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**ADERENZA ALLA TERAPIA
FARMACOLOGICA**

**OTTICA
RESPIRO**

VERONA 2017
CROWNE PLAZA

ALESSANDRO NOBILI

Dichiarazione Conflitto di Interessi

Il sottoscritto Alessandro NOBILI

*ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg.
Applicativo dell'Accordo Stato-Regione del 5 Novembre 2009,*

DICHIARA

*che negli ultimi due anni NON ha avuto rapporti diretti di
finanziamento con soggetti portatori di interessi commerciali in
campo sanitario.*

TOPICS

- Definitions and prevalence
- Problems and consequences of non-adherence in COPD
- Factors affecting non-adherence in COPD
- The role of different device
- How to improve the adherence in COPD
- Conclusions and perspectives

PREMISE

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

DRUG THERAPY

Adherence to Medication

Lars Osterberg, M.D., and Terrence Blaschke, M.D.

**“DRUGS DON’T WORK IN PATIENTS
WHO DON’T TAKE THEM”.**

C. Everett Koop

PREMISE

The average rates of **adherence in clinical trials** can be remarkably **high**, owing to the **attention study patients receive** and to **selection of the patients**, yet even clinical trials report **average adherence rates of only 43 to 78 percent** among patients receiving treatment for chronic conditions.

Patients commonly **improve their medication-taking behavior in the 5 days before and after an appointment with the health care provider**, as compared with 30 days after, in a phenomenon known as ***“white-coat adherence.”***

DEFINITIONS

COMPLIANCE

*Refers to a treatment regimen and the **following passive behavior from the patient** respect to specific prescription like an **acquiescent recipient of expert medical prescription**.*

ADHERENCE

*Considers the **approval and “active” leading part of the patient in his own health management**. It more accurately reflects a patient's active role in consenting and following prescribed treatments.*

CONCORDANCE

*Has been used to describe the **“therapeutic alliance”** that exists between patients and medical healthcare professionals.*

AGREEMENT

*Indicates a **medical treatment prescription model based on negotiation and agreement** by and between the physician and the patient, **reflecting and valuing the viewpoint of the latter**.*

ADHERENCE TO THERAPY

In a recent survey carried out with pneumunologists, the definition of ADHERENCE in Respiratory Medicine that has received the highest consensus has been the following:

“A condition that can only be fulfilled when the patient accepts the presence of the disease and the issues related to the recommended therapy”

Braido F, et a.. Respir Res 2013, 14:94.

The World Health Organization (WHO), through Mr. Clancy (Director of the Agency for Health Research and Quality) defined

“Adherence to therapy as a new pharmacological problem”.

MEDICATION NON-ADHERENCE

INTENTIONAL

*The **deliberate discontinuation or reduction** in use of therapy during periods of **symptom remission**, often resulting from an **erroneous understanding of the disease course** and the **goals of treatment**.*

UNINTENTIONAL

*Occurs when patients **do not adhere to treatment advice** due to reasons out of **their control**, often relating to **age, cognitive impairments, language barriers** and **physical disability**.*

In COPD the most commonly identified reasons are:

- *complex medication regimens,*
- *polypharmacy,*
- *multiple devices,*
- *poor awareness and understanding of COPD,*
- *confusion,*
- *depression.*

MEDICATION POSSESSION RATIO - MPR

Medication adherence, as defined by the ISPOR*, “refers to the act of conforming to the recommendations made by the provider with respect of timing, dosage and frequency of medication taking”.

(Carmer et al., 2008)

Adherence is expressed as **an index number**, which is typically given as a **percentage** and refers to a **specified time interval**. One of the most commonly used models for calculating medication compliance is the **MEDICATION POSSESSION RATIO (MPR)**.

Medication possession ratio (MPR) is the **number of days of medication supplied within the refill interval is divided by the number of days in the refill interval**.

(Peterson et al., 2007)

Drugs	Months (1 month = 30 days)									Supply (days)			MPR
A	x	x	x	x	x	x				x	x	x	9x30=270 270/360=0.75
B		x	x	x	x		x	x	x	x			8x30=240 240/360=0.66
C			x		x		x	x		x	x	x	7x30=210 210/360=0.58

$\sum \text{MPR}: ((270+240+210)/3)/360 = 0.66 \rightarrow 66\%^*$

*:Patient is non-compliant (cut-off point: 80%).

| x |: medication supplied, | |: medication not supplied

MEDICATION PERSISTENCE

According to the definition of ISPOR, **MEDICATION PERSISTENCE** may be described as “the duration of time from initiation to discontinuation of therapy” .

(Carmer et al., 2008).

Persistence analyses must also define a **permissible gap period**, which specifies the **maximum allowable time period between refills without discontinuation of the therapy**. Persistence may be **counted in days**. However, it can also be given as the percentage of the number of persistent patients at the end of a predefined time period.

(Patricia et al., 2006)

Patients	Months (1 month = 30 days)												Days persistent (gap: 30 days)*	Persisted 180 days**
A	x	x	x	x			x	x	x				120	no
B	x	x	x	x	x	x				x		x	180	yes
C	x	x				x	x			x		x	60	no

*: Patients persisted an average of 120 days $((120+180+60)/3)$

** : 33% (1/3) of the patients were persistent for 180 days

| x | : medication supplied, | | : medication not supplied

MEDICATION ADHERENCE

UNDERUSE, OVERUSE, IMPROPER USE

Underuse/overuse is defined as a reduction/increasing of the apparent daily use versus a standard dose of a medication that is indicated for the treatment or prevention of a disease or condition.

(Lipton et al 1992; Harrow et al 1997)

Improper use or inappropriate use is confirmed by determining whether a drug is ineffective, not indicated, or if there is unnecessary duplication of therapy.

(Steinman et al 2006)

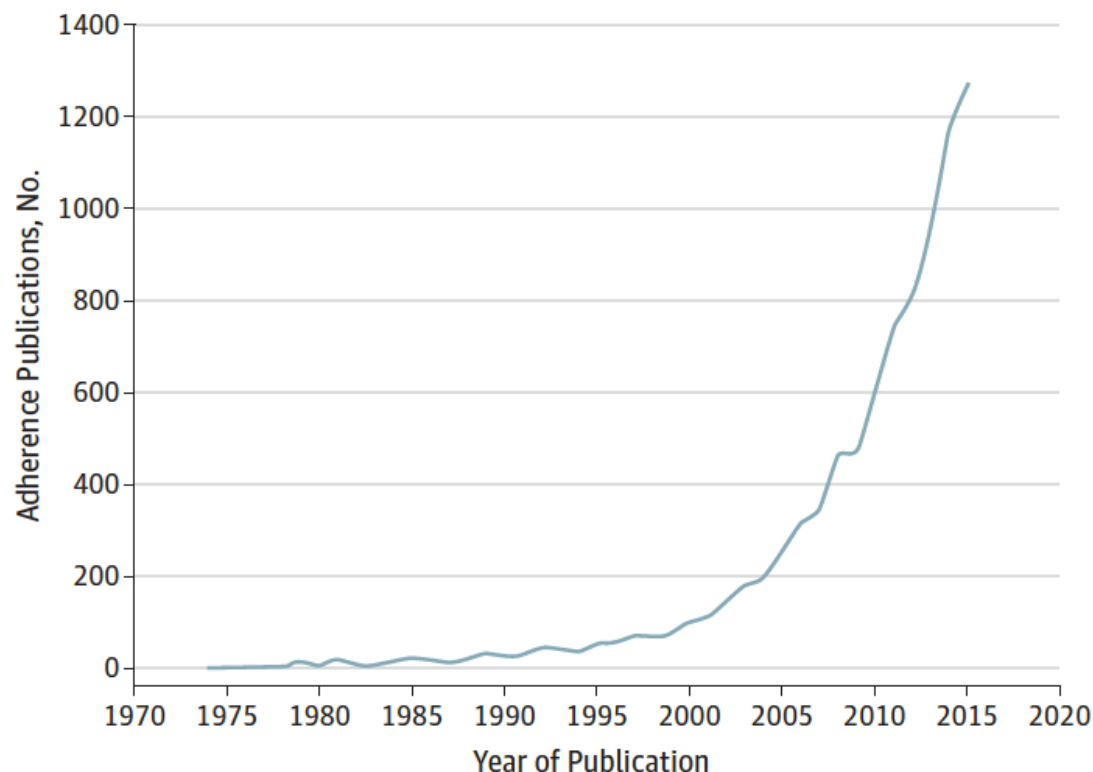
In Search of a “Magic Pill” for Medication Nonadherence

Ian M. Kronish, MD, MPH; Nathalie Moise, MD, MS

In the **mid 1970s**, David Sackett and colleagues partnered with a group of 250 hypertensive factory workers and their physicians to conduct groundbreaking research on what was then referred to as medication compliance.

In the subsequent 40 years, the amount of research dedicated to medication nonadherence increased exponentially.

Figure. Forty Years of Medication Adherence Research



Number of publications indexed in PubMed with *medication adherence* or *compliance* in the title or abstract, from 1966 to 2015.

IDENTIFYING POOR ADHERENCE

The simplest and most practical suggestion for physicians is to **ask patients nonjudgmentally how often they miss doses.**

Patients generally want **to please their physicians** and will **often say what they think their doctor wants to hear.**

It can be reassuring to the patient when the physician tells them, *“I know it must be difficult to take all your medications regularly. How often do you miss taking them?”*

This approach makes most patients feel comfortable in telling the truth and facilitates the identification of poor adherence. A patient who admits to poor adherence is generally being candid.

Patients should also be asked whether:

- they are **having any side effects** of their medications,
- they **know why they are taking** their medications,
- and **what the benefits of taking them are.**

METHODS OF MEASURING ADHERENCE

Table 1. Methods of Measuring Adherence.

Test	Advantages	Disadvantages
Direct methods		
Directly observed therapy	Most accurate	Patients can hide pills in the mouth and then discard them; impractical for routine use
Measurement of the level of medicine or metabolite in blood	Objective	Variations in metabolism and "white-coat adherence" can give a false impression of adherence; expensive
Measurement of the biologic marker in blood	Objective; in clinical trials, can also be used to measure placebo	Requires expensive quantitative assays and collection of bodily fluids
Indirect methods		
Patient questionnaires, patient self-reports	Simple; inexpensive; the most useful method in the clinical setting	Susceptible to error with increases in time between visits; results are easily distorted by the patient
Pill counts	Objective, quantifiable, and easy to perform	Data easily altered by the patient (e.g., pill dumping)
Rates of prescription refills	Objective; easy to obtain data	A prescription refill is not equivalent to ingestion of medication; requires a closed pharmacy system
Assessment of the patient's clinical response	Simple; generally easy to perform	Factors other than medication adherence can affect clinical response
Electronic medication monitors	Precise; results are easily quantified; tracks patterns of taking medication	Expensive; requires return visits and downloading data from medication vials
Measurement of physiologic markers (e.g., heart rate in patients taking beta-blockers)	Often easy to perform	Marker may be absent for other reasons (e.g., increased metabolism, poor absorption, lack of response)
Patient diaries	Help to correct for poor recall	Easily altered by the patient
When the patient is a child, questionnaire for caregiver or teacher	Simple; objective	Susceptible to distortion

ISSUES OF NONADHERENCE IN COPD

- In real-life conditions, the **percentage of compliant patients is much lower (10-40%) than the percentages reported in the literature (40-60%), and those recorded in clinical trials (70-90%).**
- **The most common type of non-adherence in COPD patients is underuse and improper use is the most frequent type of non-adherence in patients older than 65 years of age with polypharmacy.**
- **Forgetfulness probably is the most common unintentional behavior to skip doses in order to make the medication last longer.**

PREVALENCE OF MEDICATION ADHERENCE

MEDICATION POSSESSION RATIOS

Rolnick SJ, et al. Clin Med Res 2013,11(2):54–65.

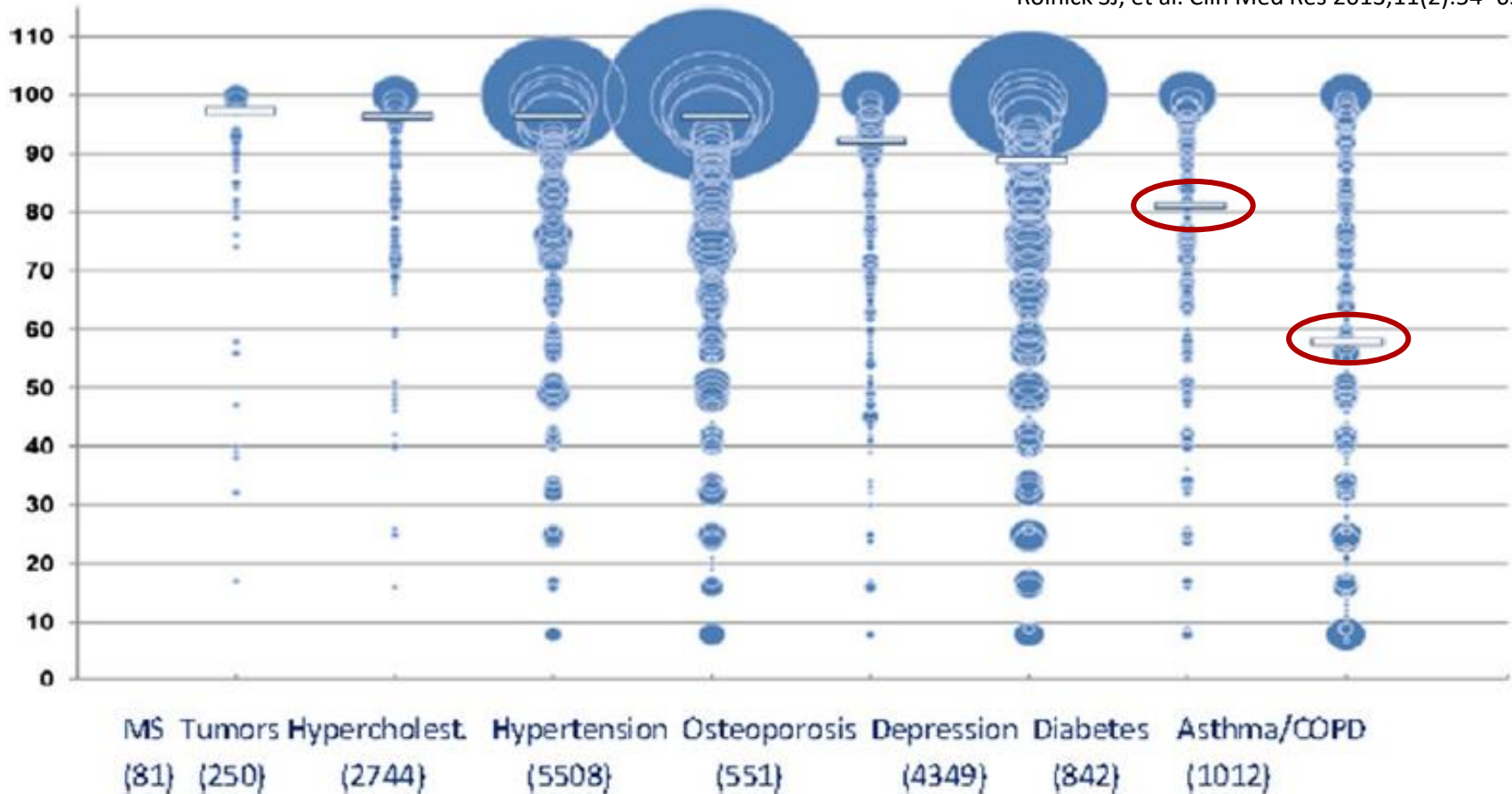


Figure 1 Distribution of medication possession ratios (MPR) for eight medical conditions among 15,334 patients (the areas of the circles are proportional to the sample sizes. **Median MPR is represented by horizontal bars**).

ADHERNENCE TO MEDICATION IN COPD

Only a limited number of studies have evaluated adherence in patients with COPD.

Jung et al. examined medication adherence and persistence among a sample of COPD patients during their last year of life. The study reviewed the use of inhaled corticosteroids (ICS), long-acting β 2 agonists (LABA), anticholinergics (AC) and methylxanthines (MTX), alone and in combination.

The overall MPR to COPD medication was 44%. Approximately 30% of the patients persisted with the therapy, and the overall time to discontinuation was 94.2 days. Differences were found between the mean **MPRs of COPD drug classes** (MTX: 52%, AC: 38%, ICS: 35%, LABA: 34%). Medication adherence was the highest with MTX.

(Jung et al., 2009)

These rates of cooperation are **much lower than the drug-taking rates in other chronic diseases**. Adherence in hypertension, dyslipidaemia and diabetes is, on average, 72% (MPR), and persistence is 63%.

(Cramer et al., 2008).

Association between adherence to medications for COPD and medications for other chronic conditions in COPD patients

14,117 patients, with a mean age of 69.9 years.

Table 3 Association between non-adherence to mCOPD medications and non-adherence to non-COPD medications: logistic regression analysis^a

Variable	Odds ratio	Lower 95% CI	Upper 95% CI	P-value
Dependent variable				
Non-adherence (PDC <0.8) to mCOPD medications	NA	NA	NA	NA
Main independent variables				
Non-adherence (PDC <0.8) to				
Statins	1.54	1.37	1.74	<0.0001
Antihypertensives	1.55	1.38	1.74	<0.0001
Anticoagulants	1.21	0.93	1.57	0.1497
Oral antihyperglycemics	1.38	1.13	1.69	0.0019
Insulins	1.78	1.28	2.47	0.0005
Antidepressants	1.73	1.50	1.99	<0.0001
NSAIDs	1.74	1.39	2.18	<0.0001
Antianxiety	1.16	0.93	1.45	0.1873
Calcium channel blockers	1.53	1.31	1.78	<0.0001
Beta-blockers	1.39	1.21	1.61	<0.0001
Bisphosphonates	1.51	1.20	1.91	0.0005
Diuretics	1.44	1.27	1.63	<0.0001

Notes: ^aStudy population, n=14,117. Baseline patient characteristics including age, sex, region, influenza vaccination status, and RxRisk-V score were included in the model as covariates.

Abbreviations: CI, confidence interval; mCOPD, maintenance COPD; NA, not applicable; NSAIDs, nonsteroidal anti-inflammatory drugs; PDC, proportion of days covered.

Non-adherence to COPD medications was associated with non-adherence to 10 of 12 non-COPD medication classes (odds ratio 1.38–1.78, all *P*0.01).

CONSEQUENCES OF NONADHERENCE IN COPD

Table 5 Negative consequences of non-adherence

- Poor control of symptoms
 - Worsening of the quality of life
 - Increasing number of relapses and more frequent need for health-care services (which account for 35-45% of the disease-related costs)
 - Higher mortality rate (2–3 times higher than in patients showing good compliance – 26.4% vs. 11.3% according to a sub-analysis made in the TORCH study [28])
 - Increase in health-care expenditure.
-

CONSEQUENCES OF NONADHERENCE IN COPD

Costs of chronic obstructive pulmonary disease (COPD) in Italy: the SIRIO study (social impact of respiratory integrated outcomes).

Considering that, in Italy, failure to use inhaled medications for chronic respiratory diseases, or wrong use thereof, leads to a **20% increase in the risk of hospitalization** and to a **50% increase in health-care expenditure** for overall direct/ indirect costs, which amount **to € 14 billion/year**, of which **€ 9 billion are for COPD alone** (with an estimated per capita cost of € 2,723), the extent of the problem is easily understood.

Valeria Belleudi¹, Mirko Di Martino¹, Silvia Cascini¹, Ursula Kirchmayer¹, Riccardo Pistelli², Giulio Formoso³, Danilo Fusco¹, Marina Davoli¹, and Nera Agabiti^{1*} on behalf of the OUTPUT Study Group

A total of 12 124 individuals were studied, 46% women, mean age 73,8 years.

Table 3. Association between inhaled drug use and survival (HR, 95%CI) both in the whole population under study and in the subgroup with previous exacerbations

Cohort: N= 12 124, mean of follow-up= 2.4 years, mortality rate = 11.9 per100 p. y.							
Treatment	% time of follow-up	Mortality rate	HR	CI95%		AR%	Number of preventable deaths
LB/ICS regular use	13.0	8.2	1	—	—	—	—
LB/ICS occasional use	45.7	11.3	1.26	1.11	1.43	20.6	280
LB regular use	12.5	9.7	1.13	0.97	1.32	11.6	39
LB occasional use	11.1	12.7	1.34	1.16	1.56	25.5	90
Respiratory drugs other than LB	17.6	17.0	1.63	1.43	1.87	38.7	261
People with exacerbation: N= 1389, mean of follow-up= 2.3 years, mortality rate = 14.9 per100 p. y.							
Treatment	% time of follow-up	Mortality rate	HR	CI95%		AR%	Number of preventable deaths
LB/ICS regular use	14.7	8.7	1	—	—	—	—
LB/ICS occasional use	45.2	14.4	1.65	1.17	2.32	39.4	82
LB regular use	13.7	11.9	1.45	0.96	2.19	30.8	17
LB occasional use	10.0	15.3	1.73	1.14	2.63	42.2	20
Respiratory drugs other than LB	16.5	23.6	2.11	1.47	3.03	52.6	51

p.y. = person years

In comparison to LB/ICS regular use, higher risks of death for all remaining treatments were found, the highest risk for respiratory drugs other than LB category (HR = 1.63, 95%CI 1.43–1.87). Patients with regular LB use had higher survival than those with LB/ICS occasional use (HR = 0.89, 95%CI 0.79–0.99).

FACTORS AFFECTING ADHERENCE IN COPD

COPD

- Progressive nature of the disease ↓*
- Poor prognosis ↓
- Lack of clinical symptoms ↓
- Disease severity —
- Lung function —

Patient

- Gender -
- Demographic factors: old age ↑
- Improved quality of life ↓
- Social support ↑
- Psychiatric co-morbidities ↓

Treatment

- Polypharmacy ↓
- Higher dosing frequency ↓
- Higher medication cost ↓
- Side effects ↓
- Oral administration ↑

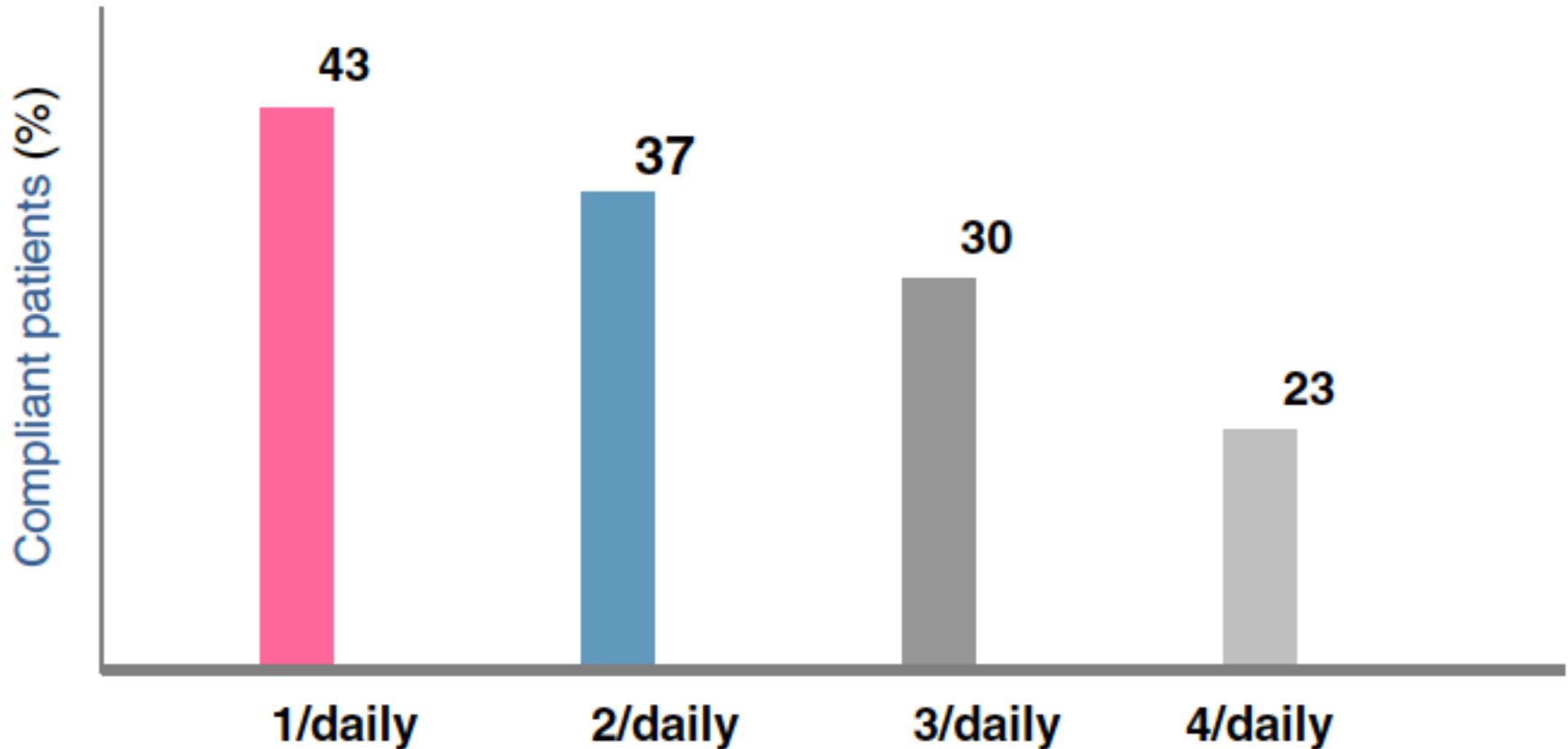
Health-care provider-patient relationship

- Higher quality of communication ↑
- Type of caregiver: specialist ↑
- Closer follow-up ↑
- Hospitalisation ↑

*Influence on adherence: decrease (↓), improve (↑), no effect (—)

FACTORS AFFECTING NON-ADHERENCE

Frequency of administration



Percentage of days under treatment as a function of the number of daily administrations in patients with chronic obstructive pulmonary disease.

PROFILE OF COPD NONADHERENT PATIENTS

- very old
- never quit smoking
- suffer from mild-moderate COPD
- take several different medications
- live alone
- depressed
- have limited economic resources
- show cognitive/cultural deficits
- have poor trust in physicians and medications
- do not realize the gravity of the disease or don't want to see themselves as such
- justify or hide their symptoms
- are reluctant to follow long-term therapies
- are well documented on their disease and know that they need to take specific medications but do not take any action and criticize any kind of pharmacological option (evolved inactivity)

FACTORS AFFECTING NON-ADHERENCE

THE ROLE OF DEVICE

Another key factor that is closely related to the patients' compliance with their medical therapy is the device.

If used incorrectly, it remarkably reduces the efficacy of the drug and, consequently, the patient's compliance.

The importance of inhaler devices: the choice of inhaler device may lead to suboptimal adherence in COPD patients

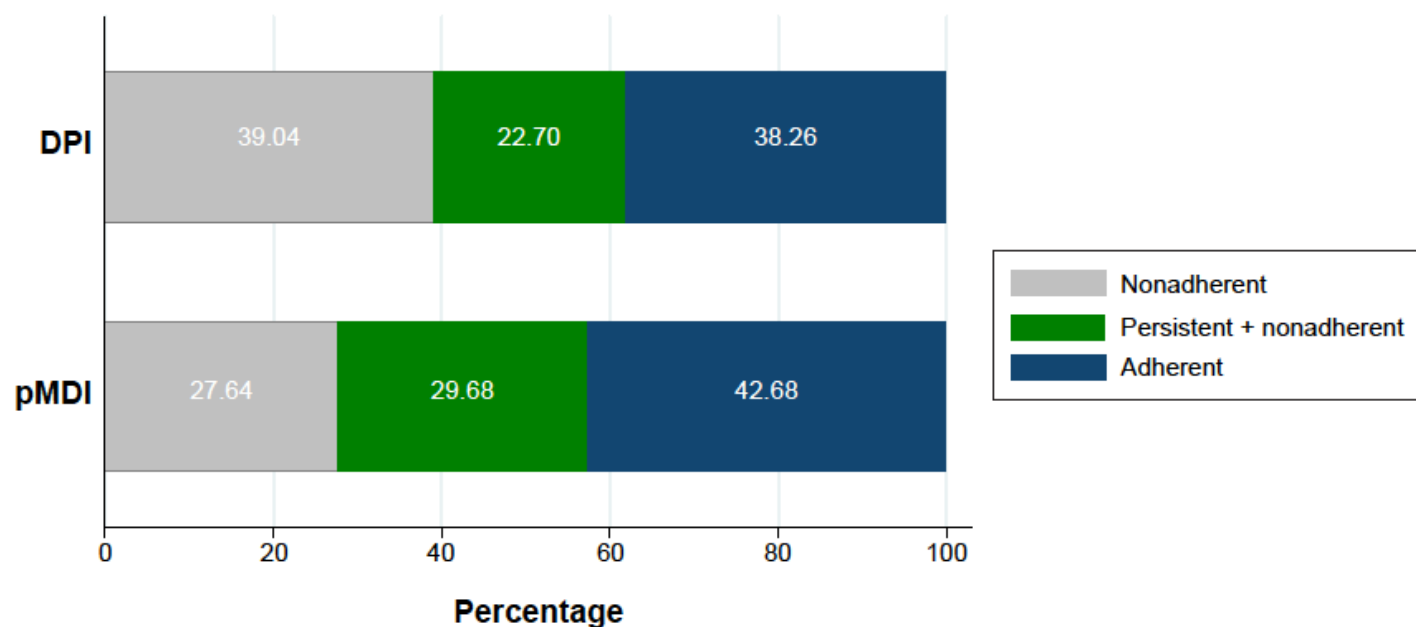
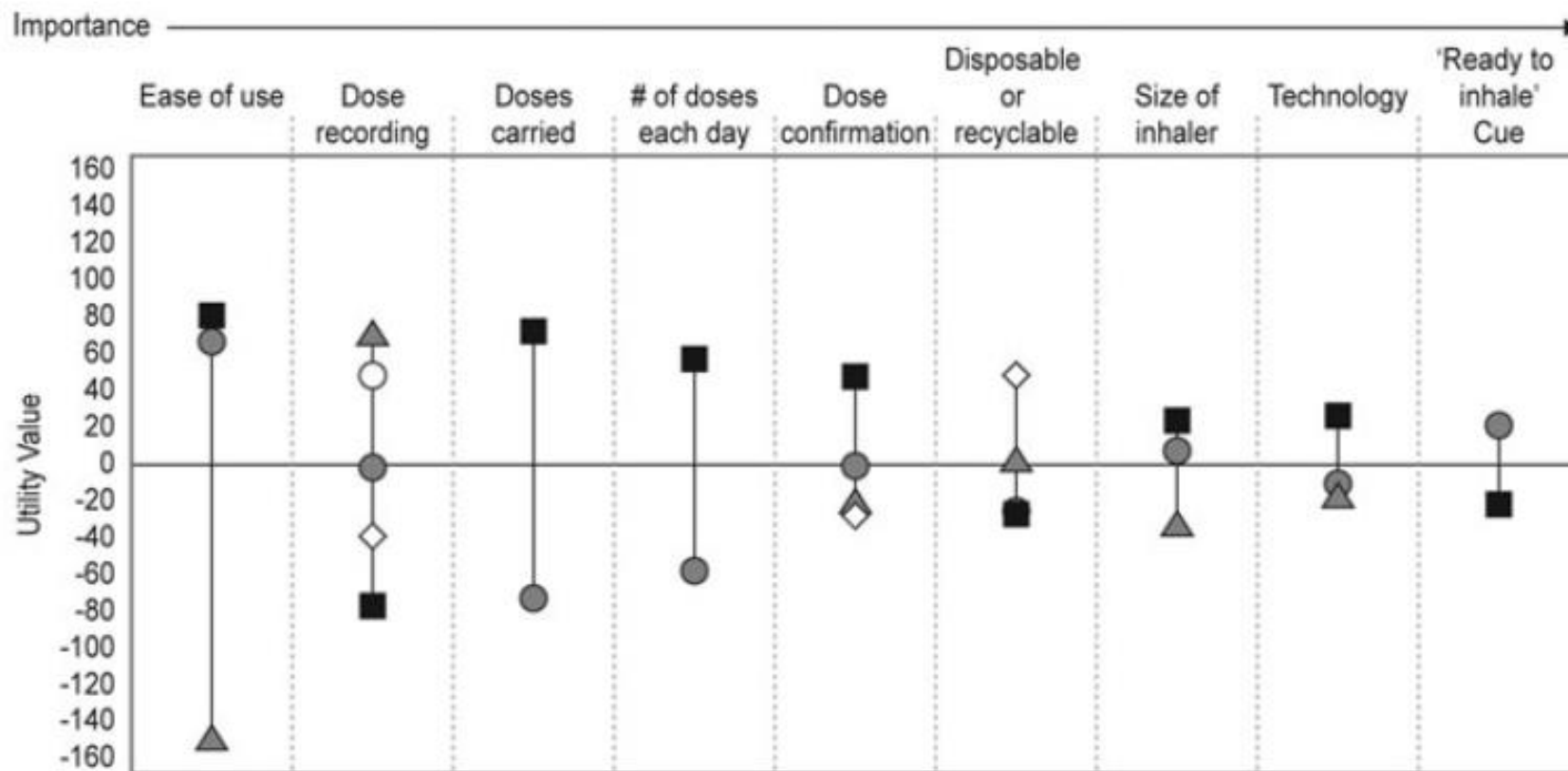


Figure 3 Percentage of adherent patients by each inhaler device (n=1,263).

Notes: Nonpersistent patient = patient who discontinued their therapy before the 18th month, persistent + nonadherent patient = patient who did not discontinue therapy but was <90% of the MPR, and adherent patient = patient who did not discontinue their therapy but was >90% of the MPR.

Abbreviations: pMDI, pressurized metered-dose inhaler; DPI, dry powder inhaler; MPR, medication possession ratio.

Mathieu Molimard, MD, PhD,¹ and Paul Colthorpe, PhD²



Choice utility values derived for patients (with number of doses each day).

Positive choice utility value for a given attribute level indicates a more desirable attribute, whereas a negative utility value of the attribute level indicates a less desirable attribute.

For each attribute, the larger the spread from the highest to lowest utility values, the higher that attribute's importance.

Teaching inhaler use in chronic obstructive pulmonary disease patients

Suzanne C. Lareau, RN, MS, FAAN (Senior Instructor)¹ & Richard Hodder, MD, FRCPC (Professor of Medicine)²

Table 1 Physical factors that may impair correct inhaler device use

Factor	Mechanism
Tremors	Intention tremors, tremors from overuse of short-acting beta-agonists, Parkinson's disease, etc., can make loading or twisting the device difficult or even impossible
Hand–eye coordination	Older people may have hand–eye coordination issues resulting in difficulty locating their mouth for delivering the spray from a pMDI
Dexterity	Patients with arthritis may have difficulty depressing the release for the pMDI or inserting the capsule into the small holding chamber of single-dose DPIs
Vision	Visual impairment problems may affect the patient's ability to see the dose counter (leading some patients to believe the device still holds medication when it is empty), or from properly loading the inhaler (single-dose DPIs)
Hearing	Patients may not hear the instructions and consequently, will not be in a position to be able to ask vital questions. Poor hearing may prevent patients from hearing the “click” indicating readiness to inhale in some DPIs, or the discharge from a pMDI into a spacer
Comorbidities	COPD patients often have multiple other health issues resulting in polypharmacy such as tablets, creams, eye drops, etc., which add to their challenge of maintaining a workable medication schedule
Economics	Financial concerns are an increasing problem in older patients, some of whom will miss doses to save the expense of buying the medication

pMDIs, pressurized metered dose inhalers; DPIs, dry powder inhalers.

HOW TO IMPROVE THE ADHERENCE IN COPD

FIVE “RIGHTS” OF MEDICATIONS

The right patient

The right medication

The right time

The right route

The right dose

Assessing medication adherence: options to consider

Audrey Lehmann • Parisa Aslani • Rana Ahmed •
Jennifer Celio • Aurelie Gauchet • Pierrick Bedouch •
Olivier Bugnon • Benoît Allenet • Marie Paule Schneider

HOW TO IMPROVE THE ADHERENCE IN COPD

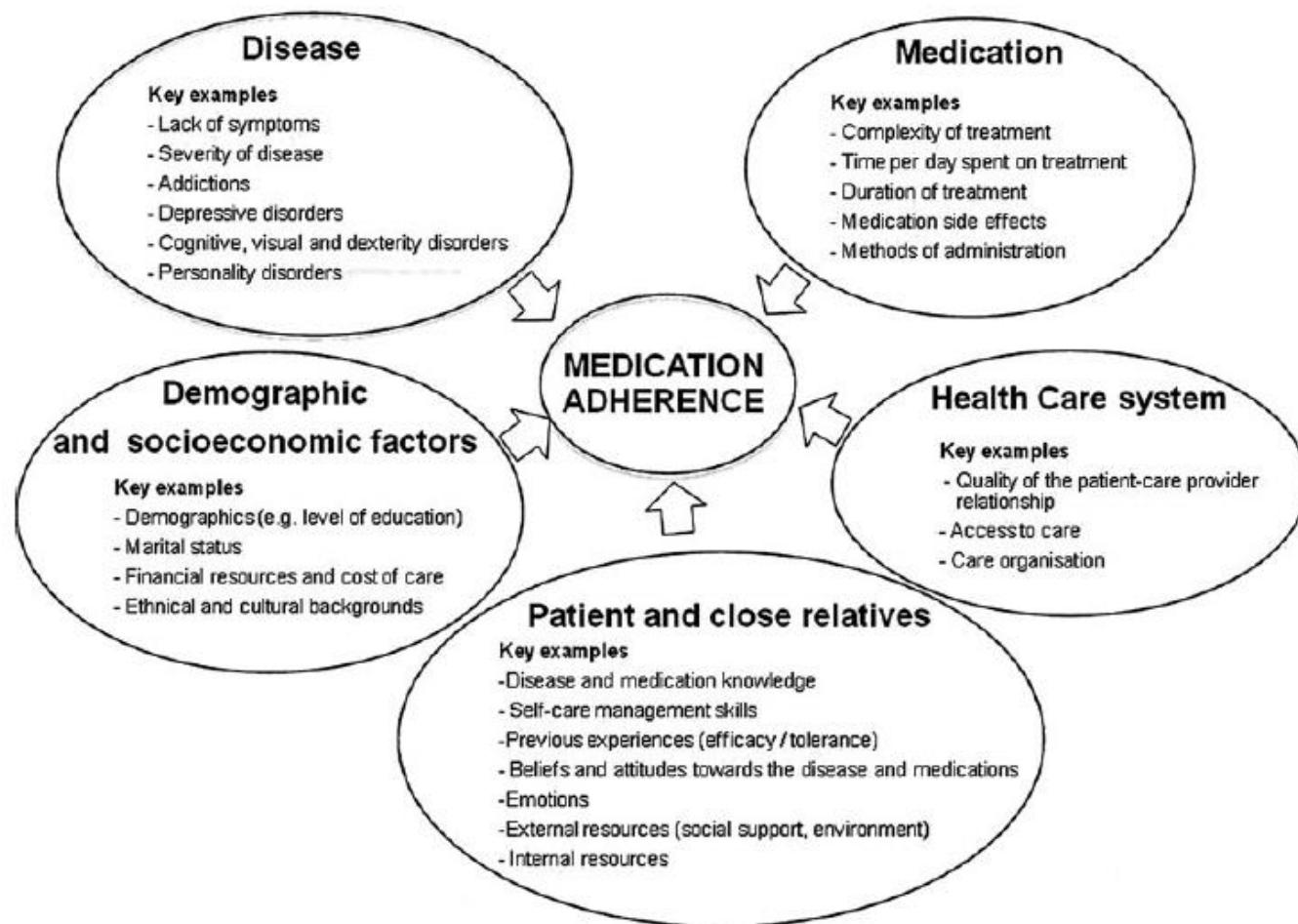


Fig. 1 Factors influencing medication adherence in chronic patients [6, 9–11]

HOW TO IMPROVE MEDICATION ADHERENCE IN COPD

INTERVENTIONS TO IMPROVE ADHERENCE

Methods that can be used to improve adherence can be grouped into four general categories:

- patient education;
- improved dosing schedules;
- Increased hours when the clinic is open (including evening hours), and therefore shorter wait times;
- improved communication between physicians and patients.



Ministero della Salute

DIREZIONE GENERALE DELLA PROGRAMMAZIONE SANITARIA

GLI ELEMENTI CHIAVE DI GESTIONE DELLA CRONICITA'

1. Aderenza

ASPETTI TRASVERSALI DELL'ASSISTENZA ALLA CRONICITA'

3. Appropriatezza nell'uso delle terapie e delle tecnologie - Aderenza alla terapia farmacologica

Piano Nazionale della Cronicità

Accordo tra lo Stato, le Regioni e le Province Autonome di Trento e di Bolzano del 15 settembre 2016

http://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=4654&area=programmazioneSanitariaLea&menu=vuoto

TERAPIE E ADERENZA TERAPEUTICA

OBIETTIVO

- Promuovere l'appropriatezza nell'uso delle terapie e delle tecnologie diagnostiche e terapeutiche
- Migliorare l'aderenza terapeutica
- Garantire il diritto all'accesso appropriato alle tecnologie diagnostiche e terapeutiche, favorendo l'impiego di strumenti di qualità tecnologica adeguata e di procedure idonee a ottenere risultati sicuri riducendo i potenziali rischi e monitorando nel tempo l'adeguatezza e la qualità

RISULTATI ATTESI

Incremento di soluzioni organizzative che favoriscano l'adesione alle prescrizioni, con particolare riferimento all'aderenza alla terapia farmacologica in caso di trattamenti farmacologici multipli (politerapie)

LINEE DI INTERVENTO PROPOSTE

1. valutare le buone pratiche presenti al fine di individuare un modello nazionale di valutazione dell'appropriatezza prescrittiva, coinvolgendo e responsabilizzando le istituzioni competenti (AIFA, ISS, Agenas ...)
2. promuovere studi di ricerca applicata e soluzioni tecnologiche e organizzative per migliorare l'aderenza terapeutica
3. valutare l'utilizzo delle linee guida e promuoverne l'implementazione per migliorare l'appropriatezza terapeutica e disincentivare l'utilizzo di farmaci non appropriati
4. diffondere le conoscenze sul rischio aumentato di reazioni avverse ai farmaci nei pazienti affetti da patologia cronica e in politerapia
5. sviluppare iniziative per far conoscere i criteri di Beers e di START and STOPP tra gli operatori sanitari
6. favorire l'implementazione di strumenti di ICT di aiuto alla prescrizione con warning per interazioni e controindicazioni
7. adottare procedure che favoriscano l'adesione alle prescrizioni mediche, con particolare riferimento all'aderenza alla terapia farmacologica in caso di trattamenti farmacologici multipli (politerapie)
8. definire modalità organizzative che consentano equità di accesso alle terapie e alle tecnologie, valorizzando le competenze dei centri specializzati a più alto livello di organizzazione
9. formare e informare le persone con cronicità e tutti gli operatori sanitari e non sanitari coinvolti sull'uso appropriato delle terapie e delle tecnologie

HOW TO IMPROVE MEDICATION ADHERENCE IN COPD

The main errors in delivery device use relate to problems with inspiratory flow, inhalation duration, coordination, dose preparation, exhalation maneuver prior to inhalation and breath-holding following dose inhalation (**Table 3.6**).¹⁷⁴ Specific instructions are available for each type of device.¹⁷⁰ Observational studies in patients with COPD show that, although the type and frequency of inhalation errors vary between devices depending on their characteristics, there is no device obviating the need to explain, demonstrate and regularly check inhalation technique.¹⁷⁷⁻¹⁸³ Strategies for inhaler choice based on patients' characteristics have been proposed by experts and consensus-based taskforces (**Table 3.6**), but none have yet been prospectively tested.^{170,183,184} There is no evidence for superiority of nebulized therapy over hand-held devices in patients who are able to use these devices properly.

Table 3.6. The inhaled route

- When a treatment is given by the inhaled route, the importance of education and training in inhaler device technique cannot be over-emphasized.
- The choice of inhaler device has to be individually tailored and will depend on access, cost, prescriber, and most importantly, patient's ability and preference.
- It is essential to provide instructions and to demonstrate the proper inhalation technique when prescribing a device, to ensure that inhaler technique is adequate and re-check at each visit that patients continue to use their inhaler correctly.
- Inhaler technique (and adherence to therapy) should be assessed before concluding that the current therapy is insufficient.

HOW TO IMPROVE MEDICATION ADHERENCE IN COPD

Improving medication adherence in chronic obstructive pulmonary disease: a systematic review

Jamie Bryant^{1*}, Vanessa M McDonald^{2,3}, Allison Boyes¹, Rob Sanson-Fisher¹, Christine Paul¹ and Jessica Melville¹

Abstract

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

Improving Medication Adherence and Health Outcomes in Older Adults: An Evidence-Based Review of Randomized Controlled Trials

Zachary A. Marcum¹ • Joseph T. Hanlon^{2,3} • Michael D. Murray⁴

Drugs Aging 2017; DOI 10.1007/s40266-016-0433-7

Abstract

Background Poor medication adherence is a major public health problem in older adults often resulting in negative health outcomes.

Objective The objective of this review was to provide an updated summary of evidence from randomized controlled studies to determine whether interventions aimed at improving medication adherence also improve the health outcomes of older adults residing in community-based settings.

Methods Articles that assessed medication adherence interventions and related health outcomes in elderly individuals were identified through searches of MEDLINE (1970–June 2016), the Cochrane Database of Systematic Reviews (through to June 2016), and Google Scholar. Across the 12 included studies, interventions were grouped into three main categories: behavioral/educational ($n = 3$), pharmacist-led ($n = 7$), and reminder/simplification ($n = 2$).

Results Among the behavioral/educational intervention studies, two showed improvements in both adherence and related health outcomes, whereas one found no changes in adherence or health outcomes. Among the pharmacist-led

studies, three showed improvements in both adherence and related health outcomes, while three reported no changes in adherence or health outcomes. One found an improvement in adherence but not health outcomes. Among the reminder/simplification studies, both studies reported improvements in adherence without a significant impact on related health outcomes.

Conclusion This evidence-based review of medication adherence interventions in older adults revealed promising strategies in the larger context of a largely mixed body of literature. Future patient-centered and multidisciplinary interventions should be developed and tested using evidence-based principles to improve medication adherence and health outcomes in older adults.

**HOW TO IMPROVE
MEDICATION ADHERENCE
IN COPD**



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Main results

The present update included 109 new RCTs published since the previous update in January 2007, bringing the total number of RCTs to 182; we found five RCTs from the previous update to be ineligible and excluded them. Studies were heterogeneous for patients, medical problems, treatment regimens, adherence interventions, and adherence and clinical outcome measurements, and most had high risk of bias. The main changes in comparison with the previous update include that we now: 1) report a lack of convincing evidence also specifically among the studies with the lowest risk of bias; 2) do not try to classify studies according to intervention type any more, due to the large heterogeneity; 3) make our database available for collaboration on sub-analyses, in acknowledgement of the need to make collective advancement in this difficult field of research. Of all 182 RCTs, 17 had the lowest risk of bias for study design features and their primary clinical outcome, 11 from the present update and six from the previous update. The RCTs at lowest risk of bias generally involved complex interventions with multiple components, trying to overcome barriers to adherence by means of tailored ongoing support from allied health professionals such as pharmacists, who often delivered intense education, counseling (including motivational interviewing or cognitive behavioral therapy by professionals) or daily treatment support (or both), and sometimes additional support from family or peers. Only five of these RCTs reported improvements in both adherence and clinical outcomes, and no common intervention characteristics were apparent. Even the most effective interventions did not lead to large improvements in adherence or clinical outcomes.

Authors' conclusions

Across the body of evidence, effects were inconsistent from study to study, and only a minority of lowest risk of bias RCTs improved both adherence and clinical outcomes. Current methods of improving medication adherence for chronic health problems are mostly complex and not very effective, so that the full benefits of treatment cannot be realized. The research in this field needs advances, including improved design of feasible long-term interventions, objective adherence measures, and sufficient study power to detect improvements in patient-important clinical outcomes. By making our comprehensive database available for sharing we hope to contribute to achieving these advances.

Interventions for enhancing medication adherence (Review)

Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, Agoritsas T, Mistry N, Iorio A, Jack S, Sivaramalingam B, Iserman E, Mustafa RA, Jedraszewski D, Cotoi C, Haynes RB

CONCLUSIONS

Invited Commentary

In Search of a “Magic Pill” for Medication Nonadherence

Ian M. Kronish, MD, MPH; Nathalie Moise, MD, MS

So where do we go from here?

- **need to improve the detection** of nonadherence;
- **objective measures**, such as pharmacy fill data, drug levels, and electronic monitoring, are needed to accurately identify nonadherence;
- targeting **intensive behavioral adherence interventions at high-risk nonadherent** patients may be an approach to achieving value;
- **streamlining medications to avoid unnecessary or outdated prescriptions** and using **once-daily dosing whenever possible** can also help to improve adherence;
- **advances in mobile health and telemonitoring** show promise for facilitating behavioral interventions and allowing physicians to tailor these interventions to a patient’s individual barriers;
- it remains to be seen **whether such technological innovations can bend the cost curve on multicomponent adherence interventions.**

CONCLUSIONS

Invited Commentary

In Search of a “Magic Pill” for Medication Nonadherence

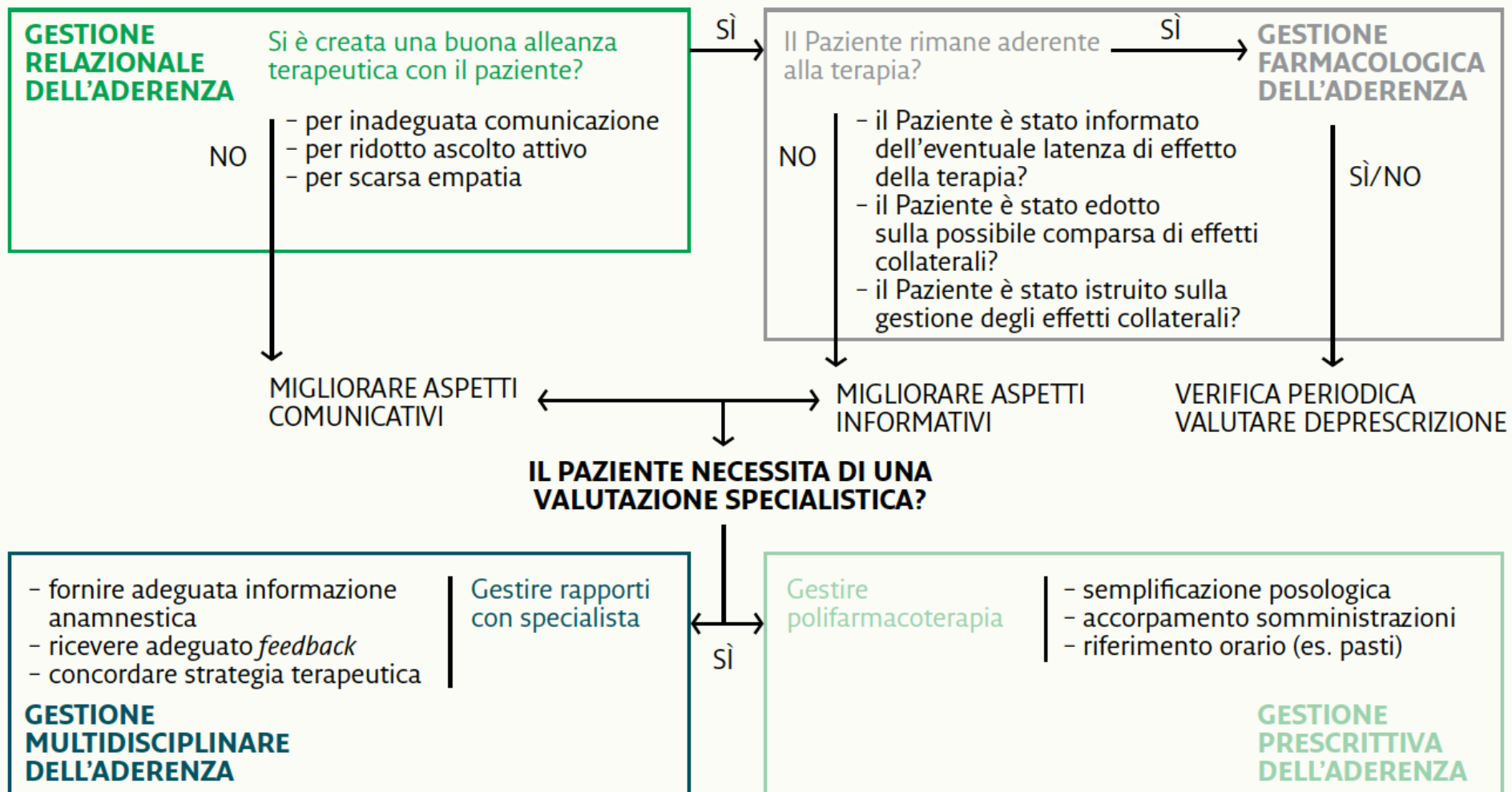
Ian M. Kronish, MD, MPH; Nathalie Moise, MD, MS

In the meantime:

- adherence researchers and practicing clinicians need to acknowledge that **there is unlikely to be a “magic pill”** that will solve medication nonadherence;
- **routinely inquiring about medication adherence** in a nonjudgmental manner remains essential to uncovering nonadherence when objective measures are unavailable;
- when nonadherence is suspected, **clinicians are encouraged to explore the reasons for nonadherence** and to **incorporate behavior-change techniques** from effective, multicomponent interventions into their practice;
- these techniques may include **providing feedback on self-monitoring**, enlisting **social supports**, and recommending use of **reminder systems**;
- **partnering with allied health professionals**, such as pharmacists or care managers, with expertise in these techniques is recommended when possible;
- **tackling nonadherence is challenging but not insurmountable**, and this work helps inform our strategies.

CONCLUSIONS

ALGORITMO RIASSUNTIVO DELLA RELAZIONE MEDICO/PAZIENTE PER MIGLIORARE L'ADERENZA ALLA TERAPIA.





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***Insanity: doing the same thing over and over again
and expecting different results.***

Albert Einstein

Grazie per l'attenzione .