

Supplementary File

Supplementary Figure S1. Tool to assess adherence for each individual drug taken by a patient (validated in French)

DRUG NAME:.....

1. Have you **definitely stopped** taking this drug? Yes No

2. If you have to take this drug several times per day, do you systematically skip a dose? Yes No

3. Do you **sometimes stop taking** this drug for a while? (forget, weekends, holidays, away from home etc.)

MON	TUE	WEN	THU	FRI	SAT	SUN
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

No, never or for one day

MON	TUE	WEN	THU	FRI	SAT	SUN
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Yes, sometimes for 2-3 days

MON	TUE	WEN	THU	FRI	SAT	SUN
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Yes, sometimes for 6-7 days or more

4. Do you **sometimes miss taking** this drug? (forget, not wanting to take it etc.)

MON	TUE	WEN	THU	FRI	SAT	SUN
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

No, never

MON	TUE	WEN	THU	FRI	SAT	SUN
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Yes, once or twice a month

MON	TUE	WEN	THU	FRI	SAT	SUN
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

Yes, once a week or more

5. Do you sometimes take this drug **later than the prescription's schedule**?

Yes, I sometimes take this drug with a delay of 12 hours or more

Yes, I sometimes take this drug with a delay of 4 hours or more

No, I always take this drug at the same time

Supplementary Table S1. Characteristics of patients in pilot testing (n=51)

Characteristics	Value
Age – median (IQR)	59.1 (42.5-70.6)
Sex – no (%)	
Male	18 (35.3)
Marital Status – no (%)	
Married or civil union	24 (47.1)
Live-in partner	13 (25.5)
Single	5 (9.9)
Separated	7 (13.7)
Widowed	2 (3.9)
Education level – no (%)	
Primary school	16 (31.3)
Secondary school	22 (43.1)
College	13 (25.6)
Place of recruitment – no (%)	
Inpatients	13 (25.5)
Outpatients	38 (74.5)
No. of medications per patient – median (IQR)	3.0 (1.0-4.0)

Supplementary Table S2. Definition of patient adherence for comparison with MMAS-4 and TBQ (validation at patient level)

Example of a patient taking 3 drugs:

<i>Metformin</i>	<i>Clopidogrel</i>	<i>Simvastatin</i>
Drug holidays 2-3 days	No drug holidays	Discontinuation
No missing doses	No missing doses	
No schedules errors	No schedule errors	
Poor drug adherence	Perfect drug adherence	Drug discontinuation
Level 4	Level 1	Level 6 (*)

(*) Maximum= Level 6

Patient adherence level as Level 6

Example of a patient taking 5 drugs:

<i>Metformin</i>	<i>Omeprazole</i>	<i>Simvastatin</i>	<i>Aspirin</i>	<i>Valsartan</i>
No drug holidays	No drug holidays	No drug holidays	No drug holidays	No drug holidays
No missing doses	No missing doses	Missing doses once a week	No missing doses	No missing doses
Schedule errors >4h	Schedules errors >4h	Schedules errors >4h	Schedule errors >4h	Schedule errors >4h
Good drug adherence	Good drug adherence	Poor drug adherence	Good drug adherence	Good drug adherence
Level 2	Level 2	Level 4 (*)	Level 2	Level 2

(*) Maximum= Level 4

Patient adherence level as Level 4

TBQ, Treatment Burden Questionnaire; MMAS, Morisky Medication Adherence Scale

Supplementary Table S3. Translation procedure and pilot testing

Objective:	
<ul style="list-style-type: none"> - To generate a French-language version of the Adherence Estimator, Lu's instrument and introductory sentences of the questionnaire - To assess clarity and feasibility of the study questionnaire 	
Stage 1: forward translation step	<p>Source language: English, target language: French</p> <p>Two reports of the translation were written by translators (CB and CZ) with additional comments about uncertainties.</p>
Stage 2: preliminary synthesis	<p>Any discrepancies with translators' reports were resolved to reach a consensus. A report was written and a preliminary questionnaire was produced by a working group (CC, SS, V-TT)</p>
Stage 3: first pilot testing	<p>34 patients were recruited and completed the questionnaire. During one-to-one debriefing interviews, patients were asked about the meaning of each item to ensure good understanding. In cases of inconsistency, patients were asked to explain their answers. The investigators (SS and CC) focused on any phrases that systematically failed to elicit an appropriate answer.</p> <p>A report was written (CC, SS).</p>
Stage 4: second synthesis	<p>A working group (CC, SS, V-TT) analyzed the report and the questionnaires. The group reworded the second and third question of Adherence Estimator to improve the clarity and adapted Lu's rating response scale to an 11-step scale, as suggested by patients. The initial planned question about generic use was removed because of misunderstanding and to reduce time needed to complete the questionnaire.</p> <p>A modified questionnaire was produced.</p>
Stage 5: second pilot testing	<p>17 patients were recruited and completed the modified questionnaire. The investigators (SS and CC) used the same method as for the first pilot testing.</p>
Stage 6: final synthesis	<p>The final questionnaire was elaborated.</p>

Supplementary Table S4. Classification of medications (n=961)

No. of molecules	292
Date of drug initiation	
< 6 months	115 (11.9)
6 months–1 year	80 (8.3)
> 1 year	726 (75.6)
Class of medications	
Cardiovascular drugs	
Beta-blockers	30 (3.1)
Calcium channel blockers	35 (3.6)
Platelet aggregation inhibitors	48 (5.0)
Anticoagulants (vitamin K antagonists, heparin)	22 (2.3)
Diuretics	45 (4.7)
Other cardiac agents (renin-angiotensin system agents, anti-arrhythmics)	101 (10.5)
Anti-diabetic drugs	
Blood glucose-lowering drugs	51 (5.3)
Insulin	29 (2.1)
Anti-rheumatic drugs	
Anti-inflammatory and anti-rheumatic products	38 (4.0)
Drugs for treating bone diseases (bisphosphonates, vitamin D, calcium)	35 (3.6)
Hormonal Drugs	
Oral contraceptives	38 (4.0)
Drugs for thyroid disorders	29 (2.1)
Hormone replacement therapy	17 (1.8)
Antipsychotics, sleep disorders drugs, antidepressants	79 (8.2)
Lipid modifying agents	71 (8.4)
Drugs for obstructive airway disease	68 (7.8)
Peptic ulcer and gastro-esophageal diseases drugs	58 (6.0)
Vitamins, iron preparations	35 (3.6)
Analgesics	30 (3.1)
Drugs for infections, prevention of infections	20 (2.0)
Ophthalmic treatments	10 (1.0)
Others (intestinal inflammatory disease Anti-migraine preparations, anti-Parkinson disease drugs)	77 (8.0)

Data are number (%).

To obtain the number of different molecules, we renamed all drugs by their International non-proprietary name, and counted all occurrences.

Supplementary Table S5. Criterion validity at the drug level: agreement between adherence measured by our tool and drug diaries (n=37 patients)

Questions	ICC	95% CI
Do you sometimes stop taking this drug for a while? (forget, weekends, holidays, away from home etc.)	0.59	0.0 to 0.92
Do you sometimes miss taking this drug? (forget, not wanting to take it etc.)	0.80	0.44 to 0.94
Do you sometimes take this drug later than the prescription's schedule?	0.24	0.0 to 0.54
Drug adherence level	0.69	0.34 to 0.91

Patients were asked to complete a 14-day diary for a randomly chosen drug. One investigator assessed drug adherence from data in diaries: each reported drug intake was considered a taken dose and each missing intake a missing dose; schedule errors were assessed by determining the time between reported doses. Agreement is described by the intraclass correlation coefficient (ICC). The 95% confidence intervals (95% CIs) were determined by a bootstrap method.

Supplementary Table S6. Reliability at the drug level: agreement between adherence measured at baseline and 1 month later (n=203 drugs taken by 53 patients)

Questions	ICC	95% CI
Do you sometimes stop taking this drug for a while? (forget, weekends, holidays, away from home etc.)	0.63	0.36 to 0.82
Do you sometimes miss taking this drug? (forget, not wanting to take it etc.)	0.65	0.42 to 0.79
Do you sometimes take this drug later than the prescription's schedule?	0.45	0.25 to 0.67
Drug adherence level	0.67	0.42 to 0.85

Test-retest agreement is described by the intraclass correlation coefficient (ICC). The 95% confidence intervals (95% CIs) were determined by a bootstrap method.

Supplementary Table S7. Impact of definition of patient adherence level on correlation with other instruments

Patient adherence level defined as the **median** of drug adherence level for the different prescribed medications

Correlation ^a with TBQ score	0.24 (p<0.01)
Correlation ^a with MMAS score	0.45 (p<0.01)

Patient adherence level defined as the **mean** of drug adherence level for the different prescribed medications

Correlation ^a with TBQ score	0.26 (p<0.01)
Correlation ^a with MMAS score	0.45 (p<0.01)

^a correlations were assessed by Spearman correlation coefficient
TBQ, Treatment Burden Questionnaire; MMAS, Morisky Medication Adherence Scale