

Is being adherent to
long-term therapies
abnormal?

Adherence

- Adherence to long-term treatments

Adherence in neurological and psychiatric disorders

- Migraine
- Schizophrenia

The background features abstract, overlapping geometric shapes in various shades of green, ranging from light lime to dark forest green. These shapes are primarily located on the left and right sides of the frame, leaving a large white central area. The shapes are layered, creating a sense of depth and movement.

Adherence

What percentage of your patients is in your opinion adherent to their treatment?



Adherence to long-term treatments

- ▶ Failure to take prescribed medicine for chronic diseases is a massive, world-wide problem. ⁽¹⁾
- ▶ Adherence to long-term therapy averages **50%**. ⁽¹⁾
- ▶ Occurs in all chronic medical disorders. ⁽²⁾
- ▶ Observed in all situations where the self-administration of treatment is required. ⁽³⁾

1. World Health Organization. Adherence to long-term therapies: evidence for action. Geneva, Switzerland: World Health Organization; 2003. Available from: <http://whqlibdoc.who.int/publications/2003/9241545992.pdf>. Accessed April 25,2022.

2. Haddad PM, et al. Patient Relat Outcome Meas, 2014;5:43-62

3. <https://www.who.int/news/item/01-07-2003-failure-to-take-prescribed-medicine-for-chronic-diseases-is-a-massive-world-wide-problem>, assessed April 25 2022

Adherence to long-term treatments

Poor adherence

- ▶ Is an important if not the primary reason for not achieving full health outcomes despite effective medications. ^(1,3)
- ▶ Consequences are
 - ▶ not achieving population health goals,
 - ▶ increased health care costs,
 - ▶ waste of health care costs. ⁽¹⁾

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Definition of adherence

Adherence is

The **extent** to which a person's behavior corresponds with **agreed recommendations** from a health care provider. ⁽¹⁾

- ▶ taking medication
- ▶ following a diet
- ▶ executing lifestyle changes

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Definition of adherence

- ▶ The patient agrees with the recommendations. ⁽¹⁾
- ▶ Adherence is different from compliance. ⁽¹⁾
- ▶ Compliance implies an unequal power balance between the prescriber and patient. ⁽²⁾

1. World Health Organization. Adherence to long-term therapies: evidence for action. Geneva, Switzerland: World Health Organization; 2003. Available from: <http://whqlibdoc.who.int/publications/2003/9241545992.pdf>. Accessed April 25, 2022.

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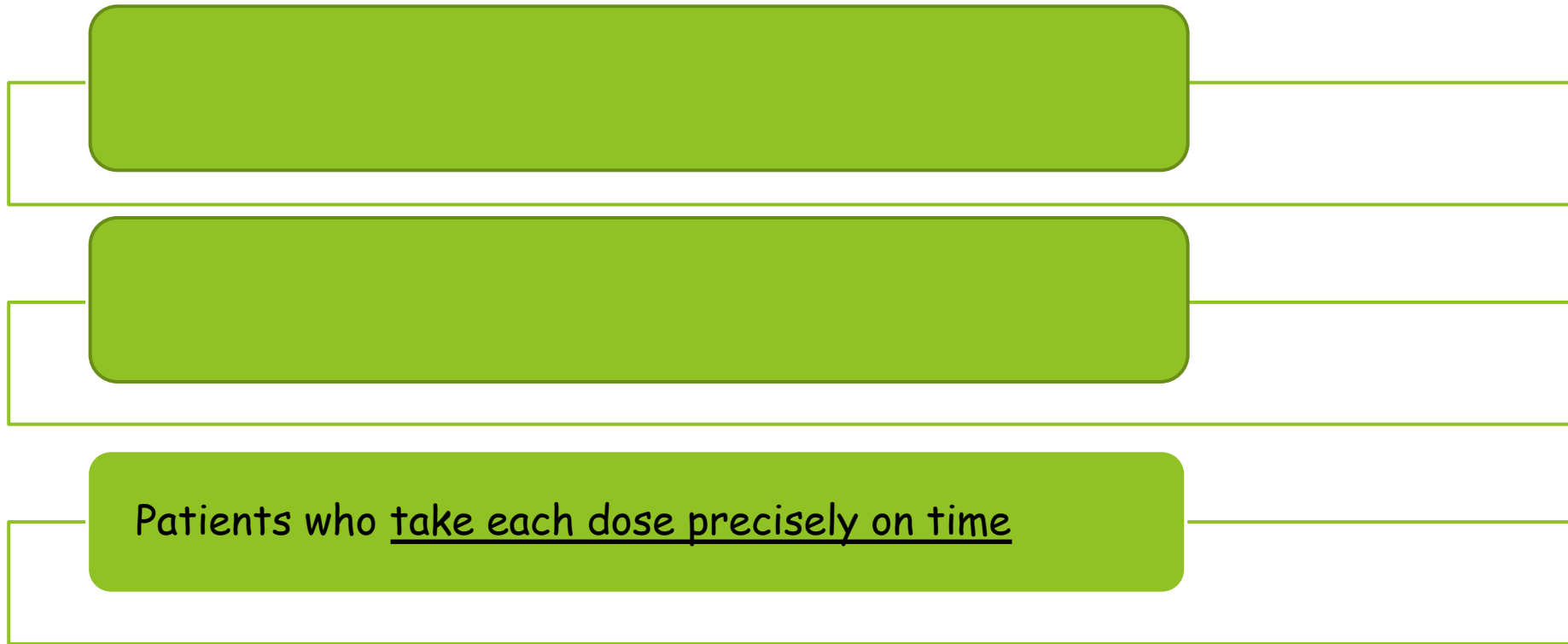
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Definition of adherence



The extent

The extent to which the patient takes the medication is dynamic (4)

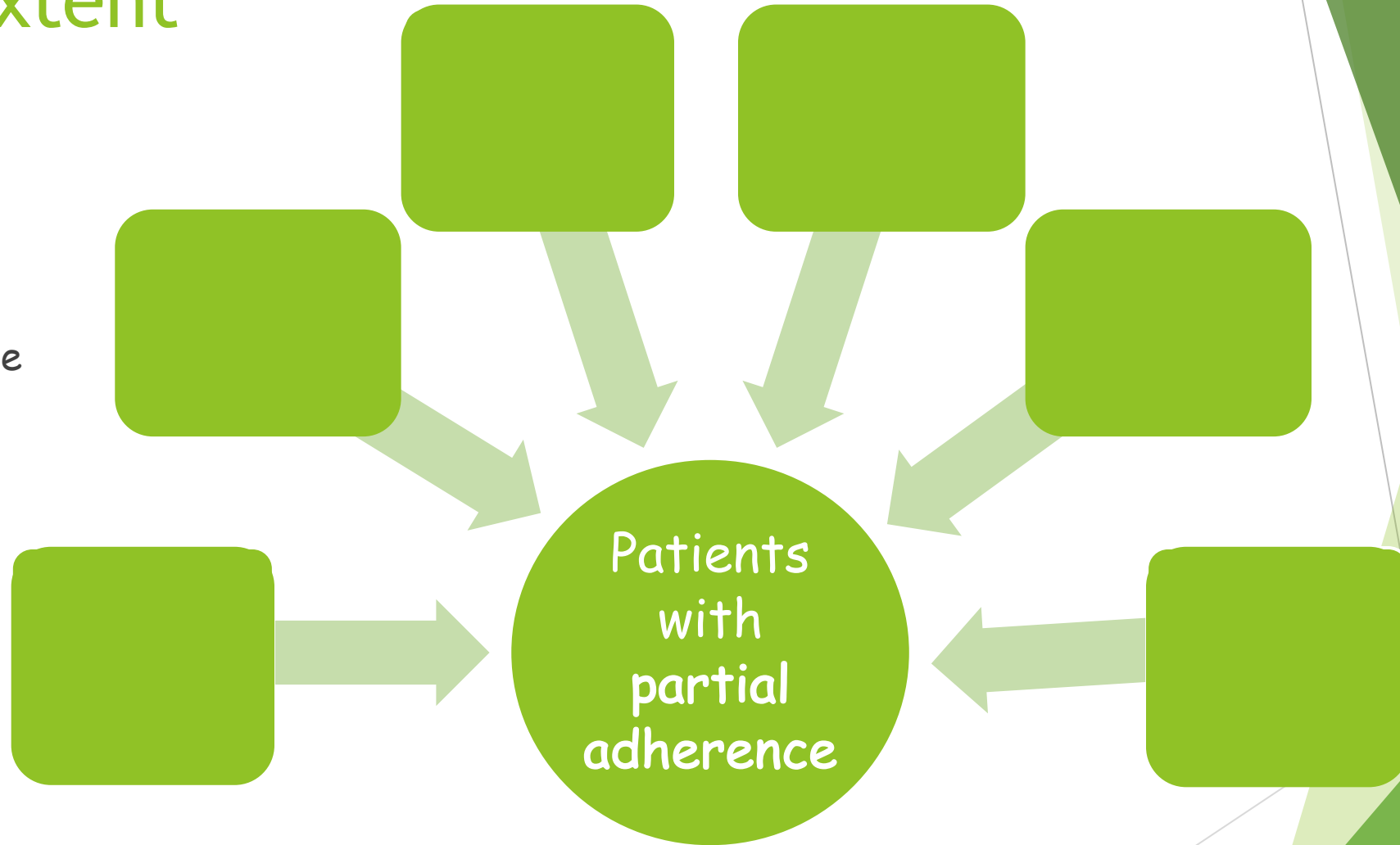


Figure based on (2, 4, 5)

2. Haddad PM, et al. Patient Relat Outcome Meas, 2014;5:43-62

4. Subotnik KL, et al. Am J Psychiatry, 2011; 168(3):286-292

5. Weiden PJ, et al. Psychiatr Serv, 2004;55(8):886-889

Adherence to long-term treatments

- ▶ Adherence is the **single most important modifiable factor** that compromises treatment outcome. ⁽¹⁾
- ▶ Increasing adherence may have a far **greater impact on the health** of the population **than any improvement** in specific medical treatments. ⁽¹⁾
- ▶ Without adherence, **advances** in biomedical technology will **fail** to reduce the burden of chronic illness. ⁽¹⁾

Reasons for nonadherence

► The patient is not solely responsible. ⁽¹⁾

► Other factors affect people's behavior and capacity to adhere to their treatment. ⁽¹⁾

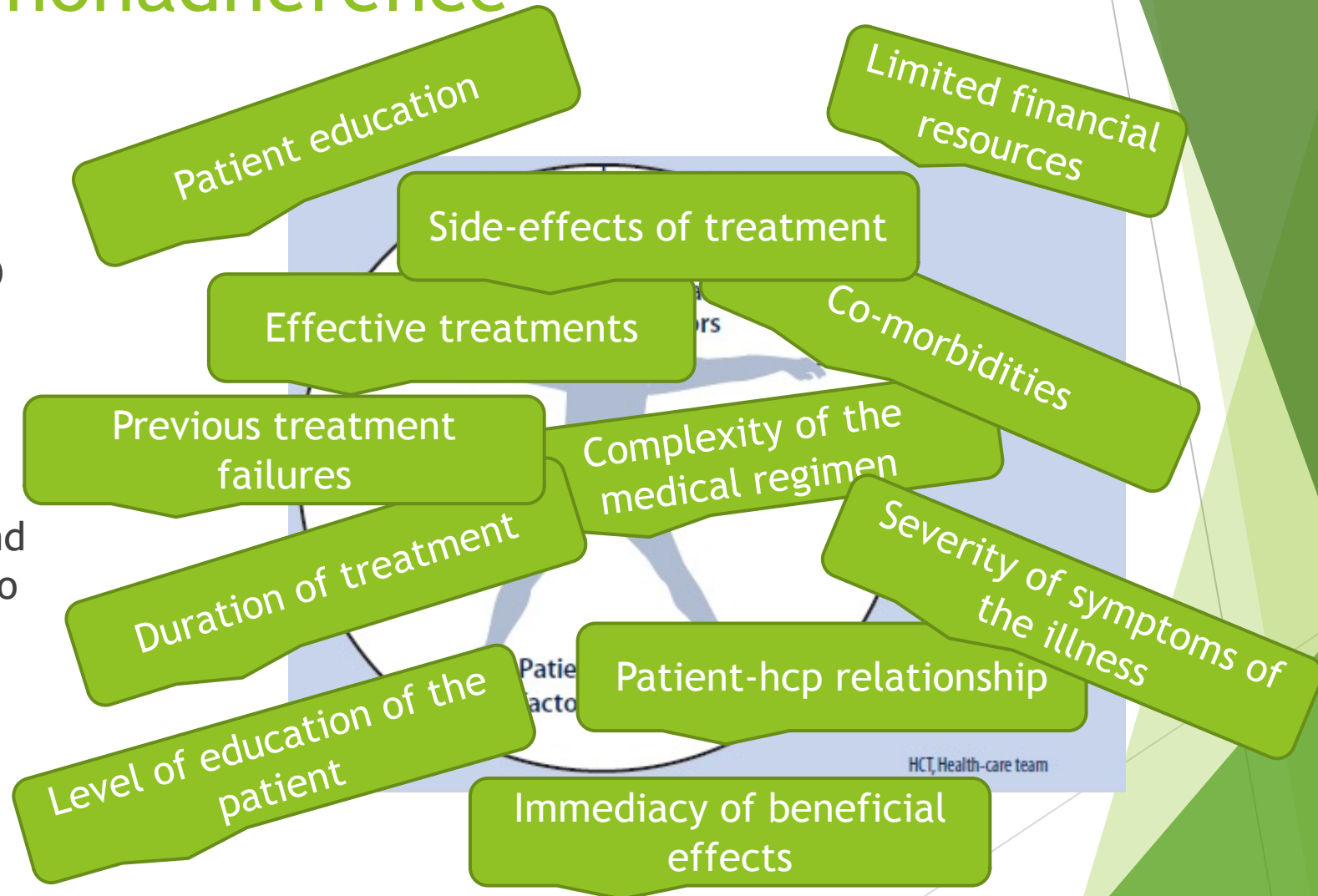


Figure based on (1)

1. World Health Organization. Adherence to long-term therapies: evidence for action. Geneva, Switzerland: World Health Organization; 2003. Available from: <http://whqlibdoc.who.int/publications/2003/9241545992.pdf>. Accessed April 25, 2022.

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Adherence in neurological and psychiatric disorders

When we compare adherence in patients with neurological disorders like Multiple Sclerosis or epilepsy with patients with somatic disorders e.g. asthma, hypertension, diabetes, adherence is ...

Worse

The same

Better

Adherence in neurological and psychiatric disorders

▶ Non-Adherence rate

- ▶ Up to 60 % of patients with multiple sclerosis ⁽⁶⁾
- ▶ 39,2% of patients with seizure disorders ⁽⁷⁾
- ▶ From 30 to 70 % in asthma ⁽¹⁾
- ▶ In Medicaid patient's nonadherence reaches⁽⁸⁾
 - ▶ 55% of patients with depression
 - ▶ 42% for antihypertensive medication
 - ▶ 46% for diabetes
 - ▶ 41% for congestive heart failure
- ▶ After hospitalization for heart failure or stroke: 24% of the do not fill their prescription within 7 days ⁽⁸⁾

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6. Mardan J, et al. J Manag Care Spec Pharm, 2021;27(9):1273-1295

7. Briesacher BA, et al. Pharmacotherapy, 2008 ;28(4):437-443

8. Unni E, et al. Pharmacy (Basel), 2022;10(2):43.

Adherence in neurological and psychiatric disorders

- ▶ 6-week study in 161 patients who admitted to the psychiatric hospital, plasma drug levels were analyzed ⁽⁹⁾
 - ▶ 52% (n=83) with plasma levels below 50% of expected plasma level
 - ▶ 21% (n= 34) with plasma levels above 200% of expected plasma level
 - ▶ 27% (n= 44) had plasma levels between 50% and 200% of the expected level
- ▶ Did not take the medication as prescribed
 - ▶ 66% of patients with schizophrenia
 - ▶ 47% of patients with affective disorders
 - ▶ 41% of patients with other psychiatric diagnoses

Migraine

The background features a series of overlapping, semi-transparent green triangles and polygons of various shades, ranging from light lime green to dark forest green. These shapes are primarily concentrated on the right side of the page, with some extending towards the left. The overall effect is a modern, abstract geometric design.

Migraine

- ▶ Characterized by recurrent attacks of moderate to severe headaches. ⁽¹⁰⁾
- ▶ **Acute treatments** ^(10,11)
 - ▶ Painkillers, triptans,....
 - ▶ Relieve pain
 - ▶ Restore function
 - ▶ Taken as needed

10. Hines DM, et al. Headache. 2021;61(4):590-602.

11. Seng E. et al. Curr Pain Headache Rep, 2015;19 (6):24

Migraine

- ▶ **Preventive treatment⁽¹¹⁾**
 - ▶ Reduce frequency of headache attacks
 - ▶ Reduce severity of headache attacks
 - ▶ Reduce risk of medication overuse

 - ▶ Taken (mostly) at least on a daily basis
- ▶ **Medication adherence to preventive treatment ⁽¹¹⁾**
 - ▶ Needed for a successful treatment
 - ▶ Suboptimal use is a risk factor for developing chronic migraine

Pharmacological treatment of migraine

- ▶ Preventive pharmacological treatments
 - ▶ Anti-epileptic drugs
 - ▶ Beta-blockers
 - ▶ Antidepressants
 - ▶ Onabotulinumtoxin A
 - ▶ ...

Adherence in patients with migraine

- ▶ Retrospective population-based study in Italy ⁽¹¹⁾
 - ▶ N= 599
 - ▶ Prophylactic treatment: antidepressants, beta-blocker, antiepileptics...
 - ▶ 73,8% discontinued their prophylactic treatment after 3,5 months
- ▶ Preventive medication for migraine ⁽¹²⁾
 - ▶ Lack specificity
 - ▶ Limited efficacy
 - ▶ Poor tolerability

11. Orlando V, et al. BMJ Open. 2020;10(11):e038972.

12. Schoenen J, et al. Rev Neurol (Paris). 2020 Dec;176(10):788-803

WHO states :

“The main role of the pharmaceutical industry is to develop safe and efficacious treatments. The development of drugs with few side-effects and easy or easier administration would promote adherence” ⁽¹⁾

New treatments for migraine

- ▶ New era with treatments specific for migraine ⁽¹²⁾
 - ▶ Treatments acting on calcitonin gene related peptide or its receptor
- ▶ Treatments with a good balance between efficacy and safety⁽¹²⁾
- ▶ Acute and prophylactic treatments (not all yet available nor reimbursed) ^(12,13)
- ▶ Dosing regimen between daily oral intake, monthly or 3-monthly subcutaneous injection or 3-monthly IV infusion. ^(14,15,16,data on file)

New treatments for migraine

- ▶ New era with treatments specific for migraine⁽¹²⁾

- ▶ Antibodies acting on Calcitonin gene-related peptide

Efficacious treatments ⁽¹²⁾

Few side effects ⁽¹²⁾

- ▶ Treatment balance between efficacy and safety ⁽¹²⁾

Safe treatments ⁽¹²⁾

- ▶ Acute and prophylactic treatments (not all yet available)

Easy or easier administration

- ▶ Dosing regimen between daily oral intake, monthly or 3-monthly subcutaneous injection or 3-monthly IV infusion. ^(14,15,16,data on file)

Schizophrenia

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Schizophrenia

- ▶ Characterized by delusions, hallucinations, negative symptoms, disorganized speech and grossly disorganized behavior ⁽¹⁸⁾

- ▶ **Acute treatment** ⁽¹⁹⁾
 - ▶ Antipsychotics

 - ▶ Mainly treatment of positive symptoms

18. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: Author.

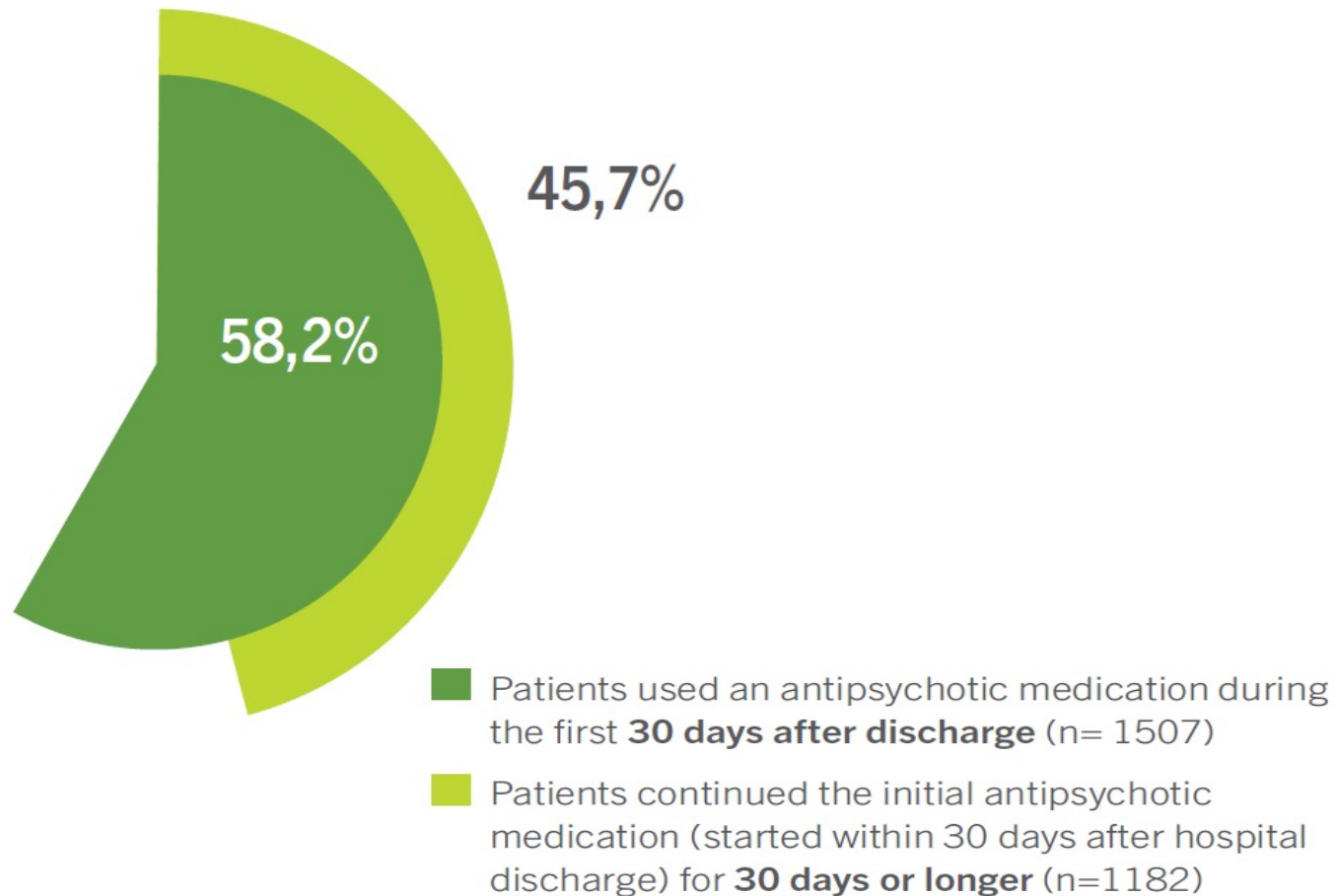
19. Tiihonen J, et al. Am J Psychiatry, 2011;168(6):603-609

Schizophrenia

- ▶ Long-term treatment (2, 19)
 - ▶ Antipsychotics
 - ▶ Reduces the risk of relapse, hospitalization, suicide attempts
 - ▶ First episode patients: at least 1 year
 - ▶ Many patients requires indefinite antipsychotic medication

Adherence in patients with schizophrenia

Patients diagnosed with schizophrenia after their first hospitalization (n=2588)

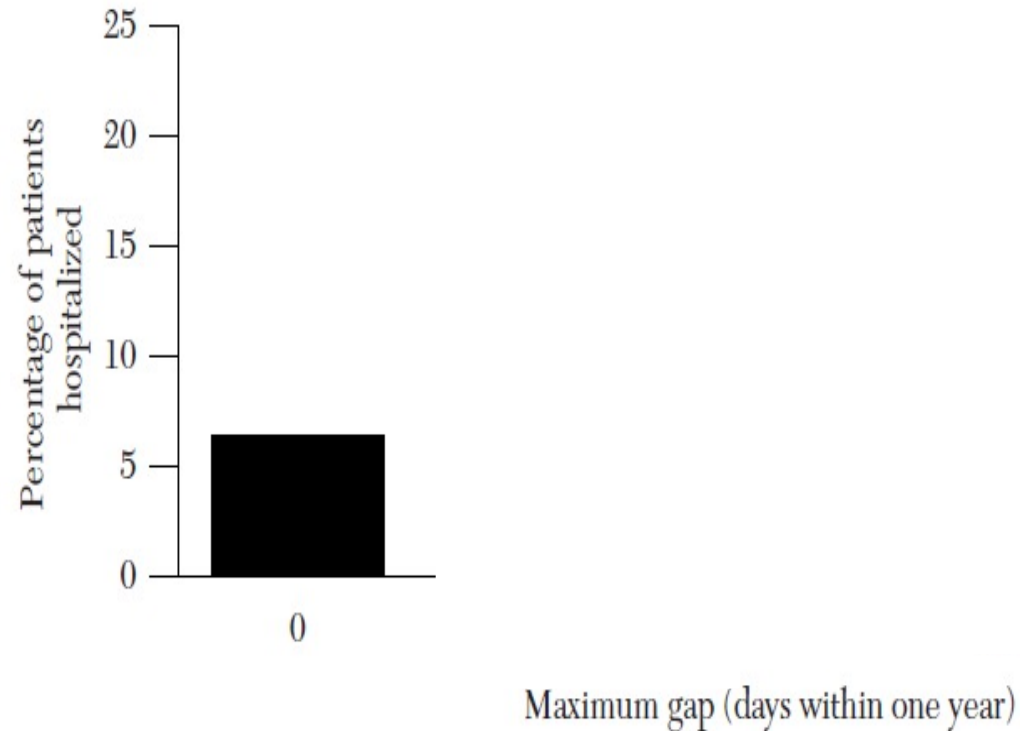


Non-adherence can be due to

- ▶ The disease itself (2,20,21)
 - ▶ lack of insight
 - ▶ positive symptoms
 - ▶ negative and depressive symptoms
 - ▶ cognitive problems
- ▶ Social isolation and stigma (2,20,21)
- ▶ Alcohol and/or drug abuse (2,20,21)
- ▶ Side effects of antipsychotics (2,20,21)

Adherence and rehospitalisation

Percentage of patients with schizophrenia who were rehospitalized, by maximum gap in therapy^a



^a All pairwise comparisons were significant at $p < .005$.

Adherence and recurrence

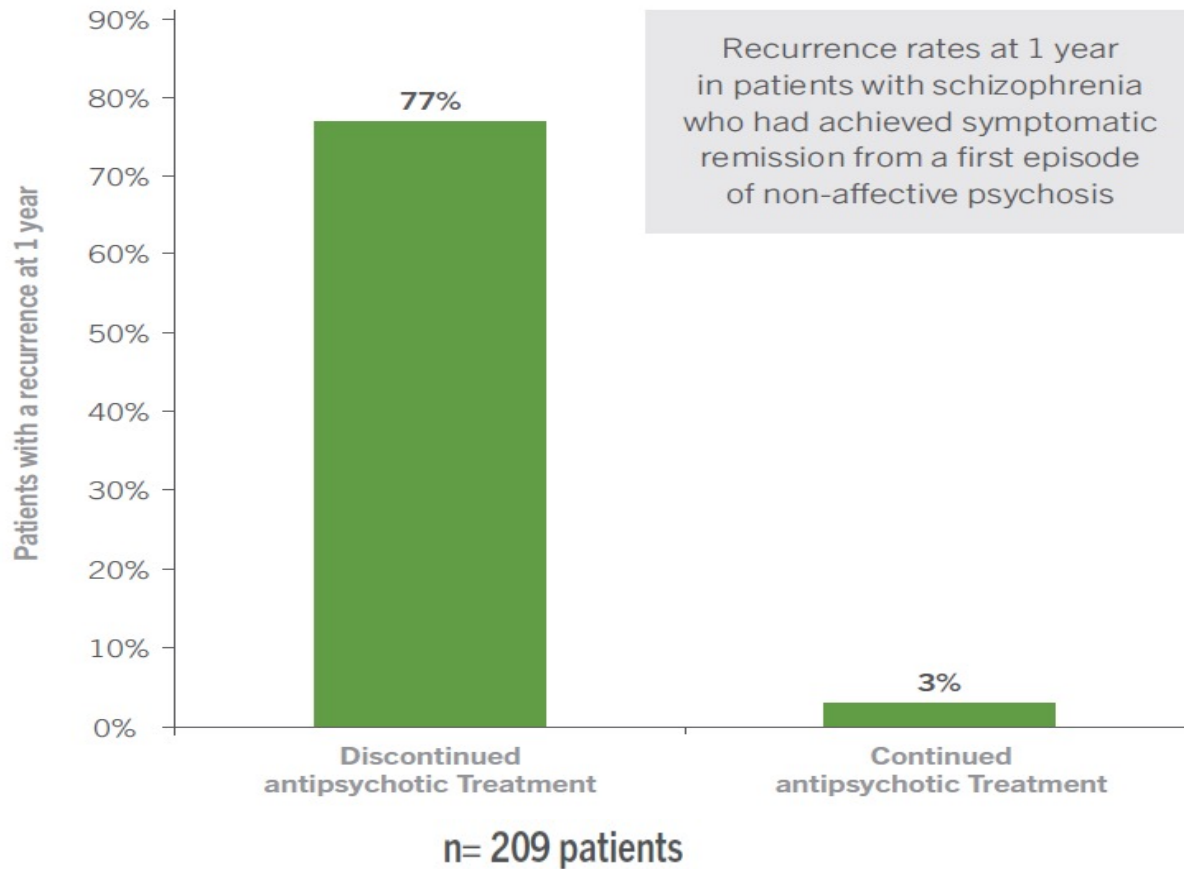


Figure based on (22)

N: number

22. Zipursky RB, et al. Schizophr Res, 2014;152(2-3):408-414

Implications of relapse

- ▶ Worse or decreased treatment response (24,25)
- ▶ Progressively longer time to achieve remission (25)
- ▶ Harder to re-establish previous gains (26)
- ▶ Higher risk on rehospitalization (5,25)
- ▶ More resistant to treatment (26)
- ▶ Chronic course of illness (25)

24. Thomas P, L'Encéphale, 2013;39 (suppl 2):S79-S82

25. Heres S, Eur Psychiatry, 2014;29 (suppl 2):1409-1413

26. Kane JM, CNS Spectr, 2007;12(10 suppl 17):21-26

WHO states

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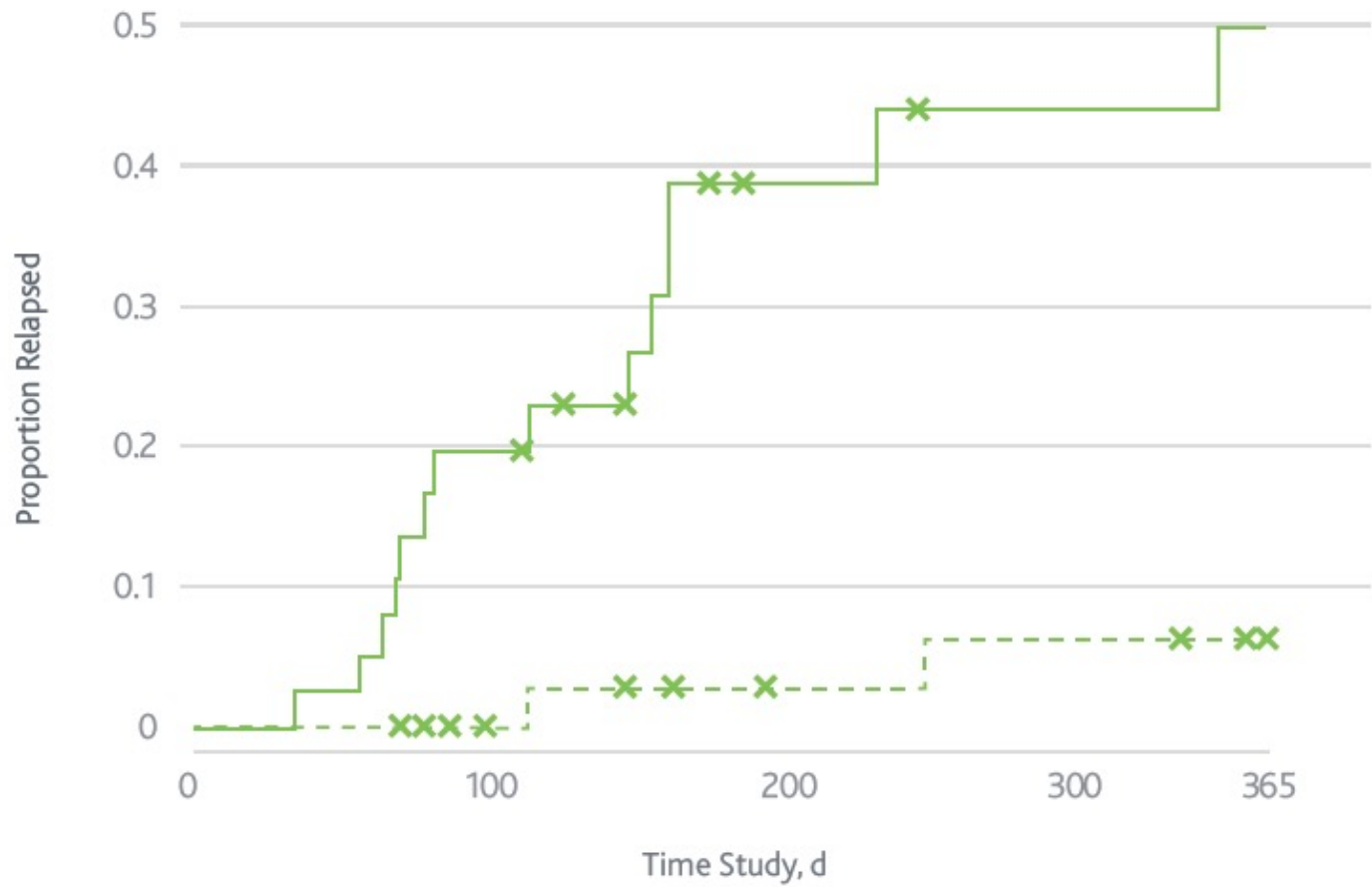


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 23. Subotnik KL, et al. JAMA Psychiatry, 2015;72(8):822-829

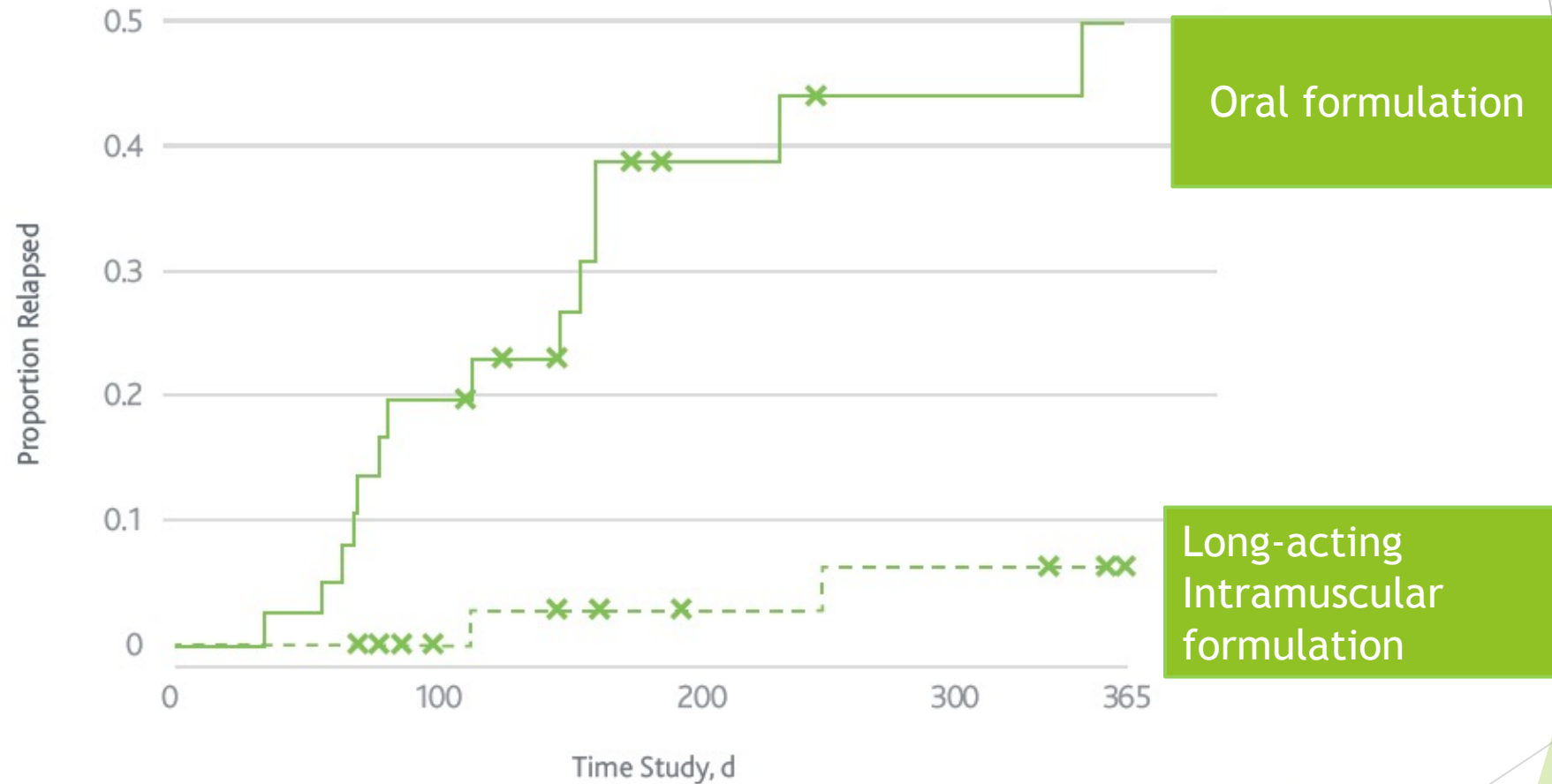
Which 2 products are here compared to each other?

Any antipsychotic
versus
placebo

'old' FGA
Versus
'new' SGA

SGA
Versus
clozapine

Same antipsychotic but



Improved treatments for schizophrenia

- ▶ Use of any antipsychotic was associated with lower mortality than no antipsychotic use. ⁽¹⁹⁾
- ▶ With Long Acting Injectables there is 59% lower risk of treatment discontinuation. ⁽¹⁹⁾
- ▶ Risk of rehospitalization for patients treated with Long Acting Injectables was about 1/3 of the risk for people treated with oral antipsychotics. ⁽¹⁹⁾

Improved treatments for schizophrenia

Safe treatments

- ▶ Use of any antipsychotic was associated with lower mortality than no antipsychotic use. ⁽¹⁹⁾

Easy or easier administration

Efficacious treatments

- ▶ With Long Acting Injectables there is 59% lower risk of treatment discontinuation. ⁽¹⁹⁾
- ▶ Risk of rehospitalization for patients treated with Long Acting Injectables was about 1/3 of the risk for people treated with oral antipsychotics. ⁽¹⁹⁾

Few side effects

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Conclusions

- ▶ Failure to take prescribed medicine for chronic diseases is a massive, world-wide problem. Adherence is the **single most important modifiable factor** that compromises treatment outcome. Increasing adherence may have a very **great impact**. ⁽¹⁾

- ▶ Adherence can be boosted by choosing treatments that are
 - ▶ safe and efficacious,
 - ▶ with few side-effects and
 - ▶ easy administration. ⁽¹⁾

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Q & A

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References

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13. Schoenen J, et al. Rev Neurol (Paris). 2020 Dec;176(10):788-803

14. Coppola G, et al. *Curr Opin Support Palliat Care*. 2012;6(2):177-182.
15. SmPC Aimovig
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