Tiltak for å bedre pasienters etterlevelse av legemiddelbehandling

Notat fra Kunnskapssenteret
Systematisk litteratursøk med sortering
Juni 2014

kunnskapssenteret

Nasjonalt kunnskapssenter for helsetjenesten
Postboks 7004, St. Olavs plass
N-0130 Oslo
(+47) 23 25 50 00
www.kunnskapssenteret.no
Notat: ISBN 978-82-8121-873-4

Juni 2014

kunnskapssenteret

Tittel	Tiltak for å bedre pasienters etterlevelse av legemiddelbehandling
English title	Interventions to improve patients' adherance to medications
Institusjon	Nasjonalt kunnskapssenter for helsetjenesten
Ansvarlig	Magne Nylenna, direktør
Forfattere	Berg, Rigmor C, prosjektleder, *forsker, Kunskapssenteret* Straumann, Gyri H., *forskningsbibliotekar, Kunnskapssenteret* Vist, Gunn E., *seksjonsleder, Kunnskapssenteret*
ISBN	978-82-8121-873-4
Notat	Juni – 2014
Prosjektnummer	1008
Publikasjonstype	Notat - Systematisk litteratursøk med sorterte referanser
Antall sider	30 (78 inklusiv vedlegg)
Oppdragsgiver	Helsedirektoraret
Emneord(MeSH)	Medication Adherance
Sitering	Berg RC, Straumann GH, Vist GE. Tiltak for å bedre pasienters etterlevelse av legemiddelbehandling. Notat. Oslo: Nasjonalt kunnskapssenter for helsetjenesten, 2014.

Nasjonalt kunnskapssenter for helsetjenesten fremskaffer og formidler kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten. Målet er å bidra til gode beslutninger slik at brukerne får best mulig helsetjenester. Kunnskapssenteret er formelt et forvaltningsorgan under Helsedirektoratet, men har ingen myndighetsfunksjoner og kan ikke instrueres i faglige spørsmål.

Nasjonalt kunnskapssenter for helsetjenesten
Oslo, juni 2014

Hovedfunn

Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag fra Helsedirektoratet å utføre et systematisk litteratursøk med påfølgende sortering av mulig relevante publikasjoner. Oppdraget var å finne systematiske oversikter om effekten av tiltak for å bedre pasienters etterlevelse av legemiddelbehandling.

Metode

Vi utarbeidet søkestrategi for et systematisk litteratursøk. Det ble søkt i syv internasjonale litteraturdatabaser. Søket ble utført i april 2014. To forskere gikk uavhengig av hverandre gjennom identifiserte publikasjoner/referanser og vurderte relevans i forhold til inklusjonskriteriene.

Resultater

Vi identifiserte totalt 3174 referanser. Av disse var 106 mulig relevante.

Vi sorterte oversiktene i ni kategorier ut fra medikamentell etterlevelsetiltak. Hovedkategoriene av tiltak benyttet for å øke etterlevelse av legemidler var:

- E-helse- eller telehelsebaserte tiltak (12 oversikter)
- Tiltak gitt av helsepersonell (8 oversikter)
- Opplæring (6 oversikter)
- Tiltak gitt av farmasøyter (5 oversikter)
- Motiverende samtale (3 oversikter)
- Påminnelsepakninger (3 oversikter)
- Andre tiltak (10 oversikter)

- Alle typer etterlevelsetiltak for ulike populasjoner (7 oversikter)
- Alle typer etterlevelsetiltak for ulike sykdommer (52 oversikter)

Tittel:

Effekten av tiltak for å bedre pasienters etterlevelse av legemiddelbehandling

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Publikasjonstype:

Systematisk litteratursøk med sortering

Systematisk litteratursøk med sortering er resultatet av å
- søke etter relevant litteratur ifølge en søkestrategi og
- eventuelt sortere denne litteraturen i grupper presentert med referanser og vanligvis sammendrag

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Svarer ikke på alt:

- Ingen kritisk vurdering av studienes kvalitet
- Ingen analyse eller sammenfatning av studiene
- Ingen anbefalinger

Hvem står bak denne publikasjonen?

Kunnskapssenteret har gjennomført oppdraget etter forespørsel fra Helsedirektoratet

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Når ble litteratursøket utført?

Søk etter studier ble avsluttet april 2014.

Key messages

The Norwegian Knowledge Centre for the Health Services was commissioned by the Health Directorate to conduct a systematic literature search with subsequent sorting of possible relevant publications. The aim was to identify systematic reviews on the effect of interventions designed to improve patients' adherance with drug therapy.

Methods

We developed a search strategy for a systematic literature search. The search was carried out in seven international literature databases in April 2014. Two researchers independently screened the identified publications / references and assessed their relevance relative to the inclusion criteria.

Results

We identified a total of 3174 references, of which there were 106 relevant publications.

We sorted the publications into nine categories, based on drug adherance intervention. The main categories of interventions used to improve adherence to drug therapy were:

- E-health or telehealth interventions (12 reviews)
- Interventions provided by healthcare personnel (8 reviews)
- Education (6 reviews)
- Interventions provided by pharmacists (5 reviews)
- Motivational Interviewing (3 reviews)
- Reminder functions (3 reviews)
- Other interventions (10 reviews)
- All types of adherance interventions for different populations (7 reviews)
- All types of adherance interventions for different diseases (52 reviews).

Title:

The effectiveness of interventions to improve patients' adherance to medications

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Type of publication:

Systematic reference list

A systematic reference list is the result of a search for relevant literature according to a specific search strategy. The references resulting from the search are then grouped and presented with their abstracts.

Doesn't answer eve-rything:

- No critical evaluation of study quality
- No analysis or synthesis of the studies
- No recommendations

Publisher:

Norwegian Knowledge Centre for the Health Services

Updated:

Last search for studies: April, 2014.

Innhold

Forord

Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag fra Helsedirektoratet å utføre et systematisk litteratursøk med påfølgende sortering av mulig relevante publikasjoner («søk og sorter»). Oppdraget var å finne systematiske oversikter om effekten av tiltak for å bedre pasienters etterlevelse av legemiddelbehandling. Denne informasjonen skal brukes som støtte til Helse- og omsorgsdepartementets (HOD) utforming av en Stortingsmelding om legemidler.

Litteraturen i vår referanseliste kan bidra til dokumentasjonsgrunnlaget for den nye Stortingsmeldingen om legemidler.

Prosjektgruppen har bestått av:

- Rigmor C Berg, forsker, Kunnskapssenteret
- Gyri H. Straumann, bibliotekar, Kunnskapssenteret
- Gunn E. Vist, seksjonsleder, Kunnskapssenteret

Gro Jamtvedt	Gunn E. Vist	Rigmor C Berg
Avdelingsdirektør	*Seksjonsleder*	*Prosjektleder*

Innledning

Bakgrunn

Uriktig bruk av legemidler kan være helseskadelig for den enkelte pasient, kan medføre resistensutvikling i tilfelle for antibiotikabruk, og er dessuten kostbart både for pasienten og for samfunnet. Det kan i tillegg skape en unødvendig belastning for helsetjenesten. Begrepet «etterlevelse» av legemiddelbruk benyttes for å beskrive i hvilken grad en pasient henter ut et legemiddel på apoteket, tar det til riktig tid, i rett dose, og eventuelt fullfører behandlingen (1).

Litteraturen tilsier at lav etterlevelse av legemiddelbehandling er et voksende problem, særlig blant eldre og pasienter med kroniske lidelser. Verdens helseorganisasjon har anslått at kun halvparten av de som bruker legemidler for en kronisk lidelse etterlever behandlingen slik legen har forskrevet (2). En norsk litteraturgjennomgang for syv vanlige legemiddelgrupper (antidiabetika, antiepileptika, antihypertensiver, statiner, psykofarmaka, antibiotika, analgetika) viste at et knippe nøkkelfaktorer er assosiert med lav etterlevelse: dosering mer enn én gang daglig, komplekse behandlingsregimer, nedsatt kognitiv funksjon og depresjon, og utilstrekkelig oppfølging. Følgelig vil tiltak rettet mot denne typen faktorer kunne øke etterlevelsen, slik som forenkling av doseringen (f.eks. depottabletter, kombinasjonspreparater), tilrettelegging av praktiske forhold (f.eks. doseringshjelpemidler, allianse med pårørende, involvering av hjemmetjenesten) og tettere oppfølging (f.eks. hyppige kontroller, korte ventetider) (1).

Eksperimentelle forsøk som undersøker effekten av ulike tiltak for å bedre etterlevelse av medikamentbruk vil kunne gi et pålitelig svar på hvilke tiltak som er mest hensiktsmessige.

Styrker og svakheter ved litteratursøk med sortering

Ved litteratursøk gjennomfører vi systematiske litteratursøk for en gitt problemstilling. Resultatene fra søket blir i sin helhet overlevert oppdragsgiver, eller vi kan gjennomgå søkeresultatet før overleveringen og sortere ut ikke-relevante artikler. Dette gjøres basert på tittel og eventuelt sammendrag. Artiklene innhentes ikke i fulltekst. Det gjør at vi kan ha inkludert titler som ville vist seg ikke å være relevante

ved gjennomlesning av fulltekst. Vi benytter kun databaser for identifisering av litteratur og kan derfor ha gått glipp av potensielt relevante studier. Andre måter å identifisere studier på, som søk i referanselister, kontakt med eksperter på fagfeltet og upublisert litteratur, er ikke utført i søk og sorter oppdrag. Vi gjennomfører ingen kvalitetsvurdering av artikler.

Ved en full forskningsoppsummering ville vi ha innhentet artiklene i fulltekst for endelig vurdering opp mot inklusjonskritene. Inkluderte studier ville så blitt kvalitetsvurdert i henhold til våre sjekklister og resultater sammenstilt og diskutert.

Begrunnelse for valg av søkestrategi

Med bakgrunn i oppdraget har vi søkt i elektroniske kilder, men ikke etter grå litteratur eller liknende. Søket er gjort for tidsperioden 2009-2014 da systematiske oversikter er mindre nyttige jo eldre de er. I søkene er det benyttet filter på systematiske oversikter for å begrense til dette studiedesignet.

Problemstilling

I prosjektet har vi søkt etter litteratur som skal belyse problemstillingen knyttet til etterlevelse av legemiddelbehandling. Målet med prosjektet var å utføre et «søk og sorter» etter systematiske oversikter. Spørsmålet som skulle besvares var: Hvilken systematisk oppsummert dokumentasjon fins om effekten av tiltak for å bedre pasienters etterlevelse av legemiddelbehandling?

Metode

Bakgrunnen for valg av metoden litteratursøk med søk og sorter er at vi allerede kjente til at det er flere mulige relevante systematiske oversikter på dette fagfeltet. I denne publikasjonen har vi utført et systematisk litteratursøk, valgt ut systematiske oversikter etter forhåndsbestemte kriterier og med påfølgende sortering av mulig relevante publikasjoner. Som del av denne bestillingen vil vi også vurdere å formidle enkelte nyere Cochrane-oversikter i egne omtaler publisert på Kunnskapssenterets nettsider.

Litteratursøking

Vi søkte systematisk etter litteratur i følgende syv internasjonale databaser:

- Cinahl
- Cochrane Database of Systematic Reviews (CDSR)
- Centre for Reviews and Dissemination (CRD)
- Embase
- Medline
- PsycInfo
- Web of Knowledge (ISI)

Forskningsbibliotekar Gyri H. Straumann planla og utførte samtlige søk i samarbeid med prosjektgruppen. Søkene ble utført 24.-25. april 2014. Søkene ble avgrenset til systematiske oversikter publisert f.o.m. 2009 t.o.m. søkedato. Vi la bestillingen til grunn ved utarbeiding av litteratursøket og søkte etter systematiske oversikter som oppfylte våre inklusjonskriterier. Det ble brukt filter for systematiske oversikter i søkene. De fullstendige søkestrategiene fins i vedlegg 1.

Inklusjonskriterier

Populasjon:	Pasienter som får legemiddelbehandling forskrevet av lege i forebyggende eller terapeutisk øyemed. Ingen begrensninger på kjønn, alder, nasjonalitet, sykdomstilstand eller annet.
Tiltak:	Tiltak som har som mål å bedre etterlevelse av legemiddelbehandling. Dette inkluderte, men var ikke begrenset til, tiltak

	som for eksempel: opplæring og informasjonstiltak, mobilapplikasjoner for å påminne om legemiddelbruk, støtte fra pasientorganisasjoner, legemiddellister, legemiddelgjennomgang.
Sammenlikning:	Vanlig praksis, ingen tiltak. Det var ingen begrensninger når det gjelder sammenligning.
Utfall:	Pasientens etterlevelse av legemiddelbehandling. Det var ingen begrensninger når det gjelder metoder for å måle etterlevelse.
Studiedesign	Systematiske oversikter. Vi definerer systematiske oversikter slik: oversikt som beskriver litteratursøk, har kriterier for inklusjon og eksklusjon av studier og metodisk kvalitetsvurdering av studier. Vi inkluderte ikke protokoller eller konferanseabstrakt.
Språk:	Engelsk, skandinaviske språk (dansk, norsk, svensk), tysk.

Artikkelutvelging

To forskere gikk gjennom alle titler og sammendrag identifisert via litteratursøket for å vurdere relevans i henhold til inklusjonskriteriene. Vurderingene ble først utført uavhengig av hverandre og deretter sammenlignet. Ved uenighet ble inklusjonsvurderingen avgjort ved konsensus. Dersom det hadde vært vedvarende uenighet ville prosjektansvarlig fattet en beslutning om inklusjon/eksklusjon, men dette ble ikke nødvendig. Et inkluderingsskjema ble utarbeidet av prosjektleder og benyttet i utvelgelsen. Utvelging av litteratur ble gjort basert på tittel og sammendrag. Vi bestilte ikke fulltekst av artiklene.

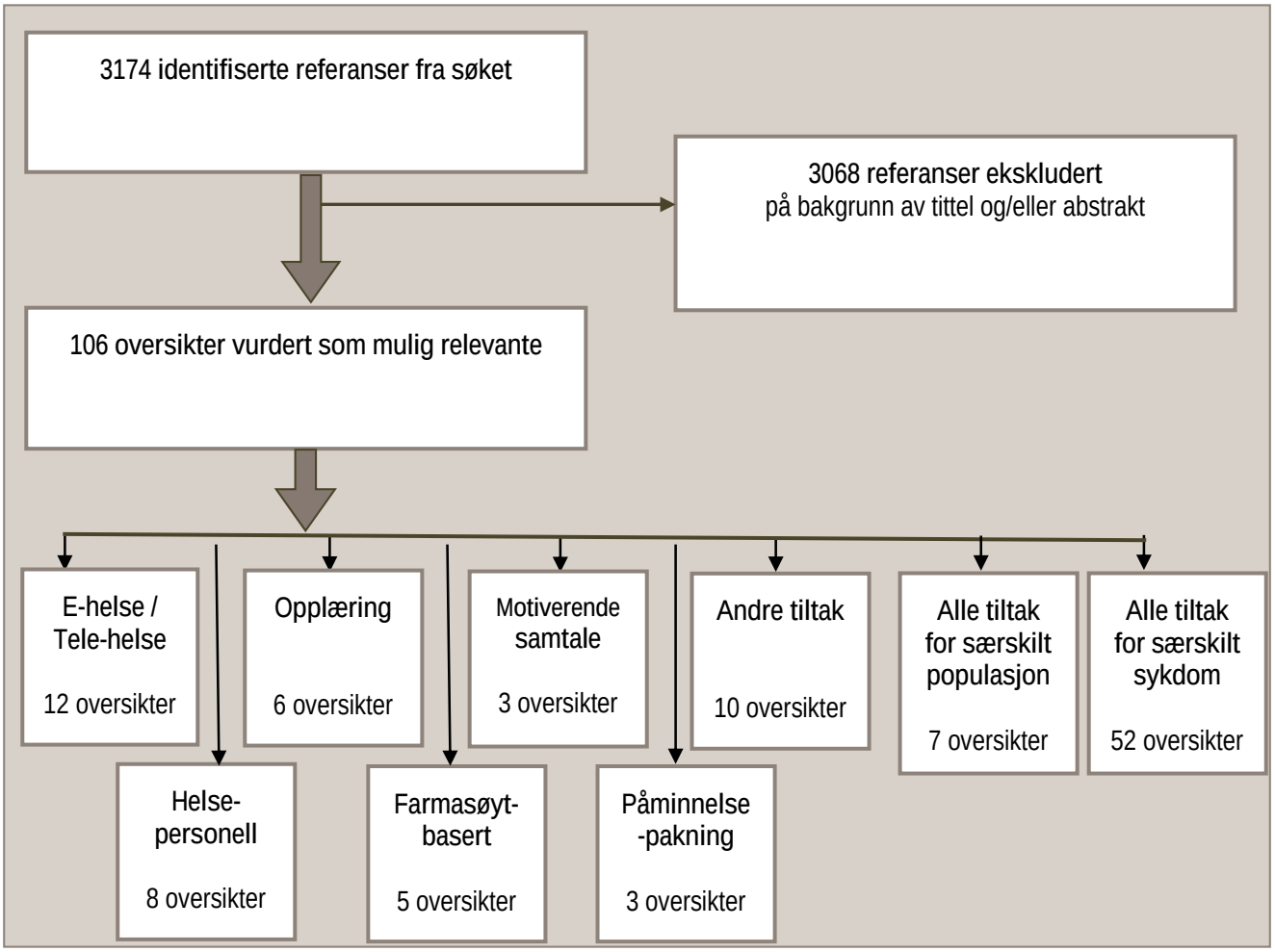
Sortering

Vi lagde en liste over alle mulig relevante oversikter og sorterte dem i henhold til tiltak. Tiltakene ble videre sortert i henhold til sykdom eller lidelse for medikamentell behandling. Det ble ikke foretatt innhenting av litteratur i fulltekst, og derfor heller ikke kvalitetsvurdering eller analyser.

Resultat

Resultat av søk

Søket resulterte i 3174 referanser (figur 1). Vi vurderte 106 av de identifiserte referansene til å være mulig relevante i henhold til inklusjonskriteriene.



Figur 1. Flytskjema over identifisert litteratur

Resultat av sorteringen

De mulig relevante systematiske oversiktene ble sortert i ni kategorier ut fra fokus på medikamentell etterlevelsetiltak (tabell 1).

Av de 106 mulig relevante systematiske oversiktene var det syv hovedkategorier av strategier eller tiltak benyttet for å øke etterlevelse av legemidler. Det var også en kategori av alle typer etterlevelsetiltak for ulike typer sykdommer. Til slutt identifiserte vi en kategori av alle typer etterlevelsetiltak for ulike populasjoner. De ni kategoriene er oppsummert i tabell 1.

Tabell 1: *Antall oversiktsartikler sortert etter tiltak*

Tiltak	Antall oversikter: 106
E-helse eller telehelse-basert	12
Tiltak gitt av helsepersonell	8
Opplæring	6
Tiltak gitt av farmasøyter	5
Motiverende samtale	3
Påminnelsepakning	3
Andre tiltak	10
Alle typer tiltak for ulike sykdommer	52
Alle typer tiltak for ulike populasjoner	7

I vedlegg 2 (fra side 35) presenterer vi de 106 referansene fordelt i henhold til våre ni sorteringskategorier. Vi oppgir forfattere, tittel på publikasjonen, publikasjonssted og sammendrag av artikkelen slik de fremkom i de elektroniske databasene.

E-helse / Telehelse-baserte tiltak

Vi identifiserte 12 systematiske oversikter som omhandlet effekten av e-helse eller telehelsetiltak for å øke etterlevelse av medisiner (tabell 2). Slike tiltak var beskrevet som påminnelser gitt via tekstmeldinger (sms), personsøker, telefonsamtale; IT-baserte; internett-baserte. Sykdommene som disse tiltakene rettet seg mot var diabetes type 2 (3); hiv (4-6), tuberkulose (7), akne (8), kronisk sykdom (9), hjertekarsykdom og diabetes (10). Fire systematiske oversikter omhandler e-helse / telehelse-baserte tiltak for alle typer sykdommer (11-14).

Tabell 2: *Oversiktsartikler som omhandlet e-helse eller telehelse-baserte tiltak, sortert alfabetisk etter forfatter (n=12)*

Forfatter, årstall (ref)	Tittel
Cassimatis 2012 (3)	Effects of type 2 diabetes behavioural telehealth interventions on glycaemic control and adherence: a systematic review
Fenerty 2012 (11)	The effect of reminder systems on patients' adherence to treatment
Finitsis 2014 (4)	Text Message Intervention designs to promote adherence to Antiretroviral Therapy (ART): A meta-analysis of randomized controlled trials
Free 2013 (12)	The effectiveness of mobile-health technology-based health behaviour change or disease management Iinterventions for health care consumers: A systematic review
Horvath 2012 (5)	Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection
Linn 2011 (13)	Effects of eHealth Interventions on medication adherence: A systematic review of the literature
McKay 2013 (14)	How personalized should we be? A systematic review of tailored & targeted health communication interventions to improve adherence
Misono 2010 (10)	Healthcare information technology interventions to improve cardiovascular and diabetes medication adherence
Nglazi 2013 (7)	Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: A systematic review
Park 2014 (8)	Improving adherence to acne treatment: The emerging role of application software
Saberi 2011 (6)	Technology-based self-care methods of improving antiretroviral adherence: A systematic review
Vervloet 2012 (9)	The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: a systematic review of the literature

Sammendragene til disse oversiktene er listet alfabetisk i vedlegg 2 (fra side 35).

Tiltak gitt av helsepersonell

Åtte systematiske oversikter omhandlet effekten av medikamentelle etterlevelsetiltak gitt av helsepersonell (tabell 3). Slike tiltak var blant annet beskrevet som samtaler med helsepersonell (ikke lege, sykepleier), direkte observert behandling ('directly observed therapy') og sykepleie-basert behandling. Tiltakene rettet seg mot personer med følgende sykdommer: hjertekarsykdom (15), diabetes (16, 17), hjertekarsykdom og diabetes (18), hiv (19-21) og kronisk sykdom (22).

Tabell 3: *Oversiktsartikler som omhandlet tiltak gitt av helsepersonell, sortert alfabetisk etter forfatter (n=8)*

Forfatter, årstall (ref)	Tittel
Cutrona 2010b (18)	Physician effectiveness in interventions to improve cardiovascular medication adherence: A systematic review

Doggrell 2010 (16)	Does intervention by an allied health professional discussing adherence to medicines improve this adherence in Type 2 diabetes?
Ford 2009 (19)	Directly observed antiretroviral therapy: a systematic review and meta-analysis of randomised clinical trials
Hart 2010 (20)	Effect of directly observed therapy for Highly Active Antiretroviral Therapy on virologic, immunologic, and adherence outcomes: A meta-analysis and systematic review
Kenya 2011 (21)	Can community health workers improve adherence to highly active antiretroviral therapy in the USA? A review of the literature
Mansoor 2013 (15)	Multiprofessional interventions to improve patient adherence to cardiovascular medications
Schoenthaler 2013 (17)	A systematic review of interventions to improve adherence to diabetes medications within the patient-practitioner interaction
Van Camp 2013 (22)	Nurse-led interventions to enhance adherence to chronic medication: systematic review and meta-analysis of randomised controlled trials

Sammendragene til disse oversiktene er tilgjengelige i vedlegg 2 (fra side 40).

Opplæring

Vi identifiserte seks systematiske oversikter som omhandlet effekten av opplæring for å øke etterlevelse av medisiner (tabell 4). Opplæring inkluderte ulike typer undervisning og trening. Diagnosene som opplæring rettet seg mot var astma (23), kreft (24), hjertekarsykdommer (25), høyt blodtrykk (26), tuberkulose (27) og glaukom (28).

Tabell 4: *Oversiktsartikler som omhandlet opplæring, sortert alfabetisk etter forfatter (n=6)*

Forfatter, årstall (ref)	Tittel
Axelsson 2012 (23)	Recent educational interventions for improvement of asthma medication adherence
Gassman 2012 (24)	Interventions promoting adherence in the care of patients with oral chemotherapy - A systematic literature review
Ghisi 2014 (25)	A systematic review of patient education in cardiac patients: Do they increase knowledge and promote health behavior change?
Li 2014 (26)	Influence of health education on medicine-taking compliance of Chinese hypertensive patients: A Bayesian meta-analysis
M'Imunya 2012 (27)	Patient education and counselling for promoting adherence to treatment for tuberculosis
Newman-Casey 2013 (28)	Systematic review of educational interventions to improve glaucoma medication adherence

I vedlegg 2 (fra side 43) presenteres sammendragene til disse seks oversiktene.

Tiltak gitt av farmasøyt

Vi identifiserte fem systematiske oversikter som omhandlet effekten av farmasøyt-baserte tiltak for å øke etterlevelse av medisiner (tabell 5). Slike tiltak var beskrevet som opplæring og monitorering gjennomført av en farmasøyt. Sykdommene som disse tiltakene rettet seg mot var: depresjon (29, 30), høyt blodtrykk (31) og diabetes type 2 (32). Én oversikt inkluderte personer med enhver type sykdom (33).

Tabell 5: *Oversiktsartikler som omhandlet tiltak gitt av farmasøyter, sortert alfabetisk etter forfatter (n=5)*

Forfatter, årstall (ref)	Tittel
Al-Jumah 2012 (29)	Impact of pharmacist interventions on patients' adherence to antidepressants and patient-reported outcomes: a systematic review
Morgado 2011 (31)	Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: Review and meta-analysis
Omran 2012 (32)	Systematic review of pharmacist interventions to improve adherence to oral antidiabetic medications in people with type 2 diabetes
Rickles 2010 (33)	Adherence: a review of education, research, practice, and policy in the United States
Rubio-Valera 2011 (30)	Effectiveness of pharmacist care in the improvement of adherence to antidepressants: A systematic review and meta-analysis

I vedlegg 2 (fra side 45) presenteres sammendragene til disse oversiktene.

Motiverende samtale

Tre systematiske oversikter omhandlet effekten av motiverende samtale som medikamentell etterlevelsetiltak (tabell 6). Motiverende samtale er en type samtaleterapi for å motivere personer til å endre uønsket atferd, slik som opphold eller avbrudd i bruk av legemidler. Tiltakene rettet seg mot personer med schizofreni (34) og hiv (35). Én systematisk oversikt omhandlet motiverende samtale for medisinsk etterlevelse blant personer med enhver type sykdom (36).

Tabell 6: *Oversiktsartikler som omhandlet motiverende samtale, sortert alfabetisk etter forfatter (n=3)*

Forfatter, årstall (ref)	Tittel
Drymalski 2009 (34)	A review of Motivational Interviewing to enhance adherence to antipsychotic medication in patients with schizophrenia: Evidence and recommendations
Easthall 2012 (36)	The impact of motivational interviewing (MI) as an intervention to improve medication adherence; A meta-analysis
Hill 2012 (35)	Motivational interviewing as a behavioral intervention to increase HAART adherence in patients who are HIV-positive: A systematic review of the literature

Sammendragene til disse oversiktene fins i vedlegg 2 (fra side 48).

Påminnelsepakning

Tre systematiske oversikter omhandlet effekten av påminnelsepakning ('reminder packaging') for å bedre etterlevelse av medikamentbruk (tabell 7). De tre systematiske oversiktene omtalte tiltakene som pakninger eller innretning med påminnelsesfunksjoner, for eksempel pakninger med dato eller tidspunkt for når medisinene skal tas. Tiltakene var ikke rettet mot personer med en spesiell type sykdom, men inkluderte personer som tok medikamenter for enhver type sykdom eller lidelse (37-39).

Tabell 7: *Oversiktsartikler som omhandlet påminnelsepakning, sortert alfabetisk etter forfatter (n=3)*

Forfatter, årstall (ref)	Tittel
Boeni 2014 (37)	Effect of drug reminder packaging on medication adherence: a systematic review revealing research gaps
Hall 2013 (38)	The effect of medical devices with dose-memory and reminder functions on patients' treatment adherence, confidence and disease self-management
Mahtani 2011 (39)	Reminder packaging for improving adherence to self-administered long-term medications

Sammendragene til disse oversiktene fins i vedlegg 2 (fra side 49).

Andre etterlevelsetiltak

Vi identifiserte ti systematiske oversikter som omhandlet effekten av andre typer tiltak (enn de angitt ovenfor) for å bedre etterlevelse av medisiner (tabell 8). Blant disse var det for eksempel elektronisk monitorering og økonomiske insentiver.

Tabell 8: *Oversiktsartikler som omhandlet andre tiltak, sortert alfabetisk etter forfatter (n=10)*

Forfatter, årstall (ref)	Tittel
Chapman 2014 (40)	Adherence to medication and self-management in stroke patients. British journal of nursing
Christensen 2009 (41)	Electronic monitoring of patient adherence to oral antihypertensive medical treatment: a systematic review
Cutrona 2010a (42)	Modes of delivery for interventions to improve cardiovascular medication adherence
DeFulio 2012 (43)	The use of incentives to reinforce medication adherence
Easthall 2013 (44)	A meta-analysis of cognitive-based behaviour change techniques as interventions to improve medication adherence
Golubev 2010 (45)	Compliance measurement-guided medication management programs in hypertension: A health technology assessment
Luersen 2012 (46)	Sticker Charts: A method for improving adherence to treatment of chronic diseases in children

Petry 2012 (47)	Financial reinforcers for improving medication adherence: Findings from a meta-analysis
Tran 2014 (48)	Patient reminder systems and asthma medication adherence: a systematic review
Van Dalem 2012 (49)	Interventions promoting adherence to cardiovascular medicines

Sammendragene til disse 10 oversiktene fins i vedlegg 2 (fra side 51).

Det var i mange tilfeller vanskelig å oversette termene for disse tiltak til norsk, i tabell 9 angir vi derfor både den norske og den engelske benevnelsen slik den er brukt i abstraktet.

Tabell 9: *Andre etterlevelsetiltak*

Tiltak (norsk)	Tiltak (engelsk)	Sykdom	Referanse
Egenmestring	Self-management	Slag	Chapman 2014 (40)
Elektronisk monitorerings-redskap	Electronic monitoring devices	Høyt blodtrykk	Christensen 2009 (41)
Personstyrt vs ikke-personstyrt	Person-independent vs person-dependent	Hjertekarsyk-dom/diabetes	Cutrona 2010a (42)
Insitament-basert	Incentives	Alle	DeFulio 2012 (43)
Kognitiv-baserte atferds-endringsteknikker	Cognitive-based behavior change techniques	Alle	Easthall 2013 (44)
Overholdelsetiltak	Compliance measurement-guided medication management prog	Høyt blodtrykk	Golubev 2010 (45)
Etikett-diagram/tabell	Sticker charts	Kronisk sykdom (barn)	Luersen 2012 (46)
Økonomiske insitament	Financial reinforcers	Alle	Petry 2012 (47)
Påminnelser	Patient reminder systems	Astma	Tran 2014 (48)
Tiltak gitt i samfunn/ lokalbefolkningen	Community-setting strategies	Hjertekarsyk-dom	Van Dalem 2012 (49)

Alle mulige tiltak for enhver type lidelse innenfor én populasjon

Vi identifiserte syv systematiske oversikter som omhandlet alle mulige etterlevelse-tiltak for enhver type lidelse innenfor én populasjonsgruppe (tabell 10). Det vil si at oversiktsforfatterne definerte oversikten kun etter populasjonen. Disse syv systematiske oversiktene omhandlet fire populasjonsgrupper: eldre, barn og unge, afroamerikanere og latinere, samt personer med kulturell- og språklig variert bakgrunn. Vi lister disse syv systematiske oversiktene nedenfor etter populasjon:

- Eldre: Banning 2009 (50); Conn 2009 (51); Patterson 2011 (52)
- Barn og unge: Lafond 2010 (53); Salema 2011 (54)
- Afroamerikanere og latinere: Hu 2014 (55)

- Personer med kulturell- og språklig variert bakgrunn: Manias 2010 (56)

Tabell 10: *Oversiktsartikler som omhandlet alle typer etterlevelsetiltak for ulike populasjoner, sortert alfabetisk etter forfatter (n=7)*

Forfatter, årstall (ref)	Tittel
Banning 2009 (50)	A review of interventions used to improve adherence to medication in older people
Conn 2009 (51)	Interventions to improve medication adherence among older adults: Meta-analysis of adherence outcomes among randomized controlled trials
Hu 2014 (55)	Interventions to increase medication adherence in African-American and Latino populations: a literature review
Lafond 2010 (53)	Medicine-taking interventions in children and young people: One size fits all, one size fits none
Manias 2010 (56)	Medication adherence in people of culturally and linguistically diverse backgrounds: A meta-analysis
Patterson 2011 (52)	Interventions to improve the appropriate use of polypharmacy for older people: A Cochrane Review
Salema 2011 (54)	A systematic review of adherence-enhancing interventions in adolescents taking long-term medicines

Sammendragene til disse syv oversiktene fins i vedlegg 2 (fra side 54).

Alle mulige tiltak for medisinsk etterlevelse innenfor én behandlingstype / diagnose

Totalt var det 52 systematiske oversikter som omhandlet tiltak for å bedre medisinsk etterlevelse blant personer med en spesiell sykdom (tabell 11). Oversiktene tok altså ikke for seg en spesiell type tiltak, men oppsummerte i stedet alle typer tiltak for å bedre medisinsk etterlevelse blant personer som behøvde medisiner for en særskilt sykdom. Alt i alt var etterlevelsetiltak for 28 ulike sykdommer oppsummert. Det fantes flest systematiske oversikter for hiv, hjertekarsykdommer og psykiske lidelser. Alle de systematiske oversiktene som omhandlet tiltak for å bedre medisinsk etterlevelse blant personer med en spesiell sykdom er listet nedenfor i alfabetisk rekkefølge etter sykdom eller lidelse:

- Astma: Andrews 2014 (57); Moullec 2012 (58)
- Bipolar lidelse: Berk 2010 (59); Crowe 2012 (60)
- Epilepsi (fallesyke): Al-Aqeel 2011 (61)
- Depresjon: Chong 2011 (62); van Servellen 2011 (63)
- Diabetes type 1: Hood 2010 (64)
- Diabetes type 2: Williams 2014 (65); Zomahoun 2012 (66)
- Hiv: Arrivillaga 2013 (67); Baernighausen 2011 (68); Bain-Brickley 2011 (69); Binford 2012 (70); Charania 2014 (71); de Bruin 2010 (72); Marcus 2014 (73); Mathes 2013 (74); Mills 2013 (75)

- Hjertekarsykdom / høyt blodtrykk og eller tar lipidsenkende medisiner: Chapman 2010 (76); Cutrona 2012 (77); de Simoni 2013 (78); Glynn 2011 (79); Gwadry-Sridhar 2013 (80); Kardas 2009 (81); Laba 2013 (82); Schedlbauer 2010 (83)
- Hjertesvikt: Molloy 2012 (84)
- Høyt intraokulært trykk: Gray 2009 (85); Waterman 2013 (86)
- Inflammatorisk tarmsykdom: Greenley 2013 (87)
- Kognitiv svekkelse (eldre): Campbell 2012 (88)
- Kreft: Mathes 2014 (89)
- Kronisk nyresykdom: Matteson 2010 (90)
- Kronisk obstruktiv lungesykdom: Bryant 2013 (91)
- Kronisk sykdom blant barn: Dean 2010 (92); Graves 2010 (93)
- Kronisk sykdom blant personer som bor i USA: Viswanathan 2012 (94)
- Malaria: Fuangchan 2014 (95)
- Organtransplantasjon: De Bleser 2009 (96)
- Osteoporose: Gleeson 2009 (97); Hiligsmann 2013 (98); White 2010 (99)
- Psykiatrisk lidelse: Garcia-Perez 2011 (100)
- Psykose: Barkhof 2012 (101)
- Revmatisme: Achaval 2010 (102)
- Schizofreni: Barry 2012 (103)
- Smerte: Argoff 2014 (104)
- Spedalskhet (Hansens sykdom): Weiand 2012 (105)
- Tuberkulose: Suwankeeree 2014 (106)

Vi nevner at det også var én systematisk oversikt som omhandlet tiltak for å bedre etterlevelse av hormonbaserte prevensjonsmidler (107) og én som så ut til å omhandle etterlevelsetiltak for enhver type sykdom der langtidsbruk av medisiner er nødvendig (108).

Tabell 11: *Oversiktsartikler som omhandlet alle typer etterlevelsetiltak for ulike sykdommer, sortert alfabetisk etter forfatter (n=52)*

Forfatter, årstall (ref)	Tittel
Achaval 2010 (102)	Treatment adherence to disease-modifying antirheumatic drugs in patients with rheumatoid arthritis and systemic lupus erythematosus
Al-Aqeel 2011 (61)	Strategies for improving adherence to antiepileptic drug treatment in patients with epilepsy
Andrews 2014 (57)	Asthma self management in adults: A review of current literature
Argoff 2014 (104)	Preventing and managing aberrant drug-related behavior in primary care: Systematic review of outcomes evidence
Arrivillaga 2013 (67)	Adherence among children and young people living with HIV/AIDS: A systematic review of medication and comprehensive interventions
Baernighausen 2011 (68)	Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies

Bain-Brickley 2011 (69)	Interventions to improve adherence to antiretroviral therapy in children with HIV infection
Barkhof 2012 (101)	Interventions to improve adherence to antipsychotic medication in patients with schizophrenia--a review of the past decade
Barry 2012 (103)	Schizophrenia
Berk 2010 (59)	Enhancing medication adherence in patients with bipolar disorder
Binford 2012 (70)	A systematic review of antiretroviral adherence interventions for HIV-infected people who use drugs
Bryant 2013 (91)	Improving medication adherence in chronic obstructive pulmonary disease: a systematic review
Campbell 2012 (88)	Medication adherence in older adults with cognitive impairment: A systematic evidence-based review
Chapman 2010 (76)	The cost and effectiveness of adherence-improving interventions for antihypertensive and lipid-lowering drugs
Charania 2014 (71)	Identification of evidence-based interventions for promoting HIV medication adherence: Findings from a systematic review of US-based studies, 1996-2011
Chong 2011 (62)	Effectiveness of interventions to improve antidepressant medication adherence: a systematic review
Crowe 2012 (60)	Effectiveness of interventions to improve medication adherence bipolar disorder
Cutrona 2012 (77)	Targeting cardiovascular medication adherence interventions
De Bleser 2009 (96)	Interventions to improve medication-adherence after transplantation: a systematic review
De Bruin 2010 (72)	Standard care impact on effects of Highly Active Antiretroviral Therapy Adherence interventions A meta-analysis of randomized controlled trials
De Simoni 2013 (78)	Trials to improve blood pressure through adherence to antihypertensives in stroke/TIA: Systematic literature review and meta-analysis
Dean 2010 (92)	A systematic review of interventions to enhance medication adherence in children and adolescents with chronic illness
Demonceau 2013 (108)	Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: A systematic literature review and meta-analysis
Fuangchan 2014 (95)	Intervention to promote patients' adherence to antimalarial medication: A systematic review
Garcia-Perez 2011 (100)	Cost-effectiveness of interventions to enhance medication adherence in psychiatric patients: a systematic review
Gleeson 2009 (97)	Interventions to improve adherence and persistence with osteoporosis medications: a systematic literature review
Glynn 2011 (79)	Cardiovascular medication: improving adherence
Graves 2010 (93)	The efficacy of adherence Interventions for chronically Ill children: A meta-analytic review
Gray 2009 (85)	Interventions for improving adherence to ocular hypotensive therapy

Greenley 2013 (87)	Practical strategies for enhancing adherence to treatment regimen in inflammatory bowel disease
Gwadry-Sridhar 2013 (80)	Impact of interventions on medication adherence and blood pressure control in patients with essential hypertension: A systematic review by the ISPOR Medication Adherence and Persistence Special Interest Group
Halpern 2013 (107)	Strategies to improve adherence and acceptability of hormonal methods of contraception
Hiligsmann 2013 (98)	Interventions to improve osteoporosis medication adherence and persistence: a systematic review and literature appraisal by the ISPOR Medication Adherence & Persistence Special Interest Group
Hood 2010 (64)	Interventions with adherence-promoting components in pediatric type 1 diabetes - Meta-analysis of their impact on glycemic control
Kardas 2009 (81)	How to improve patient compliance with lipid lowering medication?
Laba 2013 (82)	Strategies to improve adherence to medications for cardiovascular diseases in socioeconomically disadvantaged populations: A systematic review
Marcus 2014 (73)	Helping our patients take HIV pre-exposure prophylaxis (PrEP): a systematic review of adherence interventions
Mathes 2014 (89)	Adherence enhancing interventions for oral anticancer agents: A systematic review
Mathes 2013 (74)	Adherence-enhancing interventions for highly active antiretroviral therapy in HIV-infected patients - a systematic review
Matteson 2010 (90)	Interventions to improve hemodialysis adherence: A systematic review of randomized-controlled trials
Mills 2013 (75)	Adherence interventions to improve adherence to antiretroviral therapy in low income settings: An individual patient data network meta-analysis
Molloy 2012 (84)	Interventions to enhance adherence to medications in patients with heart failure - A systematic review
Moullec 2012 (58)	Efficacy of interventions to improve adherence to inhaled corticosteroids in adult asthmatics: Impact of using components of the chronic care model
Schedlbauer 2010 (83)	Interventions to improve adherence to lipid lowering medication
Suwankeeree 2014 (106)	Strategies to promote adherence to treatment by pulmonary tuberculosis patients: a systematic review
Van Servellen 2011 (63)	Factors associated with antidepressant medication adherence and adherence-enhancement programmes: a systematic literature review
Viswanathan 2012 (94)	Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review
Waterman 2013 (86)	Interventions for improving adherence to ocular hypotensive therapy
Weiand 2012 (105)	Assessing and improving adherence with multidrug therapy
White 2010 (99)	A systematic review assessing the effectiveness of interventions to improve persistence with anti-resorptive therapy in women at high risk of clinical fracture
Williams 2014 (65)	Effective interventions to improve medication adherence in Type 2 diabetes: A systematic review

Zomahoun 2012 (66)	Interventions that improve adherence to oral antidiabetic in adults with type 2 diabetes: A systematic review

Sammendragene til disse oversiktene fins i vedlegg 2 (fra side 58).

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Vedlegg 1: Søkestrategier

Database: CINAHL

Dato for søk: 25.04.2014

#	Searches	Results
1	(MH "Medication Compliance")	7564
2	TI (((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) N5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinuation))) OR AB (((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) N5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinuation)))	631
3	S1 OR S2	11609
4	(MH "Systematic Review")	17438
5	(MH "Meta Analysis")	14309
6	TI (((systematic or literature) N3 (review* or overview or search*))) OR AB (((systematic or literature) N3 (review* or overview or search*)))	55982
7	AB medline or embase or pubmed	28917
8	S4 OR S5 OR S6 OR S7	75575
9	S3 AND S8 Limiters - Exclude MEDLINE records	165
10	S3 AND S8 Limiters - Exclude MEDLINE records; Published Date: 20090101-20141231	90

Database: Cochrane Database of Systematic Reviews (CDSR)

Dato for søk: 24.04.2014

#	Searches	Results
#1	MeSH descriptor: [Medication Adherence] explode all trees	941
#2	((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) NEAR/5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinuation))	9466
#3	#1 or #2 Publication Date from 2009 to 2014, in Cochrane Reviews (Reviews and Protocols)	801

Database: Centre for Reviews and Dissemination (CRD)

Dato for søk: 25.04.2014

#	Searches	Results
1	MeSH DESCRIPTOR Medication adherence EXPLODE ALL TREES FROM 2009 TO 2014	189
2	((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) adj5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinuation)) FROM 2009 TO 2014	319
3	1 or 2	319

Database: Embase 1974 to 2014 April 25

Dato for søk: 25.04.2014

#	Searches	Results
1	medication compliance/	3405
2	((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) adj5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinuation)).ti,ab.	40855
3	1 or 2	42592
4	(medline or embase or pubmed or search*).ab.	287502
5	((systematic or literature) adj3 (review or overview)).ti,ab.	227478
6	meta analys*.mp.	117408
7	4 or 5 or 6	531315

8	3 and 7	2690
9	Limit 8 to yr=”2009-Current”	1606

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present

Dato for søk: 25.04.2014

#	Searches	Results
1	Medication Adherence/	7129
2	((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) adj5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinua-tion)).ti,ab.	28044
3	1 or 2	32033
4	(medline or embase or pubmed or search*).ab.	238574
5	((systematic or literature) adj3 (review or overview)).ti,ab.	193397
6	meta analysis.pt.	47309
7	4 or 5 or 6	406405
8	3 and 7	1937
9	Limit 8 to yr=”2009-Current”	1103

Database: PsycINFO 1806 to April Week 4 2014

Dato for søk: 25.04.2014

#	Searches	Results
1	treatment compliance/	10864
2	exp drug therapy/	109665
3	1 and 2	3773
4	((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) adj5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinua-tion)).ti,ab.	8777
5	3 or 4	10242
6	(medline or embase or pubmed or search*).ab.	56579
7	((systematic or literature) adj3 (review or overview)).ti,ab.	41600
8	meta analys*.mp.	17013

9	6 or 7 or 8	102941
10	5 and 9	546
11	limit 10 to yr="2009 -Current"	274

Database: Web of Knowledge

Dato for søk: 25.04.2014

#	Searches	Results
1	TOPIC: (((medication* or medicine* or medical* or drug* or pharmac* or psychopharma* or dose* or dosage* or dosing) NEAR/5 (adherence or compliance or concordance or nonadherence or noncompliance or nonconcordance or persistence or continuation or discontinuation))) Timespan=2009-2014 Search language=English	30603
2	TOPIC: ((((systematic or literature) NEAR/3 (review* or overview or search*)) or (meta analys*))) Timespan=2009-2014 Search language=English	261782
3	1 and 2	2089

Vedlegg 2: Abstrakt til inkluderte systematiske oversikter

Abstraktene til de inkluderte systematiske oversiktene (n=106) er listet i henhold til sorteringskategoriene, og deretter alfabetisk, nedenfor.

E-helse eller telehelse-baserte tiltak

Cassimatis M, Kavanagh DJ. Effects of type 2 diabetes behavioural telehealth interventions on glycaemic control and adherence: a systematic review. J Telemed Telecare 2012;18(8):447-450.
Abstract: We reviewed the effect of behavioural telehealth interventions on glycaemic control and diabetes self-management in patients with type 2 diabetes. The databases CINAHL, Medline and psychINFO were searched in August 2012. journal articles were selected that had been published in English with a randomized controlled trial design using a usual care comparison group, and in which the primary intervention component was delivered by telehealth. Relevant outcome measures were glycaemic control and one or more of the following diabetes self-care areas: diet, physical activity, blood glucose self-monitoring (BGSM) or medication adherence. Interventions were excluded if they were primarily based on telemonitoring. The search retrieved 1027 articles, from which 49 were selected based on their title and abstract. Fourteen articles (reporting 13 studies) met the eligibility criteria for inclusion. Four studies reported significant improvements in glycaemic control. Five of eight studies on dietary adherence reported significant treatment effects, as did five of eight on physical activity, four of nine on blood glucose self-monitoring, and three of eight on medication adherence. Overall, behavioural telehealth interventions show promise in improving the diabetes self-care and glycaemic control of people with type 2 diabetes.

Fenerty SD, West C, Davis SA, Kaplan SG, Feldman SR. The effect of reminder systems on patients' adherence to treatment. Patient Preference and Adherence 2012;6:127-135.
Abstract: Background: Patient adherence is an important component of the treatment of chronic disease. An understanding of patient adherence and its modulating factors is necessary to correctly interpret treatment efficacy and barriers to therapeutic success. Purpose: This meta-analysis aims to systematically review published randomized controlled trials of reminder interventions to assist patient adherence to prescribed medications. Methods: A Medline search was performed for randomized controlled trials published between 1968 and June 2011, which studied the effect of reminder-based interventions on adherence to self-administered daily medications. Results: Eleven published randomized controlled trials were found between 1999 and 2009 which measured adherence to a daily medication in a group receiving reminder interventions compared to controls receiving no reminders. Medication adherence was measured as the number of doses taken compared to the number prescribed within a set period of time. Meta-analysis showed a statistically significant increase in adherence in groups receiving a reminder intervention compared to controls (66.61% versus 54.71%, 95% CI for mean: 0.8% to 22.4%). Self-reported and electronically monitored adherence rates did not significantly differ (68.04% versus 63.67%, P = 1.0). Eight of eleven studies showed a statistically significant increase in adherence for at least one of the reminder group arms compared to the control groups receiving no reminder intervention. Limitations: The data are limited by imperfect measures of adherence due to variability in data collection methods. It is also likely that concomitant educational efforts in the study populations, such as instructions regarding proper administration and importance of correct dosing schedules, contributed

to improved patient adherence, both in reminder and control arms. The search strategy could have missed relevant studies which were categorized by disease rather than adherence. Conclusions: Reminder-based interventions may improve adherence to daily medications. However, the interventions used in these studies, which included reminder phone calls, text messages, pagers, interactive voice response systems, videotelephone calls, and programmed electronic audiovisual reminder devices, are impractical for widespread implementation, and their efficacy may be optimized when combined with alternative adherence-modifying strategies. More practical reminder-based interventions should be assessed to determine their value in improving patient adherence and treatment outcomes.

Finitsis DJ, Pellowski JA, Johnson BT. Text Message Intervention Designs to Promote Adherence to Antiretroviral Therapy (ART): A Meta-Analysis of Randomized Controlled Trials. PLoS One 2014;9(2).

Abstract: Background: The efficacy of antiretroviral therapy depends on patient adherence to a daily medication regimen, yet many patients fail to adhere at high enough rates to maintain health and reduce the risk of transmitting HIV. Given the explosive global growth of cellular-mobile phone use, text-messaging interventions to promote adherence are especially appropriate. This meta-analysis synthesized available text messaging interventions to promote antiretroviral therapy adherence in people living with HIV. Methods: We performed Boolean searches of electronic databases, hand searches of recent year conference abstracts and reverse searches. Included studies (1) targeted antiretroviral therapy adherence in a sample of people living with HIV, (2) used a randomized-controlled trial design to examine a text messaging intervention, and (3) reported at least one adherence measurement or clinical outcome. Results: Eight studies, including 9 interventions, met inclusion criteria. Text-messaging interventions yielded significantly higher adherence than control conditions (OR = 1.39; 95% CI = 1.18, 1.64). Sensitivity analyses of intervention characteristics suggested that studies had larger effects when interventions (1) were sent less frequently than daily, (2) supported bidirectional communication, (3) included personalized message content, and (4) were matched to participants' antiretroviral therapy dosing schedule. Interventions were also associated with improved viral load and/or CD4+ count (k = 3; OR = 1.56; 95% CI = 1.11, 2.20). Conclusions: Text-messaging can support antiretroviral therapy adherence. Researchers should consider the adoption of less frequent messaging interventions with content and timing that is individually tailored and designed to evoke a reply from the recipient. Future research is needed in order to determine how best to optimize efficacy.

Free C, Phillips G, Galli L, Watson L, Felix L, Edwards P, et al. The Effectiveness of Mobile-Health Technology-Based Health Behaviour Change or Disease Management Interventions for Health Care Consumers: A Systematic Review. PLoS Med 2013;10(1).

Abstract: Background: Mobile technologies could be a powerful media for providing individual level support to health care consumers. We conducted a systematic review to assess the effectiveness of mobile technology interventions delivered to health care consumers. . Methods and Findings: We searched for all controlled trials of mobile technology-based health interventions delivered to health care consumers using MEDLINE, EMBASE, PsycINFO, Global Health, Web of Science, Cochrane Library, UK NHS HTA (Jan 1990-Sept 2010). Two authors extracted data on allocation concealment, allocation sequence, blinding, completeness of follow-up, and measures of effect. We calculated effect estimates and used random effects meta-analysis. We identified 75 trials. Fifty-nine trials investigated the use of mobile technologies to improve disease management and 26 trials investigated their use to change health behaviours. Nearly all trials were conducted in high-income countries. trials had a low risk of bias. Two trials of disease management had low risk of bias; in one, antiretroviral (ART) adherence, use of text messages reduced high viral load (>400 copies), with a relative risk (RR) of 0.85 (95% CI 0.72-0.99), but no statistically significant benefit on mortality (RR 0.79 [95% CI 0.47-1.32]). In a second, a PDA based intervention increased scores for perceived self care agency in lung transplant patients. Two trials of health behaviour management had low risk of bias. The pooled effect of text messaging smoking cessation support on biochemically verified smoking cessation was (RR 2.16 [95% CI 1.77-2.62]). Interventions for other conditions showed suggestive benefits in some cases, but the results were not consistent. No evidence of publication bias was demonstrated on visual or statistical examination of the funnel plots for either disease management or health behaviours. To address the limitation of the older search, we also reviewed more recent literature. Conclusions: Text messaging interventions increased adherence to ART and smoking cessation and should be considered for inclusion in services. Although there is suggestive evidence of benefit in some other areas, high quality adequately powered trials of optimised interventions are required to evaluate effects on objective outcomes.

Horvath T, Azman H, Kennedy Gail E, Rutherford George W. Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd; 2012.

Abstract: Background: More than 34 million people are presently living with HIV infection. Antiretroviral therapy (ART) can help these people to live longer, healthier lives, but adherence to ART can be difficult. Mobile phone text-messaging has the potential to help promote adherence in these patients. Objectives: To determine whether mobile phone text-messaging is efficacious in enhancing adherence to ART in patients with HIV infection. Search methods: Using the Cochrane Collaboration's validated search strategies for identifying randomised controlled trials and reports of HIV interventions, along with appropriate keywords and MeSH terms, we searched a range of electronic databases, including the Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), MEDLINE (via PubMed), PsycINFO, Web of Science, and the World Health Organization (WHO) Global Index Medicus. The date range was from 01 January 1980 to 01 November 2011. There were no limits to language or publication status.Selection criteria: Randomised controlled trials (RCTs) in which patients or their caregivers (in the case of infants and children) of any age, in any setting, and receiving ART were provided with mobile phone text messages as a means of promoting adherence to ART.Data collection and analysis: Two authors independently examined the abstracts of all identified trials. We initially identified 243 references. Seventeen full-text articles were closely reviewed. Both authors abstracted data independently, using a pre-designed, standardised data collection form. When appropriate, data were combined in meta-analysis. Main results: Two RCTs from Kenya were included in the review. One trial compared short weekly text messages against standard care. The other trial compared short daily, long daily, short weekly and long weekly messages against standard care. Both trials were with adult patients. In the trial comparing only short weekly messages to standard care, text messaging was associated with a lower risk of non-adherence at 12 months (RR 0.77, 95% CI 0.63 to 0.93) and with the non-occurrence of virologic failure at 12 months (RR 0.83, 95% CI 0.69 to 0.99).In the trial that compared different intervals and lengths for text-messaging to standard care, long weekly text-messaging was not significantly associated with a lower risk of non-adherence compared to standard care (RR 0.79, 95% CI 0.60 to 1.04). Patients receiving weekly text-messages of any length were at lower risk of non-adherence at 48 weeks than were patients receiving daily messages of any length (RR 0.79, 95% CI 0.64 to 0.99). There were no significant differences between weekly text-messaging of any length (RR 1.01, 95% CI 0.75 to 1.37) and between short or long messaging at either interval (RR 0.99, 95% CI 0.78 to 1.27). Compared to standard care, any daily text-messaging, whether short or long, did not reduce the risk for non-adherence (RR 0.99, 95% CI 0.82 to 1.20).In meta-analysis of both trials, any weekly text-messaging (i.e. whether short or long messages) was associated with a lower risk of non-adherence at 48-52 weeks (RR 0.78, 95% CI 0.68 to 0.89). The effect of short weekly text-messaging was also significant (RR 0.77, 95% CI 0.67 to 0.89).Authors' conclusions: There is high-quality evidence from the two RCTs that mobile phone text-messaging at weekly intervals is efficacious in enhancing adherence to ART, compared to standard care. There is high quality evidence from one trial that weekly mobile phone text-messaging is efficacious in improving HIV viral load suppression. Policy-makers should consider funding programs proposing to provide weekly mobile phone text-messaging as a means for promoting adherence to antiretroviral therapy. Clinics and hospitals should consider implementing such programs. There is a need for large RCTs of this intervention in adolescent populations, as well as in high-income countries.

Linn AJ, Vervloet M, van Dijk L, Smit EG, Van Weert JCM. Effects of eHealth Interventions on Medication Adherence: A Systematic Review of the Literature. J Med Internet Res 2011;13(4).

Abstract: Background: Since medication nonadherence is considered to be an important health risk, numerous interventions to improve adherence have been developed. During the past decade, the use of Internet-based interventions to improve medication adherence has increased rapidly. Internet interventions have the potential advantage of tailoring the interventions to the needs and situation of the patient. Objective: The main aim of this systematic review was to investigate which tailored Internet interventions are effective in improving medication adherence. Methods: We undertook comprehensive literature searches in PubMed, PsycINFO, EMBASE, CINAHL, and Communication Abstracts, following the guidelines of the Cochrane Collaboration. The methodological quality of the randomized controlled trials and clinical controlled trials and methods for measuring adherence were independently reviewed by two researchers. Results: A total of 13 studies met the inclusion criteria. All included Internet interventions clearly used moderately or highly sophisticated computer-tailored methods. Data synthesis revealed that there is evidence for the effectiveness of Internet interventions in improving medication adherence: 5 studies (3 high-quality studies and 2 low-quality studies) showed a significant effect on

adherence; 6 other studies (4 high-quality studies and 2 low-quality studies) reported a moderate effect on adherence; and 2 studies (1 high-quality study and 1 low-quality study) showed no effect on patients' adherence. However, most studies used self-reported measurements to assess adherence, which is generally perceived as a low-quality measurement. In addition, we did not find a clear relationship between the quality of the studies or the level of sophistication of message tailoring and the effectiveness of the intervention. This might be explained by the great difference in study designs and the way of measuring adherence, which makes results difficult to compare. There was also large variation in the measured interval between baseline and follow-up measurements. Conclusion: This review shows promising results on the effectiveness of Internet interventions to enhance patients' adherence to prescribed long-term medications. Although there is evidence according to the data synthesis, the results must be interpreted with caution due to low-quality adherence measurements. Future studies using high-quality measurements to assess medication adherence are recommended to establish more robust evidence for the effectiveness of eHealth interventions on medication adherence.

McKay C, Reed M. How personalized should we be? A systematic review of tailored & targeted health communication interventions to improve adherence. Value Health 2013;16 (3):A46.
Abstract: OBJECTIVES: To target patients with "personalized" interventions with the highest probability of success, understanding what works with other behaviors provides empirical guidance, as few outcomes are explicitly medication adherence-related. This study's purpose is to glean 1) the characteristics of individuals or interventions examined in "tailored" or "targeted" health communication interventions, and 2) the components or combination of successful strategies tailored to the individual's needs and targeted to the social groups in which the patient is embedded. METHODS: A systematic review was conducted, with articles identified via searches in MEDLINE and Embase, using keywords representing individual, interventional, and behavioral factors. Inclusion criteria: published peer-reviewed articles in English, 2000-2012; 77 studies reflected behavioral outcomes (medication adherence, preventive screening, health promotion, and self-management of disease). The review specified individual factors (sociodemographic, behavioral, contextual, disease) as well as elements upon which interventions were customized (delivery, content, form, dose/frequency, setting, level of analysis). RESULTS: Across all outcomes assessed (n=133), 52.6% of tailored or targeted interventions demonstrated statistically significant benefit, with additional 12.8% effective (not statistically), 9.8% mixed, 24.8% non-significant. Regarding behaviors associated with multiple morbidities: most studies evidenced health promoting effects (medication adherence, 66.7%; diet/obesity, 65.9%; physical activity, 47.4%; screening, 71.4%). Disease-specific outcomes reflected stronger findings. Individual characteristics were clustered into groups for analysis, with significantly positive effects for 3 of 4 clusters: sociodemographic, 59.0%; behavioral, 63.4%, contextual, 52.6%. Within group differences indicated support for specific factors within each cluster (age vs. education, barriers vs. selfefficacy). Effects were moderated by intervention-type (tailored vs tailored+targeted). CONCLUSIONS: A matrix developed for this review permits a refined approach to creating interventions focusing on the interaction ("person x intervention") features of effective strategies. Several candidate characteristics of patients to prioritize in medication adherence program development were identified, using evidenced-based selection of patient-centered strategies that appropriately match what has worked and for whom.

Misono AS, Cutrona SL, Choudhry NK, Fischer MA, Stedman MR, Liberman JN, et al. Healthcare Information Technology Interventions to Improve Cardiovascular and Diabetes Medication Adherence. Am J Manag Care 2010;16:SP82-SP92.
Abstract: Objective: To determine the efficacy of healthcare information technology (HIT) interventions in improving adherence. Study Design: Systematic search of randomized controlled trials of HIT interventions to improve medication adherence in cardiovascular disease or diabetes. Methods: Interventions were classified as 1-way patient reminder systems, 2-way interactive systems, and systems to enhance patient-provider interaction. Studies were subclassified into those with and without real-time provider feedback. Cohen's d effect sizes were calculated to assess each intervention's magnitude of effectiveness. Results: We identified 7190 articles, only 13 of which met inclusion criteria. The majority of included studies (54%, 7 studies) showed a very small ES. The effect size was small in 15%, large in 8%, and was not amenable to calculation in the remainder. Reminder systems were consistently effective, showing the largest effect sizes in this review. Education/counseling HIT systems were less successful, as was the addition of real-time adherence feedback to healthcare providers. Interactive systems were rudimentary and not integrated into electronic health records; they exhibited very small effect sizes. Studies aiming to improve patient-provider communication also had very small effect sizes. Con-

clusions: There is a paucity of data about HIT's efficacy in improving adherence to medications for cardiovascular disease and diabetes, although simple patient reminder systems appear effective. Future studies should focus on more sophisticated interactive interventions that expand the functionality and capabilities of HIT and better engage patients in care.

Nglazi MD, Bekker LG, Wood R, Hussey GD, Wiysonge CS. Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: A systematic review. BMC Infect Dis 2013;13(1).

Abstract: Background: Mobile phone text messaging (SMS) has the potential to promote adherence to tuberculosis treatment. This systematic review aims to synthesize current evidence on the effectiveness of SMS interventions in improving patients' adherence to tuberculosis treatment.Methods: We searched electronic databases (PubMed, EMBASE, Science Citation Index), reference lists of relevant articles, conference proceedings, and selected websites for eligible studies available by 15 February 2013; regardless of language or publication status. Two authors independently screened selected eligible studies, and assessed risk of bias in included studies; resolving discrepancies by discussion and consensus.Results: We identified four studies that compared the outcomes of the SMS intervention group with controls. Only one of the four studies was a randomized controlled trial. This was conducted in Argentina and the SMS intervention did not significantly improve adherence to tuberculosis treatment compared to self-administration of tuberculosis treatment (risk ratio [RR] 1.49, 95% confidence intervals [CI] 0.90 to 2.42). One of the non-randomized studies, conducted in South Africa, which compared SMS reminders to directly observed therapy short course (DOTS) reported similar rates of tuberculosis cure (62.35% vs. 66.4%) and treatment success (72.94% vs. 69.4%). A second study from South Africa, utilized SMS reminders when patients delayed in opening their pill bottles and reported increased tuberculosis cure (RR 2.32, 95% CI 1.60 to 3.36) and smear conversion (RR 1.62, 95% CI 1.09 to 2.42) rates compared to DOTS. In the third non-randomized study, conducted in Kenya, use of SMS reminders increased rates of clinic attendance on scheduled days compared to standard care (RR 1.56, 95% CI 1.06 to 2.29). Using the GRADE approach, we rate the quality of the evidence as low, mainly because of the high risk of bias and heterogeneity of effects across studies.Conclusions: This systematic review indicates that there is a paucity of high-quality data on the effectiveness of SMS interventions for improving patients' adherence to tuberculosis treatment. The low quality of the current evidence implies that further studies (in particular randomized trials) on the subject are needed. In the interim, if the intervention is implemented outside research settings an impact evaluation is warranted.

Park C, Kim G, Patel I, Chang J, Tan X. Improving adherence to acne treatment: The emerging role of application software. Clin Cosmet Investig Dermatol 2014;7:65-72.

Abstract: Objective: To examine recent studies on the effect of mobile and electronic (ME)-health technology on adherence to acne treatment. Background: With emerging use of ME-health technology, there is a growing interest in evaluating the effectiveness of the tools on medication adherence. Examples of ME-health technology-based tools include text message-based pill reminders and Web-based patient education. Methods: MEDLINE, Cochrane Library, and Web of Science were searched for articles on adherence to acne treatment published through November 2013. A combination of search terms such as "acne" and "adherence" or "compliance" were used. Results: Adherence to oral acne medication was higher than for topical acne medication. The frequency of office visits was also an influencing factor for acne treatment adherence. The telephone-based reminders on a daily basis did not improve acne patients' medication adherence, whereas the Web-based educational tools on a weekly basis had a positive effect on medication adherence in acne treatment. Conclusion: In using ME-health interventions, factors such as medication dosage forms, frequency of intervention, and patients' preferences should be taken into consideration. Developing disease-specific text message reminders may be helpful to increase adherence rates. In addition, a combination of text message reminders with another type of intervention may improve medication adherence.

Saberi P, Johnson MO. Technology-Based Self-Care Methods of Improving Antiretroviral Adherence: A Systematic Review. PLoS One 2011;6(11).

Abstract: Background: As HIV infection has shifted to a chronic condition, self-care practices have emerged as an important topic for HIV-positive individuals in maintaining an optimal level of health. Self-care refers to activities that patients undertake to maintain and improve health, such as strategies to achieve and maintain high levels of antiretroviral adherence. Methodology/Principal Findings: Technology-based methods are increasingly used to enhance antiretroviral adherence; therefore, we systematically reviewed the literature to examine technology-based self-care methods that HIV-positive

individuals utilize to improve adherence. Seven electronic databases were searched from 1/1/1980 through 12/31/2010. We included quantitative and qualitative studies. Among quantitative studies, the primary outcomes included ARV adherence, viral load, and CD4+ cell count and secondary outcomes consisted of quality of life, adverse effects, and feasibility/acceptability data. For qualitative/descriptive studies, interview themes, reports of use, and perceptions of use were summarized. Thirty-six publications were included (24 quantitative and 12 qualitative/descriptive). Studies with exclusive utilization of medication reminder devices demonstrated less evidence of enhancing adherence in comparison to multicomponent methods. Conclusions/Significance: This systematic review offers support for self-care technology-based approaches that may result in improved antiretroviral adherence. There was a clear pattern of results that favored individually-tailored, multi-function technologies, which allowed for periodic communication with health care providers rather than sole reliance on electronic reminder devices.

Vervloet M, Linn AJ, van Weert JCM, de Bakker DH, Bouvy ML, van Dijk L. The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: a systematic review of the literature. J Am Med Inform Assoc 2012;19(5):696-704.
Abstract: Background Many patients experience difficulties in adhering to long-term treatment. Although patients' reasons for not being adherent are diverse, one of the most commonly reported barriers is forgetfulness. Reminding patients to take their medication may provide a solution. Electronic reminders (automatically sent reminders without personal contact between the healthcare provider and patient) are now increasingly being used in the effort to improve adherence. Objective To examine the effectiveness of interventions using electronic reminders in improving patients' adherence to chronic medication. Methods A comprehensive literature search was conducted in PubMed, Embase, PsycINFO, CINAHL and Cochrane Central Register of Controlled Trials. Electronic searches were supplemented by manual searching of reference lists and reviews. Two reviewers independently screened all citations. Full text was obtained from selected citations and screened for final inclusion. The methodological quality of studies was assessed. Results Thirteen studies met the inclusion criteria. Four studies evaluated short message service (SMS) reminders, seven audiovisual reminders from electronic reminder devices (ERD), and two pager messages. Best evidence synthesis revealed evidence for the effectiveness of electronic reminders, provided by eight (four high, four low quality) studies showing significant effects on patients' adherence, seven of which measured short-term effects (follow-up period <6 months). Improved adherence was found in all but one study using SMS reminders, four studies using ERD and one pager intervention. In addition, one high quality study using an ERD found subgroup effects. Conclusion This review provides evidence for the short-term effectiveness of electronic reminders, especially SMS reminders. However, long-term effects remain unclear.

Tiltak gitt av helsepersonell

Cutrona SL, Choudhry NK, Stedman M, Servi A, Liberman JN, Brennan T, et al. Physician Effectiveness in Interventions to Improve Cardiovascular Medication Adherence: A Systematic Review. J Gen Intern Med 2010;25(10):1090-1096.
Abstract: Medications for the prevention and treatment of cardiovascular disease save lives but adherence is often inadequate. The optimal role for physicians in improving adherence remains unclear. Using existing evidence, we set the goal of evaluating the physician's role in improving medication adherence. We conducted systematic searches of English-language peer-reviewed publications in MEDLINE and EMBASE from 1966 through 12/31/2008. We selected randomized controlled trials of interventions to improve adherence to medications used for preventing or treating cardiovascular disease or diabetes. Articles were classified as either (1) physician "active"aEuro"a physician participated in designing or implementing the intervention; (2) physician "passive"aEuro"physicians treating intervention group patients received patient adherence information while physicians treating controls did not; or (3) physicians noninvolved. We also identified studies in which healthcare professionals helped deliver the intervention. We did a meta-analysis of the studies involving healthcare professionals to determine aggregate Cohen's D effect sizes (ES). We identified 6,550 articles; 168 were reviewed in full, 82 met inclusion criteria. The majority of all studies (88.9%) showed improved adherence. Physician noninvolved studies were more likely (35.0% of studies) to show a medium or large effect on adherence compared to physician-involved studies (31.3%). Among interventions requiring a healthcare professional, physician-noninvolved interventions were more effective (ES 0.47; 95% CI 0.38-0.56) than physician-involved interventions (ES 0.25; 95% CI 0.21-0.29; p < 0.001). Among physician-involved interventions, physician-passive

interventions were marginally more effective (ES 0.29; 95% CI 0.22-0.36) than physician-active interventions (ES 0.23; 95% CI 0.17-0.28; p = 0.2). Adherence interventions utilizing non-physician healthcare professionals are effective in improving cardiovascular medication adherence, but further study is needed to identify the optimal role for physicians.

Doggrell SA. Does intervention by an allied health professional discussing adherence to medicines improve this adherence in Type 2 diabetes? Diabet Med 2010;27(12):1341-1349.
Abstract: Aims Increasing adherence to medicines should improve glycaemic control and be cost effective in patients with Type 2 diabetes. It is assumed that the intervention of an allied health professional will improve adherence to medicines, but this has not been well documented. The aim of this review was to determine whether an intervention by an allied health professional, including a discussion of adherence to medicines, improved adherence to medicines in these subjects. Methods A comprehensive review of the literature was undertaken to determine this. All available studies were included and critically reviewed. Results When adherence to medicines was high in the treatment of Type 2 diabetes, an intervention by an allied health professional did not improve adherence. In studies in which the adherence could be improved the results were varied, with some studies showing improvement and some not. This variation existed whether the allied health professional was a nurse, a pharmacist or a diabetes educator, and whether the intervention was by phone or by counselling in person. Conclusions In conclusion, prior to undertaking an intervention to improve adherence to medicines in Type 2 diabetes, it is necessary to know the baseline level of adherence, and if adherence is already high there is no point in undertaking an intervention. When adherence to medicines is low, it is not clear which interventions will improve adherence, and further studies are needed to clarify this.

Ford N, Nachega JB, Engel ME, Mills EJ. Directly observed antiretroviral therapy: a systematic review and meta-analysis of randomised clinical trials. Lancet 2009;374(9707):2064-2071.
Abstract: Background Directly observed therapy has been recommended to improve adherence for patients with HIV infection who are on highly active antiretroviral therapy, but the benefit and cost-effectiveness of this approach has not been established conclusively. We did a systematic review and meta-analysis of randomised trials of directly observed versus self-administered antiretroviral treatment. Methods We did duplicate searches of databases (from inception to July 27, 2009), searchable websites of major HIV conferences (up to July, 2009), and lay publications and websites (March-July, 2009) to identify randomised trials assessing directly observed therapy to promote adherence to antiretroviral therapy in adults. Our primary outcome was virological suppression at study completion. We calculated relative risks (95% CIs), and pooled estimates using a random-effects method. Findings 12 studies met our inclusion criteria; four of these were done in groups that were judged to be at high risk of poor adherence (drug users and homeless people). Ten studies reported on the primary outcome (n=1862 participants); we calculated a pooled relative risk of 1.04 (95% CI 0.91-1.20, p=0.55), and noted moderate heterogeneity between the studies (I(2)= 53.8%, 95% CI 0-75.7, p=0.0247) for directly observed versus self-administered treatment. Interpretation Directly observed antiretroviral therapy seems to offer no benefit over self-administered treatment, which calls into question the use of such an approach to support adherence in the general patient population.

Hart JE, Jeon CY, Ivers LC, Behforouz HL, Caldas A, Drobac PC, et al. Effect of Directly Observed Therapy for Highly Active Antiretroviral Therapy on Virologic, Immunologic, and Adherence Outcomes: A Meta-Analysis and Systematic Review. Jaids-Journal of Acquired Immune Deficiency Syndromes 2010;54(2):167-179.
Abstract: Introduction: Directly observed therapy of highly active antiretroviral therapy (DOT-HAART) is a feasible adherence intervention. Prospective DOT-HAART studies have shown mixed results, and optimal target groups have yet to be defined. We performed a meta-analysis and systematic review to assess the effect of DOT-HAART on adherence and virologic and immunologic response. Methods: We performed a comprehensive search through August 2009 to identify peer-reviewed controlled studies that involved outpatient DOT-HAART among adults and reported at least 1 outcome assessed in this meta-analysis. Random-effects meta-analyses were performed; differences in effect on virologic suppression were examined using stratified meta-analyses and meta-regression on several study characteristics. Results: Seventeen studies met inclusion criteria. Compared with control groups, DOT-HAART recipients were more likely to achieve an undetectable viral load (random effects risk ratio 1.24, 95% confidence interval (CI): 1.08 to 1.41), a greater increase in CD4 cell count (random effects weighted mean difference 43 cells/mu L, 95% CI: 12 to 74 cells/mu L), and HAART adherence of >= 95% (random effects risk ratio 1.17, 95% CI: 1.03 to 1.32). Results varied with respect to virologic response. DOT-HAART

did not have a significant effect on virologic suppression when restricted to randomized controlled studies. Post-treatment effect was not observed in a limited number of studies. Conclusions: DOT-HAART had a significant effect on virologic, immunologic, and adherence outcomes, although its efficacy was not supported when restricting analysis to randomized controlled trials. DOT-HAART shows greatest treatment effect when targeting individuals with greater risk of nonadherence and when delivering the intervention that maximizes participant convenience and provides enhanced adherence support. Further investigation is needed to assess the postintervention effect and cost-effectiveness of DOT-HAART.

Kenya S, Chida N, Symes S, Shor-Posner G. Can community health workers improve adherence to highly active antiretroviral therapy in the USA? A review of the literature. HIV Med 2011;12(9):525-534.

Abstract: Objectives Highly active antiretroviral therapy (HAART) has transformed HIV infection into a manageable chronic illness, yet AIDS mortality among ethnic minorities persists in the USA. HAART nonadherence is associated with increased HIV viral load, low CD4 cell count and racial disparities in HIV outcomes. While there is no universal consensus on how to improve medical adherence in HIV-positive populations, the community health worker (CHW) model is emerging as an effective strategy to overcome barriers to HAART adherence. Although utilized in international settings, there is little evidence regarding the effects of CHWs on HIV outcomes in the USA. Methods We performed a comprehensive search from May 2010 to November 2010 to identify studies carried out in the USA that utilized CHWs to improve HAART adherence and measured HIV viral loads and CD4 cell counts to assess intervention effects. Sixteen studies met the inclusion criteria and were reviewed for this article. All studies reported clinical HIV outcomes. Results Interventions that lasted at least 24 weeks, provided frequent contact with participants, and focused on medication management were associated with improved HAART adherence, as indicated by reduced HIV viral load and increased CD4 cell count. Conclusions Compared with current standards of care, CHW programmes may offer a practical and cost-effective alternative to improve HAART adherence, which may lead to reduced HIV viral load and increased CD4 cell counts among HIV-positive populations in the USA.

Mansoor SM, Krass I, Aslani P. Multiprofessional interventions to improve patient adherence to cardiovascular medications. J Cardiovasc Pharmacol Ther 2013;18(1):19-30.

Abstract: BACKGROUND: Poor adherence to medications is a significant health care issue, particularly among cardiovascular patients. A variety of interventions have been tested by researchers in an effort to identify the most effective approach to improving adherence. Interventions delivered by multiple health care professionals (HCPs) may have an impact on improving adherence to medications in patients with chronic conditions, although the evidence to support this is still limited. OBJECTIVE: To investigate the impact of interventions delivered by HCPs within a multiprofessional team to improve patients' adherence to cardiovascular disease medications in community settings. Search strategy: The search strategy involved the use of the following data bases: Google scholar, PubMed, Medline, Cinahl, Embase, IPA, and Cochrane Library, from 1994 to 2010. Search was restricted to articles published in English. Selection criteria: Cluster randomized trials, controlled randomized clinical trials, prospective randomized trials, and nonrandomized studies were included. We considered any intervention designed to enhance adherence to medication directed by more than 1 HCP. RESULTS: We included 17 studies testing 3 different types of interventions directed by more than 1 HCP. The HCPs received a variety of training via educational lectures or interactive workshops. Informational, behavioral, and combined interventions were delivered to cardiovascular patients. The majority of studies using only informational interventions or a combination of behavioral and informational interventions showed improvements in clinical outcomes (ie, blood pressure and total cholesterol lowering). However, only 2 studies measured improvements in adherence but the results were not significant. In contrast, all interventions based on the behavior change strategies improved both clinical outcomes and adherence to medication. CONCLUSIONS: Behavioral interventions delivered by a multiprofessional team appear to offer the best opportunity to improve clinical outcomes through improvements in adherence. However, whether interventions delivered by a multiprofessional team are more clinically effective than those delivered by a single HCP remain to be tested.

Schoenthaler A, Cuffee YL. A systematic review of interventions to improve adherence to diabetes medications within the patient-practitioner interaction. J Clin Outcomes Manag 2013;20(11):494-506.

Abstract: Objectives: To conduct a systematic review of the literature examining interventions delivered

by health care practitioners to improve medication adherence in patients with diabetes mellitus (DM). * Methods: Databases were searched up to 2 July 2013 to identify eligible studies that included interventions that were conducted in a clinic-based setting and delivered by a health care practitioner (eg, nurse, physician, diabetes educator) to improve adherence to diabetes medications (including oral hypoglycemic agents and insulin). Articles were limited to published clinical trials conducted in adults > 18 years of age and published in English-language journals. * Results: 18 papers were reviewed: 15 trials targeted patients with DM, 3 targeted health care practitioners. 7 patient-focused and 1 practitioner-focused trial demonstrated a beneficial effect of the intervention compared with a control group. The patient-focused trials were complex interventions involving a combination of adherence-enhancing strategies such as individualized patient counseling, tailored patient education, medication reminders, behavioral feedback and reinforcement, and care management by ancillary staff, nurses, text message or telephone-linked system. The practitioner-focused trial employed an electronic feedback system for individualized care and quality improvement. Limitations included the diversity in the measures employed to assess adherence; differing definitions of adherence; the inclusion of patients regardless of baseline adherence status; and the short duration of the trials. * Conclusions: Additional research is needed to understand the conditions under which interventions targeting the patient-practitioner interaction can be implemented in clinic settings to improve medication adherence in patients with DM.

Van Camp YP, Van Rompaey B, Elseviers MM. Nurse-led interventions to enhance adherence to chronic medication: systematic review and meta-analysis of randomised controlled trials. Eur J Clin Pharmacol 2013;69(4):761-770.
Abstract: Non-adherence to chronic medication remains an important problem with vast consequences and without solutions to date. Nurses are well positioned to provide adherence care, yet currently represent an underutilised force in improving adherence and outcomes. This review aims to synthesise the effect of nurse-led interventions on adherence to chronic medication. Using Review Manager software, a meta-analysis was conducted. The search term medication adherence was combined with random* and nurse in PubMed and ISI Web of Knowledge. Retrieved articles' reference lists were hand searched. Included were randomised controlled trials on nurse-led interventions, aiming to improve chronic medication adherence. Articles were to be in English and published from 2006 to 2011. Quality was assessed using an adapted version of the CONSORT tool. Ten studies met the selection criteria, seven of which were on HIV-positive patients. Their quality was acceptable to high. Counselling was the intervention most frequently assessed, mostly given face-to-face, but also in groups and via electronic messages. All interventions enhanced adherence. Of the five studies reporting adherence as mean percentage of adherence, pooled mean differences were +5.39 (1.70-9.07) (short term) and +9.49 (4.68-14.30) (long term), favouring the intervention groups. Of the studies reporting adherence dichotomously, odd's ratios were 1.55 (1.04-2.29) (short term) and 1.87 (1.35-2.61) (long term). The longer counselling was effectuated, the better the results. Counselling appears to be an effective approach that nurses can use to supplement other methods, building a multifaceted strategy to enhance adherence. Tackling non-adherence seems to demand continuous efforts and follow-up.

Opplæring

Axelsson M, Lotvall J. Recent educational interventions for improvement of asthma medication adherence. Asia Pacific allergy 2012;2(1):67-75.
Abstract: Poor adherence to asthma medication treatment is a dilemma as it decreases the chance of achieving and maintaining a proper asthma control. Another dilemma is that there seems to be a small range of functional interventions that enhance adherence to long-term medication treatments. The aim was to review the last five years of published educational interventions for improving adherence to asthma medication. Through systematic database searches 20 articles were identified, which matched the inclusion criteria and described educational interventions to improve asthma self-management including adherence. The current review showed that addressing unintentional non-adherence in terms of incorrect inhaler technique by recurrent education improved the technique among many patients, but not among all. Phoning patients, as a means to remove medication beliefs as adherence barriers, seemed to be an effective educational strategy, shown as increased adherence. Involving patients in treatment decisions and individualising or tailoring educational support also seemed to have favourable effect on adherence. To conclude, addressing specific adherence barriers such as poor inhaler technique or medication beliefs could favour adherence. To change adherence behavior, the current review

proposes that educational adherence support should be a collaborative effort between the patient and the health-care professional based on each individual patient's needs and patient factors, including elements such as personality traits.

Gassman C, Brenner A. Interventions promoting adherence in the care of patients with oral chemotherapy - A systematic literature review [German]. Pflegewissenschaft 2012;14(7-8):429-438.

Abstract: In the last years oral chemotherapies are boosting the pharmaceutical market: 25% of 400 antineoplastic agents waiting for their approval are planned as oral medications. Experts are prognosting an increase of this tendency. Up to a few years ago chemotherapies were mainly administered intravenous for in-patients. The possibility of oral administration relocates the setting from in- to outpatient. This matches the needs and preferences of the concerned patients. They percieve it as an advantage to be hospitalized less often. Additionally, they can take a more active part in their therapy and feel able to control the illness and the therapy themselves. Increasing administration of oral chemotherapies leads to a paradigm shift in oncological nursing. The nursing role shows growing emphasis in patient education rather than in the administration of medications. The aim of this systematic review was to identify effective educational methods nurses could use in the care of patients on oral chemotherapies. A systematic literature search was undertaken in the databases CINAHL, Cochrane and Medline. Seven studies fulfilled the inclusion criterias. In each of these studies the occurrence of toxic symptoms was common. A possible correlation between the occurrence of toxicity and medication adherence could be shown. Adherence and self-efficacy are used as theoretical background of this systematic review. Different interpretations of adherence are discussed; consequences are drawn for oncological populations.

Ghisi GLDM, Abdallah F, Grace SL, Thomas S, Oh P. A systematic review of patient education in cardiac patients: Do they increase knowledge and promote health behavior change? Patient Educ Couns 2014;95(2):160-174.

Abstract: Objective: (1) To investigate the impact of education on patients' knowledge; (2) to determine if educational interventions are related to health behavior change in cardiac patients; and (3) to describe the nature of educational interventions. Methods: A literature search of several electronic databases was conducted for published articles from database inception to August 2012. Eligible articles included cardiac patients, and described delivery of educational interventions by a healthcare provider. Outcomes were knowledge, smoking, physical activity, dietary habits, response to symptoms, medication adherence, and psychosocial well-being. Articles were reviewed by 2 authors independently. Results: Overall, 42 articles were included, of which 23 (55%) were randomized controlled trials, and 16 (38%) were considered "good" quality. Eleven studies (26%) assessed knowledge, and 10 showed a significant increase with education. With regard to outcomes, educational interventions were significantly and positively related to physical activity, dietary habits, and smoking cessation. The nature of interventions was poorly described and most frequently delivered post-discharge, by a nurse, and in groups. Conclusions: Findings support the benefits of educational interventions in CHD, though increase in patients' knowledge and behavior change. Practice implications: Future reporting of education interventions should be more explicitly characterized, in order to be reproducible and assessed.

Li YY, Chao JQ, Song L, Zong MM. Influence of health education on medicine-taking compliance of Chinese hypertensive patients: A Bayesian meta-analysis. Chinese Journal of Evidence-Based Medicine 2014;14(2):211-215.

Abstract: Objective To systematically review the influence of health education on medicine-taking compliance of hypertensive patients, so as to provide scientific evidence for health decision-making. Methods Literature search was performed in CBM, CNKI, WanFang Data and VIP databases to collect randomized controlled trials (RCTs) published between 1998 and 2013 concerning the effect of health education on medicine-taking compliance of hypertensive patients. Two reviewers independently screened the literature according to the inclusion and exclusion criteria, extracted the data, assessed the methodological quality of included studies, and then conducted Bayesian meta-analysis using WinBUGS 14 software after heterogeneity-test by using Stata 10.0 software. Results A total of 19 RCTs involving 3 751 participants were included. The results of Bayesian meta-analysis showed that the health education group was superior to the control group in medicine-taking compliance with a significant difference (OR=4.46, 95%CI 3.698 to 5.358). Conclusion Health education could enhance the medicine-taking compliance of Chinese hypertension patients significantly.

M'Imunya J M, Kredo T, Volmink J. Patient education and counselling for promoting adherence to treatment for tuberculosis. Cochrane Database of Systematic Reviews 2012;5:CD006591.
Abstract: BACKGROUND: Non-adherence to tuberculosis treatment can lead to prolonged periods of infectiousness, relapse, emergence of drug-resistance, and increased morbidity and mortality. In this review, we assess whether patient education or counselling, or both, promotes adherence to tuberculosis treatment. OBJECTIVES: To evaluate the effects of patient education or counselling, or both, on treatment completion and cure in people requiring treatment for active or latent tuberculosis. SEARCH METHODS: Without language restriction, we searched for eligible studies in the Cochrane Infectious Diseases Group Specialized Register, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, and LILACS; checked reference lists of relevant articles; and contacted relevant researchers and organizations up to 24 November 2011. SELECTION CRITERIA: Randomized controlled trials examining the effects of education or counselling, or both, on treatment completion and cure in people with clinical tuberculosis; and treatment completion and clinical tuberculosis in people with latent disease. DATA COLLECTION AND ANALYSIS: We independently screened identified studies for eligibility, assessed methodological quality, and extracted data; with differences resolved by consensus. We expressed study results as risk ratios (RRs) with 95% confidence intervals (CI). MAIN RESULTS: We found three trials, with a total of 1437 participants, which examined the effects of different educational and counselling interventions on adherence to treatment for latent tuberculosis. All three trials reported the proportion of people who successfully completed treatment for latent tuberculosis. Overall, education or counselling interventions may increase successful treatment completion but the magnitude of benefit is likely to vary depending on the nature of the intervention, and the setting (data not pooled, 923 participants, three trials, low quality evidence).In a four-arm trial in children from Spain, counselling by nurses via telephone increased the proportion of children completing treatment from 65% to 94% (RR 1.44, 95% CI 1.21 to 1.72; 157 participants, one trial), and counselling by nurses through home visits increased completion to 95% (RR 1.46, 95% CI 1.23 to 1.74; 156 participants, one trial). Both of these interventions were superior to counselling by physicians at the tuberculosis clinic (RR 1.20, 95% CI 0.98 to 1.47; 159 participants, one trial). In the USA, a programme of peer counselling for adolescents failed to show an effect on treatment completion rates at six months (RR 1.01, 95% CI 0.90 to 1.13; 394 participants, one trial). In this trial treatment completion was around 75% even in the control group. In the third study, in prisoners from the USA, treatment completion was very low in the control group (12%), and although counselling significantly improved this, completion in the intervention group remained low at 24% (RR 1.94, 95% CI 1.03 to 3.68; 211 participants, one trial).None of these trials aimed to assess the effect of these interventions on the subsequent development of active tuberculosis, and we found no trials that assessed the effects of patient education or counselling on adherence to treatment for active tuberculosis. AUTHORS' CONCLUSIONS: Educational or counselling interventions may improve completion of treatment for latent tuberculosis. As would be expected, the magnitude of the benefit is likely to depend on the nature of the intervention, and the reasons for low completion rates in the specific setting.

Newman-Casey PA, Weizer JS, Heisler M, Lee PP, Stein JD. Systematic Review of Educational Interventions to Improve Glaucoma Medication Adherence. Semin Ophthalmol 2013;28(3):191-201.
Abstract: Adherence to prescribed glaucoma medications is often poor, and proper adherence can be challenging for patients. We systematically reviewed the literature and identified eight studies using educational interventions to improve glaucoma medication adherence. Overall, five of the eight studies found that educational interventions lead to a significant improvement in medication adherence, and two additional studies found a trend towards improvement. Using information from this systematic review and Health Behavior Theory, we constructed a conceptual framework to illustrate how counseling and education can improve glaucoma medication adherence. More rigorous studies grounded in Health Behavior Theory with adequately powered samples and longer follow-up are needed.

Tiltak gitt av farmasøyter

Al-Jumah KA, Qureshi NA. Impact of pharmacist interventions on patients' adherence to antidepressants and patient-reported outcomes: a systematic review. Patient Preference and Adherence 2012;6:87-100.
Abstract: Background: Pharmacist intervention in improving patient adherence to antidepressants is coupled with better outcomes. Aims: The aim of this investigation was to systematically examine the

published literature to explore different types of pharmacist interventions used for enhancing patient adherence to antidepressant medications. Three specific questions guided the review: what is the impact of pharmacist interventions on adherence to antidepressant medication? What is the impact of pharmacist interventions on patient-reported outcomes and patient satisfactions? What are the types of interventions used by pharmacists to enhance patients' adherence to antidepressants? Search strategies: A systematic review of the literature was conducted during August-November 2010 using PubMed, BIOSIS Previews (R) Web of Science, ScienceDirect, the Cochrane Library, PsycINFO (R), Ingenta-Connect (TM), Cambridge Journals Online, and Medscape databases. Key text words and medical subject headings included pharmacist intervention, medication intervention, depression, medication adherence, health-related quality of life, patient-reported outcomes, and antidepressants. Results: A total of 119 peer-reviewed papers were retrieved; 94 were excluded on the basis of abstract review and 13 after full-text analysis, resulting in twelve studies suitable for inclusion and intensive review. The most common intervention strategy that pharmacists utilized was a combination of patient education and drug monitoring. A cumulative patient adherence improvement in this review ranged from 15% to 27% attributed to utilization of different interventions and different combinations of interventions together with patient satisfaction with the treatment when depression improved. Conclusion: This review suggests that pharmacist intervention is effective in the improvement of patient adherence to antidepressants. This may be a basis for more studies examining the effectiveness of innovative interventions by pharmacists to enhance patient adherence to antidepressant medications.

Morgado MP, Morgado SR, Mendes LC, Pereira LJ, Castelo-Branco M. Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: Review and meta-analysis. Am J Health Syst Pharm 2011;68(3):241-253.

Abstract: Purpose. Pharmacist interventions to enhance blood pressure (BP) control and adherence to antihypertensive therapy in adults with essential hypertension were reviewed. Methods. A literature search was conducted to identify relevant articles describing pharmacist interventions intended to improve adherence to antihypertensive medications. Studies were included if they described a pharmacist intervention to improve medication adherence and analyzed adherence to therapy and BP control as outcomes. A fixed-effects model was used to combine data from randomized controlled trials. Results. A total of 15 studies were identified, testing 16 different interventions and containing data on 3280 enrolled patients. Although 87.5% of the interventions resulted in significant improvements in treatment outcomes, only 43.8% of the interventions were associated with significant increases in medication adherence. All interventions that increased antihypertensive medication adherence also significantly reduced BP. Almost all the interventions that were effective in increasing adherence to medication were complex, including combinations of different strategies. Meta-analysis of 2619 patients in 8 studies found that pharmacist interventions significantly reduced systolic blood pressure (SBP) ($p < 0.001$) and diastolic blood pressure (DBP) ($p = 0.002$) and that the meta-analytic differences in SBP and DBP changes from baseline to endpoint in intervention and control groups were -4.9 +/- 0.9 mm Hg ($p < 0.001$) and -2.6 +/- 0.9 mm Hg ($p < 0.001$), respectively. Conclusion. A literature review and meta-analysis showed that pharmacist interventions can significantly improve medication adherence, SBP, DBP, and BP control in patients with essential hypertension. Interventions were complex and multifaceted and included medication management in all analyzed studies.

Omran D, Guirguis LM, Simpson SH. Systematic review of pharmacist interventions to improve adherence to oral antidiabetic medications in people with type 2 diabetes. Canadian Journal of Diabetes 2012;36(5):292-299.

Abstract: Objective: Poor adherence is an important challenge to healthcare professionals because it jeopardizes treatment success and increases the risk of serious complications, especially in patients with chronic diseases like diabetes. The purpose of this study was to summarize the effects of pharmacist interventions aimed at enhancing adherence to oral antidiabetic medications in patients with type 2 diabetes mellitus. Methods: Five electronic databases were searched through to March 12, 2011 to identify controlled trials reporting the effects of pharmacist interventions to improve medication adherence rates in adults with type 2 diabetes. Components of the intervention were categorized as educational, behavioural, affective or provider-targeted strategies. In addition to the impact on medication adherence rates, we recorded any reported effects on health outcomes. Results: Eight studies were included in this review. Education-related strategies were the most frequent (7 of 8 studies), and 6 of 8 studies used a combination of 2 or more strategies for the adherence intervention. Change in adherence rate was assessed using a variety of measurement methods, and 6 studies reported the effect of pharmacist

intervention on clinical, economic or humanistic outcomes. Compared to a control group, 5 studies reported significant improvements in adherence rate with pharmacist intervention; however, glycemic control improved significantly in only 2 studies. Conclusions: Pharmacist interventions to improve medication adherence in diabetes generally use an educational component combined with behavioural, affective or provider-targeted strategies. Although these interventions appear to improve adherence, the effect on health outcomes has not been established. 2012 Canadian Diabetes Association.

Rickles NM, Brown TA, McGivney MS, Snyder ME, White KA. Adherence: a review of education, research, practice, and policy in the United States. Pharmacy Practice (Internet) 2010;8(1):1-17.
Abstract: Objective: To describe the education, research, practice, and policy related to pharmacist interventions to improve medication adherence in community settings in the United States. Methods: Authors used MEDLINE and International Pharmaceutical Abstracts (since 1990) to identify community and ambulatory pharmacy intervention studies which aimed to improve medication adherence. The authors also searched the primary literature using Ovid to identify studies related to the pharmacy teaching of medication adherence. The bibliographies of relevant studies were reviewed in order to identify additional literature. We searched the tables of content of three US pharmacy education journals and reviewed the American Association of Colleges of Pharmacy website for materials on teaching adherence principles. Policies related to medication adherence were identified based on what was commonly known to the authors from professional experience, attendance at professional meetings, and pharmacy journals. Results: Research and Practice: 29 studies were identified: 18 randomized controlled trials; 3 prospective cohort studies; 2 retrospective cohort studies; 5 case-controlled studies; and one other study. There was considerable variability in types of interventions and use of adherence measures. Many of the interventions were completed by pharmacists with advanced clinical backgrounds and not typical of pharmacists in community settings. The positive intervention effects had either decreased or not been sustained after interventions were removed. Although not formally assessed, in general, the average community pharmacy did not routinely assess and/or intervene on medication adherence. Education: National pharmacy education groups support the need for pharmacists to learn and use adherence-related skills. Educational efforts involving adherence have focused on students´ awareness of adherence barriers and communication skills needed to engage patients in behavioral change. Policy: Several changes in pharmacy practice and national legislation have provided pharmacists opportunities to intervene and monitor medication adherence. Some of these changes have involved the use of technologies and provision of specialized services to improve adherence. Conclusions: Researchers and practitioners need to evaluate feasible and sustainable models for pharmacists in community settings to consistently and efficiently help patients better use their medications and improve their health outcomes.

Rubio-Valera M, Serrano-Blanco A, Magdalena-Belio J, Fernandez A, Garcia-Campayo J, March Pujol M, et al. Effectiveness of Pharmacist Care in the Improvement of Adherence to Antidepressants: A Systematic Review and Meta-Analysis. Ann Pharmacother 2011;45(1):39-48.
Abstract: BACKGROUND: Pharmacists can play a decisive role in the management of ambulatory patients with depression who have poor adherence to antidepressant drugs. OBJECTIVE: To systematically evaluate the effectiveness of pharmacist care in improving adherence of depressed outpatients to antidepressants. METHODS: A systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted. RCTs were identified through electronic databases (MEDLINE, Cochrane Central Register of Controlled Trials, Institute for Scientific Information Web of Knowledge, and Spanish National Research Council) from inception to April 2010, reference lists were checked, and experts were consulted. RCTs that evaluated the impact of pharmacist interventions on improving adherence to antidepressants in depressed patients in an outpatient setting (community pharmacy or pharmacy service) were included. Methodologic quality was assessed and methodologic details and outcomes were extracted in duplicate. RESULTS: Six RCTs were identified. A total of 887 patients with an established diagnosis of depression who were initiating or maintaining pharmacologic treatment with antidepressant drugs and who received pharmacist care (459 patients) or usual care (428 patients) were included in the review. The most commonly reported interventions were patient education and monitoring, monitoring and management of toxicity and adverse effects, adherence promotion, provision of written or visual information, and recommendation or implementation of changes or adjustments in medication. Overall, no statistical heterogeneity or publication bias was detected. The pooled odds ratio, using a random effects model, was 1.64 (95% CI 1.24 to 2.17). Subgroup analysis showed no statistically significant differences in results by type of pharmacist involved, adherence measure, diagnostic tool, or analysis strategy. CONCLUSIONS: These results suggest that pharmacist intervention is effective in the improvement

of patient adherence to antidepressants. However, data are still limited and we would recommend more research in this area, specifically outside of the US.

Motiverende samtale

Drymalski WM, Campbell TC. A review of Motivational Interviewing to enhance adherence to antipsychotic medication in patients with schizophrenia: Evidence and recommendations. Journal of Mental Health 2009;18(1):6-15.

Abstract: Background: Non-adherence with treatment is a serious concern for many behavioral health problems, and nowhere is this issue more acute than among patients with schizophrenia who are non-adherent to antipsychotic medications. Aims: Motivational Interviewing (MI) is a psychotherapeutic intervention which has been demonstrated to be effective at increasing adherence to behavioral health regimens. The aim of this article was to review the empirical literature on the use of MI to increase adherence to antipsychotics among patients with schizophrenia. Method: A literature review utilizing PubMed and PsycINFO from 1965 to 2006 was conducted. Results: The literature review produced only five empirical studies which utilized MI to increase antipsychotic adherence. Two studies found an increase in antipsychotic adherence following the MI-based intervention, while the other three found no change in adherence. Conclusions: The small sample of studies and the methodological limitations of each made it difficult to draw any meaningful conclusions. Suggestions to address these methodological issues in future research are provided.

Easthall C, Watson S, Wright D, Wood J, Bhattacharya D. The impact of motivational interviewing (MI) as an intervention to improve medication adherence; A meta-analysis. Int J Pharm Pract 2012;20:48.

Abstract: Medication adherence is a determinant of treatment efficacy, yet 30-50% of patients prescribed medication for chronic illnesses do not take their medicines as prescribed[1]. Evidence suggests that complex, multi-faceted interventions, tailored to meet individual needs are most efficacious[2], however, a gold standard adherence intervention remains elusive. MI is a patient-centred technique intended to facilitate behaviour change by resolving patient ambivalence[3] and may therefore be useful in cases of intentional non-adherence where patients choose not to take their medications as prescribed. Metaanalyses have reported MI efficacy in facilitating health related behaviour change, but have not explored its effects on medication adherence. This study provides a meta-analysis of MI as an intervention to improve medication adherence. Ethical approval was not required. Articles were identified from a larger systematic review of MI and other cognitive based techniques used as adherence interventions by searching the Medline, Embase and PsychInfo databases using the Ovid interface, the Cinahl database and The National Electronic Library for Medicines (NELM), on the 4th and 5th of August 2011. Bibliographies of identified articles and relevant reviews were also handsearched. Variations of the terms 'medication adherence' and 'cognitive-based techniques' were combined using Boolean operators where permitted. Searches were restricted to title and abstract fields, without date, language or study design restrictions. Studies describing an intervention to improve medication adherence, using MI or other cognitive based techniques which reported medication adherence were included in the larger study. Studies involving interventions for the treatment of addiction or in mental health were excluded. Randomised controlled trials (RCTs), using MI as the adherence intervention, were then selected for this substudy. Random effects meta-analysis using 'Comprehensive Meta-Analysis' was employed to determine the efficacy of MI compared to standard care with results reported as Cohen's d with 95% confidence intervals. Potential reporting bias explored by visual analysis of a funnel plot. Following the removal of duplicate articles, 299 abstracts were identified for the larger study. Eight of these were RCT's using MI as the main intervention (n = 1,742) and have therefore been included in this sub-study. Included studies were drawn from a ten year time period, with the earliest study published in 2001. MI was associated with a small improvement in medication adherence when compared to usual care, d (95% CI) = 0.268 (0.157, 0.379) p < 0.0001. There was no evidence for excessive heterogeneity (Cochran's Q = 5.870, p = 0.555, I2 = 0.000). Visual inspection of the funnel plot did not provide any indication of reporting bias. Relative to estimates of the effect size of other reported adherence interventions (0.08 (0.04-0.12))[4], whilst still small, MI has demonstrated a greater effect. The low heterogeneity is encouraging and indicates little systematic variation between studies. Further work is needed to fully elucidate the value of MI as an adherence intervention, and the associated variables which influence its effect size.

Hill S, Kavookjian J. Motivational interviewing as a behavioral intervention to increase HAART adherence in patients who are HIV-positive: A systematic review of the literature. Aids Care-Psychological and Socio-Medical Aspects of Aids/Hiv 2012;24(5):583-592.
Abstract: As HIV infection rates continue to rise, more and more people are faced with a complex, life-altering highly active antiretroviral therapy (HAART) regimen. With some researchers reporting as few as 50-70% of patients achieving adherence in the first six months of a HAART regimen, many behavioral interventions to increase HAART adherence have been examined. One such intervention, motivational interviewing (MI), has shown promise in previous studies and reviews as a possible successful intervention. Researchers conducted a review of the literature to identify studies analyzing the effect of a MI intervention on HAART adherence, with the objectives of examining this relationship and identifying gaps in the literature. To draw definitive conclusions about these questions and to maintain high methodological quality in the search, researchers used the Cochrane method for systematic reviews while conducting this review. Five studies were retained for review from the search and all were RCTs. Sample sizes ranged from 141 to 326 patients. Three of the five studies showed a significant increase in adherence rates, two studies reported a significant decrease in viral load, and one study showed an increase in CD4 cell count as a result of the intervention. A lack of a universally accepted definition of adherence and large gaps in the areas of humanistic and economic outcomes in the literature creates challenges in comparing improvements in HAART adherence across studies. Despite these challenges in comparison, MI appears to be a promising intervention to improve HAART adherence in HIV-positive individuals, but further studies of rigorous methodological quality are needed to fully understand the effect of this intervention.

Påminnelsepakning

Boeni F, Spinatsch E, Suter K, Hersberger KE, Arnet I. Effect of drug reminder packaging on medication adherence: a systematic review revealing research gaps. Systematic reviews 2014;3(1):29-29.
Abstract: BACKGROUND: This was a systematic review of the literature in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Evidence mapping was used to reveal the effect of drug reminder packaging on medication adherence, to identify research gaps and to make suggestions for future research. METHODS: PubMed, Embase, CINAHL and PsycINFO were searched with an end date of September 2013 using the Medical Subject Headings (MeSH) term 'medication adherence' and 20 different search terms for 'drug reminder packaging', limited to the English and German languages. Additional references were identified through cross-referencing. All prospective controlled trials with an intervention using drug reminder packaging for patients taking at least one medication without the assistance of a health-care professional were included in the evidence mapping of the effect of drug reminder packaging on adherence and outcomes according to the Economic, Clinical and Humanistic Outcomes (ECHO) model. RESULTS: A total of 30 studies met the inclusion criteria: 10 randomized controlled trials, 19 controlled clinical trials and 1 cohort study. Drug reminder packaging had a significant effect on at least one adherence parameter in 17 studies (57%). The methodological quality was strong in five studies. Two studies provided complete information. Clear research gaps emerged. CONCLUSIONS: Overall, the studies showed a positive effect of drug reminder packaging on adherence and clinical outcomes. However, poor reporting and important gaps like missing humanistic and economic outcomes and neglected safety issues limit the drawing of firm conclusions. Suggestions are made for future research.

Hall R, Harald-Kongso J, Humphrey L, Willgoss T. The effect of medical devices with dose-memory and reminder functions on patients' treatment adherence, confidence and disease self-management. Value Health 2013;16 (7):A336.
Abstract: Objectives: Adherence to treatment is an important issue in the management of chronic diseases and an indicator of patients' ability to self-manage their condition. Some medical devices have been designed to help support patients' self-management and adherence by including dose-memory and reminder functions. This literature review explored the role and impact of these devices on patients' adherence to treatment, confidence and disease self-management. Methods: A search of Medline, Embase and PsycInfo was performed to identify articles published in English from 2003-2013, which studied the effect of devices with memory and/or reminder functions on treatment adherence,

confidence and self-management. The main attributes of the abstracts selected for inclusion and full-text review, were summarized. Results: The database searches yielded 940 abstracts. Of the 47 meeting the inclusion criteria, 32 were retained. The articles explored the impact of memory and/or reminder devices on treatment adherence, device usability and users' (patients, health care professionals (HCPs) and caregivers) relationship and attitudes towards the devices. Devices with memory and/or reminder functions were found to improve self-reported and electronically-monitored treatment adherence in prophylactic medication use (e.g. contraceptives) and a range of chronic diseases including HIV, diabetes and asthma. Memory functions were considered valuable in disease management by patients and HCPs. Of particular value was that memory and/or reminder functions provided dose-history information, enhanced patients' confidence with, and ability to manage their medication and condition, and helped reduce forgotten or incorrect medication dosing. Conclusions: The incorporation of memory functions alone and in combination with reminder features in medical devices can improve patient's adherence, confidence and self-management. This can lead to improvements in disease control and clinical outcomes, thereby offering clinical and economic value. This review highlights the importance of conducting further qualitative and quantitative research in this area to fully understand the value of these types of devices to patients and HCPs.

Mahtani Kamal R, Heneghan Carl J, Glasziou Paul P, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd; 2011.

Abstract: Background: Current methods of improving medication adherence for health problems are mostly complex, labour-intensive, and not reliably effective. Medication 'reminder packaging', which incorporates a date or time for a medication to be taken in the packaging, can act as a reminder to improve adherence. This review of reminder packaging is an update of our 2006 Cochrane review. Objectives: The objective of this review was to determine the effects of reminder packaging aids for self-administered medication/s taken for at least one month, on adherence and other outcomes.Search methods: We updated searches of the Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE) (The Cochrane Library Issue 9, 2010), MEDLINE, EMBASE, CINAHL and PsycINFO from the database start dates to September 2010. We searched Current Controlled Trials to identify trials in progress. We performed a cited reference search on the Science Citation Index to identify papers that had cited the original systematic review. We also searched the Internet, contacted packaging manufacturers, and checked abstracts from the Pharm-line database and reference lists from relevant articles. We did not apply any language restrictions. Selection criteria: We selected randomised controlled trials with at least 80% follow up. We intended to do a sensitivity analysis of those studies that analysed their data on an intention-to-treat basis. Included studies compared a reminder packaging device with no device, for participants taking self-administered medications for at least one month. Data collection and analysis: Three review authors independently assessed studies for inclusion, assessed quality, and extracted data from included studies. Where considered appropriate, data were combined for meta-analysis, or were reported and discussed in a narrative. Main results: We included twelve studies containing data on 2196 participants; four of these studies were newly included in this 2011 update of our 2006 Cochrane review. Six intervention groups in four trials provided data on the percentage of pills taken. Reminder packaging increased the percentage of pills taken (mean difference (MD) 11% (95% confidence interval (CI) 6% to 17%)). Notable heterogeneity occurred among these trials (I2 = 96.3%). Two trials provided data for the proportion of self-reported adherent patients, reporting a reduction in the intervention group which was not statistically significant (odds ratio = 0.89 (95% CI 0.56 to 1.40)). We conducted meta-analysis on data from two trials assessing the effect of reminder packaging on blood pressure measurements. We found that reminder packaging significantly decreased diastolic blood pressure (MD = -5.89 mmHg (95% CI -6.70 to -5.09; P < 0.00001; I2 = 0%). No effect was seen on systolic blood pressure (mean change -1.01, 95% CI -2.22 to 0.20; P = 0.1, I2 = 0%). We also conducted meta-analysis on extracted data from two trials that looked at change in glycated haemoglobin. We found that reminder packaging significantly reduced glycated haemoglobin levels (MD -0.72; 95% CI -0.83 to -0.60; P < 0.00001; I2 = 92%), although there was considerable heterogeneity.No appropriate data were available for meta-analysis of remaining clinical outcomes, which included serum vitamin C and E levels, and self-reported psychological symptoms (one trial each). We reported remaining data narratively. In one study the presence of a reminder packaging aid was found to be preferred by patients with low literacy levels. Authors' conclusions: Reminder packing may represent a simple method for improving adherence for patients with selected conditions. Further research is warranted to improve the design and targeting of these devices.

Chapman B, Bogle V. Adherence to medication and self-management in stroke patients. British journal of nursing (Mark Allen Publishing) 2014;23(3):158-166.
Abstract: BACKGROUND: Stroke is the third most common cause of mortality and one of the leading causes of adult physical disability in England. Medical treatment is imperative for the management of stroke and the risk reduction of recurrent stroke. The success of a medical treatment is determined largely by adherence. However, research has shown that adherence to medication in patients who have had a stroke is often suboptimal. Self-management interventions have been shown to improve adherence in long-term conditions. The impact of self-management interventions specifically on adherence to stroke medication is unknown. OBJECTIVE: To review systematically the impact that self-management interventions have on adherence to stroke medication. Method: The online databases that were systematically searched included PsychINFO, MEDLINE, EMBASE, Scopus, Cochrane Database of Systematic Reviews, CINAHL and Web of Science. Reference lists of retrieved studies were hand-searched. RESULTS: Six studies met the criteria for inclusion in the systematic review. Self-management interventions for stroke patients were effective in improving adherence to stroke medication in the short term. However, in the longer term, these benefits were not maintained. CONCLUSIONS: Applying self-management interventions to improve medication adherence in stroke patients across integrated clinical settings shows promise. However, further development of such interventions and research is recommended, with more stringent methodologies and longer follow-up periods.

Christensen A, Osterberg LG, Hansen EH. Electronic monitoring of patient adherence to oral antihypertensive medical treatment: a systematic review. J Hypertens 2009;27(8):1540-1551.
Abstract: Poor patient adherence is often the reason for suboptimal blood pressure control. Electronic monitoring is one method of assessing adherence. The aim was to systematically review the literature on electronic monitoring of patient adherence to self-administered oral antihypertensive medications. We searched the Pubmed, Embase, Cinahl and Psychinfo databases and websites of suppliers of electronic monitoring devices. The quality of the studies was assessed according to the quality criteria proposed by Haynes et al. Sixty-two articles were included; three met the criteria proposed by Haynes et al. and nine reported the use of electronic adherence monitoring for feedback interventions. Adherence rates were generally high, whereas average study quality was low with a recent tendency towards improved quality. One study detected investigator fraud based on electronic monitoring data. Use of electronic monitoring of patient adherence according to the quality criteria proposed by Haynes et al. has been rather limited during the past two decades. Electronic monitoring has mainly been used as a measurement tool, but it seems to have the potential to significantly improve blood pressure control as well and should be used more widely.

Cutrona SL, Choudhry NK, Fischer MA, Servi A, Liberman JN, Brennan TA, et al. Modes of Delivery for Interventions to Improve Cardiovascular Medication Adherence. Am J Manag Care 2010;16(12):929-942.
Abstract: Objective: To determine the optimal modes of delivery for interventions to improve adherence to cardiovascular medications. Study Design: Systematic review. Methods: We conducted systematic searches of English-language, peer-reviewed publications in MEDLINE and EMBASE, 1966 through December 31, 2008. We selected randomized controlled trials of interventions to improve adherence to medications for preventing or treating cardiovascular disease or diabetes. Articles were classified based on mode of delivery of the main intervention as (1) person-independent interventions (mailed, faxed, or hand distributed; or delivered via electronic interface) or (2) person-dependent interventions (nonautomated phone calls, in-person interventions). Results: We identified 6550 articles. Of these, 168 were reviewed in full and 51 met inclusion criteria. Among person-independent interventions (56% successful), electronic interventions were most successful (67%). Among person-dependent interventions (52% successful), phone calls showed low success rates (38%). In-person interventions at hospital discharge were more effective (67%) than clinic interventions (47%). In-person pharmacist interventions were effective when held in a pharmacy (83% successful), but were less effective in clinics (38%). Conclusions: Future medication adherence studies should explore new electronic approaches and in-person interventions at the site of medication distribution. Identifying times of increased patient receptivity to the adherence message such as hospital discharge also will be important.

DeFulio A, Silverman K. The use of incentives to reinforce medication adherence. Prev Med 2012;55:S86-S94.

Abstract: Objective. Poor medication adherence is a longstanding problem, and is especially pertinent for individuals with chronic conditions or diseases. Adherence to medications can improve patient outcomes and greatly reduce the cost of care. The purpose of the present review is to describe the literature on the use of incentives as applied to the problem of medication adherence. Methods. We conducted a systematic review of peer-reviewed empirical evaluations of incentives provided to patients contingent upon medication adherence. Results. This review suggests that incentive-based medication adherence interventions can be very effective, but there are few controlled studies. The studies on incentive-based medication adherence interventions most commonly feature patients taking medication for drug or alcohol dependence. HIV, or latent tuberculosis. Across studies that reported percent adherence comparisons, incentives increased adherence by a mean of 20 percentage points, but effects varied widely. Cross-study comparisons indicate a positive relationship between the value of the incentive and the impact of the intervention. Post-intervention evaluations were rare, but tended to find that adherence effects diminish after the interventions are discontinued. Conclusions. Incentive-based medication adherence interventions are promising but understudied. A significant challenge for research in this area is the development of sustainable and cost-effective long-term interventions.

Easthall C, Song F, Bhattacharya D. A meta-analysis of cognitive-based behaviour change techniques as interventions to improve medication adherence. BMJ Open 2013;3(8).

Abstract: Objective: To describe and evaluate the use of cognitive-based behaviour change techniques as interventions to improve medication adherence. Design: Systematic review and meta-analysis of interventions to improve medication adherence. Data sources: Search of the MEDLINE, EMBASE, PsycINFO, CINAHL and The Cochrane Library databases from the earliest year to April 2013 without language restriction. References of included studies were also screened to identify further relevant articles. Review methods: We used predefined criteria to select randomised controlled trials describing a medication adherence intervention that used Motivational Interviewing (MI) or other cognitive-based techniques. Data were extracted and risk of bias was assessed by two independent reviewers. We conducted the meta-analysis using a random effects model and Hedges' g as the measure of effect size. Results: We included 26 studies (5216 participants) in the meta-analysis. Interventions most commonly used MI, but many used techniques such as aiming to increase the patient's confidence and sense of self-efficacy, encouraging support-seeking behaviours and challenging negative thoughts, which were not specifically categorised. Interventions were most commonly delivered from community-based settings by routine healthcare providers such as general practitioners and nurses. An effect size (95% CI) of 0.34 (0.23 to 0.46) was calculated and was statistically significant ($p < 0.001$). Heterogeneity was high with an I-2 value of 68%. Adjustment for publication bias generated a more conservative estimate of summary effect size of 0.21 (0.08 to 0.33). The majority of subgroup analyses produced statistically nonsignificant results. Conclusions: Cognitive-based behaviour change techniques are effective interventions eliciting improvements in medication adherence that are likely to be greater than the behavioural and educational interventions largely used in current practice. Subgroup analyses suggest that these interventions are amenable to use across different populations and in differing manners without loss of efficacy. These factors may facilitate incorporation of these techniques into routine care.

Golubev S. Compliance measurement-guided medication management programs in hypertension: A health technology assessment. J Hypertens 2010;28:e269.

Abstract: Objective: Many approaches were suggested to measure and manage patients' attitude to antihypertensive medication in clinical settings but whether inclusion of such interventions in hypertension management programs affects their effectiveness is unclear. This systematic review aims to determine the influence of compliance measurement-guided medication management programs on outcomes in essential hypertensives. Design and Method: All-language search of all articles in the Cochrane Controlled Trials Register (CENTRAL, The Cochrane Library, Issue 4, 2009),MEDLINE (1970to2009),EMBASE (1974to2009),CINAHL(1982 to 2009), PsycINFO and ISI Web of Science. RCTs of interventions designed to influence not only patient compliance, but any clinical (BP, morbidity, mortality), patient-reported (health-related quality of life (QL)) or organizational outcomes of hypertension management via application of compliance monitoring and feedback in adults with essential hypertension under long-term antihypertensive medication in primary care. Each study was assessed and data were extracted according to the criteria outlined by the Cochrane Handbook for Systematic Reviews ofInterventions, Version 5.0.2. Results: 4 studies were included testing different compliance monitoring approaches. Due to heterogeneitybetween studiesintermsofparticipantsand compliance interventions

the results were not pooled. In 3 studies compliance measurement-guided medication management was a part of complex interventions (patient motivation, support and reminders, delivered by telecommunication, nursing or pharmacy care) which makes these trials inconclusive. Electronic compliance monitoring in one study had no effect on BP, but led to fewer drug changes and less drug use during 5-months follow-up. None ofthe trials evaluated effects on patient-reported or hard clinical outcomes. Conclusions: Electronic compliance monitoring appears to have some positive organizational impact, although it is not possible to say whether compliance monitoring and feedback have an effect on BP or other clinical outcomes. There is insufficient evidence for effectiveness of this health technology in clinical management of hypertension.

Luersen K, Davis SA, Kaplan SG, Abel TD, Winchester WW, Feldman SR. Sticker Charts: A Method for Improving Adherence to Treatment of Chronic Diseases in Children. Pediatr Dermatol 2012;29(4):403-408.

Abstract: Poor adherence is a common problem and may be an underlying cause of poor clinical outcomes. In pediatric populations, positive reinforcement techniques such as sticker charts may increase motivation to adhere to treatment regimens. To review the use of sticker charts to improve adherence in children with chronic disease, Medline and PsycINFO searches were conducted using the key words positive reinforcement OR behavior therapy and adherence OR patient compliance and child. Randomized controlled retrospective cohort or single-subject-design studies were selected. Studies reporting adherence to the medical treatment of chronic disease in children using positive reinforcement techniques were included in the analysis. The systematic search was supplemented by identifying additional studies identified through the reference lists and authors of the initial articles found. Positive reinforcement techniques such as sticker charts increase adherence to medical treatment regimens. In several studies, this effect was maintained for months after the initial intervention. Better adherence correlated with better clinical outcomes in some, but not all, studies. Few studies examining the use of sticker charts were identified. Although single-subject-design studies are useful in establishing the effect of a behavioral intervention, larger randomized controlled trials would help determine the precise efficacy of sticker chart interventions. Adherence to medical treatments in children can be increased using sticker charts or other positive reinforcement techniques. This may be an effective means to encourage children with atopic dermatitis to apply their medications and improve clinical outcomes.

Petry NM, Rash CJ, Byrne S, Ashraf S, White WB. Financial Reinforcers for Improving Medication Adherence: Findings from a Meta-analysis. Am J Med 2012;125(9):888-896.

Abstract: BACKGROUND: Increasingly, financial reinforcement interventions based on behavioral economic principles are being applied in health care settings, and this study examined the use of financial reinforcers for enhancing adherence to medications. METHODS: Electronic databases and bibliographies of relevant references were searched, and a meta-analysis of identified trials was conducted. The variability in effect size and the impact of potential moderators (study design, duration of intervention, magnitude of reinforcement, and frequency of reinforcement) on effect size were examined. RESULTS: Fifteen randomized studies and 6 nonrandomized studies examined the efficacy of financial reinforcement interventions for medication adherence. Financial reinforcers were applied for adherence to medications for tuberculosis, substance abuse, human immunodeficiency virus, hepatitis, schizophrenia, and stroke prevention. Reinforcement interventions significantly improved adherence relative to control conditions with an overall effect size of 0.77 (95% confidence interval, 0.70-0.84; P < .001). Nonrandomized studies had a larger average effect size than randomized studies, but the effect size of randomized studies remained significant at 0.44 (95% confidence interval, 0.35-0.53; P < .001). Interventions that were longer in duration, provided an average reinforcement of $50 or more per week, and reinforced patients at least weekly resulted in larger effect sizes than those that were shorter, provided lower reinforcers, and reinforced patients less frequently. CONCLUSION: These results demonstrate the efficacy of medication adherence interventions and underscore principles that should be considered in designing future adherence interventions. Financial reinforcement interventions hold potential for improving medication adherence and may lead to benefits for both patients and society. Published by Elsevier Inc. The American Journal of Medicine (2012) 125, 888-896

Tran N, Coffman JM, Sumino K, Cabana MD. Patient reminder systems and asthma medication adherence: a systematic review. J Asthma 2014:epub.

Abstract: Objective: One of the most common reasons for medication non-adherence for asthma patients is forgetfulness. Daily medication reminder system interventions in the form of text messages, automated phone calls and audiovisual reminder devices can potentially address this problem. The aim

of this review was to assess the effectiveness of reminder systems on patient daily asthma medication adherence. Methods: We conducted a systematic review of the literature to identify randomized controlled trials (RCTs) which assessed the effect of reminder systems on daily asthma medication adherence. We searched all English-language articles in Pub Med (MEDLINE), CINAHL, EMBASE, PsychINFO and the Cochrane Library through May 2013. We abstracted data on the year of study publication, location, inclusion and exclusion criteria, patient characteristics, reminder system characteristics, effect on patient adherence rate and other outcomes measured. Descriptive statistics were used to summarize the characteristics and results of the studies. Results: Five RCTs and one pragmatic RCT were included in the analysis. Median follow-up time was 16 weeks. All of the six studies suggested that the reminder system intervention was associated with greater levels of participant asthma medication adherence compared to those participants in the control group. None of the studies documented a change in asthma-related quality of life or clinical asthma outcomes. Conclusion: All studies in our analysis suggest that reminder systems increase patient medication adherence, but none documented improved clinical outcomes. Further studies with longer intervention durations are needed to assess effects on clinical outcomes, as well as the sustainability of effects on patient adherence

van Dalem J, Krass I, Aslani P. Interventions promoting adherence to cardiovascular medicines. Int J Clin Pharm 2012;34(2):295-311.
Abstract: Background Cardiovascular diseases (CVDs) are a large burden on the healthcare system. Medicines are the primary treatment for these diseases; however, adherence to therapy is low. To optimise treatment and health outcomes for patients, it is important that adherence to cardiovascular medicines is maintained at an optimal level. Therefore, identifying effective interventions to improve adherence and persistence to cardiovascular therapy is of great significance. Aim of the Review This paper presents a review of the literature on interventions used in the community setting which aim to improve adherence to cardiovascular medicines in patients with hypertension, dyslipidaemia, congestive heart failure or ischaemic heart disease. Methods Several databases (Medline, EMBASE, PsychINFO, IPA, CINAHL, Pubmed, Cochrane) were searched for studies which were published from 19792009, evaluated interventions intended to improve adherence to cardiovascular medicines in the community setting, had at least one measure of adherence, and consisted of an intervention and comparison/control group. Results Among 36 eligible studies (consisting of 7 informational, 15 behavioural, 1 social, and 13 combined strategy interventions), 17 (1 informational, 10 behavioural, and 6 combined) reported a significant improvement in adherence and/or persistence. Behavioural interventions were the most successful. Twenty-one studies (4 informational, 9 behavioural, and 8 combined) also demonstrated improvements in clinical outcomes, though, effects were frequently variable, contradictory and not related to changes in adherence. Conclusion Several types of interventions are effective in improving adherence and/or persistence within the CVD area and in the community setting. Behavioural interventions have shown the greatest success (compared to other types of interventions); and adding informational strategies has not resulted in further improvements in adherence. Improving adherence and persistence to cardiovascular medicines is a dynamic process that is influenced by many factors, and one which requires long term multiple interventions to promote medicine taking in patients.

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Banning M. A review of interventions used to improve adherence to medication in older people. Int J Nurs Stud 2009;46(11):1505-1515.
Abstract: Background: Medication mismanagement is a continuous problem particularly in older people. Numerous interventions have been developed and tested in an attempt to improve adherence with medication in this client group. Objectives: This review aimed to examine the simple to complex interventions that have been used to assess and improve adherence with medication in older people. Design: An extensive review of the literature was performed and 20 relevant research papers and one report were chosen. Findings: Research papers were evaluated according to design, RCTs were analysed using the JADAD scoring system, systematic reviews and reviews of the literature were reviewed using the Critical Appraisal Skills Programme and subjected to a narrative analysis. This process assisted the development to emerging themes. Four themes were developed: patient barriers, health professional involvement, and health related outcomes and formation giving. Conclusions: The salient findings of the review infer that there is no clear definition of non-adherent behaviour. Quantitative interventions

fail to assess patient choice in relation to medication taking. Pharmacist-driven interventions are resource intensive. Health care outcomes and clinical effectiveness are seldom addressed in interventions. Among the many difficulties encountered when attempting to use interventions to promote adherence with medication in older people is their perceptions and beliefs, the appropriateness of the medicines prescribed as well as the impact of lifestyle patterns: smoking, alcohol and diet. Many intervention studies are of poor quality and do not include a theoretical framework to underpin the interventions being used. More focused research is needed to improve understanding of the theoretical knowledge that underpins the complexities of adherence with medication in older people. In-depth qualitative studies can be used to develop such theory. In addition, the quality of intervention research can be improved by the inclusion of a research framework such as the Medical Research Council model.

Conn VS, Hafdahl AR, Cooper PS, Ruppar TM, Mehr DR, Russell CL. Interventions to Improve Medication Adherence Among Older Adults: Meta-Analysis of Adherence Outcomes Among Randomized Controlled Trials. Gerontologist 2009;49(4):447-462.

Abstract: Purpose: This study investigated the effectiveness of interventions to improve medication adherence (MA) in older adults. Design and Methods: Meta-analysis was used to synthesize results of 33 published and unpublished randomized controlled trials. Random-effects models were used to estimate overall mean effect sizes (ESs) for MA, knowledge, health outcomes, and health services utilization. Results: Data were synthesized across 11,827 participants. Interventions significantly improved MA (ES = 0.33), knowledge (ES = 0.48), and diastolic blood pressure (ES = 0.19). Nonsignificant effects were found for systolic blood pressure (ES = 0.21), other health outcomes (ES = 0.04), and health services utilization (ES = 0.16). Moderator analyses showed larger adherence ESs for interventions employing special medication packaging, dose modification, participant monitoring of medication effects and side effects, succinct written instructions, and standardized (not tailored) interventions. Larger effects were found when a moderate proportion of participants were women, for participants taking 3-5 medications, and when pill count adherence was measured. Implications: The findings document that interventions increase MA in older adults. The considerable heterogeneity in the magnitude of effects across studies and results of the moderator analyses demonstrate the need for additional empirical research to optimize interventions.

Hu D, Juarez DT, Yeboah M, Castillo TP. Interventions to increase medication adherence in African-American and Latino populations: a literature review. Hawai'i journal of medicine & public health : a journal of Asia Pacific Medicine & Public Health 2014;73(1):11-18.

Abstract: The objective of this systematic review was to investigate the effectiveness of interventions to improve medication adherence in ethnic minority populations. A literature search from January 2000 to August 2012 was conducted through PubMed/Medline, Web of Science, The Cochrane Library, and Google Scholar. Search terms used included: medication (MeSH), adherence, medication adherence (MeSH), compliance (MeSH), persistence, race, ethnicity, ethnic groups (MeSH), minority, African-American, Hispanic, Latino, Asian, Pacific Islander, and intervention. Studies which did not have ≥75% of the sample population comprised of individuals of any one ethnic background were excluded, unless the authors performed sub-group analyses by race/ethnicity. Of the 36 studies identified, 20 studies showed significant post-intervention differences. Sample population sizes ranged from 10 to 520, with a median of 126.5. The studies in this review were conducted with patients of mainly African-American and Latino descent. No studies were identified which focused on Asians, Pacific Islanders, or Native Americans. Interventions demonstrating mixed results included motivational interviewing, reminder devices, community health worker (CHW) delivered interventions, and pharmacist-delivered interventions. Directly observed therapy (DOT) was a successful intervention in two studies. Interventions which did not involve human contact with patients were ineffective. In this literature review, studies varied significantly in their methods and design as well as the populations studied. There was a lack of congruence among studies in the way adherence was measured and reported. No single intervention has been seen to be universally successful, particularly for patients from ethnic minority backgrounds.

Lafond NA, Churchill R, Pandya H, Smyth A, Williams J, Elliott RA. Medicine-taking interventions in children and young people: One size fits all, one size fits none. Int J Pharm Pract 2010;18:11-12.

Abstract: Background: One in five UK children under 16 years has long-standing illnesses and may need medicines. Adherence with medicines is worse in children, especially adolescents, than in adults. Many interventions designed to improve adherence stop at the patient-provider level and are criticised for

lack of integration in service provision.^[1,2] There have been no published systematic reviews of adherence enhancing interventions carried out in children and adolescent populations. As part of our overall study, we conducted a critical evidence synthesis to review interventions designed to improve adherence in this patient group. Methods: A critical evidence synthesis was carried out to elicit child-parent feedback and provide experience to identify perceptions of roles, empowerment, rights and responsibilities associated with long-term medicine use. Systematic searches of seven electronic databases were conducted including The Cochrane Library, MEDLINE, EMBASE, PsycINFO, (all via OVID), CINAHL (via EBSCOhost), ePIC and Econlit (via CSA). Databases were searched for papers relating to adherence to medicines in children and adolescents with chronic illness requiring regular daily medication, from 1970 to 2007, with English as a language restriction. Ethical approval was not required for the evidence synthesis. Studies had to be concurrent control or randomised controlled trials and had to measure medicines adherence. Results: Searches identified 3343 papers. There were a total of 47 papers included in the interventions review. Of 47 studies, 25 were American and only 5 were from the United Kingdom. Most interventions were carried out in asthma (26) and diabetes (5). Many studies included a wide age range and there appeared to be little age-specific adjustment of interventions. Interventions aimed to improve medicines adherence in a variety of ways including using health education or training interventions (24), educational-behavioural interventions (6), drug delivery, drug dosing and regimen-focused interventions (12) and parent, family and peer-led interventions (4). Many interventions were aimed at parents or carers. Only 11 studies reported a theoretical basis for their intervention. Power calculations were not reported by 29 studies, and small sample size meant that half of the studies probably lacked power to detect clinically important effects. Patient or carer reported adherence was used in 19 studies. Seventeen studies had follow-up periods of 1 year or more. Thirty-four studies had Jadad scores of 0-2, low quality. Eighteen studies found a statistically significant difference in adherence and 25 studies reported statistically significant differences in outcomes. Discussion: Due to the heterogeneity of these studies, it is difficult to conclude whether interventions to improve adherence in children are effective. Poor quality study design precludes appropriate assessment of effectiveness in many studies. In many cases, interventions appeared to demonstrate a lack of understanding of reasons for nonadherence, were not tailored appropriately for different age groups and were complex and costly. Studies that demonstrated effectiveness were from a range of disease states and used a range of intervention types, so we can conclude that one type of intervention will not suit all types of nonadherence.

Manias E, Williams A. Medication Adherence in People of Culturally and Linguistically Diverse Backgrounds: A Meta-Analysis. Ann Pharmacother 2010;44(6):964-982.

Abstract: BACKGROUND: Medication adherence is of particular importance for people of culturally and linguistically diverse (CALD) backgrounds due to language difficulties, lack of social and organizational supports, lack of access to healthcare resources, and disengagement with the health-care system. OBJECTIVE: To evaluate the impact of interventions to improve medication adherence in people of CALD backgrounds through a systematic review and meta-analysis. METHODS: A search was performed using the following databases: Cochrane Database of Systematic Reviews, Cumulative Index to Nursing & Allied Health Literature, EMBASE, Journals@Ovid, PsychInfo, PubMed, Science Direct, Scopus, and Web of Science. Databases were searched from January 1978 to October 2009. RESULTS: Forty-six articles reviewed were assessed as being relevant, which included 36 randomized controlled trials, 2 observational cohort studies, and 8 quasi-experimental studies. The most common method for assessing medication adherence was self-reporting measures, such as the Morisky Scale and its modifications. Few studies used combinations of adherence measures, and adherence involving a medication event monitoring system (MEMS) was used in only 6 studies. Individuals of CALD backgrounds were recruited with people of non-CALD backgrounds and subsequent analyses tended to be undertaken of the whole sample. Twenty studies showed statistically significant improvements in medication adherence, 15 of which were randomized controlled trials. Six of the successful interventions involved delivery by a bilingual person or the use of translated materials and 4 involved the use of a conceptual model. Meta-analyses demonstrated modest improvements in medication adherence. CONCLUSIONS: Relatively little high-quality work has been conducted on adherence-enhancing interventions for people of CALD backgrounds. Greater attention needs to be given to examining the needs of specific CALD population groups. Future researchers should consider rigorously testing interventions that take into account the enormous diversity and differences that exist within any particular CALD group.

Patterson SM, Bradley MC, Kerse N, Cardwell CR, Hughes CM. Interventions to improve the appropriate use of polypharmacy for older people: A Cochrane Review. Int J Pharm Pract 2011;19:17-18.

Abstract: Introduction: Polypharmacy, defined as, "the administration of more medicines than are clinically indicated, representing unnecessary drug use"^[1] is a particular concern in older persons. It is associated with a range of negative health outcomes,^[2] hence, choosing the best interventions to improve appropriate poly-pharmacy is a priority. The objectives of this systematic review [supported by the Cochrane Effective Practice and Organisation of Care (EPOC) Cochrane Review Group] were to determine which interventions alone, or in combination, are effective in improving the appropriate use of poly-pharmacy and reducing medication-related problems in older people. Methods: A range of literature databases such as The Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, MEDLINE, EMBASE, CINAHL, ISI Web of Science, International Pharmaceutical Abstracts, PsycINFO, PubMed, The Health Management Information Consortium database, Pharmline (NELM) and NHS Evidence were searched to identify suitable studies, in addition to hand-searching reference lists. Search terms included polypharmacy, Beers criteria, medication appropriateness, inappropriate, suboptimal. A range of study designs, e.g. randomised and non-randomised controlled trials (RCTs/CCTs), controlled before-and-after studies (CBAs) and interrupted time series (ITS) studies were eligible for inclusion. Studies were eligible if they described interventions which directly or indirectly affected prescribing and were aimed at improving appropriate poly-pharmacy in those aged 65 years and older. Outcomes of interest were appropriateness of medications prescribed, measured by a validated instrument, e.g. Beers' criteria or the Medication Appropriateness Index (MAI), prevalence of appropriate medication as defined by a validated tool and hospital admissions. Secondary outcomes were medication-related problems, medication adherence and quality of life. Study specific estimates were pooled, using a random effects model to yield summary estimates of effect and 95% confidence intervals. Results: The electronic searches identified 2200 potentially relevant citations, of which 138 appeared to meet the inclusion criteria. Following detailed assessment, 10 studies were included in the review and 128 citations were excluded primarily due to the outcome measure used. All studies described interventions that were organisational according to EPOC definitions. Nine were complex, multifaceted interventions of pharmaceutical care in a variety of settings and one examined computerised decision support provided to general physicians. Seven studies measured appropriateness of prescribing using the summated (MAI) score post-intervention. The Beers' criteria were used to assess the appropriateness of medications post-intervention in four studies. The pharmaceutical care and computerised decision support interventions included in this review demonstrated a reduction in inappropriate medication use. Pooled data from 5 studies showed a mean improvement of -3.88 (95% CI: -5.40, -2.35) in the summated MAI score, post-intervention, in favour of the intervention group. Data from 4 studies showed a mean difference of -6.78 (95% CI: -12.34, -1.22) in the change in MAI score in favour of the intervention group. The pooled data from 3 studies, demonstrated a mean reduction -0.06 (95% CI: -0.16, 0.04) in the number of Beers drugs per patient, post-intervention. Hospital admissions were measured in 4 studies; however, evidence of the effect of the interventions on this outcome was conflicting. Medication-related problems were reported as adverse drug events (ADEs) in 3 studies, but only one of these found a significant reduction (35%), in the number of ADEs, post-intervention. Conclusions: Interventions to improve appropriate polypharmacy, such as pharmaceutical care, appear beneficial in terms of reducing inappropriate prescribing and reducing some medication related problems.

Salema N-EM, Elliott RA, Glazebrook C. A Systematic Review of Adherence-Enhancing Interventions in Adolescents Taking Long-term Medicines. J Adolesc Health 2011;49(5):455-466.

Abstract: Purpose: To assess the effectiveness of adherence-enhancing interventions (AEIs) aimed at adolescents (10-19-year-olds). Methods: An extensive search of seven bibliographic databases was conducted at the end of 2009 to identify comparative studies evaluating AEIs targeting adolescents. Data describing study characteristics and intervention effects on adherence to medicines or health outcomes were extracted and summarized using qualitative and quantitative methods. Results: A total of 17 AEIs were identified: 12 studies (70%) were conducted in the United States, 10 (59%) included adolescents with type 1 diabetes mellitus, and 14 (82%) considered the developmental tasks of adolescence. In all, 12 AEIs successfully improved outcome measures. Features of successful interventions included targeting AEIs to a narrow age range, including family in type 1 diabetes mellitus management, and improving access to care. Poor quality and underpowered studies limit the inferences drawn from this review. Conclusions: More diverse and robust studies are needed to identify strategies to help adolescents manage medicines.

Achaval SD, Suarez-Almazor ME. Treatment adherence to disease-modifying antirheumatic drugs in patients with rheumatoid arthritis and systemic lupus erythematosus. Int J Clin Rheumtol 2010;5(3):313-326.

Abstract: Treatment adherence is critical in the management of rheumatic diseases. Recent advances in therapy for rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are promising, although the impact on quality of life may be limited due to nonadherence. Databases including Ovid Medline, Scopus and the Epub-ahead-of-print subset of PubMed were searched for the period of the last 10 years using combined keywords patient compliance, medication adherence, disease modifying antirheumatic drug (DMARD), rheumatoid arthritis and systemic lupus erythematosus. Additional references from retrieved papers were considered. Inclusion criteria were the following: identification of a quantitative measure of adherence to medications including DMARDs and biologics; inclusion of well-defined measures of adherence; and patients with RA or SLE. Studies in RA and SLE patients demonstrated overall inadequate treatment adherence. Adherence was measured using multiple methods including pharmacy records, electronic monitoring, self-report and physician report. The evidence for interventions to improve treatment adherence was limited and demonstrated various results. Future research should further explore determinants of nonadherence and continue to examine the efficacy of implementing various strategies to improve medication management in this patient population.

Al-Aqeel S, Al-Sabhan J. Strategies for improving adherence to antiepileptic drug treatment in patients with epilepsy. Cochrane Database of Systematic Reviews 2011 (1):CD008312.

Abstract: BACKGROUND: Poor adherence to antiepileptic medications is associated with increased mortality and morbidity. In this review we focus on interventions designed to assist patients with adherence to antiepileptic medications. OBJECTIVES: To determine the effectiveness of interventions aimed at improving adherence to antiepileptic medications in adults and children with epilepsy. SEARCH STRATEGY: We searched the Epilepsy Group's Specialised Register (24 June 2010), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2010, Issue 2) and electronic databases: MEDLINE (OVID) (1950 to June 2010); EMBASE (OVID) (1980 to 2010 Week 24); CINAHL (1982 to June 2010) and PsycINFO (22 June 2010), and the reference lists of relevant articles. SELECTION CRITERIA: Randomised or quasi-randomised controlled trials of adherence-enhancing interventions aimed at patients with clinical diagnosis of epilepsy (as defined in individual studies), of any age and of either gender, treated with antiepileptic drugs in a primary care, outpatient or other community setting. DATA COLLECTION AND ANALYSIS: We screened titles and abstracts for eligibility. Two review authors independently extracted data and assessed each study according to the Cochrane criteria. The studies differed widely according to intervention and measures of adherence, therefore combining data was not appropriate. MAIN RESULTS: Six trials met our inclusion criteria: five targeted adult epileptic patients with a combined patient number of 222 and one targeted parents of children with epilepsy (n = 51). Follow-up time was generally short: from one to six months. Two main types of intervention were examined: educational and behavioural modification. Each study compared treatment with no intervention 'usual care'. None compared one intervention with another. Due to heterogeneity between studies in terms of interventions and the methods used to measure adherence, we did not pool the results. Education and counselling of patients with epilepsy have shown mixed success. Behavioural interventions such as the use of intensive reminders and 'implementation intention' interventions provided more positive effects on adherence. AUTHORS' CONCLUSIONS: Intensive reminders and 'implementation intention' interventions appear promising in enhancing adherence to antiepileptic mediations, however we need more reliable evidence on their efficacy from carefully designed randomised controlled trials before a firm conclusion can be reached.

Andrews KL, Jones SC, Mullan J. Asthma self management in adults: A review of current literature. Collegian 2014;21(1):33-41.

Abstract: Self management programs for chronic conditions, such as asthma, have an important place in healthcare delivery. When properly implemented, they can curb the impact of disease and reduce both the high personal costs for individuals and significant financial costs for health care systems. The purpose of this review was to establish an understanding of current published literature on asthma self management programs in adults and to identify any reported attributes or components which serve to

either assist or obstruct the uptake of self management strategies. Electronic data sources including Scopus, Proquest 5000, CINAHL, PubMed and Web of Science were accessed and literature searches were conducted using the key terms: asthma, chronic disease, self management, morbidity, quality of life, health outcomes, patient education and best practice. Inclusion criteria for the search included journal articles relating to adults with asthma published in English in peer reviewed journals from 1995 to 2011. Exclusion criteria included research targeting children, parents of children or families; and articles examining Asthma and COPD (or any other co-morbidity). Sixty four articles were included in this review due to their relevance to the major components of asthma self management, as defined by the Australian Asthma Management Handbook. A major conclusion from this review was that the uptake of asthma self management strategies is poor despite global recommendations for over twenty years; and that a likely reason for this is that generic asthma self management advice does not engage the individual with asthma.

Argoff CE, Kahan M, Sellers EM. Preventing and managing aberrant drug-related behavior in primary care: Systematic review of outcomes evidence. Journal of opioid management 2014;10(2):119-134.

Abstract: Several strategies for preventing, identifying, and responding to aberrant opioid-related behaviors are recommended in pain management guidelines. This systematic review evaluated data supporting basic strategies for addressing aberrant opioid-related behaviors. Risk reduction strategies were identified via a review of available guidelines. Systematic literature searches of PubMed (May 1, 2007-January 18, 2013) identified articles with evidence relevant to nine basic strategies. Reference lists from relevant articles were reviewed for additional references of interest. Levels of evidence for articles identified were graded on a four-point scale (strongest evidence = level 1; weakest evidence = level 4) using Oxford Centre for Evidence-Based Medicine Levels of Evidence criteria. Weak to moderate evidence supports the value of thorough patient assessment, risk-screening tools, controlled-substance agreements, careful dose titration, opioid dose ceilings, compliance monitoring, and adherence to practice guidelines. Moderate to strong evidence suggests that prescribing tamper-resistant opioids may help prevent misuse but may also have the unintended consequence of prompting a migration of users to other marketed opioids, heroin, or other substances. Similarly, preliminary evidence suggests that although recent regulatory and legal efforts may reduce misuse, they also impose barriers to the legitimate treatment of pain. Despite an absence of consistent, strong supporting evidence, clinicians are advised to use each of the available risk-mitigation strategies in combination in an attempt to minimize the risk of abuse in opioid treatment patients. Physicians must critically evaluate their opioid prescribing and not only increase their efforts to prevent substance abuse but also not compromise pain management in patients who benefit from it.

Arrivillaga M, Martucci V, Hoyos PA, Arango A. Adherence among children and young people living with HIV/AIDS: A systematic review of medication and comprehensive interventions. Vulnerable Children and Youth Studies 2013;8(4):321-337.

Abstract: Advancements in therapy, including the use of highly active antiretroviral therapy, have increased survival and decreased opportunistic infections in HIV pediatric and adolescent population. Previous studies have found that in general HIV persons who maintained consistent ad had lower viral loads and improved health status. Nevertheless, adherence among children, adolescents, and youth has been found to be suboptimal. This systematic review describes interventions that have been conducted to improve adherence among these segments of the population diagnosed with HIV/AIDS, in both developed and developing settings. We found 16 interventions and clinical trials conducted between 2000 and 2011; these were grouped into studies that focused strictly on the medication (n = 6) and others that focused on factors associated with medication adherence (n = 10). The results indicate that, in 11 years, few treatment adherence interventions were conducted, most of which took place in the United States; although some articles reported more comprehensive interventions, all of them ultimately aimed only to promote adherence to antiretrovirals. We conclude that interventions need to be more specifically created for children and youth in order to improve adherence and promote self-care in general, incorporating the social determinants approach with special emphasis on the needs of children, adolescents, and youth according to their age. It is also concluded that interventions should be implemented and evaluated in contexts where children and youth are severely affected by HIV in regions like Africa, Latin America, and the Caribbean.

Baernighausen T, Chaiyachati K, Chimbindi N, Peoples A, Haberer J, Newell M-L. Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies. Lancet Infect Dis 2011;11(12):942-951.

Abstract: The success of potent antiretroviral treatment for HIV infection is primarily determined by adherence. We systematically review the evidence of effectiveness of interventions to increase adherence to antiretroviral treatment in sub-Saharan Africa. We identified 27 relevant reports from 26 studies of behavioural, cognitive, biological, structural, and combination interventions done between 2003 and 2010. Despite study diversity and limitations, evidence suggests that treatment supporters, directly observed therapy, mobile-phone text messages, diary cards, and food rations can effectively increase adherence in sub-Saharan Africa. However, some interventions are unlikely to have large or lasting effects, and others are effective only in specific settings. These findings emphasise the need for more research, particularly for randomised controlled trials, to examine the effect of context and specific features of intervention content on effectiveness. Future work should assess intervention targeting and selection of interventions based on behavioural theories relevant to sub-Saharan Africa.

Bain-Brickley D, Butler Lisa M, Kennedy Gail E, Rutherford George W. Interventions to improve adherence to antiretroviral therapy in children with HIV infection. Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd; 2011.

Abstract: Background: Achieving and maintaining high levels of medication adherence are required to achieve the full benefits of antiretroviral therapy (ART), yet suboptimal adherence among children is common in both developed and developing countries. Objectives: To conduct a systematic review of the literature of evaluations of interventions for improving paediatric ART adherence. Search methods: We created a comprehensive search strategy in order to identify all studies relevant to this topic. In July 2010, we searched the following electronic databases: EMBASE, MEDLINE, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, LILACS, Web of Science, Web of Social Science, NLM Gateway (supplemented by a manual search of the most recent abstracts not included in the Gateway database). We searched abstracts from the International AIDS Conference from 2002 to 2010, the International AIDS Society Conference on Pathogenesis, Treatment and Prevention from 2003 to 2009, and from the Conference on Retroviruses and Opportunistic Infections from 1997 to 2010. We used search strategies determined by the Cochrane Review Group on HIV/AIDS. We also contacted researchers who work in this field and checked reference lists of related systematic reviews and of all included studies. Selection criteria: Randomised and non-randomised controlled trials of interventions to improve adherence to ART among children and adolescents (age ?18 years) were included. Studies had to report adherence to ART as an outcome .Data collection and analysis: After one author performed an initial screening to exclude citations that did not meet the inclusion criteria, two authors did a second screening of those citations that likely met the criteria. For all articles that passed the second screening, full articles were pulled in order to make a final determination. Two authors then extracted data and graded methodological quality independently. Differences were resolved through discussion. Main results: Four studies met the inclusion criteria. No single intervention was evaluated by more than one trial. Two studies were conducted in low-income countries. Two studies were randomised controlled trials (RCT), and two were non-randomised trials. An RCT of a home-based nursing programme showed a positive effect of the intervention on knowledge and medication refills (p=.002), but no effect on CD4 count and viral load. A second RCT of caregiver medication diaries showed that the intervention group had fewer participants reporting no missed doses compared to the control group (85% vs. 92%, respectively), although this difference was not statistically significant (p=.08). The intervention had no effect on CD4 percentage or viral load. A non-randomised trial of peer support group therapy for adolescents demonstrated no change in self-reported adherence, yet the percentage of participants with suppressed viral load increased from 30% to 80% (p=.06). The second non-randomised trial found that the percentage of children achieving >80% adherence was no different between children on a lopinavir-ritonavir (LPV/r) regimen compared to children on a non-nucleoside reverse transcriptase regimen (p=.781). However, the proportion of children achieving virological suppression was significantly greater for children on the LPV/r regimen than for children on the NNRTI-containing regimen (p=.002).Authors' conclusions: A home-based nursing intervention has the potential to improve ART adherence, but more evidence is needed. Medication diaries do not appear to have an effect on adherence or disease outcomes. Two interventions, an LPV/r-containing regimen and peer support therapy for adolescents, did not demonstrate improvements in adherence, yet demonstrated greater viral load suppression compared to control groups, suggesting a different mechanism for improved health outcomes. Well-designed evaluations of interventions to improve paediatric adherence to ART are needed.

Barkhof E, Meijer CJ, de Sonneville LM, Linszen DH, de Haan L. Interventions to improve adherence to antipsychotic medication in patients with schizophrenia--a review of the past decade. European Psychiatry: the Journal of the Association of European Psychiatrists 2012;27(1):9-18.
Abstract: OBJECTIVE: Nonadherence to antipsychotic medication is highly prevalent in patients with schizophrenia and has a deleterious impact on the course of the illness. This review seeks to determine the interventions that were examined in the past decade to improve adherence rates. METHOD: The literature between 2000 and 2009 was searched for randomized controlled trials which compared a psychosocial intervention with another intervention or with treatment as usual in patients with schizophrenia. RESULTS: Fifteen studies were identified, with a large heterogeneity in design, adherence measures and outcome variables. Interventions that offered more sessions during a longer period of time, and especially those with a continuous focus on adherence, seem most likely to be successful, as well as pragmatic interventions that focus on attention and memory problems. The positive effects of adapted forms of Motivational Interviewing found in earlier studies, such as compliance therapy, have not been confirmed. CONCLUSION: Nonadherence remains a challenging problem in schizophrenia. The heterogeneity of factors related to nonadherence calls for individually tailored approaches to promote adherence. More evidence is required to determine the effects of specific interventions.

Barry SJ, Gaughan TM, Hunter R. Schizophrenia. Clin Evid 2012;2012.
Abstract: INTRODUCTION: The lifetime prevalence of schizophrenia is approximately 0.7% and incidence rates vary between 7.7 and 43.0 per 100,000; about 75% of people have relapses and continued disability, and one third fail to respond to standard treatment. Positive symptoms include auditory hallucinations, delusions, and thought disorder. Negative symptoms (demotivation, self-neglect, and reduced emotion) have not been consistently improved by any treatment. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of drug treatments for positive, negative, or cognitive symptoms of schizophrenia? What are the effects of drug treatments in people with schizophrenia who are resistant to standard antipsychotic drugs? What are the effects of interventions to improve adherence to antipsychotic medication in people with schizophrenia? We searched: Medline, Embase, The Cochrane Library, and other important databases up to May 2010 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 51 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: amisulpride, chlorpromazine, clozapine, depot haloperidol decanoate, haloperidol, olanzapine, pimozide, quetiapine, risperidone, sulpiride, ziprasidone, zotepine, aripiprazole, sertindole, paliperidone, flupentixol, depot flupentixol decanoate, zuclopenthixol, depot zuclopenthixol decanoate, behavioural therapy, clozapine, compliance therapy, first-generation antipsychotic drugs in treatment-resistant people, multiple-session family interventions, psychoeducational interventions, and second-generation antipsychotic drugs in treatment-resistant people.

Berk L, Hallam KT, Colom F, Vieta E, Hasty M, Macneil C, et al. Enhancing medication adherence in patients with bipolar disorder. Hum 2010;25(1):1-16.
Abstract: OBJECTIVES: Medication adherence contributes to the efficacy-effectiveness gap of treatment in patients with bipolar disorder. This paper aims to examine the challenges involved in improving medication adherence in bipolar disorder, and to extract some suggestions for future directions from the core psychosocial studies that have targeted adherence as a primary or secondary outcome. METHODS: A search was conducted for articles that focused on medication adherence in bipolar disorder, with emphasis on publications from 1996 to 2008 using Medline, Web of Science, CINAHL PLUS, and PsychINFO. The following key words were used: adherence, compliance, alliance, adherence assessment, adherence measurement, risk factors, psychosocial interventions, and psycho-education. RESULTS: There are a number of challenges to understanding non-adherence including the difficulty in defining and measuring it and the various risk factors that need to be considered when aiming to enhance adherence. Nevertheless, the importance of addressing adherence is evidenced by the connection between adherence problems and poor outcome. Despite these challenges, a number of small psychosocial studies targeting adherence as a primary outcome point to the potential usefulness of psycho-education aimed at improving knowledge, attitudes, and adherence behavior, but more large scale randomized controlled trials are needed in this area. Evidence of improved outcomes from larger

randomized controlled trials of psychosocial interventions that target medication adherence as a secondary outcome suggests that tackling other factors besides medication adherence may also be an advantage. While some of these larger studies demonstrate an improvement in medication adherence, the translation of these interventions into real life settings may not always be practical. A person centered approach that considers risk factors for non-adherence and barriers to other health behaviors may assist with the development of more targeted briefer interventions. Integral to improving medication adherence is the delivery of psycho-education, and attention needs to be paid to the implementation, and timing of psycho-education. Progress in the understanding of how medicines work may add to the credibility of psycho-education in the future. CONCLUSIONS: Enhancement of treatment adherence in bipolar patients is a necessary and promising management component as an adjunct to pharmacotherapy. The current literature on psychosocial interventions that target medication adherence in bipolar disorder points to the possibility of refining the concept of non-adherence and adapting psycho-education to the needs of certain subgroups of people with bipolar disorder. Large scale randomized controlled trials of briefer or more condensed interventions are needed that can inform clinical practice.

Binford MC, Kahana SY, Altice FL. A systematic review of antiretroviral adherence interventions for HIV-infected people who use drugs. Current HIV/AIDS reports 2012;9(4):287-312.
Abstract: HIV-infected persons who use drugs (PWUDs) are particularly vulnerable for suboptimal combination antiretroviral therapy (cART) adherence. A systematic review of interventions to improve cART adherence and virologic outcomes among HIV-infected PWUDs was conducted. Among the 45 eligible studies, randomized controlled trials suggested directly administered antiretroviral therapy, medication-assisted therapy (MAT), contingency management, and multi-component, nurse-delivered interventions provided significant improved short-term adherence and virologic outcomes, but these effects were not sustained after intervention cessation. Cohort and prospective studies suggested short-term increased cART adherence with MAT. More conclusive data regarding the efficacy on cART adherence and HIV treatment outcomes using cognitive behavioral therapy, motivational interviewing, peer-driven interventions and the integration of MAT into HIV clinical care are warranted. Of great concern was the virtual lack of interventions with sustained post-intervention adherence and virologic benefits. Future research directions, including the development of interventions that promote long-term improvements in adherence and virologic outcomes, are discussed.

Bryant J, McDonald VM, Boyes A, Sanson-Fisher R, Paul C, Melville J. Improving medication adherence in chronic obstructive pulmonary disease: a systematic review. Respir Res 2013;14.
Abstract: Adherence to medication among individuals with chronic obstructive pulmonary disease (COPD) is suboptimal and has negative impacts on survival and health care costs. No systematic review has examined the effectiveness of interventions designed to improve medication adherence. Electronic databases Medline and Cochrane were searched using a combination of MeSH and keywords. Eligible studies were interventions with a primary or secondary aim to improve medication adherence among individuals with COPD published in English. Included studies were assessed for methodological quality using the Effective Practice and Organisation of Care (EPOC) criteria. Of the 1,186 papers identified, seven studies met inclusion criteria. Methodological quality of the studies was variable. Five studies identified effective interventions. Strategies included: brief counselling; monitoring and feedback about inhaler use through electronic medication delivery devices; and multi-component interventions consisting of self-management and care co-ordination delivered by pharmacists and primary care teams. Further research is needed to establish the most effective and cost effective interventions. Special attention should be given to increasing patient sample size and using a common measure of adherence to overcome methodological limitations. Interventions that involve caregivers and target the healthcare provider as well as the patient should be further explored.

Campbell NL, Boustani MA, Skopeljia EN, Gao S, Unverzagt FW, Murray MD. Medication Adherence in Older Adults With Cognitive Impairment: A Systematic Evidence-Based Review. Am J Geriatr Pharmacother 2012;10(3):165-177.
Abstract: Background: Cognitive impairment challenges the ability to adhere to the complex medication regimens needed to treat multiple medical problems in older adults. Objective: Our aim was to conduct a systematic evidence-based review to identify barriers to medication adherence in cognitively impaired older adults and interventions aimed at improving medication adherence. Methods: A search of MEDLINE, EMBASE, PsycINFO, GoogleDocs, and CINAHL for articles published between 1966 and February 29, 2012 was performed. Studies included older adults with a diagnosis of cognitive impairment

of any degree (mild cognitive impairment or mild, moderate, or severe dementia). To identify barriers to adherence, we reviewed observational studies. To identify relevant interventions, we reviewed clinical trials targeting medication adherence in cognitively impaired older adults. We excluded studies lacking a measure of medication adherence or lacking an assessment of cognitive function, case reports or series, reviews, and those focusing on psychiatric disorders or infectious diseases. Population demographics, baseline cognitive function, medication adherence methods, barriers to adherence, and prospective intervention methodologies were extracted. Results: The initial search identified 594 articles. Ten studies met inclusion criteria for barriers to adherence and three met inclusion criteria for interventional studies. Unique barriers to adherence included understanding new directions, living alone, scheduling medication administration into the daily routine, using potentially inappropriate medications, and uncooperative patients. Two studies evaluated reminder systems and showed no benefit in a small group of participants. One study improved adherence through telephone and televideo reminders at each dosing interval. The results of the review are limited by reviewing only published articles, missing barriers or interventions due to lack of subgroup analysis, study selection and extraction completed by 1 reviewer, and articles with at least an abstract published in English. Conclusions: The few studies identified limit the assessment of barriers to medication adherence in the cognitively impaired population. Successful interventions suggest that frequent human communication as reminder systems are more likely to improve adherence than nonhuman reminders.

Chapman RH, Ferrufino CP, Kowal SL, Classi P, Roberts CS. The cost and effectiveness of adherence-improving interventions for antihypertensive and lipid-lowering drugs. Int J Clin Pract 2010;64(2):169-181.

Abstract: AIMS: Adherence to cardiovascular medications is poor. Accordingly, interventions have been proposed to improve adherence. However, as intervention-associated costs are rarely considered in full, we sought to review the effectiveness and costs associated with different adherence-improving interventions for cardiovascular disease therapies. METHODS: We reviewed MEDLINE to update a prior review of interventions to improve adherence with antihypertensive and/or lipid-lowering therapy covering January 1972 to June 2002, to add studies published from July 2002 to October 2007. Eligible studies evaluated > or = 1 intervention compared with a control, used measures other than self-report, reported significant improvement in adherence and followed patients for > or = 6 months. Effectiveness was measured as relative improvement (RI), the ratio of adherence in the intervention group to the control group. Costs were calculated based on those reported in the analysis, if available or estimated based on resource use described. All costs were truncated to 6 months and adjusted to 2007 US$. RESULTS: Of 755 new articles, five met all eligibility criteria. Combining with the prior review gave 23 interventions from 18 studies. RI in adherence ranged from 1.11 to 4.65. Six-month intervention costs ranged from $10 to $142 per patient. Reminders had the lowest effectiveness (RI: 1.11-1.14), but were least costly ($10/6 months). Case management was most effective (RI: 1.23-4.65), but the most costly ($90-$130/6 months). CONCLUSIONS: Generally, we found a positive association between intervention costs and effectiveness. Therefore, consideration of intervention costs, along with the benefits afforded to adherence, may help guide the design and implementation of adherence-improving programs.

Charania MR, Marshall KJ, Lyles CM, Crepaz N, Kay LS, Koenig LJ, et al. Identification of Evidence-Based Interventions for Promoting HIV Medication Adherence: Findings from a Systematic Review of US-Based Studies, 1996-2011. AIDS Behav 2014;18(4):646-660.

Abstract: A systematic review was conducted to identify evidence-based interventions (EBIs) for increasing HIV medication adherence behavior or decreasing HIV viral load among persons living with HIV (PLWH). We conducted automated searches of electronic databases (i.e., MEDLINE, EMBASE, PsycINFO, CINAHL) and manual searches of journals, reference lists, and listservs. Interventions were eligible for the review if they were U.S.-based, published between 1996 and 2011, intended to improve HIV medication adherence behaviors of PLWH, evaluated the intervention using a comparison group, and reported outcome data on adherence behaviors or HIV viral load. Each intervention was evaluated on the quality of study design, implementation, analysis, and strength of findings. Of the 65 eligible interventions, 10 are EBIs. The remaining 55 interventions failed to meet the efficacy criteria primarily due to null findings, small sample sizes, or low retention rates. Research gaps and future directions for development of adherence EBIs are discussed.

Chong WW, Aslani P, Chen TF. Effectiveness of interventions to improve antidepressant medication adherence: a systematic review. Int J Clin Pract 2011;65(9):954-975.
Abstract: Non-adherence to antidepressant medications is a significant barrier to the successful treatment of depression in clinical practice. This review aims to systematically assess the effectiveness of interventions for improving antidepressant medication adherence among patients with unipolar depression, and to evaluate the effect of these interventions on depression clinical outcomes. MEDLINE, PsycINFO and EMBASE databases were searched for English-language randomised controlled trials published between January 1990 and December 2010 on interventions to improve antidepressant adherence. The impact of interventions on antidepressant medication adherence (compliance and persistence) and depression clinical outcomes was evaluated. Data concerning the quality of the included studies were also extracted. Twenty-six studies met the inclusion criteria. Interventions were classified as educational, behavioural and multifaceted interventions. A total of 28 interventions were tested, as two studies investigated two interventions each. Sixteen (57%) of the 28 interventions showed significant effects on antidepressant adherence outcomes, whereas 12 (43%) interventions demonstrated significant effects on both antidepressant adherence and depression outcomes. The interventions which showed significant improvement in outcomes were primarily multifaceted and complex, with proactive care management and involvement of mental health specialists. The most commonly used elements of multifaceted interventions included patient educational strategies, telephone follow-up to monitor patients' progress, as well as providing medication support and feedback to primary care providers. Overall, educational interventions alone were ineffective in improving antidepressant medication adherence. In conclusion, improving adherence to antidepressants requires a complex behavioural change and there is some evidence to support behavioural and multifaceted interventions as the most effective in improving antidepressant medication adherence and depression outcomes. More carefully designed and well-conducted studies are needed to clarify the effect of interventions in different patient populations and treatment settings.

Crowe M, Porter R, Inder M, Lacey C, Carlyle D, Wilson L. Effectiveness of interventions to improve medication adherence bipolar disorder. Aust N Z J Psychiatry 2012;46(4):317-326.
Abstract: Objective: To identify interventions that improve medication adherence in bipolar disorder. Method: A review of the literature from 2004 to 2011 was conducted using Medline and manual searching. Results: Eleven studies were identified as meeting inclusion criteria. Five studies demonstrated improved medication adherence. No characteristics of the interventions, clinical characteristics of the groups or methodological factors distinguished those psychosocial interventions that demonstrated improvement from those that did not. Conclusions: While only a few interventions improved adherence, most improved clinical outcomes. Issues were also identified about the way in which adherence is defined. It is proposed that incorporating patient preferences into measures of adherence within the context of a disorder-specific psychosocial intervention may provide an approach that demonstrates both improved adherence and improved clinical outcomes. However this requires further research.

Cutrona SL, Choudhry NK, Fischer MA, Servi AD, Stedman M, Liberman JN, et al. Targeting cardiovascular medication adherence interventions. J Am Pharm Assoc (2003) 2012;52(3):381-397.
Abstract: Objectives: To determine whether adherence interventions should be administered to all medication takers or targeted to nonadherers. Data sources and study selection: Systematic search (Medline and Embase, 1966-2009) of randomized controlled trials of interventions to improve adherence to medications for preventing or treating cardiovascular disease or diabetes. Data extraction: Articles were classified as (1) broad interventions (targeted all medication takers), (2) focused interventions (targeted nonadherers), or (3) dynamic interventions (administered to all medication takers; real-time adherence information targets nonadherers as intervention proceeds). Cohen's d effect sizes were calculated. Data synthesis: We identified 7,190 articles; 59 met inclusion criteria. Broad interventions were less likely (18%) to show medium or large effects compared with focused (25%) or dynamic (32%) interventions. Of the 33 dynamic interventions, 6 used externally generated adherence data to target nonadherers. Those with externally generated data were less likely to have a medium or large effect (20% vs. 34.8% self-generated data). Conclusion: Adherence interventions targeting nonadherers are heterogeneous but may have advantages over broad interventions. Dynamic interventions show promise and require further study.

De Bleser L, Matteson M, Dobbels F, Russell C, De Geest S. Interventions to improve medication-adherence after transplantation: a systematic review. Transpl Int 2009;22(8):780-797.
Abstract: Reports of interventions to improve adherence to medical regimens in solid organ transplant recipients are scarce. A systematic review identified 12 intervention studies. These studies focused on renal, heart, and liver transplant recipients. Five reports used randomized controlled trial (RCT) designs. Sample sizes varied between 18 and 110 subjects. The interventions are difficult to evaluate and categorize because of brief descriptions of intervention details. Of the 12 studies identified in this review, only five studies found a statistically significant improvement in at least one medication-adherence outcome with the intervention. In general, most included a combination of patient-focused cognitive/educational, counseling/behavioral, and psychologic/affective dimensions. Eight studies intervened at the healthcare provider, healthcare setting or healthcare system level, but showed a limited improvement in adherence. No single intervention proved to be superior at increasing medication-adherence in organ transplantation, but a combination of interventions in a team approach for the chronic disease management of organ transplant patients may be effective in a long-term perspective. In conclusion, finding the most effective combination of interventions to enhance adherence is vital. Utilizing an RCT design and adhering to the CONSORT guidelines can lead to higher quality studies and possibly more effective intervention studies to enhance medication-adherence.

de Bruin M, Viechtbauer W, Schaalma HP, Kok G, Abraham C, Hospers HJ. Standard Care Impact on Effects of Highly Active Antiretroviral Therapy Adherence Interventions A Meta-analysis of Randomized Controlled Trials. Arch Intern Med 2010;170(3):240-250.
Abstract: Background: Poor adherence to medication limits the effectiveness of treatment for human immunodeficiency virus. Systematic reviews can identify practical and effective interventions. Meta-analyses that control for variability in standard care provided to control groups may produce more accurate estimates of intervention effects. Methods: To examine whether viral load and adherence success rates could be accurately explained by the active content of highly active antiretroviral therapy (HAART) adherence interventions when controlling for variability in care delivered to controls, databases were searched for randomized controlled trials of HAART adherence interventions published from 1996 to January 2009. A total of 1342 records were retrieved, and 52 articles were examined in detail. Directly observed therapy and interventions targeting specific patient groups (ie, psychiatric or addicted patients, patients < 18 years) were excluded, yielding a final sample of 31 trials. Two coders independently retrieved study details. Authors were contacted to complete missing data. Results: Twenty studies were included in the analyses. The content of adherence care provided to control and intervention groups predicted viral load and adherence success rates in both conditions (P<.001 for all comparisons), with an estimated impact of optimal adherence care of 55 percentage points. After controlling for variability in care provided to controls, the capacity of the interventions accurately predicted viral load and adherence effect sizes (R-2=0.78, P=.02; R-2=0.28, P<.01). Although interventions were generally beneficial, their effectiveness reduced noticeably with increasing levels of standard care. Conclusions: Intervention and control patients were exposed to effective adherence care. Future meta-analyses of (behavior change) interventions should control for variability in care delivered to active controls. Clinical practice may be best served by implementing current best practice.

De Simoni A, Hardeman W, Mant J, Farmer AJ, Kinmonth AL. Trials to Improve Blood Pressure Through Adherence to Antihypertensives in Stroke/TIA: Systematic Review and Meta-Analysis. Journal of the American Heart Association 2013;2(4).
Abstract: Background-The purpose of this study was to determine whether interventions including components to improve adherence to antihypertensive medications in patients after stroke/transient ischemic attack (TIA) improve adherence and blood pressure control. Methods and Results-We searched MEDLINE, EMBASE, CINAHL, BNI, PsycINFO, and article reference lists to October 2012. Search terms included stroke/TIA, adherence/prevention, hypertension, and randomized controlled trial (RCT). Inclusion criteria were participants with stroke/TIA; interventions including a component to improve adherence to antihypertensive medications; and outcomes including blood pressure, antihypertensive adherence, or both. Two reviewers independently assessed studies to determine eligibility, validity, and quality. Seven RCTs were eligible (n=1591). Methodological quality varied. All trials tested multifactorial interventions. None targeted medication adherence alone. Six trials measured blood pressure and 3 adherence. Meta-analysis of 6 trials showed that multifactorial programs were associated with improved blood pressure control. The difference between intervention versus control in mean improvement in systolic blood pressure was -5.3 mm Hg (95% CI, -10.2 to -0.4 mm Hg, P=0.035; I-2=67% [21% to 86%]) and in diastolic blood pressure was -2.5 mm Hg (-5.0 to -0.1 mm Hg, P=0.046; I-2=47% [0% to 79%]).

There was no effect on medication adherence where measured. Conclusions-Multifactorial interventions including a component to improve medication adherence can lower blood pressure after stroke/TIA. However, it is not possible to say whether or not this is achieved through better medication adherence. Trials are needed of well-characterized interventions to improve medication adherence and clinical outcomes with measurement along the hypothesized causal pathway.

Dean AJ, Walters J, Hall A. A systematic review of interventions to enhance medication adherence in children and adolescents with chronic illness. Arch Dis Child 2010;95(9):717-723.
Abstract: Introduction Poor medication adherence is common in children and adolescents with chronic illness, but there is uncertainty about the best way to enhance medication adherence in this group. The authors conducted a systematic review of controlled trials examining interventions that aim to improve medication adherence. Method A comprehensive literature search was undertaken to locate controlled trials that described specific interventions aiming to improve adherence to long-term medication, where participants were aged 18 years and under, medication adherence was reported as an outcome measure, and which could be implemented by individual health practitioners. Studies were reviewed for quality and outcome. Results 17 studies met inclusion criteria: seven studies examined educational strategies, seven studies examined behavioural interventions and three studies examined educational intervention combined with other forms of psychological therapies. Only two of seven studies reported a clear benefit for education on medication adherence, whereas four of seven trials indicated a benefit of behavioural approaches on medication adherence. One trial reported that combining education with behavioural management may be more effective than education alone. Studies which combined education with other non-medication specific psychological interventions failed to demonstrate a beneficial effect on medication adherence. Only two studies examined adherence-promoting interventions in young people with established adherence problems. Conclusion These findings suggest that education interventions alone are insufficient to promote adherence in children and adolescents, and that incorporating a behavioural component to adherence interventions may increase potential efficacy. Future research should examine interventions in high-risk groups.

Demonceau J, Ruppar T, Kristanto P, Hughes DA, Fargher E, Kardas P, et al. Identification and Assessment of Adherence-Enhancing Interventions in Studies Assessing Medication Adherence Through Electronically Compiled Drug Dosing Histories: A Systematic Literature Review and Meta-Analysis. Drugs 2013;73(6):545-562.
Abstract: Background Non-adherence to medications is prevalent across all medical conditions that include ambulatory pharmacotherapy and is thus a major barrier to achieving the benefits of otherwise effective medicines. Objective The objective of this systematic review was to identify and to compare the efficacy of strategies and components thereof that improve implementation of the prescribed drug dosing regimen and maintain long-term persistence, based on quantitative evaluation of effect sizes across the aggregated trials. Data sources MEDLINE, EMBASE, CINAHL, the Cochrane Library, and PsycINFO were systematically searched for randomized controlled trials that tested the efficacy of adherence-enhancing strategies with self-administered medications. The searches were limited to papers in the English language and were included from database inception to 31 December 2011. Study selection Our review included randomized controlled trials in which adherence was assessed by electronically compiled drug dosing histories. Five thousand four hundred studies were screened. Eligibility assessment was performed independently by two reviewers. A structured data collection sheet was developed to extract data from each study. Study appraisal and synthesis methods The adherence-enhancing components were classified in eight categories. Quality of the papers was assessed using the criteria of the Cochrane Handbook for Systematic Reviews of Interventions guidelines to assess potential bias. A combined adherence outcome was derived from the different adherence variables available in the studies by extracting from each paper the available adherence summary variables in a pre-defined order (correct dosing, taking adherence, timing adherence, percentage of adherent patients). To study the association between the adherence-enhancing components and their effect on adherence, a linear meta-regression model, based on mean adherence point estimates, and a meta-analysis were conducted. Results Seventy-nine clinical trials published between 1995 and December 2011 were included in the review. Patients randomized to an intervention group had an average combined adherence outcome of 74.3 %, which was 14.1 % higher than in patients randomized to the control group (60.2 %). The linear meta-regression analysis with stepwise variable selection estimated an 8.8 % increase in adherence when the intervention included feedback to the patients of their recent dosing history (EM-feedback) ($p < 0.01$) and a 5.0 % increase in adherence when the intervention included a cognitive-educational component ($p = 0.02$). In addition, the effect of interventions on adherence decreased by 1.1 %

each month. Sensitivity analysis by selecting only high-quality papers confirmed the robustness of the model. The random effects model in the meta-analysis, conducted on 48 studies, confirmed the above findings and showed that the improvement in adherence was 19.8 % (95 % CI 10.7-28.9 %) among patients receiving EM-feedback, almost double the improvement in adherence for studies that did not include this type of feedback [10.3 % (95 % CI 7.5-13.1 %)] ($p < 0.01$). The improvement in adherence was 16.1 % (95 % CI 10.7-21.6 %) in studies that tested cognitive-educational components versus 10.1 % (95 % CI 6.6-13.6 %) in studies that did not include this type of intervention ($p = 0.04$). Among 57 studies measuring clinical outcomes, only 8 reported a significant improvement in clinical outcome. Limitations Despite a common measurement, the meta-analysis was limited by the heterogeneity of the pooled data and the different measures of medication adherence. The funnel plot showed a possible publication bias in studies with high variability of the intervention effect. Conclusions Notwithstanding the statistical heterogeneity among the studies identified, and potential publication bias, the evidence from our meta-analysis suggests that EM-feedback and cognitive-educational interventions are potentially effective approaches to enhance patient adherence to medications. The limitations of this research highlight the urgent need to define guidelines and study characteristics for research protocols that can guide researchers in designing studies to assess the effects of adherence-enhancing interventions.

Fuangchan A, Dhippayom T, Kongkaew C. Intervention to Promote Patients' Adherence to Antimalarial Medication: A Systematic Review. Am J Trop Med Hyg 2014;90(1):11-19.
Abstract: Non-adherence as a major contributor to poor treatment outcomes. This study aimed to explore the effectiveness of existing interventions promoting adherence to antimalarial drugs by systematic review. The following databases were used to identify potential articles: MEDLINE, EMBASE, the Cochrane CENTRAL, and CINAHL (through March 2013). From 1,813 potential papers identified, 16 studies met the selection criteria comprising 9,247 patients. Interventions were classified as packaging aids, visual media, combined visual media and verbal information, community education, medication supervision, and convenient regimen. These interventions were shown to increase adherence to antimalarial drugs (median relative risk = 1.4, interquartile range 1.2-2.0). Although a most effective intervention did not emerge, community education and visual media/verbal information combinations may well have most potential to improve adherence to antimalarial medication. These interventions should be implemented in combination to optimize their beneficial effects. The current understanding on improved adherence would facilitate to contain outbreaks of malaria cost effectively.

Garcia-Perez L, Serrano-Aguilar P. Cost-effectiveness of interventions to enhance medication adherence in psychiatric patients: a systematic review. Curr Clin Pharmacol 2011;6(2):115-124.
Abstract: It was conducted a systematic review of economic evaluations that assessed the cost-effectiveness of interventions to enhance the medication adherence in psychiatric patients. Several bibliographic databases were searched: MEDLINE, MEDLINE in process, PSYCINFO, EMBASE, Cochrane Controlled Trials Register, CINAHL, CRD, EconLit, Science Citation Index and Social Science Citation Index. Full economic evaluations which assessed interventions to enhance the adherence to drug therapy in adult patients with a mental illness were included. Data were extracted and the methodological quality of selected studies was assessed. The information was synthesized through narrative procedures. Four clinical trials and two ongoing studies fulfilled the selection criteria. Two studies did not find significant differences in adherence between the interventions (a compliance-enhancing program, a therapeutic drug monitoring and a pharmacy-based intervention) and the control groups; one study found that a compliance program was more effective than a non-specific counselling intervention over 18 months in psychotic patients; another study found better results in terms of adherence among high-severity depressed patients receiving a stepped collaborative care during 12 months in comparison to a control group; in moderate-severity patients the differences disappeared after the first 6 months. None of the four studies found significant differences in costs between groups because of the low statistical power. In summary, adherence enhancing programs could be cost-effective in psychiatric patients although this statement is based on few studies with limited methodological quality. It is necessary more and better research on the cost-effectiveness of interventions in the field of mental health.

Gleeson T, Iversen MD, Avorn J, Brookhart AM, Katz JN, Losina E, et al. Interventions to improve adherence and persistence with osteoporosis medications: a systematic literature review. Osteoporos Int 2009;20(12):2127-2134.
Abstract: Adherence and persistence with osteoporosis medications are poor. We conducted a systematic literature review of interventions to improve adherence and persistence with osteoporosis medications. Seven studies met eligibility requirements and were included in the review. Few interventions

were efficacious, and no clear trends regarding successful intervention techniques were identified. However, periodic follow-up interaction between patients and health professionals appeared to be beneficial. Adherence and persistence with pharmacologic therapy for osteoporosis are suboptimal. Our goal was to examine the design and efficacy of published interventions to improve adherence and persistence. We searched medical literature databases for English-language papers published between January 1990 and July 2008. We selected papers that described interventions and provided results for control and intervention subjects. We assessed the design and methods of each study, including randomization, blinding, and reporting of drop-outs. We summarized the results and calculated effect sizes for each trial. Seven studies met eligibility requirements and were included in the review. Five of the seven studies provided adherence data. Of those five studies, three showed a statistically significant (p a parts per thousand currency signaEuro parts per thousand 0.05) improvement in adherence by the intervention group, with effect sizes from 0.17 to 0.58. Five of the seven studies provided persistence data. Of those five, one reported statistically significant improvement in persistence by the intervention group, with an effect size of 0.36. Few interventions were efficacious, and no clear trends regarding successful intervention techniques were identified in this small sample of studies. However, periodic follow-up interaction between patients and health professionals appeared to be beneficial.

Glynn L, Fahey T. Cardiovascular medication: improving adherence. Clin Evid 2011;2011.
Abstract: INTRODUCTION: Adherence to medication is generally defined as the extent to which people take medications as prescribed by their healthcare providers. It can be assessed in many ways (e.g., by self-reporting, pill counting, direct observation, electronic monitoring, or by pharmacy records). This review reports effects of intervention on adherence to cardiovascular medications however adherence has been measured. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of interventions to improve adherence to long-term medication for cardiovascular disease in adults? We searched: Medline, Embase, The Cochrane Library, and other important databases up to April 2010 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 39 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: patient health education, prescriber education, prompting mechanisms, reminder packaging (calendar [blister] packs, multi-dose pill boxes), and simplified dosing.

Graves MM, Roberts MC, Rapoff M, Boyer A. The Efficacy of Adherence Interventions for Chronically Ill Children: A Meta-Analytic Review. J Pediatr Psychol 2010;35(4):368-382.
Abstract: Objectives To provide quantitative information about the overall effectiveness of adherence interventions to improve adherence and health outcomes for children with chronic illnesses. To evaluate statistically the potential moderators. Methods A meta-analysis was performed on 71 adherence intervention studies. Results Weighted-mean effect size (ES) across all the adherence outcomes for group design studies was in the medium range (mean d = 0.58) and for single-subject design studies was in the large range (mean d = 1.44). The weighted mean ES across all health outcome measures for studies using group designs was in the medium range (mean d = 0.40) and for studies using single-subject designs was in the large range (mean d = 0.74). Conclusions Adherence interventions for children with chronic illnesses effectively increase adherence and result in some positive health benefits. Intervention and methodological variables had significant impact on ESs. High levels of heterogeneity characterized the data.

Gray TA, Orton LC, Henson D, Harper R, Waterman H. Interventions for improving adherence to ocular hypotensive therapy. Cochrane Database of Systematic Reviews 2009 (2).
Abstract: Background Poor adherence to therapy is a significant healthcare issue, particularly in patients with chronic disease such as open angle glaucoma. Treatment failure may necessitate unwarranted changes of medications, increased healthcare expenditure and risk to the patient if surgical intervention is required. Simplifying eye drop regimes, providing adequate information and ongoing support according to patient need, may have a positive effect on improving adherence. Objectives To summarise the effects of interventions for improving adherence to ocular hypotensive therapy in people with ocular hypertension (OHT) or glaucoma. Search strategy We searched CENTRAL, MEDLINE, EMBASE, CINAHL, PsycINFO, Web of Science, ZETOC and OpenSIGLE. In addition, we searched research registers of

ongoing studies. We contacted pharmaceutical manufacturers to request unpublished data and searched conference proceedings for the Association for Research in Vision and Ophthalmology (ARVO), and the Annual Congress for the Royal College of Ophthalmologists (RCO). There were no language or date restrictions in the search for trials. The electronic databases were last searched on 15 January 2009. Selection criteria We included randomised controlled trials (RCTs) and quasi RCTs that compared interventions to improve adherence to ocular hypotensive therapy for patients with OHT or glaucoma. Data collection and analysis At least two authors independently assessed the search results for eligibility and extracted data for included trials onto specifically designed forms. We calculated the mean difference for continuous data and relative risks for dichotomous data. Where appropriate, we pooled data using a fixed-effect model. Main results Eight trials met the inclusion criteria. There was considerable heterogeneity of interventions and reported outcome measures and therefore, meta-analysis was limited to two studies. Overall, studies were not of high quality due to small sample sizes, missing data and short term follow-up. Three of five drug comparison studies provided evidence that reducing the frequency of drops can improve adherence. However, the study that compared the least frequent regime with one of the most complicated, showed no difference in reported adherence. A small study of thirteen patients found a reminder device beneficial to adherence levels yet only one of two studies involving education and individualised care planning was found to be successful. Authors' conclusions Interventions involving simplified dosing regimes, reminder devices, education and individualised care planning, did show improvements in adherence rates. However, due to inadequate methodological quality and heterogeneity of study design we are unable to advocate any particular interventions at this time.

Greenley RN, Kunz JH, Walter J, Hommel KA. Practical Strategies for Enhancing Adherence to Treatment Regimen in Inflammatory Bowel Disease. Inflamm Bowel Dis 2013;19(7):1534-1545.
Abstract: Promoting adherence to treatment among pediatric and adult patients with inflammatory bowel disease (IBD) is a critical yet challenging task for health care providers. Several existing interventions to enhance adherence among individuals with IBD offer useful information about practical strategies to enhance adherence. The current review article has 3 goals. First, the review provides a context for understanding treatment regimen adherence in IBD by reviewing key definitional, measurement, and conceptual challenges in this area. Next, published studies focused on interventions to enhance adherence in IBD are briefly summarized, followed by a synthesis of practical adherence promotion strategies for use in IBD by health care providers. Strategies are distinguished by the level of evidence supporting their utility as well as by age group. Finally, recommendations for future research to facilitate the development and implementation of practical, evidence-based strategies for adherence promotion in IBD are provided. Findings from the literature review suggest that strategies including education, regimen simplification, and use of reminder systems and organizational strategies (e.g., pill boxes) are likely to be best suited for addressing accidental nonadherence. In contrast, addressing motivational issues, teaching problem-solving skills, and addressing problematic patterns of family functioning are more likely to benefit individuals displaying intentional nonadherence.

Gwadry-Sridhar FH, Manias E, Lal L, Salas M, Hughes DA, Ratzki-Leewing A, et al. Impact of Interventions on Medication Adherence and Blood Pressure Control in Patients with Essential Hypertension: A Systematic Review by the ISPOR Medication Adherence and Persistence Special Interest Group. Value Health 2013;16(5):863-871.
Abstract: Objectives: To systematically review the evidence on the impact of interventions to improve medication adherence in adults prescribed antihypertensive medications. Methods: An electronic search was undertaken of articles published between 1979 and 2009, without language restriction, that focused on interventions to improve antihypertensive medication adherence among patients (>= 18 years) with essential hypertension. Studies must have measured adherence as an outcome of the intervention. We followed standard guidelines for the conduct and reporting of the review and conducted a narrative synthesis of reported data. Results: Ninety-seven articles were identified for inclusion; 35 (35 of 97, 36.1%) examined interventions to directly improve medication adherence, and the majority (58 of 97, 59.8%) were randomized controlled trials. Thirty-four (34 of 97, 35.1%) studies reported a statistically significant improvement in medication adherence. Discussion/Conclusions: Interventions aimed at improving patients' knowledge of medications possess the greatest potential clinical value in improving adherence with antihypertensive therapy. However, we identified several limitations of these studies, and advise future researchers to focus on using validated adherence measures, well-designed randomized controlled trials with relevant adherence and clinical outcomes, and guidelines on the appropriate design and analysis of adherence research.

Halpern V, Lopez LM, Grimes DA, Stockton LL, Gallo MF. Strategies to improve adherence and acceptability of hormonal methods of contraception. Cochrane Database of Systematic Reviews 2013 (10).

Abstract: Background Worldwide, hormonal contraceptives are among the most popular reversible contraceptives. Despite their high theoretical effectiveness, typical use results in much lower effectiveness. In large part, this disparity reflects difficulties in adherence to the contraceptive regimen and low rates for long-term continuation. Objectives The intent was to determine the effectiveness of ancillary counseling techniques to improve adherence to, and continuation of, hormonal methods of contraception. Search methods Through August 2013, we searched computerized databases for randomized controlled trials (RCTs) comparing client-provider interventions with standard family planning counseling. Sources included CENTRAL, MEDLINE, EMBASE, POPLINE, ClinicalTrials.gov and ICTRP. Earlier searches also included LILACS, PsycINFO, Dissertation Abstracts, African Index Medicus, and IMEMR. Selection criteria We included RCTs of an intensive counseling technique or other client-provider intervention compared to routine family planning counseling. Interventions included group motivation; structured, peer, or multi-component counseling; and intensive reminders of appointments or next dosing. Outcome measures were discontinuation, reasons for discontinuation, number of missed pills or on-time injections, and pregnancy. Data collection and analysis One author evaluated the titles and abstracts from the searches to determine eligibility. Two authors extracted data from the included studies. We calculated the Mantel-Haenszel odds ratio (OR) for dichotomous outcomes. For continuous variables, the mean difference (MD) was computed; RevMan uses the inverse variance approach. For all analyses, 95% confidence intervals (CI) were also computed. Since the studies identified differed in both interventions and outcome measures, we did not conduct a meta-analysis. Main results Nine RCTs met our inclusion criteria. Five involved direct counseling; of those, two also provided multiple contacts by telephone. Four other trials provided intensive reminders, two of which also provided health education information. Three trials showed some benefit of the experimental intervention. In a counseling intervention, women who received repeated structured information about the injectable depot medroxyprogesterone acetate (DMPA) were less likely to discontinue the method by 12 months (OR 0.27; 95% CI 0.16 to 0.44) than women who had routine counseling. The intervention group was also less likely to discontinue due to menstrual disturbances (OR 0.20; 95% CI 0.11 to 0.37). Another trial showed a group with special counseling plus phone calls was more likely than the special-counseling group to report consistent use of oral contraceptives (OC) at 3 months (OR 1.41; 95% CI 1.06 to 1.87), though not at 12 months. The group with only special counseling did not differ significantly from those with standard care for any outcome. The third trial compared daily text-message reminders about OCs plus health information versus standard care. Women in the text-message group were more likely than the standard-care group to continue OC use by six months (OR 1.54; 95% CI 1.14 to 2.10). The text-message group was also more likely to avoid an interruption in OC use longer than seven days (OR 1.53; 95% CI 1.13 to 2.07). Authors' conclusions Only three trials showed some benefit of strategies to improve adherence and continuation. However, several had small sample sizes and six had high losses to follow up. The overall quality of evidence was considered moderate. The intervention type and intensity varied greatly across the studies. A combination of intensive counseling and multiple contacts and reminders may be needed to improve adherence and acceptability of contraceptive use. High-quality RCTs with adequate power and well-designed interventions could help identify ways to improve adherence to, and continuation of, hormonal contraceptive methods.

Hiligsmann M, Salas M, Hughes DA, Manias E, Gwadry-Sridhar FH, Linck P, et al. Interventions to improve osteoporosis medication adherence and persistence: a systematic review and literature appraisal by the ISPOR Medication Adherence & Persistence Special Interest Group. Osteoporos Int 2013;24(12):2907-2918.

Abstract: This study aims to systematically review, critically appraise and identify from the published literature, the most effective interventions to improve medication adherence in osteoporosis. A literature search using Medline, EMBASE, Cochrane library, and Cumulative Index to Nursing and Allied Health Literature was undertaken to identify prospective studies published between January 1, 1999 and June 30, 2012. We included studies on adult users of osteoporosis medications that tested a patient adherence intervention (e. g., patient education, intensified patient care, different dosing regimens) and reported quantitative results of adherence. The Delphi list was modified to assess the quality of studies. Of 113 articles identified, 20 studies fulfilled the inclusion criteria. The most frequent intervention was education (n = 11) followed by monitoring/supervision (n = 4), drug regimens (n = 2), drug regimens

and patient support (n = 1), pharmacist intervention (n = 1), and electronic prescription (n = 1). Although patient education improved medication adherence in four studies, two large-scale randomized studies reported no benefits. Simplification of dosing regimens (with and without patient support program) was found to have a significant clinical impact on medication adherence and persistence. Monitoring/supervision showed no impact on medication persistence while electronic prescription and pharmacist intervention increased medication adherence or persistence. In conclusion, this review found that simplification of dosing regimens, decision aids, electronic prescription, or patient education may help to improve adherence or persistence to osteoporosis medications. We identified wide variation of quality of studies in the osteoporosis area. The efficacy of patient education was variable across studies, whilemonitoring/supervision does not seem an effective way to enhance medication adherence or persistence.

Hood KK, Ronan JM, Peterson CM, Drotar D. Interventions With Adherence-Promoting Components in Pediatric Type 1 Diabetes Meta-analysis of their impact on glycemic control. Diabetes Care 2010;33(7):1658-1664.
Abstract: OBJECTIVE - To review interventions with adherence-promoting components and document their impact on glycemic control via meta-analysis. RESEARCH DESIGN AND METHODS - Data from 15 studies that met the following criteria were subjected to meta-analysis: 1) randomized, controlled trial, 2) study sample included youth aged <19 years, 3) youth had type 1 diabetes, 4) study reported results on glycemic control; and 5) study reported use of adherence- or self-management promoting components. RESULTS - The 15 studies included 997 youth with type 1 diabetes. The mean effect size for pre- to posttreatment change for the intervention versus control group comparison was 0.11 (95% CI -0.01 to 0.23). This is a small effect, demonstrating very modest improvements in glycemic control. However, analysis for the pre- to posttreatment effects for the intervention group alone did show significant variability [Q(14) = 33.11; P < 0.05]. Multicomponent interventions, those that targeted emotional, social, or family processes that facilitate diabetes management, were more potent than interventions just targeting a direct, behavioral process (e.g., increase in blood glucose monitoring frequency). CONCLUSIONS - Interventions that focus on direct, behavioral processes and neglect emotional, social, and family processes are unlikely to have an impact on glycemic control; multicomponent interventions showed more robust effects on A1C. Future clinical research should focus on refining interventions and gathering more efficacy and effectiveness data on health outcomes of the pediatric patients treated with these interventions.

Kardas P. How to improve patient compliance with lipid lowering medication? Atherosclerosis Supplements 2009;10 (2).
Abstract: Objectives: Poor patient adherence is a major barrier for realising the benefits of evidence-based therapies with lipid-lowering medication. An important portion of patients is non-compliant with their daily statin medication. No more than 50% continues their treatment after two years, at the time when the first documented benefits of treatment come. Thus, assuring good patient compliance with statins is a need of the day. On the other hand, asymptomatic nature of hyperlipidaemia makes this goal even more challenging. The aim of this study was to perform a systematic review of randomised controlled trials that assess the effectiveness of compliance-enhancing interventions aimed at the improvement of patient compliance with lipid-lowering medication. Methods: A MEDLINE database search as well as manual search in the bibliographies of identified publications was performed in January 2009. Results: Twelve randomised controlled trials were included in this review. Identified interventions included simplification of drug regimen, patient information and education, and intensified patient care. Seven studies reported significantly improved adherence rates. None of the identified interventions had significant advantage over the other types. Conclusion: Currently available studies can not point at the golden standard in compliance-enhancing interventions with lipid lowering medications. On the other hand, similar effectiveness of the available interventions should encourage clinicians to use all of them more frequently, in order to improve compliance, and assure better outcomes of patients on statins.

Laba T-L, Bleasel J, Brien J-a, Cass A, Howard K, Peiris D, et al. Strategies to improve adherence to medications for cardiovascular diseases in socioeconomically disadvantaged populations: A systematic review. Int J Cardiol 2013;167(6):2430-2440.
Abstract: Medication non-adherence poses a major barrier to reducing cardiovascular disease (CVD) burden globally, and is increasingly recognised as a socioeconomically determined problem. Strategies

promoting CVD medication adherence appear of moderate effectiveness and cost-effectiveness. Potentially, 'one-size-fits-all' measures are ill-equipped to address heterogeneous adherence behaviour between social groups. This review aims to determine the effects of strategies to improve adherence to CVD-related medications in socioeconomically disadvantaged groups. Randomised/quasi-randomised controlled trials (1996-June 2012, English), testing strategies to increase adherence to CVD-related medications prescribed to adult patients who may experience health inequity (place of residence, occupation, education, or socioeconomic position) were reviewed. 772 abstracts were screened, 111 full-text articles retrieved, and 16 full-text articles reporting on 14 studies, involving 7739 patients (age range 41-66 years), were included. Methodological and clinical heterogeneity precluded quantitative data synthesis. Studies were thematically grouped by targeted outcomes; underlying interventions and policies were classified using Michie et al.'s Behaviour Change Wheel. Contrasting with patient or physician/practice strategies, those simultaneously directed at patients and physicians/practices resulted in statistically significant improvements in relative adherence (16-169%). Comparative cost and cost-effectiveness analyses from three studies did not find cost-saving or cost-effective strategies. Unlike much current evidence in general populations, promising evidence exists about what strategies improve adherence in disadvantaged groups. These strategies were generally complex: simultaneously targeting patients and physicians; addressing social, financial, and treatment-related adherence barriers; and supported by broader guidelines, regulatory and communication-based policies. Given their complexity and potential resource implications, comprehensive process evaluations and cost and cost-effectiveness evidence are urgently needed.

Marcus J, Buisker T, Horvath T, Amico K, Fuchs J, Buchbinder S, et al. Helping our patients take HIV pre-exposure prophylaxis (PrEP): a systematic review of adherence interventions. HIV Med 2014:epub.

Abstract: Objectives: Adherence is critical for maximizing the effectiveness of pre-exposure prophylaxis (PrEP) in preventing HIV infection. Strategies for promoting adherence to HIV treatment, and their potential application to PrEP adherence, have received considerable attention. However, adherence promotion strategies for prevention medications have not been well characterized and may be more applicable to PrEP. We aimed to identify adherence support interventions that have been effective in other prevention fields and could be applied in the HIV prevention context to support pill taking among PrEP users. Methods: To identify adherence support interventions that could be evaluated and applied in the PrEP context, we conducted a systematic review across the following prevention fields: hypertension, latent tuberculosis infection, hyperlipidaemia, oral contraceptives, osteoporosis, malaria prophylaxis, and post-exposure prophylaxis for HIV infection. We included randomized controlled trials that evaluated the efficacy of interventions to improve adherence to daily oral medications prescribed for primary prevention in healthy individuals or for secondary prevention in asymptomatic individuals. Results: Our searches identified 585 studies, of which 48 studies met the eligibility criteria and were included in the review; nine evaluated multiple strategies, yielding 64 separately tested interventions. Interventions with the strongest evidence for improving adherence included complex, resource-intensive interventions, which combined multiple adherence support approaches, and low-cost, low-intensity interventions that provided education or telephone calls for adherence support. Conclusions: Our review identified adherence interventions with strong evidence of efficacy across prevention fields and provides recommendations for evaluating these interventions in upcoming PrEP studies.

Mathes T, Antoine S-L, Pieper D, Eikermann M. Adherence enhancing interventions for oral anticancer agents: A systematic review. Cancer Treat Rev 2014;40(1):102-108.

Abstract: Background: The use of oral anticancer agents has increased in the last decades. Adherence is a crucial factor for the success of oral anticancer agent therapy. However, many patients are non-adherent. Objective: The objective was to evaluate the effectiveness of adherence interventions in patients taking oral anticancer agents. Methods: A systematic literature search was performed in Medline and Embase. Titles and abstracts and in case of potential relevance, full-texts were assessed for eligibility according to the predefined inclusion criteria. The study quality was evaluated. Both process steps were carried out independently by two reviewers. Relevant data on study design, patients, interventions and results were extracted in standardized tables by one reviewer and checked by a second reviewer. Results: Six controlled studies were included. Only one study was randomized. The study quality was moderate to low. One study showed statistically significant results in favor of the adherence intervention, two studies showed a tendency in favor of the intervention, one study showed an inconsistent result depending on the adherence definition and one study showed almost identical adherence rates in both groups. One study showed a tendency in favor of the control group. Conclusions: Although most of the

interventions are not very effective, it appears that certain adherence enhancing interventions could have a promising effect. One crucial point is the consideration of the baseline adherence when choosing patients to avoid ceiling effects. The evidence is limited due to lack of sufficient studies and partly inconsistent results. Further high quality studies are needed.

Mathes T, Pieper D, Antoine SL, Eikermann M. Adherence-enhancing interventions for highly active antiretroviral therapy in HIV-infected patients - a systematic review. HIV Med 2013;14(10):583-595.

Abstract: ObjectivesThe objective of this systematic review was to evaluate the effectiveness of adherence-enhancing interventions for highly active antiretroviral therapy (HAART) in HIV-infected patients in developed countries. MethodsA systematic literature search was performed (January 2001 to May 2012) in EMBASE, including MEDLINE records, CENTRAL and PsycInfo. Trials meeting the following predefined inclusion criteria were included: adult patients with an HIV infection treated with HAART, an intervention to enhance patient adherence, adherence as the outcome, clinical outcomes, randomized controlled trial (RCT), article written in English or German, patient enrolment after 2001, and trial conducted in World Health Organization (WHO) stratum A. Selection was performed by two reviewers independently. All relevant data on patient characteristics, interventions, adherence measures and results were extracted in standardized tables. The methodological trial quality was evaluated by two reviewers independently. All discrepancies were discussed until a consensus was reached. A meta-analysis could not be performed because of the heterogeneity of trials. Results In total, 21 trials fulfilled all inclusion criteria. Of 21 trials, only one that examined motivational interviewing for alcohol-dependent patients showed statistically significant results for adherence rates and viral load in favour of the intervention. One trial showed a statistically significant clinical effect of the intervention; however, inconsistent results were presented for adherence depending on the underlying adherence definition. The results of the remaining 19 trials were not statistically significant or were conflicting for adherence and/or clinical outcomes. However, the methodological trial quality was low. Conclusions It is not possible to definitively assess the effectiveness of adherence-enhancing interventions. However, it appears that most adherence interventions have no effect.

Matteson ML, Russell C. Interventions to improve hemodialysis adherence: A systematic review of randomized-controlled trials. Hemodialysis International 2010;14(4):370-382.

Abstract: Over 485,000 people in the United States have chronic kidney disease, a progressive kidney disease that may lead to hemodialysis. Hemodialysis involves a complex regimen of treatment, medication, fluid, and diet management. In 2005, over 312,000 patients were undergoing hemodialysis in the United States. Dialysis nonadherence rates range from 8.5% to 86%. Dialysis therapy treatment nonadherence, including treatment, medication, fluid, and diet nonadherence, significantly increases the risk of morbidity and mortality. The purpose of this paper is to systematically review randomized-controlled trial intervention studies designed to increase treatment, medication, fluid, and diet adherence in adult hemodialysis patients. A search of Cumulative Index of Nursing and Allied Health Literature (CINAHL) (1982 to May 2008), MEDLINE (1950 to May 2008), PsycINFO (1806 to May 2008), and all Evidence-Based Medicine (EBM) Reviews (Cochran DSR, ACP Journal Club, DARE, and CCTR) was conducted to identify randomized-controlled studies that tested the efficacy of interventions to improve adherence in adult hemodialysis patients. Eight randomized-controlled trials met criteria for inclusion. Six of the 8 studies found statistically significant improvement in adherence with the intervention. Of these 6 intervention studies, all studies had a cognitive component, with 3 studies utilizing cognitive/behavioral intervention strategies. Based on this systematic review, interventions utilizing a cognitive or cognitive/behavioral component appear to show the most promise for future study.

Mills EJ, Nachega J, Lester R, Thorlund K, Ioannidis J, Linnemayr S, et al. Adherence interventions to improve adherence to antiretroviral therapy in low income settings: An individual patient data network meta-analysis. Value Health 2013;16 (7):A361.

Abstract: Objectives: To determine the comparative effectiveness of different interventions for improving antiretroviral medication adherence in low-income settings. Methods: We obtained individual patient data from all randomized trials that have evaluated an adherence intervention to promote antiretroviral adherence within low-income countries. We created a treatment network of the differing interventions by pooling the individual patient data from comparable treatments and comparing them across the individual interventions using a Bayesian network meta-analysis approach. Outcomes included self-reported adherence and viral suppression. Results: We obtained data on 11 randomized,

involving 5432 patients. Interventions included daily and weekly text messaging, calendars, peer supporters, alarms, counseling, and basic clinical care. For self-reported adherence, we found compelling evidence for the role of weekly text messages (Odds ratio [OR] 1.57, 95% Confidence Intervals [CI] 1.22-2.02), counseling (OR 1.43, 95% CI, 1.06-1.94), and peer supporters (OR 1.72, 95% CI, 1.28-2.29). We found no compelling evidence for daily text messaging, alarms, calendars, or unsupported clinical care. Results were similar when using viral suppression as an outcome, although not all trials reported viral outcomes. Treatment supporters (OR 1.36, 95% CI, 1.02-1.82) and weekly text messages (OR, 1.56, 95% CI, 1.01-2.39) were superior to basic clinical care. Conclusions: Using individual patient data allowed us to increase precision to determine what interventions appear to work. Several common recommendations for improving adherence are unsupported by the available evidence. These findings should influence guidance documents on improving antiretroviral adherence in poor settings.

Molloy GJ, O'Carroll RE, Witham MD, McMurdo MET. Interventions to Enhance Adherence to Medications in Patients With Heart Failure A Systematic Review. Circulation-Heart Failure 2012;5(1):126-133.
Abstract: Doesn't exist – free full text online: http://circheartfailure.ahajournals.org/content/5/1/126

Moullec G, Gour-Provencal G, Bacon SL, Campbell TS, Lavoie KL. Efficacy of interventions to improve adherence to inhaled corticosteroids in adult asthmatics: Impact of using components of the chronic care model. Respir Med 2012;106(9):1211-1225.
Abstract: Background: Adherence to inhaled corticosteroids (ICS) remains poor among asthmatics, yet little is known about the efficacy of interventions to improve adherence. Implementing the Chronic Care Model (CCM) components among patients with respiratory disorders has been associated with an improvement in outcomes, yet little is known about its effects on ICS adherence in asthmatics. Objective: We conducted a systematic review to assess the efficacy of interventions to improve ICS adherence among adult-asthmatics, and whether the use of CCM components (i.e., teaching self-management skills, providing decision support, delivery system design, and clinical information systems) resulted in greater ICS adherence. Methods: All English language articles testing the efficacy of an intervention including ICS medication on outcome from MEDLINE and PsychINFO databases through Aug-2010 were reviewed. Interventions were categorized based on the inclusion of CCM components. We standardized treatment effects to obtain effect-size's (ES's) and we combined the ES's of studies according to the number of CCM components included in their interventions. Results: Eighteen studies met inclusion criteria. Inclusion of a greater number of CCM components within interventions was associated with stronger effects on ICS adherence outcomes, with interventions featuring one, two, and four CCM components having medium (ES = 0.29; 95%CI, 0.16-0.42), large (0.53; 0.40-0.66), and very-large (0.83; 0.69-0.98) effects respectively. Conclusions: Findings provide support for using the CCM as a framework for the design and implementation of interventions to improve adherence among adult-asthmatics.

Schedlbauer A, Davies P, Fahey T. Interventions to improve adherence to lipid lowering medication. Cochrane Database of Systematic Reviews 2010 (3).
Abstract: Background Lipid lowering drugs are still widely underused, despite compelling evidence about their effectiveness in the treatment and prevention of cardiovascular disease. Poor patient adherence to a medication regimen is a major factor in the lack of success in treating hyperlipidaemia. In this updated review we focus on interventions which encourage patients at risk of heart disease or stroke to take lipid lowering medication regularly. Objectives To assess the effects of interventions aimed at improved adherence to lipid lowering drugs, focusing on measures of adherence and clinical outcomes. Search strategy We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2008, Issue 1), MEDLINE, EMBASE, PsycINFO and CINAHL (March 2008). No language restrictions were applied. Selection criteria Randomised controlled trials of adherence-enhancing interventions for lipid lowering medication in adults for both primary and secondary prevention of cardiovascular disease in an ambulatory setting looking at adherence, serum lipid levels, adverse effects and health outcomes. Studies were selected independently by two review authors. Data collection and analysis Data were extracted and assessed by two review authors following criteria outlined by the Cochrane Handbook for Systematic Reviews of Interventions. Main results Three additional studies were found in the update and, in total, 11 studies were included in this review. The studies included interventions that caused a change in adherence ranging from -3% to 25% (decrease in adherence by 3% to increase in adherence by 25%). Patient reenforcement and reminding was the most promising category of interventions, investigated in six trials of which four showed improved adherent behaviour of

statistical significance (absolute increase: 24%, 9%, 8% and 6%). Other interventions associated with increased adherence were simplification of the drug regimen (absolute increase 11%) and patient information and education (absolute increase 13%). The methodological and analytical quality of some studies was low and results have to be considered with caution. Authors' conclusions At this stage, reminding patients seems the most promising intervention to increase adherence to lipid lowering drugs. The lack of a gold standard method of measuring adherence is one major barrier in adherence research. More reliable data might be achieved by newer methods of measurement, more consistency in adherence assessment and longer duration of follow up. More recent studies have started using more reliable methods for data collection but follow-up periods remain too short. Increased patient-centredness with emphasis on the patient's perspective and shared decision-making might lead to more conclusive answers when searching for tools to encourage patients to take lipid lowering medication.

Suwankeeree W, Picheansathian W. Strategies to promote adherence to treatment by pulmonary tuberculosis patients: a systematic review. International journal of evidence-based healthcare 2014;12(1):3-16.

Abstract: OBJECTIVE: The objective of this study is to review and synthesise the best available research evidence that investigates the effectiveness of strategies to promote adherence to treatment by patients with newly diagnosed pulmonary tuberculosis (TB). METHODS: The search sought to find published and unpublished studies. The search covered articles published from 1990 to 2010 in English and Thai. The database search included Cumulative Index to Nursing and Allied Health Literature (CINAHL), EMBASE, Cochrane Library, PubMed, Science Direct, Current Content Connect, Thai Nursing Research Database, Thai thesis database, Digital Library of Thailand Research Fund, Research of National Research Council of Thailand and Database of Office of Higher Education Commission. Studies were additionally identified from reference lists of all studies retrieved. Eligible studies were randomised controlled trials that explored different strategies to promote adherence to TB treatment of patients with newly diagnosed pulmonary TB and also included quasiexperimental studies. Two of the investigators independently assessed the studies and then extracted and summarised data from eligible studies. Extracted data were entered into Review Manager software and analysed. RESULTS: A total of 7972 newly diagnosed pulmonary TB patients participated in 10 randomised controlled trials and eight quasiexperimental studies. The studies reported on the effectiveness of a number of specific interventions to improve adherence to TB treatment among newly diagnosed pulmonary TB patients. These interventions included directly observed treatment (DOT) coupled with alternative patient supervision options, case management with DOT, short-course directly observed treatment, the intensive triad-model programme and an intervention package aimed at improved counselling and communication, decentralisation of treatment, patient choice of a DOT supporter and reinforcement of supervision activities. CONCLUSION: This review found evidence of beneficial effects from the DOT with regard to the medication adherence among TB patients in terms of cure rate and success rate. However, no beneficial effect was found from DOT intervention with increasing completion rate. In addition, the combined interventions to improve adherence to tuberculosis treatment included case management with directly observed treatment short-course program, the intensive triad-model programme and intervention package. These interventions should be implemented by healthcare providers and tailored to local contexts and circumstances, wherever appropriate.

van Servellen G, Heise BA, Ellis R. Factors associated with antidepressant medication adherence and adherence-enhancement programmes: a systematic literature review. Mental health in family medicine 2011;8(4):255-271.

Abstract: Medication adherence is critical to the efficacy of available treatment for depression in primary care settings. This review identifies factors associated with adherence and what is known about the effectiveness of adherence-enhancement programmes. A comprehensive systematic review of English language publications from January 2002 to October 2011 was conducted using the following databases: PUBMED/MEDLINE, PsycINFO and the Cochrane database. Twenty-one studies met the inclusion criteria for adherence-enhancement evaluations. Eleven of the studies evaluated demonstrated significantly positive effects on adherence; the remaining 10 reported mixed or no effects. Similar to previous literature reviews, factors shown to be associated with adherence were multifactorial and in this analysis were grouped as patient, condition and comorbidities, therapy or treatment, patient-provider relationship and healthcare system level. Adherence improved most notably in studies that included sustainable system and patient-targeted changes. Evaluating adherence-enhancement interventions is key to

promoting successful approaches; however, a number of gaps exist between intervention and implementation: (1) the cost in resources and time to implement and sustain these programmes is unknown, (2) specific details about which subgroups of patients are best helped with such programmes is not clear, and (3) what specific processes or content are critical to programme success is still to be identified. There are sufficient data supporting the substantial need for planning and implementing adherence interventions despite reported mixed results. Primary care providers are often positioned to impact patients' adherence; however, practice constraints can limit their implementation.

Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RCM, et al. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. Ann Intern Med 2012;157(11):785-795.

Abstract: BACKGROUND: Suboptimum medication adherence is common in the United States and leads to serious negative health consequences but may respond to intervention. PURPOSE: To assess the comparative effectiveness of patient, provider, systems, and policy interventions that aim to improve medication adherence for chronic health conditions in the United States. DATA SOURCES: Eligible peer-reviewed publications from MEDLINE and the Cochrane Library indexed through 4 June 2012 and additional studies from reference lists and technical experts. STUDY SELECTION: Randomized, controlled trials of patient, provider, or systems interventions to improve adherence to long-term medications and nonrandomized studies of policy interventions to improve medication adherence. DATA EXTRACTION: Two investigators independently selected, extracted data from, and rated the risk of bias of relevant studies. DATA SYNTHESIS: The evidence was synthesized separately for each clinical condition; within each condition, the type of intervention was synthesized. Two reviewers graded the strength of evidence by using established criteria. From 4124 eligible abstracts, 62 trials of patient-, provider-, or systems-level interventions evaluated 18 types of interventions; another 4 observational studies and 1 trial of policy interventions evaluated the effect of reduced medication copayments or improved prescription drug coverage. Clinical conditions amenable to multiple approaches to improving adherence include hypertension, heart failure, depression, and asthma. Interventions that improve adherence across multiple clinical conditions include policy interventions to reduce copayments or improve prescription drug coverage, systems interventions to offer case management, and patient-level educational interventions with behavioral support. LIMITATIONS: Studies were limited to adults with chronic conditions (excluding HIV, AIDS, severe mental illness, and substance abuse) in the United States. Clinical and methodological heterogeneity hindered quantitative data pooling. CONCLUSION: Reduced out-of-pocket expenses, case management, and patient education with behavioral support all improved medication adherence for more than 1 condition. Evidence is limited on whether these approaches are broadly applicable or affect longterm medication adherence and health outcomes. PRIMARY FUNDING SOURCE: Agency for Healthcare Research and Quality.

Waterman H, Evans Jennifer R, Gray Trish A, Henson D, Harper R. Interventions for improving adherence to ocular hypotensive therapy. Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd; 2013.

Abstract: Background: Poor adherence to therapy is a significant healthcare issue, particularly in patients with chronic disease such as open-angle glaucoma. Treatment failure may necessitate unwarranted changes of medications, increased healthcare expenditure and risk to the patient if surgical intervention is required. Simplifying eye drop regimes, providing adequate information, teaching drop instillation technique and ongoing support according to the patient need may have a positive effect on improving adherence.Objectives: To summarise the effects of interventions for improving adherence to ocular hypotensive therapy in people with ocular hypertension (OHT) or glaucoma .Search methods: We searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library 2012, Issue 6), MEDLINE (June 1946 to June 2012), EMBASE (June 1980 to June 2012), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (June 1937 to June 2012), PsycINFO (1806 to June 2012), PsycEXTRA (1908 to June 2012), Web of Science (1970 to June 2012), ZETOC (1993 to June 2012), OpenGrey (System for Information on Grey Literature in Europe) (www.opengrey.eu/), the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We did not use any date or language restrictions in the electronic searches for trials. The electronic databases were last searched on 26 June 2012. We did not search the National Research Register (NNR) as this resource has now been now archived. We contacted pharmaceutical manufacturers to request unpublished data and searched conference proceedings for the Association for Research

in Vision and Ophthalmology (ARVO), and the Annual Congress for the Royal College of Ophthalmologists (RCO).Selection criteria: We included randomised controlled trials (RCTs) and quasi-RCTs that compared interventions to improve adherence to ocular hypotensive therapy for patients with OHT or glaucoma.Data collection and analysis: At least two authors independently assessed the search results for eligibility and extracted data for included trials onto specifically designed forms. We did not pool data due to clinical and methodological heterogeneity. Main results: Sixteen trials (1565 participants) met the inclusion criteria. Seven studies investigated some form of patient education. In six of these studies this education was combined with other behavioural change interventions including tailoring daily routines to promote adherence to eye drops. Eight studies compared different drug regimens (one of these trials also compared open and masked monitoring) and one study investigated a reminder device. The studies were of variable quality and some were at considerable risk of bias; in general, the length of follow-up was short at less than six months with only two studies following up to 12 months. Different interventions and outcomes were reported and so it was not possible to produce an overall estimate of effect. There was some evidence from three studies that education combined with personalised interventions, that is, more complex interventions, improved adherence to ocular hypotensive therapy. There was less information on other outcomes such as persistence and intraocular pressure, and no information on visual field defects, quality of life and cost. There was weak evidence as to whether people on simpler drug regimens were more likely to adhere and persist with their ocular hypotensive therapy. A particular problem was the interpretation of cross-over studies, which in general were not reported correctly. One study investigated a reminder device and monitoring but the study was small and inconclusive. Authors' conclusions: Although complex interventions consisting of patient education combined with personalised behavioural change interventions, including tailoring daily routines to promote adherence to eye drops, may improve adherence to glaucoma medication, overa l there is insufficient evidence to recommend a particular intervention. The interventions varied between studies and none of the included studies reported on the cost of the intervention. Simplified drug regimens also could be of benefit but again the current published studies do not provide conclusive evidence. Future studies should follow up for at least one year, and could benefit from standardised outcomes.

Weiand D, Thoulass J, Smith WCS. Assessing and improving adherence with multidrug therapy. Lepr Rev 2012;83(3):282-291.

Abstract: Introduction: Adherence with multidrug therapy (MDT) in the treatment of leprosy is important to minimise the risk of relapse and avoid the emergence of drug resistance. Adherence is defined as the extent to which the patient's behaviour matches recommendations from the prescriber. This paper reviews the methods for assessing adherence with MDT in leprosy, and community approaches to improving adherence based on evidence from the treatment of tuberculosis (TB) and HIV, as well as leprosy. Methods: To identify and summarise the available literature regarding the assessment of treatment regularity in leprosy, a literature search of MEDLINE was conducted using the following search terms: 'leprosy' AND ('adherence' OR 'compliance' OR 'concordance'). To identify evidence for interventions that have involved community members in HIV, TB or leprosy adherence support, a literature search was conducted using the key terms and medical subject headings 'treatment or adherence' 'community', 'HIV, TB or Leprosy' and low and middle income countries' combined using Boolean operators. Results: Leprosy programmes routinely use defaulting and treatment completion as proxy measures of adherence as recommended by the WHO global strategy. However, a number of other methods have been used to assess adherence including questionnaires, pill counts, as well as direct measures based on testing urine for the presence of dapsone. Direct methods were extensively used during the dapsone mono-therapy era but there is little evidence of their use in MDT. Use of multiple methods of assessing adherence improves the accuracy and reliability of the results. Community activities in TB and HIV such as variants of treatment observation, and/or wider programmes of counselling or direct support to the patient or their family or to increase community or social support were shown to improve treatment outcomes. Outcomes evaluated included treatment default and completion, clinical indicators, and adherence (pill-count, self report). Conclusions: Adherence is very important in leprosy and regular assessment of medication adherence together with constructive feedback and counselling of patients is likely to be beneficial. Leprosy programme can learn from adherence support interventions developed by both TB and HIV programmes.

White HJ, Bettiol SS, Perera R, Roberts NW, Javaid MK, Farmer AJ. A systematic review assessing the effectiveness of interventions to improve persistence with anti-resorptive therapy in women at high risk of clinical fracture. Fam Pract 2010;27(6):593-603.

Abstract: Objective. To identify randomized controlled trials (RCTs) evaluating interventions intended to improve persistence with anti-resorptive therapy for treating women with osteoporosis or osteopenia. The design of the study is a systematic review and meta-analysis of RCTs. Methods. Included trials were those reporting interventions to improve persistence with or adherence to anti-resorptive treatment compared to a control medication or usual care. A search of MEDLINE, EMBASE, CINAHL and the Cochrane Library was supplemented by review of cited literature. Reports were reviewed and data pooled where appropriate. The primary outcome was duration of persistence with medication. Results. Six trials met inclusion criteria, including four reporting persistence as an outcome measure indicating a relative reduction in non-persistence of 22% (pooled relative risk: 0.78, 95% confidence interval 0.65-0.95) for active compared to control interventions. Heterogeneity between the trial effects was present but not significant (I(2) = 47%, P = 0.11). Interventions were varied in design, and some measurements of adherence were subject to self-report bias. Two trials included the majority of participants (3386/3497), accounting for > 90% of the weight in the pooled estimate. Conclusions. Trials to date suggest potential for improving persistence with medication taking thus improving treatment outcomes and reducing fracture risk. More precise measurement of medication taking and promoting fidelity to a precisely defined intervention protocol may lead to better assessment of impact on clinically important outcomes.

Williams JLS, Walker RJ, Smalls BL, Campbell JA, Egede LE. Effective interventions to improve medication adherence in Type 2 diabetes: A systematic review. Diabetes Management 2014;4(1):29-48.

Abstract: Aim: Medication adherence is associated with improved outcomes in diabetes. Interventions have been established to help improve medication adherence; however, the most effective interventions in patients with Type 2 diabetes remain unclear. The goal of this study was to distinguish whether interventions were effective and identify areas for future research. Methods: Medline was searched for articles published between January 2000 and May 2013, and a reproducible strategy was used. Study eligibility criteria included interventions measuring medication adherence in adults with Type 2 diabetes. Results: Twenty seven studies met the inclusion criteria and 13 showed a statistically significant change in medication adherence. Conclusion: Heterogeneity of the study designs and measures of adherence made it difficult to identify effective interventions that improved medication adherence. Additionally, medication adherence may not be solely responsible for achieving glycemic control. Researchers must emphasize tailored interventions that optimize management and improve outcomes, and examine the need for clear indicators of medication adherence.

Zomahoun HTV, Guenette L, Moisan J. Interventions that improve adherence to oral antidiabetic in adults with type 2 diabetes: A systematic review. J Popul Ther Clin Pharmacol 2012;19 (2):e135.

Abstract: Background: Poor adherence to drug treatment is a concern, particularly in chronic conditions including diabetes. Few interventions to improve adherence have been proven effective and little is known on the characteristics of effective interventions. Objectives: To evaluate the quality of studies on intervention aiming at improving adherence to oral antidiabetic drugs treatment (OADT) in adults with type 2 diabetes (T2DM) and to describe the characteristics of interventions that are most likely to succeed. Methods: We carried out a systematic review using PubMed, Embase and the Cochrane Library. All databases were searched from their start date until October 2011. Studies were included if at least one component of the intervention aimed to improve adherence to OADT in adults with T2DM. Quality of studies (poor, medium or good) was evaluated using nine criteria recognized as essential in the report or planning of intervention studies. Characteristics of studies with at least medium overall quality and for which interventions had a positive effect on adherence were described. Results: Among the eight studies included five had at least a medium overall quality score and two had a positive effect on adherence. Characteristics of effective interventions were: the use of socio-ecological theory; the use of behavioral determinants as empowerment, self-efficacy and barriers to medication; specific behavior change techniques. Interventions that were effective were delivered by health educators and mostly via phone calls. Conclusion: The characteristics of identified effective interventions could inform in the planning of new interventions to improve adherence to OADT.