Ikke-medikamentelle tiltak for å redusere risiko for hjerte- og karsykdommer: en oppsummering av systematiske oversikter

Rapport fra Kunnskapssenteret nr 19–2008

Kunnskapsoppsummering

kunnskapssenteret

Bakgrunn: Kunnskapssenteret fikk i oppgave av Sosial- og helsedirektoratet å utføre en kunnskapsoppsummering av ikke-medikamentelle tiltak for å redusere risiko for hjerte- og karsykdommer. Vi ble bedt om å kort omtale kunnskapsgrunnlaget med hensyn på effekter av ikke-medikamentell forebygging, både individrettede tiltak og tiltak rettet mot befolkningen. **Metode:** Vi søkte etter systematiske oversikter i databaser i Cochrane Library om effektene av ikke-medikamentelle tiltak for å redusere risiko for hjerte- og karsykdommer, samt medikamentelle tiltak for røykeslutt, vektreduksjon og forebygging av diabetes. To personer leste uavhengig av hverandre alle unike titler og sammendrag som vi identifiserte i litteratursøket og vurderte disse i forhold til inklusjonskriteriene. Tiltakene ble sortert i 1) Tiltak som synes å virke, 2) Tiltak som synes å ikke virke og 3) Ukjent effekt. **Resultat:** Vi identifiserte 81 oversikter fra Cochrane Database of Systematic Reviews, og 159 potensielt relevante oversikter i DARE- og HTA-databasene. De 81 identifiserte Cochrane-oversiktene handlet om røykeslutt, fysisk aktivitet og vektreduksjon og diettråd for å redusere *(fortsetter på baksiden)*

Nasjonalt kunnskapssenter for helsetjenesten
Postboks 7004, St. Olavsplass
N-0130 Oslo
(+47) 23 25 50 00
www.kunnskapssenteret.no
Rapport: ISBN 978-82-8121-236-7 ISSN 1890-1298

nr 19–2008

kunnskapssenteret

(fortsettelsen fra forsiden) risiko for hjerte- og karsykdom. **Konklusjon:** Det er rom for ytterligere reduksjon i forekomst av hjerte- og karsykdommer ved i større grad å ta i bruk oppsummert kunnskap om effektene av ikke-medikamentelle tiltak for å påvirke risikofaktorene for hjerte- og karsykdommer. Det er fornuftig å satse på enkle og veldokumenterte tiltak som har positiv effekt på røykeslutt, fysisk aktivitet, overvekt og kosthold, framfor mer komplekse og mindre kostnadseffektive tiltak, eller tiltak som mangler dokumentasjon. Det er behov for mer kunnskap om effektene av tiltak for å redusere sosioøkonomiske forskjeller i risiko for og forekomst av hjerte- og karsykdommer. En rekke av oversiktene vurderte tiltak som viste seg å ha manglende eller usikker dokumentasjon. Det er derfor behov for flere gode studier av ikke-medikamentelle intervensjoner for å redusere risiko for hjerte- og karsykdommer.

Tittel Ikke-medikamentelle tiltak for å redusere risiko for hjerte- og karsykdommer: en oppsummering av systematiske oversikter.
Institusjon Nasjonalt kunnskapssenter for helsetjenesten
Ansvarlig John-Arne Røttingen, *direktør*
Forfattere Signe Flottorp, *forskningsleder (prosjektleder)*
Mohamed Guled Farah, *forsker*
Hanne Thürmer, *avdelingsdirektør*
Marit Johansen, *bibliotekar*
Atle Fretheim, *forskningsleder*
ISBN 978-82-8121-236-7
ISSN 1890-1298
Rapport nr 19 – 2008
Prosjektnr 206
Rapporttype Kunnskapsoppsummering
Antall sider 123 (med vedlegg)
Oppdragsgiver Sosial- og helsedirektoratet
Sitering Flottorp S, Farah MG, Thürmer H, Johansen M, Fretheim A. Ikke-medikamentelle tiltak for å redusere risiko for hjerte- og karsykdommer: en oppsummering av systematiske oversikter. Rapport Nr 33-2008. Oslo: Nasjonalt kunnskapssenter for helsetjenesten, 2008.

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. Senteret er formelt et forvaltningsorgan under Sosial- og helsedirektoratet, uten myndighetsfunksjoner. Kunnskapssenteret kan ikke instrueres i faglige spørsmål.

Nasjonalt kunnskapssenter for helsetjenesten
Oslo, november 2008

1-side oppsummering

- Flere tiltak for å støtte røykeslutt, økt fysisk aktivitet, vektreduksjon og fornuftig kosthold kan redusere risikofaktorer for hjerte- og karsykdommer. Ingen av tiltakene ser ut til å ha stor effekt, og det mangler dokumentasjon på effekter på sykelighet og dødelighet. En liten eller moderat effekt på risikofaktorer kan likevel være viktig, både for den enkelte, men særlig i et folkehelseperspektiv.
- En rekke tiltak kan bidra til at folk slutter å røyke: massemedia-tiltak rettet både mot ungdom og voksne, råd fra helsepersonell i primærhelsetjenesten og på sykehus, selvhjelpsprogrammer, gruppebehandling, telefonrådgiving, tiltak på arbeidsplassen, nikotinerstatning, bupropion og vareniklin.
- Massemedia-kampanjer rettet mot voksne etablerte røykere så ut til å ha samme effekt uavhengig av alder, kjønn, etnisitet og utdanning.
- Det er ikke mulig å trekke konklusjoner om effekter på røykeslutt av opplæring av helsepersonell, skolebaserte programmer, tiltak for å hindre salg til mindreårige, fysisk aktivitet og familiebaserte programmer.
- Rådgiving, veiledning, telefon- og annen støtte for å øke fysisk aktivitet har vist positive effekter på selvrapportert fysisk aktivitet, evne til å nå et forhåndsbestemt aktivitetsnivå og på hjerte- og lungefunksjon.
- Trening ved overvekt og ved type 2 diabetes gjør det lettere å gå ned i vekt, og reduserer risikofaktorer for hjerte- og karsykdom selv uten vektnedgang.
- Dietter med kalorirestriksjon for overvektige med høyt blodtrykk gir en beskjeden reduksjon i vekt og blodtrykk, og kan redusere behovet for legemidler.
- Ulike vektreduserende tiltak ved prediabetes gir redusert forekomst av diabetes.
- Diettråd, råd om redusert eller modifisert fettinntak og redusert saltinntak kan ha en liten, men viktig effekt på risikofaktorer for hjerte- og karsykdom.
- Effektene av diettråd ved diabetes og familiær hyperkolesterolemi er ukjent.
- Velorganisert oppfølging av blodtrykkspasienter gir bedre blodtrykkskontroll.
- Vi har ikke vurdert kostnadseffektiviteten av tiltakene. Vi har heller ikke vurdert i hvilken grad tiltakene kan eller bør gjennomføres i vanlig praksis.
- Vi trenger mer kunnskap om effekt av tiltak for å redusere sosioøkonomiske forskjeller i risiko for og forekomst av hjerte- og karsykdommer.
- Det er mangelfull dokumentasjon for flere av tiltakene som er vurdert. Vi trenger gode studier av ikke-medikamentelle tiltak for å forebygge hjerte- og karsykdom, med lengre oppfølgingstid og med måling av sykelighet og dødelighet.

Sammendrag

BAKGRUNN

Sosial- og helsedirektoratet ga i sitt tildelningsbrev av 21.04.2004 Nasjonalt kunnskapssenter for helsetjenesten i oppgave å utføre en "Metodevurdering knyttet til nasjonale retningslinjer for medikamentell forebygging av hjerte- og karsykdommer". Det siste av tre punkter i bestillingen var:

"Nasjonalt kunnskapssenter for helsetjenesten bes om å kort omtale kunnskapsgrunnlaget med hensyn på effekter av ikke-medikamentell forebygging. Både individrettede tiltak og tiltak rettet mot befolkningen skal omtales."

I den foreliggende rapporten oppsummerer vi Cochrane-oversikter om effektene av ikke-medikamentelle tiltak for å redusere risiko for hjerte- og karsykdommer, samt medikamentelle tiltak for røykeslutt, vektreduksjon og forebygging av diabetes. Til forskjell fra hovedrapporten avgrenser vi oss ikke til utfallsmål som sykdom og dødelighet.

METODE

Vi søkte etter systematiske oversikter i følgende databaser i The Cochrane Library:

- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of Reviews of Effects (DARE)
- Health Technology Assessment Database (HTA)

Vi søkte etter systematiske oversikter som vurderte ikke-medikamentelle tiltak for primærforebygging av hjerte- og karsykdommer, som diett, fysisk aktivitet, vektkontroll og vektreduksjon, røykeslutt, komplementære og alternative tiltak hos personer uten diagnostisert hjerte- og karsykdom, samt oversikter over medikamentelle tiltak for å støtte vektreduksjon og røykeslutt og forebygge utvikling av diabetes. Relevante utfall var dødelighet og sykelighet og viktige utfall ved livsstilstiltak som f. eks. røykeslutt, økt fysisk aktivitet, vektreduksjon og endring av risikofaktorer. To personer leste uavhengig av hverandre alle unike titler og sammendrag som vi identifiserte i litteratursøket og vurderte disse i forhold til inklusjonskriteriene.

Vi gjorde en enkel oppsummering av de inkluderte Cochrane-oversiktene. Vi baserte oss på informasjonen i sammendragene i oversiktene og forfatternes konklusjoner.

To prosjektmedarbeidere sorterte uavhengig av hverandre effekten av tiltakene i:
- Tiltak som synes å virke
- Tiltak som synes å ikke virke
- Ukjent effekt

RESULTAT

- Vi identifiserte 81 oversikter fra Cochrane Database of Systematic Reviews, og 159 potensielt relevante oversikter i DARE- og HTA-databasene.

Vi har listet alle identifiserte oversikter i vedlegg, men vi har ikke analysert oversiktene fra HTA og DARE databasene nærmere.

De 81 identifiserte Cochrane-oversiktene handlet om (antall oversikter i parentes):
- røykeslutt (42)
- fysisk aktivitet (6)
- vektreduksjon og diettråd for å redusere risiko for hjerte- og karsykdom (27)
- annet (6)

Hovedkonklusjonene basert på disse oversiktene er:
- En rekke tiltak for røykeslutt, økt fysisk aktivitet, vektreduksjon og fornuftig kosthold kan redusere risikofaktorer for hjerte- og karsykdommer. Ingen av tiltakene ser ut til å ha stor effekt. Det mangler dokumentasjon på effekter på sykelighet og dødelighet. En liten eller moderat effekt på risikofaktorer kan likevel være viktig, både for den enkelte, men særlig i et folkehelseperspektiv.
- En rekke tiltak kan bidra til at folk slutter å røyke: massemedia-tiltak rettet både mot ungdom og voksne, råd fra helsepersonell i primærhelsetjenesten og på sykehus, selvhjelpsprogrammer, gruppebehandling, telefonrådgiving, tiltak på arbeidsplassen, nikotinerstatning, bupropion og vareniklin.
- Massemedia-kampanjer rettet mot voksne etablerte røykere så ut til å ha samme effekt uavhengig av alder, kjønn, etnisitet og utdanning.
- Måling av karbonmonoksyd, spirometri og andre biomedisinske målinger for å motivere til røykeslutt, og hypnose, synes ikke å være til noen hjelp.
- Det er ikke mulig å trekke konklusjoner om effekter på røykeslutt av opplæring av helsepersonell, skolebaserte programmer, tiltak for å hindre salg til mindreårige, fysisk aktivitet og familiebaserte programmer.
- Rådgiving, veiledning, telefon- og annen støtte for å øke fysisk aktivitet har vist positive effekter på selvrapportert fysisk aktivitet, evne til å nå et forhåndsbestemt aktivitetsnivå og på hjerte- og lungefunksjon.

- Trening ved overvekt og ved type 2 diabetes gjør det lettere å gå ned i vekt, og reduserer risikofaktorer for hjerte- og karsykdom selv uten vektnedgang.
- Dietter med kalorirestriksjon for overvektige med høyt blodtrykk gir en beskjeden reduksjon i vekt og blodtrykk, og kan redusere behovet for legemidler.
- Ulike vektreduserende tiltak ved prediabetes gir redusert forekomst av diabetes.
- Diettråd, råd om redusert eller modifisert fettinntak og redusert saltinntak kan ha en liten, men viktig effekt på risikofaktorer for hjerte- og karsykdom.
- Velorganisert oppfølging av blodtrykkspasienter med aktiv opptrapping av medikamentell behandling gir bedre blodtrykkskontroll, og viste også lavere mortalitet i en stor randomisert kontrollert studie.
- For en rekke av de undersøkte tiltakene var effekten ukjent eller usikker på grunn av manglende eller ikke konklusiv dokumentasjon.

DISKUSJON

Det er dokumentasjon for at en rekke tiltak kan ha positiv effekt på livsstilsfaktorer som er knyttet til risiko for hjerte- og karsykdommer, som røyking, fysisk aktivitet, overvekt og kosthold. Ingen av de vurderte tiltakene ser ut til å ha stor effekt ut fra de oversiktene vi har inkludert. En liten, men varig gunstig endring av livsstils- og risikofaktorer for hjerte- og karsykdom vil imidlertid kunne ha en viktig effekt både for enkeltindivider og i et folkehelseperspektiv.

Vi har ikke vurdert kvaliteten av dokumentasjonen for utfallene. Vi har ikke vurdert kostnadseffektiviteten av tiltakene, og heller ikke i hvilken grad tiltakene kan eller bør gjennomføres i vanlig praksis.

KONKLUSJON

Det er rom for ytterligere reduksjon i forekomst av hjerte- og karsykdommer ved i større grad å ta i bruk oppsummert kunnskap om effektene av ikke-medikamentelle tiltak for å påvirke risikofaktorene for hjerte- og karsykdommer. Det er fornuftig å satse på enkle og veldokumenterte tiltak som har positiv effekt på røykeslutt, fysisk aktivitet, overvekt og kosthold, framfor mer komplekse og mindre kostnadseffektive tiltak, eller tiltak som mangler dokumentasjon.

Det er behov for mer kunnskap om effektene av tiltak for å redusere sosioøkonomiske forskjeller i risiko for og forekomst av hjerte- og karsykdommer.

En rekke av oversiktene vurderte tiltak som viste seg å ha manglende eller usikker dokumentasjon. Det er derfor behov for flere gode studier av ikke-medikamentelle intervensjoner for å redusere risiko for hjerte- og karsykdommer. Studiene bør være tilstrekkelig store med lang nok oppfølgingstid, og helst med måling av harde endepunkter som sykelighet og dødelighet av hjerte- og karsykdommer.

Key messages

Non-pharmacological interventions to reduce the risk for cardiovascular disease: a summary of systematic reviews

- Many interventions to quit smoking, increase physical activity, reduce weight and improve diet can reduce risk factors for cardiovascular disease. The interventions seem to produce only small effects, if any, and there is a lack of evidence regarding effects on morbidity and mortality. A small or moderate effect may be important, though, both for the individual but particularly at population level.
- Several interventions support smoking cessation: mass media campaigns targeted at young people and adults, advice from health professionals both in primary care and hospitals, self help programs, group therapy, telephone advice, interventions in the workplace, nicotine replacement, bupropion and varenicline.
- Mass media campaigns aimed at adult established smokers seemed to have similar effects regardless of age, gender, ethnicity or education.
- Biomedical risk assessments and hypnosis are unlikely to help smokers to quit.
- We can not draw conclusions on the effects on smoking rates of training of health professionals, school-based or family-based programs, acupuncture, physical activity, interventions for preventing tobacco sales to minors or relapse prevention.
- Physical activity interventions moderately improve self-reported physical activity and cardio-respiratory fitness, and help achieving a predetermined activity level.
- Exercise for overweight and type 2 diabetes supports weight reduction and reduces cardiovascular disease risk factors even if no weight is lost.
- Calorie restricted diets in overweight hypertensive persons can give modest weight loss and blood pressure decreases.
- Weight loss strategies in prediabetes may reduce weight and diabetes incidence.
- Dietary advice, advice to reduce or modify fat intake and reduce intake of salt may have a small, but important effect on cardiovascular risk factors.
- There are no high quality data on the efficacy of the dietary treatment of type 2 diabetes or familial hypercholesterolaemia.
- An organized system of regular review may reduce blood pressure.
- We have not assessed cost effectiveness of the interventions.
- We need more evidence on effects of interventions to reduce social inequalities in risk for and incidence of cardiovascular disease.
- We need evidence from studies of high quality and longer follow-up measuring morbidity and mortality, for several of the interventions that we have assessed.

Executive summary

Non-pharmacological interventions to reduce the risk for cardiovascular disease: a summary of systematic reviews

BACKGROUND

The Norwegian Directorate for Health asked the Norwegian Knowledge Centre for the Health Services to perform a health technology assessment related to the development of national guidelines for the pharmacological prevention of cardiovascular disease. The last of three issues in the request was:

”Norwegian Knowledge Centre for the Health Services is asked to briefly refer to the evidence regarding the effects of non-pharmacological prevention. Both individual interventions and intervention at the population level should be discussed.”

In this report we summarise Cochrane reviews on the effects of non-pharmacological interventions to reduce risk factors for cardiovascular diseases, together with pharmacological interventions to support smoking cessation, weight reduction and diabetes prevention. In contrast to the main report outcomes were not limited to morbidity and mortality.

METHODS

We searched for systematic reviews in these databases in the Cochrane Library:

- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of Reviews of Effects (DARE)
- Health Technology Assessment Database (HTA)

We searched for systematic reviews examining non-pharmacological interventions for primary prevention of cardiovascular diseases, as diet, physical activity, weight control and weight reduction, smoking cessation, complementary and alternative treatments in persons without diagnosed cardiovascular disease, and also Cochrane reviews of pharmacological interventions to support weight reduction, smoking cessation and diabetes prevention. Relevant outcomes were mortality and morbidity and important outcomes in life style interventions as quit rate, increased physical

activity, weight reduction, and reduction in level of risk factors. Two persons independently read all unique titles and abstracts identified in the literature search, and assessed them towards the inclusion criteria.

We made a simple summary of the included Cochrane reviews, mainly based on information in the abstracts in the summaries and the authors' conclusions.

Two persons independently assessed and sorted the effects of the interventions in:
- Interventions likely to be effective
- Interventions unlikely to be effective
- Interventions with unknown effect

RESULTS

- We identified 81 reviews from the Cochrane Database of Systematic Reviews, and 159 potentially relevant reviews in the DARE and HTA databases.

We have listed all identified reviews in the appendices, but we have not further analysed the reviews from DARE and the HTA databases.

The 81 Cochrane reviews dealt with (number of reviews in parenthesis):
- smoking cessation (42)
- physical activity (6)
- weight reduction and dietary advice to reduce the risk for cardiovascular disease (27)
- other interventions (6)

The main conclusions based on these reviews are:
- Many interventions to quit smoking, increase physical activity, reduce weight and improve diet can reduce risk factors for cardiovascular disease. The interventions seem to produce only small effects, if any, and there is a lack of evidence regarding effects on morbidity and mortality. A small or moderate effect may be important, though, both for the individual but particularly at population level.
- Several interventions support smoking cessation: mass media campaigns targeted at young people and adults, advice from health professionals both in primary care and hospitals, self help programs, group therapy, telephone advice, interventions in the workplace, nicotine replacement, bupropion and varenicline.
- Mass media campaigns aimed at adult established smokers seemed to have similar effects regardless of age, gender, ethnicity or education.
- Biomedical risk assessments and hypnosis are unlikely to help smokers to quit.
- We can not draw conclusions on the effects on smoking rates of training of health professionals, school-based or family-based programs, acupuncture, physical activity, interventions for preventing tobacco sales to minors or relapse prevention.

- Physical activity interventions moderately improve self-reported physical activity and cardio-respiratory fitness, and help achieving a predetermined activity level.
- Exercise for overweight and type 2 diabetes supports weight reduction and reduces cardiovascular disease risk factors even if no weight is lost.
- Calorie restricted diets in overweight hypertensive persons can give modest weight loss and blood pressure decreases.
- Weight loss strategies in prediabetes may reduce weight and diabetes incidence.
- Dietary advice, advice to reduce or modify fat intake and reduce intake of salt may have a small, but important effect on cardiovascular risk factors.
- An organized system of regular review may reduce blood pressure.
- We have not assessed cost effectiveness of the interventions.
- We need more evidence on effects of interventions to reduce social inequalities in risk for and incidence of cardiovascular disease.
- We need evidence from studies of high quality and longer follow-up measuring morbidity and mortality, for several of the interventions that we have assessed.

DISCUSSION

There is evidence that several interventions may have positive effects on lifestyle factors related to risk for cardiovascular diseases, as smoking, physical activity, overweight and diet. The interventions seem to have a small or moderate effect, if any. A small but lasting change in lifestyle and other risk factors may be important both at individual and at population health level.

We have not assessed the quality of the evidence for the outcomes. We have not assessed the cost-effectiveness of the interventions, and not the degree to which it is feasible or desirable to implement the interventions in daily practice.

CONCLUSION

The incidence of cardiovascular disease in Norway may be additionally reduced by using and acting upon evidence of effects of non pharmacological interventions to influence the risk factors for cardiovascular diseases. It seems sensible to implement simple interventions supported by high quality evidence for effect on smoking cessation, physical activity, overweight and diet, rather than complex and less cost-effective interventions, or interventions with unknown effects.

We need more evidence of the effects of interventions to reduce socioeconomic inequalities in risk for and incidence of cardiovascular diseases.

Several of the reviews examined interventions for which there were lacking or low quality evidence. We need more and better studies to assess the effects of non pharmacological interventions to prevent the risk for cardiovascular diseases. The studies

should be well designed, with sufficient sample sizes and long enough follow up, and preferably measuring cardiovascular morbidity and mortality.

Norwegian Knowledge Centre for the Health Services summarizes and disseminates evidence concerning the effect of treatments, methods, and interventions in health services, in addition to monitoring health service quality. Our goal is to support good decision making in order to provide patients in Norway with the best possible care. The Centre is organized under The Directorate for Health and Social Affairs, but is scientifically and professionally independent. The Centre has no authority to develop health policy or responsibility to implement policies.

Norwegian Knowledge Centre for the Health Services
PB 7004 St. Olavs plass
N-0130 Oslo, Norway
Telephone: +47 23 25 50 00
E-mail: post@kunnskapssenteret.no
Full report (pdf): www.kunnskapssenteret.no

Innhold

Forord

Sosial- og helsedirektoratet (nå Helsedirektoratet) ved avdeling for retningslinjer, prioritering og kvalitet utformer nasjonale retningslinjer for medikamentell primærforebygging av hjerte- og karsykdommer.

På oppdrag fra Sosial- og helsedirektoratet har Kunnskapssenteret i samarbeid med en utredningsgruppe av fageksperter gjennomført en medisinsk metodevurdering om tiltak for å forebygge hjerte- og karsykdommer, for å understøtte arbeidet med disse retningslinjene. Hovedrapporten omfatter i hovedsak behandling med legemidler, og har kun vurdert effekter på sykelighet og dødelighet (harde endepunkter). Kunnskapssenteret har også utarbeidet en helseøkonomisk vurdering av kostnadseffektiviteten av behandling med forskjellige legemidler.

I denne rapporten har vi oppsummert resultatene fra Cochrane-oversikter om ikke-medikamentelle tiltak for å redusere risiko for hjerte- og karsykdom, samt medikamentelle tiltak for å få folk til å slutte å røyke. Det er få slike studier som har rapportert effekter på sykelighet og dødelighet (harde endepunkter). Vi har oppsummert oversikter over studier som rapporterer andre utfall som er av interesse i arbeidet med å forebygge hjerte- og karsykdom. Vi har basert oss på forfatternes konklusjoner. Rapporten er utarbeidet av medarbeidere ved Kunnskapssenteret.

Interne fagfeller ved Kunnskapssenteret har vært Krystyna Hviding og Michael de Vibe. Tor-Erik Widerøe, Eivind Meland og Serena Tonstad har vært eksterne fagfeller.

Anne Karin Lindahl
Avdelingsdirektør

Signe Flottorp
Forskningsleder/prosjektleder

Problemstilling

På bestilling fra Sosial- og helsedirektoratet (nå Helsedirektoratet) har Kunnskapssenteret utarbeidet en systematisk kunnskapsoppsummering om effekter av tiltak for forebygging av hjerte- og karsykdom. I hovedrapporten ble både medikamentelle og ikke-medikamentelle tiltak vurdert, men avgrenset til effekter som gjaldt sykelighet og død "(”harde endepunkt”).

Slike effektmål mangler for en stor del av de ikke-medikamentelle tiltakene som er aktuelle å vurdere.

Det er derfor behov for også å oppsummere studier som rapporterer andre effekter av ikke-medikamentelle tiltak som kan være relevante med tanke på forebygging av hjerte- og karsykdom. Vi har også vurdert medikamentelle tiltak for å få folk til å slutte å røyke, gå ned i vekt og forebygge diabetes.

Innledning

BAKGRUNN OG MANDAT

Dødeligheten av hjerte- og karsykdommer har falt i flere tiår i Norge. I 1996 døde 324 av 100 000 innbyggere av hjerte- og karsykdommer, mens tallet var 211 per 100 000 i 2005. Det er en nedgang på 35 % over ti år, og 70 % av disse dødsfallene skjer nå etter 80 år (1;2). Hjerte- og karsykdommer er ved siden av kreft den viktigste dødsårsaken i Norge. Om lag 500 menn og 120 kvinner mellom 45 og 56 år dør av hjerteinfarkt og annen åresykdom i hjertet, og i denne aldersgruppen ser det ut til at nedgangen i dødelighet har stoppet opp (3).

Både medikamentelle og ikke-medikamentelle tiltak kan forebygge hjerte- og karsykdommer. Ikke-medikamentelle tiltak er viktige både på individnivå og i et folkehelseperspektiv.

Oppsummering av tilgjengelig forskningsbasert kunnskap er viktig for å kunne gi kunnskapsbaserte anbefalinger og prioritere rett mellom de ulike tiltakene.

Sosial- og helsedirektoratet (nå Helsedirektoratet) ga i sitt tildelningsbrev av 21.04.2004 Nasjonalt kunnskapssenter for helsetjenesten i oppgave å utføre en "Metodevurdering knyttet til nasjonale retningslinjer for medikamentell forebygging av hjerte- og karsykdommer". Begrunnelsen var:

"Retningslinjer på området er prioritert på bakgrunn av at det finnes flere retningslinjer for medikamentell forebygging, som til dels gir ulike anbefalinger."

Begrunnelsen ble utdypet i brev av 13.07.2004 med at det er stor variasjon i praksis og uenighet i fagmiljøene. Fra samfunnets side er interessen knyttet til de store kostnadene og nytten/ helsegevinsten som slik behandling gir. Sosial- og helsedirektoratet kom med følgende bestilling:

"Nasjonalt kunnskapssenter for helsetjenesten bes om å:

- gjøre rede for kunnskapsgrunnlaget med hensyn på effekter av medikamentell primærforebygging av hjerte- og karsykdommer, med særlig vekt på interven-

sjonsgrenser. Begrepet primærforebygging er reservert for intervensjoner rettet mot personer med forhøyet risiko for hjerte- og karsykdommer uten etablert sykdom. Sekundærforebyggende tiltak, rettet mot pasienter med etablert sykdom (for eksempel gjennomgått hjerteinfarkt) inngår ikke. Medikamentelle intervensjoner inkluderer alle medikamenter som kan redusere risiko, som for eksempel alle typer anti-hypertensiva, statiner og acetylsalisylsyre.

- gjøre rede for kunnskapsgrunnlaget for hvilke medikamenter som bør anbefales for medikamentell forebygging av hjerte- og karsykdom.
- kort omtale kunnskapsgrunnlaget med hensyn på effekter av ikke-medikamentell forebygging. Både individrettede tiltak og tiltak rettet mot befolkningen skal omtales."

Kunnskapssenteret har, i samarbeid med en utredningsgruppe av fageksperter, utarbeidet en rapport som besvarer de to første disse problemstillingene (4), og en helseøkonomisk vurdering av kostnadseffektiviteten av behandling med forskjellige legemidler (5).

I tillegg har vi utarbeidet denne rapporten hvor vi gjør rede for resultater fra eksisterende systematiske oversikter om effektene av ikke-medikamentelle tiltak, samt medikamentelle tiltak for røykeslutt, vektreduksjon og forebygging av type 2 diabetes. Til forskjell fra hovedrapporten avgrenser vi oss ikke til utfallsmål som sykdom og dødelighet, men har også inkludert systematiske oversikter som rapporterer for eksempel hvor mange som slutter å røyke, går ned i vekt, begynner å trimme osv.

Fordi feltet er omfattende, og fordi oppgaven kun var å gi en mer begrenset omtale av kunnskapsgrunnlaget av ikke-medikamentelle tiltak, og fordi vi hadde begrensede ressurser, har vi gjort dette arbeidet mer summarisk. Vi har lagt vekt på å gjennomføre gode søk og identifisere relevante systematiske oversikter. Vi har ikke gjort en vurdering av oversiktenes kvalitet. Vi har presentert resultatene fra identifiserte Cochrane-oversikter slik de framgår av oversiktene, uten nærmere kritisk vurdering.

Denne rapporten ble gjort i sluttfasen av arbeidet med hovedrapporten. Arbeidet er utført av medarbeidere i Kunnskapssenteret, uten medvirkning av utredningsgruppens medlemmer. Utkastet til rapport er revidert på grunnlag av innspill fra interne og eksterne fagfeller.

Metode

LITTERATURSØK

Vi søkte etter systematiske oversikter i følgende databaser i The Cochrane Library Issue 4 2007:

- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of Reviews of Effects (DARE)
- Health Technology Assessment Database (HTA)

Prosjektmedarbeiderne planla søket i samarbeid med forskningsbibliotekar Marit Johansen som utførte samtlige søk. Søkestrategien er vist i vedlegg 1.

INKLUSJONSKRITERIER

Studiedesign:	Systematiske oversikter (med eksplisitt søkestrategi og klare kriterier for inklusjon og eksklusjon av studier).
Populasjon:	Personer uten diagnostisert hjerte- og karsykdom
Tiltak:	Ikke-medikamentelle tiltak for primærforebygging av hjerte- og karsykdommer, f. eks. diett, fysisk aktivitet, vektkontroll, røykeslutt, komplementære og alternative tiltak. Medikamentelle tiltak for røykeslutt.*
Utfall:	Total dødelighet (uansett årsak), kardiovaskulær dødelighet, akutt hjerteinfarkt, hjerneslag, angina pectoris, hjertesvikt, utvikling av diabetes, revaskularisering, kombinerte endepunkter. Dessuten viktige surrogatutfall ved livsstilstiltak som f. eks. røykeslutt, økt fysisk aktivitet, vektreduksjon, endring av risikofaktorer. Kostnadseffektivitet.
Språk:	Ingen restriksjoner.

* Etter forslag fra ekstern fagfelle inkluderte vi dessuten Cochrane-oversikter over medikamentelle tiltak for vektreduksjon og forebygging av type 2 diabetes, og vi gjennomførte et enkelt søk etter slike oversikter.

EKSKLUSJONSKRITERIER

Studiedesign:	Ikke systematiske oversikter, primærstudier.
Populasjon:	Personer med etablert hjerte- og karsykdom.
Tiltak:	Ordinære medikamentelle forebyggende tiltak.

ARTIKKELUTVELGELSE

To personer leste uavhengig av hverandre alle unike titler og sammendrag som vi identifiserte i litteratursøket og vurderte disse i forhold til inklusjons- og eksklusjonskriteriene. MGF leste alle, mens HT og SF leste halvparten hver. Vi løste uenighet ved konsensus, eventuelt etter diskusjon med tredje medarbeider. Vi har benyttet nyere versjoner av Cochrane-oversikter som har blitt oppdatert etter vårt søk. Inkluderte Cochrane-oversikter er listet i vedlegg 2, andre oversikter i vedlegg 3.

ANALYSER

Vi gjennomgikk titlene på de potensielt relevante systematiske oversiktene fra Database of Abstracts of Reviews of Effects og Health Technology Assessment Database, og utarbeidet en liste over hvilke temaer de handlet om. For øvrig har vi ikke analysert disse oversiktene nærmere, men kun listet dem i vedlegg 3.

Vi har oppsummert Cochrane-oversiktene basert på informasjonen i sammendragene og forfatternes konklusjoner, og supplert med tekst fra oversiktene ved behov. Vi leste ikke de inkluderte Cochrane-oversiktene i fulltekst, og vi gjorde ingen kvalitetsvurderinger av dem. I vedlegg 4 har vi beskrevet studiedesign, populasjon, intervensjon, utfall, hovedresultater og forfatternes konklusjoner for de inkluderte Cochrane-oversiktene, og i resultatkapitlet har vi redegjort for resultatene.

To prosjektmedarbeidere kategoriserte uavhengig av hverandre effekten av tiltakene for de viktigste sammenlikninger og utfallsmål i følgende kategorier:

- Tiltak som synes å virke (likely to be effective)
- Tiltak som synes å ikke virke (unlikely to be effective)
- Ukjent effekt (unknown effectiveness)

Det er flere grunner til at tiltak har ukjent effekt. Dokumentasjon kan være mangelfull fordi spørsmålet ikke er belyst i forskningen, eller fordi studiene ikke har hatt tilstrekkelig antall deltakere og lang nok varighet til å påvise en eventuell statistisk og klinisk signifikant effekt. Kvaliteten av dokumentasjonen kan være lav og resultatene fra ulike studier kan være inkonsistente slik at det ikke er forsvarlig å trekke sikre konklusjoner. I resultatkapitlet har vi forsøkt å gjøre rede for dette for hver enkelt av de intervensjonene som er kategorisert til å ha ukjent effekt.

Resultat

KUNNSKAPSGRUNNLAGET

Identifiserte systematiske oversikter

Vi fant 1820 unike titler i søket etter systematiske oversikter, herav 841 i Cochrane Database of Systematic Reviews (CDSR), 777 i Database of Abstracts of Reviews of Effects (DARE) og 202 Health Technology Assessment Database (HTA).

Vi identifiserte 80 relevante titler fra Cochrane Database of Systematic Reviews. Sju av disse var kun protokoller, og vi satt derfor igjen med 73 Cochrane-oversikter fra CDSR (vedlegg 2). Blant titler og sammendrag i DARE- og HTA-databasene i Cochrane Library identifiserte vi 159 potensielt relevante oversikter (vedlegg 3). Vi har ikke gjort noen nærmere analyse av oversiktene fra DARE- og HTA-databasene.

Etter forslag fra ekstern fagfelle valgte vi også å inkludere oversikter over medikamentelle tiltak for vektreduksjon og medikamentelle og ikke-medikamentelle tiltak for å forebygge utvikling av type 2 diabetes. I et enkelt søk i Cochrane Database of Systematic Reviews fant vi ytterligere åtte relevante oversikter som vi inkluderte.

Hvilke intervensjoner er studert?

En gjennomgang av titlene på oversiktene fra DARE og HTA-databasene viste at de handlet om (antall oversikter i parentes):

- røykeslutt (32)
- fysisk aktivitet (50)
- vektreduksjon og diettråd for å redusere risiko for hjerte- og karsykdom (59)
- annet (20)

Cochrane-oversiktene som vi identifiserte handlet om (antall oversikter i parentes):

- røykeslutt (42)
    - ikke-farmakologiske tiltak (32)
    - farmakologiske tiltak (10)
- fysisk aktivitet (6)
- vektreduksjon og diettråd for å redusere risiko for hjerte- og karsykdom (27)
- annet (6)

Førti av de inkluderte Cochrane-oversiktene konkluderte med at de vurderte tiltakene syntes å være effektive; det gjaldt 20 av oversiktene om røykeslutt, fire av oversiktene om fysisk aktivitet, 13 av oversiktene om vektreduksjon og diett og tre oversikter i kategorien "annen". Effekten var ukjent eller usikker for 29 av tiltakene som var undersøkt: 16 om røykeslutt, to om fysisk aktivitet, ti om vektreduksjon/diett og to om andre typer tiltak. Ti av oversiktene gjaldt tiltak som syntes å ikke være effektive: seks om røykeslutt, fire om vektreduksjon/diett og en "annen".

To medarbeidere valgte ut relevante titler uavhengig av hverandre, og vi vurderte uavhengig av hverandre hovedkonklusjonen i oversiktene, basert på de viktigste sammenlikningene og utfallene. Det var stort samsvar i våre vurderinger.

Hva slags deltakere er inkludert i Cochrane-oversiktene?

Oversiktene har omhandlet intervensjoner rettet mot personer uten etablert hjerte- og karsykdom, eventuelt har bare et mindretall av deltakerne hatt etablert sykdom. De fleste oversiktene har inkludert personer fra normal befolkning med ulik grad av risiko for hjerte- og karsykdommer. Noen oversikter inkluderte deltakere med spesielle risikofaktorer, som overvekt, økt risiko for type 2 diabetes, type 2 diabetes, hypertensjon og hyperkolesterolemi. Oversiktene over tiltak for røykeslutt har inkludert røykere uten spesielle diagnoser.

Vi gjør først rede for resultatene i forhold til hvilke tiltak som ble studert, uavhengig av målgruppe. Deretter gir vi en tabellarisk oversikt over effekten av intervensjoner som er rettet mot personer med spesielle risikofaktorer.

TILTAK FOR RØYKESLUTT

Vi fant til sammen 42 Cochrane-oversikter som omhandlet tiltak mot røyking og tobakksbruk, se oversikt i tabell 1.1. Vi valgte å se på både ikke-medikamentelle og medikamentelle tiltak, og fant henholdsvis 32 og ti oversikter. Tjue av oversiktene gjaldt tiltak som syntes å være effektive, seks oversikter gjaldt tiltak som syntes å være ineffektive, mens 16 oversikter konkluderte med at effekten var ukjent.

Tabell 1.1. *Tiltak for røykeslutt*

Tiltak for å få folk til å slutte å røyke	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Massemedia - voksne	x			Bala 2008 (6)
Reklame – ungdom	x [1]			Lovato 2003 (7)

[1] Negativ effekt: reklame for tobakk økte andelen unge som rapporterte at de røykte

Massemedia – ungdom	x			Sowden 1998 (8)
Råd fra lege	x			Lancaster 2004 (9)
Råd fra sykepleier	x			Rice 2008 (10)
Støtte til pas. innlagt i sykehus	x			Rigotti 2007 (11)
Råd fra farmasøyt	x			Sinclair 2004 (12)
Rådgiving av trenet rådgiver, ikke lege/sykepleier	x			Lancaster 2005 (13)
Selvhjelpsprogrammer	x			Lancaster 2005 (14)
Tiltak på arbeidsplassen	x			Moher 2005 (15)
Hindre røyk på offentlige steder	x			Serra 2000 (16)
Lokalsamfunnstiltak rettet mot ungdom	x			Sowden 2003 (17)
Gruppebehandling	x			Stead 2005 (18)
Telefonrådgiving	x			Stead 2006 (19)
Vareniklin	x			Cahill 2007 (20)
Clonidin	x			Gourlay 2004 (21)
Antidepressiver	x			Hughes 2007 (22)
Nikotinerstatning (tyggegummi, plaster, spray, tabletter)	x			Stead 2008 (23)
Finansielle tiltak rettet mot røyker eller helsepersonell	x			Kaper 2005 (24)
Hypnose		x		Abbot 1998 (25)
Biomedisinsk risikovurdering (CO, spirometri, genetisk testing)		x		Bize 2005 (26)
Konkurranser og insentiver		x		Cahill 2008 (27)
Sølvacetat		x		Lancaster 1997 (28)
Støtte til røykers partner (ektefelle, venn, kollega)		x		Park 2004 (29)
Lokalsamfunnstiltak – voksne		x		Secker-Walker 2002 (30)
Råd fra tannlege			x	Carr 2006 (31)
Opplæring av helsepersonell			x	Lancaster 2000 (32)
Opioid-antagonister			x	David 2006 (33)
Anxiolytika			x	Hughes 2000 (34)
Mecamylamin (en nikotinantagonist)			x	Lancaster 1998 (35)
Lobelin,			x	Stead 1997 (36)
Nicobrevine			x	Stead 2006 (37)
Programmer rettet mot ungdom			x	Grimshaw 2006 (38)
Aversiv røyking			x	Hajek 2001 (39)
Befolkningsbaserte konkurranser			x	Cahill 2008 (40)

Hindre salg til mindreårige	x	Stead 2005 (41)
Begrense skader ved fortsatt bruk	x	Stead 2007 (42)
Skolebaserte programmer	x	Thomas 2006 (43)
Familiebaserte programmer	x	Thomas 2007 (44)
Fysisk aktivitet	x	Ussher 2005 (45)
Akupunktur, akupressur, laser	x	White 2006 (46)

Røykeslutt - tiltak som synes å virke

Massemedia-tiltak rettet mot voksne røykere kan påvirke røykeatferd og redusere røyking blant voksne røykere (6). Det ble ikke funnet noen konsistent sammenheng mellom effekten av kampanjene rettet mot voksne etablerte røykere, og alder, kjønn, etnisitet eller utdanning. *Massemedia-tiltak* rettet mot ungdom syntes også å forebygge røyking blant unge (8).

En oversikt over longitudinelle studier viste en sammenheng mellom ulike former for reklame og en økt sannsynlighet for at unge under 18 år begynte å røyke (7).

Enkle råd og mer omfattende støtte og oppfølging fra helsepersonell (leger, sykepleiere og farmasøyter) førte til en liten økning i andelen som sluttet å røyke (9;10;12). Oppfølging ga en økt effekt i forhold til kortvarige tiltak. Tilleggseffekten av mer omfattende intervensjoner var marginal, slik at bruk av hjelpemidler og lignende kun synes aktuelt hos mer motiverte røykere. Intensiv rådgiving rettet mot pasienter innlagt i sykehus som startet under sykehusoppholdet og fortsatte med støtte minst en måned etter utskrivelsen, førte til en økning i andelen som sluttet å røyke. Disse intensive intervensjonene var effektive uavhengig av diagnosen som førte til sykehusinnleggelse. Mindre intensive intervensjoner på sykehus, og med kortere oppfølging etter utskrivelsen, viste ingen effekt på røykeslutt (11).

Individuell rådgiving gitt i direkte kontakt mellom røyker og en person som hadde fått opplæring i å gi støtte til røykeslutt, selvhjelpstiltak, gruppebehandling og telefonrådgiving hadde positiv effekt for å øke andelen som sluttet å røyke (13;14;18;19).

Det var god dokumentasjon for at individrettede *tiltak initiert på arbeidsplassen* økte sjansen for at ansatte sluttet å røyke (15). Dette gjaldt de samme tiltak som er vist effektive også i andre sammenhenger: råd fra helsepersonell, individuell eller gruppebasert rådgiving og farmakologisk behandling mot nikotinavhengighet. Røykeforbud eller restriksjoner reduserte røyking på arbeidsplassen. Det var usikkert om dette førte til redusert bruk av tobakk eller redusert andel røykere samlet sett.

En oversikt over effekten av *tiltak mot røyking på offentlige steder* identifiserte 11 ukontrollerte før- og etterstudier. Godt planlagte og sammensatte strategier med

forbud mot røyking på offentlige steder og i institusjoner var effektive, mens mindre omfattende strategier viste mindre effekt (16). En oversikt som omhandlet *tiltak basert i lokalsamfunn for å forebygge røyking blant ungdom* inkluderte 17 kontrollerte studier der skoledistrikt eller lokalsamfunn var fordelt til intervensjons- eller kontrollgruppe. Oversikten fant en begrenset støtte for effekten av slike tiltak (17).

Flere *farmakologiske tiltak* var mer effektive enn placebo for å øke andelen som klarte å slutte å røyke. Dette gjaldt midler med partiell agonisteffekt overfor nikotinreseptorer (vareniklin) (20), tilførsel av nikotin i form av tyggegummi, plaster, nesespray, inhalasjon eller tabletter (10), noen antidepressiver (bupropion og nortryptilin hjalp for røykeslutt, men selektive serotonin reopptakshemmere hadde ingen effekt) (22) og klonidin (21). Det så ut til at virkningen av bupropion og nortryptilin var uavhengig av antidepressiv effekt, og at effekten var på nivå med effekten av nikotinerstatning. I Norge er det kun nikotinerstatning, bupropion og vareniklin som er godkjent for røykeavvenning.

Det ble også funnet noe dokumentasjon for at *finansiell støtte* til røykere og helsepersonell ga positiv effekt på røykeslutt (24).

Røykeslutt - tiltak som synes å ikke virke

Hypnoterapi hadde ikke effekt på røykeslutt etter seks måneder (25). Eksisterende dokumentasjon av lavere kvalitet støtter ikke hypotesen om at motivasjonen for å slutte å røyke kan økes ved *biomedisinsk risikovurdering* ved f. eks. måling av karbonmonoksyd (CO) i ekspirasjonsluft, spirometri eller genetisk testing (26). *Insentiver og konkurranser* syntes ikke å øke sjansen for å lykkes med å slutte å røyke på lang sikt. En viss tidlig suksess syntes å fortape seg når insentivene ikke ble opprettholdt (27).

Det ble ikke funnet økt sjanse for røykeslutt i studier som undersøkte effekten av å *støtte partnere (ektefelle, venner, arbeidskolleger)* til røykere som en del av program for røykeslutt (29).

En oversikt over *tiltak i lokalsamfunn rettet mot voksne røykere* inkluderte 37 studier og fant at de største og best gjennomførte studiene ikke viste noen effekt på forekomsten av røykere (30).

Røykeslutt - tiltak med ukjent effekt

Råd fra tannleger økte sjansen for å kutte ut annen tobakksbruk enn sigaretter, mens dokumentasjonen for råd om røykeslutt hos tannleger var for svak til å trekke sikre konklusjoner (31).

Opplæring av helsepersonell i metoder for å fremme røykeslutt blant pasientene viste en målbar effekt på helepersonellets praksis, men det var ingen sterk dokumentasjon på at dette førte til endret røykeatferd blant pasientene (32).

Oversikter over studier av opioidantagonister (33), anxiolytika (34) og nikotin antagonist (mekamylamin) (35) har konkludert med at tilgjengelig dokumentasjon ikke er tilstrekkelig til å avgjøre om disse midlene er effektive for røykeslutt. Oversikter over lobelin og nicobrevin fant ingen studier som tilfredsstilte inklusjonskriteriene (36;37).

En oversikt som vurderte effekt av intervensjoner rettet mot unge røykere inkluderte 15 studier med 3 605 unge deltakere (38). Tre av studiene brukte den transteoretiske modellen om stadier av endring, to testet farmakologisk støtte for røykeslutt, og de resterende brukte ulike psykososiale intervensjoner som motivasjonsforsterking og kognitiv atferdsbehandling. Forfatterne konkluderte at komplekse intervensjoner virket lovende, særlig de som benyttet elementer fra modellen om stadier av endring, men forskjeller mellom og svakheter ved studiene gjorde det vanskelig å trekke sikre slutninger (38).

En oversikt over tiltak som skal gi aversjon mot røyking inkluderte 25 studier. Tolv studier av rask røyking viste en tilsynelatende positiv effekt på røykeslutt, men fordi de fleste studiene hadde metodologiske problemer konkluderte forfatterne at dokumentasjonen var utilstrekkelig til å vurdere effekten av rask røyking (39).

Befolkningsbaserte konkurranser på lokalt og regionalt nivå (”quit and win”) så ut til å gi høyere andel av folk som sluttet å røyke, men innvirkningen på befolkningen syntes å være liten. Dessuten viste det seg at andelen som jukset var høy, der det var mulig å kontrollere, slik at validiteten av slike studier er usikker (40).

Tiltak rettet mot detaljister for å hindre salg av tobakk til mindreårige er ikke sikkert vist å føre til at det blir vanskeligere for unge å få tak i tobakk, eller at det påvirker røykeatferd blant ungdom (41).

Oversikter over tiltak for å begrense røyking og redusere skader ved fortsatt røyking, skolebaserte og familiebaserte programmer for å forebygge røyking blant barn og unge, programmer med fysisk trening (alene eller i tillegg til andre røykeslutt-tiltak) og akupunktur og liknende ikke-farmakologisk stimulering som akupressur og laser kunne heller ikke gi sikre konklusjoner om eventuelle effekter (42-46).

Tabell 1.2. *Fysisk aktivitet*

Tiltak for å øke fysisk aktivitet	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Råd, støtte og veiledning	x			Foster 2005 (47)
Trening for å forebygge type 2 diabetes	x			Orozco 2008 (48)
Foreskrive trening ved overvekt	x			Shaw 2006 (49)
Trening ved type 2 diabetes	x			Thomas 2006 (50)
Hjemmebasert vs. senterbasert trening - eldre			x	Ashworth 2005 (51)
Policytiltak for å fremme sunn livsstil gjennomført i idrettsorganisasjoner			x	Jackson 2005 (52)

Fysisk aktivitet - tiltak som synes å virke

Ulike *tiltak for å fremme fysisk aktivitet* har en moderat effekt på selvrapportert fysisk aktivitet, på oppnåelse av et forhåndsbestemt nivå av fysisk aktivitet og på fysisk kondisjon (47).

En oversikt over 43 studier om effekt av *trening ved overvekt* fant støtte for bruk av trening for å gå ned i vekt, særlig når trening var kombinert med endring av kosten. Trening ved overvekt var også assosiert med redusert nivå av risikofaktorer for hjerte- og karsykdommer (forhøyet blodtrykk, serumlipidnivå, blodsukker) også uten vektreduksjon (49).

En oversikt over effekt av *trening for pasienter med type 2 diabetes* viste at selv uten vektreduksjon ga treningen forbedret glykemisk kontroll, reduksjon av visceralt fettvev og reduksjon av triglyserider i plasma, men ikke av kolesterolnivået (50).

En oversikt over effektene av *trening alene, eller trening og diett blant personer med økt risiko* identifiserte åtte studier med ett til seks års oppfølging. Livsstilstiltakene førte til redusert forekomst av type 2 diabetes. Ingen av studiene rapporterte data på kardiovaskulær morbiditet eller mortalitet (48).

Fysisk aktivitet - tiltak med ukjent effekt

En oversikt over seks studier som sammenliknet hjemmebasert versus senterbasert program for fysisk aktivitet blant eldre fant ingen sikker forskjell i effekt i forhold til fysisk funksjon eller kardiovaskulære risikofaktorer, men det var holdepunkter for at de eldre i større grad fulgte opp hjemmebaserte program, særlig på lang sikt (51).

En oversikt over effekten av tiltak i regi av idrettsorganisasjoner for å fremme sunn livsstil identifiserte ingen metodesterke studier (52).

TILTAK FOR VEKTREDUKSJON OG DIETT

Tabell 1.3. Vektreduksjon og diett

Tiltak for å vektreduksjon og diett	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Kalorirestriksjon ved overvekt og hypertensjon	x			Mulrow 1998 (53)
Diettråd for å forebygge type 2 diabetes	x			Nield 2008 (54)
Vektreduksjon eller vektkontroll ved prediabetes	x			Norris 2005 (55)
Vektreduksjon eller vektkontroll – type 2 diabetes	x			Norris 2005 (56)
Farmakoterapi for vektreduksjon ved type 2 diabetes	x			Norris 2005 (57)
Farmakoterapi ved fedme og overvekt	x			Padwal 2003 (58)
Psykologiske intervensjoner ved overvekt	x			Shaw 2005 (59)
Lav glykemisk indeks diett ved overvekt	x			Thomas 2007 (60)
Langvarig moderat saltreduksjon	x			He 2004 (61)
Diettråd for å redusere risiko for hjerte- og karsykdom	x			Brunner 2007 (62)
Råd om saltreduksjon for å redusere risiko for hjerte- og karsykdom	x			Hooper 2004 (63)
Redusert eller modifisert fettinntak	x			Hooper 2000 (64)
Diett med lavt vs. høyt saltinntak	x			Jürgens 2004 (65)
Råd om fettredusert diett vs. diett med lavt kaloriinnhold ved overvekt		x		Pirozzo 2002 (66)
Kombinert kalsium, magnesium og kaliumtilskudd		x		Beyer 2006 (67)
Kitosan for vektreduksjon		x		Ni Mhurchu 2005 (68)
Fullkornrik kost for å forebygge type 2 diabetes		x		Priebe 2008 (69)
Sink for å forebygge type 2 diabetes			x	Beletate 2007 (70)
Vektreduksjon ved overvekt for primærforebygging av slag			x	Curioni 2006 (71)
Omega 3 for pasienter med type 2 diabetes			x	Hartweg 2008 (72)
Omega 3 for å forebygge hjerte- og			x	Hooper 2004 (73)

karsykdommer		
Dietter med lav glykemisk indeks for pasienter med forhøyet hjertek-risiko	x	Kelly 2004 (74)
Fullkornrike dietter	x	Kelly 2007 (75)
Diettråd ved type 2 diabetes	x	Nield 2007 (76)
Artisjokkbladekstrakt ved hyperkolesterolemi	x	Pittler 2002 (77)
Diett ved familiær hyperkolesterolemi	x	Poustie 2001 (78)
Diettråd gitt av dietetiker vs. annet helsepersonell	x	Thompson 2003 (79)

Diett og vektreduksjon - tiltak som synes å virke

En oversikt over *diett med kalorirestriksjon hos overvektige med hypertensjon* identifiserte 18 studier, og viste at dette førte til vekttap i størrelsesorden 3-9 % av kroppsvekten samt en reduksjon av systolisk og diastolisk blodtrykk på omkring 3 mm Hg (53). *Langvarige ikke-farmakologiske intervensjoner rettet mot vekttap eller vektreduksjon hos personer med prediabetes* ga gunstig effekt på vekt og en reduksjon i forekomst av diabetes. Videre forskning er nødvendig for å få kunnskap om langtidseffektene av disse tiltakene, og kunnskap om hvordan de eventuelt kan gjennomføres i ulike lokale settinger (55). Tilsvarende tiltak for *pasienter med diabetes* viste en litt større vektreduksjon i intervensjonsgruppen i forhold til sammenlikningsgruppen (56).

En oversikt over effekten av *dietter med lav glykemisk indeks* identifiserte seks randomiserte kontrollerte studier (202 personer), og viste større vekttap og større forbedringer i lipidprofiler ved slik diett i forhold til andre dietter (60).

Overvektige personer kan ha nytte av *psykologiske intervensjoner* i form av kognitiv behandling og/eller atferdsbehandling. Dette ga økt vektreduksjon, særlig i kombinasjon med diett og fysisk aktivitet. Det mangler god dokumentasjon for effekten av andre psykologiske tiltak ved overvekt (59).

Farmakologisk behandling for vektreduksjon hos pasienter med type 2 diabetes og overvekt med fluoxetine, orlistat og sibutramin førte til et beskjedent, men signifikant vekttap over 12-57 uker (57). De eventuelle helseeffekter på sikt er uklare. *Vektreduserende medikamenter (orlistat og sibutramin)* førte også til en signifikant vektreduksjon hos andre pasienter med overvekt og fedme. De hadde noe varierende effekter på risikofaktorer for hjerte- og karsykdommer, og ulike profiler med hensyn til bivirkninger. Frafallet i disse studiene var stort (58).

En metaanalyse av randomiserte kontrollerte studier av *en beskjeden reduksjon i saltinntak i fire uker eller mer* viste en gunstig effekt på blodtrykket både hos personer med normalt og forhøyet blodtrykk. Effekten på blodtrykket var korrelert til

nivået på saltreduksjonen. Forfatterne konkluderte med at dette er viktig fra et folkehelseperspektiv, ved at en beskjeden og varig reduksjon i saltinntaket på befolkningsnivå kunne føre til redusert forekomst av slag, hjerteinfarkt og hjertesvikt (61). En annen oversikt over *råd for å redusere saltinntak for å forebygge kardiovaskulær sykdom* med oppfølgingstid fra seks måneder til sju år viste at intensive intervensjoner som er uegnet i primærhelsetjenesten eller i vanlige befolkningsrettede forebyggingsprogrammer, kun førte til minimale reduksjoner i blodtrykket. Pasienter i intervensjonsgruppen kunne stoppe med blodtrykksmedisiner oftere enn pasientene i kontrollgruppen, og opprettholde samme blodtrykkskontroll (63). En tredje oversikt sammenliknet *dietter med lavt natriuminntak med dietter med høyt natriuminntak* (65). I 57 studier av hovedsakelig hvite personer med normalt blodtrykk, førte diett med lavt natriuminntak til en endring i systolisk blodtrykk på -1.27 mmHg (KI: -0,94; -0,14). I 58 studier av personer med høyt blodtrykk førte diett med lavt natriuminntak til endring av systolisk blodtrykk på -4,18 mmHg (KI -5,08; - 3,27) og diastolisk blodtrykk -1,98 mmHg sammenliknet med diett med høyt natriuminntak. Forfatterne av denne oversikten konkluderte med at størrelsen av effekten på blodtrykksreduksjonen hos hvite med normalt blodtrykk ikke gir grunnlag for en generell anbefaling om å redusere natriuminntaket, mens redusert saltinntak har en gunstig effekt på kort sikt hos hvite med forhøyet blodtrykk. Resultatene kunne tyde på at effektene av lavt versus høyt natriuminntak var større hos svarte og asiatiske pasienter i forhold til hos hvite, men dokumentasjonen var utilstrekkelig for å gi grunnlag for ulike anbefalinger.

En oversikt over *diettråd for å redusere risikofaktorer for hjerte- og karsykdommer* identifiserte 38 randomiserte kontrollerte studier. Diettrådene syntes å føre til små gunstige endringer i kost og risikofaktorer for hjerte- og karsykdom over omtrent ti måneder. Langtidseffektene av slike råd er ukjente (62).

En oversikt over *diettråd for å forebygge type 2 diabetes* inkluderte to randomiserte studier med 358 deltakere og viste redusert forekomst av diabetes i intervensjonsgruppen (54). Intervensjonen i disse to studiene innebar en diett med redusert inntak av energi og sukker, og økt inntak av frukt og grønnsaker. Deltakerne hadde hyppig kontakt med rådgivere for å motivere til støtte for diettforandringer. Det er behov for flere gode studier for å kunne konkludere hvordan diettråd best kan forebygge diabetes hos risikoindivider.

En oversikt over 27 studier av *redusert inntak av mettet fett og delvis erstatning med umettet fett* viste signifikant effekt på kardiovaskulære hendelser, og en mulig beskyttelse for dødelighet av hjerte- og karsykdom i studier som varte i minst to år (64). Forfatterne konkluderte at livsstilsråd til pasienter med økt risiko for hjerte- og karsykdom, og også til befolkningsgrupper med lavere risiko, fortsatt bør inneholde råd om varig reduksjon av mettet fett og erstatning med umettet fett.

Diett og vektreduksjon - tiltak som synes å ikke virke

Råd om fettreduserte dietter hos overvektige førte til et beskjedent vekttap, men fettreduserte dietter var ikke mer effektive enn andre kaloriredusерte dietter for å oppnå vektreduksjon på lang sikt. Fettreduserte dietter ved overvekt førte til ikke-signifikante endringer i blodtrykk og lipidnivå (66).

Det var ingen robust dokumentasjon for at *supplement av kalium, magnesium eller kalsium* reduserte blodtrykksnivå, sykelighet eller dødelighet (67). Resultater fra studier av høy kvalitet indikerte at kitosan ved overvekt hadde en ubetydelig effekt på vekta (68).

En oversikt over effektene av *omega 3 fettsyrer i kost eller som tilskudd* identifiserte 48 randomiserte kontrollerte studier og 41 kohortstudier. Metaanalyser viste ingen reduksjon i total mortalitet eller hjerte- og karsykdom blant dem som tok omega 3 fettsyrer (73).

Diett og vektreduksjon - tiltak med ukjent effekt

Det ble ikke identifisert studier som hadde undersøkt *om vektreduksjon kan forebygge hjerneslag hos overvektige* (71).

Det manglet dokumentasjon til støtte for *supplement av sink for å forebygge diabetes* (70). *Omega-3 flerumettede fettsyrer (PUFA) ved type 2 diabetes mellitus* førte til gunstige endringer mht. triglyserider og VLDL kolesterol, men førte kanskje også til økning av LDL kolesterol (72).

Metaanalyser av 21 randomiserte studier av *dietter med lav glykemisk indeks* viste en liten reduksjon i totalkolesterol og HbA1c, men ingen sikker reduksjon i andre risikofaktorer for hjerte- og karsykdom (74). Mange av studiene var av dårlig kvalitet, med få deltakere og kort oppfølgingstid. Det er behov for studier av bedre kvalitet og lengre oppfølgingstid for å kunne vurdere effektene av dietter med lav glykemisk indeks på hjerte- og karsykdommer.

Det ble funnet ti studier av effekten av *dietter rike på fullkorn* sammenliknet med dietter uten eller med lavere nivå av fullkorn med 4-8 ukers varighet. Det ble funnet en reduksjon av total kolesterol og LDL kolesterol med fullkorn hvete. Studiene var av dårlig kvalitet, med få deltakere og av kort varighet. Derfor var det ikke mulig å trekke sikre konklusjoner selv om studiene viste konsistente positive effekter (75). Dokumentasjonen var også for svak til at det var mulig å trekke en sikker konklusjon om *dietter rike på fullkorn* kan forebygge type 2 diabetes hos personer med økt risiko (69).

Det ble ikke funnet data av høy kvalitet på effekten av diettbehandling av type 2 diabetes i en oversikt som omfattet 18 studier med 1 467 deltakere omtalt i 36 artikler (76). Tilgjengelige data tydet på at trening kan bedre nivået på HbA1c hos pasienter med type 2 diabetes. Det var ikke mulig å trekke konklusjoner om effekten av *diettbehandling ved familiær hyperkolesterolemi*, på grunn av mangel på data (78).

En oversikt over studier som sammenliknet effekten av *diettråd gitt av dietetiker versus annet helsepersonell eller selvhjelpsressurser*, fant ikke god nok dokumentasjon for å kunne trekke sikre konklusjoner. Dietetikere syntes å være bedre enn leger for å redusere kolesterolnivået (79). Det er rapportert om positive effekter av *preparater med ekstrakter av artisjokkblader for å behandle hyperkolesterolemi*, men dokumentasjonen var for svak til å kunne trekke noen konklusjoner (77).

ANDRE TILTAK

Tabell 1.4. *Andre tiltak*

Andre tiltak	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Tiltak for bedret blodtrykkskontroll	x			Fahey 2006 (80)
Kulturelt tilpassede intervensjoner for pasienter fra etniske minoriteter med type 2 diabetes	x			Hawthorne 2008 (81)
Alfaglukosidasehemmere (akarbose) ved prediabetes	x			Van de Laar 2006 (82)
Multippel risikofaktoriintervensjon		x		Ebrahim 2006 (83)
Kontrakter mellom pasient og behandler for å øke etterlevelse			x	Bosch-Capblanch 2007 (84)
Avspenningsbehandlinger (ulike biofeedback- og kognitive tiltak) ved hypertensjon			x	Heather 2008 (85)

Andre tiltak - som synes å virke

En oversikt som undersøkte ulike tiltak for å forbedre kontrollen av blodtrykket for pasienter med forhøyet blodtrykk inkluderte 56 randomiserte kontrollerte studier av varierende kvalitet. Tiltakene ble klassifisert som egenkontroll, opplæring rettet mot pasient og mot helsepersonell, behandling ledet av sykepleier eller farmasøyt, organisatoriske tiltak for å gi bedre behandling og systemer for å minne om kontrollavtaler. Et organisert system med regelmessige kontroller koblet til en kraftfull behandling med blodtrykkssenkende medisiner førte til redusert blodtrykk og redusert total dødelighet (6,4 % versus 7,8 %, forskjell 1,4 %, KI ikke oppgitt) etter 5 års oppfølging i en enkelt stor randomisert kontrollert studie sammenliknet med ordi-

nær oppfølging. Forfatterne konkluderte med at legekontor bør ha gode systemer for å sikre regelmessig og god oppfølging av sine blodtrykkspasienter, og blodtrykksmedisineringen bør trappes opp når pasientene ikke når sine behandlingsmål (80).

Etniske minoritetsgrupper har ofte høyere forekomst av type 2 diabetes enn befolkningen for øvrig, og har ofte lavere sosioøkonomiske status. *Intervensjoner som er kulturelt tilpasset pasienter med type 2 diabetes i etniske minoritetsgrupper* har vist seg å ha positive effekter på glykemisk kontroll, kunnskap om diabetes og livsstil på kort sikt (81). Oversikten identifiserte 11 randomiserte kontrollerte studier, men fant ingen studier av mer enn 12 måneders varighet. Vi mangler derfor kunnskap om eventuelle helseeffekter av slike intervensjoner på lengre sikt.

Alfaglukosidasehemmere (akarbose) kan redusere forekomsten av type 2 diabetes i pasienter med nedsatt glukosetoleranse (82).

Andre tiltak - som synes å ikke virke

En oversikt om *multippel risikofaktorintervensjon (rådgiving eller opplæringstiltak, med eller uten farmakologisk behandling)* inkluderte 39 studier av minst seks måneders varighet. Studiene undersøkte effektene av tiltak for å redusere mer enn en risikofaktor for hjerte- og karsykdom (f. eks. blodtrykk, røyking, totalkolesterol, fysisk aktivitet, diett) hos deltakere uten kliniske holdepunkter for hjerte- og karsykdom. Det var ingen statistisk signifikant effekt på dødelighet eller ikke dødelige hjerteinfarkt, men 10 % reduksjon av dødelighet av hjerte- og karsykdom kunne ikke utelukkes. Endringene i risikofaktorer var beskjedne, og relatert til hvor mye farmakologisk behandling som ble gitt. Intervensjoner med rådgiving og opplæring rettet mot individer eller familier med høy risiko for hjerte- og karsykdom syntes å være mer effektive. I den vanlige befolkning, overfor personer med lav risiko, er eventuell nytte av multippel risikofaktorintervensjon begrenset (83).

Andre tiltak – med ukjent effekt

En oversikt som inkluderte 30 studier med 4 691 deltakere undersøkte effekten av *kontrakter mellom pasienter og helsepersonell for å øke pasientenes tilslutning til behandling, forebygging og helsefremmende aktiviteter*. Studiene vurderte kontrakter ved avhengighet (10 studier), høyt blodtrykk (fire studier), vektkontroll (3 studier) og en rekke andre tilstander (13 studier). Oversikten fant at det var utilstrekkelig dokumentasjon for å rutinemessig anbefale slike kontrakter (84).

Effekten av intervensjoner for å *fremme avslapning* blant pasienter med høyt blodtrykk var undersøkt i 25 studier. Kvaliteten av studiene var dårlig, og det var variasjoner mellom studien som ikke kunne forklares. Forfatterne konkluderte derfor at det var svak dokumentasjon for en kausal sammenheng mellom avslapning og blodtrykk (85).

TILTAK RETTET MOT PERSONER MED IDENTIFISERTE RISIKOFAKTORER

Røykere

Tabell 1.1. gir oversikt over tiltak for å hjelpe røykere til å slutte å røyke.

Overvekt

	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Foreskrive trening ved overvekt	x			Shaw 2006 (49)
Kalorirestriksjon ved overvekt og hypertensjon	x			Mulrow 1998 (53)
Farmakoterapi ved fedme og overvekt	x			Padwal 2003 (58)
Psykologiske intervensjoner ved overvekt	x			Shaw 2005 (59)
Lav glykemisk indeks diett ved overvekt	x			Thomas 2007 (60)
Vektreduksjon ved overvekt for primærforebygging av slag			x	Curioni 2006 (71)
Kitosan for vektreduksjon		X		Ni Mhurchu 2005 (68)

Økt risiko for diabetes

Flere oversikter har vurdert tiltak for å forebygge diabetesutvikling og redusere andre risikofaktorer for hjerte- og karsykdommer. Populasjonen med økt risiko for diabetes er litt ulikt definert i de ulike oversikter, men kan omfatte pasienter med nedsatt glukosetoleranse (prediabetes), tidligere svangerskapsdiabetes, hypertensjon, familiehistorie med type 2 diabetes hos førstegradsslektning, fedme, dyslipidemi og etnisk gruppe med økt risiko for type 2 diabetes (48).

	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Trening og diett for å forebygge type 2 diabetes	x			Orozco 2008 (48)
Diettråd for å forebygge type 2 diabetes	x			Nield 2008 (54)
Vektreduksjon eller vektkontroll ved prediabetes	x			Norris 2005 (55)
Fullkornrik kost for å forebygge type 2		x		Priebe 2008 (69)

diabetes				
Sink for å forebygge type 2 diabetes			x	Beletate 2007 (70)
Alfaglukosidasehemmere (akarbose) ved prediabetes	x			Van de Laar 2006 (82)

Diabetes

Personer med diabetes har betydelig økt risiko for å utvikle hjerte- og karsykdom. Effektive primærforebyggende tiltak er derfor viktig.

	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Trening ved type 2 diabetes	x			Thomas 2006 (50)
Vektreduksjon eller vektkontroll – type 2 diabetes	x			Norris 2005 (56)
Farmakoterapi for vektreduksjon ved type 2 diabetes	x			Norris 2005 (57)
Omega 3 ved med type 2 diabetes			x	Hartweg 2008 (72)
Diettråd ved type 2 diabetes			x	Nield 2007 (76)
Kulturelt tilpassede intervensjoner for pasienter fra etniske minoriteter med type 2 diabetes	x			Hawthorne 2008 (81)

Hypertensjon

	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Kalorirestriksjon ved overvekt og hypertensjon	x			Mulrow 1998 (53)
Tiltak for bedret blodtrykkskontroll	x			Fahey 2006 (80)
Avspenningsbehandlinger (ulike biofeedback- og kognitive tiltak) ved hypertensjon			x	Heather 2008 (85)

Hyperkolesterolemi

	Sannsynlig effekt			Oversikt (forfatter – år)
	Virker	Virker ikke	Ukjent	
Ekstrakt av artisjokkblader			x	Pittler 2002 (77)
Diett ved familiær hyperkolesterolemi			x	Poustie 2001 (78)

Diskusjon

Vi har oppsummert 81 Cochrane-oversikter som rapporterte resultater fra studier om effekter av ikke-medikamentelle tiltak som kan forebygge hjerte- og karsykdommer. Vi har valgt å inkludere oversikter over medikamentelle tiltak for å fremme røykeslutt, vektreduksjon og forebygging av type 2 diabetes. I tillegg har vi identifisert 159 andre relevante oversikter fra DARE og HTA databasene i Cochrane Library som er listet i vedlegg 3.

NOEN HOVEDFUNN

Det finnes en omfattende dokumentasjon fra systematiske oversikter over effektene av en rekke ulike ikke-medikamentelle tiltak for å endre livsstil og redusere risiko for hjerte- og karsykdom, og over farmakologiske tiltak for å gjøre det lettere å slutte å røyke. Det er dokumentasjon for at en rekke tiltak kan ha positiv effekt på livsstilsfaktorer som er knyttet til risiko for hjerte- og karsykdommer, som røyking, fysisk inaktivitet, overvekt og uheldig kosthold.

Massemediatiltak, rådgiving gitt av helsepersonell og av ikke-profesjonelle, selvhjelp, gruppebehandling, telefonrådgiving, tiltak på arbeidsplassen og farmakologisk behandling har en veldokumentert, men begrenset effekt for å øke andelen som slutter å røyke. Flere ulike intervensjoner for å øke fysisk aktivitet har en moderat effekt på egenrapportert aktivitet og målt fysisk kondisjon. Trening har gunstig effekt på risikofaktorer ved overvekt og type 2 diabetes. Vektreduserende dietter kan gi en beskjeden vektreduksjon ved overvekt, prediabetes og type 2 diabetes. Diettråd kan gi beskjedne positive endringer i kost og risikofaktorer. Saltredusert diett er gunstig for pasienter med høyt blodtrykk.

Hypnose, biomedisinske målinger (f. eks. spirometri og måling av karbonmonoksyd), konkurranser og lokalsamfunnsbaserte tiltak syntes ikke å ha effekt på røykeslutt.

For en rekke av de undersøkte tiltakene var effekten ukjent eller usikker på grunn av manglende eller ikke konklusiv dokumentasjon.

Ingen av de vurderte tiltakene ser ut til å stor effekt ut fra de oversiktene vi har inkludert. De fleste studiene hadde relativt kort oppfølgingstid, og det manglet data for effekter av tiltakene på sykelighet og dødelighet av hjerte- og karsykdommer. En liten, men gunstig endring av livsstils- og risikofaktorer for hjerte- og karsykdom vil imidlertid kunne ha en viktig effekt i et folkehelseperspektiv.

STYRKE VED RAPPORTEN

Vi har gjennomført en systematisk innhenting av litteraturen, basert på eksplisitte inklusjons- og eksklusjonskriterier og systematisk søk etter systematiske oversikter i Cochrane Library.

Vi har identifisert et stort materiale, med 81 Cochrane-oversikter og 159 oversikter fra DARE- og HTA-databasene i Cochrane Library. Disse oversiktene omfatter en rekke studier med mange deltakere og gir informasjon om effekter av en rekke ulike tiltak for å påvirke livsstil og forebygge hjerte- og karsykdom.

Vi valgte å basere oss på Cochrane-oversiktene, som utarbeides etter en eksplisitt metode. Det er dokumentert at Cochrane-oversikter jevnt over har bedre kvalitet enn andre oversikter (86-88).

For interesserte håper vi at listen i vedlegg 3 over andre oversikter kan være en nyttig kilde til ytterligere informasjon.

Vi har valgt å ta stilling til om tiltakene synes å virke eller ikke virke, eller om de har ukjent effekt, for å gjøre det enklere å få oversikt over den omfattende dokumentasjonen. To medarbeidere gjorde disse vurderingene uavhengig av hverandre. Det var godt samsvar i våre vurderinger.

BEGRENSNINGER VED RAPPORTEN

Vi har kun søkt etter systematiske oversikter, ikke primærstudier. Noen emner kan derfor mangle på områder der det finnes primærstudier, men ikke systematiske oversikter.

Innholdet i rapporten er bestemt av de oversiktene vi har funnet, ikke av viktighet eller relevans av de foreslåtte tiltakene. Vi har valgt også å ta med oversikter over tiltak som er lite aktuelle i Norge i dag.

Vi har ikke vurdert den metodologiske kvaliteten av oversiktene. De inkluderte Cochrane-oversiktene har vært gjennom omfattende kvalitetsprosedyrer før publisering, og de angir resultater på en standardisert måte. Selv om Cochrane-oversikter jevnt over er av god kvalitet, kan imidlertid disse også ha svakheter (89).

Studiene som er inkludert i oversiktene er av varierende kvalitet. Flere av oversiktene er basert på studier med svakt design, og med kort oppfølgingstid. Vi har ikke vurdert i hvilken grad oversiktene har tatt hensyn til dette i analysene.

I hovedsak har vi kun basert oss på en gjennomgang av sammendragene, de rapporterte resultatene og forfatternes konklusjoner. Vi har forsøkt å vurdere om det er samsvar mellom forfatternes konklusjoner og resultatene slik de er presentert i sammendragene. Vi har undersøkt nærmere i fulltekst der vi har vært i tvil om dette. Vi har utarbeidet en summarisk oversikt over Cochrane-oversiktene i vedlegg 4. Vi har ikke gradert kvaliteten av dokumentasjonen for utfallene. Funnene bør derfor tolkes med varsomhet.

Vi har i liten grad tatt med informasjon om størrelsene på effektestimatene i resultatkapitlet. Eventuelle effekter er jevnt over ganske små, men likevel potensielt viktige. Det er noe mer informasjon om effektstørrelser i vedlegg 4.

En grov forenklet inndeling av tiltakene i forhold til sannsynlig effekt er noe misvisende for oversikter over ulike intervensjoner der effekten varierte. Vi har valgt å forenkle budskapet. Budskapet blir da selvsagt mindre nyansert. Selv om vi hadde godt samsvar i våre vurderinger, erkjenner vi at flere av kategoriseringene kan diskuteres.

Vi har i liten grad analysert tilsynelatende inkonsistente funn i beslektede oversikter.

Flere av de inkluderte oversiktene er gamle, og noen er sannsynligvis utdaterte. I prinsippet skal Cochrane-oversikter oppdateres regelmessig, men dette skjer ikke alltid, selv der det kan ha kommet nye studier som kan endre resultatene i oversiktene. Vi har ikke oppdatert søkene for å lete etter nye studier.

Når det gjelder saltreduksjon er det verdt å nevne at nyere studier støtter opp om funnene fra de relativt gamle Cochrane-oversiktene. Det er holdepunkter for en signifikant og doseavhengig reduksjon av blodtrykket relatert til daglig saltinntak. Det synes ikke å være bivirkninger av en saltreduksjon innenfor det som det er realistisk å gjennomføre i en befolkning. En oppfølging etter 10-15 år av to randomiserte kontrollerte studier med støtte for redusert saltinntak til personer med ”prehypertensjon” eller normalt blodtrykk på grensen til høyt blodtrykk, viste en relativ risiko for kardiovaskulær sykdom på 0,75 (95 % KI 0,57-0,99) (90). En systematisk oversikt viste også signifikant blodtrykksreduksjon helt ned i spedbarnsalder ved 35-40 % saltreduksjon (91).

Vi har ikke søkt etter data om kostnadseffektiviteten for tiltakene. Vi har heller ikke vurdert i hvilken grad eller på hvilken måte de dokumentert effektive tiltakene kan gjennomføres i vanlig praksis i Norge.

Oversiktene i rapporten omhandler i all hovedsak forebyggende tiltak som starter i voksen alder. Ingen av oversiktene omhandler befolkningsrettede tiltak som starter i tidlig barnealder, som for eksempel tiltak i skolen for å oppmuntre barn til fysisk aktivitet og fornuftig kosthold. Politiske tiltak som har som mål å legge forholdene til rette for godt kosthold og fysisk aktivitet er også i liten grad omtalt i oversiktene.

I denne rapporten har vi begrenset oss til Cochrane-oversikter. Systematiske oversikter over randomiserte kontrollerte studier er vanligvis den beste kilde til kunnskap om effekt av tiltak, inkludert forebyggende tiltak. Når vi gir råd og veiledning om forebyggende tiltak, er det som oftest mulig å vurdere effektene av dette med studier av god design, helst ved randomiserte kontrollerte studier.

Prospektive kohortstudier kan imidlertid også gi viktig informasjon om effekter av livsstil, og om effekter av å endre livsstil, slik som oppfølgingsstudien av britiske leger som har skaffet informasjon om dødelighet ved røyking (92;93).

Flere av Cochrane-oversiktene har inkludert observasjonelle studier, for eksempel av lovregulerende tiltak.

IMPLIKASJONER

Data fra observasjonelle studier har vist at risikoen for hjerte- og karsykdom påvirkes av kjente modifiserbare faktorer som røyking, diabetes, forhøyet blodtrykk og forhøyet kolesterol (92-95). En kasus-kontroll studie i 52 land identifiserte ni faktorer som forklarte 90 % av risikoen for hjerteinfarkt blant menn, og 94 % blant kvinner globalt (96). De ni risikofaktorene var røyking, hypertensjon, diabetes, abdominal fedme, psykososialt stress, forhøyede lipidnivåer i blodet, uregelmessig inntak av frukt og grønnsaker, null inntak av alkohol og mangel på regelmessig fysisk aktivitet.

En stor kohortstudie med 50 års oppfølging av britiske leger viste at røykere som sluttet å røyke reduserte risikoen for hjerte- og karsykdommer sammenliknet med dem som fortsatte å røyke (92). Vi tar for gitt at tiltak som får folk til å slutte å røyke vil føre til redusert sykelighet og dødelighet.

Tilsvarende kan vi regne med at tiltak som fører til varig og positiv endring i livsstil og til reduksjon i risikofaktorer som forhøyet blodtrykks- eller kolesterolnivå, også vil redusere forekomsten av hjerte- og karsykdommer. Informasjon om effekter av forebyggende tiltak på livsstil og andre etablerte risikofaktorer er derfor viktig i arbeidet for å forebygge hjerte- og karsykdom.

Det er imidlertid svært sparsom dokumentasjon for effekter på harde endepunkter som sykelighet og dødelighet av hjerte- og karsykdom ved livsstilstiltak. Det er ønskelig med gode studier med lengre oppfølgingstid som også kan rapportere slike

harde endepunkter. Slik vil vi få et bedre grunnlag for å satse på de mest effektive forebyggende tiltakene.

Det er veldokumenterte forskjeller i sykelighet og dødelighet av hjerte- og karsykdommer knyttet til sosioøkonomiske ulikheter både i Norge og andre vestlige land, til tross for en generell velstandsutvikling. Det har vært diskutert om disse forskjellene skyldes materielle forhold, psykososiale forhold, "programmering" ved ugunstige forhold i fosterstadiet og tidlig barndom, eller om de kan forklares ved sosioøkonomiske forskjeller i helserelatert atferd eller livsstil (97-102).

Ulikheter i livsstil eller helserelatert atferd (røyking, uheldig kosthold, overvekt og mindre fysisk aktivitet) er viktige faktorer for å forklare økt forekomst av hjerte- og karsykdommer i lavere sosiale lag. Det er verdt å merke seg at kampanjer i media rettet mot voksne røykere så ut til å ha samme effekt uavhengig av alder, kjønn, etnisitet og utdanning. For øvrig har vi ikke funnet oversikter som omhandler tiltak for å motvirke sosioøkonomiske skjevheter i risikofaktorer eller sykelighet. Vi har heller ikke identifisert oversikter som sammenlikner politiske tiltak for å utjevne skjevheter i utdanning og inntekt, med individrettede tiltak for å påvirke helserelatert atferd. Tradisjonelle tiltak for å få folk til å slutte å røyke, trene mer og spise sunnere, har gjerne større effekt i grupper med høyere utdanning. Det er derfor et stort behov for å utvikle og evaluere intervensjoner som kan utjevne sosioøkonomiske ulikheter i risiko for hjerte- og karsykdom (103;104).

Det er omdiskutert hvordan man mest effektivt kan oppnå slik risikoreduksjon i befolkningen, og derved forebygge flest mulig tilfeller av hjerte- og karsykdom. NICE arbeider med retningslinjer for forebygging av hjerte- og karsykdom på populasjonsnivå. Dette arbeidet forventes ferdig i mars 2010 (105).

Det er ingen uenighet om at pasienter med høy risiko for hjerte- og karsykdom bør få både medikamentell behandling, rådgiving og god oppfølging og støtte for å redusere sin risiko. Men intervensjonsgrenser og behandlingsmål er kontroversielle. Flere har advart mot retningslinjer som diagnostiserer en stor andel av den voksne del av befolkningen som risiko-individer (106). Retningslinjer med aggressive anbefalinger kan føre til uheldig medikalisering av friske personer med gode leveutsikter, og en ressurskrevende jakt etter og oppfølging av risikofaktorer i allmennpraksis (106).

Gjennomgangen av dokumentasjonen fra de identifiserte Cochrane-oversiktene viste at flere ikke-medikamentelle tiltak, både individrettede og befolkningsrettede, hadde effekt på risikofaktorer for hjerte- og karsykdom. Selv om det mangler data på sykelighet og dødelighet, kan vi gå ut fra at det å få folk til å slutte å røyke, øke fysisk aktivitet og spise sunt, fører til redusert forekomst av hjerte- og karsykdommer – i større eller mindre grad.

Enkle tiltak med dokumentert effekt, som f. eks. enkel rådgiving om røykeslutt gitt av helsepersonell i forbindelse med konsultasjoner, er åpenbart kostnadseffektive. Andre programmer for å få folk til å endre livsstil har vært svært ressurskrevende, både med hensyn til faglig kompetanse og økonomisk og personellmessig ressursinnsats. Det kan derfor være vanskelig å gjennomføre slike program i ordinær praksis.

Det er behov for mer kunnskap om effekter på lengre sikt av ulike tiltak for å forebygge hjerte- og karsykdom. Beslutningstakere vil også ha behov for å sammenlikne kostnadseffektivitet av alternative intervensjoner for å ha bedre grunnlag for å foreta fornuftige prioriteringer mellom ulike strategier for å redusere forekomsten av hjerte- og karsykdommer i befolkningen.

Konklusjon

Velkjente risikofaktorer for hjerte- og karsykdommer som røyking, høyt blodtrykk, fysisk inaktivitet, overvekt, diabetes, høyt kolesterolnivå og uheldig kosthold kan påvirkes både av medikamentelle og ikke-medikamentelle tiltak. Det er rom for ytterligere reduksjon i forekomst av hjerte- og karsykdommer ved i større grad å ta i bruk eksisterende kunnskap om effektene av ikke-medikamentelle tiltak for å påvirke risikofaktorene for hjerte- og karsykdommer.

Vi har ikke vurdert kostnadseffektiviteten av tiltakene i forhold til hverandre, i forhold til medikamentell behandling for å forebygge hjerte- og karsykdommer eller i forhold til andre forebyggende tiltak. Ingen av de ikke-medikamentelle tiltakene ser ut til å ha stor effekt, ut fra de oversiktene som vi har vurdert. En vedvarende liten eller moderat effekt kan likevel være viktig, både for den enkelte, og i et folkehelseperspektiv.

Det er fornuftig å satse på enkle veldokumenterte tiltak, framfor mer komplekse og kanskje lite kostnadseffektive tiltak, eller tiltak som mangler dokumentasjon.

BEHOV FOR VIDERE FORSKNING

Det er behov for mer kunnskap om effektene av tiltak for å redusere sosioøkonomiske forskjeller i risiko for og forekomst av hjerte- og karsykdommer.

En rekke av oversiktene vurderte tiltak som viste seg å ha manglende eller usikker dokumentasjon. Det er derfor behov for flere gode studier av ikke-medikamentelle intervensjoner for å redusere risiko for hjerte- og karsykdommer. Studiene bør være tilstrekkelig store med lang nok oppfølgingstid, og helst med måling av harde endepunkter som kardiovaskulær sykelighet og dødelighet.

Referanser

1. Dødsårsaker 2006. 27-6-2008. Statistisk sentralbyrå. http://www.ssb.no/emner/03/01/10/dodsarsak/
2. Dødsårsaker 2005. 2008. Statistisk sentralbyrå. http://www.ssb.no/vis/emner/03/01/10/dodsarsak/arkiv/art-2007-10-19-01.html
3. Dødsårsaksstatistikken 2006. Nedgangen i hjertedødsfall stopper opp. 19-10-2007. Folkehelseinstituttet. http://www.fhi.no/eway/default.aspx?pid=233&trg=MainLeft_5565&MainArea_5661=5565:0:15,3408:1:0:0:::0:0&MainLeft_5565=5544:66403::1:5569:5:::0:0
4. Håheim LL, Fretheim A, Brørs O, Kjeldsen SE, Kristiansen IS, Madsen S et al. Primærforebygging av hjerte- og karsykdom. Rapport nr. 20-2008. Oslo: Nasjonalt kunnskapssenter for helsetjenesten, 2008.
5. Wisløff T, Norheim OF, Halvorsen S, Selmer RM, Kristiansen IS. Kostnader og leveårsgevinster ved medikamentell primærforebygging av hjertekarsykdom. Rapport nr. 34-2008. Oslo: Nasjonalt kunnskapssenter for helsetjenesten, Oslo.
6. Bala M, Strzeszynski L, Cahill K. Mass media interventions for smoking cessation in adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
7. Lovato C, Linn G, Stead LF, Best A. Impact of tobacco advertising and promotion on increasing adolescent smoking behaviours. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2003;(3).
8. Sowden AJ, Arblaster L. Mass media interventions for preventing smoking in young people. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001006. Cochrane Database Syst Rev 1998;(4).
9. Lancaster T, Stead LF. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(4).
10. Rice VH, Stead LF. Nursing interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
11. Rigotti NA, Munafo MR, Stead LF. Interventions for smoking cessation in hospitalised patients. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).

12. Sinclair HK, Bond CM, Stead LF. Community pharmacy personnel interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).
13. Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
14. Lancaster T, Stead LF. Self-help interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(3).
15. Moher M, Hey K, Lancaster T. Workplace interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
16. Serra C, Cabezas C, Bonfill X, Pladevall-Vila M. Interventions for preventing tobacco smoking in public places. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(3).
17. Sowden A, Stead L. Community interventions for preventing smoking in young people. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2003;(1).
18. Stead LF, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
19. Stead LF, Perera R, Lancaster T. Telephone counselling for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).
20. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
21. Gourlay SG, Stead LF, Benowitz NL. Clonidine for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(3).
22. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
23. Stead LF, Perera R, Bullen C, Mant D, Lancaster T. Nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
24. Kaper J, Wagena EJ, Severens JL, Van Schayck CP. Healthcare financing systems for increasing the use of tobacco dependence treatment. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
25. Abbot NC, Stead LF, White AR, Barnes J. Hypnotherapy for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001008. Cochrane Database Syst Rev 1998;(2).

26. Bize R, Burnand B, Mueller Y, Cornuz J. Biomedical risk assessment as an aid for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(4).
27. Cahill K, Perera R. Competitions and incentives for smoking cessation. Cochrane Database Syst Rev 2008;(3).
28. Lancaster T, Stead LF. Silver acetate for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1997 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000191. Cochrane Database Syst Rev 1997;(3).
29. Park E-W, Schultz JK, Tudiver F, Campbell T, Becker L. Enhancing partner support to improve smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(3).
30. Secker-Walker RH, Gnich W, Platt S, Lancaster T. Community interventions for reducing smoking among adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2002;(2).
31. Carr AB, Ebbert JO. Interventions for tobacco cessation in the dental setting. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(1).
32. Lancaster T, Silagy C, Fowler G. Training health professionals in smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(3).
33. David S, Lancaster T, Stead LF, Evins AE. Opioid antagonists for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database of Systematic Reviews 2006 Issue 4. Chichester (UK): John Wiley & Sons, Ltd, 2006.
34. Hughes JR, Stead LF, Lancaster T. Anxiolytics for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(4).
35. Lancaster T, Stead LF. Mecamylamine (a nicotine antagonist) for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001009. Cochrane Database Syst Rev 1998;(2).
36. Stead LF, Hughes JR. Lobeline for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1997 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000124. Cochrane Database Syst Rev 1997;(3).
37. Stead LF, Lancaster T. Nicobrevin for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(2).
38. Grimshaw GM, Stanton A. Tobacco cessation interventions for young people. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
39. Hajek P, Stead LF. Aversive smoking for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2001;(3).
40. Cahill K, Perera R. Quit and Win contests for smoking cessation. Cochrane Database Syst Rev 2008;(4).

41. Stead LF, Lancaster T. Interventions for preventing tobacco sales to minors. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
42. Stead LF, Lancaster T. Interventions to reduce harm from continued tobacco use. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).
43. Thomas R, Perera R. School-based programmes for preventing smoking. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).
44. Thomas RE, Baker P, Lorenzetti D. Family-based programmes for preventing smoking by children and adolescents. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
45. Ussher M. Exercise interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
46. White AR, Rampes H, Campbell JL. Acupuncture and related interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(1).
47. Foster C, Hillsdon M, Thorogood M. Interventions for promoting physical activity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
48. Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roque IF, Richter B, Mauricio D. Exercise or exercise and diet for preventing type 2 diabetes mellitus. Cochrane Database Syst Rev 2008;(3):CD003054.
49. Shaw K, Gennat H, O'Rourke P, Del Mar C. Exercise for overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
50. Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).
51. Ashworth NL, Chad KE, Harrison EL, Reeder BA, Marshall SC. Home versus center based physical activity programs in older adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
52. Jackson NW, Howes FS, Gupta S, Doyle JL, Waters E. Policy interventions implemented through sporting organisations for promoting healthy behaviour change. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
53. Mulrow CD, Chiquette E, Angel L, Cornell J, Summerbell C, Anagnostelis B et al. Dieting to reduce body weight for controlling hypertension in adults. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000484. Cochrane Database Syst Rev 1998;(4).
54. Nield L, Summerbell CD, Hooper L, Whittaker V, Moore H. Dietary advice for the prevention of type 2 diabetes mellitus in adults. Cochrane Database Syst Rev 2008;(3):CD005102.

55. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Long-term non-pharmacological weight loss interventions for adults with prediabetes. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
56. Norris SL, Zhang X, Avenell A, Gregg E, Brown TJ, Schmid CH et al. Long-term non-pharmacological weight loss interventions for adults with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
57. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus. Cochrane Database Syst Rev 2005;(1).
58. Padwal R, Li SK, Lau DC. Long-term pharmacotherapy for obesity and overweight. Cochrane Database Syst Rev 2003;(4).
59. Shaw K, O'Rourke P, Del Mar C, Kenardy J. Psychological interventions for overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
60. Thomas DE, Elliott EJ, Baur L. Low glycaemic index or low glycaemic load diets for overweight and obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).
61. He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).
62. Brunner EJ, Rees K, Ward K, Burke M, Thorogood M. Dietary advice for reducing cardiovascular risk. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(4).
63. Hooper L, Bartlett C, Davey SG, Ebrahim S. Advice to reduce dietary salt for prevention of cardiovascular disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).
64. Hooper L, Summerbell CD, Higgins JPT, Thompson RL, Clements G, Capps N et al. Reduced or modified dietary fat for preventing cardiovascular disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(2).
65. Jürgens G, Graudal NA. Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).
66. Pirozzo S, Summerbell C, Cameron C, Glasziou P. Advice on low-fat diets for obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2002;(2).
67. Beyer FR, Dickinson HO, Nicolson DJ, Ford GA, Mason J. Combined calcium, magnesium and potassium supplementation for the management of primary hypertension in adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).

68. Ni MC, Dunshea-Mooij CAE, Bennett D, Rodgers A. Chitosan for overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(3).
69. Priebe MG, van Binsbergen JJ, de Vos R, Vonk RJ. Whole grain foods for the prevention of type 2 diabetes mellitus. Cochrane Database Syst Rev 2008;(1):CD006061.
70. Beletate V, El Dib RP, Atallah AN. Zinc supplementation for the prevention of type 2 diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
71. Curioni C, André C, Veras R. Weight reduction for primary prevention of stroke in adults with overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
72. Hartweg J, Perera R, Montori V, Dinneen S, Neil HAW, Farmer A. Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
73. Hooper L, Thompson RL, Harrison RA, Summerbell CD, Moore H, Worthington HV et al. Omega 3 fatty acids for prevention and treatment of cardiovascular disease. Cochrane Database Syst Rev 2004;(4):CD003177.
74. Kelly S, Frost G, Whittaker V, Summerbell C. Low glycaemic index diets for coronary heart disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(4).
75. Kelly SAM, Summerbell CD, Brynes A, Whittaker V, Frost G. Wholegrain cereals for coronary heart disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database of Systematic Reviews 2007 Issue 2. Chichester (UK): John Wiley & Sons, Ltd, 2007.
76. Nield L, Moore HJ, Hooper L, Cruickshank JK, Vyas A, Whittaker V et al. Dietary advice for treatment of type 2 diabetes mellitus in adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).
77. Pittler MH, Thompson CJ, Ernst E. Artichoke leaf extract for treating hypercholesterolaemia. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2002;(3).
78. Poustie VJ, Rutherford P. Dietary treatment for familial hypercholesterolaemia. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2001;(2).
79. Thompson RL, Summerbell CD, Hooper L, Higgins JPT, Little PS, Talbot D et al. Dietary advice given by a dietitian versus other health professional or self-help resources to reduce blood cholesterol. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2003;(3).
80. Fahey T, Schroeder K, Ebrahim S. Interventions used to improve control of blood pressure in patients with hypertension. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
81. Hawthorne K, Robles Y, Cannings-John R, Edwards AG. Culturally appropriate health education for type 2 diabetes mellitus in ethnic minority groups. Cochrane Database Syst Rev 2008;(3).

82. Van de Laar FA, Lucassen PL, Akkermans RP, van De Lisdonk EH, De Grauw WJ. Alpha-glucosidase inhibitors for people with impaired glucose tolerance or impaired fasting blood glucose. Cochrane Database Syst Rev 2006;(4).
83. Ebrahim S, Beswick A, Burke M, Davey SG. Multiple risk factor interventions for primary prevention of coronary heart disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
84. Bosch-Capblanch X, Abba K, Prictor M, Garner P. Contracts between patients and healthcare practitioners for improving patients' adherence to treatment, prevention and health promotion activities. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(2).
85. Heather OD, Fiona C, Fiona RB, Donald JN, Julia VC, Gary AF et al. Relaxation therapies for the management of primary hypertension in adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
86. Sheikh L, Johnston S, Thangaratinam S, Kilby MD, Khan KS. A review of the methodological features of systematic reviews in maternal medicine. BMC Med 2007; 5: 10.
87. Jadad AR, Cook DJ, Jones A, Klassen TP, Tugwell P, Moher M et al. Methodology and reports of systematic reviews and meta-analyses: a comparison of Cochrane reviews with articles published in paper-based journals. JAMA 1998; 280: 278-80.
88. Jorgensen AW, Hilden J, Gotzsche PC. Cochrane reviews compared with industry supported meta-analyses and other meta-analyses of the same drugs: systematic review. BMJ 2006; 333: 782.
89. Shea B, Boers M, Grimshaw JM, Hamel CD, Bouter LM. Does updating improve the methodological and reporting quality of systematic reviews? BMC Medical Research Methodology 2006; 6: 27.
90. Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ 2007; 334: 885.
91. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. Hypertension 2006; 48:861-9.
92. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ 2004; 328: 1519.
93. Doll R, Hill AB. The mortality of doctors in relation to their smoking habits: a preliminary report: (Reprinted from Br Med J 1954:ii;1451-5). BMJ 2004; 328: 1529-33.
94. Canto JG, Iskandrian AE. Major risk factors for cardiovascular disease: debunking the "only 50%" myth. JAMA 2003; 290: 947-9.
95. Greenland P, Knoll MD, Stamler J, Neaton JD, Dyer AR, Garside DB et al. Major Risk Factors as Antecedents of Fatal and Nonfatal Coronary Heart Disease Events. JAMA: The Journal of the American Medical Association 2003; 290: 891-7.

96. Yusuf S, Hawken S, Èunpuu S, Dans T, Avezum A, Lanas F et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. The Lancet 2004; 364: 937-52.
97. Strand BH, Tverdal A. Can cardiovascular risk factors and lifestyle explain the educational inequalities in mortality from ischaemic heart disease and from other heart diseases? 26 year follow up of 50 000 Norwegian men and women. J Epidemiol Community Health 2004; 58: 705-9.
98. Laaksonen M, Talala K, Martelin T, Rahkonen O, Roos E, Helakorpi S et al. Health behaviours as explanations for educational level differences in cardiovascular and all-cause mortality: a follow-up of 60 000 men and women over 23 years. Eur J Public Health 2008; 18: 38-43.
99. Schrijvers CT, Stronks K, van de Mheen HD, Mackenbach JP. Explaining educational differences in mortality: the role of behavioral and material factors. Am J Public Health 1999; 89: 535-40.
100. van Oort FVA, van Lenthe FJ, Mackenbach JP. Material, psychosocial, and behavioural factors in the explanation of educational inequalities in mortality in the Netherlands. J Epidemiol Community Health 2005; 59:214-20.
101. Graham H, Power C. Childhood disadvantage and health inequalities: a framework for policy based on lifecourse research. Child Care Health Dev 2004; 30: 671-8.
102. Elstad JI. Sosioøkonomiske ulikheter i helse - teorier og forklaringer. Rapport 07/2005. Oslo: Sosial- og helsedirektoratet, 2005.
103. Whitehead M. A typology of actions to tackle social inequalities in health. J Epidemiol Community Health 2007; 61: 473-8.
104. Smedslund G, Steiro A, Winsvold A, Hammerstrøm K. Effekt av tiltak for å fremme et sunnere kosthold og økt fysisk aktivitet, spesielt i grupper med lav sosioøkonomisk status.. Rapport fra Kunnskapssenteret nr 08 - 2008. Oslo: Nasjonalt kunnskapssenter for helsetjenesten, 2008.
105. Prevention of cardiovascular disease. Guidance on the prevention of cardiovascular disease at the population level. Expected date of issue March 2010. NICE, 2008. http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11881
106. Getz L, Sigurdsson JA, Hetlevik I, Kirkengen AL, Romundstad S, Holmen J. Estimating the high risk group for cardiovascular disease in the Norwegian HUNT 2 population according to the 2003 European guidelines: modelling study. BMJ 2005; 331: 551.

Vedlegg 1 Søkestrategi

Cochrane Library Issue 4 2007 CDSR, DARE og HTA

#1 MeSH descriptor Exercise, this term only
#2 MeSH descriptor Exercise Therapy, this term only
#3 MeSH descriptor Sports, this term only
#4 MeSH descriptor Gymnastics, this term only
#5 MeSH descriptor Bicycling, this term only
#6 MeSH descriptor Running, this term only
#7 MeSH descriptor Jogging, this term only
#8 MeSH descriptor Skiing, this term only
#9 MeSH descriptor Swimming, this term only
#10 MeSH descriptor Walking, this term only
#11 MeSH descriptor Physical Fitness, this term only
#12 MeSH descriptor Physical Education and Training, this term only
#13 MeSH descriptor Diet, this term only
#14 MeSH descriptor Diet, Atherogenic, this term only
#15 MeSH descriptor Diet Therapy, this term only
#16 MeSH descriptor Caloric Restriction, this term only
#17 MeSH descriptor Diabetic Diet, this term only
#18 MeSH descriptor Diet, Carbohydrate-Restricted, this term only
#19 MeSH descriptor Diet, Fat-Restricted, this term only
#20 MeSH descriptor Diet, Mediterranean, this term only
#21 MeSH descriptor Diet, Reducing, this term only
#22 MeSH descriptor Diet, Sodium-Restricted, this term only
#23 MeSH descriptor Diet, Vegetarian, this term only
#24 MeSH descriptor Diet, Macrobiotic, this term only
#25 MeSH descriptor Diet, Carbohydrate-Restricted, this term only
#26 MeSH descriptor Nutrition Therapy, this term only
#27 MeSH descriptor Weight Loss, this term only
#28 MeSH descriptor Smoking, this term only
#29 MeSH descriptor Smoking Cessation, this term only
#30 MeSH descriptor Complementary Therapies explode all trees
#31 (exercis* or walk or walking or cycling or bikeing or bicycling or jogging or swimming or running or gymnastics):ti or (exercis* or walk or walking or cycling or bikeing or bicycling or jogging or swimming or running or gymnastics):ab

#32 (physical NEXT (fitness or condition$ or activit$ or training)):ti or (physical NEXT (fitness or condition$ or activit$ or training)):ab
#33 (diet or diets or nutrition NEXT therap$):ti or (diet or diets or nutrition NEXT therap$):ab
#34 (salt or sodium) NEAR/3 (free or low or restrict$ or reduc$):ti or (salt or sodium) NEAR/3 (free or low or restrict$ or reduc$):ab
#35 (caloric or calory or calorie or calories) NEAR/3 (restrict$ or reduc$ or free):ti or (caloric or calory or calorie or calories) NEAR/3 (restrict$ or reduc$ or free):ab
#36 (weight NEAR/3 (loss or lose or losing or reduc*)):ti or (weight NEAR/3 (loss or lose or losing or reduc*)):ab
#37 (smoking):ti or (smoking):ab
#38 (complementary or alternative or traditional) NEXT (therap$ or medicine):ti or (complementary or alternative or traditional) NEXT (therap$ or medicine):ab
#39 (acupuncture or acupressure or homeopathy or yoga or relaxation or relaxing):ti or (acupuncture or acupressure or homeopathy or yoga or relaxation or relaxing):ab
#40 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39)

Vedlegg 2 Inkluderte Cochrane-oversikter

1. Abbot NC, Stead LF, White AR, Barnes J. Hypnotherapy for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 2 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001008. Cochrane Database Syst Rev 1998;(2).
2. Ashworth NL, Chad KE, Harrison EL, Reeder BA, Marshall SC. Home versus center based physical activity programs in older adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
3. Bala M, Strzeszynski L, Cahill K. Mass media interventions for smoking cessation in adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
4. Beletate V, El Dib RP, Atallah AN. Zinc supplementation for the prevention of type 2 diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
5. Beyer FR, Dickinson HO, Nicolson DJ, Ford GA, Mason J. Combined calcium, magnesium and potassium supplementation for the management of primary hypertension in adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).
6. Bize R, Burnand B, Mueller Y, Cornuz J. Biomedical risk assessment as an aid for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(4).
7. Bosch-Capblanch X, Abba K, Prictor M, Garner P. Contracts between patients and healthcare practitioners for improving patients' adherence to treatment, prevention and health promotion activities. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(2).
8. Brunner EJ, Rees K, Ward K, Burke M, Thorogood M. Dietary advice for reducing cardiovascular risk. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(4).
9. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
10. Cahill K, Perera R. Quit and Win contests for smoking cessation. Cochrane Database Syst Rev 2008;(4).

11. Cahill K, Perera R. Competitions and incentives for smoking cessation. Cochrane Database Syst Rev 2008;(3).
12. Carr AB, Ebbert JO. Interventions for tobacco cessation in the dental setting. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(1).
13. Curioni C, André C, Veras R. Weight reduction for primary prevention of stroke in adults with overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
14. David S, Lancaster T, Stead LF, Evins AE. Opioid antagonists for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database of Systematic Reviews 2006 Issue 4. Chichester (UK): John Wiley & Sons, Ltd, 2006.
15. Ebrahim S, Beswick A, Burke M, Davey SG. Multiple risk factor interventions for primary prevention of coronary heart disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
16. Fahey T, Schroeder K, Ebrahim S. Interventions used to improve control of blood pressure in patients with hypertension. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
17. Foster C, Hillsdon M, Thorogood M. Interventions for promoting physical activity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
18. Gourlay SG, Stead LF, Benowitz NL. Clonidine for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(3).
19. Grimshaw GM, Stanton A. Tobacco cessation interventions for young people. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
20. Hajek P, Stead LF. Aversive smoking for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2001;(3).
21. Hajek P, Stead LF, West R, Jarvis M, Lancaster T. Relapse prevention interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
22. Hartweg J, Perera R, Montori V, Dinneen S, Neil HAW, Farmer A. Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
23. Hawthorne K, Robles Y, Cannings-John R, Edwards AG. Culturally appropriate health education for type 2 diabetes mellitus in ethnic minority groups. Cochrane Database Syst Rev 2008;(3).
24. He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).
25. Heather OD, Fiona C, Fiona RB, Donald JN, Julia VC, Gary AF et al. Relaxation therapies for the management of primary hypertension in adults. Coch-

rane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
26. Hooper L, Summerbell CD, Higgins JPT, Thompson RL, Clements G, Capps N et al. Reduced or modified dietary fat for preventing cardiovascular disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(2).
27. Hooper L, Bartlett C, Davey SG, Ebrahim S. Advice to reduce dietary salt for prevention of cardiovascular disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).
28. Hooper L, Thompson RL, Harrison RA, Summerbell CD, Moore H, Worthington HV et al. Omega 3 fatty acids for prevention and treatment of cardiovascular disease. Cochrane Database Syst Rev 2004;(4).
29. Hughes JR, Stead LF, Lancaster T. Anxiolytics for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(4).
30. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
31. Jackson NW, Howes FS, Gupta S, Doyle JL, Waters E. Policy interventions implemented through sporting organisations for promoting healthy behaviour change. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
32. Jürgens G, Graudal NA. Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).
33. Kaper J, Wagena EJ, Severens JL, Van Schayck CP. Healthcare financing systems for increasing the use of tobacco dependence treatment. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
34. Kelly S, Frost G, Whittaker V, Summerbell C. Low glycaemic index diets for coronary heart disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(4).
35. Kelly SAM, Summerbell CD, Brynes A, Whittaker V, Frost G. Wholegrain cereals for coronary heart disease. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database of Systematic Reviews 2007 Issue 2. Chichester (UK): John Wiley & Sons, Ltd, 2007.
36. Lancaster T, Stead LF. Silver acetate for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1997 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000191. Cochrane Database Syst Rev 1997;(3).
37. Lancaster T, Stead LF. Mecamylamine (a nicotine antagonist) for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 2

John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001009. Cochrane Database Syst Rev 1998;(2).
38. Lancaster T, Silagy C, Fowler G. Training health professionals in smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(3).
39. Lancaster T, Stead LF. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(4).
40. Lancaster T, Stead LF. Self-help interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(3).
41. Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
42. Lovato C, Linn G, Stead LF, Best A. Impact of tobacco advertising and promotion on increasing adolescent smoking behaviours. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2003;(3).
43. Moher M, Hey K, Lancaster T. Workplace interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
44. Mulrow CD, Chiquette E, Angel L, Cornell J, Summerbell C, Anagnostelis B et al. Dieting to reduce body weight for controlling hypertension in adults. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000484. Cochrane Database Syst Rev 1998;(4).
45. Ni MC, Dunshea-Mooij CAE, Bennett D, Rodgers A. Chitosan for overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(3).
46. Nield L, Moore HJ, Hooper L, Cruickshank JK, Vyas A, Whittaker V et al. Dietary advice for treatment of type 2 diabetes mellitus in adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).
47. Nield L, Summerbell CD, Hooper L, Whittaker V, Moore H. Dietary advice for the prevention of type 2 diabetes mellitus in adults. Cochrane Database Syst Rev 2008;(3).
48. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus. Cochrane Database Syst Rev 2005;(1)
49. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Long-term non-pharmacological weight loss interventions for adults with prediabetes. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
50. Norris SL, Zhang X, Avenell A, Gregg E, Brown TJ, Schmid CH et al. Long-term non-pharmacological weight loss interventions for adults with type 2

diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
51. Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roque IF, Richter B, Mauricio D. Exercise or exercise and diet for preventing type 2 diabetes mellitus. Cochrane Database Syst Rev 2008;(3).
52. Padwal R, Li SK, Lau DC. Long-term pharmacotherapy for obesity and overweight. Cochrane Database Syst Rev 2003;(4).
53. Park E-W, Schultz JK, Tudiver F, Campbell T, Becker L. Enhancing partner support to improve smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(3).
54. Pirozzo S, Summerbell C, Cameron C, Glasziou P. Advice on low-fat diets for obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2002;(2).
55. Pittler MH, Thompson CJ, Ernst E. Artichoke leaf extract for treating hypercholesterolaemia. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2002;(3).
56. Poustie VJ, Rutherford P. Dietary treatment for familial hypercholesterolaemia. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2001;(2).
57. Priebe MG, van Binsbergen JJ, de Vos R, Vonk RJ. Whole grain foods for the prevention of type 2 diabetes mellitus. Cochrane Database Syst Rev 2008;(1).
58. Rice VH, Stead LF. Nursing interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
59. Rigotti NA, Munafo MR, Stead LF. Interventions for smoking cessation in hospitalised patients. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).
60. Secker-Walker RH, Gnich W, Platt S, Lancaster T. Community interventions for reducing smoking among adults. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2002;(2).
61. Serra C, Cabezas C, Bonfill X, Pladevall-Vila M. Interventions for preventing tobacco smoking in public places. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2000;(3).
62. Shaw K, O'Rourke P, Del Mar C, Kenardy J. Psychological interventions for overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
63. Shaw K, Gennat H, O'Rourke P, Del Mar C. Exercise for overweight or obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(4).
64. Sinclair HK, Bond CM, Stead LF. Community pharmacy personnel interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2004;(1).

65. Sowden A, Stead L. Community interventions for preventing smoking in young people. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2003;(1).
66. Sowden AJ, Arblaster L. Mass media interventions for preventing smoking in young people. Cochrane Database of Systematic Reviews: Reviews 1998 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD001006. Cochrane Database Syst Rev 1998;(4).
67. Stead LF, Hughes JR. Lobeline for smoking cessation. Cochrane Database of Systematic Reviews: Reviews 1997 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD000124. Cochrane Database Syst Rev 1997;(3).
68. Stead LF, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(2).
69. Stead LF, Lancaster T. Interventions for preventing tobacco sales to minors. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
70. Stead LF, Perera R, Lancaster T. Telephone counselling for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).
71. Stead LF, Lancaster T. Nicobrevin for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(2).
72. Stead LF, Lancaster T. Interventions to reduce harm from continued tobacco use. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).
73. Stead LF, Perera R, Bullen C, Mant D, Lancaster T. Nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2008;(1).
74. Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).
75. Thomas DE, Elliott EJ, Baur L. Low glycaemic index or low glycaemic load diets for overweight and obesity. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(3).
76. Thomas R, Perera R. School-based programmes for preventing smoking. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(3).
77. Thomas RE, Baker P, Lorenzetti D. Family-based programmes for preventing smoking by children and adolescents. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2007;(1).
78. Thompson RL, Summerbell CD, Hooper L, Higgins JPT, Little PS, Talbot D et al. Dietary advice given by a dietitian versus other health professional or self-help resources to reduce blood cholesterol. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2003;(3).

79. Ussher M. Exercise interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2005;(1).
80. Van de Laar FA, Lucassen PL, Akkermans RP, van De Lisdonk EH, De Grauw WJ. Alpha-glucosidase inhibitors for people with impaired glucose tolerance or impaired fasting blood glucose. Cochrane Database Syst Rev 2006;(4).
81. White AR, Rampes H, Campbell JL. Acupuncture and related interventions for smoking cessation. Cochrane Database of Systematic Reviews: Reviews. Cochrane Database Syst Rev 2006;(1).

Vedlegg 3 Oversikter fra DARE og HTA databasene

1. Ackermann RT, Mulrow CD, Ramirez G, Gardner CD, Morbidoni L, Lawrence VA. Garlic shows promise for improving some cardiovascular risk factors (DARE structured abstract). Archives of Internal Medicine 2001; 161: 813-824.
2. Alam S, Johnson AG. A meta-analysis of randomised controlled trials (RCT) among healthy normotensive and essential hypertensive elderly patients to determine the effect of high salt (NaC1) diet on blood pressure (DARE structured abstract). Journal of Human Hypertension 1999; 13: 367-374.
3. Allison DB, Faith MS. Hypnosis as an adjunct to cognitive-behavioral psychotherapy for obesity: a meta-analytic reappraisal (DARE structured abstract). Journal of Consulting and Clinical Psychology 1996; 64: 513-516.
4. Ammerman A, Pignone M, Fernandez L, Lohr K, Driscoll JA, Nester C et al. Counseling to promote a healthy diet (DARE structured abstract). 18. 2002.
5. Andersen S, Keller C, McGowan N. Smoking cessation: the state of the science. The utility of the transtheoretical model in guiding interventions in smoking cessation (DARE structured abstract). Online Journal of Knowledge Synthesis for Nursing 1999; 6.
6. Anderson JW, Konz EC, Frederich RC, Wood CL. Long-term weight-loss maintenance: a meta-analysis of US studies (DARE structured abstract). American Journal of Clinical Nutrition 2001; 74: 579-584.
7. Armstrong N, Simons-Morton B. Physical activity and blood lipids in adolescents (DARE structured abstract). Pediatric Exercise Science 1994; 6: 381-405.
8. Ashenden R, Silagy CA, Lodge M, Fowler G. A meta-analysis of the effectiveness of acupuncture in smoking cessation (DARE structured abstract). Drug and Alcohol Review 1997; 16: 33-40.
9. Ashenden R, Silagy C, Weller D. A systematic review of the effectiveness of promoting lifestyle change in general practice (DARE structured abstract). Family Practice 1997; 14: 160-175.
10. Asikainen TM, Kukkonen-Harjula K, Miilunpalo S. Exercise for health for early postmenopausal women: a systematic review of randomised con-

trolled trials (DARE provisional record). Sports Medicine 2004; 34: 753-778.

11. Astrup A, Grunwald GK, Melanson EL, Saris WH, Hill JO. The role of low-fat diets in body weight control: a meta-analysis of ad libitum dietary intervention studies (DARE structured abstract). International Journal of Obesity 2000; 24: 1545-1552.
12. Atlantis E, Barnes EH, Singh MA. Efficacy of exercise for treating overweight in children and adolescents: a systematic review (DARE provisional record). International Journal of Obesity 2006; 30:1027-1040.
13. Baer RA. Mindfulness training as a clinical intervention: a conceptual and empirical review (DARE provisional record). Clinical Psychology: Science and Practice 2003; 10:125-143.
14. Bains N, Pickett W, Hoey J. The use and impact of incentives in population-based smoking cessation programs: a review (DARE structured abstract). American Journal of Health Promotion 1998; 12: 307-320.
15. Bautista-Castana I, Doreste J, Serra-Majem L. Effectiveness of interventions in the prevention of childhood obesity (DARE structured abstract). European Journal of Epidemiology 2004; 19: 617-622.
16. Bent S, Padula A, Neuhaus J. Safety and efficacy of citrus aurantium for weight loss (DARE structured abstract). American Journal of Cardiology 2004; 94: 1359-1361.
17. Berry D, Sheehan R, Heschel R, Knafl K, Melkus G, Grey M. Family-based interventions for childhood obesity: a review (DARE structured abstract). Journal of Family Nursing 2004; 10: 429-449.
18. Blue CL, Black DR. Synthesis of intervention research to modify physical activity and dietary behaviors (DARE provisional record). Research and Theory for Nursing Practice 2005; 19: 25-61.
19. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials (DARE structured abstract). Jama 2001; 286: 1218-1227.
20. Boule NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in type 2 diabetes mellitus (DARE structured abstract). Diabetologia 2003; 46: 1071-1081.
21. Brandsma JW, Robeer BG, van den HS, Smit B, Wittens CH, Oostendorp RA. The effect of exercises on walking distance of patients with intermittent claudication: a study of randomized clinical trials (DARE structured abstract). Physical Therapy 1998; 78: 278-286.
22. Bravata DM, Sanders L, Huang J, Krumholz HM, Olkin I, Gardner CD et al. Efficacy and safety of low-carbohydrate diets: a systematic review (DARE structured abstract). Jama 2003; 289: 1837-1850.

23. Brown SA, Winter M, Upchurch S, Ramirez G, Anding R. Promoting weight loss in type II diabetes (DARE structured abstract). Diabetes Care 1996; 19: 613-624.
24. Brunner E, White I, Thorogood M, Bristow A, Curle D, Marmot M. Can dietary interventions change diet and cardiovascular risk factors: a meta-analysis of randomized controlled trials (DARE structured abstract). American Journal of Public Health 1997; 87: 1415-1422.
25. Castera P, Nguyen J, Gerlier JL, Robert S. L'acupuncture est-elle benefique dans le sevrage tabagique, son action est-elle specifique: une meta-analyse [Is acupuncture beneficial in smoking cessation, is its action specific: a meta-analysis] (DARE provisional record). Acupuncture and Moxibustion 2002; 1: 76-85.
26. Ciliska D, Kelly C, Petrov N, Chalmers J. A review of the weight loss interventions for obese people with non-insulin-dependent diabetes mellitus (DARE structured abstract). Canadian Journal of Diabetes Care 1995; 19: 10-15.
27. Clemmens D, Hayman LL. Increasing activity to reduce obesity in adolescent girls: a research review (DARE provisional record). Journal of Obstetric, Gynecologic and Neonatal Nursing 2004; 33: 801-808.
28. Conn VS, Minor MA, Burks KJ, Rantz MJ, Pomeroy SH. Integrative review of physical activity intervention research with aging adults (DARE structured abstract). Journal of the American Geriatrics Society 2003; 51: 1159-1168.
29. Cornelissen VA, Fagard RH. Effect of resistance training on resting blood pressure: a meta-analysis of randomized controlled trials (DARE structured abstract). Journal of Hypertension 2005; 23: 251-259.
30. Cutler JA, Follmann D, Allender PS. Randomized trials of sodium reduction: an overview (DARE structured abstract). American Journal of Clinical Nutrition 1997; 65: 643S-651S.
31. Dickinson HO, Mason JM, Nicolson DJ, Campbell F, Beyer FR, Cook J, V et al. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials (DARE structured abstract). Journal of Hypertension 2006; 24: 215-233.
32. Dodd K, Shields N. A systematic review of the outcomes of cardiovascular exercise programs for people with Down syndrome (DARE structured abstract). Archives of Physical Medicine and Rehabilitation 2005; 86: 2051-2058.
33. Drukker M, de Bie RA, van Rossum E. The effects of exercise training in institutionalized elderly people: a systematic review (DARE structured abstract). Physical Therapy Reviews 2001; 6: 273-285.
34. Eakin EG, Glasgow RE, Riley KM. Review of primary care-based physical activity intervention studies: effectiveness and implications for practice and future research (DARE structured abstract). Journal of Family Practice 2000; 49: 158-168.

35. Ebrahim S, Smith GD. Systematic review of randomised controlled trials of multiple risk factor interventions for preventing coronary heart disease (DARE structured abstract). Bmj 1997; 314:1666-1674.
36. Epstein LH, Coleman KJ, Myers MD. Exercise in treating obesity in children and adolescents (DARE structured abstract). Medicine and Science in Sports and Exercise 1996; 28: 428-435.
37. Eriksen MP, Gottlieb NH. A review of the health impact of smoking control at the workplace (DARE structured abstract). American Journal of Health Promotion 1998; 13: 83-104.
38. Ernst E, Pittler MH. Chitosan as a treatment for body weight reduction: a meta-analysis (DARE structured abstract). Perfusion 1998; 11: 461-465.
39. Ernst E. Acupuncture/acupressure for weight reduction: a systematic review (DARE structured abstract). Wiener Klinische Wochenschrift 1997; 109: 60-62.
40. Canter PH, Ernst E. Insufficient evidence to conclude whether or not transcendental meditation decreases blood pressure: results of a systematic review of randomized clinical trials (DARE structured abstract). Journal of Hypertension 2004; 22: 2049-2054.
41. Ernst E, Huntley A. Tea tree oil: a systematic review of randomized clinical trials (DARE structured abstract). Forschende Komplementarmedizin und Klassische Naturheilkunde 2000; 7: 17-20.
42. Ernst E, Pittler MH. The efficacy and safety of feverfew (Tanacetum parthenium L.): an update of a systematic review (DARE structured abstract). Public Health Nutrition 2000; 3: 509-514.
43. Faas A. Exercises: which ones are worth trying, for which patients, and when? (DARE structured abstract). Spine 1996; 21: 2874-2878.
44. Fagard RH. Prescription and results of physical activity (DARE structured abstract). Journal of Cardiovascular Pharmacology 1995; 25: S20-S27.
45. Fagard RH. The role of exercise in blood pressure control: supportive evidence (DARE structured abstract). Journal of Hypertension 1995; 13: 1223-1227.
46. Finlay SJ, Faulkner G. Physical activity promotion through the mass media: inception, production, transmission and consumption (DARE structured abstract). Preventive Medicine 2005; 40: 121-130.
47. Fletcher A, Rake C. Effectiveness of interventions to promote healthy eating in elderly people living in the community: a review (DARE structured abstract). 78. 1998.
48. Flodmark CE, Marcus C, Britton M. Interventions to prevent obesity in children and adolescents: a systematic literature review (DARE structured abstract). International Journal of Obesity 2006; 30: 579-589.
49. Fogelholm M, Lahti-Koski M. Community health-promotion interventions with physical activity: does this approach prevent obesity? (DARE structured abstract). Scandinavian Journal of Nutrition 2002; 46: 173-177.

50. Fogelholm M, Kukkonen-Harjula K. Does physical activity prevent weight gain: a systematic review (DARE structured abstract). Obesity Reviews 2000; 1: 95-111.
51. France EK, Glasgow RE, Marcus AC. Smoking cessation interventions among hospitalized patients: what have we learned? (DARE structured abstract). Preventive Medicine 2001; 32: 376-388.
52. Franz MJ. Effectiveness of weight loss and maintenance interventions in women (DARE structured abstract). Current Diabetes Reports 2004; 4: 387-393.
53. Gibson LJ, Peto J, Warren JM, dos SS, I. Lack of evidence on diets for obesity for children: a systematic review (DARE provisional record). International Journal of Epidemiology 2006; 35: 1544-1552.
54. Gorin SS, Heck JE. Meta-analysis of the efficacy of tobacco counseling by health care providers (DARE provisional record). Cancer Epidemiology, Biomarkers and Prevention 2004; 13: 2012-2022.
55. Graudal NA, Galloe AM, Garred P. Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride: a meta-analysis (DARE structured abstract). Jama 1998; 279:1383-1391.
56. Halbert JA, Silagy CA, Finucane P, Withers RT, Hamdorf PA. Exercise training and blood lipids in hyperlipidemic and normolipidemic adults: a meta-analysis of randomized, controlled trials (DARE structured abstract). European Journal of Clinical Nutrition 1999; 53: 514-522.
57. Halbert JA, Silagy CA, Finucane P, Withers RT, Hamdorf PA, Andrews GR. The effectiveness of exercise training in lowering blood pressure: a meta-analysis of randomised controlled trials of 4 weeks or longer (DARE structured abstract). Journal of Human Hypertension 1997; 11 :641-649.
58. Hamer M, Taylor A, Steptoe A. The effect of acute aerobic exercise on stress related blood pressure responses: a systematic review and meta-analysis (DARE provisional record). Biological Psychology 2006; 71: 183-190.
59. Heymsfield SB, van Mierlo CA, van der Knaap HC, Heo M, Frier H, I. Weight management using a meal replacement strategy: meta and pooling analysis from six studies (DARE structured abstract). International Journal of Obesity 2003; 27:537-549.
60. Hillsdon M, Thorogood M, Anstiss T, Morris J. Randomised controlled trials of physical activity promotion in free living populations: a review (DARE structured abstract). Journal of Epidemiology and Community Health 1995; 49: 448-453.
61. Hopkins DP, Briss PA, Ricard CJ, Husten CG, Carande-Kulis VG, Fielding JE et al. Reviews of evidence regarding interventions to reduce tobacco use and exposure to environmental tobacco smoke (DARE structured abstract). American Journal of Preventive Medicine 2001; 20: 16-66.

62. Innes KE, Bourguignon C, Taylor AG. Risk indices associated with the insulin resistance syndrome, cardiovascular disease, and possible protection with yoga: a systematic review (DARE structured abstract). Journal of the American Board of Family Practice 2005; 18: 491-519.
63. Kanji N, White AR, Ernst E. Anti-hypertensive effects of autogenic training: a systematic review (DARE structured abstract). Perfusion 1999; 12: 279-282.
64. Kanji N, Ernst E. Autogenic training for stress and anxiety: a systematic review (DARE structured abstract). Complementary Therapies in Medicine 2000; 8: 106-110.
65. Kelley G. Dynamic resistance exercise and resting blood pressure in adults: a meta-analysis (DARE structured abstract). Journal of Applied Physiology 1997; 82: 1559-1565.
66. Kelley G. Effects of aerobic exercise on ambulatory blood pressure: a meta-analysis (DARE structured abstract). Sports Medicine Training and Rehabilitation 1996; 7: 115-131.
67. Kelley GA. Aerobic exercise and resting blood pressure among women: a meta-analysis (DARE structured abstract). Preventive Medicine 1999; 28: 264-275.
68. Kelley GA, Sharpe KK. Aerobic exercise and resting blood pressure in older adults: a meta-analytic review of randomized controlled trials (DARE structured abstract). Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2001; 56A: M298-M303.
69. Kelley GA, Kelley KS, Tran Z, V. Aerobic exercise and lipids and lipoproteins in women: a meta-analysis of randomized controlled trials (DARE structured abstract). Journal of Women's Health 2004; 13: 1148-1164.
70. Kelley GA, Kelley KS. Aerobic exercise and HDL2-C: a meta-analysis of randomized controlled trials (DARE structured abstract). Atherosclerosis 2006; 184: 207-215.
71. Kelley GA, Kelley KS, Vu TZ. Aerobic exercise, lipids and lipoproteins in overweight and obese adults: a meta-analysis of randomized controlled trials (DARE structured abstract). International Journal of Obesity 2005; 29: 881-893.
72. Kelley GA, Kelley KS, Tran Z, V. Exercise, lipids, and lipoproteins in older adults: a meta-analysis (DARE structured abstract). Preventive Cardiology 2005; 8: 206-214.
73. Kelley GA, Sharpe KK. Progressive resistance exercise and resting blood pressure: a meta-analysis of randomized controlled trials (DARE structured abstract). Hypertension 2000; 35: 838-843.
74. Kelley GA, Kelley KS, Tran Z, V. Walking, lipids, and lipoproteins: a meta-analysis of randomized controlled trials (DARE structured abstract). Preventive Medicine 2004; 38: 651-661.

75. Ketola E, Sipila R, Makela M. Effectiveness of individual lifestyle interventions in reducing cardiovascular disease and risk factors (DARE structured abstract). Annals of Medicine 2000; 32: 239-251.
76. Keysor JJ, Jette AM. Have we oversold the benefit of late-life exercise? (DARE structured abstract). Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2001; 56A: M412-M423.
77. Kodama S, Tanaka S, Saito K, Shu M, Sone Y, Onitake F et al. Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis (DARE provisional record). Archives of Internal Medicine 2007; 167: 999-1008.
78. Kumanyika SK, Cutler JA. Dietary sodium reduction: is there cause for concern? (DARE structured abstract). Journal of the American College of Nutrition 1997; 16: 192-203.
79. Law M, Tang JL. An analysis of the effectiveness of interventions intended to help people stop smoking (DARE structured abstract). Archives of Internal Medicine 1995; 155: 1933-1941.
80. Lawlor DA, Hanratty B. The effect of physical activity advice given in routine primary care consultations: a systematic review (DARE structured abstract). Journal of Public Health Medicine 2001; 23: 219-226.
81. Lawrence D, Graber JE, Mills SL, Meissner H, I, Warnecke R. Smoking cessation interventions in U.S. racial/ethnic minority populations: an assessment of the literature (DARE structured abstract). Preventive Medicine 2003; 36: 204-216.
82. Manterola C, Pineda V, Vial M, Losada H, Munoz S. Surgery for morbid obesity: selection of operation based on evidence from literature review (DARE structured abstract). Obesity Surgery 2005; 15: 106-113.
83. Marckmann P, Gronbaek M. Fish consumption and coronary heart disease mortality: a systematic review of prospective cohort studies (DARE structured abstract). European Journal of Clinical Nutrition 1999; 53: 585-590.
84. McArthur DB. Heart healthy eating behaviors of children following a school-based intervention: a meta-analysis (DARE structured abstract). Issues in Comprehensive Pediatric Nursing 1998; 21: 35-48.
85. McLean N, Griffin S, Toney K, Hardeman W. Family involvement in weight control, weight maintenance and weight-loss interventions: a systematic review of randomised trials (DARE provisional record). International Journal of Obesity 2003; 27: 987-1005.
86. Mcrae M. A review of studies of garlic (Allium sativum) on serum lipids and blood pressure before and after 1994: does the amount of allicin released from garlic powder tablets play a role? (DARE provisional record). Journal of Chiropractic Medicine 2005; 4: 182-190.
87. McTigue KM, Hess R, Ziouras J. Obesity in older adults: a systematic review of the evidence for diagnosis and treatment (DARE provisional record). Obesity 2006; 14: 1485-1497.

88. Midgley JP, Matthew AG, Greenwood CM, Logan AG. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials (DARE structured abstract). Jama 1996; 275: 1590-1597.
89. Miller WC, Koceja DM, Hamilton EJ. A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention (DARE structured abstract). International Journal of Obesity 1997; 21: 941-947.
90. Mizushima S, Cappuccio FP, Nichols R, Elliott P. Dietary magnesium intake and blood pressure: a qualitative overview of the observational studies (DARE structured abstract). Journal of Human Hypertension 1998; 12: 447-453.
91. Morgan O. Approaches to increase physical activity: reviewing the evidence for exercise-referral schemes (DARE provisional record). Public Health 2005; 119: 361-370.
92. Mukuddem-Petersen J, Oosthuizen W, Jerling JC. A systematic review of the effects of nuts on blood lipid profiles in humans (DARE structured abstract). Journal of Nutrition 2005; 135: 2082-2089.
93. Mulrow C, Lawrence V, Ackerman R, Ramirez G, Morbidoni L, Aguilar C et al. Garlic: effects on cardiovascular risks and disease, protective effects against cancer, and clinical adverse effects (DARE structured abstract). 140. 2000.
94. Murphy MH, Nevill AM, Murtagh EM, Holder RL. The effect of walking on fitness, fatness and resting blood pressure: a meta-analysis of randomised, controlled trials (DARE provisional record). Preventive Medicine 2007; 44: 377-385.
95. Nakao M, Yano E, Nomura S, Kuboki T. Blood pressure-lowering effects of biofeedback treatment in hypertension: a meta-analysis of randomized controlled trials (DARE structured abstract). Hypertension Research 2003; 26: 37-46.
96. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS, Brehm BJ et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials (DARE structured abstract). Archives of Internal Medicine 2006; 166: 285-293.
97. Opperman AM, Venter CS, Oosthuizen W, Thompson RL, Vorster HH. Meta-analysis of the health effects of using the glycaemic index in meal-planning (DARE provisional record). British Journal of Nutrition 2004; 92: 367-381.
98. Pittler MH, Stevinson C, Ernst E. Chromium picolinate for reducing body weight: a meta-analysis of randomized trials (DARE structured abstract). International Journal of Obesity 2003; 27: 522-529.
99. Pittler MH, Ernst E. Ginkgo biloba extract for the treatment of intermittent claudication: a meta-analysis of randomized trials (DARE structured abstract). American Journal of Medicine 2000; 108: 276-281.

100. Pittler MH, Ernst E. Guar gum for body weight reduction: meta-analysis of randomized trials (DARE structured abstract). American Journal of Medicine 2001; 110: 724-730.
101. Proper K, I, Koning M, van der Beek AJ, Hildebrandt VH, Bosscher RJ, van Mechelen W. The effectiveness of worksite physical activity programs on physical activity, physical fitness, and health (DARE structured abstract). Clinical Journal of Sport Medicine 2003; 13: 106-117.
102. Ritvo PG, Irvine MJ, Lindsay EA, Kraetschmer N, Blair N, Shnek ZM. A critical review of research related to family physician-assisted smoking cessation interventions (DARE structured abstract). Cancer Prevention and Control 1997; 1: 289-303.
103. Robeer GG, Brandsma JW, van den Heuvel SP, Smit B, Oostendorp RA, Wittens CH. Exercise therapy for intermittent claudication: a review of the quality of randomised clinical trials and evaluation of predictive factors (DARE structured abstract). European Journal of Vascular and Endovascular Surgery 1998; 15: 36-43.
104. Rydwik E, Frandin K, Akner G. Effects of physical training on physical performance in institutionalised elderly patients (70+) with multiple diagnoses (DARE provisional record). Age and Ageing 2004; 33: 13-23.
105. Shekelle PG, Hardy M, Morton SC, Coulter I, Venuturupalli S, Favreau J et al. Are Ayurvedic herbs for diabetes effective? (DARE provisional record). Journal of Family Practice 2005; 54: 876-886.
106. Stevinson C, Pittler MH, Ernst E. Garlic for treating hypercholesterolemia: a meta-analysis of randomized clinical trials (DARE structured abstract). Annals of Internal Medicine 2000; 133: 420-429.
107. Studer M, Briel M, Leimenstoll B, Glass TR, Bucher HC. Effect of different antilipidemic agents and diets on mortality: a systematic review (DARE structured abstract). Archives of Internal Medicine 2005; 165: 725-730.
108. Tang JL, Armitage JM, Lancaster T, Silagy CA, Fowler GH, Neil HA. Systematic review of dietary intervention trials to lower blood total cholesterol in free-living subjects (DARE structured abstract). Bmj 1998; 316: 1213-1220.
109. Thompson Coon JS, Ernst E. Herbs for serum cholesterol reduction: a systematic review (DARE structured abstract). Journal of Family Practice 2003; 52: 468-478.
110. Tsukayama H, Yamashita H. Systematic review of clinical trials on acupuncture in the Japanese literature (DARE provisional record). Clinical Acupuncture and Oriental Medicine 2002; 3: 105-113.
111. Ulbricht C, Basch E, Szapary P, Hammerness P, Axentsev S, Boon H et al. Guggul for hyperlipidemia: a review by the Natural Standard Research Collaboration (DARE provisional record). Complementary Therapies in Medicine 2005; 13: 279-290.
112. van Dixhoorn J, White A. Relaxation therapy for rehabilitation and prevention in ischaemic heart disease: a systematic review and meta-analysis

(DARE provisional record). European Journal of Cardiovascular Prevention and Rehabilitation 2005; 12: 193-202.

113. van Sluijs EM, van Poppel MN, van Mechelen W. Stage-based lifestyle interventions in primary care: are they effective? (DARE provisional record). American Journal of Preventive Medicine 2004; 26: 330-343.
114. Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials (DARE structured abstract). Annals of Internal Medicine 2002; 136: 493-503.
115. Wilcox S, Parra-Medina D, Thompson-Robinson M, Will J. Nutrition and physical activity interventions to reduce cardiovascular disease risk in health care settings: a quantitative review with a focus on women (DARE structured abstract). Nutrition Reviews 2001; 59: 197-214.
116. Wu P, Wilson K, Dimoulas P, Mills EJ. Effectiveness of smoking cessation therapies: a systematic review and meta-analysis (DARE provisional record). BMC Public Health 2006; 6: 300.
117. Yamaoka K, Tango T. Efficacy of lifestyle education to prevent type 2 diabetes: a meta-analysis of randomized controlled trials (DARE provisional record). Diabetes Care 2005; 28: 2780-2786.
118. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes (DARE structured abstract). Diabetes Care 2003; 26: 1277-1294.
119. Yu-Poth S, Zhao G, Etherton T, Naglak M, Jonnalagadda S, Kris-Etherton PM. Effects of the National Cholesterol Education Program's step I and step II dietary intervention programs on cardiovascular disease risk factors: a meta-analysis (DARE structured abstract). American Journal of Clinical Nutrition 1999; 69: 632-646.
120. Yucha CB, Clark L, Smith M, Uris P, LaFleur B, Duval S. The effect of biofeedback in hypertension (DARE structured abstract). Applied Nursing Research 2001; 14: 29-35.
121. Wang D, Connock M, Barton P, Fry-Smith A, Aveyard P, Moore D. Cut down to quit with nicotine replacement therapies (NRT) for smoking cessation: systematic review and economic analysis (update of NICE Guidance 39) - HTA technology assessment report, ref 06/09/01 (project) (Brief record). 2008.
122. Adelaide Health Technology Assessment on behalf of National Horizon Scanning Unit (HealthPACT and MSAC). Program for the distribution of nicotine patches; horizon scanning prioritising summary - volume 13 (Brief record). 2006.
123. Agency for Healthcare Research and Quality. Ayurvedic interventions for diabetes mellitus: a systematic review (DARE structured abstract). 2001.
124. Basque Office for Health Technology Assessment, Department of Health, Basque Government O. Evaluation of the impact of different interventions in smoking cessation in the Basque Country and comparison between primary and specialised care (project) (Brief record). 2008.

125. Carroll R, Ali N, Azam N. Promoting physical activity in South Asian Muslim women through 'exercise on prescription' (DARE structured abstract). 2002.
126. Catalan Agency for Health Technology Assessment and Research. Tobacco control: a review of the strategies (DARE structured abstract). 2003.
127. Centre for Reviews and Dissemination (CRD). Systematic overview of population tobacco control interventions and their effects on social inequalities in health - systematic review (Brief record). 2008.
128. Cohen D, Eliasson M, Eriksson C, Gilljam H, Hedin A, Hellnius M-L et al. Smoking cessation methods (DARE structured abstract). 1998.
129. Danish Centre for Evaluation and Health Technology Assessment (DACEHTA). Health Technology Assessment of an Educational Program for patients with Type 2 Diabetes in a Continuation School after a Diabetes School Program - miscellaneous (Brief record). 2008.
130. Danish Centre for Evaluation and Health Technology Assessment (DACEHTA). Health technology assessment of the Diabetes School for type 2 diabetics - miscellaneous (Brief record). 2008.
131. Danish Centre for Evaluation and Health Technology Assessment (DACEHTA). Smoking cessation among patients in general practice. Which method is the most cost-effective? (Brief record). 2008.
132. Danish Institute for Health Services Research. Smoking cessation interventions in pharmacies. Demand from smokers and the ability of general practitioners to recruit participants (Brief record). 2004.
133. Eden KB, Orleans CT, Mulrow CD, Pender NJ, Teutsch SM. Clinical counseling and physical activity (DARE structured abstract). 2002.
134. German Agency of Health Technology Assessment at German Institute for Medical Documentation and Information (DAHTA). Efficiency and the effectiveness of behaviour related measures for the prevention of smoking cigarettes - an international review for evaluating the transferability to Germany (Brief record). 2008.
135. Gorgojo JL, Gonzalez EJ, Salvador LT. Efficacy, effectiveness and cost-effectiveness of interventions for smoking cessation IPE-03/40 (Public report) (DARE structured abstract). 2003.
136. HAYES, Inc. Biofeedback for the treatment of hypertension (Brief record). 2006.
137. Health Council of the Netherlands, Gezondheidsraad. Guidelines for a healthy diet 2006 (Brief record). 2006.
138. Hermes-DeSantis E. Smoking cessation therapies (Brief record). 2001.
139. Holtzman J, Schmitz K, Babes G, Kane RL, Duval S, Wilt TJ et al. Effectiveness of behavioral interventions to modify physical activity behaviors in general populations and cancer patients and survivors (DARE provisional record). 2004.
140. Institut fuer Qualitaet und Wirtschaftlichkeit im Gesundheitswesen (IQWiG). Evaluation of the benefits and harms of non-drug treatment

strategies in patients with essential hypertension: weight reduction (DARE structured abstract). 2006.
141. Institute for Clinical Systems Improvement. Behavioral therapy programs for weight loss in adults (DARE structured abstract). 2005.
142. Institute for Clinical Systems Improvement. Diet programs for weight loss in adults (DARE structured abstract). 2004.
143. Institute for Clinical Systems Improvement. Treatment of obesity in children and adolescents (DARE structured abstract). 2005.
144. National Horizon Scanning Centre. Rimonabant for smoking cessation, weight loss and cardiovascular risk factors of overweight/obesity - horizon scanning review (DARE structured abstract). 2004.
145. National Institute for Health and Clinical Excellence. Brief interventions and referral for smoking cessation in primary care and other settings (DARE structured abstract). 2006.
146. National Institute for Health and Clinical Excellence. Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling (DARE structured abstract). 2006.
147. National Institute for Clinical Excellence. Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation (DARE structured abstract). 2002.
148. National Institute for Health and Clinical Excellence. Workplace health promotion: how to help employees to stop smoking (DARE structured abstract). 2007.
149. New Zealand Health Technology Assessment. In adults without clinical cardiovascular disease what is the dose, intensity and type of physical activity required to produce an effect on the risk factors of blood pressure, lipid profiles and weight? Evidence Tables (Brief record). 2003.
150. NHS Centre for Reviews and Dissemination. A systematic review of interventions in the treatment and prevention of obesity (DARE structured abstract). 1997.
151. NHS Centre for Reviews and Dissemination. Preventing the uptake of smoking in young people (DARE structured abstract). 1999.
152. NHS Centre for Reviews and Dissemination. Smoking cessation: what the health service can do (DARE structured abstract). 1998.
153. NHS Q, I. Nicotine replacement therapy (NRT) and bupropion (Zyban) to help quit smoking (Brief record). 2001.
154. Ranney L, Melvin C, Lux L, McClain E, Morgan L, Lohr K. Tobacco use: prevention, cessation, and control (DARE structured abstract). 2006.
155. The Netherlands Organisation for Health Research and Development (ZonMw). Motivational interviewing embedded in planned diabetes care for Type 2 patients: effectiveness and efficiency in general practice especially to improve guideline recommendations on diet and exercise (Brief record). 2008.

156. U.S.Preventive Services Task Force. Behavioral counseling in primary care to promote physical activity: recommendations and rationale (Brief record). 2002.
157. Van den BA, Cleemput I, Van Linden A, Schoefs D, Ramaekers D, Bonneux L. Effectiveness and cost-effectiveness of treatments for smoking cessation (Brief record). 2004.
158. Woolacott NF, Jones L, Forbes CA, Mather LC, Sowden AJ, Song FJ et al. The clinical effectiveness and cost-effectiveness of bupropion and nicotine replacement therapy for smoking cessation: a systematic review and economic evaluation (DARE structured abstract). Health Technology Assessment 2002; 6:1-245.
159. NHS Centre for Reviews and Dissemination. The prevention and treatment of obesity (DARE structured abstract). 1997.

Vedlegg 4 Summaries of included Cochrane reviews

SMOKING CESSATION INTERVENTIONS LIKELY TO BE EFFECTIVE

Mass media interventions likely to be effective

Bala 2008	Mass media interventions for smoking cessation in adults
Study design	Randomized or quasi-randomized controlled trials allocating communities, regions or states to intervention or control conditions. Controlled trials without randomization, allocating communities, regions or states to intervention or to control conditions. Interrupted time series.
Population	Adults, 25 years or older who regularly smoke cigarettes
Intervention	Mass media defined as channels of communication such as television, radio, newspapers, billboards, posters, leaflets or booklets tended to reach large numbers of people, and which are not dependent on person-to-person contact.
Outcomes	Primary: Tobacco cessation, covered by prevalence rates, quit rates. Secondary: Tobacco reduction, covered by changes in the number of cigarettes purchased or smoked, prevalence of daily smoking, quit attempts.
Main results	Eleven campaigns met the inclusion criteria for this review. Studies differed in design, settings, duration, content and intensity of intervention, length of follow up, methods of evaluation and also in definitions and measures of smoking behaviour used. Among nine campaigns reporting smoking prevalence, significant decreases were observed in the California and Massachusetts state wide tobacco control campaigns compared with the rest of the USA. Some positive effects on prevalence in the whole population or in the subgroups were observed in three of the remaining seven studies. Three large-scale campaigns of the seven presenting results for tobacco consumption found statistically significant decreases. Among the seven studies presenting abstinence or quit rates, four showed some positive effect, although in one of them the effect was measured for quitting and cutting down combined. Among the three that did not show significant decreases, one demonstrated a significant intervention effect on smokers and ex-smokers combined.
Authors' conclusions	There is evidence that comprehensive tobacco control programmes which include mass media campaigns can be effective in changing smoking behaviour in adults, but the evidence comes from a heterogeneous group of studies of variable methodological quality. The intensity and duration of mass media campaigns may influence effectiveness, but length of follow up and concurrent secular trends and events can make this difficult to quantify. No consistent relationship was observed between campaign effectiveness and age, education, ethnicity or gender.

Lovato 2003	Impact of tobacco advertising and promotion on increasing adolescent smoking behaviours
Study design	Longitudinal studies that assessed individuals' smoking behaviour and exposure to advertising, receptivity or attitudes to tobacco advertising, or brand awareness at baseline, and assessed smoking behaviour at follow-ups.
Population	Adolescents 18 years of age or younger who were not regular smokers at baseline.
Intervention	The 'interventon' is tobacco mass media advertising by the industry, including tobacco promotion. Mass media channels of communication include advertising delivered through television, radio, newspapers, billboards, posters etc. Tobacco promotion includes give-aways such as t-shirts and other items bearing tobacco industry logos.
Outcomes	Self-reported smoking status (nonsmoker, current smoker, exsmoker).
Main results	Nine longitudinal studies that followed up a total of over 12,000 baseline nonsmokers met inclusion criteria. The studies measured exposure or receptivity to advertising and promotion in a variety of ways. All studies assessed smoking behaviour change in participants who reported not smoking at baseline. In all studies the nonsmoking adolescents who were more aware of tobacco advertising or receptive to it, were more likely to have experimented with cigarettes or become smokers at follow-up. There was variation in the strength of association, and the degree to which potential confounders were controlled for.
Authors' conclusions	Longitudinal studies consistently suggest that exposure to tobacco advertising and promotion is associated with the likelihood that adolescents will start to smoke. The strength of this association, the consistency of findings across numerous observational studies, temporality of exposure and smoking behaviours observed, as well as the theoretical plausibility regarding the impact of advertising supported this conclusion.

Sowden 1998	Mass media interventions for preventing smoking in young people
Study design	Randomised controlled trial in which the unit of randomisation was the school, community or geographical region. Controlled trial without randomisation allocating schools, communities or geographical regions. Time series.
Population	Young people aged less than 25 years.
Intervention	Mass media defined as channels of communication such as television, radio, newspapers, bill boards, posters, leaflets or booklets intended to reach large numbers of people and which are not dependent on person to person contact..
Outcomes	Primary measures of smoking behaviour: objective measures of smoking (saliva thiocyanate levels, alveolar CO) and self-reported smoking behaviour. Intermediate measures: intentions to smoke, attitudes to smoking, knowledge about smoking, decision making skills. refusal skills and self esteem/self-efficacy.
Main results	Six out of a total of 63 studies reporting information about mass media smoking campaigns met all of the inclusion criteria. All six studies used a controlled trial design. Two studies concluded that the mass media were effective in influencing the smoking behaviour of young people. Both of the effective campaigns had a solid theoretical basis, used formative research in designing the campaign messages and message broadcast was of reasonable intensity over extensive periods of time.
Authors' conclusions	There is some evidence that the mass media can be effective in preventing the uptake of smoking in young people, but overall the evidence is not strong.

Interventions given by health professionals likely to be effective

Carr 2006	Interventions for tobacco cessation in the dental setting
Study design	Randomized and pseudo-randomized controlled trials. The unit of randomization was the dentist or practice for the studies in the dental office setting, and college or high school for the studies in the community setting.
Population	Patients or subjects of any age reporting tobacco use and receiving oral health interventions by dental professionals.
Intervention	Any intervention to promote tobacco use cessation which included a component delivered by a dentist, dental hygienist, dental assistant or office staff in the dental practice setting or as part of a community effort.
Outcomes	Smoking and tobacco use cessation, assessed at least six months from the delivery of the intervention.
Main results	Six trials met the criteria for inclusion in this review. All studies employed behavioural interventions and only one offered pharmacotherapy as an interventional component. All studies assessed the efficacy of interventions for smokeless tobacco users, one of which included cigarettes smokers. All studies included an oral examination component. Pooling of the studies suggested that interventions conducted by oral health professionals increase tobacco abstinence rates (odds ratio [OR] 1.44; 95% confidence interval [CI]: 1.16 to 1.78) at 12 months or longer. Heterogeneity was evident (I^2 = 75%) and could not be adequately explained through subgroup or sensitivity analyses.
Authors' conclusions	Interventions for smokeless tobacco users in the dental setting, either in the dental office or in the school community, may increase the odds of quitting tobacco. Insufficient evidence exists to make conclusions about the effectiveness of these interventions for cigarette smokers. Differences between the studies limit the ability to make conclusive recommendations regarding the intervention components that should be incorporated into clinical practice.

Lancaster 2004	Physician advice for smoking cessation
Study design	Randomized controlled trials.
Population	Smokers of either gender recruited in any setting. Trials which only recruited pregnant women were excluded.
Intervention	Studies included if they compared physician advice to stop smoking versus no advice (or usual care), or differing levels of physician advice to stop smoking.
Outcomes	Primary: smoking cessation, or reduction in amount of cigarettes smoked. Secondary: effect of smoking advice on subsequent mortality and morbidity.
Main results	39 trials, conducted between 1972 and 2003, including over 31,000 smokers, were identified. In some trials, subjects were at risk of specified diseases (chest disease, diabetes, ischaemic heart disease), but most were from unselected populations. The most common setting for delivery of advice was primary care. Other settings included hospital wards and outpatient clinics, and industrial clinics. Pooled data from 17 trials of brief advice versus no advice (or usual care) revealed a significant increase in quit rates (relative risk (RR) 1.66, 95% confidence interval (CI) 1.42 to 1.94). Amongst 11 trials where the intervention was judged to be more intensive the estimated effect was higher (RR 1.84, 95% CI 1.60 to 2.13) but there was no statistical difference between the intensive and minimal subgroups. Direct comparison of intensive versus minimal advice showed a small advantage of intensive advice (RR 1.37, 95% CI 1.20 to 1.56). Direct comparison also suggested a small benefit of follow-up visits. Only one study determined the effect of smoking

	advice on mortality. This study found no statistically significant differences in death rates at 20 years follow up. Assuming an unassisted quit rate of 2 to 3%, a brief advice intervention can increase quitting by a further 1to 3%. Additional components appear to have only a small effect, though there is a small additional benefit of more intensive interventions compared to very brief interventions.
Authors' conclusions	Simple advice given by physicians to their smoking patients had a small effect on cessation rates. Providing follow up, if possible, is likely to produce additional benefit. However, the marginal benefits of more intensive interventions, including use of aids is small, and cannot be justified as a routine intervention in unselected smokers. They may, however, be of benefit for individual, motivated smokers.

Rice 2008	Nursing interventions for smoking cessation
Study design	Randomized controlled trials.
Population	Adult smokers, 18 years and older, of either gender and recruited in any type of healthcare setting.
Intervention	Nursing intervention was defined as the provision of advice, counselling, and/or strategies to help patients quit smoking.
Outcomes	Smoking cessation, or reduction in amount of cigarettes smoked.
Main results	Forty-two studies met the inclusion criteria. Thirty-one studies comparing a nursing intervention to a control or to usual care found the intervention to significantly increase the likelihood of quitting (RR 1.28, 95% CI 1.18 to 1.38). In a subgroup analysis there was weaker evidence that lower intensity interventions were effective (RR 1.27, 95% CI 0.99 to 1.62). There was limited indirect evidence that interventions were more effective for hospital inpatients with cardiovascular disease than for inpatients with other conditions. Interventions in non-hospitalized patients also showed evidence of benefit. Nine studies comparing different nurse-delivered interventions failed to detect significant benefit from using additional components. Five studies of nurse counselling on smoking cessation during a screening health check, or as part of multifactorial secondary prevention in general practice (not included in the main meta-analysis) found nursing intervention to have less effect under these conditions.
Authors' conclusions	The results indicate the potential benefits of smoking cessation advice and/or counselling given by nurses to patients. The evidence of an effect is weaker when interventions are brief and are provided by nurses whose main role is not health promotion or smoking cessation. The challenge will be to incorporate smoking behaviour monitoring and smoking cessation interventions as part of standard practice.

Rigotti 2007	Interventions for smoking cessation in hospitalised patients
Study design	Randomized or quasi-randomized controlled trials.
Population	Hospitalised patients who were currently smoking or had recently quit.
Intervention	Any intervention that was initiated during the hospitalization and that aimed to increase motivation to quit, to assist a quit attempt, or to help recent quitters avoid relapse.
Outcomes	Abstinence from smoking, at least six months after the start of the intervention.

Main results	Thirty-three trials met the inclusion criteria. Intensive counselling interventions that began during the hospital stay and continued with supportive contacts for at least one month after discharge increased smoking cessation rates after discharge (Odds Ratio (OR) 1.65, 95% confidence interval (CI) 1.44 to 1.90; 17 trials). No statistically significant benefit was found for less intensive counselling interventions. The one study that tested a single brief (<=15 minutes) in-hospital intervention did not find it to be effective (OR 1.16, 95% CI 0.80 to 1.67). Counselling of longer duration during the hospital stay was not associated with a higher quit rate (OR 1.08, 95% CI 0.89 to 1.29, eight trials). Even counselling that began in the hospital but had less than one month of supportive contact after discharge did not show significant benefit (OR 1.09, 95% CI 0.91 to 1.31, six trials). Adding nicotine replacement therapy (NRT) did not produce a statistically significant increase in cessation over what was achieved by intensive counselling alone (OR 1.47, 95% CI 0.92 to 2.35, five studies). The one study that tested the effect of adding bupropion to intensive counselling had a similar nonsignificant effect (OR 1.56, 95% CI 0.79 to 3.06). A similar pattern of results was observed in smokers admitted to hospital because of cardiovascular disease (CVD). In this subgroup, intensive intervention with follow-up support increased the odds of smoking cessation (OR 1.81, 95% CI 1.54 to 2.15, 11 trials), but less intensive interventions did not. One trial of intensive intervention including counselling and pharmacotherapy for smokers admitted with CVD assessed clinical and health care utilization endpoints, and found significant reductions in all-cause mortality and hospital readmission rates over a two-year follow-up period.
Authors' conclusions	High intensity behavioural interventions that begin during a hospital stay and include at least one month of supportive contact after discharge promote smoking cessation among hospitalised patients. These interventions are effective regardless of the patient's admitting diagnosis. Interventions of lower intensity or shorter duration have not been shown to be effective in this setting.

Sinclair 2004	Community pharmacy personnel interventions for smoking cessation
Study design	Randomized controlled trials.
Population	Community pharmacy clients who are smokers and who wish to stop.
Intervention	Any intervention by community pharmacy personnel to promote smoking cessation amongst their clients.
Outcomes	Rates of abstinence from smoking afteer six months or more.
Main results	Two trials met the selection criteria. They included a total of 976 smokers. Both trials were set in the UK and involved a training intervention which included the Stages of Change Model; they then compared a support programme involving counselling and record keeping against a control receiving usual pharmacy support. In both studies a high proportion of intervention and control participants began using nicotine replacement therapy (NRT). Both studies reported smoking cessation outcomes at three time points. However, the follow-up points were not identical (three, six and 12 months in one, and one, four and nine months in the other), and the trend in abstinence over time was not linear in either study, so the data could not be combined. One study showed a significant difference in self-reported cessation rates at 12 months: 14.3% versus 2.7% ($p < 0.001$); the other study showed a positive trend at each follow-up with 12.0% versus 7.4% ($p = 0.09$) at nine months.
Authors' conclusions	The limited number of studies to date suggests that trained community pharmacists, providing a counselling and record keeping support programme for their customers, may have a positive effect on smoking cessation rates. The strength of evidence is limited because only one of the trials showed a statistically significant effect.

Non health care smoking cessation interventions likely to be effective

Lancaster 2005	Individual behavioural counselling for smoking cessation
Study design	Randomized or quasi-randomized controlled trials with a minimum follow up of six months, where at least one treatment arm consisted of an unconfounded intervention from a counsellor
Population	Any smokers, except pregnant women. Trials recruiting only children and adolescents were excluded.
Intervention	Individual counselling defined as a face-to-face encounter between a smoking patient and a counsellor trained in assisting smoking cessation. The review excluded studies of counselling delivered by doctors and nurses.
Outcomes	Sustained abstinence or multiple point prevalence.
Main results	21 trials with over 7000 participants were identified. Eighteen trials compared individual counselling to a minimal behavioural intervention, four compared different types or intensities of counselling. Individual counselling was more effective than control. The odds ratio for successful smoking cessation was 1.56 (95% confidence interval 1.32 to 1.84). In a subgroup of three trials where all participants received nicotine replacement therapy the point estimate of effect was smaller and did not reach significance (odds ratio 1.34, 95% confidence interval 0.98 to 1.83). It was failed to detect a greater effect of intensive counselling compared to brief counselling (odds ratio 0.98, 95% confidence interval 0.61 to 1.56).
Authors' conclusions	Counselling interventions given outside routine clinical care by smoking cessation counsellors assist smokers to quit.

Lancaster 2005	Self-help interventions for smoking cessation
Study design	Randomized or quasi-randomized controlled trials with a minimum follow up of six months, where at least one arm consisted of a self-help intervention without repeated face-to-face therapist contact.
Population	Any smokers except pregnant smokers and adolescent smokers.
Intervention	Self-help interventions defined as any manual or programme to be used by individuals to assist a quit attempt not aided by health professionals, counsellors or group support. They include written materials, audio- or videotape or computer programmes. Materials may be aimed at smokers in general, may target particular populations of smokers, for example different ages or ethnic groups, or may be interactively tailored to individual smoker characteristics. Brief leaflets on the health effects of smoking were not included - they were considered to be a control intervention if compared to a more substantial manual. Interventions with a minimal face-to-face contact for the purpose of supplying the self-help programme materials were regarded as self help alone. Where a face-to-face meeting included discussion of the programme contents it was categorized as brief advice in addition to self-help materials.
Outcomes	Sustained abstinence, or two-point prevalence.
Main results	Sixty trials were identified. Thirty-three compared self-help materials to no intervention or tested materials used in addition to advice. In 11 trials in which self help was compared to no intervention there was a pooled effect that just reached statistical significance (N = 13,733; odds ratio [OR] 1.24, 95% confidence interval [CI] 1.07 to 1.45). This analysis excluded two trials with strongly positive outcomes that introduced significant heterogeneity. Four further trials in which the control group received alternative written materials did not show evidence for an effect of

	the smoking self-help materials. There was no evidence of benefit from adding self-help materials to face-to-face advice, or to nicotine replacement therapy. There were seventeen trials using materials tailored for the characteristics of individual smokers, where meta-analysis supported a small benefit of tailored materials (N = 20,414; OR 1.42, 95% CI 1.26 to 1.61). The evidence is strongest for tailored materials compared to no intervention, but also supports tailored materials as more helpful than standard materials. Part of this effect could be due to the additional contact or assessment required to obtain individual data. A small number of other trials failed to detect benefits from using additional materials or targeted materials, or to find differences between different self-help programmes.
Authors' conclusions	Standard self-help materials may increase quit rates compared to no intervention, but the effect is likely to be small. There was no additional benefit when self-help materials was used alongside other interventions such as advice from a healthcare professional, or nicotine replacement therapy. There is evidence that materials that are tailored for individual smokers are effective, and are more effective than untailored materials, although the absolute size of effect is still small.

Moher 2005	Workplace interventions for smoking cessation
Study design	For interventions aimed at helping individuals to stop smoking, it was included only randomized controlled trials allocating individuals, workplaces or companies to intervention or control conditions. For studies of restrictions and bans, it was also included controlled trials with baseline and post-intervention outcomes and interrupted times series studies.
Population	Adults over 18 years of age, in employment, who smoked.
Intervention	1. Smoking cessation interventions aimed at individuals in the workforce. 2. Interventions aimed at the workforce as a population.
Outcomes	Employee smoking behaviour (cessation rates for programmes, workplace prevalence data), preferably sustained cessation for at least six months.
Main results	Workplace interventions aimed at helping individuals to stop smoking included ten studies of group therapy, seven studies of individual counselling, nine studies of self-help materials and five studies of nicotine replacement therapy. The results were consistent with those found in other settings. Group programmes, individual counselling and nicotine replacement therapy increased cessation rates in comparison to no treatment or minimal intervention controls. Self-help materials were less effective. Workplace interventions aimed at the workforce as a whole included 14 studies of tobacco bans, two studies of social support, four studies of environmental support, five studies of incentives, and eight studies of comprehensive (multi-component) programmes. Tobacco bans decreased cigarette consumption during the working day but their effect on total consumption was less certain. The review did not detect an increase in quit rates from adding social and environmental support to these programmes. There was a lack of evidence that comprehensive programmes reduced the prevalence of smoking. Competitions and incentives increased attempts to stop smoking, though there was less evidence that they increased the rate of actual quitting.
Authors' conclusions	Strong evidence that interventions directed towards individual smokers increase the likelihood of quitting smoking. These include advice from a health professional, individual and group counselling and pharmacological treatment to overcome nicotine addiction. All these interventions are effective whether offered in the workplace or elsewhere. Although people taking up these interventions are more likely to stop, the absolute numbers who quit are low. Limited evidence that participation in programmes can be increased by competitions

	and incentives organized by the employer. Consistent evidence that workplace tobacco policies and bans can decrease cigarette consumption during the working day by smokers and exposure of non-smoking employees to environmental tobacco smoke at work, but conflicting evidence about whether they decrease prevalence of smoking or overall consumption of tobacco by smokers. A lack of evidence that comprehensive approaches reduce the prevalence of smoking, despite the strong theoretical rationale for their use. A lack of evidence about the cost-effectiveness of workplace programmes.

Serra 2000	Interventions for preventing tobacco smoking in public places
Study design	Randomized and controlled trials, controlled before and after studies and interrupted time series. After an initial literature search identified few such studies in this area, it was also decided to include uncontrolled before and after studies.
Population	Users of public places where restrictions or bans on smoking were implemented.
Intervention	Interventions to reduce smoking in public places, including restrictions and bans, educational materials, signs and strategies that used a combination of different interventions, that were aimed at populations. Interventions aimed at individuals.
Outcomes	1. Objective measures: a) direct observation of people smoking b) indirect observation of tobacco consumption (presence of cigarette butts, ash-trays and/or odour of tobacco) or other tests (for example, simulation tests) c) environmental measures of the concentration of tobacco smoke. 2. Subjective measures: surveys of directors, workers and/or clients.
Main results	Eleven of 22 studies reporting information about interventions to reduce smoking in public places met all the inclusion criteria. All included studies were uncontrolled before and after studies. The most effective strategies used comprehensive, multicomponent approaches to implement policies banning smoking within institutions. Less comprehensive strategies, such as posted warnings and educational material had a moderate effect. Five studies showed that prompting individual smokers had an immediate effect, but such strategies are unlikely to be acceptable as a public health intervention.
Authors' conclusions	Carefully planned and resourced, multicomponent strategies effectively reduced smoking within public places. Less comprehensive strategies were less effective. All studies used relatively weak designs. Most studies were done in the USA.

Sowden 2003	Community interventions for preventing smoking in young people
Study design	Randomised and non-randomised controlled trial allocating communities, geographical regions or school districts.
Population	Young people aged less than 25 years.
Intervention	Interventions targeted at entire or parts of entire communities or large areas with the intention of influencing the smoking behaviour of young people. Community interventions defined as co-ordinated, widespread programmes in a particular geographical area (e.g. school districts) or region or in groupings of people who share common interests or needs, which support non-smoking behaviour.
Outcomes	Primary measures of smoking behaviour: a) objective measures of smoking (saliva thiocyanate levels, alveolar CO). b) self reported smoking. Intermediate outcomes (impact): intentions to smoke, attitudes to smoking, knowledge about smoking, decision making and refusal skills.

Main results	Seventeen studies were included in the review. All studies used a controlled trial design, with six using random allocation of schools or communities. Of thirteen studies which compared community interventions to no intervention controls, two, which were part of cardiovascular disease prevention programmes, reported lower smoking prevalence. Of three studies comparing community interventions to school-based programmes only, one found differences in reported smoking prevalence. One study reported a lower rate of increase in prevalence in a community receiving a multi-component intervention compared to a community exposed to a mass media campaign alone. One study reported a significant difference in smoking prevalence between a group receiving a media, school and homework intervention compared to a group receiving the media component only.
Authors' conclusions	There is some limited support for the effectiveness of community interventions in helping prevent the uptake of smoking in young people.

Stead 2005	Group behaviour therapy programmes for smoking cessation
Study design	Randomized trials that compared group therapy with self help, individual counselling, another intervention or no intervention (including usual care or a waiting list control), and trials that compared more than one group programme.
Population	Smokers of either gender irrespective of their initial level of nicotine dependency, recruited from any setting, with the exception of pregnant women.
Intervention	Studies in which smokers met for scheduled meetings and received some form of behavioural intervention, such as information, advice and encouragement or cognitive behavioural therapy (CBT) delivered over at least two sessions, and studies in which group therapy was tested as an adjunct to nicotine replacement .
Outcomes	The main outcome was abstinence from cigarettes at follow up at least six months after the start of treatment.
Main results	A total of 55 trials met inclusion criteria. Sixteen studies compared a group programme with a self-help programme. There was an increase in cessation with the use of a group programme (N = 4395, odds ratio (OR) 2.04, 95% confidence interval (CI) 1.60 to 2.60). Group programmes were more effective than no intervention (seven trials, N = 815, OR 2.17, 95% CI 1.37 to 3.45). There was no evidence that group therapy was more effective than a similar intensity of individual counselling. There was limited evidence that the addition of group therapy to other forms of treatment, such as advice from a health professional or nicotine replacement, produced extra benefit. There was variation in the extent to which those offered group therapy accepted the treatment. There was limited evidence that programmes which included components for increasing cognitive and behavioural skills and avoiding relapse were more effective than same length or shorter programmes without these components. This analysis was sensitive to the way in which one study with multiple conditions was included. It was not found an effect of manipulating the social interactions between participants in a group programme on outcome.
Authors' conclusions	Group therapy is better for helping people stop smoking than self help, and other less intensive interventions. There is not enough evidence to evaluate whether groups are more effective, or cost-effective, than intensive individual counselling. There is not enough evidence to support the use of particular psychological components in a programme beyond support and skills training normally included.

Stead 2006	Telephone counselling for smoking cessation
Study design	Randomized or quasi-randomized controlled trials, with the unit of allocation individual participants, group, intervention site or geographical area.

Population	Smokers or recent quitters.
Intervention	Provision of proactive or reactive telephone counselling to assist smoking cessation.
Outcomes	Smoking cessation at least six months after the start of intervention.
Main results	Forty-eight trials met the inclusion criteria. Among smokers who contacted helplines, quit rates were higher for groups randomised to receive multiple sessions of call-back counselling (eight studies, >18,000 participants, odds ratio (OR) for long term cessation 1.41, 95% confidence interval (CI) 1.27 to 1.57). Two of these studies showed a significant benefit of more intensive compared to less intensive intervention. Telephone counselling not initiated by calls to helplines also increased quitting (29 studies, >17,000 participants, OR 1.33, 95% CI 1.21 to 1.47). A meta-regression detected a significant association between the maximum number of planned calls and the effect size. There was clearer evidence of benefit in the subgroup of trials recruiting smokers motivated to quit. Of two studies that provided access to a hotline one showed a significant benefit and one did not. Two studies comparing different counselling approaches during a single session did not detect significant differences. A further seven studies were too diverse to contribute to meta-analyses.
Authors' conclusions	Proactive telephone counselling helps smokers interested in quitting. There is evidence of a dose response; one or two brief calls are less likely to provide a measurable benefit. Three or more calls increases the odds of quitting compared to a minimal intervention such as providing standard self-help materials, brief advice, or compared to pharmacotherapy.

Pharmacologically assisted smoking cessation likely to be effective

Cahill 2007	Nicotine receptor partial agonists for smoking cessation
Study design	Randomized controlled trials.
Population	Adult smokers.
Intervention	Selective nicotine receptor partial agonists.
Outcomes	A minimum of six months abstinence.
Main results	Five trials of varenicline compared with placebo for smoking cessation were found; three of these also included a bupropion experimental arm. One additional trial studied relapse prevention, comparing varenicline with placebo. The six trials covered 4924 participants, 2451 of whom used varenicline. We identified one trial of cytisine (Tabex) for inclusion. The pooled odds ratio (OR) for continuous abstinence at 12 months for varenicline versus placebo was 3.22 (95% confidence interval [CI] 2.43 to 4.27). The pooled OR for varenicline versus bupropion was 1.66 (95% CI 1.28 to 2.16). The main adverse effect of varenicline was nausea, which was mostly at mild to moderate levels and usually subsided over time. The two trials which tested the use of varenicline beyond the 12-week standard regimen found the drug to be well-tolerated and effective during long-term use. The one cytisine trial included found that more participants taking cytisine stopped smoking compared with placebo at two-year follow up, with an OR of 1.77 (95% CI 1.30 to 2.40).
Authors' conclusions	Varenicline increased the odds of successful long-term smoking cessation approximately threefold compared with pharmacologically unassisted quit attempts. In trials reported so far, more participants quit successfully with varenicline than with bupropion. The effectiveness of varenicline as an aid to relapse prevention has not

	been clearly established. The main adverse effect of varenicline is nausea, but this is mostly at mild to moderate levels. There is a need for independent trials of varenicline versus placebo, to test the early findings. There is also a need for direct comparisons with nicotine replacement therapy, and for further trials with bupropion, to establish the relative efficacy of the treatments. Cytisine may also increase the chances of quitting, but the evidence at present is inconclusive.

Gourlay 2004	Clonidine for smoking cessation
Study design	Randomized placebo-controlled studies.
Population	Any smokers.
Intervention	Treatment with oral or transdermal clonidine, maximum daily dosage of >=0.2 mg.
Outcomes	Smoking cessation, assessed through follow up at least 12 weeks following the end of drug treatment.
Main results	Six trials met the inclusion criteria. There were three trials of oral, and three of transdermal clonidine. Some form of behavioural counselling was offered to all participants in five of the six trials. There was a statistically significant effect of clonidine in one of these trials. The pooled odds ratio for success with clonidine versus placebo was 1.89 (95% confidence interval 1.30 to 2.74). There was a high incidence of dose-dependent side-effects, particularly dry mouth and sedation.
Authors' conclusions	Based on a small number of trials, in which there are potential sources of bias, clonidine is effective in promoting smoking cessation. Prominent side-effects limit the usefulness of clonidine for smoking cessation.

Hughes 2007	Antidepressants for smoking cessation
Study design	Randomized controlled trialos.
Population	Current smokers or recent quitters.
Intervention	Treatment with any medication with antidepressant properties to aid a smoking cessation attempt or to prevent relapse, or in the case of trials for harm reduction, to reduce the number of cigarettes smoked and aid subsequent cessation.
Outcomes	a) abstinence from smoking, assessed at follow up after at least six months from start of treatment or b) incidence of reducing cigarette consumption to 50% or less of baseline, and abstinence. Safety was assessed by incidence of serious and other adverse events, and drop-outs due to adverse events.
Main results	Fiftythree trials were included. There were 40 trials of bupropion and eight trials of nortriptyline. When used as the sole pharmacotherapy, bupropion (31 trials, odds ratio [OR] 1.94, 95% confidence interval [CI] 1.72 to 2.19) and nortriptyline (four trials, OR 2.34, 95% CI 1.61 to 3.41) both doubled the odds of cessation. There is insufficient evidence that adding bupropion or nortriptyline to nicotine replacement therapy provides an additional long-term benefit. Three trials of extended therapy with bupropion to prevent relapse after initial cessation did not find evidence of a significant long-term benefit. From the available data bupropion and nortriptyline appear to be equally effective and of similar efficacy to nicotine replacement therapy. Pooling three trials comparing bupropion to varenicline showed a lower odds of quitting with bupropion (OR 0.60, 95% CI 0.46 to 0.78). There is a risk of about 1 in 1000 of seizures associated with bupropion use. Concerns that bupropion may increase suicide risk are currently unproven. Nortriptyline has the potential for serious side-effects, but none have been seen in the few small trials for smoking

	cessation. There were six trials of selective serotonin reuptake inhibitors; four of fluoxetine, one of sertraline and one of paroxetine. None of these detected significant long-term effects, and there was no evidence of a significant benefit when results were pooled. There was one trial of the monoamine oxidase inhibitor moclobemide, and one of the atypical antidepressant venlafaxine. Neither of these detected a significant long-term benefit.
Authors' conclusions	Bupropion and nortriptyline aid smoking cessation but selective serotonin reuptake inhibitors do not. Evidence suggests that the mode of action is independent of their antidepressant effect and that they are of similar efficacy to nicotine replacement.

Stead 2008	Nicotine replacement therapy for smoking cessation
Study design	Randomized and quasi-randomized controlled trials.
Population	Men or women who smoked.
Intervention	Nicotine replacement therapy (NRT) (including chewing gum, transdermal patches, nasal spray, inhalers and tablets or lozenges) versus placebo or no NRT control. Trials comparing different doses of NRT and comparing more than one type of NRT to a single type.
Outcomes	Smoking cessatio after at least six months.
Main results	The authors identified 132 trials; 111 with over 40,000 participants contributed to the primary comparison between any type of NRT and a placebo or non-NRT control group. The RR of abstinence for any form of NRT relative to control was 1.58 (95% confidence interval [CI]: 1.50 to 1.66). The pooled RR for each type were 1.43 (95% CI: 1.33 to 1.53, 53 trials) for nicotine gum; 1.66 (95% CI: 1.53 to 1.81, 41 trials) for nicotine patch; 1.90 (95% CI: 1.36 to 2.67, 4 trials) for nicotine inhaler; 2.00 (95% CI: 1.63 to 2.45, 6 trials) for oral tablets/lozenges; and 2.02 (95% CI: 1.49 to 3.73, 4 trials) for nicotine nasal spray. The effects were largely independent of the duration of therapy, the intensity of additional support provided or the setting in which the NRT was offered. The effect was similar in a small group of studies that aimed to assess use of NRT obtained without a prescription. In highly dependent smokers there was a significant benefit of 4 mg gum compared with 2 mg gum, but weaker evidence of a benefit from higher doses of patch. There was evidence that combining a nicotine patch with a rapid delivery form of NRT was more effective than a single type of NRT. Only one study directly compared NRT to another pharmacotherapy. In this study quit rates with nicotine patch were lower than with the antidepressant bupropion.
Authors' conclusions	All of the commercially available forms of NRT (gum, transdermal patch, nasal spray, inhaler and sublingual tablets/lozenges) can increase the chance of successfully stopping smoking. NRTs increase the rate of quitting by 50-70%, regardless of setting. The effectiveness of NRT appears to be largely independent of the intensity of additional support provided to the individual. Provision of more intense levels of support, although beneficial in facilitating the likelihood of quitting, is not essential to the success of NRT.

Healthcare financing interventions likely to be effective

Kaper 2005	Healthcare financing systems for increasing the use of tobacco dependence treatment
Study design	Randomized controlled trials, controlled trials and interrupted time series.

Population	Smokers or healthcare providers.
Intervention	Healthcare financing interventions directed at patients or providers for increasing the use of smoking cessation treatment (e.g. delivered by government or healthcare insurance plans).
Outcomes	Primary: abstinence from smoking. Secondary: number of participants making a quit attempt and use of smoking cessation treatment.
Main results	Four RCTs and two CTs were directed at smokers. Five studies compared the effect of a full benefit with no benefit of which four reported the prolonged self-reported abstinence rate and showed an increase of 2% (95% confidence interval [CI] 0.00 to 0.05). The pooled OR for achieving abstinence for a period of six months was 1.48 (95% 1.17 to 1.88). Two studies directed at smokers compared a full benefit with a partial benefit and showed that the odds of being abstinent were 2.49 times higher with a full benefit (95% CI 1.59 to 3.90). The pooled RD showed a non-significant increase (RD 0.05; 95% CI -0.07 to 0.16). Only one study compared a partial benefit with no benefit and only one study was directed at healthcare providers.
Authors' conclusions	There is some evidence that healthcare financing systems directed at smokers which offer a full financial benefit can increase the self-reported prolonged abstinence rates at relatively low costs when compared with a partial or no benefit. Since there were some limitations to the methodological quality of the studies the results should be interpreted with caution. More studies are needed on the effects of healthcare financing systems directed at healthcare providers.

SMOKING CESSATION INTERVENTIONS UNLIKELY TO BE EFFECTIVE

Abbot 1998	Hypnotherapy for smoking cessation
Study design	Randomized controlled trials.
Population	Smokers who wish to stop smoking, irrespective of gender, number of years smoking or level of nicotine dependence.
Intervention	Any trial of hypnotherapy for smoking cessation.
Outcomes	Abstinence from smoking assessed at least six months from the start of treatment.
Main results	Nine studies compared hypnotherapy with 14 different control interventions. There was significant heterogeneity between the results of the individual studies, with conflicting results for the effectiveness of hypnotherapy compared to no treatment or to advice. We therefore did not attempt to calculate pooled odds ratios for the overall effect of hypnotherapy. There was no evidence of an effect of hypnotherapy compared to rapid smoking or psychological treatment.
Authors' conclusions	It was not shown that hypnotherapy has a greater effect on six month quit rates than other interventions or no treatment. The effects of hypnotherapy on smoking cessation claimed by uncontrolled studies were not confirmed by analysis of randomized controlled trials.

Bize 2005	Biomedical risk assessment as an aid for smoking cessation
Study design	Randomized controlled trials.
Population	Individuals who smoked and who participated in smoking cessation programmes, or in screening for respiratory disease, or in health check-ups. No restriction on whether participants were hospitalized or not, or suffering from co-existent illness..
Intervention	Any intervention in which a physical measurement, such as exhaled carbonmonoxide (CO) measurement, spirometry or genetic testing, was used as a way to increase motivation to quit..
Outcomes	Abstinence from smoking at least six months after the start of the intervention.
Main results	Eight trials were included. One of the eight used CO alone and CO + Genetic Susceptibility as two different intervention groups, giving rise to three possible comparisons. Three of the trials isolated the effect of exhaled CO on smoking cessation rates resulting in the following odds ratios (ORs) and 95% confidence intervals (95% CI): 0.73 (0.38 to 1.39), 0.93 (0.62 to 1.41), and 1.18 (0.84 to 1.64). Combining CO measurement with genetic susceptibility gave an OR of 0.58 (0.29 to 1.19). Exhaled CO measurement and spirometry were used together in three trials, resulting in the following ORs (95% CI): 0.6 (0.25 to 1.46), 2.45 (0.73 to 8.25), and 3.50 (0.88 to 13.92). Spirometry results alone were used in one other trial with an OR of 1.21 (0.60 to 2.42). Two trials used other motivational feedback measures, with an OR of 0.80 (0.39 to 1.65) for genetic susceptibility to lung cancer alone, and 3.15 (1.06 to 9.31) for ultrasonography of carotid and femoral arteries performed in light smokers (average 10 to 12 cigarettes a day).
Authors' conclusions	Due to the scarcity of evidence of sufficient quality, it can not be made definitive statements about the effectiveness of biomedical risk assessment as an aid for smoking cessation. Current evidence of lower quality does not however support the hypothesis that biomedical risk assessment increases smoking cessation.

Hey 2005	Competitions and incentives for smoking cessation
Study design	Randomized controlled trials allocating individuals, communities, workplaces or groups within workplaces to intervention or to control conditions. Controlled trials with baseline measures and post-intervention outcomes.
Population	Adult smokers, either gender, in any setting.
Intervention	Contests, competitions, incentive schemes, lotteries, raffles, and contingent payments, to reward cessation and continuous abstinence in smoking cessation programmes.
Outcomes	1. Cessation rates, point prevalence and sustained abstinence, for a minimum of six months from the start of the intervention. 2. Rates of recruitment to and participation in smoking cessation programmes, where they are reported in addition to cessation rates.
Main results	Fifteen studies were included. None of the studies demonstrated significantly higher quit rates for the incentives group than for the control group beyond the six-month assessment. There was no clear evidence that participants who committed their own money to the programme did better than those who did not, or that different types of incentives were more or less effective. There is some evidence that although cessation rates have not been shown to differ significantly, recruitment rates can be improved by rewarding participation, which may be expected to deliver higher absolute numbers of successful quitters. Cost effectiveness analysis was not appropriate, since the efficacy of the intervention has not been demonstrated.
Authors' conclusions	Incentives and competitions do not appear to enhance long-term cessation rates, with early success tending to dissipate when the rewards are no longer offered. Rewarding participation and compliance in contests and cessation programmes may have more potential to deliver higher absolute numbers of quitters.

Lancaster 1997	Silver acetate for smoking cessation
Study design	Randomized controlled trials.
Population	Adult smokers.
Intervention	Silver acetate compared with placebo, or with other smoking cessation treatments were included. Silver acetate products included lozenges, gums and sprays.
Outcomes	Sustained abstinence from smoking at 6 to12 months.
Main results	Two studies provided long-term follow-up data on patients randomised to silver acetate or placebo. The combined odds ratio for quitting for silver acetate vs placebo was 1.05 (95% confidence interval 0.63 to 1.73).
Authors' conclusions	Existing trials show little evidence for a specific effect of silver acetate in promoting smoking cessation.

Park 2004	Enhancing partner support to improve smoking cessation
Study design	Randomized controlled trials.
Population	Smokers of either gender or age, irrespective of their initial level of nicotine dependency, from any setting, who agreed to participate in a smoking cessation program. Pregnant/non-pregnant and married/ non-married smokers were included.

Intervention	Partners were defined as spouses, friends, co-workers, buddies, or other significant others who supported the smokers as a part of the cessation program they were assigned. A partner support intervention could be directed at the smoker, the partner or both, with the aim of assisting the smoker to quit.
Outcomes	Primary outcome: abstinence from smoking of the smoker assessed at least 6 months following the initiation of treatment.
Main results	Eight articles (nine studies) met the inclusion criteria. The definition of partner varied among the studies. The odds ratio for self-reported abstinence at 6-9 months was 1.08 (CI 95%, 0.81 -1.44); and at 12 months post-treatment was 1.0 (CI 95%, 0.75 - 1.34). Of the six studies that measured partner support at follow-up, only two studies reported significant increase in partner support in the intervention groups.
Authors' conclusions	This review failed to detect an increase in quit rates. Limited data from several of the trials suggest that these interventions did not increase partner support either. No conclusions can be made about the impact of partner support on smoking cessation. More systematic intervention to affect partnership significantly should be delivered if partner support were part of an existing cessation program.

Secker-Walker 2002	Community interventions for reducing smoking among adults
Study design	Randomized and non-randomized controlled trials allocating communities or geographical regions
Population	Adults, 18 years or older.
Intervention	A community intervention considered as a co-ordinated, multidimensional programme aimed at changing adult smoking behaviour, involving several segments of the community and conducted in a defined geographical area, such as a town, city, county or other administrative district.
Outcomes	a) Smoking status (current smoker, recent ex-smoker - during time of intervention) b) Cigarette consumption (cigarettes per day).
Main results	Thirty-seven studies were included, of which 17 included only one intervention and one comparison community. Only four studies used random assignment of communities to either the intervention or comparison group. The population size of the communities ranged from a few thousand to over 100,000 people. Change in smoking prevalence was measured using cross-sectional follow-up data in 21 studies. The estimated net decline ranged from -1.0% to +3.0% for men and women combined (11 studies). For women, the decline ranged from -0.2% to + 3.5% per year (n=11), and for men the decline ranged from -0.4% to +1.6% per year (n=12). Cigarette consumption and quit rates were only reported in a small number of studies. The two most rigorous studies showed limited evidence of an effect on prevalence. In the US COMMIT study there was no differential decline in prevalence between intervention and control communities, and there was no significant difference in the quit rates of heavier smokers who were the target intervention group. In the Australian CART study there was a significantly greater quit rate for men but not women.
Authors' conclusions	The failure of the largest and best conducted studies to detect an effect on prevalence of smoking is disappointing. A community approach will remain an important part of health promotion activities, but designers of future programmes will need to take account of this limited effect in determining the scale of projects and the resources devoted to them.

SMOKING CESSATION INTERVENTIONS WITH UNKNOWN EFFECTIVENESS

Training health professionals – unknown effectiveness

Lancaster 2000	Training health professionals in smoking cessation
Study design	Randomized controlled trials.
Population	Trials in which the unit of randomisation was a healthcare practitioner or practice, and that reported the effects on patients who were smokers were included.
Intervention	Health care professionals were trained in methods to promote smoking cessation among their patients. Only studies allocating healthcare professionals to at least two groups (including one which received some form of training) by a formal randomisation process were included.
Outcomes	Rates of abstinence from smoking at least six months after the start of the intervention. The number of smokers who were counselled, asked to set a date for stopping (quit date), given a follow up appointment, given self help materials, offered nicotine gum, or prescribed a quit date.
Main results	Healthcare professionals who had received training were more likely to perform tasks of smoking cessation than untrained controls. Of eight studies that compared patient smoking behaviour between trained professionals and controls, six found no effect of intervention. The effects of training on process outcomes increased if prompts and reminders were used.
Authors' conclusions	Training health professionals to provide smoking cessation interventions had a measurable effect on professional performance. There was no strong evidence that it changed smoking behaviour.

Pharmacological interventions with unknown effectiveness

David 2006	Opioid antagonists for smoking cessation
Study design	Randomized controlled trials.
Population	Adult smokers.
Intervention	Naltrexone, naloxone, buprenorphine or other opioid antagonists, with or without concurrent nicotine replacement therapy.
Outcomes	Primary outcome: Six-month abstinence. Secondary outcome: withdrawal, reinforcing or hedonic effects of smoking, mood states, and ad libitum smoking.
Main results	Four trials of naltrexone met inclusion criteria for meta-analyses for long-term cessation. All four trials failed to detect a significant difference in quit rates between naltrexone and placebo. In a pooled analysis there was no significant effect of naltrexone on long-term abstinence, and confidence intervals were wide (odds ratio 1.26, 95% confidence interval 0.80 to 2.01). No trials of naloxone or buprenorphine reported long-term follow up.
Authors' conclusions	Based on limited data from four trials it is not possible to confirm or refute whether naltrexone helps smokers quit. The confidence intervals are compatible with both clinically significant benefit and possible negative effects of naltrexone.

Hughes 2000	Anxiolytics for smoking cessation

Study design	Randomized controlled trials.
Population	Any smokers.
Intervention	Treatment with any drug with anxiolytic properties, but excluding clonidine.
Outcomes	Abstinence from smoking at least six months from start of treatment.
Main results	There was one trial each of the anxiolytics diazepam, meprobamate, metoprolol and oxprenolol. There were two trials of the anxiolytic buspirone. None of the trials showed strong evidence of an effect for any of these drugs in helping smokers to quit. However, confidence intervals were wide, and an effect of anxiolytics cannot be ruled out on current evidence.
Authors' conclusions	There is no consistent evidence that anxiolytics aid smoking cessation, but the available evidence does not rule out a possible effect.

Lancaster 1998	Mecamylamine (a nicotine antagonist) for smoking cessation
Study design	Randomized controlled trials.
Population	Adult smokers.
Intervention	Treatment with mecamylamine, with or without nicotine replacement therapy.
Outcomes	Abstinence from smoking at least six months from start of treatment.
Main results	Two studies were identified, both from the same investigators. In a study of 48 volunteers, a combination of mecamylamine plus nicotine patch was more effective than nicotine patch alone (abstinence rate at one year 37.5% vs 4.2%). In a second study, 80 volunteers were treated for four weeks prior to cessation with one of four treatments: 1. Nicotine patch plus mecamylamine capsules 2. Nicotine alone 3. Mecamylamine alone 4. No active drug. All four groups received combination treatment with nicotine and mecamylamine after the scheduled quit date. The abstinence rates in these four groups were respectively 40%, 20%, 15% and 15%. The higher abstinence rate in the group treated with combination therapy was not statistically significant. In the doses used, mecamylamine was well tolerated, although up to 40% of subjects required reductions in dose, usually because of constipation.
Authors' conclusions	Data from two small studies suggest that the combination of nicotine and mecamylamine may be superior to nicotine alone in promoting smoking cessation. However, these results require confirmation in larger studies before the treatment can be recommended clinically.

Stead 1997	Lobeline for smoking cessation.
Study design	Randomized controlled trials.
Population	Any smokers.
Intervention	Treatment with any form of lobeline.
Outcomes	Smoking cessation, assessed at follow-up at least 6 months from start of treatment.

Main results	No trials meeting the full inclusion criteria including long term follow-up were identified.
Authors' conclusions	There is no evidence available from long term trials that lobeline can aid smoking cessation.

Stead 2006	Nicobrevin for smoking cessation
Study design	Randomized controlled trials.
Population	Smokers wishing to quit.
Intervention	Treatment with Nicobrevin (a 28-day course of tablets).
Outcomes	Smoking cessation, assessed at follow up at least six months from the start of treatment.
Main results	No trials meeting the full inclusion criteria including long term follow-up were identified.
Authors' conclusions	There is no evidence available from long-term trials that Nicobrevin can aid smoking cessation.

Other smoking cessation interventions, with unknown effectiveness

Grimshaw 2006	Tobacco cessation interventions for young people
Study design	Randomized controlled trials, cluster-randomized controlled trials and controlled trials.
Population	Young people, aged less than 20, who are regular tobacco smokers.
Intervention	The interventions ranged from simple ones such as pharmacotherapy, targeting individual young people, through complex programmes targeting people or organizations associated with young people (for example, their families or schools), or the community in which young people live. It was included cessation programmes but excluded programmes primarily aimed at prevention of uptake.
Outcomes	The primary outcome was smoking status at six months follow up, among those who smoked at baseline.
Main results	Fifteen trials were found, covering 3605 young people. Three trials used or tested the transtheoretical model stages of change (TTM) approach, two tested pharmacological aids to quitting (nicotine replacement and bupropion), and the remaining trials used various psycho-social interventions, such as motivational enhancement or behavioural management. The trials evaluating TTM interventions achieved moderate long-term success, with a pooled odds ratio (OR) at one year of 1.70 (95% confidence interval (CI) 1.25 to 2.33) persisting at two-year follow up with an OR of 1.38 (95% CI 0.99 to 1.92). Neither of the pharmacological intervention trials achieved statistically significant results (data not pooled), but both were small-scale, with low power to detect an effect. The three interventions (5 trials) which used cognitive behavioural therapy interventions did not individually achieve statistically significant results, although when the three Not on Tobacco trials were pooled the OR 1.87; (95% CI 1.00 to 3.50) suggested some measure of effectiveness. Although the three trials that incorporated motivational interviewing as a component of the intervention achieved a pooled OR of 2.05 (95% CI 1.10 to 3.80), the impossibility of isolating the effect of the motivational interviewing in these trials meant that we could not draw meaningful inferences from that analysis.

Authors' conclusions	Complex approaches show promise, especially those incorporating elements sensitive to stage of change. There were few trials with evidence about pharmacological interventions, and none demonstrated effectiveness for adolescent smokers. Psycho-social interventions have not so far demonstrated effectiveness, although pooled results for the Not on Tobacco trials suggest that that this approach may yet prove to be effective; however, their definition of cessation (one or more smoke-free days) may not adequately account for the episodic nature of much adolescent smoking.

Hajek 2001	Aversive smoking for smoking cessation
Study design	Randomized controlled trials.
Population	Any smokers.
Intervention	Any non-pharmacological aversion treatment.
Outcomes	Abstinence from smoking at least six months from beginning of treatment.
Main results	Twenty-five trials met the inclusion criteria. Twelve included rapid smoking and nine used other aversion methods. Ten trials included two or more conditions allowing assessment of a dose-response to aversive stimulation. The odds ratio (OR) for abstinence following rapid smoking compared to control was 2.01 (95% confidence intervals (CI): 1.36 to 2.95). Several factors suggest that this finding should be interpreted cautiously. A funnel plot of included studies was asymmetric, due to the relative absence of small studies with negative results. Most trials had a number of serious methodological problems likely to lead to spurious positive results. The only trial using biochemical validation of all self reported cessation gave a non-significant result. Other aversion methods were not shown to be effective (OR 1.15, 95% CI 0.73 to 1.82). There was a borderline dose-response to the level of aversive stimulation (OR 1.67, 95% CI 0.99 to 2.81).
Authors' conclusions	The existing studies provide insufficient evidence to determine the efficacy of rapid smoking, or whether there is a dose-response to aversive stimulation. Milder versions of aversive smoking seem to lack specific efficacy.

Hajek 2005	Relapse prevention interventions for smoking cessation
Study design	Randomized controlled trials.
Population	1)People who had quit smoking on their own; 2) People who were undergoing enforced abstinence, whether or not they intended to quit permanently; 3)Smokers participating in treatment programmes to assist initial cessation.
Intervention	Interventions identified by study investigators as intended to prevent relapse, compared to either no intervention or to a shorter intervention or to an intervention not oriented towards relapse prevention. Behavioural interventions delivered in any format, including group meetings, face to face sessions, written or other materials, proactive or reactive telephone support, and pharmacological interventions were considered.
Outcomes	The preferred outcome was prolonged or multiple point prevalence abstinence at follow-up of at least six months since randomization. Trials that only reported point prevalence abstinence (number of participants not smoking at point when assessment is made - abstinent at that time but not necessarily continuously since treatment) at six months or more were included. Studies with less than six months

	follow-up were excluded.
Main results	Forty studies met inclusion criteria, but were heterogeneous in terms of populations and interventions. Studies that randomized abstainers separately from studies that randomized participants prior to their quit date were considered. No benefit of brief and 'skills-based' relapse prevention interventions for women who had quit smoking due to pregnancy, or for smokers undergoing a period of enforced abstinence was detected. It was also failed to detect significant effects in trials in other smokers who had quit on their own or with a formal programme. Amongst trials recruiting smokers and evaluating the effect of additional relapse prevention components it was also found no evidence of benefit in any subgroup. It was not found that providing training in skills thought to be needed for relapse avoidance reduced relapse, but most studies did not use experimental designs best suited to the task, and had limited power to detect expected small differences between interventions.
Authors' conclusions	There is insufficient evidence to support the use of any specific intervention for helping smokers who have successfully quit for a short time to avoid relapse. The verdict is strongest for interventions focusing on identifying and resolving tempting situations, as most studies were concerned with these. There is very little research available regarding other approaches. Until more evidence becomes available it may be more efficient to focus resources on supporting the initial cessation attempt rather than on additional relapse prevention efforts.

Cahill 2005	Quit and Win contests for smoking cessation
Study design	Randomized and non-randomised controlled trials trials allocating communities to intervention or to control conditions.
Population	Adult smokers, either gender, within the targeted community.
Intervention	Population-based quit and win contests at local, national and international levels.
Outcomes	1. Cessation rates and sustained abstinence, for a minimum of six months from the start of the intervention. 2. Rates of recruitment to and participation in smoking cessation programmes.
Main results	Four studies met inclusion criteria. Three demonstrated significantly higher quit rates (8% to 20%) for the quit and win group than for the control group at the 12-month assessment. However, the population impact measure, where available, suggests that the effect of contests on community prevalence of smoking is small, with fewer than one in 500 smokers quitting because of the contest. Levels of deception, where they could be quantified, were high. Although surveys suggest that international quit and win contests may be effective, especially in developing countries, the lack of controlled studies precludes any firm conclusions from this review.
Authors' conclusions	Quit and win contests at local and regional level appear to deliver quit rates above baseline community rates, although the population impact of the contests seems to be relatively low. Contests may be subject to levels of deception which could compromise the validity of the intervention. International contests may prove to be an effective mechanism, particularly in developing countries, but a lack of well-designed comparative studies precludes any firm conclusions.

Stead 2007	Interventions for preventing tobacco sales to minors
Study design	Randomized and non-randomized controlled trials allocating retail outlets, communities or geographical regions, time series studies and uncontrolled before

	and after studies.
Population	Retailers. Minors were defined by the legal age limit in the communities studied.
Intervention	Education, law enforcement, community mobilization, or combinations of strategies that aimed to deter retailers from selling tobacco to minors.
Outcomes	1. Illegal tobacco sales, assessed by attempted purchase by young people. 2. Perceived ease of access to cigarettes by young people. 3. Prevalence of tobacco use among young people.
Main results	Thirty four studies of which 14 had data from a control group for at least one outcome were identified . Giving retailers information was less effective in reducing illegal sales than active enforcement or multicomponent educational strategies, or both. No strategy achieved complete, sustained compliance. In three controlled trials, there was little effect of intervention on youth perceptions of access or prevalence of smoking.
Authors' conclusions	Interventions with retailers can lead to large decreases in the number of outlets selling tobacco to youths. However, few of the communities studied in this review achieved sustained levels of high compliance. This may explain why there is limited evidence for an effect of intervention on youth perception of ease of access to tobacco, and on smoking behaviour.

Stead 2007	Interventions to reduce harm from continued tobacco use
Study design	Randomized or quasi-randomized controlled trials.
Population	Tobacco users.
Intervention	Interventions to reduce amount smoked, or to reduce harm from smoking by means other than cessation, including switching to a Potential Reduced-Exposure Product (PREP), or making other changes to cigarette characteristics. Interventions where a reduction in number of cigarettes smoked over a short period, or a change in type of cigarette smoked (e.g. nicotine fading), was intended as a precursor to quitting completely were excluded.
Outcomes	Change in cigarette consumption, markers of cigarette exposure and any markers of damage or benefit to health, at least six months from the start of the intervention.
Main results	The 13 included trials all evaluated interventions to help smokers cut down the amount smoked. Most trials tested nicotine replacement therapy (NRT) to assist reduction. In a pooled analysis of eight trials, NRT significantly increased the odds of reducing CPD by 50% or more for people using nicotine gum or inhaler or a choice of product compared to placebo (n=3273, odds ratio [OR] 2.02, 95% confidence interval [CI] 1.55 to 2.62). Whilst the effect for NRT was significant, small numbers of people in either treatment or control group successfully sustained a reduction of 50% or more. Use of NRT also significantly increased the odds of quitting (OR 1.90, 95% CI 1.46 to 2.47). Four trials of different types of advice and instructions on reducing CPD did not provide clear evidence.
Authors' conclusions	There is insufficient evidence about long-term benefit to give firm support the use of interventions intended to help smokers reduce but not quit tobacco use. Some people who do not wish to quit can be helped to cut down the number of cigarettes smoked by using nicotine gum or nicotine inhaler. Because the long-term health benefit of a reduction in smoking rate is unclear this application of NRT is more appropriately used as a precursor to quitting.

Thomas 2006	School-based programmes for preventing smoking
Study design	Randomized controlled trials allcoating individual students, classes, schools, or school districts.
Population	Children (aged 5 to12) or adolescents (aged 13 to18) in school settings.
Intervention	Classroom programmes or curricula, including those with associated family and community interventions, intended to deter use of tobacco. Programmes or curricula that provided information, those that used social influences approaches, those that taught generic social competence, and those that included interventions beyond the school into the community were included. Programmes with a drug or alcohol focus were included if outcomes for tobacco use were reported.
Outcomes	Prevalence of non-smoking at follow up among those not smoking at baseline.
Main results	Of the 94 randomized controlled trials identified, twenty three were classified as category one (most valid), evaluating for instance information-giving (one study), teaching social competence (two studies) and social influences interventions (13 studies). Of these, nine found some positive effect of intervention on smoking prevalence, and four failed to detect an effect on smoking prevalence. The largest and most rigorous study, the Hutchinson Smoking Prevention Project, found no long-term effect of an intensive eight-year programme on smoking behaviour. There were three category one RCTs of combined social influences and social competence interventions: one provided significant results and one only for instruction by health educators compared to self-instruction. There was a lack of high quality evidence about the effectiveness of combinations of social influences and social competence approaches. There was one category one study providing data on social influences compared with information giving. There were four category one studies of multi-modal approaches providing limited evidence about the effectiveness of multi-modal approaches including community initiatives.
Authors' conclusions	There is no strong evidence for offering school-based programmes that provide information only. The most widely used school interventions draw on social influence models. Although half of the high quality randomized controlled trials (RCTs) found positive significant results, there is conflicting evidence about the effects of such programmes, and the largest and most rigorous test of a social influences model, found no evidence of a sustained effect on smoking prevalence. Three of the four high quality multi-modal intreventions showed a positive significant effect. Cost is an important factor in planning school-based programmes. The Hutchinson Smoking Prevention Project delivered 65 classroom sessions to each group of students. This requires investment in teacher training, and diverts from other academic uses of classroom time. Those planning services will need to determine whether these costs are justified in the light of the existing evidence.

Thomas 2007	Family-based programmes for preventing smoking by children and adolescents
Study design	Randomized controlled trials.
Population	Children (aged 5-12) and adolescents (aged 13-18) and family members.
Intervention	Interventions with children and family members intended to deter the use of tobacco. Those with school- or community-based components were included provided the effect of the family-based intervention could clearly be measured and separated from the wider school- or community-based interventions. Interventions

	that focus on preventing drug or alcohol use were included if outcomes for tobacco use were reported. The family-based intervention could include any components to change parenting behaviour, parental or sibling smoking behaviour, or family communication and interaction.
Outcomes	Primary outcome: the smoking status of children who reported no use of tobacco at baseline, measured at least six months from the start of the intervention.
Main results	Twenty two RCTs of family interventions to prevent smoking were identified. Six RCTs were identified in Category 1 (minimal risk of bias on all counts); nine in Category 2 (a risk of bias in one or more areas); and five in Category 3 (risks of bias in design and execution such that reliable conclusions cannot be drawn from the study). Considering the fifteen Category 1 and 2 studies together: (1) four of the nine that tested a family intervention against a control group had significant positive effects, but one showed significant negative effects; (2) one of the five RCTs that tested a family intervention against a school intervention had significant positive effects; (3) none of the six that compared the incremental effects of a family plus a school programme to a school programme alone had significant positive effects; (4) the one RCT that tested a family tobacco intervention against a family non-tobacco safety intervention showed no effects; and (5) the trial that used general risk reduction interventions found the group which received the parent and teen interventions had less smoking than the one that received only the teen intervention. In the trial of CD-ROMs to reduce alcohol use, both groups which received the alcohol reduction intervention had less smoking than the control group. In neither trial was there a tobacco intervention, but tobacco outcomes were measured. For the included trials the amount of implementer training and the fidelity of implementation were related to positive outcomes, but the number of sessions was not.
Authors' conclusions	Some well-executed RCTs show family interventions may prevent adolescent smoking, but RCTs which were less well executed had mostly neutral or negative results. There is thus a need for well-designed and executed RCTs in this area.

Ussher 2005	Exercise interventions for smoking cessation
Study design	Randomized controlled trials.
Population	Smokers wishing to quit or recent quitters.
Intervention	Programmes of supervised or unsupervised exercise alone or as an adjunct to a smoking cessation intervention, compared to a smoking cessation programme alone. Interventions which included exercise in a multiple component smoking cessation programme were excluded since the specific effects of exercise on smoking abstinence could not be addressed. Multiple risk factor interventions where smoking cessation was one of a number of health-related outcomes were excluded for the same reason.
Outcomes	Smoking cessation at longest follow up after six months.
Main results	Eleven trials were identified, six of which had fewer than 25 people in each treatment arm. They varied in the timing and intensity of the smoking cessation and exercise programmes. Three studies showed significantly higher abstinence rates in a physically active group versus a control group at end of treatment. One study showed significantly higher abstinence rates for the exercise group versus a control group at the three-month follow up but not at the end of treatment or 12-month follow up. The other studies showed no significant effect for exercise on abstinence.
Authors'	Only one of the 11 trials offered evidence for exercise aiding smoking cessation at a

conclusions	12-month follow up. All but one of the other trials were too small to exclude reliably an effect of intervention, or included an exercise intervention which was insufficiently intense to achieve the desired level of exercise.

White 2006	Acupuncture and related interventions for smoking cessation
Study design	Randomized controlled trials
Population	Tobacco smokers of any age who wished to stop smoking.
Intervention	Non-pharmacological stimulation interventions involving needle puncture or finger pressure or laser therapy in areas of the body described by the study's author as acupuncture points, which includes points on the ear, face and body, or the related intervention of electrostimulation to the head region, either through surface electrodes or through needles.
Outcomes	Abstinence from smoking.
Main results	Twenty four reports of studies were identified. The only comparison for which there were sufficient studies to combine meaningfully, was acupuncture compared with sham acupuncture. The long-term result shows no effect of acupuncture compared with sham acupuncture. There was no consistent evidence that acupuncture is superior to no treatment, and no evidence that the effect of acupuncture was different from that of other anti-smoking interventions, or that any particular acupuncture technique is superior to other techniques.
Authors' conclusions	There is no consistent evidence that acupuncture, acupressure, laser therapy or electrostimulation are effective for smoking cessation, but methodological problems mean that no firm conclusions can be drawn. Further research using frequent or continuous stimulation is justified.

INTERVENTIONS TO PROMOTE PHYSICAL ACTIVITY LIKELY TO BE EFFECTIVE

Foster 2005	Interventions for promoting physical activity
Study design	Randomised controlled trials.
Population	Community dwelling adults with no more than 10% of subjects with pre-existing medical conditions that may limit participation in physical activity
Intervention	One only or a combination of: One-to-one counselling/advice or group counselling/advice; Self-directed or prescribed physical activity; Supervised or unsupervised physical activity; Home-based or facility-based physical activity; Ongoing face-to-face support; Telephone support; Written education/motivation support material; Self monitoring. The interventions were conducted by one or a combination of practitioners including a physician, nurse, health educator, counsellor, exercise leader or peer. Mass media interventions and multiple risk factor interventions were excluded. The interventions were compared with a no intervention control, attention control (receiving attention matched to length of intervention, e.g. general health check) and/or minimal intervention control group.
Outcomes	1. Change in self-reported physical activity between baseline and follow-up. 2. Cardio-respiratory fitness. 3. Adverse events.
Main results	The effect of interventions on self-reported physical activity (19 studies; 7598 participants) was positive and moderate (pooled SMD random effects model 0.28 95% CI 0.15 to 0.41) as was the effect of interventions (11 studies; 2195 participants) on cardio-respiratory fitness (pooled SMD random effects model 0.52 95% CI 0.14 to 0.90). There was significant heterogeneity in the reported effects as well as in characteristics of the interventions. The heterogeneity in reported effects was reduced in higher quality studies, when physical activity was self-directed with some professional guidance and when there was on-going professional support.
Authors' conclusions	The review suggests that physical activity interventions have a moderate effect on self-reported physical activity, on achieving a predetermined level of physical activity and cardio-respiratory fitness. Due to the clinical and statistical heterogeneity of the studies, only limited conclusions can be drawn about the effectiveness of individual components of the interventions.

Orozco 2008	Exercise or exercise and diet for preventing type 2 diabetes mellitus
Study design	RCTs
Population	Participants of any age, sex or ethnicity belonging to any of the major risk groups for the development of type 2 diabetes (impaired glucose tolerance, impaired fasting glucose, previous gestational diabetes, hypertension equal to or greater than 140/90 mmHg, family history of type 2 diabetes in first degree relatives, obesity, dyslipidaemia, high risk ethnic groups
Intervention	Exercise versus standard recommendations or no intervention; exercise and diet versus standard recommendations or no intervention; exercise versus diet.
Outcomes	Primary: development of type 2 diabetes mellitus (incidence); diabetes and cardiovascular related morbidity Secondary: development of impaired glucose tolerance, development of impaired fasting glucose, anthropometric measures: body weight, body mass index (BMI) and waist-to-hip-ratio, systolic and diastolic blood pressure; lipid levels: total cholesterol,

	LDL- and HDL-cholesterol, triglycerides; quality of life, adverse effects, all-cause mortality; costs. Covariates, effect modifiers and confounders: compliance; co-morbidities; age.
Main results	Eight trials had an exercise plus diet (2241 participants) and a standard recommendation arm (2509 participants). Two studies had a diet only (167 participants) and exercise only arm (178 participants). Study duration ranged from one to six years. Overall, exercise plus diet interventions reduced the risk of diabetes compared with standard recommendations (RR 0.63, 95% CI 0.49 to 0.79). This had also favourable effects on weight and body mass index reduction, waist-to-hip ratio and waist circumference. However, statistical heterogeneity was very high for these outcomes. Exercise and diet interventions had a very modest effect on blood lipids. However, this intervention improved systolic and diastolic blood pressure levels (weighted mean difference -4 mmHg, 95% CI -5 to -2 and -2 mmHg, 95% CI -3 to -1, respectively). No statistical significant effects on diabetes incidence were observed when comparing exercise only interventions either with standard recommendations or with diet only interventions. No study reported relevant data on diabetes and cardiovascular related morbidity, mortality and quality of life.
Authors' conclusions	Interventions aimed at increasing exercise combined with diet are able to decrease the incidence of type 2 diabetes mellitus in high risk groups (people with impaired glucose tolerance or the metabolic syndrome). There is a need for studies exploring exercise only interventions and studies exploring the effect of exercise and diet on quality of life, morbidity and mortality, with special focus on cardiovascular outcomes.

Shaw 2006	Exercise for overweight or obesity
Study design	Randomized controlled trials.
Population	Adult participants (aged over 18 years) with overweight or obesity.
Intervention	The studies included had an exercise prescription. Exercise was defined as any form of physical activity performed on a repeated basis for a defined period of time (exercise training). Exercise prescriptions include specific recommendations for the type, intensity, frequency and duration of any physical activity with a specific objective (e.g. increase fitness, lose weight). Studies stating that they simply recommended increasing physical activity were not included within the analyses unless it was possible to quantify the exercise stimulus by some means.
Outcomes	Primary: weight or another indicator of body mass (e.g. body mass index, waist measurement, waist-to-hip ratio); morbidity and mortality; well-being and quality of life, with a follow-up period of at least three months. Secondary: serum lipids; serum glucose; systolic and diastolic blood pressure.
Main results	The 43 studies included 3476 participants. Although significant heterogeneity in some of the main effects' analyses limited ability to pool effect sizes across some studies, a number of pooled effect sizes were calculated. When compared with no treatment, exercise resulted in small weight losses across studies. Exercise combined with diet resulted in a greater weight reduction than diet alone (WMD - 1.0 kg; 95% confidence interval (CI) -1.3 to -0.7). Increasing exercise intensity increased the magnitude of weight loss (WMD - 1.5 kg; 95% CI -2.3 to -0.7). There were significant differences in other outcome measures such as serum lipids, blood pressure and fasting plasma glucose. Exercise as a sole weight loss intervention resulted in significant reductions in diastolic blood pressure (WMD - 2 mmHg; 95% CI -4 to -1), triglycerides (WMD - 0.2 mmol/L; 95% CI -0.3 to -0.1) and fasting glucose (WMD - 0.2 mmol/L; 95% CI -0.3 to -0.1). Higher intensity exercise resulted

	in greater reduction in fasting serum glucose than lower intensity exercise (WMD -0.3 mmol/L; 95% CI -0.5 to -0.2). No data were identified on adverse events, quality of life, morbidity, costs or on mortality.
Authors' conclusions	The results of this review support the use of exercise as a weight loss intervention, particularly when combined with dietary change. Exercise is associated with improved cardiovascular disease risk factors even if no weight is lost.

Thomas 2006	Exercise for type 2 diabetes mellitus
Study design	Randomised controlled trials.
Population	Males and females with type 2 diabetes.
Intervention	A prescribed exercise intervention, defined as a pre-determined program of physical activity. The included studies involved three types of intervention: (1) exercise versus non-exercise control; (2) exercise plus diet versus diet alone; (3) exercise plus medication versus medication alone.
Outcomes	Primary: glycaemic control; body mass indices; adverse events (hypoglycaemic reactions, exercise induced injuries). Secondary: insulin sensitivity; blood lipids; blood pressure; quality of life; fitness; diabetic complication rates; mortality.
Main results	Fourteen randomised controlled trials comparing exercise against no exercise in type 2 diabetes were identified involving 377 participants. Trials ranged from eight weeks to twelve months duration. Compared with the control, the exercise intervention significantly improved glycaemic control as indicated by a decrease in glycated haemoglobin levels of 0.6% (-0.6 % HbA_{1c}, 95% confidence interval (CI) -0.9 to -0.3; $P < 0.05$). This result is both statistically and clinically significant. There was no significant difference between groups in whole body mass, probably due to an increase in fat free mass (muscle) with exercise, as reported in one trial (6.3 kg, 95% CI 0.0 to 12.6). There was a reduction in visceral adipose tissue with exercise (-45.5 cm^2, 95% CI -63.8 to -27.3), and subcutaneous adipose tissue also decreased. No study reported adverse effects in the exercise group or diabetic complications. The exercise intervention significantly increased insulin response (131 AUC, 95% CI 20 to 242) (one trial), and decreased plasma triglycerides (-0.25 mmol/L, 95% CI -0.48 to -0.02). No significant difference was found between groups in quality of life (one trial), plasma cholesterol or blood pressure.
Authors' conclusions	The meta-analysis shows that exercise significantly improves glycaemic control and reduces visceral adipose tissue and plasma triglycerides, but not plasma cholesterol, in people with type 2 diabetes, even without weight loss.

INTERVENTIONS TO PROMOTE PHYSICAL ACTIVITY WITH UNKNOWN EFFECTIVENESS

Ashworth 2005	Home versus center based physical activity programs in older adults
Study design	Randomised or quasi-randomised controlled trials.
Population	Older adults with either a recognised cardiovascular risk factor, or existing cardiovascular disease, chronic obstructive airways disease or osteoarthritis.
Intervention	'Home based' physical activity versus a program of center based' physical activity.
Outcomes	1. Primary: Measures of functional activity. 2. Secondary: Long-term maintenance of physical activity, Measures of Quality of Life, Cost and Health Service utilization. 3. Secondary Cardiovascular related: Mortality, Rates of Cardiovascular diseases, Exercise capacity and CV Risk factor reduction. 4. Other.
Main results	Six trials including 224 participants who received a 'home based' exercise program and 148 who received a 'center based' exercise program were included. Five studies were of medium quality and one poor. A meta-analysis was not undertaken. Home based programs appeared to have a significantly higher adherence rate than center based programs, but this was based on the one study (with the highest quality rating of the studies found) of sedentary older adults. This showed an adherence rate of 68% in the home based program at two year follow-up compared with a 36% adherence in the center based group. There was essentially no difference in treadmill performance or cardiovascular risk factors between groups.
Authors' conclusions	Home based programs appear to be superior to center based programs in terms of the adherence to exercise (especially in the long-term).

Jackson 2005	Policy interventions implemented through sporting organisations for promoting healthy behaviour change
Study design	RCTs)/cluster RCTs, Quasi-randomised' trials, CBA studies.
Population	Persons of all ages.
Intervention	Any policy intervention implemented through sporting organisations to instigate and/or sustain healthy behaviour change, intention to change behaviour, or changes in attitudes, knowledge or awareness of healthy behaviour. Policies must address any of the following: smoking, alcohol, healthy eating, sun protection, access for disadvantaged groups, physical safety (not including injuries), and social and emotional health (e.g.. anti-vilification, anti-discrimination).
Outcomes	Behaviour change, intention to change behaviour, change in attitudes, knowledge or awareness of healthy behaviour, and policy presence.
Main results	No rigorous studies were located to test the effectiveness of policy interventions organised through sporting organisations to increase healthy behaviours, attitudes, knowledge or inclusion of health oriented policies within the organisations.
Authors' conclusions	The authors were unable to find any controlled studies to guide the use of policy interventions used in sporting settings. The search process revealed a number of case studies with anecdotal reporting of outcomes. They strongly recommend that rigorous evaluation techniques are employed more commonly in this field to illuminate the impact of health promoting policy on outcomes, and the contexts and processes which are likely to be effective in reducing harmful behaviours.

DIETARY AND WEIGHT REDUCTION INTERVENTIONS LIKELY TO BE EFFECTIVE

Weight reduction interventions likely to be effective

Mulrow 1998	Dieting to reduce body weight for controlling hypertension in adults
Study design	Randomized controlled trials.
Population	Adults with hypertension (ie, systolic blood pressure at least 140 mm Hg and/or diastolic blood pressure at least 90 mm Hg; or receiving antihypertensives).
Intervention	Calorie restricted diets intended to produce weight reduction.
Outcomes	Weight, Total mortality, Cardiovascular mortality and morbidity, Quality of life, Functional status and Blood pressure.
Main results	Eighteen trials were found. Only one small study of inadequate power reported morbidity and mortality outcomes. None addressed quality of life or general well being issues. In general, participants assigned to weight-reduction groups lost weight compared to control groups. Six trials involving 361 participants assessed a weight-reducing diet versus a normal diet. The data suggested weight loss in the range of 4% to 8% of body weight was associated with a decrease in blood pressure in the range of 3 mm Hg systolic and diastolic. Three trials involving 363 participants assessed a weight-reducing diet versus treatment with antihypertensive medications. These suggested that a stepped-care approach with antihypertensive medications produced greater decreases in blood pressure (in the range of 6/5 mm Hg systolic/diastolic) than did a weight-loss diet. Trials that allowed adjustment of participants' antihypertensive regimens suggested that patients required less intensive antihypertensive drug therapy if they followed a weight-reducing diet. Data was insufficient to determine the relative efficacy of weight-reduction versus changes in sodium or potassium intake or exercise.
Authors' conclusions	Weight-reducing diets in overweight hypertensive persons can affect modest weight loss in the range of 3-8% of body weight and are probably associated with modest blood pressure decreases of roughly 3 mm Hg systolic and diastolic. Weight-reducing diets may decrease dosage requirements of antihypertensive medications.

Norris 2005	Long-term non-pharmacological weight loss interventions for adults with prediabetes
Study design	Randomized controlled trials.
Population	Persons 18 years or greater with prediabetes.
Intervention	Interventions had to have weight loss or weight control as one of their primary goals. Focus on the patient rather than the provider or health care system.
GOutcomes	1. Main outcome measures: Weight, BMI, or percentage weight loss from baseline; Mortality: diabetes-related, cardiovascular disease, total; Quality of life. 2. Additional outcome measures: Morbidity; Cardiovascular disease events; Glycemic control; Serum lipid concentrations; Blood pressure.
Main results	Nine studies were identified, with a total of 5,168 participants. Follow-up ranged from 1 to 10 years. Quantitative synthesis was limited by the heterogeneity of populations, settings, and interventions and by the small number of studies that

	examined outcomes other than weight. Overall, in comparisons with usual care, four studies with a follow-up of one year reduced weight by 2.8 kg (95 % confidence interval (CI) 1.0 to 4.7) (3.3% of baseline body weight) and decreased body mass index by 1.3 kg/m^2 (95% CI 0.8 to 1.9). Weight loss at two years was 2.6 kg (95% CI 1.9 to 3.3) (three studies). Modest improvements were noted in the few studies that examined glycemic control, blood pressure, or lipid concentrations (P > 0.05). No data on quality of life or mortality were found. The incidence of diabetes was significantly lower in the intervention groups versus the controls in three of five studies examining this outcome at 3 to 6 years follow-up.
Authors' conclusions	Overall, weight loss strategies using dietary, physical activity, or behavioural interventions produced significant improvements in weight among persons with prediabetes and a significant decrease in diabetes incidence. Further work is needed on the long-term effects of these interventions on morbidity and mortality and on how to implement these interventions in diverse community settings.

Norris 2005	Long-term non-pharmacological weight loss interventions for adults with type 2 diabetes mellitus
Study design	Randomized controlled trials.
Population	Persons ≥18 years of age with type 2 diabetes.
Intervention	Interventions having weight loss or weight control as one of the primary stated goals of the intervention., they were classified as dietary, physical activity, or behavioral.
Outcomes	1. Main outcome measures: weight; mortality; quality of life. 2. Additional outcome measures: morbidity; cardiovascular disease events; glycated hemoglobin (GHb); fasting blood sugar; serum lipids; blood pressure; adverse events; cardiovascular fitness; incidence of hypertension; biliary tract disease. 3. Studies with a follow-up period of 12 months or greater were included in this review.
Main results	The 22 studies of weight loss interventions identified had a 4,659 participants and follow-up of 1 to 5 years. The pooled weight loss for any intervention in comparison to usual care among 585 subjects was 1.7 kg (95 % confidence interval [CI] 0.3 to 3.2), or 3.1% of baseline body weight among 517 subjects. Other main comparisons demonstrated non-significant results: among 126 persons receiving a physical activity and behavioural intervention, those who also received a very low calorie diet lost 3.0 kg (95% CI -0.5 to 6.4), or 1.6% of baseline body weight, more than persons receiving a low-calorie diet. Among 53 persons receiving identical dietary and behavioural interventions, those receiving more intense physical activity interventions lost 3.9 kg (95% CI -1.9 to 9.7), or 3.6% of baseline body weight, more than those receiving a less intense or no physical activity intervention. Comparison groups often achieved significant weight loss (up to 10.0 kg), minimizing between-group differences. Changes in glycated hemoglobin generally corresponded to changes in weight and were not significant when between-group differences were examined. No data were identified on quality of life and mortality.
Authors' conclusions	Weight loss strategies using dietary, physical activity, or behavioural interventions produced small between-group improvements in weight. These results were minimized by weight loss in the comparison group. Multicomponent interventions including very low calorie diets or low calorie diets may hold promise for achieving weight loss in adults with type 2 diabetes.

Norris 2005	Pharmacotherapy for weight loss in adults with type 2 diabetes mellitus
Study design	Randomised controlled trials only

Population	Adults 18 years or older with type 2 diabetes, overweight as defined in the study.
Intervention	Any drug therapy delivered for the primary purpose of losing and/or controlling weight.
Outcomes	Main: Weight and body fat distribution, drug-related morbidity, quality of life. Secondary: Glycemic control: glycated hemoglobin, fasting blood sugar; Serum lipids; Blood pressure; Non drug-related morbidity; Mortality.
Main results	A sufficient number of studies were available for a quantitative synthesis for fluoxetine, orlistat, and sibutramine. Twenty two randomized controlled trials were included in the review, with a total of 296 participants for fluoxetine, 2036 for orlistat, and 1047 for sibutramine. Pharmacotherapy produced modest reductions in weight for fluoxetine (5.1 kg (95% CI, 3.3 - 6.9) at 24 to 26 weeks follow up; orlistat 2.0 kg (CI, 1.3 - 2.8) at 12 to 57 weeks follow-up, and sibutramine 5.1 kg (CI, 3.2 - 7.0) at 12 to 52 weeks follow-up. Glycated hemoglobin also modestly and significantly reduced for fluoxetine and orlistat. Gastrointestinal side effects were common with orlistat; tremor, somnolence and sweating with fluoxetine; and palpitations with sibutramine.
Authors' conclusions	Fluoxetine, orlistat, and sibutramine can achieve statistically significant weight loss over 12 to 57 weeks. The magnitude of weight loss is modest, however, and the long-term health benefits remain unclear. The safety of sibutramine is uncertain.

Padwal 2003	Long-term pharmacotherapy for obesity and overweight
Study design	Placebo controlled RCTs
Population	Adults (age 18 or over) with either: body mass index (BMI) 30 kg/m2 or greater or BMI 27 kg/m2 or greater plus obesity-related co-morbidity
Intervention	Weight loss and weight maintenance studies evaluating the following medications: sibutramine, phentermine, mazindol, diethylpropion, benzphetamine, phendimetrazine, benzocaine rimonabant and orlistat.
Outcomes	Primary: Weight loss, expressed as number of kilograms lost, percentage of baseline weight lost, or both. Secondary: weight loss expressed as the proportion of patients achieving 5% and 10% weight loss (5% and 10% responders), change in BMI and change in waist circumference, total and cardiovascular mortality; myocardial infarction; stroke; medication intolerance; change in blood pressure; change in lipid profile; change in Hb A1C; side effects of therapy.
Main results	Sixteen orlistat (n = 10,631), 10 sibutramine (n = 2623) and four rimonabant trials (n = 6365) met inclusion criteria. Attrition rates averaged 30% to 40%. Compared to placebo, orlistat reduced weight by 2.9 kg (95% confidence interval (CI) 2.5 to 3.2 kg), sibutramine by 4.2 kg (95% CI 3.6 to 4.7 kg). Patients on active drug therapy were significantly more likely to achieve 5% and 10% weight loss thresholds. Placebo-controlled weight losses were consistently lower in patients with diabetes. Orlistat reduced diabetes incidence, improved total cholesterol, LDL-cholesterol, blood pressure, and glycaemic control in patients with diabetes but increased rates of gastrointestinal side effects and slightly lowered HDL levels. Sibutramine improved HDL and triglyceride levels but raised blood pressure and pulse rate.
Authors' conclusions	Orlistat and sibutramine have been studied in trials of one year or longer. Internal validity of studies was limited by high attrition rates. The antiobesity agents are

	modestly effective in reducing weight and have differing effects on cardiovascular risk and adverse effects profiles. Longer and more methodologically rigorous studies that are powered to examine endpoints such as mortality and cardiovascular morbidity are required.

Shaw 2005	Psychological interventions for overweight or obesity
Study design	Randomised and quasi-randomised controlled clinical
Population	Adult participants aged over 18 years with overweight or obesity at study baseline.
Intervention	All types of psychological interventions were considered for inclusion.
Outcomes	1. Main outcome measures: Weight or another indicator of body mass; Morbidity and mortality; ell-being and quality of life measures. 2. Additional outcome measures: Cost of implementing the psychological intervention; Measured psychological functioning; Fasting plasma glucose and hba1c; Plasma triglycerides, high-density lipoprotein, low-density lipoprotein and very-low-density lipoprotein ; Adverse effects. 3. Specific effect modifiers: Compliance.
Main results	A total of 36 studies met the inclusion criteria and were included in the review. Overall, 3495 participants were evaluated. The majority of studies assessed behavioural and cognitive-behavioural weight reduction strategies. Cognitive therapy, psychotherapy, relaxation therapy and hypnotherapy were assessed in a small number of studies. Behaviour therapy was found to result in significantly greater weight reductions than placebo when assessed as a stand-alone weight loss strategy (WMD -2.5 kg; 95% CI -1.7 to -3.3). When behaviour therapy was combined with a diet / exercise approach and compared with diet / exercise alone, the combined intervention resulted in a greater weight reduction. Studies were heterogeneous however the majority of studies favoured combining behaviour therapy with dietary and exercise interventions to improve weight loss. Increasing the intensity of the behavioural intervention significantly increased the weight reduction (WMD -2.3 kg; 95% CI -1.4 to - 3.3). Cognitive-behaviour therapy, when combined with a diet / exercise intervention, was found to increase weight loss compared with diet / exercise alone (WMD -4.9 kg; 95% CI -7.3 to - 2.4). No data on mortality, morbidity or quality of life were found.
Authors' conclusions	People who are overweight or obese benefit from psychological interventions, particularly behavioural and cognitive-behavioural strategies, to enhance weight reduction. They are predominantly useful when combined with dietary and exercise strategies. The bulk of the evidence supports the use of behavioural and cognitive-behavioural strategies. Other psychological interventions are less rigorously evaluated for their efficacy as weight loss treatments.

Thomas 2007	Low glycaemic index or low glycaemic load diets for overweight and obesity
Study design	Randomised controlled trials.
Population	Males and females of any age who were classified as overweight or obese. People with diabetes mellitus were excluded.
Intervention	Included were studies that compared a low glycaemic index, or low glycaemic load, diet with a higher glycaemic index or load diet or any other diet.
Outcomes	Primary outcomes: body mass, body mass index (BMI), BMI adjusted for age; adiposity (cm2) and fat distribution; adverse effects. Secondary outcomes: insulin action; glycaemic control; cardiovascular risk factors;

	satiety; other metabolic indices; quality of life; mortality.
Main results	Six eligible randomised controlled trials (total of 202 participants) were identified. Interventions ranged from five weeks to six months duration with up to six months follow-up after the intervention ceased. The decrease in body mass (WMD -1.1 kg, 95% confidence interval (CI) -2.0 to -0.2, P < 0.05) (n = 163), total fat mass (WMD -1.1 kg, 95% CI -1.9 to -0.4, P < 0.05) (n =147) and body mass index (WMD -1.3, 95% CI -2.0 to -0.5, P < 0.05) (n = 48) was significantly greater in participants receiving LGI compared to Cdiets. The decrease in total cholesterol was significantly greater with LGI compared to Cdiets (WMD -0.22 mmol/L, 95% CI -0.43 to -0.02, P < 0.05), as was the change in LDL-cholesterol (WMD -0.24 mmol/L, 95% CI -0.44 to -0.05, P < 0.05). No study reported adverse effects, mortality or quality of life data.
Authors' conclusions	Overweight or obese people on LGI lost more weight and had more improvement in lipid profiles than those receiving Cdiets. Body mass, total fat mass, body mass index, total cholesterol and LDL-cholesterol all decreased significantly more in the LGI group. In studies comparing ad libitum LGI diets to conventional restricted energy low-fat diets, participants fared as well or better on th LGI diet, even though they could eat as much as desired. Lowering the glycaemic load of the diet appears to be an effective method of promoting weight loss and improving lipid profiles and can be simply incorporated into a person's lifestyle. Further research with longer term follow-up will determine whether improvement continues long-term and improves quality of life.

Other dietary interventions aimed at reducing cardiovascular risk likely to be effective

He 2004	Effect of longer-term modest salt reduction on blood pressure.
Study design	Randomized controlled trials.
Population	Adults (18 years or older) with normal or elevated blood pressure, irrespective of gender and ethnicity. Children or pregnant women were excluded.
Intervention	The interventions included were to reduce salt intake. Studies with concomitant interventions (i.e. nonpharmacololgical interventions, antihypertensive or other medications) were excluded. One trial with factorial design (i.e. the Trials of Hypertension Prevention, Phase II) was included (TOHPRG 1997), however, in this trial the low salt arm (without weight intervention) was compared to the control group (without salt or weight intervention).
Outcomes	Changes in systolic and diastolic blood pressure, and 24h urinary sodium excretion.
Main results	Twenty trials in individuals with elevated blood pressure (n=802) and 11 trials in individuals with normal blood pressure (n=2220) were included. In individuals with elevated blood pressure the median reduction in urinary sodium was 78 mmol/24h (4.6 g/day of salt), the mean reduction in blood pressure was -5.06 mmHg (95%CI:-5.81 to -4.31) for systolic and -2.70 mmHg (95% CI:-3.16 to -2.24) for diastolic. In individuals with normal blood pressure the median reduction in urinary sodium was 74 mmol/24h (4.4 g/day of salt), the mean reduction in blood pressure was -2.03 mmHg (95% CI: -2.56 to -1.50) for systolic and -0.99 mmHg (-1.40 to -0.57) for diastolic. Weighted linear regression showed a significant relationship between the reduction in urinary sodium and the reduction in blood pressure.
Authors' conclusions	The meta-analysis demonstrates that a modest reduction in salt intake for a duration of 4 or more weeks has a significant and, from a population viewpoint, important effect on blood pressure in both individuals with normal and elevated blood pressure. These results support other evidence suggesting that a modest and long-

	term reduction in population salt intake could reduce strokes, heart attacks, and heart failure. Furthermore, our meta-analysis demonstrates a correlation between the magnitude of salt reduction and the magnitude of blood pressure reduction. Within the daily intake range of 3 to 12 g/day, the lower the salt intake achieved, the lower the blood pressure.

Brunner 2007	Dietary advice for reducing cardiovascular risk
Study design	Randomised controlled trials
Population	Healthy community-dwelling adults aged 18 years or older. Less than 25% of the participants in any trial had diagnosed cardiovascular disease at recruitment. Reported use of pharmacological therapy (e.g. statins or diuretics), during the trial was no greater than 10% of participants in any arm of the trial. Trials involving pregnant women or children and trials to reduce weight were excluded.
Intervention	Dietary interventions involve verbal or written advice delivered in person or over the phone to individuals or small groups. The advice could include a combination of such approaches, and be given by health professionals or other personnel. Trials could include additional interventions such as posters in a works canteen.
Outcomes	Primary outcomes: a) Cardiovascular risk factors. b) Bio-markers of dietary intake. Secondary outcomes: Self-reported measures of dietary intake, including fat, fat fractions, dietary fibre, fish, fruit and vegetables, vitamin C, vitamin E, carotenoids, flavonoids, and folic acid. Follow up: Trials were included if they had at least 3 months follow up from baseline.
Main results	Thirty-eight trials with 46 intervention arms (comparisons) comparing dietary advice with no advice were included in the review. 17,871 participants/clusters were randomised. Twenty-six of the 38 included trials were conducted in the USA. Dietary advice reduced total serum cholesterol by 0.16 mmol/L (95% CI 0.06 to 0.25) and LDL cholesterol by 0.18 mmol/L (95% CI 0.1 to 0.27) after 3-24 months. Mean HDL cholesterol levels and triglyceride levels were unchanged. Dietary advice reduced blood pressure by 2.07 mmHg systolic (95% CI 0.95 to 3.19) and 1.15 mmHg diastolic (95% CI 0.48 to 1.85) and 24-hour urinary sodium excretion by 44.2 mmol (95% CI 33.6 to 54.7) after 3-36 months. Three trials reported plasma antioxidants where small increases were seen in lutein and β-cryptoxanthin, but there was heterogeneity in the trial effects. Self-reported dietary intake may be subject to reporting bias, and there was significant heterogeneity in all the following analyses. Compared to no advice, dietary advice increased fruit and vegetable intake by 1.25 servings/day (95% CI 0.7 to 1.81). Dietary fibre intake increased with advice by 5.99 g/day (95% CI 1.12 to 10.86), while total dietary fat as a percentage of total energy intake fell by 4.49 % (95% CI 2.31 to 6.66) with dietary advice and saturated fat intake fell by 2.36 % (95% CI 1.32 to 3.39).
Authors' conclusions	Dietary advice appears to be effective in bringing about modest beneficial changes in diet and cardiovascular risk factors over approximately 10 months but longer term effects are not known.

Hooper 2004	Advice to reduce dietary salt for prevention of cardiovascular disease
Study design	Randomised controlled trials with at least 26 weeks of follow up.
Population	Adults (16 years or older) with normal or raised blood pressure.
Intervention	The interventions included were designed to reduce sodium intake. The control group received a placebo intervention or no active intervention. Studies were not

	included if they used a multiple risk factor intervention intending to alter lifestyle or dietary factors other than sodium (unless the effect of the low sodium diet could be separated out from the other interventions).
Outcomes	Primary outcomes: total mortality and combined cardiovascular events. Secondary outcomes: Changes in systolic and diastolic blood pressure (mm Hg), quality of life, weight (kg), nutrient intakes, urinary sodium excretion (mmol/24 hours) and numbers and doses of anti-hypertensive medication used.
Main results	Three trials in normotensives (n=2326), five in untreated hypertensives (n=387) and three in treated hypertensives (n=801) were included, with follow up from six months to seven years. The large, high quality (and therefore most informative) studies used intensive behavioural interventions. Deaths and cardiovascular events were inconsistently defined and reported; only 17 deaths equally distributed between intervention and control groups occurred. Systolic and diastolic blood pressures were reduced at 13 to 60 months in those given low sodium advice as compared with controls (systolic by 1.1 mm Hg, 95% CI 1.8 to 0.4, diastolic by 0.6 mm hg, 95% CI 1.5 to -0.3), as was urinary 24 hour sodium excretion (by 35.5 mmol/ 24 hours, 95% CI 47.2 to 23.9). Degree of reduction in sodium intake and change in blood pressure were not related. People on anti-hypertensive medications were able to stop their medication more often on a reduced sodium diet as compared with controls, while maintaining similar blood pressure control.
Authors' conclusions	Intensive interventions, unsuited to primary care or population prevention programmes, provide only minimal reductions in blood pressure during long-term trials. Further evaluations to assess effects on morbidity and mortality outcomes are needed for populations as a whole and for patients with elevated blood pressure. Evidence from a large and small trial showed that a low sodium diet helps in maintenance of lower blood pressure following withdrawal of antihypertensives. If this is confirmed, with no increase in cardiovascular events, then targeting of comprehensive dietary and behavioural programmes in patients with elevated blood pressure requiring drug treatment would be justified.

Hooper 2000	Reduced or modified dietary fat for preventing cardiovascular disease
Study design	Randomized controlled trials.
Population	Adults (18 years or older) at any risk of cardiovascular disease (with or without existing cardiovascular disease)
Intervention	Interventions stating an intention to reduce or modify dietary fat or cholesterol, such as would be expected to result in improvement of serum lipid profile, such as dietary advice, supplementation (of fats, oils or modified or low fat foods) or a provided diet, and the control group usual diet, placebo or a control diet.
Outcomes	Primary: total and cardiovascular mortality, combined cardiovascular events (cardiovascular deaths, cardiovascular morbidity and unplanned cardiovascular interventions). Secondary: risk factor changes (weight, blood pressure, total, LDL or HDL cholesterol and triglyceride levels) and quality of life measures.
Main results	Twenty seven studies were included (40 intervention arms, 30,901 person-years). There was no significant effect on total mortality (rate ratio 0.98, 95% CI 0.86 to 1.12), a trend towards protection form cardiovascular mortality (rate ratio 0.91, 95% CI 0.77 to 1.07), and significant protection from cardiovascular events (rate ratio 0.84, 95% CI 0.72 to 0.99). The latter became non-significant on sensitivity analysis. Trials where participants were involved for more than 2 years showed significant reductions in the rate of cardiovascular events and a suggestion of protection from total mortality. The degree of protection from cardiovascular events appeared similar

	in high and low risk groups, but was statistically significant only in the former.
Authors' conclusions	The findings are suggestive of a small but potentially important reduction in cardiovascular risk in trials longer than two years. Lifestyle advice to all those at high risk of cardiovascular disease (especially where statins are unavailable or rationed), and to lower risk population groups, should continue to include permanent reduction of dietary saturated fat and partial replacement by unsaturates.

Jürgens 2004	Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride
Study design	Randomized controlled trials.
Population	Adults (> 15 years) with normal or elevated blood pressure irrespective of race.
Intervention	The intervention was changed sodium intake: comparisons between a group eating a low sodium diet and a group eating high sodium diet.
Outcomes	SBP, DBP, renin, aldosterone, adrenaline, noradrenaline, triglyceride, cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL).
Main results	In 57 trials of mainly Caucasians with normal blood pressure, low sodium intake reduced SBP by -1.27 mm Hg (CI: -1.76; -0.77)(p<0.0001) and DBP by -0.54 mm Hg (CI: -0.94; -0.14) (p = 0.009) as compared to high sodium intake. In 58 trials of mainly Caucasians with elevated blood pressure, low sodium intake reduced SBP by -4.18 mm Hg (CI: -5.08; - 3.27) (p < 0.0001) and DBP by -1.98 mm Hg (CI: -2.46; -1.32) (p < 0.0001) as compared to high sodium intake. The median duration of the intervention was 8 days in the normal blood pressure trials (range 4-1100) and 28 days in the elevated blood pressure trials (range 4-365). Multiple regression analyses showed no independent effect of duration on the effect size. In 8 trials of blacks with normal or elevated blood pressure, low sodium intake reduced SBP by -6.44 mm Hg (CI: -9.13; -3.74) (p < 0.0001) and DBP by -1.98 mm Hg (CI: -4.75; 0.78) (p = 0.16) as compared to high sodium intake.
Authors' conclusions	The magnitude of the effect in Caucasians with normal blood pressure does not warrant a general recommendation to reduce sodium intake. Reduced sodium intake in Caucasians with elevated blood pressure has a useful effect to reduce blood pressure in the short-term. The results suggest that the effect of low versus high sodium intake on blood pressure was greater in Black and Asian patients than in Caucasians. However, the number of studies in black and Asian patients was insufficient for different recommendations.

Nield 2008	Dietary advice for the prevention of type 2 diabetes mellitus in adults
Study design	Randomised controlled clinical trials
Population	Participants who were 18 years or older
Intervention	Dietary advice aiming at reducing weight and risk of developing type 2 diabetes.
Outcomes	Primary: Incidence of type 2 diabetes. Glycaemic control measures (oral glucose tolerance test, both fasting and 2-hour and glycated haemoglobin; for the detection of impaired glucose tolerance); Time to development or diagnosis of type 2 diabetes mellitus. Secondary: Quality of life (ideally, measured using a validated instrument); Mortality; Morbidity; Weight; body mass index (BMI); Cost of intervention(s); Serum

	cholesterol (LDL and/or HDL) and serum triglycerides; Blood pressure; Maximal exercise capacity; Adverse effects.
Main results	Two trials which randomised 358 people to dietary treatment and control groups were identified. Longest duration of follow-up was six years. In the 6-year Da Qing IGT & Diabetes study, the incidence of type 2 diabetes in the control group was 67.7% (95% CI 59.8% to 75.2%) which was reduced to 43.8% (95% CI 35.5% to 54.7%) in the diet group. Overall, the dietary intervention group had a 33% reduction in the incidence of diabetes after six years ($P < 0.03$). The Oslo Diet & Exercise Study (ODES) found significant ($P<0.05$) reductions in insulin resistance, fasting insulin (pmol/L), fasting C-peptide (pmol/L), fasting proinsulin (pmol/L), fasting blood glucose (mmol/L), BMI (kg/m²), mBP (mmHg) and fasting triglycerides (mmol/L), and a significant increase in fasting HDL cholesterol (mmol/L) and PAI-1 (U/ml) after 12 months of dietary intervention. Data on mortality, morbidity, health-related quality of life, adverse effects, costs were not reported in either study.
Authors' conclusions	There are no high quality data on the efficacy of dietary intervention for the prevention of type 2 diabetes. More well-designed, long-term studies, providing well-reported, high-quality data are required before proper conclusions can be made into the best dietary advice for the prevention of diabetes mellitus in adults.

DIETARY AND WEIGHT REDUCTION INTERVENTIONS UNLIKELY TO BE EFFECTIVE

Pirozzo 2002	Advice on low-fat diets for obesity
Study design	Randomised controlled clinical trials
Population	Adults living in the community, 18 years or older, who were overweight or obese (BMI >25 kg/m2) at baseline.
Intervention	The intervention must have included advice about how to achieve a diet with less than or equal to 30% of calories coming from total fat or advice which would lead to an eating pattern that would achieve this. Advice could be provided by dietitians, health professionals, or investigators in verbal or written form.
Outcomes	Main outcome measure: Indicators of body mass. Additional outcome measures: Mortality, Cardiovascular events, Serum lipids, Blood pressure, Glycated haemoglobin and fasting plasma glucose, Adverse effects of diet, Quality of life.
Main results	Four studies were included at six month follow-up, five studies at12 month follow-up and three studies at 18 month follow-up. There was no significant difference in weight loss between the two groups at six months (WMD 1.7 kg, 95% CI -1.4 to 4.8 kg). There was no significant difference in weight loss between the two groups at 12 months (WMD 1.1 kg, 95% CI -1.6 to 3.8 kg). There was no significant difference in weight loss between the two groups at 18 months (WMD 3.7 kg, 95% CI - 1.8 to 9.2). The weighted sum of weight loss in the control group was -2.3 kg (95% CI -3.5 to -1.2 kg) and in the low fat group there was a weight gain of 0.1 kg (95% CI -0.8 to 1 kg). There was significant heterogeneity in the results for weight loss at six months and 12 months. There were no significant differences between the dietary groups for other outcome measures such as serum lipids, blood pressure and fasting plasma glucose.
Authors' conclusions	The review suggests that fat-restricted diets are no better than calorie restricted diets in achieving long term weight loss in overweight or obese people.

Beyer 2006	Combined calcium, magnesium and potassium supplementation for the management of primary hypertension in adults
Study design	Randomized controlled trials
Population	Adults over 18 years of age, with elevated BP (a minimum of 140 mmHg for SBP or 85 mmHg for DBP), without a known primary cause.
Intervention	Increased consumption of at least two of calcium, potassium, or magnesium simultaneously, compared to placebo, no treatment, or usual care.
Outcomes	Primary: death from all causes, coronary heart disease events, cerebrovascular events, SBP at end of follow-up, DBP at end of follow-up. Secondary: total withdrawals from treatment, reported adverse effects, serum electrolyte levels at end of follow-up.
Main results	Included were three RCTs (n=277) with between 24 and 28 weeks follow-up. Three combinations of minerals were investigated: potassium & magnesium, calcium & magnesium, and calcium & potassium. One trial investigated combinations of calcium & magnesium and of calcium & potassium, and for each found a statistically non-significant increase in both SBP and DBP. All three trials investigated the combination of potassium & magnesium. None of the trials provided data on mortality or morbidity. The combination of potassium & magnesium compared to

	control resulted in statistically non-significant reductions in both SBP (mean difference = -4.6 mmHg, 95% CI: -9.9 to 0.7) and DBP (mean difference = -3.8 mmHg, 95% CI: -9.5 to 1.8), although the results were heterogeneous (I^2=68% and 85% for SBP and DBP respectively). A sensitivity analysis using alternative reported values which accounted for missing data had very little effect on DBP but resulted in a larger, statistically significant reduction in SBP (mean difference = -5.8 mmHg, 95% CI: -10.5 to -1.0). The quality of the trials was not well reported.
Authors' conclusions	There was no robust evidence that supplements of any combination of potassium, magnesium or calcium reduced mortality, morbidity or BP in adults.

Hooper 2004	Omega 3 fatty acids for prevention and treatment of cardiovascular disease
Study design	RCTs and cohorts (if omega 3 intake estimated).
Population	Studies of adults (18 years or older, men and/or women) at any risk of cardiovascular disease
Intervention	Dietary supplementation, a provided diet or advice on diet. The foodstuffs or supplements must have been: oily fish (including mackerel, dogfish, salmon, herring, trout, tuna, sturgeon, stablefish, anchovy, sprat, coho, capelin, sardines, swordfish, sild, pilchard, brisling, menhaden, bloater, whitebait, crab and conger eel); fish oils (made from any of the above or a mixture of fish, or cod liver oil); linseed (flax), canola (rapeseed), perilla, purslane, mustard seed, candlenut, stillingia or walnut as a food, oil, made into a spreading fat or supplementing another food (such as bread or eggs) such that the product consumed had an omega 3 fat content of at least 10% of the total fat content. Refined eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) or alpha-linolenic acids, or concentrated fish oils, were also accepted. Supplementation may have been in oil or capsule form or as food stuffs provided.
Outcomes	Main: total all-cause mortality, combined cardiovascular events, cancers and other adverse events. Secondary: cardiovascular events, risk factor changes and quality of life measures.
Main results	Forty eight randomised controlled trials (36,913 participants) and 41 cohort analyses were included. Pooled trial results did not show a reduction in the risk of total mortality or combined cardiovascular events in those taking additional omega 3 fats (with significant statistical heterogeneity). Sensitivity analysis, retaining only studies at low risk of bias, reduced heterogeneity and again suggested no significant effect of omega 3 fats. Restricting analysis to trials increasing fish-based omega 3 fats, or those increasing short chain omega 3s, did not suggest significant effects on mortality or cardiovascular events in either group. Subgroup analysis by dietary advice or supplementation, baseline risk of CVD or omega 3 dose suggested no clear effects of these factors on primary outcomes. Neither RCTs nor cohorts suggested increased relative risk of cancers with higher omega 3 intake but estimates were imprecise so a clinically important effect could not be excluded.
Authors' conclusions	It is not clear that dietary or supplemental omega 3 fats alter total mortality, combined cardiovascular events or cancers in people with, or at high risk of, cardiovascular disease or in the general population. There is no evidence we should advise people to stop taking rich sources of omega 3 fats, but further high quality trials are needed to confirm suggestions of a protective effect of omega 3 fats on cardiovascular health. There is no clear evidence that omega 3 fats differ in effectiveness according to fish or plant sources, dietary or supplemental sources, dose or presence of placebo.

Ni Mhurchu 2005	Chitosan for overweight or obesity
Study design	Randomised controlled trials.
Population	Free-living adults (18 years and older), defined as overweight/obese at baseline.
Intervention	Chitosan versus placebo; Variable doses of chitosan versus placebo; Chitosan plus diet versus placebo plus diet; Chitosan versus any other pharmacological intervention; Chitosan versus a non-pharmacological intervention.
Outcomes	Main outcome measures: Total mortality/obesity-related mortality; Morbidity; Quality of life. Additional outcome measures: Indicators of body mass; Blood pressure; Blood lipid levels; Adverse effects of the treatment; Faecal fat excretion; HbA1c.
Main results	Fourteen trials including a total of 1131 participants met the inclusion criteria. No trial to date has measured the effect of chitosan on mortality or morbidity. Analyses including all trials indicated that chitosan preparations result in a significantly greater weight loss (weighted mean difference -1.7 kg; 95% confidence interval (CI) -2.1 to -1.3 kg; P < 0.00001), decrease in total cholesterol (-0.2 mmol/L; 95% CI -0.3 to -0.1; P < 0.00001), decrease in systolic (-5.9 mmHg; 95% CI -7.3 to -4.6; P < 0.0001) and diastolic (-3.4 mmHg; 95% CI -4.4 to -2.4; P < 0.00001) blood pressure compared with placebo. There were no clear differences between intervention and control groups in terms of frequency of adverse events or in faecal fat excretion. However, the quality of many studies was sub-optimal and analyses restricted to studies that met allocation concealment criteria, were larger, or of longer duration showed that such trials produced substantially smaller decreases in weight and total cholesterol.
Authors' conclusions	There is some evidence that chitosan is more effective than placebo in the short-term treatment of overweight and obesity. However, many trials to date have been of poor quality and results have been variable. Results obtained from high quality trials indicate that the effect of chitosan on body weight is minimal and unlikely to be of clinical significance.

DIETARY AND WEIGHT REDUCTION INTERVENTIONS WITH UNKNOWN EFFECTIVENESS

Beletate 2007	Zinc supplementation for the prevention of type 2 diabetes mellitus
Study design	Randomised and quasi-randomised controlled clinical trials.
Population	Non-diabetic adults living in the community, 18 years or older with insulin resistance.
Intervention	Zinc (different doses) versus placebo or no intervention.
Outcomes	Primary: incidence of type 2 diabetes mellitus. Secondary decreased insulin resistance; all-cause mortality; costs; adverse effects; cholesterol levels.
Main results	Only one study met the inclusion criteria of this review. There were 56 normal glucose tolerant obese. Follow-up was four weeks. There were no statistically significant differences favouring participants receiving zinc supplementation compared to placebo concerning any outcome measured by the study.
Authors' conclusions	There is currently no evidence to suggest the use of zinc supplementation to prevent type 2 diabetes mellitus.

Curioni 2006	Weight reduction for primary prevention of stroke in adults with overweight or obesity
Study design	Randomized controlled trials.
Population	Adults (at least 18 years) diagnosed as overweight
Intervention	Any intervention for weight reduction compared with placebo or no intervention.
Outcomes	Primary: incidence of first stroke; all -cause mortality; health-related quality of life.
Main results	No trials were found in the literature for inclusion in this review.
Authors' conclusions	Obesity seems to be associated with an increased risk of stroke and it has been suggested that weight loss may lead to a reduction of stroke occurrence. However, this hypothesis is not based on strong scientific evidence resulting from randomised controlled clinical trials.

Hartweg 2008	Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus
Study design	Randomized controlled trials
Population	Adults with type 2 diabetes mellitus.
Intervention	Any type of dietary supplementation with omega-3 PUFA
Outcomes	Primary: fatal myocardial infarction or sudden cardiac death; proven non-fatal myocardial infarction; coronary or peripheral revascularization procedures. Secondary: Triglycerides, Total cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol, HbA1c, Fasting glucose, Fasting insulin, Body weight, Adverse effects.
Main results	Twenty three randomised controlled trials (1075 participants) were included with a mean treatment duration of 8.9 weeks. The mean dose of omega-3 PUFA used in

	the trials was 3.5 g/d. No trials with vascular events or mortality endpoints were identified. Among those taking omega-3 PUFA triglyceride levels were significantly lowered by 0.45 mmol/L (95% confidence interval (CI) -0.58 to -0.32, P < 0.00001) and VLDL cholesterol lowered by -0.07 mmol/L (95% CI -0.13 to 0.00, P = 0.04). LDL cholesterol levels were raised by 0.11 mmol/L (95% CI 0.00 to 0.22, P = 0.05). No significant change in or total or HDL cholesterol, HbA1c, fasting glucose, fasting insulin or body weight was observed. The increase in VLDL remained significant only in trials of longer duration and in hypertriglyceridemic patients. The elevation in LDL cholesterol was non-significant in subgroup analyses. No adverse effects of the intervention were reported.
Authors' conclusions	Omega-3 PUFA supplementation in type 2 diabetes lowers triglycerides and VLDL cholesterol, but may raise LDL cholesterol (although results were non-significant in subgroups) and has no statistically significant effect on glycemic control or fasting insulin. Trials with vascular events or mortality defined endpoints are needed.

Kelly 2004	Low glycaemic index diets for coronary heart disease
Study design	Randomised controlled studies.
Population	Non-institutionalised people (age >16) with at least one major risk factor for coronary heart disease or with diagnosed coronary heart disease were included.
Intervention	Advice on diet or carbohydrate foods, or a prescribed diet when the glycaemic index of the diet or carbohydrate foods were reported or compared and the effect on risk factors for CHD or CHD events or mortality were reported. Studies needed to have a minimum of four weeks intervention period. Comparisons had to be between diets with similar overall carbohydrate and fat levels and similar levels of energy and macronutrients.
Outcomes	Total CHD mortality; Combined CHD events and morbidity; Changes in the severity of major risk factors for CHD including lipids, measures of diabetic control, overweight, blood pressure.
Main results	Fifteen randomised controlled trials met the inclusion criteria. No studies reported the effect of low glycaemic index diets on CHD mortality or CHD events and morbidity. All fifteen included studies report the effect of low glycaemic index diets on major risk factors for CHD. Meta-analysis detected limited and weak evidence of a relationship between low glycaemic index diets and slightly lower total cholesterol, compared with higher glycaemic index diets. There is also limited and weak evidence of a small reduction in HbA1c after 12 weeks on low glycaemic index diets but not at 4 to 5 weeks. There is no evidence that low glycaemic index diets have an effect on LDL cholesterol or HDL cholesterol, triglycerides, fasting glucose or fasting insulin levels.
Authors' conclusions	Evidence from randomised controlled trials showing that low glycaemic index diets reduces coronary heart disease and CHD risk factors is weak. Many of the trials identified were short-term, of poor quality and conducted on small sample sizes.

Kelly 2007	Wholegrain cereals for coronary heart disease
Study design	Randomised controlled studies.
Population	Non-institutionalised adults of either sex with diagnosed CHD, or with at least one major risk factor for CHD.
Intervention	Comparisons of the effect of individual wholegrain foods, or diets high in wholegrain foods, with other diets or foods with lower levels or no wholegrains. Comparisons

	were between diets with similar overall carbohydrate, fat, protein and energy levels.
Outcomes	Primary: Total CHD mortality; Combined CHD events and morbidity; Changes in major risk factors for CHD including overweight, lipids, blood pressure, measures of diabetic control.
Main results	Ten trials met the inclusion criteria. None of the studies found reported the effect of wholegrain diets on CHD mortality or CHD events or morbidity. All 10 included studies reported the effect of wholegrain foods or diets on risk factors for CHD. Studies ranged in duration from 4 to 8 weeks. In eight of the included studies, the wholegrain component was oats. Seven of the eight studies reported lower total and low density lipoproteins (LDL) cholesterol with oatmeal foods than control foods. When the studies were combined in a meta-analysis lower total cholesterol (-0.20 mmol/L, 95% confidence interval (CI) -0.31 to -0.10, P = 0.0001) and LDL cholesterol (0.18 mmol/L, 95% CI -0.28 to -0.09, P < 0.0001) were found with oatmeal foods. However, there is a lack of studies on other wholegrains or wholegrain diets.
Authors' conclusions	Despite the consistency of effects seen in trials of wholegrain oats, the positive findings should be interpreted cautiously. Many of the trials identified were short term, of poor quality and had insufficient power. Most of the trials were funded by companies with commercial interests in wholegrains.

Nield 2007	Dietary advice for treatment of type 2 diabetes mellitus in adults
Study design	Randomised controlled clinical trials.
Population	Adult participants (18 years or older) diagnosed with type 2 diabetes.
Intervention	Studies where the intervention was dietary advice with an aim of reducing weight and the severity of type 2 diabetes were included in the review. Dietary advice is taken to mean advice given with the intention of improving dietary habits (i.e. to either produce weight loss or to change diet composition).
Outcomes	Primary: Weight; Development of micro and macrovascular diabetic complications. Secondary: Quality of life; Change in anti-diabetic medication use; Overall cardiovascular disease risk assessment; Mortality; Glycated haemoglobin; Serum cholesterol (LDL and/or HDL) and serum triglycerides; Maximal exercise capacity (VO_2 max); Blood pressure; Compliance.
Main results	Thirty-six articles reporting a total of eighteen trials following 1467 participants were included. Dietary approaches assessed in this review were low-fat/high-carbohydrate diets, high-fat/low-carbohydrate diets, low-calorie (1000 kcal per day) and very-low-calorie (500 kcal per day) diets and modified fat diets. Two trials compared the American Diabetes Association exchange diet with a standard reduced fat diet and five studies assessed low-fat diets versus moderate fat or low-carbohydrate diets. Two studies assessed the effect of a very-low-calorie diet versus a low-calorie diet. Six studies compared dietary advice with dietary advice plus exercise and three other studies assessed dietary advice versus dietary advice plus behavioural approaches. The studies all measured weight and measures of glycaemic control although not all studies reported these in the articles published. Other outcomes which were measured in these studies included mortality, blood pressure, serum cholesterol (including LDL and HDL cholesterol), serum triglycerides, maximal exercise capacity and compliance. The results suggest that adoption of regular exercise is a good way to promote better glycaemic control in type 2 diabetic patients, however all of these studies were at high risk of bias.
Authors'	There are no high quality data on the efficacy of the dietary treatment of type 2

conclusions	diabetes. The data available indicate that the adoption of exercise may improve glycated haemoglobin at six and twelve months in people with type 2 diabetes

Pittler 2002	Artichoke leaf extract for treating hypercholesterolaemia
Study design	Randomised controlled trials
Population	Patients with hypercholesterolaemia.
Intervention	Oral preparations containing ALE as the only component (mono-preparation).
Outcomes	Total serum cholesterol, cholesterol subfractions and adverse events as reported in the included trials.
Main results	Two randomised trials including 167 participants met all inclusion criteria. In one trial ALE reduced total cholesterol levels from 7.74 mmol/l to 6.31 mmol/l after 42 ± 3 days of treatment whereas the placebo reduced cholesterol from 7.69 mmol/l to 7.03 mmol/l (p=0.00001). Another trial did state that ALE significantly (p<0.05) reduced blood cholesterol compared with placebo in a sub-group of patients with baseline total cholesterol levels of more than 230 mg/dl. Trial reports and post-marketing surveillance studies indicate mild, transient and infrequent adverse events.
Authors' conclusions	There are few data from rigorous clinical trials assessing ALE for treating hypercholesterolaemia. Beneficial effects are reported, the evidence however is not compelling. The limited data on safety suggest only mild, transient and infrequent adverse events with the short term use of ALE

Poustie 2001	Dietary treatment for familial hypercholesterolaemia
Study design	Randomised controlled trials.
Population	Children and adults with Familial hypercholesterolaemia (FH).
Intervention	Cholesterol-lowering diet or any other dietary intervention intended to lower serum total and LDL cholesterol, for a period of at least six months.
Outcomes	Primary: ischaemic heart disease and atheromatous disease; deaths; total cholesterol; LDL cholesterol; HDL cholesterol; triglyceride; weight, height and other measures of nutritional status; Secondary: Quality of life; Compliance; Morbidity.
Main results	Only short-term outcomes could be assessed in this review due to the length of the seven studies. Compliance to treatment, quality of life, mortality and evidence of ischaemic or atheromatous disease were not assessed. No differences were found between the cholesterol-lowering diet and other diets for the outcomes assessed.
Authors' conclusions	No conclusions can be made about the effectiveness of cholesterol-lowering diets, or other dietary interventions for familial hypercholesterolaemia, due to the lack of adequate data. Until further evidence is available current dietary treatment of familial hypercholesterolaemia should continue to be observed and monitored with care.

Thompson 2003	Dietary advice given by a dietitian versus other health professional or self-help resources to reduce blood cholesterol
Study design	Randomised controlled trials.
Population	Adults, with or without existing heart disease or previous myocardial infarction.

Intervention	All interventions including dietary advice to reduce blood cholesterol. Accepted interventions included dietary advice given by a dietitian or a nutritionist compared with another health professional (e.g. doctor or nurse) or self-help resources.
Outcomes	Primary outcomes: The main outcome was difference in blood cholesterol between dietitian group compared with other intervention groups. 2. Secondary outcomes: It was examined data on change in low density lipoprotein cholesterol, high density lipoprotein cholesterol, body mass index (or body weight) and blood pressure. Since patient preference and acceptability of methods are important, data on patient satisfaction with the interventions were also examined.
Main results	Twelve studies with 13 comparisons were included. Four studies compared dietitian with doctor, seven with self-help resources, and only one study was found for dietitian versus nurse and dietitian versus counsellor comparisons. Participants receiving advice from dietitians experienced a greater reduction in blood cholesterol than those receiving advice only from doctors (-0.25 mmol/L (95% CI -0.37, -0.12 mmol/L)). There was no statistically significant difference in change in blood cholesterol between dietitians and self-help resources (-0.10 mmol/L (95% CI -0.22, 0.03 mmol/L)). No statistically significant differences were detected for secondary outcome measures between any of the comparisons with the exception of dietitian versus nurse for HDLc, where the dietitian group showed a greater reduction (-0.06 mmol/L (95% CI -0.11, -0.01)) and dietitian versus counsellor for body weight, where the dietitian group showed a greater reduction (-5.80 kg (95% CI -8.91, -2.69 kg)).
Authors' conclusions	Dietitians were better than doctors at lowering blood cholesterol in the short to medium term, but there was no evidence that they were better than self-help resources. There was no evidence that dietitians provided better outcomes than nurses. The results should be interpreted with caution as the studies were not of good quality and the analysis was based on a limited number of trials.

OTHER INTERVENTIONS TO PREVENT CARDIOVASCULAR DISEASES LIKELY TO BE EFFECTIVE

Fahey 2006	Interventions used to improve control of blood pressure in patients with hypertension
Study design	Randomized controlled trials
Population	Adult patients (18 years or over) with essential hypertension (treated or not currently treated with blood pressure lowering drugs) in a primary care, outpatient or community setting.
Intervention	The interventions were aimed at improving control of blood pressure or clinic attendance and were classified as: self-monitoring; educational interventions directed to the patient; educational interventions directed to the health professional; health professional (nurse or pharmacist) led care; organisational interventions that aimed to improve the delivery of care; appointment reminder systems.
Outcomes	Mean systolic and diastolic blood pressure; control of blood pressure; proportion of patients followed up at clinic.
Main results	56 RCTs met our inclusion criteria. The methodological quality of included studies was variable. An organized system of regular review allied to vigorous antihypertensive drug therapy was shown to reduce blood pressure (weighted mean difference -8.2/-4.2 mmHg, -11.7/-6.5 mmHg, -10.6/-7.6 mmHg for 3 strata of entry blood pressure) and all-cause mortality at five years follow-up (6.4% versus 7.8%, difference 1.4%) in a single large RCT- the Hypertension Detection and Follow-Up study. Other interventions had variable effects. Self-monitoring was associated with moderate net reduction in diastolic blood pressure (weighted mean difference (WMD): -2.0 mmHg, 95%CI: -2.7 to -1.4 mmHg, respectively. Appointment reminders increased the proportion of individuals who attended for follow-up. RCTs of educational interventions directed at patients or health professionals were heterogeneous but appeared unlikely to be associated with large net reductions in blood pressure by themselves. Health professional (nurse or pharmacist) led care may be a promising way of delivering care, with the majority of RCTs being associated with improved blood pressure control, but requires further evaluation.
Authors' conclusions	Family practices and community-based clinics need to have an organized system of regular follow-up and review of their hypertensive patients. Antihypertensive drug therapy should be implemented by means of a vigorous stepped care approach when patients do not reach target blood pressure levels.

Hawthorne 2008	**Culturally appropriate health education for type 2 diabetes mellitus in ethnic minority groups**
Study design	Randomised controlled trials
Population	People with type 2 diabetes mellitus, belonging to ethnic minority communities. Ethnic minority communities refers to upper middle and high income countries, where there are sizeable numbers of people resident who originate from other countries, with identifiable differences in culture, religion or language, from the majority (or dominant) population and likely to be in health disadvantage. The search was restricted to the following countries: European Economic Area (EEA), Switzerland, USA, Canada, South Africa, New Zealand and Australia.

Intervention	The effects of culturally appropriate (or adapted) diabetes health education for ethnic minority communities were considered, both separately and in comparison to conventional (usual in the country being investigated) diabetes health education. One of the interventions should be culturally appropriate to the intervention group or groups. We also considered interventions that compared two different types of culturally appropriate health education.
Outcomes	The three main outcomes: (1) glycosylated haemoglobin, (2) blood pressure, (3) validated questionnaires of quality of life (QoL) (validated for use within the minority group in the study). Secondary outcomes: Biomedical measures: BMI, lipid levels, main long-term complications of diabetes: retinopathy, neuropathy, nephropathy, cardiovascular, mortality rates from causes attributable to diabetes, hospital admissions, hypoglycaemic and hyperglycaemic episodes. Patient orientated measures: attitude scales, patient satisfaction scores, measures of patient empowerment and self efficacy, adverse effects such as deteriorating quality of life or biomedical parameters, validated questionnaires of knowledge of disease. Health economics (resource use and implications).
Main results	Eleven trials involving 1603 people were included, with ten trials providing suitable data for entry into meta-analysis. Glycaemic control (HbA1c), showed an improvement following culturally appropriate health education at three months (weight mean difference (WMD) - 0.3%, 95% CI -0.6 to -0.01), and at six months (WMD -0.6%, 95% CI -0.9 to -0.4), compared with control groups who received 'usual care'. This effect was not significat at 12 months post intervention (WMD -0.1%, 95% CI -0.4 to 0.2). Knowledge scores also improved in the intervention groups at three months (standardised mean difference (SMD) 0.6, 95% CI 0.4 to 0.7), six months (SMD 0.5, 95% CI 0.3 to 0.7) and twelve months (SMD 0.4, 95% CI 0.1 to 0.6) post intervention. Other outcome measures both clinical (such as lipid levels, and blood pressure) and patient centred (quality of life measures, attitude scores and measures of patient empowerment and self-efficacy) showed no significant improvement compared with control groups.
Authors' conclusions	Culturally appropriate diabetes health education appears to have short term effects on glycaemic control and knowledge of diabetes and healthy lifestyles. None of the studies were long-term, and so clinically important long-term outcomes could not be studied. No studies included an economic analysis. The heterogeneity of studies made subgroup comparisons difficult to interpret with confidence. There is a need for long-term, standardised multi-centre RCTs that compare different types and intensities of culturally appropriate health education within defined ethnic minority groups.

Van de Laar 2006	Alpha-glucosidase inhibitors for people with impaired glucose tolerance or impaired fasting blood glucose
Study design	RCTs
Population	Patients having prediabetes, that is impaired glucose tolerance or impaired fasting glucose, or both.
Intervention	Monotherapy with AGIs (acarbose, miglitol or voglibose) compared with: placebo; a non-pharmacological intervention (for example: diet therapy, exercise); biguanides (for example, metformin); thiazolidinediones (for example, pioglitazone); sulphonylurea (for example, glibenclamide); meglitinide (for example, nateglinide); any other pharmacological intervention
Outcomes	Primary (1) incidence of type 2 diabetes mellitus: diagnosed with criteria prevailing

	at the time of the diagnosis ; (2) morbidity related to impaired glucose metabolism, the metabolic syndrome or type 2 diabetes; (3) mortality; Secondary: glycaemic control: glycated haemoglobin levels, fasting and post-load blood glucose levels; plasma lipids; blood pressure: diastolic and systolic blood pressure; fasting and post-load insulin and C-peptide levels; body weight (or body mass index); adverse effects; quality of life; costs.
Main results	Five trials (2360 participants) investigated acarbose in patients 'at increased risk for diabetes' (n = 1). Study duration was one, three, five and six years. One study was at low risk of bias and four studies at high risk of bias. The study at low risk of bias suggested that acarbose decreased the occurrence of type 2 diabetes (NNT = 10), post-load blood glucose (-0.6 mmol/L, 95% CI -1.0 to -0.3) and body mass index (0.3 kg/m2, 95% CI -0.1 to -0.5). No statistically significant effects were observed on mortality, other morbidity, HbA1c, fasting blood glucose, lipids or blood pressure. The effects on the incidence of type 2 diabetes were confirmed in two studies at high risk of bias (OR 0.2, 95% CI 0.1 to 0.6). Adverse effects were mostly of gastro-intestinal origin (OR 3.5, 95% CI 2.7 to 4.4).
Authors' conclusions	There is evidence that acarbose reduces the incidence of type 2 diabetes in patients with IGT. However, it is unclear whether this should be seen as prevention, delay or masking of diabetes. Acarbose may prevent the occurrence of cardiovascular events, but this finding needs to be confirmed in more studies.

OTHER INTERVENTIONS UNLIKELY TO BE EFFECTIVE

Ebrahim 2006	Multiple risk factor interventions for primary prevention of coronary heart disease
Study design	Randomized controlled trials of at least 6 months duration. Trials may be randomized by individual or by group (e.g. family, workplace site).
Population	Adults aged at least 40 years old. General populations, workforce populations and high risk groups. Participants without clinical evidence of cardiovascular diseases.
Intervention	Counselling or educational interventions, with or without pharmacological treatments, which aim to reduce more than one cardiovascular risk factor (i.e. blood pressure, smoking, total blood cholesterol, physical activity, diet).
Outcomes	Total mortality, CHD mortality, net change in blood pressure, smoking and total blood cholesterol.
Main results	A total of 39 trials were found of which ten reported clinical event data. In the ten trials with clinical event end-points, the pooled odds ratios for total and CHD mortality were 0.96 (95% confidence intervals (CI) 0.92 to 1.01) and 0.96 (95% CI 0.89 to 1.04) respectively. Net changes in systolic and diastolic blood pressure, and blood cholesterol were (weighted mean differences) -3.6 mmHg (95% CI -3.9 to -3.3 mmHg), -2.8 mmHg (95% CI -2.9 to -2.6 mmHg) and -0.07 mMol/l (95% CI -0.8 to -0.06 mMol/l) respectively. Odds of reduction in smoking prevalence was 20% (95% CI 8% to 31%). Statistical heterogeneity between the studies with respect to mortality and risk factor changes was due to trials focusing on hypertensive participants and those using considerable amounts of drug treatment.
Authors' conclusions	The pooled effects suggest multiple risk factor intervention has no effect on mortality. However, a small, but potentially important, benefit of treatment (about a 10% reduction in CHD mortality) may have been missed. Risk factor changes were relatively modest, were related to the amount of pharmacological treatment used, and in some cases may have been over-estimated because of regression to the mean effects, lack of intention to treat analyses, habituation to blood pressure measurement, and use of self-reports of smoking. Interventions using personal or family counselling and education with or without pharmacological treatments appear to be more effective at achieving risk factor reduction and consequent reductions in mortality in high risk hypertensive populations. The evidence suggests that such interventions have limited utility in the general population.

OTHER INTERVENTIONS WITH UNKNOWN EFFECTIVENESS

Bosch-Capblanch 2007	Contracts between patients and healthcare practitioners for improving patients' adherence to treatment, prevention and health promotion activities
Study design	Randomised controlled trials.
Population	Patients or their carers, of any gender and age, with any health condition and in any health setting. Practitioners, including clinicians, nurses and any worker or service providing screening, diagnosis, therapeutics, rehabilitation, prevention or health promotion activities.
Intervention	Contracts concerning treatment, prevention and health promotion activities aimed at improving patients' adherence. Contracts included any verbal or written statement specifying at least one treatment, prevention or health promotion activity to be observed, and a commitment of adherence to it. Contracts could take place between healthcare practitioners or services and patients or their carers, between patients and their carers, or between patients themselves (self-commitment). Contracts could relate to any diagnostic procedure, therapeutic regimen, rehabilitation measure, general health advice, referral instruction, or any other activity or combination of activities involved in the management of patients.
Outcomes	Primary: Patients' adherence. Secondary: Participation in the contractual process.
Main results	Thirty trials were included, all conducted in high income countries, involving 4691 participants. The quality of each trial was examined against eight standard criteria, and all trials were inadequate in relation to three or more of these standards. Trials evaluated contracts in addiction (10 trials), hypertension (4 trials), weight control (3 trials) and a variety of other areas (13 trials). Sixteen trials reported at least one outcome that showed statistically significant differences favouring the contracts group, five trials reported at least one outcome that showed differences favouring the control group and 26 trials reported at least one outcome without differences between groups. Effects on adherence were not detected when measured over longer periods.
Authors' conclusions	There is limited evidence that contracts can potentially contribute to improving adherence, but there is insufficient evidence from large, good quality studies to routinely recommend contracts for improving adherence to treatment or preventive health regimens.

Heather 2008	Relaxation therapies for the management of primary hypertension in adults
Study design	Randomised controlled trials.
Population	Adults over 18 years of age, with elevated blood pressure (a minimum of 140 mmHg for SBP or 85 mmHg for DBP), without a known primary cause.
Intervention	Intervention designed to promote relaxation. Control: (i) no active treatment: this included usual treatment, or BP monitoring only; or (ii) sham therapy designed to control for non-specific features of the treatment setting, in particular an equivalent level of treatment time and therapist contact, a highly credible treatment rationale, a high level of patient motivation and involvement with therapy.
Outcomes	Primary: death from all causes; coronary heart disease events; SBP at end of follow-up; DBP at end of follow-up. Secondary: adverse events; total withdrawals from treatment.

Main results	25 trials assessing 1,198 participants were included, but adequate randomisation was confirmed in only seven trials and concealment of allocation in only one. Only one trial reported deaths, heart attacks and strokes (one of each). Meta-analysis indicated that relaxation resulted in small, statistically significant reductions in SBP (mean difference: -5.5 mmHg, 95% CI: -8.2 to -2.8, I2 =72%) and DBP (mean difference: -3.5 mmHg, 95% CI: -5.3 to -1.6, I2 =75%) compared to control. The substantial heterogeneity between trials was not explained by duration of follow-up, type of control, type of relaxation therapy or baseline blood pressure. The nine trials that reported blinding of outcome assessors found a non-significant net reduction in blood pressure (SBP mean difference: -3.2 mmHg, 95% CI: -7.7 to 1.4, I^2 =69%) associated with relaxation. The 15 trials comparing relaxation with sham therapy likewise found a non-significant reduction in blood pressure (SBP mean difference: -3.5 mmHg, 95% CI: -7.1 to 0.2, I^2 =63%).
Authors' conclusions	In view of the poor quality of included trials and unexplained variation between trials, the evidence in favour of causal association between relaxation and blood pressure reduction is weak. Some of the apparent benefit of relaxation was probably due to aspects of treatment unrelated to relaxation.