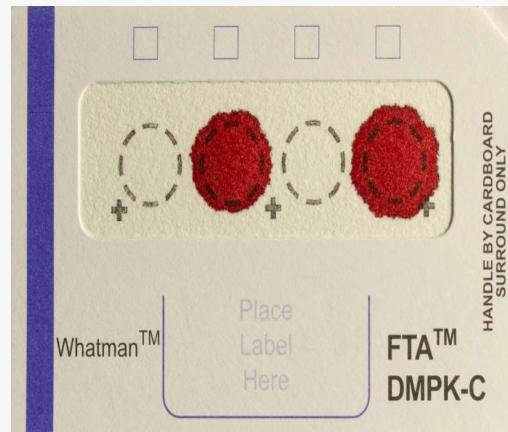
- **Bloed**
 - Drug monitoring (TDM)
- **Speeksel**
 - Drug of abuse monitoring
- **Urine**
 - Drug of abuse monitoring
- **Haar**
 - Forensisch





Bloed: kan het beter?

- “Dried blood spots” minder invasief
- Minder vaak naar het ziekenhuis (COVID)
- Toepassing o.a. bij adalimumab, azathioprine, MTX



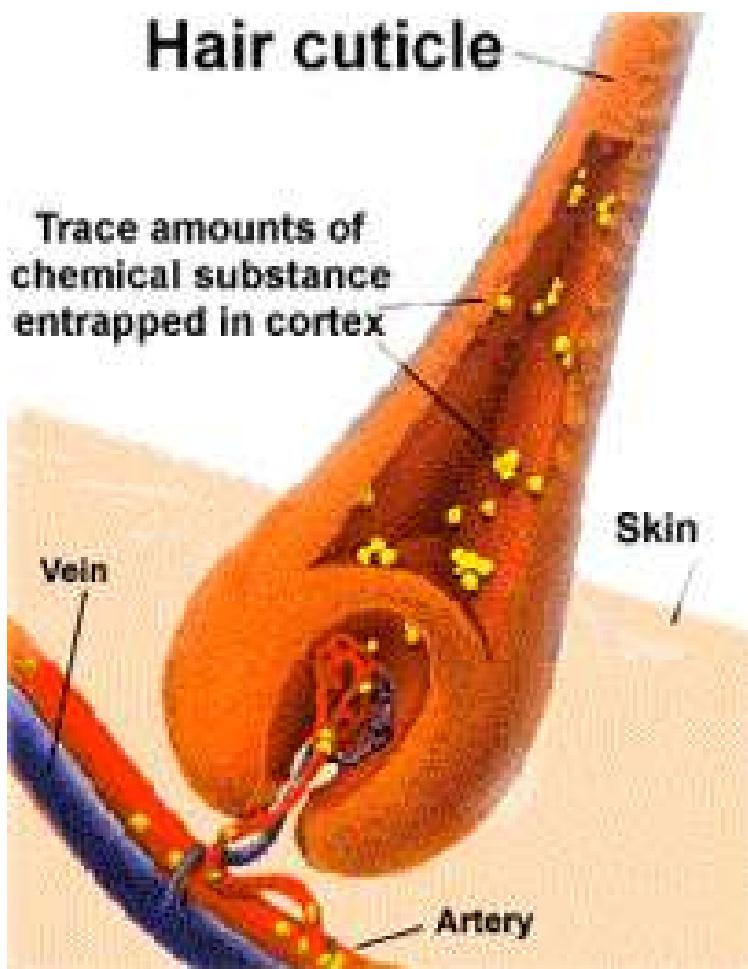
+: dagelijkse variatie, werkelijke exposure

-: PK variatie, white coat adherence, short term, frequente afname...





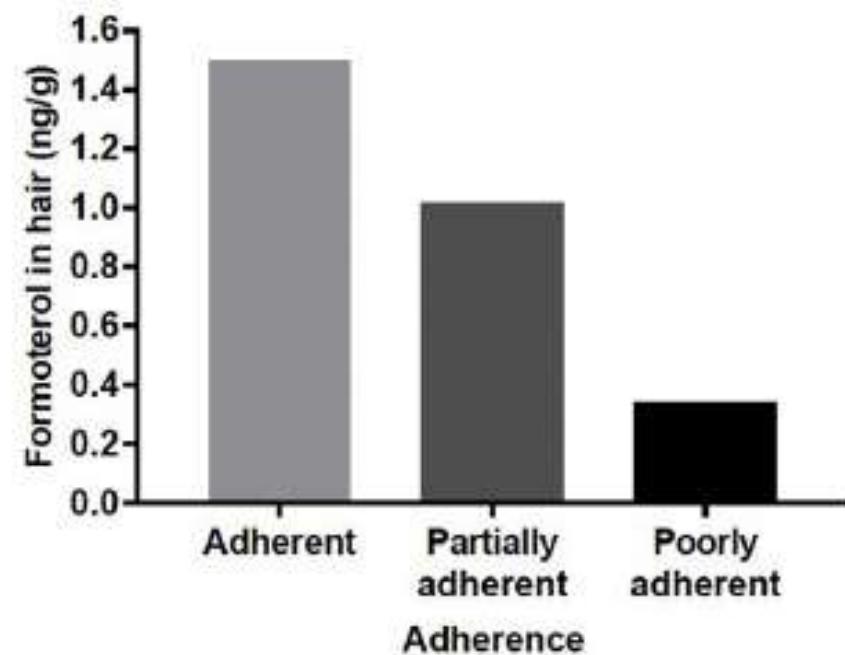
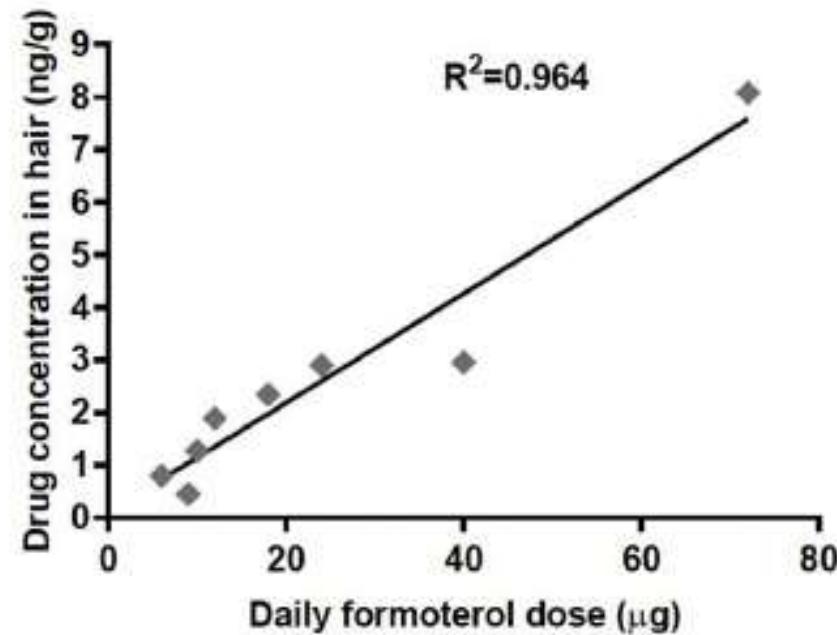
Haar analyse?



- In hoofdhuid zitten kleine bloedvaatjes
 - Van bijna alles wat er doorstroomt wordt een klein beetje in het haar afgezet
 - Haar groeit +/- 1 cm per maand
 - Traditioneel: drugs aanwezig?
-
- Ook ideale meting van **lange termijn** geneesmiddel concentraties?

Haar analyse

- N=200 met stabiel astma en/of COPD, haar geanalyseerd met LC-MS/MS
- NB haar kleur had invloed op de detectie
- In RA: o.a. ciclosporine



Dus we kunnen meten, maar...



Wat werkt?



Prevention, screening, assessing and managing of non-adherent behaviour in people with rheumatic and musculoskeletal diseases: systematic reviews informing the 2020 EULAR points to consider

Valentin Ritschl ,¹ Tanja A Stamm ,¹ Daniel Aletaha ,² Johannes W J Bijlsma ,³ Peter Böhm ,⁴ Razvan Dragoi ,⁵ Emma Dures ,^{6,7} Fernando Estévez-López ,⁸ Laure Gossec ,^{9,10} Annamaria Iagnocco ,¹¹ José B Negrón ,¹² Michal Nudel,¹³ Andréa Marques ,¹⁴ Ellen Moholt,¹⁵ Conni Skrubbeltrang ,¹⁶ Bart Van den Bemt ,^{17,18} Kirsten Viktil ,^{19,20} Marieke Voshaar ,²¹ Loreto Carmona ,²² Annette de Thurah ,^{23,24}

Table 2 Summary of the included studies, PICO 1

	Dx	Edu	Beh	CBT	Mot	Sup	MCo	Oth
Medication	RA	3+/3-	1+/1-	1+			2+	1~
	SLE	1+	1-					
	Psoriasis						1+	
	OP							1~/1-
	Total	4+/3-	1+/2-	1+			3+	2~/1-

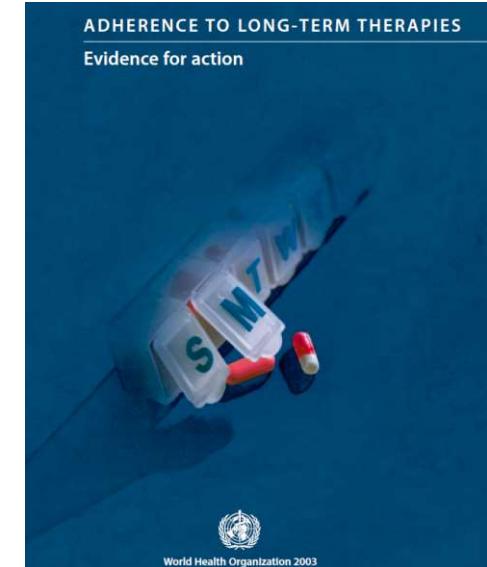
Education, behavioural interventions, cognitive behavioural therapy, motivation, supervised exercise, multicomponent, other



Verschillende achtergronden

- Erratic non-adherence
 - Intelligent non-adherence
 - Unwitting non-adherence
-
- NB In één patient kunnen verschillende vormen voorkomen

Elke vorm vraagt om een andere aanpak (op maat)!





'Erratic' non-adherence

- Niet-intentionele therapieontrouw; vergeetachtigheid
- Patiënten willen graag zo therapietrouw mogelijk zijn maar kunnen het medicatie regimen niet combineren met hun (drukke of weinig gestructureerde) leven



Mogelijke interventies: reminders, simplificeer regimens, linken aan dagelijkse gewoonte, familie/mantelzorger



Intelligent non-adherence

- Intentionele therapieontrouw: bewust aanpassen, stoppen of niet eens beginnen met voorgeschreven therapie (initiele medicatie trouw)
- **Waarom?:** (angst voor) bijwerkingen; smaak; complexiteit; interfereert met druk leven; kosten; oneens met voorschrijver over noodzaak (ziekte perceptie speelt belangrijke rol)

Mogelijke interventies: motivational interviewing, educatie, shared decision making, link met persoonlijke doelen



Unwitting non-adherence

- Niet-intentionele vorm van therapieontrouw
- Patiënt begrijpt niet volledig hoe/wanneer (en of chronisch) de medicatie moet worden ingenomen:
 - Ziet verschil niet tussen “indien nodig” medicatie en onderhouds medicatie
 - Suboptimale toediening medicatie



**Mogelijke interventies: educatie, pillbox,
instructie, training, zelf-management plan**



EULAR recommendations

Adherence is defined as the extent to which a person's behaviour corresponds with the agreed prescription*⁴

Overarching principles

- A Adherence impacts the outcomes of people with RMDs.
- B Shared decision making is key, since adherence is a behaviour following an agreed prescription.
- C Adherence is influenced by multiple factors.
- D Adherence is a dynamic process that requires continuous evaluation.

Points to consider

- 1 All HCPs involved in the management of people with RMDs should take responsibility for promoting adherence.
- 2 Effective patient-health professional communication should be applied to enhance adherence.
- 3 Barriers and facilitators of adherence of a specific patient to a specific prescription should be appropriately evaluated.
- 4 Patient education should be provided for people with RMDs as an integral part of standard care.
- 5 Care should be tailored to patient preferences and goals to enhance adherence.
- 6 Adherence should be discussed regularly based on open questions and particularly when disease is not well controlled.
- 7 The HCP should explore which factors might negatively influence adherence, including: opportunity (eg, availability or cost), capability (eg, memory problems), motivation (eg, concerns).
- 8 Together with the patient, the HCP should tailor the approach to overcome individual barriers to adherence, for example, simplifying the regimen, using reminders, providing education, discussing the patient's beliefs on treatments.
- 9 When specific expertise or interventions for adherence are needed, they should be made available to patients.



Stappenplan

Identificeer

- Wie?: Vin
- Waarom?: "therapie-ontrouw"
- Wat?: Inter



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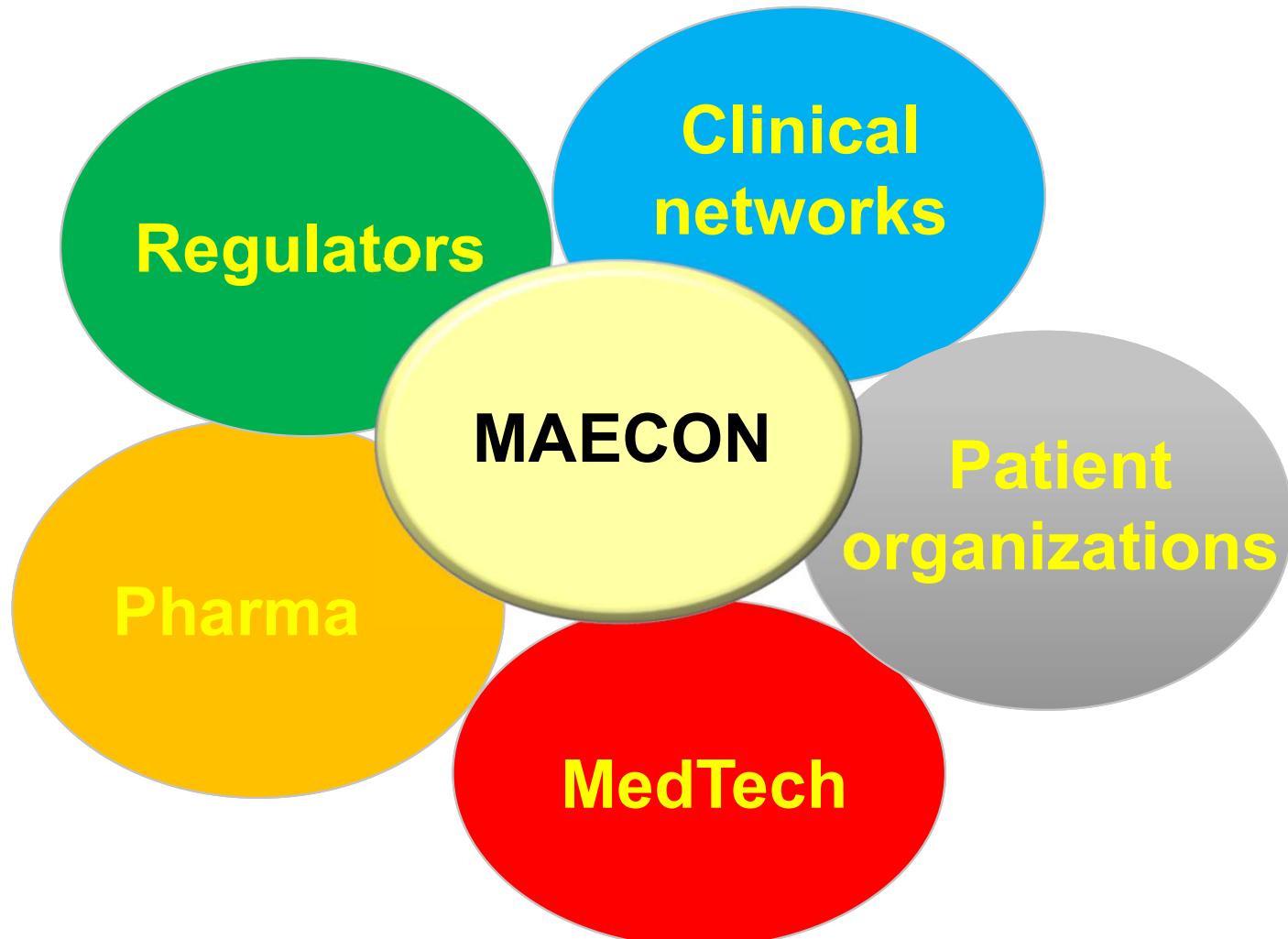
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enieur

"therapie-ontrouw



Therapietrouw Expertise Center MAECON





Referenties

- van Boven JFM, Dierick BJH, Usmani OS. When biology meets behaviour: can medication adherence mask the contribution of pharmacogenetic effects in asthma? *Eur Respir J.* 2021; 58(3):2100304
- Scheiman-Elazary A, Duan L, Shourt C, Agrawal H, Ellashof D, Cameron-Hay M, Furst DE. The Rate of Adherence to Antiarthritis Medications and Associated Factors among Patients with Rheumatoid Arthritis: A Systematic Literature Review and Metaanalysis. *J Rheumatol.* 2016;43(3):512-23
- van den Bemt BJ, van den Hoogen FH, Benraad B, Hekster YA, van Riel PL, van Lankveld W. Adherence rates and associations with nonadherence in patients with rheumatoid arthritis using disease modifying antirheumatic drugs. *J Rheumatol.* 2009; 36(10):2164-70
- Waimann CA, Marengo MF, de Achaval S, Cox VL, Garcia-Gonzalez A, Reveille JD, Richardson MN, Suarez-Almazor ME. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: consequences of low adherence. *Arthritis Rheum.* 2013; 65(6):1421-9
- Chan AHY, Horne R, Hankins M, Chisari C The Medication Adherence Report Scale: A measurement tool for eliciting patients' reports of nonadherence. *Br J Clin Pharmacol.* 2020;86(7):1281-1288
- Hughes LD, Done J, Young A. A 5 item version of the Compliance Questionnaire for Rheumatology (CQR5) successfully identifies low adherence to DMARDs. *BMC Musculoskelet Disord.* 2013; 14:286
- Li P, Blum MA, Von Feldt J, Hennessy S, Doshi JA. Adherence, discontinuation, and switching of biologic therapies in medicaid enrollees with rheumatoid arthritis. *Value Health.* 2010;13(6):805-12
- Zijp TR, Mol PGM, Touw DJ, van Boven JFM. Smart Medication Adherence Monitoring in Clinical Drug Trials: A Prerequisite for Personalised Medicine? *EClinicalMedicine.* 2019;15:3-4
- Hassall et al. Hair analysis to monitor adherence to prescribed chronic inhaler drug therapy in patients with asthma or COPD. *Pulm Pharmacol Ther.* 2018;51:59-64
- Ritschl V, Stamm TA, Aletaha D, et al. Prevention, screening, assessing and managing of non-adherent behaviour in people with rheumatic and musculoskeletal diseases: systematic reviews informing the 2020 EULAR points to consider. *RMD Open.* 2020; 6(3):e001432
- Ritschl V, Stamm TA, Aletaha D, et al. 2020 EULAR points to consider for the prevention, screening, assessment and management of non-adherence to treatment in people with rheumatic and musculoskeletal diseases for use in clinical practice. *Ann Rheum Dis.* 2021; 80(6):707-713
- World Health Organization: Adherence to long-term therapies – Evidence for action. 2003