7’ ΕΠΙΣΤΗΜΟΝΙΚΟ ΣΥΜΠΟΣΙΟ ΕΠΕΜΥ

ΚΑΛΑΜΑΤΑ 21-24 /05

ΔΟΡΥΦΟΡΙΚΟ ΣΥΜΠΟΣΙΟ

(Roche)

«Παράμετροι που καθορίζουν τη θεραπευτική απάντηση πέραν των δεδομένων των κλινικών μελετών»

Συντονιστής: Ανδρέας Μπούνας

1. Συμμόρφωση (adherence), Παραμονή (persistence), Προτίμηση (preference), Ικανοποίηση (satisfaction) των ασθενών και των επαγγελματιών υγείας (15΄)
   Ανδρέας Μπούνας, Ρευματολόγος, Πάτρα

2. Η οπτική των ασθενών σχετικά με τη θεραπεία (15΄)
   Καραϊσαρίδου Χρυστάλα, Αντιπρόεδρος ΕΛΕΑΝΑ

3. Δεδομένα υποδόριας χορήγησης του Tocilizumab (15΄)
   Παπαγόρας Χαράλαμπος, Ρευματολόγος, Αλεξανδρούπολη

Συζήτηση και παρουσίαση περιστατικών (15΄)

ΔΗΛΩΣΗ ΣΥΜΦΕΡΟΝΤΩΝ

Συμμετοχή την τελευταία 10ετία ως ομιλητής ή παρέχοντας συμβουλευτικές υπηρεσίες σε συναντήσεις στις κάτωθι φαρμακευτικές εταιρείες

- AbbVie (Abbott)
- Bristol-Mayer Squibb
- MSD
- Novartis Hellas
- Pfizer Hellas
- Roche Hellas

C. Everett Koop, M.D.

"Drugs don't work in patients who don't take them"

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, M.D.

- Συμμόρφωση (adherence),
- Παραμονή (persistence),
- Προτίμηση (preference),
- Ικανοποίηση (satisfaction)

των ασθενών και των επαγγελματιών υγείας

adherence

- ‘following medical advice sufficiently to achieve the therapeutic goal’

Kelly (1995)

- ‘the extent to which a person’s behaviour coincides with medical or health advice’

Haynes et al. (2002)

Compliance,adherence or concordance?

- Compliance : συμμόρφωση,υποταγή,υποχωρητικότητα (paternalistic)

  Oxford Dictionary

- Adherence : προσκόλληση

- Concordance : συμφωνία (partnership)

Table 1 Recommendations for the management of rheumatoid arthritis with non-biological and biological disease-modifying antirheumatic drugs.

Overarching principles	
A	Rheumatologists are the specialists who should primarily care for patients with RA
B	Treatment of patients with RA should aim at the best care and must be based on a shared decision between the patient and the rheumatologist
C	RA is expensive in regards to medical costs and productivity costs, both of which should be considered by the treating rheumatologist.

Final set of 15 recommendations for the management of RA	
1	Treatment with synthetic DMARDs should be started as soon as the diagnosis of RA is made
2	Treatment should be aimed at reaching a target of

Recommendation

Table 1 2013 Update of the EULAR recommendations (the table of 2010 recommendations can be seen in the online sup original publication)

	Overarching principles
A.	Treatment of RA patients should aim at the best care and must be based on a shared decision between the patient and the rheumatologist
B.	Rheumatologists are the specialists who should primarily care for RA patients
C.	RA incurs high individual, societal and medical costs, all of which should be considered in its management by the treating rheumatologist
	Recommendations
1.	Therapy with DMARDs should be started as soon as the diagnosis of RA is made
2.	Treatment should be aimed at reaching a target of remission or low disease activity in every patient
3.	Monitoring should be frequent in active disease (every 1–3 months); if there is no improvement by at most 3 months after the start of treatm been reached by 6 months, therapy should be adjusted
4.	MTX should be part of the first treatment strategy in patients with active RA
5.	In cases of MTX contraindications (or early intolerance), sulfasalazine or leflunomide should be considered as part of the (first) treatment stra
6.	In DMARD-naïve patients, irrespective of the addition of glucocorticoids, csDMARD monotherapy or combination therapy of csDMARDs shoul
7.	Low-dose glucocorticoids should be considered as part of the initial treatment strategy (in combination with one or more csDMARDs) for up t be tapered as rapidly as clinically feasible
8.	If the treatment target is not achieved with the first DMARD strategy, in the absence of poor prognostic factors, change to another csDMARD considered; when poor prognostic factors are present, addition of a bDMARD should be considered
9.	In patients responding insufficiently to MTX and/or other csDMARD strategies, with or without glucocorticoids, bDMARDs (TNF inhibitors*, ab and, under certain circumstances, rituximab†) should be commenced with MTX

adherence

- Judgenental ?
- Blame ?

  ΌΧΙ
- ….it is a statement of fact !!!!

adherence

- Πσσοστό %... ασθενών
- Πσσοστό %…ασθενούς

adherence

- Αποδεκτό > 80%
- > 95% (μελέτες HIV)

adherence

- Υψηλότερα ποσοστά :

  - σε acute conditions &
  - σε μελέτες

- Αλλά ακόμα και σε μελέτες….
  συμμόρφωση 43-78% (χρόνια νοσήματα)

- Δραματική μείωση μετά το 6μηνο !!!!

adherence

- Για συγκεκριμένο ασθενή…
- Ποσοστό 0% - >100% !!!

Osterberg NEJM (2005)

adherence

- Σε χρόνια νοσήματα

  (ΣΝ,ΣΔ,ΑΥ,RA,Νεοπλάσματα..)

- Μόνο 50% των ασθενών !!!!

Sackett DL (1979)

adherence

- 10 ημέρες…από συνταγογράφηση
- 30% παραλείπει τουλάχιστον 1 δόση
- Οι μισοί (50%) χωρίς λόγο

Barber N (2004)

….Intentionally (σκόπιμα)

- ΦΑΡΜΑΚΑ : -Φόβος παρενεργειών
  -Άγνοια χρησιμότητας
  -Φόβος εξάρτησης

- ΝΟΣΟΣ : Ανεπαρκής ενημέρωση

adherence

Φόβος ασθένειας vs Φόβος φαρμάκου

Poor adherence…

- Επιδείνωση νόσου
- Αναπηρία
- Θάνατος
- & αύξηση κόστους περίθαλψης

Poor adherence…

- ….33-69% ‘φαρμακογενών’ εισαγωγών σε νοσοκομεία (ΗΠΑ)
- $ 100.000.000.000 ετησίως

Poor adherence…

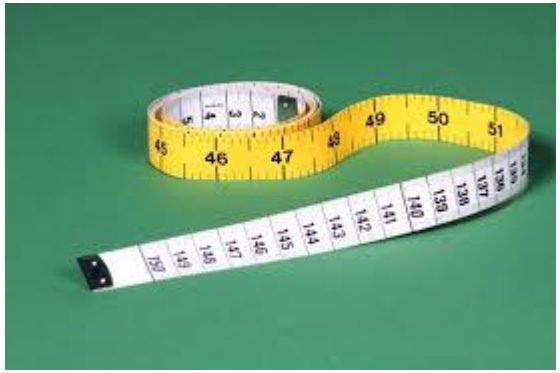
…σε μελέτες…..

…χειρότερη πρόγνωση και από PLACEBO !

WHO evidence-based guide for clinicians to improve strategies of medication adherence

- Sabate E. Adherence to long-term therapies:evidence for action. Geneva: World Health Organization, 2003.(Accessed July11, 2005, at http://www.who.int/chronic_conditions/en/adherence_report.pdf.)

?



Rheumatology 2006;45:1–5 doi:10.1093/rheumatology/kei223

Editorial

'Compliance' is futile but is 'concordance' between rheumatology patients and health professionals attainable?

The extent to which patients take prescribed medications 'as directed' and why they do not have been important issues in health research for many decades [1] and subject to recent review [2–6]. These issues are important in rheumatic diseases, given the primary reliance upon medication to control symptoms and improve patients' functional ability and longevity [7]. Not taking required medications can therefore have both a personal health impact and health-economics consequences [3]. In recent years patients have shown increased interest in their health-care; this is partially due to a boom in access to information technology coupled with increased health coverage in traditional media sources [8]. A fresh approach to medication prescribing is required, one that evolves away from the paternalistic approach of patient

about the medication and an expressed need for further information about the disease or medication itself, particularly among intentionally non-adherent patients.

Medication compliance/adherence may be operationalized (i.e. conceptualized and measured) in many different ways [5], including multi-item questionnaire scales, individual ordinal/categorical questionnaire items, patients' and physicians' categorizations and independent observations such as prescription refill monitoring, electronic dispenser monitoring or metabolite/tracer measuring. We will now describe how estimates of adherence may differ depending on the ways in which adherence is assessed, as well as the exact disease and medication investigated. We also provide details of example studies that raise some of the central issues

The authors have declared no conflicts of interest.

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Correspondence to: G. J. Treharne, School of Psychology, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK. E-mail: G.J.Treharne@bham.ac.uk

References

1. Sackett DL, Snow JC. The magnitude of compliance and non-compliance. In: Haynes RB, Taylor WD, Sackett DL, eds. Compliance in Health Care. Baltimore, MD: Johns Hopkins

TABLE 1. Definitions and recommended measures of key concepts around medication-taking in rheumatology

Concept	Summary definition	Recommended measure
Compliance	The paternalistic view that the patient is a passive party who has their prescribed treatment enforced (after [9])	Serum concentration of a tracer in the medication [38]
Adherence	The (still paternalistic) view that the informed (but still passive) patient will stick to taking their recommended treatment, barring errors (after [13])	The Compliance Questionnaire – Rheumatology (CQR [30, 31])
Concordance	The process of enlightened communication between the patient and their health-care professional, leading to an agreed treatment and ongoing assessment of this as the optimal course (after [42, 43])	The Leeds Attitude To Concordance scale (LATCon [57])
Beliefs about medications	Perceptions of one's need for medication balanced against personal and general concerns about medications (after [65])	The Beliefs about Medications Questionnaire (BMQ [33, 34])
Self-efficacy	Belief in one's ability to exert control over an outcome (after [66])	The Arthritis Self-Efficacy Scale (ASES [67, 68])[a]

[a]The ASES measures perceived control over pain, fatigue, function and mood; extension of this scale to cover patients and health-care professionals' perceived ability to achieve concordance/adherence would be theoretically and operationally useful.

MEASURES OF ADHERENCE

- Άμεσες (Direct methods)
- Έμμεσες (Indirect methods)

Άμεσες (Direct methods)

- Άμεση παρατήρηση ασθενούς
- Μέτρηση φαρμάκου στο αίμα
- Μέτρηση βιολογικού δείκτη στο αίμα

Έμμεσες (Indirect methods

- Ερωτηματολόγια ασθενών (self-reports)
- Μετρήσεις χαπιών
- Έλεγχος συνταγογράφησης
- Εκτίμηση κλινικής απάντησης
- Μετρήσεις (ΑΠ, σφύξεις)
- Ηλεκρονική παρακολούθηση χαπιών

…όμως

… ο συνδυασμός μετρήσεων αυξάνει την ακρίβεια !!!

Επιδημιολογία λήψης φαρμάκων

- “white-coat adherence”
- 6 μοντέλα συμμόρφωσης (του 1/6)
- Με απλά σχήματα…αύξηση συμμόρφωσης

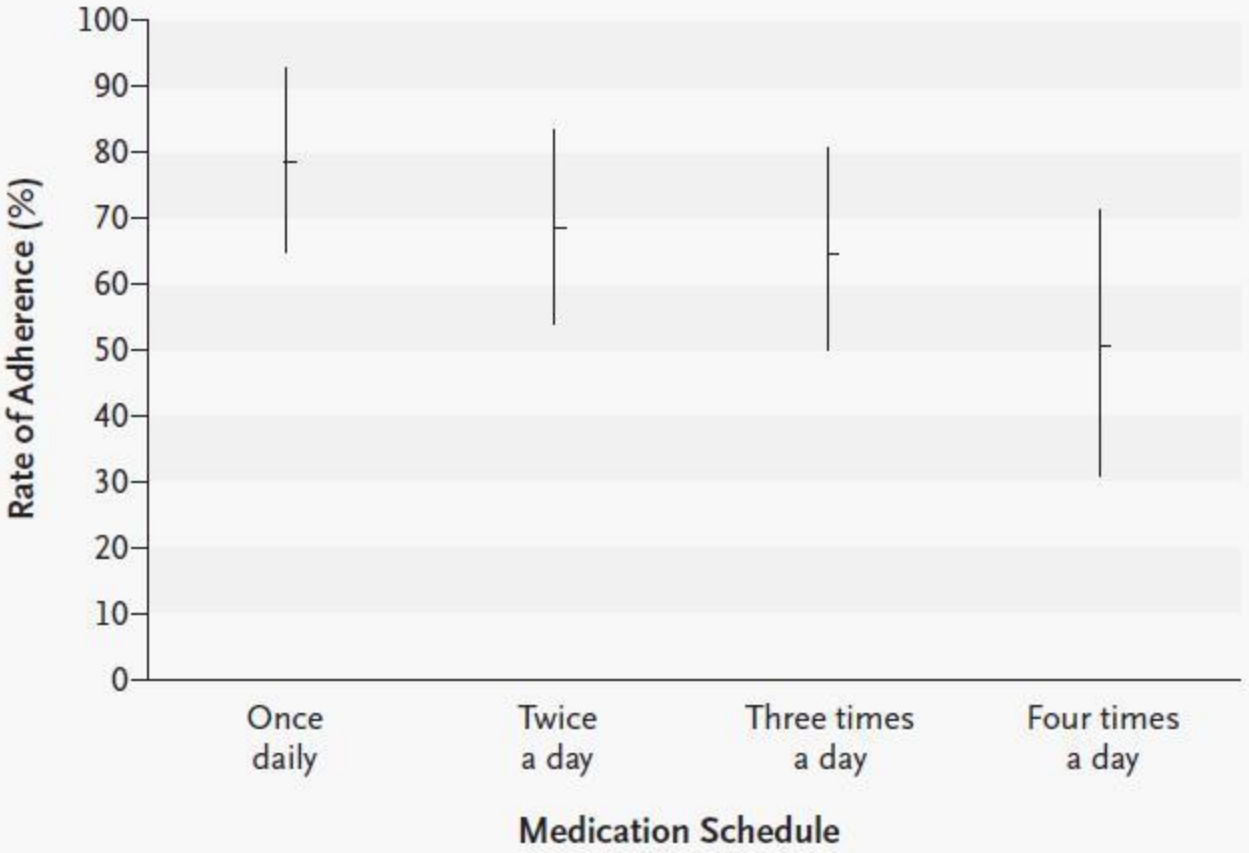


Figure 1. Adherence to Medication According to Frequency of Doses.

Vertical lines represent 1 SD on either side of the mean rate of adherence (horizontal bars). Data are from Claxton et al.[7]

Διερευνώντας πτωχή συμμόρφωση…

- Σκέψη ΠΑΝΤΑ σε απουσία κλινικής απάντησης !
- Καθησυχαστικές ερωτήσεις διερεύνησης !
- Ερωτήσεις για παρενέργειες
  & για τα οφέλη χορήγησης

Table 2. Major Predictors of Poor Adherence to Medication, According to Studies of Predictors.

Predictor	Study
Presence of psychological problems, particularly depression	van Servellen et al.,[51] Ammassari et al.,[52] Stilley et al.[53]
Presence of cognitive impairment	Stilley et al.,[53] Okuno et al.[54]
Treatment of asymptomatic disease	Sewitch et al.,[55]
Inadequate follow-up or discharge planning	Sewitch et al.,[55] Lacro et al.[56]
Side effects of medication	van Servellen et al.[51]
Patient's lack of belief in benefit of treatment	Okuno et al.,[54] Lacro et al.[56]
Patient's lack of insight into the illness	Lacro et al.,[56] Perkins[57]
Poor provider–patient relationship	Okuno et al.,[54] Lacro et al.[56]
Presence of barriers to care or medications	van Servellen et al.,[51] Perkins[57]
Missed appointments	van Servellen et al.,[51] Farley et al.[58]
Complexity of treatment	Ammassari et al.[52]
Cost of medication, copayment, or both	Balkrishnan,[59] Ellis et al.[60]

Φραγμοί στην συμμόρφωση (…under patient's control…)

- 30% ξεχνούν

- 16% άλλες προτεραιότητες
- 11% συνειδητή μείωση
- 9% έλλειψη ενημέρωσης
- 7% ψυχολογικοί λόγοι

- 27% χωρίς σαφή λόγο

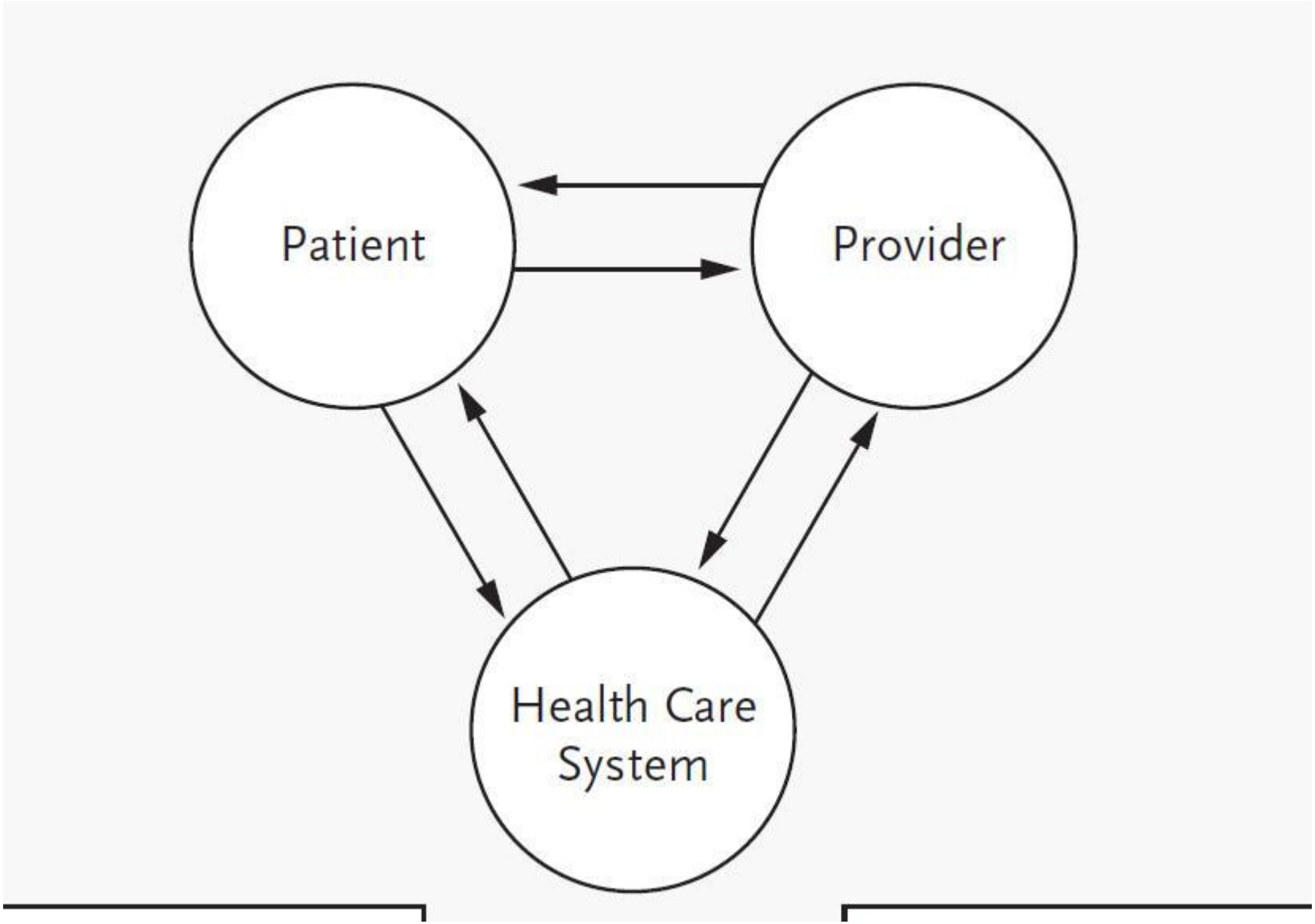
Cramer J.

Το μερίδιο των γιατρών

- Σύνθετη συνταγογράφηση
- Ελλιπής ενημέρωση για οφέλη & παρενέργειες
- Πτωχή θεραπευτική σχέση
- Αδιαφορία για κόστος φαρμάκου
- Αδιαφορία για lifestyle ασθενούς
- Poor job satisfaction !!

Το μερίδιο του συστήματος (ΕΟΠΥΥ-ΕΣΥ)

- Δυσκολία πρόσβασης
- Ελλείψεις φαρμάκων
- Αυξημένο ποσοστό συμμετοχής
- Απώλειες ραντεβού


Patient
Provider
Health Care System

ΠΑΡΕΜΒΑΣΕΙΣ

- Εκπαίδευση ασθενών
- Βελτίωση δοσολογίας
- Αύξηση ωραρίων πρόσβασης
- Βελτίωση επικοινωνίας γιατρού-ασθενούς

ΕΚΠΑΙΔΕΥΣΗ

- Ασθενών- Συγγενών
- Ημερολόγια
- Boxes δόσεων
- Υπενθυμήσεις

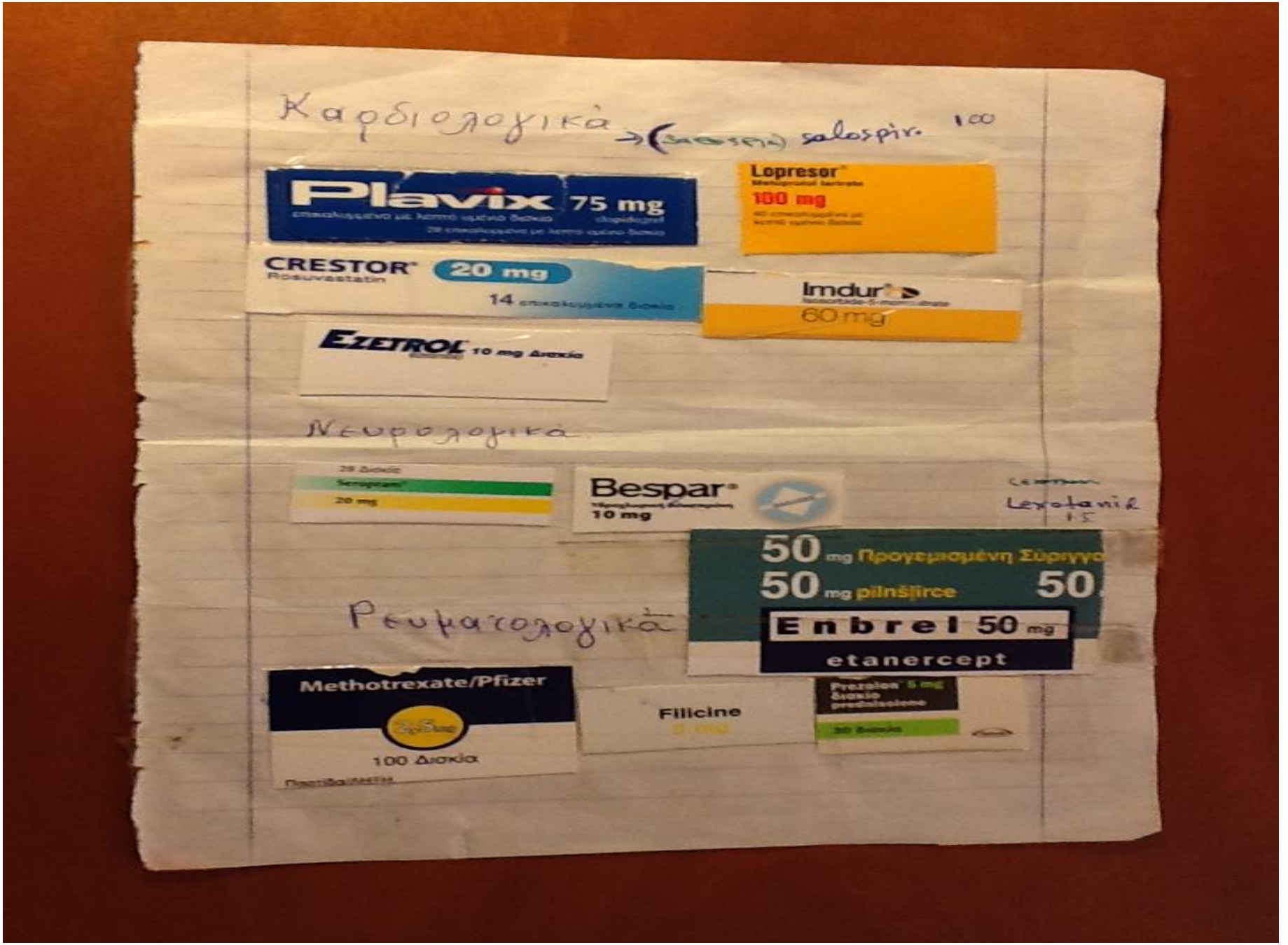

Καρδιολογικά
Plavix 75 mg
Lopresor
100 mg
CRESTOR
Rosuvastatin
20 mg
14
Imdur
60 mg
EZETROL 10 mg Διασκία
Νευρολογικά
Bespar
10 mg
50 mg Προγεμισμένη Σύριγγα
50 mg pilnšlirce 50
Enbrel 50 mg
etanercept
Ρευματολογικά
Methotrexate/Pfizer
100 Διασκία
Filicine

Table 1

The AIDES method for improving adherence to medications

A: Assessment	Assess all medications
I: Individualization	Individualize the regimen
D: Documentation	Provide written communication
E: Education	Provide accurate and continuing education tailored to the needs of the individual
S: Supervision	Provide continuing supervision of the regimen

Adherence in rheumatic diseases

- Gout 10%
- RA 30%
- SLE 49%

Jessica S Galo ARD (2015)

Interventions in adherence ?

in rheumatic diseases ?

Εως το 2008 (Cochrane) 2 μελέτες !!!

Εως το 2014 6 μελέτες σε RA

First, published on February 13, 2015 as 10.1136/annrheumdis-2014-206593

EXTENDED REPORT

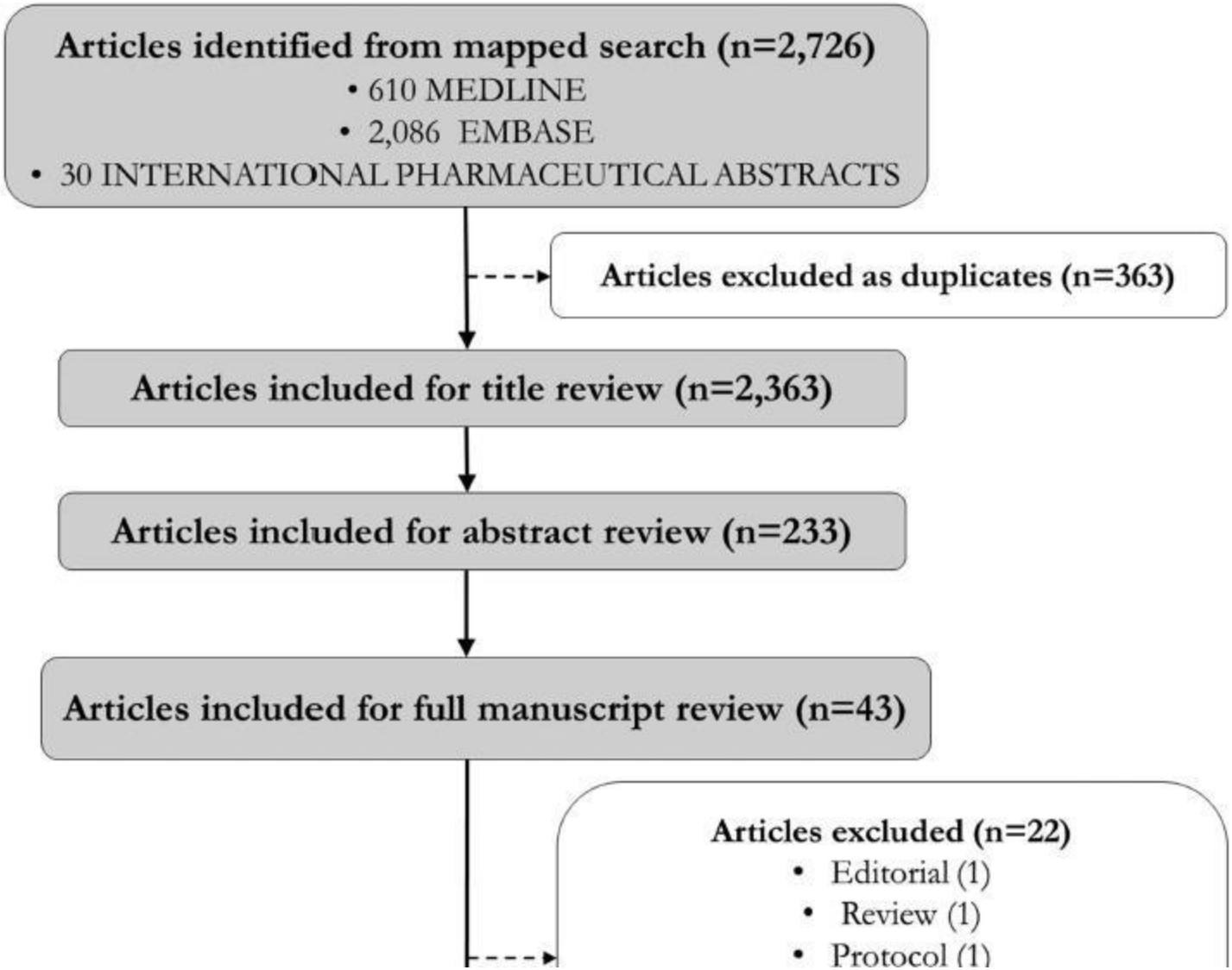
What are the effects of medication adherence interventions in rheumatic diseases: a systematic review

Jessica S Galo,[1] Pavandeep Mehat,[1,2] Sharan K Rai,[2,3] Antonio Avina-Zubieta,[2,3,4] Mary A De Vera[1,2]

ABSTRACT

Objectives Consistent reports of suboptimal treatment adherence among patients with inflammatory arthritis underscore the importance of understanding how adherence can be promoted and supported. Our objectives were to identify and classify adherence interventions; and assess the evidence on the effects of adherence interventions on outcomes of patients with rheumatic diseases.

While the problem of medication non-adherence is well described in rheumatology, solutions are not. Systematic reviews on adherence interventions in chronic disease including elderly[15] patients with hypertension[16] and diabetes[17] are available, yet to our knowledge, there are none specifically among patients with rheumatic diseases. A 2014 update of a 2008 Cochrane review of adherence interventions increased included trials in RA from 2[19 20] to 6.[18]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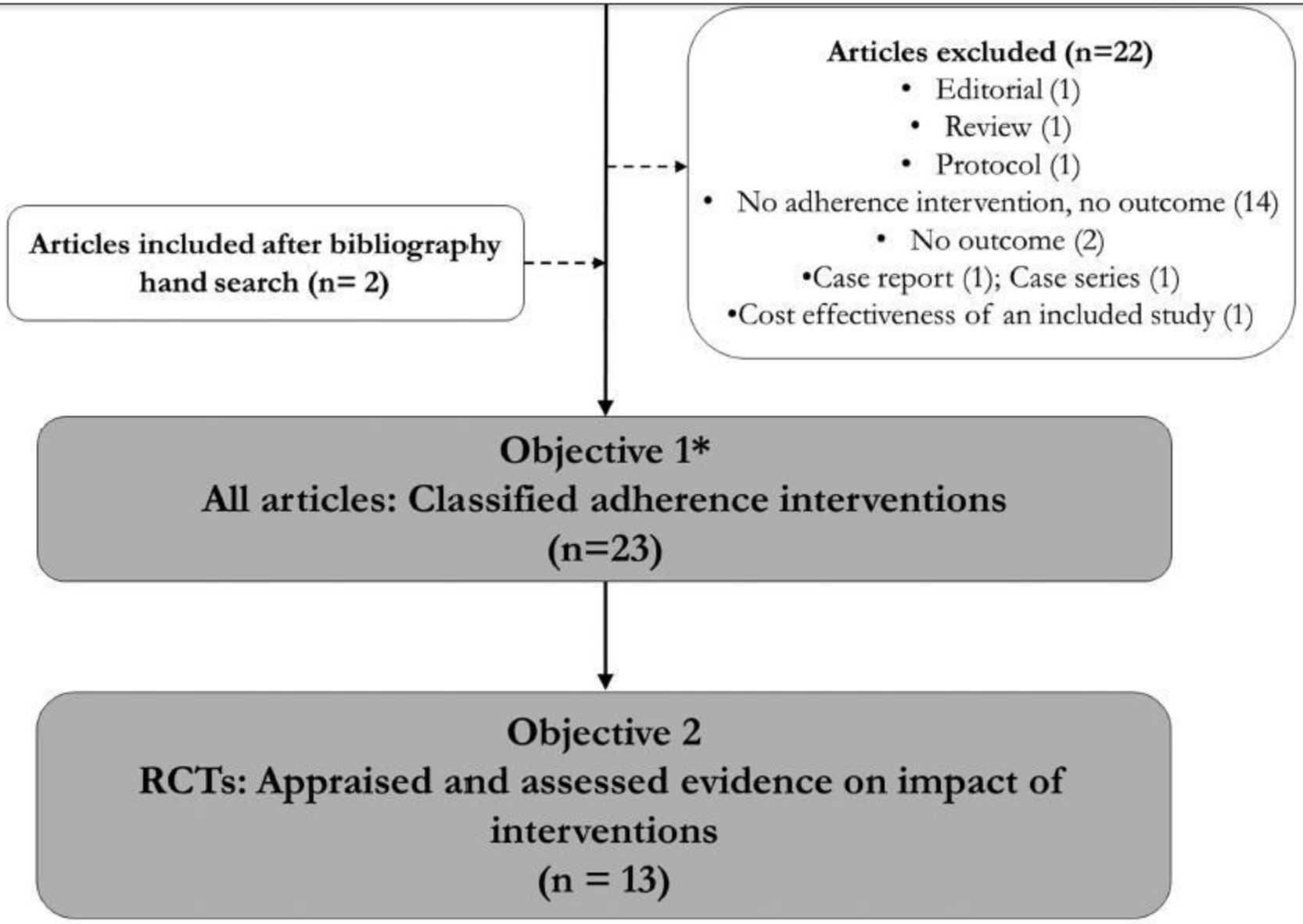
• 610 MEDLINE
• 2,086 EMBASE
• 30 INTERNATIONAL PHARMACEUTICAL ABSTRACTS
Articles excluded as duplicates (n=363)
Articles included for title review (n=2,363)
Articles included for abstract review (n=233)
Articles included for full manuscript review (n=43)
Articles excluded (n=22)
• Editorial (1)
• Review (1)
• Protocol (1)



Key: * List of studies and categorised intervention available in Online Table S3

Identification of adherence interventions in rheumatic diseases (classification)

- **Target** (patient vs provider)
- **Focus** (educational vs behavioural)
- **Complexity** (single vs multifaced)
- **Implementation** (generalised vs tailored)
- **Provider** (physician, nurse ,pharmacist)

Αποτελέσματα (θετικά) σε adherence

ΌΤΑΝ,

- direct intervention... (φάρμακο)
- Target …ο ασθενής
- Focus …Εκπαίδευση (…& risks-benefits)
- Provider …ο γιατρός
- Multifocal

Αποτελέσματα (θετικά) σε adherence (patients profile)

- Ασθενείς :

  - με ERA ή VERA

  - με υψηλό DAS28

- McEvoy DeVellis *et al*

Βοήθησε ακόμα και το απλή συνέντευξη !!!

- El Miedany *et al (2012)*

  - tailored,multifaced
  - *adherence 89 % vs 64 % control*
  - *μεγάλη βελτίωση σε DAS,πόνο,εξάρσεις,λειτουργικότητα,HAQ*

that were not shown to have impacts, reasons may be those related to the intervention itself, patient characteristics or study methodology.

Conclusions Our systematic review shows limited research on adherence interventions in rheumatic diseases with inconsistent impacts on adherence or disease outcome.

INTRODUCTION

Adherence to long-term pharmacotherapy is paramount to the management of inflammatory arthritis

specific rheumatic diseases may also be a limitation,[47] however we did not appraise this study as it was a RCT. Finally, due to the heterogeneity across interventions, adherence and disease outcomes, a quantitative meta-analysis was not performed.

Overall, our systematic review shows limited research on adherence interventions in rheumatic diseases with inconsistent impacts on adherence or disease outcome. Given the substantial burden of treatment non-adherence across inflammatory arthritis, there is need for further work in designing and evaluating interventions that promote and support treatment adherence.

Correction notice This article has been corrected since it was published Online First. 'Rheumatology arthritis' has been corrected to 'Rheumatoid arthritis (RA)' in table 1.

Contributors JSG—Executed searches, extracted data, interpreted findings, drafted

Rheumatology Advance Access published May 13, 2015

RHEUMATOLOGY

53,

Original article

doi:10.1093/rheumatology/k

The influence of behavioural and psychological factors on medication adherence over time in rheumatoid arthritis patients: a study in the biologics era

Catharine Morgan[1], John McBeth[1,2], Lis Cordingley[3], Kath Watson[1], Kimme L. Hyrich[1,4], Deborah P. M. Symmons[1,4] and Ian N. Bruce[1,4]

Abstract

Objectives. To investigate levels of self-reported adherence to biologic treatment and establish the tribution of demographic, physical and psychological factors to biologic medication adherence in a cohort

Introduction

Ασθενείς με καλή adherence in rheumatic diseases

- *Καλύτερη έκβαση*
- *Υψηλά ποσοστά ύφεσης*
- *Καλύτερη λειτουργικότητα*
- *Lower rates of escalation to aggressive treatments*

DiMatteo MedCare 2002
Pascual-Ramos V Artr ResTher 2009

Lower persistence…

…σε βιολογικούς παράγοντες **=>**

υψηλότερα μη-φαρμακευτικά κόστη

Tang B. Clin Ther (2008)

Σκοπός

- Μελέτη (με ατομικά ερωτηματολόγια)

  - adherence σε adalimumab (για 2 έτη) &

  - επίδραση σ’αυτή ψυχολογικών,φυσικών και δημογραφικών παραγόντων

adherence

- > 50% ασθενών …score < 75
- Παρόμοια με …των sDMARDs

Higher adherence

- Ηλικιωμένοι
- Μικρότερη διάρκεια νόσου
- Φόβος για χρονιότητα & επιπτώσεις νόσου
- Πίστη στην αναγκαιότητα φαρμάκων
- Μικρότερη ανησυχία για τα φάρμακα
- Αυξημένη οικογενειακή & ιατρο-νοσηλευτική υποστήριξη (x 3.6)

Several studies of oral sDMARD adherence, as well as studies in other conditions, have also shown similar importance of medication beliefs [4, 5, 23]. Non-adherence may therefore owe more to individual patient beliefs than to the actual disease or route of drug administration. A patient's level of medication belief may of course be influenced by the perceived intensity of the drug and/or its mode of administration. However, our data suggest that the influence on adherence remains qualitatively similar across therapy types.

Our findings reflect those of other studies showing that older age is associated with higher adherence [14]. Others

Rheumatology 2006;45:1–5 doi:10.1093/rheumatology/kei223

Editorial

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The extent to which patients take prescribed medications 'as directed' and why they do not have been important issues in health research for many decades [1] and subject to recent review [2–6]. These issues are important in rheumatic diseases, given the primary reliance upon medication to control symptoms and improve patients' functional ability and longevity [7]. Not taking required medications can therefore have both a personal health impact and health-economics consequences [3]. In recent years patients have shown increased interest in their health-care; this is partially due to a boom in access to information technology coupled with increased health coverage in traditional media sources [8]. A fresh approach to medication prescribing is required, one that evolves away from the paternalistic approach of patient

about the medication and an expressed need for further information about the disease or medication itself, particularly among intentionally non-adherent patients.

Medication compliance/adherence may be operationalized (i.e. conceptualized and measured) in many different ways [5], including multi-item questionnaire scales, individual ordinal/categorical questionnaire items, patients' and physicians' categorizations and independent observations such as prescription refill monitoring, electronic dispenser monitoring or metabolite/tracer measuring. We will now describe how estimates of adherence may differ depending on the ways in which adherence is assessed, as well as the exact disease and medication investigated. We also provide details of example studies that raise some of the central issues

Adherence

- Χωρίς επικοινωνία (ιατρού-ασθενούς)….
  ….ισως είναι επικίνδυνη !

Concordance

- Ιδιαίτερα σημαντική όταν(έχουμε δυνητικά) ….ισοδύναμες παρεμβάσεις

Concordance

- Πόσο πρέπει να «πιεστεί» ο ασθενής που δεν επιθυμεί συμμετοχή ;

- Ισως χρήσιμη μόνο για μερικούς (τους επιθυμούντες)

Concordance

- Και αυτός που αρνείται θεραπεία ;
- Να αφεθεί ;
- Πρέπει να «πιεστεί» ;
- Κι αν πιέσουμε πολύ ;

Concordance

- Πιθανότατα ωφέλιμη για
  - συγκεκριμένους ασθενείς
  - συγκεκριμένα νοσήματα
  - συγκεκριμένα φάρμακα

Επ’αυτού χρειάζονται καλά σχεδιασμένες ΜΕΛΕΤΕΣ !!!