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The value of tailored communication in promoting medication intake behavior

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Appendix 1

	Database	Authors	Title	Reason for exclusion
1.	PubMed	Bender BG, Apter A, Bogen DK, Dickinson P, Fisher L, Wamboldt FS, Westfall JM.	Test of an interactive voice response intervention to improve adherence to controller medications in adults with asthma.	No Internet intervention
2.	PubMed	Watson AJ, Kvedar JC, Rahman B, Pelletier AC, Salber G, Grant RW.	Diabetes connected health: a pilot study of a patient- and provider-shared glucose monitoring web application.	Medication adherence not as outcome measure
3.	PubMed	Mulvaney SA, Rothman RL, Wallston KA, Lybarger C, Dietrich MS.	An Internet-based program to improve self-management in adolescents with type 1 diabetes.	Medication adherence not as outcome measure
4.	PubMed	Svetkey LP, Pollak KI, Yancy WS Jr, Dolor RJ, Batch BC, Samsa G, Matchar DB, Lin PH.	Hypertension improvement project: randomized trial of quality improvement for physicians and lifestyle modification for patients.	Medication adherence not as outcome measure
5.	PubMed	McTigue KM, Conroy MB, Hess R, Bryce CL, Fiorillo AB, Fischer GS, Milas NC, Simkin-Silverman LR.	Using the Internet to translate an evidence-based lifestyle intervention into practice.	Medication adherence not as outcome measure
6.	PubMed	Decker V, Spoelstra S, Miezo E, Bremer R, You M, Given C, Given B.	A pilot study of an automated voice response system and nursing intervention to monitor adherence to oral chemotherapy agents.	No Internet intervention
7.	PubMed	Tamblyn R, Reidel K, Huang A, Taylor L, Winslade N, Bartlett G, Grad J, Jacques A, Dawes M, Larochelle P, Pinsonneault A.	Increasing the detection and response to adherence problems with cardiovascular medication in primary care through computerized drug management systems: a randomized controlled trial.	Intervention not patient-centered
8.	PubMed	Yoo HJ, Park MS, Kim TN, Yang SJ, Cho GJ, Hwang TG, Baik SH, Choi DS, Park GH, Choi KM.	A Ubiquitous Chronic Disease Care system using cellular phones and the Internet.	Medication adherence not as outcome measure
9.	PubMed	McCarrier KP, Ralston JD, Hirsch IB, Lewis G, Martin DP, Zimmerman FJ, Goldberg HI.	Web-based collaborative care for type 1 diabetes: a pilot randomized trial.	Medication adherence not as outcome measure

10.	PubMed	Cho JH, Lee HC, Lim DJ, Kwon HS, Yoon KH.	Mobile communication using a mobile phone with a glucometer for glucose control in Type 2 patients with diabetes: as effective as an Internet-based glucose monitoring system.	Full text could not be obtained
11.	PubMed	Lorig KR, Ritter PL, Dost A, Plant K, Laurent DD, McNeil I.	The Expert Patients Programme online, a 1-year study of an Internet-based self-management programme for people with long-term conditions.	Medication adherence not as outcome measure
12.	PubMed	Ralston JD, Hirsch IB, Hoath J, Mullen M, Cheadle A, Goldberg HI.	Web-based collaborative care for type 2 diabetes: a pilot randomized trial.	Medication adherence not as outcome measure
13.	PubMed	Cocosila M, Archer N, Haynes RB, Yuan Y.	Can wireless text messaging improve adherence to preventive activities? Results of a randomized controlled trial.	No chronic medication
14.	PubMed	Lawrence DB, Allison W, Chen JC, Demand M.	Improving medication adherence with a targeted, technology-driven disease management intervention.	No Internet intervention
15.	PubMed	Faridi Z, Liberti L, Shuval K, Northrup V, Ali A, Katz DL.	Evaluating the impact of mobile telephone technology on type 2 diabetic patients' self-management: the NICHE pilot study.	Medication adherence not as outcome measure
16.	PubMed	Basheti IA, Armour CL, Bosnic-Anticevich SZ, Reddel HK.	Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique.	Medication adherence not as outcome measure
17.	PubMed	Schulz PJ, Rubinell S, Hartung U.	An Internet-based approach to enhance self-management of chronic low back pain in the Italian-speaking population of Switzerland: results from a pilot study.	Medication adherence not as outcome measure
18.	PubMed	Kim SI, Kim HS.	Effectiveness of mobile and Internet intervention in patients with obese type 2 diabetes.	Medication adherence not as outcome measure
19.	PubMed	O'Shea SI, Arcasoy MO, Samsa G, Cummings SE, Thames EH, Surwit RS, Ortel TL.	Direct-to-patient expert system and home INR monitoring improves control of oral anticoagulation.	No Internet intervention
20.	PubMed	Hee-Sung K.	Impact of Web-based nurse's education on glycosylated haemoglobin in type 2 Diabetic patients.	Medication adherence not as outcome measure

21.	PubMed	Kim HS, Jeong HS.	A nurse short message service by cellular phone in type-2 diabetic patients for six months.	Medication adherence not as outcome measure
22.	PubMed	Wangberg SC.	An Internet-based diabetes self-care intervention tailored to self-efficacy.	Medication adherence not as outcome measure
23.	PubMed	Wu AW, Snyder CF, Huang IC, Skolasky R, McGruder HF, Celano SA, Selnes OA, Andrade AS.	A randomized trial of the impact of a programmable medication reminder device on quality of life in patients with AIDS.	No Internet intervention
24.	PubMed	Cho JH, Chang SA, Kwon HS, Choi YH, Ko SH, Moon SD, Yoo SJ, Song KH, Son HS, Kim HS, Lee WC, Cha BY, Son HY, Yoon KH.	Long-term effect of the Internet-based glucose monitoring system on HbA1c reduction and glucose stability: a 30-month follow-up study for diabetes management with a ubiquitous medical care system.	Medication adherence not as outcome measure
25.	PubMed	Gerber BS.	The chronic disease self-management program: extending reach through the Internet.	Full text could not be obtained
26.	PubMed	Roumie CL, Elasy TA, Greevy R, Griffin MR, Liu X, Stone WJ, Wallston KA, Dittus RS, Alvarez V, Cobb J, Speroff T.	Improving blood pressure control through provider education, provider alerts, and patient education: a cluster randomized trial.	No patient centered intervention
27.	PubMed	Chatkin JM, Blanco DC, Scaglia N, Wagner MB, Fritscher CC.	Impact of a low-cost and simple intervention in enhancing treatment adherence in a Brazilian asthma sample.	No Internet intervention
28.	PubMed	Puccio JA, Belzer M, Olson J, Martinez M, Salata C, Tucker D, Tanaka D.	The use of cell phone reminder calls for assisting HIV-infected adolescents and young adults to adhere to highly active antiretroviral therapy: a pilot study.	No Internet intervention
29.	PubMed	Hornick TR, Higgins PA, Stollings C, Wetzel L, Barzilai K, Wolpaw D.	Initial evaluation of a computer-based medication management tool in a geriatric clinic.	Medication adherence not as outcome measure
30.	PubMed	Feldstein A, Elmer PJ, Smith DH, Herson M, Orwoll E, Chen C, Aickin M, Swain MC.	Electronic medical record reminder improves osteoporosis management after a fracture: a randomized, controlled trial.	Medication adherence not as outcome measure
31.	PubMed	Fonseca JA, Costa-Pereira A, Delgado L, Fernandes L, Castel-Branco MG.	Asthma patients are willing to use mobile and web technologies to support self-management.	Medication adherence not as outcome measure

32.	PubMed	Bray P, Roupe M, Young S, Harrell J, Cummings DM, Whetstone LM.	Feasibility and effectiveness of system redesign for diabetes care management in rural areas: the eastern North Carolina experience.	No patient centered intervention
33.	PubMed	Pines A.	Compliance with hormone therapy after Women's Health Initiative: who is to blame?	No intervention study
34.	PubMed	Ryan D, Cobern W, Wheeler J, Price D, Tarassenko L.	Mobile phone technology in the management of asthma.	No Internet intervention
35.	PubMed	Bush N, Donaldson G, Moinpour C, Haberman M, Milliken D, Markle V, Lauson J.	Development, feasibility and compliance of a web-based system for very frequent QOL and symptom home self-assessment after hematopoietic stem cell transplantation.	Medication adherence not as outcome measure
36.	PubMed	Hagström B, Mattsson B, Rost IM, Gunnarsson RK.	What happened to the prescriptions? A single, short, standardized telephone call may increase compliance.	No Internet intervention
37.	PubMed	Kwon HS, Cho JH, Kim HS, Song BR, Ko SH, Lee JM, Kim SR, Chang SA, Kim HS, Cha BY, Lee KW, Son HY, Lee JH, Lee WC, Yoon KH.	Establishment of blood glucose monitoring system using the Internet.	No intervention study
38.	PubMed	Fairley CK, Levy R, Rayner CR, Allardice K, Costello K, Thomas C, McArthur C, Kong D, Mijch A, Melbourne Adherence Group; Melbourne Adherence Group.	Randomized trial of an adherence programme for clients with HIV.	No Internet intervention
39.	PubMed	Larsen DL, Cannon W, Towner S.	Longitudinal assessment of a diabetes care management system in an integrated health network.	Medication adherence not as outcome measure
40.	PubMed	Cramer J, Rosenheck R, Kirk G, Krol W, Krystal J; VA Naltrexone Study Group 425.	Medication compliance feedback and monitoring in a clinical trial: predictors and outcomes	No patient centered intervention
41.	PubMed	Safren SA, Hendriksen ES, Desousa N, Boswell SL, Mayer KH.	Use of an on-line pager system to increase adherence to antiretroviral medications.	No Internet intervention
42.	PubMed	Akron General Medical Center, Akron, Ohio 44333, USA.	The use of non-face-to-face communication to enhance preventive strategies.	No intervention study
43.	PubMed	McAlindon T, Formica M, Kabbara K, LaValley M, Lehmer M.	Conducting clinical trials over the Internet: feasibility study.	No chronic medication

44.	PubMed	Hart T, Hawkey K, Whyte J.	Use of a portable voice organizer to remember therapy goals in traumatic brain injury rehabilitation: a within-subjects trial.	Medication adherence not as outcome measure
45.	PubMed	Stuart GW, Laraia MT, Ornstein SM, Nietert PJ.	An interactive voice response system to enhance antidepressant medication compliance.	No Internet intervention
46.	PubMed	Burkhart PV, Dunbar-Jacob JM, Fireman P, Rohay J.	Children's adherence to recommended asthma self-management.	No Internet intervention
47.	PubMed	Finkelstein J, O'Connor G, Friedmann RH.	Development and implementation of the home asthma telemonitoring (HAT) system to facilitate asthma self-care.	Medication adherence not as outcome measure
48.	PubMed	Andrade A.	HIV adherence strategies take a high-tech route.	Full text could not be obtained
49.	PubMed	Frances CD, Alperin P, Adler JS, Grady D.	Does a fixed physician reminder system improve the care of patients with coronary artery disease? A randomized controlled trial.	No Internet intervention
50.	PubMed	Bennett SJ, Hays LM, Embree JL, Arnould M.	Heart Messages: a tailored message intervention for improving heart failure outcomes.	No intervention study
51.	PubMed	Johnson BF, Hamilton G, Fink J, Lucey G, Bennet N, Lew R.	A design for testing interventions to improve adherence within a hypertension clinical trial.	No Internet intervention
52.	PubMed	Curtin K, Hayes BD, Holland CL, Katz LA.	Computer-generated intervention for asthma population care management.	Medication adherence not as outcome measure
53.	PubMed	Cramer JA, Rosenheck R.	Enhancing medication compliance for people with serious mental illness.	No Internet intervention
54.	PubMed	Legorreta AP, Hasan MM, Peters AL, Pelletier KR, Leung KM.	An intervention for enhancing compliance with screening recommendations for diabetic retinopathy. A bicoastal experience.	Medication adherence not as outcome measure
55.	PubMed	Milch RA, Ziv L, Evans V, Hillebrand M.	The effect of an alphanumeric paging system on patient compliance with medicinal regimens.	No Internet intervention
56.	PubMed	Casebeer L, Roesener GH.	Patient informatics: using a computerized system to monitor patient compliance in the treatment of hypertension.	Full text could not be obtained
57.	PubMed	Schectman G, Hiatt J, Hartz A.	Telephone contacts do not improve adherence to niacin or bile acid sequestrant therapy.	No Internet intervention

58.	PubMed	Skaer TL, Sclar DA, Markowski DJ, Won JK.	Effect of value-added utilities on prescription refill compliance and health care expenditures for hypertension.	No Internet intervention
59.	PubMed	Turner BJ, Day SC, Borenstein B.	A controlled trial to improve delivery of preventive care: physician or patient reminders?	No Internet intervention
60.	PubMed	Simkins CV, Wenzloff NJ.	Evaluation of a computerized reminder system in the enhancement of patient medication refill compliance.	No Internet intervention
61.	PubMed	Ascione FJ, Brown GH, Kirking DM.	Evaluation of a medication refill reminder system for a community pharmacy.	No Internet intervention
62.	PubMed	Heard C, Blackburn JL, Thompson MS, Wallace SM.	Evaluation of a computer-assisted medication refill reminder system for improving patient compliance.	No Internet intervention
63.	EMBASE	Viera AJ, Jamieson B	How effective are hypertension self-care interventions	No Internet intervention
64.	EMBASE	Shanovich KK, Sorkness CA, wise M, Pulvermacher AD, Bhattacharya A, Gustafson DH.	Internet telehealth for pediatric nurse case management improves asthma control.	No patient centered intervention
65	EMBASE	Benhamou PY, Melki V, Boizel R, Perreal F, Quesada JL, Bessieres-Lacombe S <i>et al.</i>	One-year efficacy and safety of Web-based follow-up using cellular phone in type 1 diabetic patients under insulin pump therapy: the PumpNet study	No Internet intervention
66.	EMBASE	Bond GE, Burr R, Wolf FM, Price M, McCurry SM, Teri L.	The effects of a web-based intervention on the physical outcomes associated with diabetes among adults age 60 and older: A randomized trial.	Medication adherence not as outcome measure
67.	EMBASE	McMahon GT, Gomes HE, Hohne SH, Hu TMJ, Levine BA, Conlin PR.	Web-based care management in patients with poorly controlled diabetes.	Medication adherence not as outcome measure
68.	CINAHL	Phillips A.	Web based care management improved glucose control in patients with poorly controlled diabetes.	Medication adherence not as outcome measure
69.	CINAHL	Pontin D.	An interactive monitoring device reduced asthma symptoms and functional limitations in inner city children with asthma	Medication adherence not as outcome measure

Appendix 2

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Artinian RCT	Patients with symptomatic left ventricular dysfunction	A web-based monitoring system	- Tailored content - Nature of expert/therapist contact	N=18 Mean age: 68 17 males	- Pill counts - Baseline and 3 months	Medication compliance rate was 94% for the monitor group as measured by the monitor system
Jan RCT	Paediatric asthma patients	Blue Angel for Asthma Kids variability	- Tailored content - Nature of expert/therapist contact	Intervention group n=9 Control group n=9 N = 164 Intervention group n= 88 Mean age 10.9 35 males Control group n=76 Mean age 9.9 28 males	- Self-reported use and test score for dry powder inhaler (DPI) or metered dose inhaler (MDI) with the spacer technique - Baseline and 12 weeks	The Blue Angel for Asthma Kids, has the potential for improving asthma outcome compared with conventional treatment over a period of 12 weeks

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Chan RCT	Paediatric asthma patients	A customized educational and monitoring Web site	- Tailored content - Nature of expert/therapist contact	N=120 Intervention group n=60 Mean age 10.2 37 males Control group n= 60 Mean age 9.0 38 males	Computerized prescription refill record - Baseline, 26 and 52 weeks	No difference in adherence between both groups
Chan RCT	Paediatric asthma patients	A customized educational and monitoring Web site	- Tailored content - Nature of expert/therapist contact	N=10 Mean age: 7 5 males Intervention group n=5 Mean age 6.6 1 male Control group N=5 Mean age 8.7 4 males	- Self reported asthma diary and computerized prescription refill record - 90 days and 180 days	After the intervention, the use of β -agonist decreased, which is an indication of better adherence

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Joseph RCT	Patients with asthma	Web-based asthma management program	- Tailored content - User control	N=314 Mean age 15.3 36.6% male Intervention group: n=162 Control group n=152	- Self-reported - Baseline and 12 months	Positive changes in controller medication adherence
Ross RCT	Patients with Heart Failure	The SPPARO (System Providing Access to Records Online)	- Tailored content - Nature of expert/therapist contact	N= 104 Intervention group n= 54 Mean age 57 80% male Control group n=50 Mean age 55 74% male	- Self-reported - Baseline, 6 months, 12 months	Providing patients access to an online medical record improved adherence
Cherry Prospective design	Patients with diabetes	Telemedicine diabetes disease management program.	- Tailored content - Nature of expert/therapist contact	Intervention group n=169 Mean age 53 39 males Historical group (usual care)	- Self-reported - Baseline, 12 months	Outcomes offer encouraging evidence that telemedicine technology coupled with daily remote monitoring may improve appropriate utilization of healthcare services

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Guendelman RCT	Persistent asthma.	Health Buddy, an interactive device connected to a home telephone	- Tailored content - Nature of expert/therapist contact	N=134 Intervention group mean age 12.0 40 male Control group Mean age 12.2 37 male	- Self-reported - Baseline, 6 and 12 weeks	Patients were more likely to take their asthma medication without additional reminders
DeVito Dabbs RCT	Patients who received a lung transplantation	Pocket Personal Assistant for Tracking Health	- Tailored content - Nature of expert/therapist contact	N = 30 Intervention group n=15 Mean age 55 60% male Control group n=15 Mean age 57 60% male	- Self reported - Baseline, 2 months	Patients who received the PATH were more likely to show high adherence to the medical regimen
Van der Meer RCT	Patients with asthma	Internet-based self-management programme	- Customized Health program - User control	N = 200 Intervention Group n=101 Mean age 36 29% male Control Group n=99 Mean age 37 29% male	Adherence: self-reported. Baseline, 3 months and 6 months	In the first 3 months, many patients had uncontrolled asthma and were advised to increase their inhaled corticosteroid doses. The improvement in asthma control after 3 months allowed a decrease in medication over the next 9 months without loss of asthma control. This suggests tailoring medication to patients' needs rather than increasing medication for the whole study sample

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Van der Meer RCT	Patients with mild to moderate persistent asthma	Internet-based self-management programme	- Customized Health program - User control	N= 200 Intervention n=111 Mean age 36 28 males Group 1 (well controlled) n=37 Group 2 (partly controlled) n=38 Group 3 (uncontrolled) n=36 Control group n = 89 Mean age 36.6 28 male Group 1 (well controlled) n=38 Group 2 (partly controlled) n=33 Group 3 (uncontrolled) n=28	- Self-reported - Baseline and after 3 months and 1 year	Weekly self-monitoring and subsequent treatment adjustment leads to improved asthma control in patients with partly and uncontrolled asthma at baseline and tailors asthma medication to individual patients' needs

Author, publication year & design	Type of disease	Type of intervention	Delivering of tailored message	Study population	Name of instrument adherence, moment of measuring adherence	Conclusions
Dilorio	Patients with Epilepsy	WebEase	- Customized Health Program	N = 35	- Self-reported	Participants showed some improvement in adherence following the program
Survey			- User control	Mean age 37.5 40% male	- Baseline and 6 weeks	
Dew	Heart recipients and their family caregivers	Website including skills workshops, discussion group, ask an expert, question and answer, health tips, recourses and references	- Customized Health Program - Nature of expert/therapist contact.	N=64 Intervention group n= 24 Mean age 45.8 18 males Control group n= 40 Mean age = 57.5 30 males	- Self-reported - Baseline, 4 months	The intervention appeared to be most weakly associated with medical compliance change
Prospective design						

Appendix 3: List of excluded studies with reason for exclusion

Database	Year	Authors	Title	Reason for exclusion
PubMed	2011	Harris LT, Lehavot K, Huh D, Yard S, Andrasik MP, Dunbar PJ, Simoni JM.	Two-Way Text Messaging for Health Behavior Change Among Human Immunodeficiency Virus–Positive Individuals	Medication adherence not as outcome measure
PubMed	2010	Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, Jack W, Habyarimana J, Sadatsafavi M, Najafzadeh M, <i>et al.</i>	Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomized trial	Reminder not specifically for medication intake
PubMed	2010	Simoni JM, Chen WT, Huh D, Fredriksen-Goldsen KI, Pearson C, Zhao H, Shiu CS, Wang X, Zhang F.	A Preliminary Randomized Controlled Trial of a Nurse-Delivered Medication Adherence Intervention Among HIV-Positive Outpatients Initiating Antiretroviral Therapy in Beijing, China	Only total effect of intervention on adherence reported (reminder was one aspect)
PubMed	2010	Bender BG, Apter A, Bogen DK, Dickinson P, Fisher L, Wamboldt FS, Westfall JM.	Test of an Interactive Voice Response Intervention to Improve Adherence to Controller Medications in Adults with Asthma	Reminder not specifically for medication intake
PubMed	2010	Marciel KK, Saiman L, Quittell LM, Dawkins K, Quittner AL.	Cell phone intervention to improve adherence: cystic fibrosis care team, patient, and parent perspectives	Medication adherence not as outcome measure
PubMed	2009	Decker V, Spoelstra S, Miezo E, Bremer R, You M, Given C, Given B.	A pilot study of an automated voice response system and nursing intervention to monitor adherence to oral chemotherapy agents	No reminder (only information exchange)
PubMed	2009	Düsing R, Handrock R, Klebs S, Tousset E, Vrijens B.	Impact of supportive measures on drug adherence in patients with essential hypertension treated with valsartan: the randomized, open-label, parallel group study	Only total effect of intervention on adherence reported (reminder was one aspect)
PubMed	2008	Lawrence DB, Allison W, Chen JC, Demand M.	Improving Medication Adherence with a Targeted, Technology-Driven Disease Management Intervention	Reminder is not directed to patient (not patient-centered)

PubMed	2008	Tsur L, Kozer E, Berkovitch M.	The Effect of Drug Consultation Center Guidance on Contraceptive Use Among Women Using Isotretinoin: A Randomized, Controlled Study	No reminder (only information exchange)
PubMed	2008	Mollon B, Holbrook AM, Keshavjee K, Troyan S, Gaebel K, Thabane L, Perera G.	Automated Telephone Reminder Messages Can Assist Electronic Diabetes Care	Medication adherence not as outcome measure
PubMed	2006	Fonseca JA, Costa-Pereira A, Delgado L, Fernandes L, Castel-Branco MG.	Asthma patients are willing to use mobile and web technologies to support self-management.	Medication adherence not as outcome measure
PubMed	2005	Ryan D, Cobern W, Wheeler J, Price D, Tarassenko L.	Mobile phone technology in the management of asthma	Medication adherence not as outcome measure
PubMed	2003	Fairley CK, Levy R, Rayner CR, Allardice K, Costello K, Thomas C, McArthur C, Kong D, Mijch A, Melbourne Adherence Group.	Randomized trial of an adherence program for clients with HIV	Only total effect of intervention on adherence reported (reminder was one aspect)
PubMed	2003	Larsen DL, Cannon W, Towner S.	Longitudinal Assessment of a Diabetes Care Management System in an Integrated Health Network	Medication adherence not as outcome measure
PubMed	2003	Stuart GW, Laraia MT, Ornstein SM, Nietert PJ.	An interactive voice response system to enhance antidepressant medication compliance.	No reminder (only information exchange)
PubMed	1999	Cramer JA, Rosenheck R.	Enhancing Medication Compliance for People with Serious Mental Illness	No electronic reminder
PubMed	1993	Raynor DK, Booth TG, Blenkinsopp A.	Effects of computer generated reminder charts on patients' compliance with drug regimens	No electronic reminder
Ref from review	2006	Mannheimer SB, Morse E, Matts JP, Andrews L, Child C, Schmetter B, Friedland GH; Terry Beirn Community Programs for Clinical Research on AIDS	Sustained Benefit From a Long-Term Antiretroviral Adherence Intervention Results of a Large Randomized Clinical Trial	Medication adherence not as outcome measure

Ref from review	2003	Dunbar PJ, Madigan D, Grohskopf LA, Revere D, Woodward J, Minstrell J, Frick PA, Simoni JM, Hooton TM.	A two-way messaging system to enhance antiretroviral adherence	Medication adherence not as outcome measure
Ref from review	1991	Leirer VO, Morrow DG, Tanke ED, Pariente GM.	Elders' nonadherence: its assessment and medication reminding by voice mail.	No chronic medication
Embase	2006	Franklin VL, Waller A, Pagliari C, Greene SA.	A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes	Only total effect of intervention on adherence reported (reminder was one aspect)
Embase	2005	Ostojic V, Cvoriscec B, Ostojic SB, Reznikoff D, Stipic-Markovic A, Tudjman Z.	Improving Asthma Control Through Telemedicine: A Study of Short-Message Service	Medication adherence not as outcome measure
PsycINFO	2009	Basheti IA, Armour CL, Bosnic-Anticevich SZ, Reddel HK.	Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique	Medication adherence not as outcome measure
PsycINFO	2009	Enriquez M, Cheng AL, McKinsey DS, Stanford J.	Development and Efficacy of an Intervention to Enhance Readiness for Adherence among Adults Who Had Previously Failed HIV Treatment	No electronic reminder
PsycINFO	2000	Ostrop NJ, Gill MJ.	Antiretroviral Medication Adherence and Persistence with Respect to Adherence Tool Usage	Only total effect of intervention on adherence reported (reminder was one aspect)
PsycINFO	2006	Robertson L, Smith M, Castle D, Tannenbaum D.	Using the Internet to enhance the treatment of depression	Reminder not specifically for medication intake
PsycINFO	2009	Scherr D, Kastner P, Kollmann A, Hallas A, Auer J, Krappinger H, Schuchlenz H, Stark G, Grander W, Jakl G, Schreier G, Fruhwald FM; MOBITEL Investigators.	Effect of Home-Based Telemonitoring Using Mobile Phone Technology on the Outcome of Heart Failure Patients After an Episode of Acute Decompensation: Randomized Controlled Trial	No reminder (only information exchange)

Cochrane Register Controlled Trials	1999	Fulmer TT, Feldman PH, Kim TS, Carty B, Beers M, Molina M, Putnam M.	An intervention study to enhance medication compliance in community-dwelling elderly individuals.	No electronic reminder
Cochrane Register Controlled Trials	1998	Keder LM, Rulin MC, Gruss J.	Compliance with depot medroxyprogesterone acetate: A randomized, controlled trial of intensive reminders	No electronic reminder

Appendix 4: Detailed characteristics of included studies (ordered on type of reminder and year of publication)

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Hardy 2011 RCT parallel	<p>Patients with HIV</p> <p><u>Intervention:</u> n=10, mean age 42, 50% male.</p> <p><u>Control:</u> n=9, mean age 44, 50% male.</p>	<p><u>Intervention:</u> daily personalized text messages sent for each scheduled ART dose. Patients had to respond with a text message when taking ART.</p> <p><u>Control:</u> use of beeper, which would beep for 30 sec at time ART dose should be taken and would not repeat if the reminder was not acknowledged.</p> <p><i>Type: SMS versus beeper</i></p>	<p>Self-report (SR), pill count (PC), electronic monitoring (MEMS) and composite adherence score (CAS).</p> <p>Baseline, week 3, week 6.</p>	<p><u>Baseline:</u> no significant differences in PC and SR between two groups.</p> <p><u>Week 3:</u> significant difference in MEMS adherence between intervention and control group: 85.3% vs. 57.2% (p=0.0129), and with CAS: 81.5% vs. 56.7% (p=0.0176).</p> <p><u>Week 6:</u> significant difference in MEMS adherence: 89.7% vs. 56.3% (p=0.002) and with CAS: 83.4% vs. 53.6% (p=0.0094).</p>	<p>First RCT of a personalized cellular phone reminder system to show significantly better short term improvements in adherence to ART in comparison to a beeper reminder system.</p>

Author, publication year & design	Study population (size, baseline characteristics)	Intervention & type of reminder	Type of adherence measure & timing measurement	Results	Authors' conclusions
Pop-Eleches 2011 RCT parallel	<p>Patients with HIV</p> <p><u>Group 1:</u> n=70, mean age 35.6, 67% female.</p> <p><u>Group 2:</u> n=72, mean age 35.7, 69% female.</p> <p><u>Group 3:</u> n=73, mean age 37.7, 59% female.</p> <p><u>Group 4:</u> n=74, mean age 36.8, 69% female.</p> <p><u>Control:</u> n=139, mean age 35.7, 66% female.</p>	<p><u>Intervention:</u></p> <p>1) daily, short reminder; or</p> <p>2) daily, long reminder; or</p> <p>3) weekly, short reminder; or</p> <p>4) weekly, long reminder; or</p> <p>Short messages were simple ("This is your reminder"), long messages provided additional support ("This is your reminder. Be strong and courageous, we care about you").</p> <p><u>Control:</u> no reminder</p> <p><i>Type: SMS</i></p>	<p>Electronic monitoring (MEMS).</p> <p>Every 12-week period in 48 weeks.</p>	<p>Over 48 weeks, participants with adherence $\geq 90\%$ in 2 groups receiving weekly reminders was 53% vs. 40% in control group (P=0.03). Participants with adherence $\geq 90\%$ receiving daily reminders was 41% vs. 40% in control group (P=0.92). Participants with adherence $\geq 90\%$ was 47% in 2 groups receiving long reminders, 40% in the control group (P=0.24). Participants with adherence $\geq 90\%$ in two groups receiving short reminders was 47% vs. 40% in control group (P=0.24).</p>	<p>Weekly SMS reminders increased percentage of participants achieving 90% adherence to ART by 13–16% compared with no reminder. A longer reminders was not more effective than either a short reminder or no reminder. Daily reminders did not improve adherence.</p>

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Hou 2010 RCT parallel	<p>Women on oral contraceptives</p> <p><u>Intervention:</u> n=36, mean age 22.</p> <p><u>Control:</u> n=37, mean age 22.</p>	<p><u>Intervention:</u> daily text message "Please remember to take your birth control pill" sent at a designated time chosen by the participant.</p> <p><u>Control:</u> no reminder</p> <p><i>Type: SMS</i></p>	<p>Electronic monitoring (SIMPill) and self-report (diary).</p> <p>Every month for 3 months.</p>	<p><u>SIMPill:</u> rate of missed pills per cycle for intervention and control group did not differ: 4.9 ± 3.0 vs. 4.6 ± 3.5 ($P=.60$). Number of missed pills increased with each cycle for entire cohort ($P=.02$) but did not increase according to arm ($P=.58$).</p> <p><u>Diary:</u> mean of 1.4 ± 1.9 missed pills per cycle in intervention group, and 1.1 ± 1.2 in control group.</p>	<p>Although women receiving reminders felt that the text messages were useful and relied on them, there were no significant differences in mean number of missed pills per cycle between women who received daily text message reminders and women who did not.</p>

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Strandbygaard 2010 RCT parallel	<p>Patients with asthma</p> <p><u>Intervention:</u> n=12, mean age 34.4, 50% male.</p> <p><u>Control:</u> n=14, mean age 30.7, 57% male.</p>	<p><u>Intervention:</u> daily SMS reminder ("Remember to take your asthma medication morning and evening. From the Respiratory Unit").</p> <p><u>Control:</u> no reminder.</p> <p><u>All patients</u> received education concerning necessity of ICS treatment, and were provided with knowledge of the disease mechanisms and correct inhaler technique. <i>Type: SMS</i></p>	<p>Electronic monitoring (medicine dose-count on inhaler device).</p> <p>Week 4 and week 12.</p>	<p>Mean adherence rate in SMS group increased from 77.9% (week 4) to 81.5% (week 12); mean change: 3.6% (p=0.52). Mean adherence in control group decreased from 84.2% to 70.1%; mean change: -14.2% (p=0.01). Absolute difference in mean adherence rate between two groups after 12 weeks was 17.8% (p=0.019).</p>	<p>This study showed that asthmatic patients who receive a daily SMS reminder remember to take, on average, about 18% more doses of their anti-asthmatic medication compared with patients who do not receive a SMS reminder.</p>

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Christensen 2010 RCT cross-over	<p>Patients with hypertension</p> <p><u>Intervention:</u> n=219, age <45y 5.5%, 46-65y 60.3%, >65y 34.2%, 45.2% male.</p> <p><u>Control:</u> n=179, age <45y 10.1%, 46-65y 62.5%, >65y 27.3%, 50.2% male.</p>	<p><u>Intervention:</u> use of electronic monitoring device (Helping Hand Data Capture (HHDC)) which is operated with tablet blister cards. The device gives an audiovisual reminder when it is time to take medication.</p> <p><u>Control:</u> standard therapy.</p> <p>After 6 months patients were crossed over.</p> <p><i>Type: ERD with audiovisual reminder</i></p>	<p>Self-report and electronic monitoring (HHDC).</p> <p>At 6 months and 12 months.</p>	<p>First 6 months: patients using HHDC reported 90.6% compliance vs. 85.1% in control group (NS). After crossover, patients using HHDC reported 86.3% compliance vs. 88.4% in control group (NS).</p> <p>Taking, dosing and timing compliance (electronic monitoring data) was 45-52% in group 1, and 32-38% in group 2. Group differences are close to significance. After 6 months, 50% of patients was persistent, 30% took their tablets on a daily basis.</p>	<p>Use of the HHDC device improved self-reported compliance in patients starting on treatment with telmisartan by 5.5% compared to usual care. BP values were unaffected. The HHDC device is most suitable for newly diagnosed patients.</p>

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Ho 2008	<p>Patients with glaucoma</p> <p><u>Total group:</u> n=42, mean age 69.1, 23 female</p> <p><u>Intervention:</u> n=20</p> <p><u>Control:</u> n=22</p>	<p><u>Intervention:</u> use of Travatan Dosing Aid (TDA) with audiovisual reminder. TDA has a LCD screen that displays a flashing eye drop symbol on the front as a visible reminder when patients are supposed to give themselves a dose of medication and it emits an audible beep as an audible reminder. Prescribed dosing time were programmed into the TDA.</p> <p><u>Control:</u> use of TDA without audiovisual reminder.</p> <p><i>Type: ERD with audiovisual reminder</i></p>	<p>Electronic monitoring (TDA).</p> <p>At 3-5 weeks.</p> <p>Observation duration intervention group: 9-84 days (M=37.6), control group: 6-63 days (M=35.4).</p>	<p>Adherence rates were 87.9% and 79.7% (p=0.02), rates of missed dosing were 7.6% and 14.4% (p=0.03), rates of dosing at incorrect times were 7.1% and 9.8% (p=0.19), respectively for alarm on versus alarm off groups. Mean range of time between dose administration and scheduled dose time was 207 ± 108 minutes for the alarm on group and 424 ± 405 minutes for the alarm off group (p=0.08).</p>	<p>In the reminder group there were trends toward fewer days of dosing at incorrect times and smaller average range of time between scheduled dose time and drop administration. Difference in adherence rate and rate of missed doses was significant, suggesting that the presence of audible and visible alarms improved adherence and decreased likelihood of missing a dose.</p>

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Charles 2007 RCT parallel	<p>Patients with asthma</p> <p><u>Intervention:</u> n=44, mean age 39, 28 male.</p> <p><u>Control:</u> n=46, mean age 35, 22 male.</p>	<p><u>Intervention:</u> use of SmartInhaler with audiovisual reminder function (AVRF). The alarm was a single beep, which sounded at predetermined times (twice a day) once every 30 sec for 60 min after predetermined time and stopped if the device was actuated or after 60 min if not taken. The AVRF had a light, which was green before device was actuated, changing to red once the dose was taken.</p> <p><u>Control:</u> use of SmartInhaler without AVRF.</p> <p><i>Type: ERD with audiovisual reminder</i></p>	<p>Self-report and electronic monitoring (SmartInhaler).</p> <p>Baseline and at 6, 12, 18 and 24 weeks.</p>	<p>Mean and median % medication taken in last 12 weeks: AVRF: 88% and 93%, control: 66% and 74%. Absolute difference in median: 18% (P< .0001).</p> <p>Taking >50% of their medication: AVRF: 95.5%, control: 71.7%.</p> <p>Taking >80% of their medication: AVRF: 88.6%, control: 39.1%.</p> <p>Taking >90% of their medication: AVRF: 63.6%, control: 19.6%.</p> <p>At all-time points, adherence was higher in AVRF group (difference in median adherence 7-21%; P< .0001).</p> <p>Last 4 weeks, underestimated mean missed doses: AVRF: 3, control: 12.2 doses. Median difference: 8 (P=.001).</p>	<p>AVRF improved adherence from a median of 74% to 93%, with a 2- to 3-fold greater number of subjects achieving 80% and 90% adherence with AVRF, respectively. Around 1 in 4 subjects had <50% adherence in the control group, compared with around 1 in 20 with AVRF.</p>

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Santschi 2007 RCT cross-over	<p>Patients with hypertension</p> <p><u>Total group:</u> n=25, mean age 58.0, 12 male.</p>	<p><u>Intervention:</u> use of Intelligent Drug Administration System (IDAS II), an electronic device that accommodates blister packs. Electric foil is fixed upon the tablet slots, which activates recording of date and hour at which the drug was removed from the blister. Visual reminder (indicating time elapsed since last dose) and audible reminder, which sounds at chosen and fixed time for 1 min or until the device is opened, and can be deactivated upon request.<u>Control:</u> use of MEMS 6 SmartCap with LCD display on top indicating number of daily openings and number of hours elapsed since last opening.After 2 months patients were crossed over.</p> <p><i>Type: ERD with audiovisual reminder</i></p>	<p>Electronic monitoring (MEMS or IDAS II).</p> <p>Baseline and at the end of each two-month period (3 measurements).</p>	<p>Over the 4-month study, adherence was very high whatever the device, with a median taking adherence of 99.2% (range 62.7–100%). During the first 2-month period, median taking adherence was 100% (range 40.3–100%), with only two patients having a taking adherence <80%. During the last 2-month period, median taking adherence was 98.4% (range 84.1–100%). Median distribution index was lower with IDAS II, indicating that patients showed a stricter adherence to taking their drug at the same time, day after day with the IDAS II than with the MEMS device.</p>	<p>Both devices were considered to be reliable reminders supporting drug intake even though many patients had already established a daily routine for their drug intake. Overall adherence was very high and comparable with both devices.</p> <p>Our study shows that IDAS II is well accepted by patients and could represent a valuable device for the clinical management of patients with chronic diseases.</p>

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Andrade 2005 RCT parallel	<p>Patients with HIV</p> <p><u>Intervention:</u> n=29, mean age 38, 16 male.</p> <p><u>Control:</u> n=29, mean age 38, 18 male.</p>	<p><u>Intervention:</u> use of Disease Management Assistance System (DMAS) device, programmed with reminder messages and dosing times for each medication in the HAART regimen.</p> <p><u>Control:</u> no use of DMAS</p> <p>All patients participated in an individualized, 30 min adherence counseling session each month and received adherence feedback from a clinical pharmacist.</p> <p><i>Type: audiovisual reminder</i></p>	<p>Self-report and electronic monitoring (eDEM caps).</p> <p>At 4, 8, 12, 16, 20, 24 weeks.</p>	<p>Overall mean adherence from EM data was not significantly different between DMAS (80%) and control (65%). Effect size: 0.51 (95% CI for Cohen's d, 0.26–0.76).</p> <p>Among memory-impaired subjects (DMAS n=14, control n=17), overall mean adherence was higher for DMAS (77%) than control (57%) (P=.001). Among memory-intact subjects, adherence did not differ significantly between DMAS (83%) and control (77%).</p>	<p>An electronic verbal prompting device can improve adherence to HAART by HIV-infected subjects who have memory impairment. The effect of the DMAS device at 24 weeks was only evident in the memory-impaired group, resulting in a 20% increase in adherence rate, compared with 6% for the memory-intact patients.</p>

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Da Costa 2005 RCT parallel	<p>Patients with hypertension</p> <p><u>Intervention:</u> n=35, mean age 57, 45.7% male.</p> <p><u>Control:</u> n=36, mean age 59, 47.2% male.</p>	<p><u>Intervention:</u> use of reminder alarm card set up to beep every day at the same time, preselected by pharmacist and/or patient in accordance with prescription's specifications. The reminder card was similar in size to a credit card with a single button. If the patient failed to acknowledge the alarm, it would beep every 20s for 3h, then it would stop and re-initiate 8h later, beeping every 20s for 1h.</p> <p><u>Control:</u> no alarm card.</p> <p><i>Type: ERD with audible reminder</i></p>	<p>Self-report and pill count.</p> <p>Baseline and at 1, 2 and 3 months.</p>	<p>Intervention group: compliance of about 97% throughout the study.</p> <p>Control group: compliance dropped from 94.9% after 1 month to 87.3% after 3 months. Compliance in the intervention group was higher at all time; reaching statistical significance at the third month ($p=0.01$).</p> <p>For the first and third month, 36 and 29 patients had compliance rates >80% and were rated as compliant. In both first and third month, 3 patients classified as compliant reported that they had stopped taking their medication. For the last month, 7 patients classified as non-compliant reported that they were still taking their medication.</p>	<p>This study indicates that reminder 'alarm' cards may have a positive effect on compliance with antihypertensive medication in patients taking ACE inhibitors once daily over three months. Mean compliance differences between groups were 10% in the last period of follow-up.</p>

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Laster 1996 RCT cross-over	<p>Patients with glaucoma</p> <p><u>Total group:</u> n=13, age not reported, 11 female.</p>	<p><u>Intervention:</u> use of TimeCap, a medication alarm device serving as cap on conventional medication bottle. It has a digital display that shows time and day of week when the vial was last opened and an alarm that beeps when a dose is due. If the beep is ignored, the digital face flashes to provide a visual reminder that a dose has been missed.</p> <p><u>Control:</u> no use of TimeCap</p> <p>After 30 days, patients were crossed over.</p> <p><i>Type: audiovisual reminder</i></p>	<p>Self-report and amount of solution used estimated by weighing of bottle.</p> <p>At 30 and 60 days.</p>	<p>Mean difference (\pmSD) between amount of medication used with TimeCap and amount used without TimeCap was $+2.867\text{g} \pm 2.138\text{g}$ ($p < 0.0001$). Patients reported using their medication an average of 95.8% of the time with TimeCap and an average of 83.1% of the time without TimeCap.</p>	<p>Results indicate that patients used on average 2.867g more pilocarpine over the 30-day period with TimeCap. This results translates into 57 drops and into 29 medication doses or 1 additional dose of pilocarpine per day. The results indicate that a medication alarm device may effectively improve compliance in glaucoma patients.</p>

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Simoni 2009 RCT parallel	<p>Patients with HIV</p> <p><u>Group 1</u>: n=57; <u>Group 2</u>: n=56; <u>Group 3</u>: n=54;</p> <p><u>Control</u>: n=57.</p> <p>Total group: n=224, mean age 40, 76% male.</p>	<p><u>Intervention</u>:</p> <p>1) peer support: 6 twice monthly 1-hour peer meetings held at the clinic with peers and participants, and weekly phone calls from peers to participants.</p> <p>2) use of a 2-way pager system. The message schedule is customized to participants' daily regimen. In addition to dose reminders, including medication names and number of pills to be taken, 3 other types of messages were sent: 1) educational; 2) entertainment; 3) adherence assessments. Minimum of 3 pager messages sent daily for 2 months. Pages gradually tapered in third month. Confirmation page was requested.</p> <p>3) combination of peer support and pager.</p>	<p>Self-report and electronic monitoring (MEMS).</p> <p>At 3 (directly post-intervention), 6 and 9 months.</p>	<p>Self-report 100% adherence last 7 days at 2 weeks, 3, 6, 9 months:</p> <p>Group 1: 63.2%, 56.1%, 42.1%, 43.9%</p> <p>Group 2: 80.4%, 57.1%, 42.9%, 58.9%</p> <p>Group 3: 70.4%, 70.4%, 55.6%, 50.0%</p> <p>Control: 64.9%, 47.4%, 63.2%, 43.9%</p> <p>EM adherence last 7 days at 2 weeks, 3, 6, 9 months:</p> <p>Group 1: 61.7%, 47.0%, 37.2%, 32.3%</p> <p>Group 2: 63.0%, 41.8%, 36.9%, 36.5%</p> <p>Group 3: 63.2%, 50.1%, 35.4%, 32.1%</p> <p>Control: 63.0%, 38.7%, 41.0%, 29.1%</p> <p>Peer support: a 2-fold increase in the odds of self-report 100% adherence for those receiving vs. not receiving peer support at post-intervention (OR=2.10, 95% CI 1.10-4.01, P=0.02). Peer support vs. no peer support was associated with 9% higher adherence</p>	<p>Findings indicated a 2-fold greater odds of self-reported 100% adherence at immediate post-intervention among individuals receiving peer support vs not receiving peer support. EDM data partially supported this finding. However, neither effect was maintained at follow-up. Receiving informational, emotional, affirmational support from peers might promote adherence, but that effect did not persist when the support was discontinued.</p> <p>The pager intervention did not seem to be successful in promoting adherence at any time point.</p>

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		<p><u>Control</u>: no peer support or pager.</p> <p>All <u>patients</u> participated in the HAART protocol (clinic-based program designed to provide education regarding HAART and adherence and to identify and correct adherence barriers before HAART initiation).</p> <p><i>Type: pager</i></p>		<p>at post-intervention with EM data (estimate=8.88, 95% CI 22.09-19.85, P=0.11). This did not persist at 6 and 9-month follow-up for self-report (P>0.77) nor EM adherence (P>0.74). Pager support did not predict improved odds of 100% adherence at 3 or 9 months (P> 0.74), but was associated with a decrease in 100% adherence at 6 months (OR=0.50, 95% CI 0.24-1.03, P=0.06). EM adherence also indicated no effect for pager support at 3, 6, or 9 months (P> 0.54)</p>	

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Safren 2003 RCT parallel	Patients with HIV Total: n=70, 56 male, age not reported.	<p><u>Intervention</u>: website used to input patients' schedule of daily pages. A paging service delivered text messages (e.g. "Take 2 Combivir with water" every day at 9 AM, or "Take the 2 blue pills now") to patients' pagers at designated times. The system allowed staff members to incorporate other reminders (e.g. timing of meals or appointment reminders).</p> <p><u>Control</u>: no reminders</p> <p><i>Type: pager</i></p>	Electronic monitoring (MEMS). At baseline, 2 and 12 weeks.	<p>For week 2 ($F(1,58)=8.24, p<0.01$) and week 12 ($F(1,43)=5.79, p<0.03$), there were significant interactions revealing greater improvement in the pager arm.</p> <p>On average, the intervention group started with 55% adherence, went up to 70% at 2 weeks and 64% at 12 weeks. The control group started with 57% adherence, and remained at 56% (week 2) and 52% (week 12).</p>	A reminder device (pager) revealed improvements relative to monitoring alone at 2 and 12 weeks. However, at both assessment points, in both groups, adherence was less than optimal, revealing the need for more intensive intervention efforts among patients with pre-existing adherence problems.