Medications for Opioid Use Disorder: Who should get what when?

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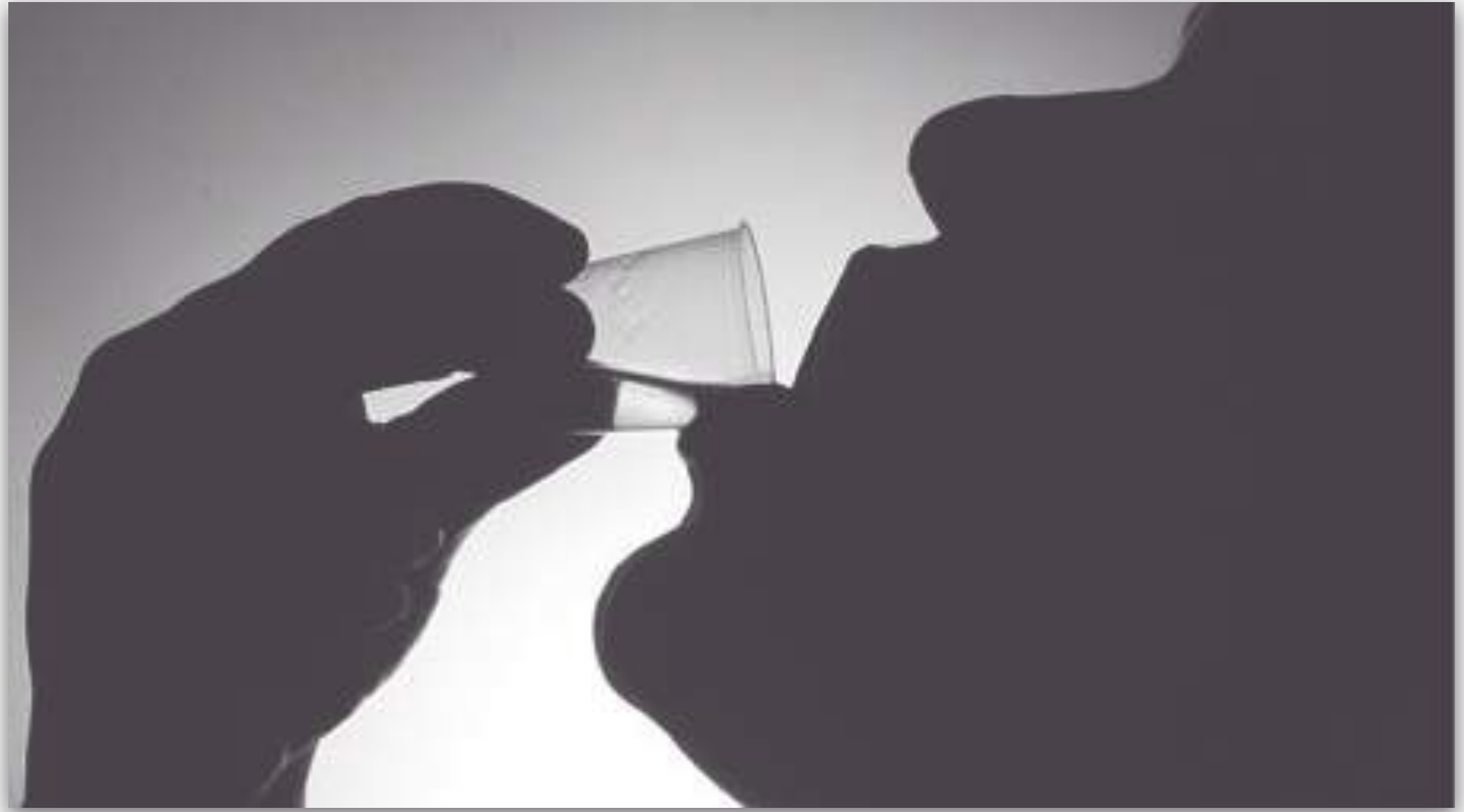
Disclosure Information

- Speaker – Jessica Gregg MD, PhD has nothing to disclose

OBJECTIVES

Compare methadone, buprenorphine, and extended release naltrexone in terms of:

1. Efficacy (on a stable dose)
2. Induction, retention, and other clinical variables
3. Operational/Systems level constraints



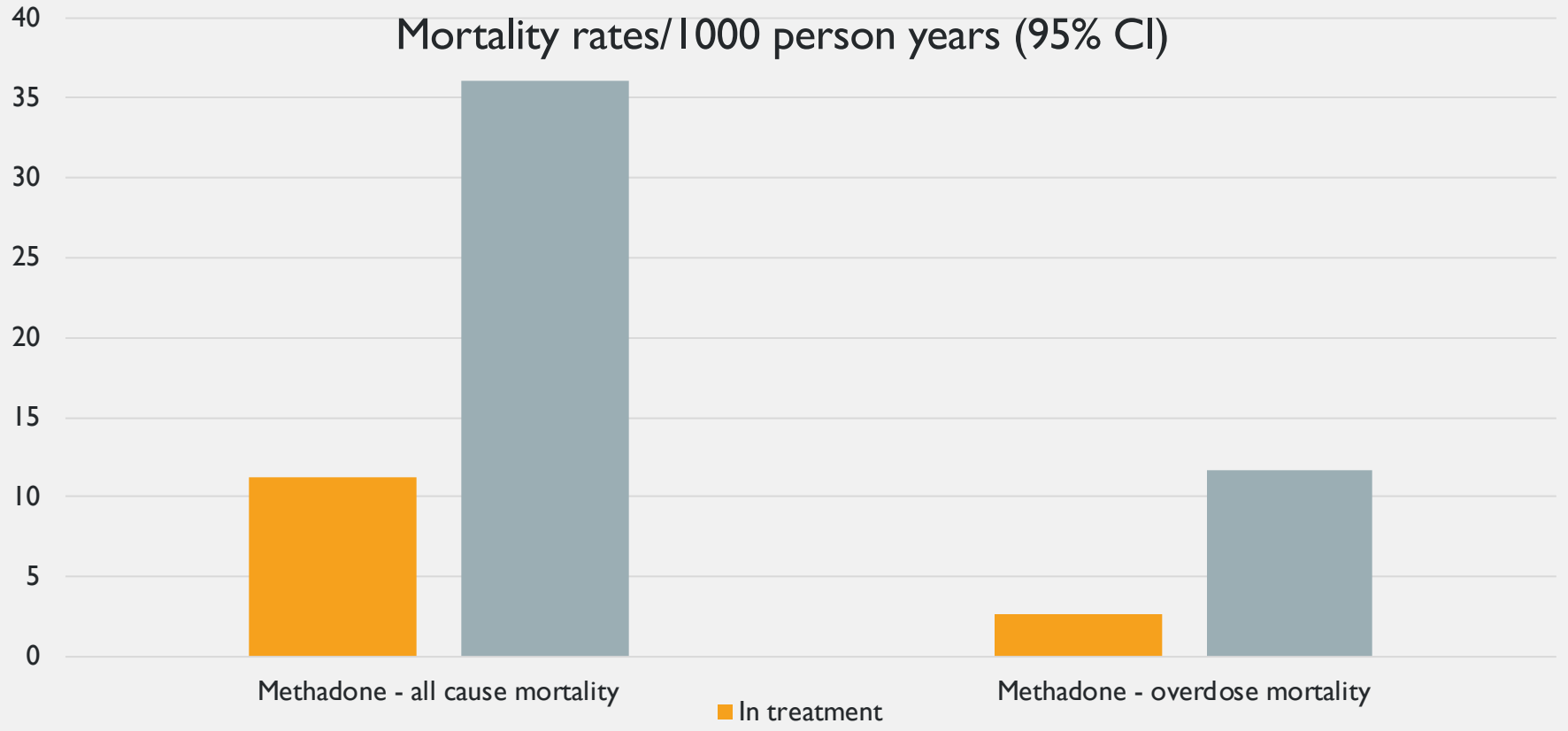
METHADONE: EFFICACY

Cochrane review 2009

- methadone v treatment without medication
- Patients on methadone significantly less likely to have positive urine drug screen
- Decreased new infections with Hep C/HIV
- Decreased criminality

Mattick RP, et al. *Cochrane Database of Systematic Reviews* 2009

MORTALITY RISK DURING AND AFTER METHADONE TREATMENT



Mortality Risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. Sordo, et al. BMJ 2017.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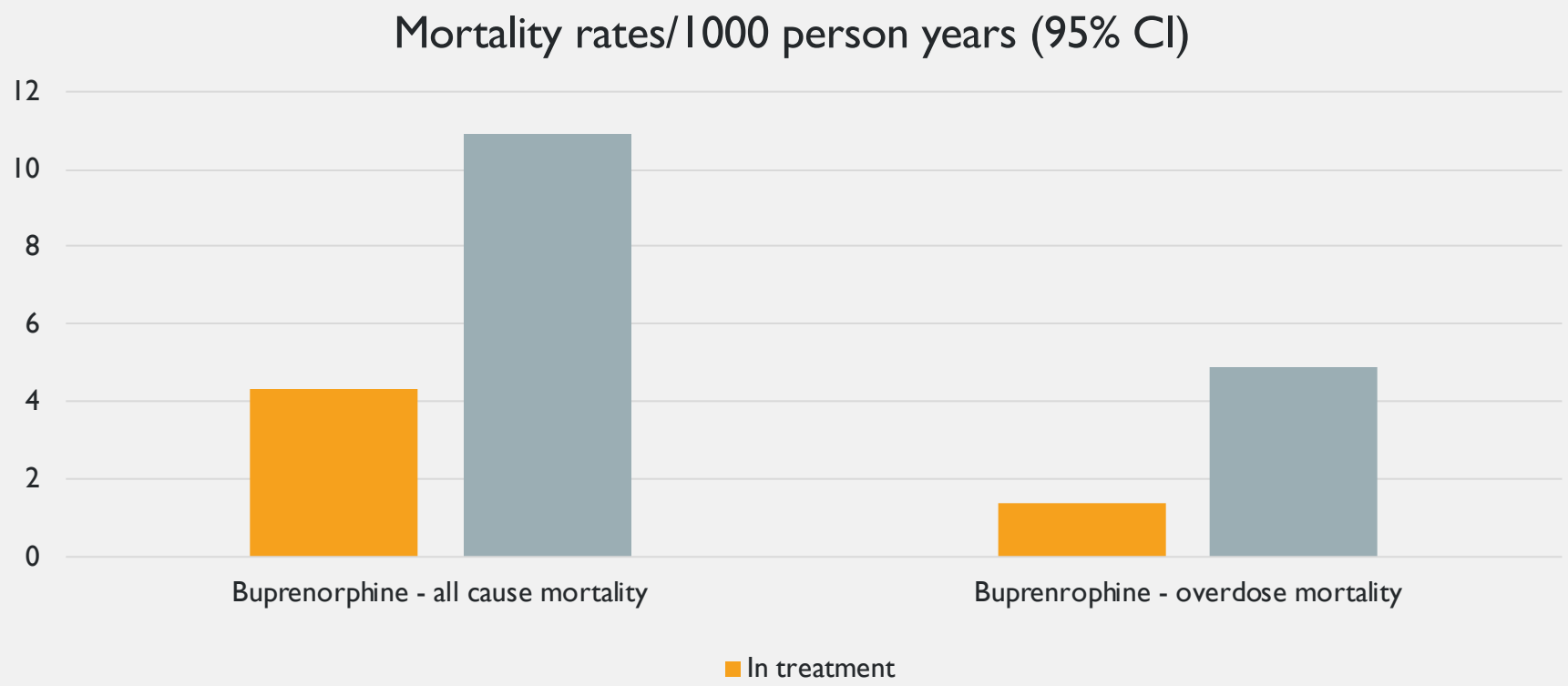
BUPRENORPHINE: EFFICACY

Cochrane review 2014

- low dose, medium dose, high dose, or flexible dosing
- Buprenorphine equivalent to methadone for suppression of illicit drug use except at very low doses
- No difference in mortality

Mattick RP, et al. *Cochrane Database of Systematic Reviews* 2014.

MORTALITY RISK DURING AND AFTER BUPRENORPHINE TREATMENT



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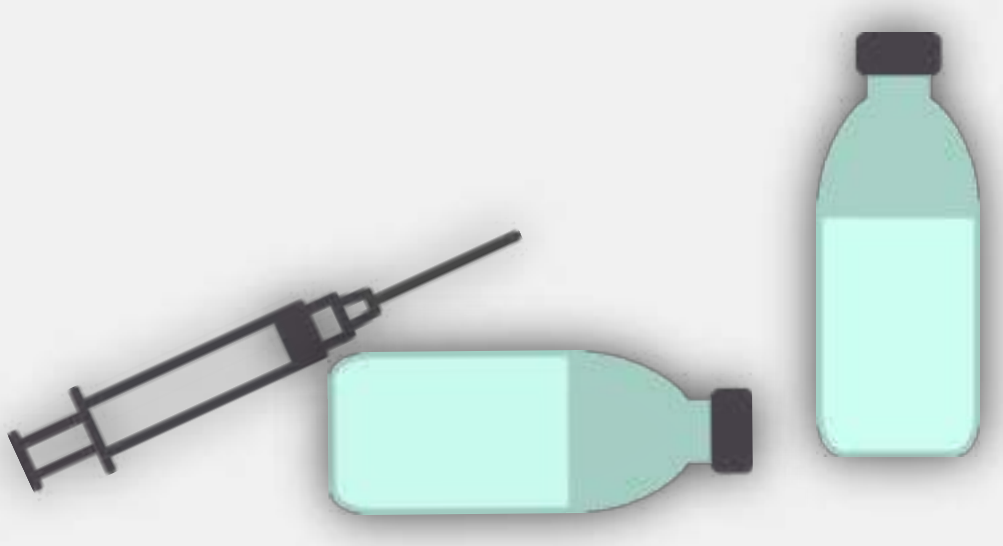
Naltrexone for Extended Release Injectable Suspension



NALTREXONE ER: EFFICACY

Efficacious compared to placebo

- Comer: 60 U.S. heroin users, 8 weeks (retention in tx and opioid negative urines)
- Krupitsky: 250 Russian heroin users, 24 wks (retention in tx without relapse)

- Efficacious compared to buprenorphine
  - Tanum: Non-inferior to buprenorphine for decreasing opioid use at 12 wks
  - Lee: Non-inferior to buprenorphine for decreasing opioid use at 24 weeks

Comer Arch Gen Psych 2006
Krupitsky Lancet 2011
Tanum JAMA Psychiatry 2017
Lee Lancet 2017

Outcome	XR-NXT (n=283)	BUP-NX (n-287)	Treatment Effect
Inducted to study medication (ITT)	204 (72%)	270 (94%)	OR 0.16, 0.09-0.28; P<0.0001
Relapse-free survival (weeks)	8.4 (3-23.4)	14.4 (5.1-23.4)	HR 1.36, 1.10-1.68; p=0.0040
	20.4 (5.4-23.4)	15.2 (5.7-23.4)	HR 0.92, 0.71-1.18, p=0.49
Opioid relapse, weeks 3-24	185 (65%)	163 (57%)	OR 1.44, 1.02-2.01; p=0.036
	106/204 (52%)	150/270 (56%)	OR 0.87, 0.60-1.25; p=0.44

Lee JD, et al. *Lancet* 2017

EFFICACY: CONCLUSIONS

- All three medications are efficacious **once a patient is on the medication**
- Buprenorphine is equivalent to methadone in terms of decreased illicit drug at higher doses and with flexible dosing
- Extended release naltrexone is equivalent to buprenorphine in terms of decreased illicit drug use.
- Both buprenorphine and methadone decrease mortality by more than ½ for patients with OUD

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METHADONE INDUCTION

No need for withdrawal

BUT the risk of death while on methadone is highest during the initial four weeks of treatment, the induction phase

Mortality Risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. Sordo, et al. BMJ 2017.

BUPRENORPHINE INDUCTION

Requires a brief period of withdrawal (usually 12 – 18 hours off opioids)

No increased mortality during induction

EXTENDED RELEASE NALTREXONE: INDUCTION

Requires abstinence from opioids 4 – 7 days

About 25% of patients will not complete induction

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WHAT ABOUT RETENTION?

- Highest mortality **out of treatment** is in first four weeks off methadone and buprenorphine

- For methadone, the highest mortality **in treatment** is in the first four weeks on methadone

- ??? risk of overdose after cessation of naltrexone ER

Persistent engagement is critical

RETENTION: METHADONE V. BUPRENORPHINE

- Buprenorphine at medium and high doses is equivalent to methadone at medium and high doses for retention.

Mattick RP, et al. *Cochrane Database of Systematic Reviews* 2014.

RETENTION: NALTREXONE ER

- Discontinuation rates of extended release naltrexone are at least two times higher than discontinuation rates of SL buprenorphine.

- More than half of those discontinuations occur after the first injection

Morgan JR, et al. JSAT 2016

SUMMARY: INDUCTION, AND RETENTION

- Induction and retention are most challenging for naltrexone
- Methadone retains patients slightly better than buprenorphine
- Due to increased mortality with cessation of medication, persistent engagement is critical when people need the medication, and extreme care should be taken when tapering

OTHER CLINICAL/PATIENT LEVEL CONSIDERATIONS

- Prolonged QT, family hx of arrhythmia or sudden death – methadone risk
- Known need for opioids in the future (surgery, sickle cell) – Naltrexone contraindication
- Safe place to store medication - methadone, buprenorphine consideration
- Other use disorders

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OPERATIONAL/SYSTEMS VARIABLES: METHADONE

- When used to treat an OUD, can only be dispensed only from an opioid treatment program

- Patients are eligible only if they have an OUD and have had it for a least a year prior to admission (exceptions: incarceration, pregnant, previous methadone treatment)

- Requirements: daily dispense for a minimum of 90 days, perhaps more

- +/-insurance

OPERATIONAL/SYSTEMS VARIABLES: BUPRENORPHINE

- Provider with a DATA waiver
- Clinic level support (help with UDS, tracking numbers of patients, PDMP, refills)
- +/- space for inductions
- Insurance coverage has (mostly) become less of a barrier

OPERATIONAL/SYSTEMS VARIABLES: EXTENDED RELEASE NALTREXONE

- Insurance coverage
- Clinician comfort

	Methadone	Buprenorphine	Naltrexone ER
Available?	+	+	+
Does your patient need daily dispense?	+	+/-	n/a
Is daily dispense problematic (illness, geography)?	X	+	+
Does your patient have a place to store medication?	+/-	+	n/a
Will your patient require opioids in the future?	+	+	X
Is a period of abstinence unlikely/difficult?	+	+/-	X
Does your patient want this medication?	+	+	+
Other clinical variables	+	+	+

Discussion?