

## ESITI CLINICI: UN IMPEGNO ED UNA RESPONSABILITÀ CONDIVISI



10° CONGRESSO NAZIONALE SIFaCT

24-26 novembre 2022  
Centro congressi Fontana di Trevi  
Roma

- Il Farmacista e la misurazione degli outcome: l'aderenza terapeutica
- Ruggero Lasala

**Drugs don't work in patients who don't take them  
(Everett Koop)**

Treatment Adherence is the extent to which a person's behavior — taking medication, following a diet, and/or executing lifestyle changes — corresponds with the **agreed recommendations** from a healthcare provider.

World Health Organization. Adherence to Long-Term Therapies: Evidence for Action. Geneva: WHO; 2003.

# Perché l'aderenza al trattamento?

**Table 3 Calculated average adherence rates (mean, SD, min, and max)**

	Overall adherence rate (%) (main phase)			Overall adherence rate (%) (extension phase)			Adherence rate for placebo (%)			Adherence rate for IP (%) (all arms)		
	<i>n</i>	Mean (SD)	Min, max	<i>n</i>	Mean (SD)	Min, max	<i>n</i>	Mean (SD)	Min, max	<i>n</i>	Mean (SD)	Min, max
All trials that provided adherence rates	125	97.40 (2.80)	84.54, 109.9	10	93.32 (3.15)	89, 98.1	65	97.87 (2.59)	90.15, 107.1	129	97.35 (3.47)	78.09, 111.3
Therapeutic area												
Diabetes	34	97.89 (1.27)	93.41, 100.06	5	94.94 (1.55)	94.07, 97.69	22	98.08 (1.86)	92.75, 101.10	37	97.71 (1.44)	93.49, 101.54
Respiratory	23	97.62 (2.19)	92.7, 99.73	2	90.1 (0.22)	89.94, 90.25	18	97.11 (3.02)	90.42, 100.30	23	97.78 (1.84)	92.6, 100.2
CVD	21	98.18 (1.85)	93, 102	1	98.1	NA	11	97.71 (0.92)	95.95, 99.16	21	98.27 (4.06)	89.3, 114.9
Anti-infectives	35	96.48 (2.89)	90.65, 100.1	1	91.2	NA	5	97.97 (2.13)	94.95, 99.8	35	96.91 (3.86)	78.09, 100.72
Oncology	12	96.93 (6.06)	84.54, 109.9	1	89	NA	9	99.04 (4.33)	90.15, 107.1	13	94.70 (7.71)	78.94, 111.3

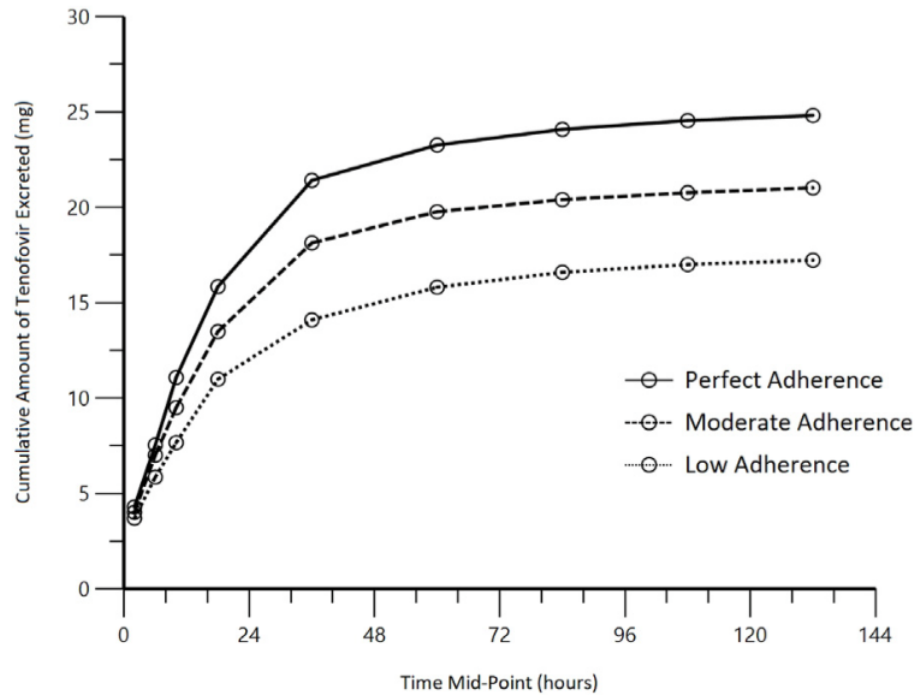
Calculated average adherence rates (mean, SD, min, max), overall and by therapeutic area, for the 131 trials that presented adherence rates using summary statistics (i.e., excluding adherence categories).

*n* = number of trials that presented the rate by using descriptive statistics (mean, min, max).

CVD, cardiovascular disease; IP, investigational product; max, maximum; min, minimum; SD, standard deviation.

Montila KM, Pasmooij AMG et al. Medication Adherence Measurement Methods in Registration Trials Supporting the Approval of New Medicines: A Cross-Sectional Analysis of Centralized Procedures in the European Union 2010–2020. *Clinical Pharmacology and Therapeutics*. 2022

# Aderenza al trattamento



**Figure 2.** Mean cumulative excretion of tenofovir in urine following the last dose of tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) in adults who had followed 6 weeks of a perfect (daily), moderate (four times weekly), or low (two times weekly) adherence dosing regimen. \* $p < 0.05$  across the three study arms.

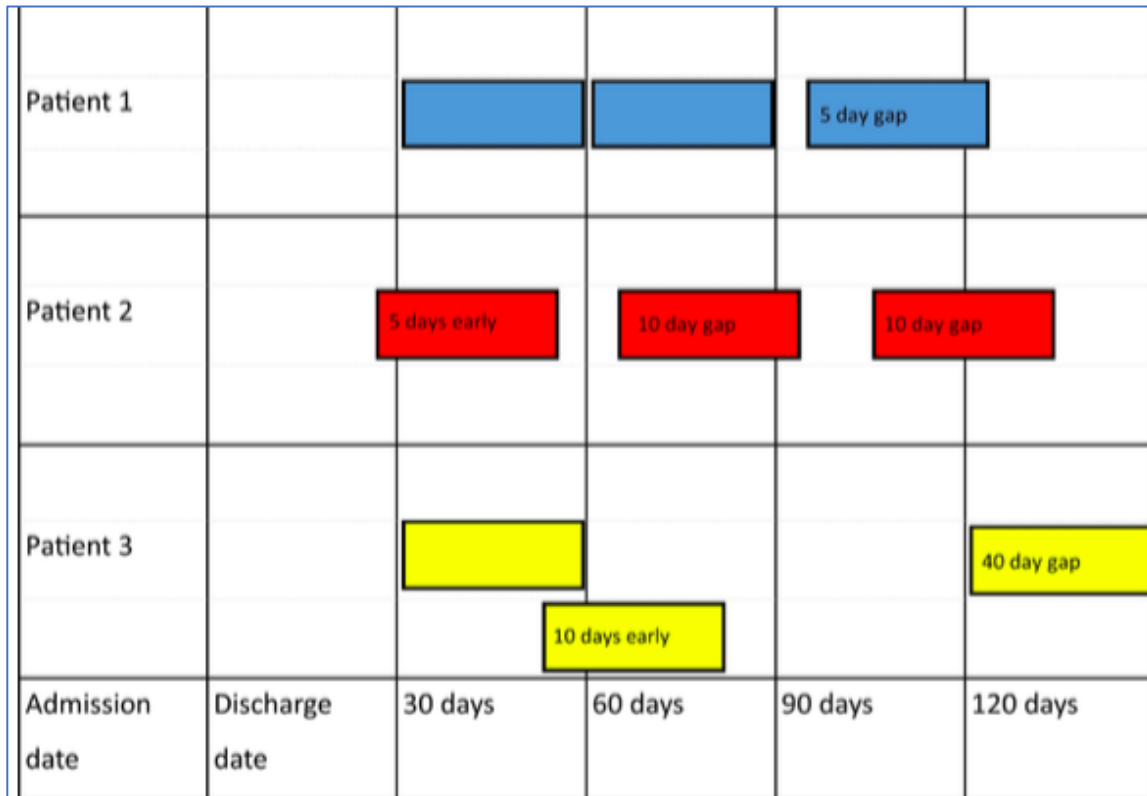
	YES	NO
1. Do you sometimes forget to take your medication?		
2. People sometimes miss taking their medications for reasons other than forgetting. Over the past 2 weeks, were there any days when you did not take your medication?		
3. Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?		
4. When you travel or leave home, do you sometimes forget to bring your medication?		
5. Did you take all your medication yesterday?		
6. When you feel like your symptoms are under control, do you sometimes stop taking your medication?		
7. Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
8. How often do you have difficulty remembering to take all your medication? Never/Rarely..... Once in a while..... Sometimes..... Usually..... All the time.....		

© Morisky Medication Adherence Scale (MMAS-8-Item). Use of the ©MMAS is protected by US copyright laws. Permission for use is required. A license agreement is available from: Donald E Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772.

Morisky D et al. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. Journal of clinical hypertension. 2008

Cressey TR et al. Plasma pharmacokinetics and urinary excretion of tenofovir following cessation in adults with controlled levels of adherence to tenofovir disoproxil fumarate. International Journal of Infectious Disease. 2020

# Aderenza al trattamento



**Figure 1** Examples of proportion of days covered calculated using multiple 30-day intervals.



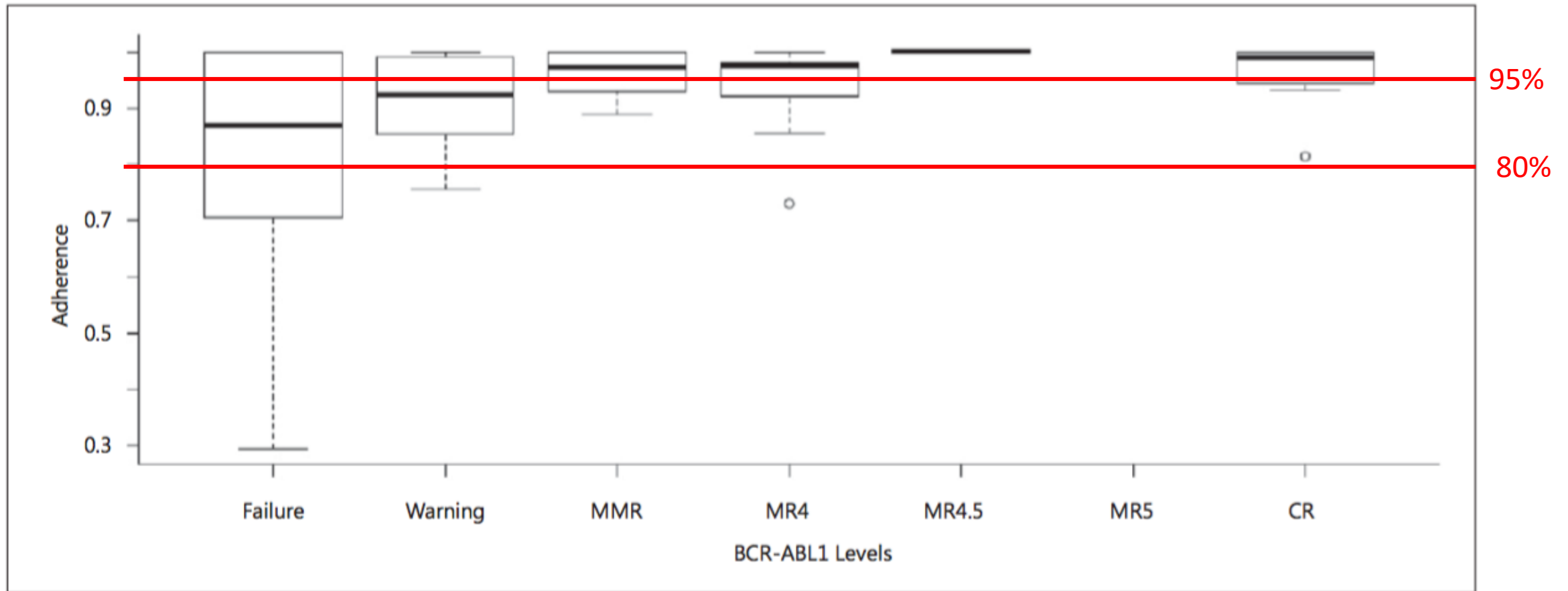
<https://www.aardexgroup.com>

Cut – Off che discrimina il paziente aderente dal non aderente è = 80% (generalmente accettato)

Fattibilità nella pratica quotidiana

Use of a patient-centred educational exchange (PCEE) to improve patient's self-management of medicines after a stroke: a randomised controlled trial study protocol. Coombes J.A. BMJ open. 2018.

# Aderenza al trattamento – Outcome clinico



**Fig. 2.** Adherence rate according to the level of response in the 1st year.

Santoleri F, Lasala R. et al. Medication Adherence to Tyrosine Kinase Inhibitors: 2-Year Analysis of Medication Adherence to Imatinib Treatment for Chronic Myeloid Leukemia and Correlation with the Depth of Molecular Response. *Acta Haematologica*. 2016

# Aderenza al trattamento – Outcome clinico

## Scope:

Oncology = 14 (15, 25, 21, 22, 23, 24, 27, 42, 43, 44, 48, 49, 52, 69)

Haematological = 28 (14, 16, 17, 18, 32, 19, 20, 26, 28, 29, 30, 31, 33, 34, 35, 36, 37, 38, 8, 39, 40, 41, 46, 47, 48, 9, 67, 68)

## Methods used in calculating adherence:

MPR = 8 studies (25, 18, 32, 24, 29, 42, 34, 36)

PDC = 4 studies (47, 48, 49, 67)

MEMS = 7 studies (16, 21, 22, 34, 37, 8, 52, 70)

Dose intensity = 1 (9)

8-MMAS = 5 studies (18, 28, 40, 41, 69)

9-MMAS = 3 studies (20, 33, 34)

4-MMAS = 1 study (46)

## Adherence cut-offs used:

80% = 12 (25, 18, 21, 22, 42, 34, 47, 48, 49, 9, 67, 44)

85% = 2 (35, 37)

90% = 8 (16, 32, 43, 34, 36, 8, 49, 68)

## Outcomes assessed in studies:

OS = 10 (15, 23, 26, 44, 47, 48, 52, 9, 17, 32)

PFS = 6 (15, 32, 23, 47, 52, 9)

DFS = 3 (42, 43, 44)

Laboratory assessment = 14 (14, 16, 18, 20, 33, 34, 35, 36, 37, 8, 39, 40, 41, 68)

## Adherence-outcome correlation:

Yes = 24 studies (26, 27, 42, 43, 44, 33, 34, 35, 36, 37, 38, 8, 39, 40, 41, 46, 47, 48, 49, 52, 9, 67, 68, 69)

No = 14 studies (14, 15, 16, 25, 17, 18, 19, 20, 21, 22, 23, 24, 26, 40)

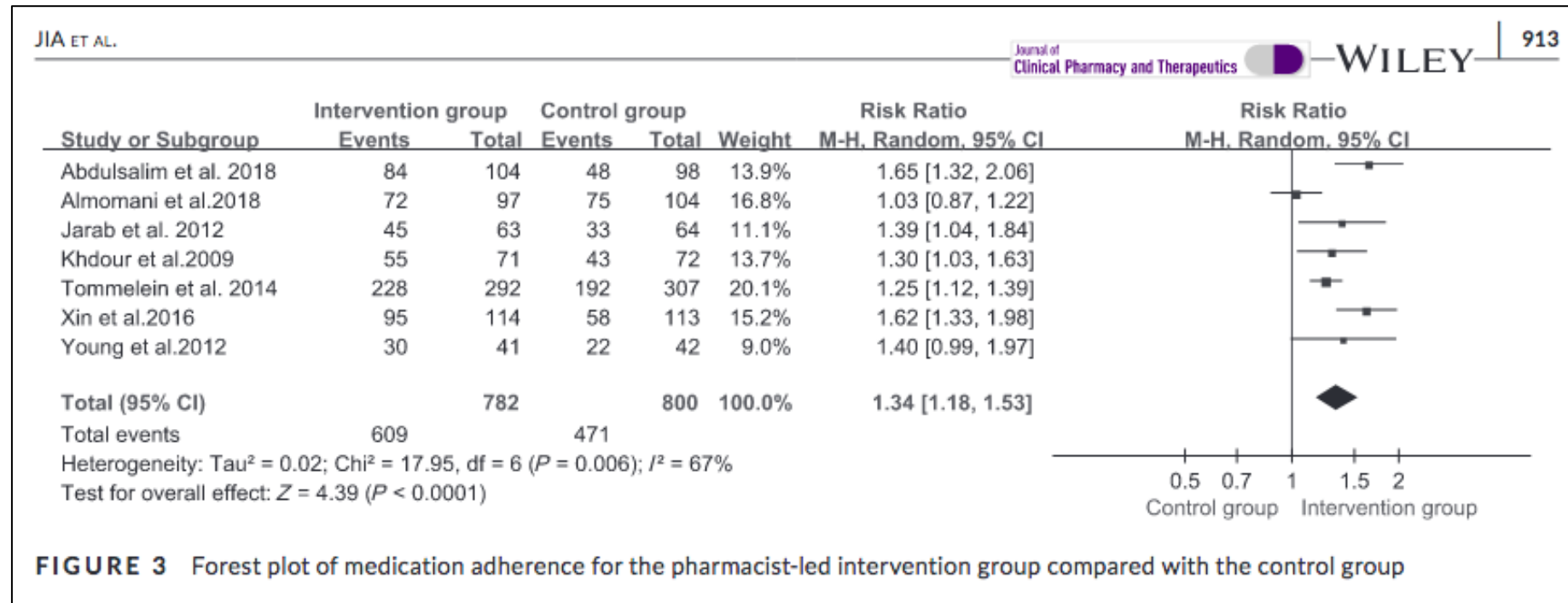
Correlation reported but not statistically significant = 5 studies (32, 28, 29, 30, 31)

Grande variabilità in termini di:

- Metodo di calcolo dell'aderenza al trattamento
- Cut-off di aderenza considerato
- Tipo di outcome valutato

Lasala R, Santoleri F. Association between adherence to oral therapies in cancer patients and clinical outcome: A systematic review of the literature. British Journal of Clinical Pharmacology. 2022

# Strategie per il miglioramento

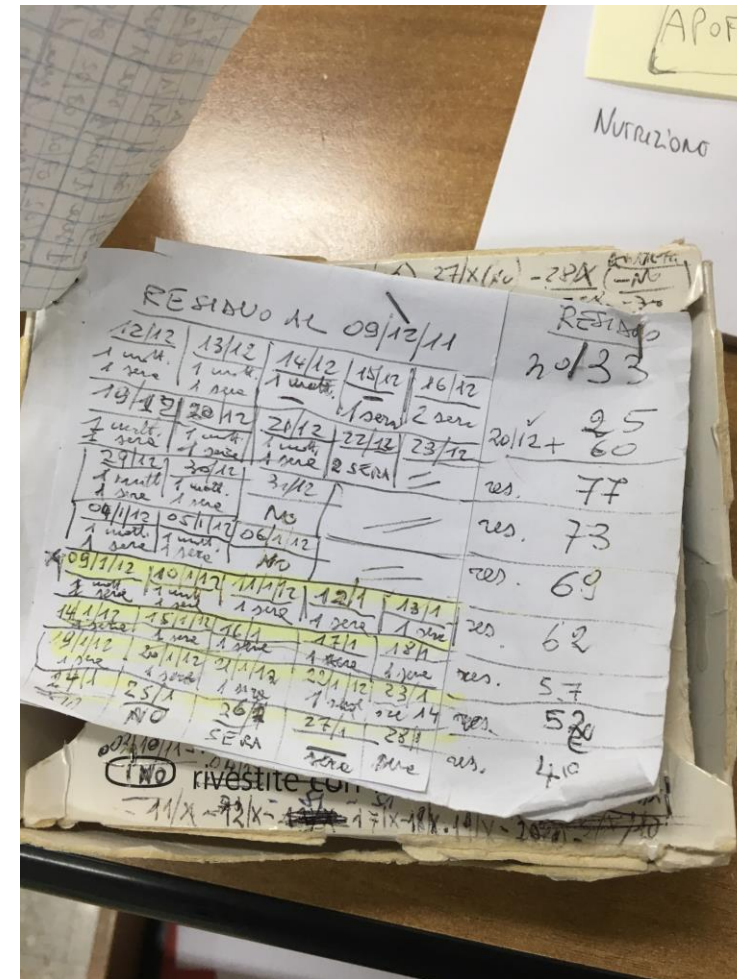
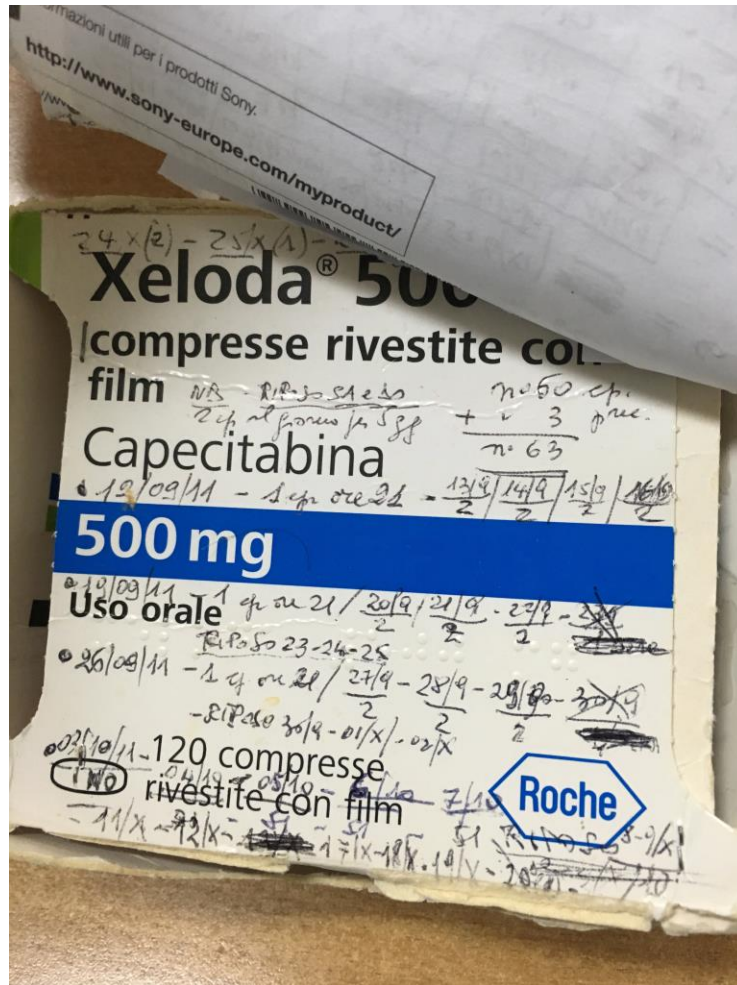


Information  
Motivation  
Behavioural skills

Jia X, Zhou S et al. Effect of pharmacist-led interventions on medication adherence and inhalation technique in adult patients with asthma or COPD: A systematic review and meta-analysis. Journal of Clinical Pharmacy and Therapeutics. 2020



# Aderenza al trattamento - strumenti



# Aderenza al trattamento - Interventi

Progetto di Farmacoutilizzazione e Farmacovigilanza Farmacia Ospedaliera Distribuzione Diretta AUSL Pescara

Cognome..... Nome.....

Mese..... Anno.....

1°gg	Ora	N° cps	1	2	3	4	5
...../.....							

**Table 2.** Medication adherence.

	Imatinib	Nilotinib	Dasatinib	Total
MedA with diary (patient reported) (A)	98.6%	96.9%	95%	97.4%
MedA with diary (RDD/PDD) (B)	94.9%	91.1%	95.8%	93.6%
MedA without diary (RDD/PDD) (C)	84.9%	87.4%	90%	86.5%
Quality of life scores	3.18 (±0.78)	3.66 (±0.73)	3.79 (±0.96)	3.46 (±0.82)
Causes of non-adherence				
Forgetfulness	33.3%	80%	100%	
Vomiting	22.2%	–	–	
Not indicated	44.5%	20%	–	

RDD/PDD: received daily dose/prescribed daily dose.

A versus C:  $p < 0.0001$ ; B versus C:  $p = 0.007$  Determined by Wilcoxon test.

Santoleri F, Lasala R, et al. Using a treatment diary to improve the medication adherence in patients with chronic myeloid leukaemia. JOPP. 2019

Rosso: Non mi sento in forma (1)  
 Giallo: Potrei sentirmi meglio (2 - 3)  
 Verde: Mi sento in forma (4 - 5)

L'aderenza al trattamento:

- È un fattore-chiave per l'ottenimento dell'outcome clinico
- Deve essere misurata
- Deve essere monitorata
- Può essere migliorata

GRAZIE PER L'ATTENZIONE!

Ruggero Lasala

[lasalaruggero@gmail.com](mailto:lasalaruggero@gmail.com)

3283319034