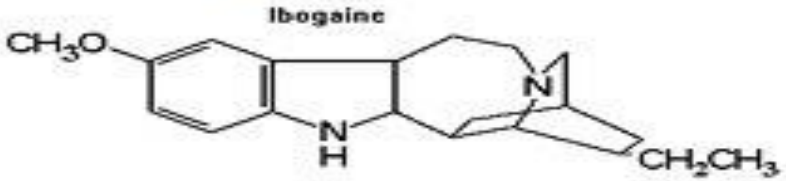
New Zealand Ibogaine treatment outcomes for opioid dependence: Another string to the bow?

Geoff Noller, PhD; Chris Frampton, PhD; Berra Yazar-Klosinski, PhD

Addiction Research Symposium, Christchurch, 8 May 2018



Ibogaine treatment for opioid dependence

- Background
- The New Zealand study
  - Description
  - Results
- Implications
  - Treatment support
  - Safety
  - Future

Ibogaine—the substance

One of 12 indole alkaloids found in the root bark of a West African shrub, *Tabernanthe iboga*

- Used by Gabonese Bwiti of West Africa (syncretic cult)
- Has been used medically for over a century, e.g.
  - as an anti-parasitic
  - as *Lambarene*, a 1930's pharmacological preparation marketed as "a neuromuscular stimulant, promoting cell combusations and getting rid of fatigue, indicated in cases of depression, asthenia, in convalescence, infectious diseases."

Popik et al, 1995:237

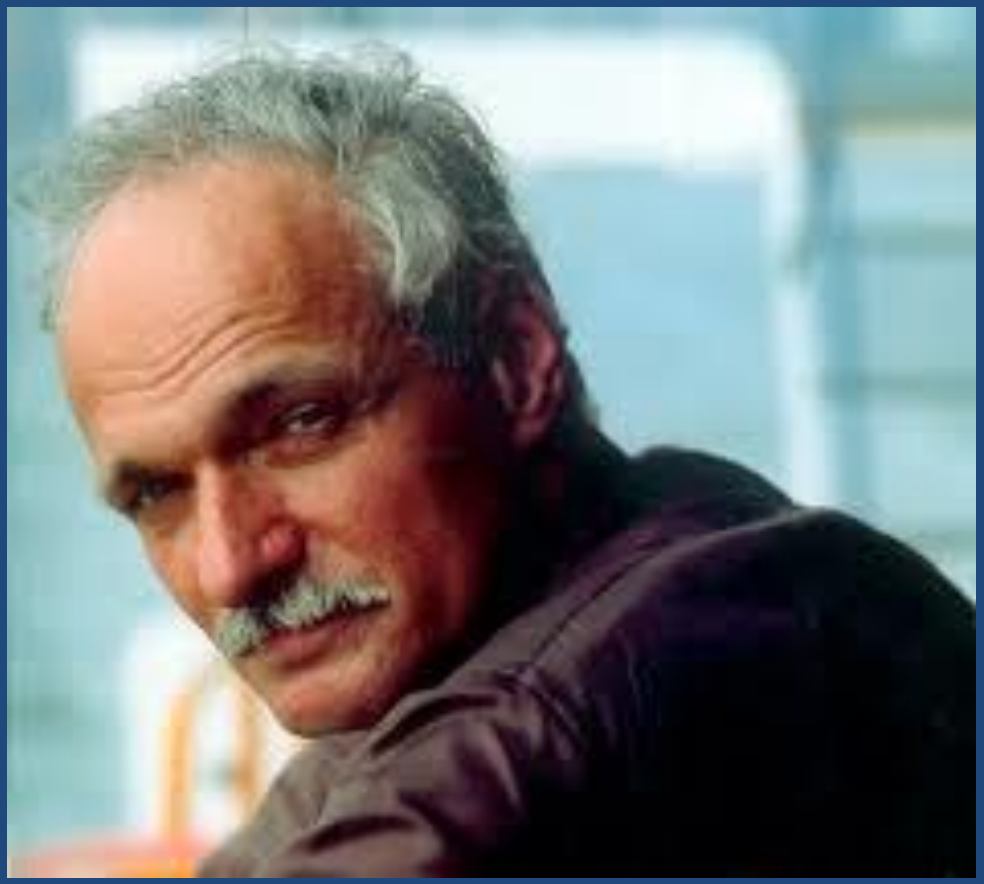
Ibogaine “breaking open the head”

Cultic practices amongst the Bwiti

- Iboga consumed as the “one true sacrament”
- Ground / rasped root consumed
- Six to 10 grams of powdered root may be considered a psychedelic dose
- Bwiti initiates may consume 50-200 gm

For opioid dependence

An addiction interrupter?



Howard Lotsof

The New Zealand study

12-month observational follow-up study of ibogaine treatments for opioid dependence

- Ibogaine prescribable in NZ (2009)
- A response to the Medsafe decision
- Funding to MAPS via Matt & Kristi Bowden's family trust
- Subsequent funding from The Star Trust
- Using the pre-existing protocol from a MAPS US study of Mexican treatments

Matt Bowden

Study—objectives / outcome measures

Primary objective:

Determine the effectiveness of ibogaine-assisted therapy in elimination or reduction of OPIOID usage, craving and withdrawal, and in improving other aspects of life.

Primary Outcome Measure:

Addiction Severity Index (ASI-Lite) composite scores for 7 life areas over a period of 12 months following the therapy.

Secondary Measures:

SOWS, SOCQ, BDI Client treatment expectations;
Drug screens.

Study protocol – interview schedule

Interview	Months Post-tx	ASI	BDI	SOWS	Drug Screen	Brief Talk
1	Pre-tx	X	X	X		
2	Post-tx		X	X		
3	1	X	X			
4	2					X
5	3	X	X			
6	4					X
7	5					X
8	6	X	X		X	
9	7					X
10	8					X
11	9	X	X		X	
12	10					X
13	11					X
14	12	X	X		X	

Table 1: Ibogaine study protocol / interview schedule

Results – The Numbers

	US / Mexico	NZ / Aotearoa
Subjects		
Contacted	67	20
Recruited	30	15
Lost to follow-up (relapsed)	15 (50%)	2 (14%)
Withdrew	2	1
Death in treatment		1
Followed to 12-months	13	11
Opioid-free @ 12-months	6 (20%)	7 (50%)

Table 2: Recruited subjects in two ibogaine studies (US/Mexico, New Zealand)

Drug Tx and drug use landscape

Drugs	Mexico % Drugs Tx (n=30)	NZ % Drugs Tx (n=14)	2013 BBVNEX Survey Drugs reported injected % previous month (n=718)
Heroin	50		14
Oxycodone	43		
Suboxone	3		
Opium (incl. poppy tea)	3	7	
Methadone		71	58
Morphine		7	50
Dihydrocodeine (DHC)		14	

Table 3: Percentages of Mexico and NZ study subjects treated for opioid dependence with ibogaine, reporting pre-tx use of opioids, by drug and 2013 NZ Needle Exchange survey previous month use.

ID	Age (Year)	Sex	Weight (kg)	Opioid	Ibogaine Dose (mg/kg)	Dosing Time (Hours)	Follow-up Post-tx (Months)
1	40	F	70.0	Methadone	31.4	17	12
2	45	F	120.0	Methadone	25.3	72	11*
3	39	F	88.0	Methadone	29.5	42	12
4	33	F	73.0	Methadone	35.6	21	11*
5	39	M	88.0	Methadone	25.0	19	12
6	42	M	81.0	Methadone	24.6	72	7**
7	47	F	57.0	Methadone	38.5	54	12
8	33	M	74.0	Methadone	27.0	41	12
9	29	F	92.0	Methadone	28.2	38	12
10	40	M	56.0	Dihydrocodeine	25.0	65	12
11	34	F	54.5	Methadone	55.0	81	12
12	36	M	70.0	Poppy seed	34.2	77	12
13	41	M	75.0	Dihydrocodeine	26.6	51	12
14	39	M	79.5	Dihydrocodeine	25.1	71	12

S1: Demographics, drug of dependence, ibogaine dose and period of administration, and follow-up period for each participant (n=14) receiving ibogaine treatment for opioid dependence. Post-tx = post-treatment.
* Lost to follow-up
** Withdrew from study

Table 4: Subjects completing treatment (n=14) for NZ ibogaine study, showing:

- Age 29-47 years; Median 39
- Sex (50% female)
- Drug of dependence 71% methadone
- Ibogaine dose/kg: range 25-55 mg/kg; mean 30.8 mg/kg
- Dosing duration: range 17-81 hours; median 48.4 hours

Results – outcomes

At 12-months post treatment:

- Full data set (n=8) – significant reduction, ASI-Lite drug use composite score (p=0.002) (Friedman Test, non-parametric)
- Reductions in BDI-II scores from baseline to 12-month follow-up were also significant ($p < 0.001$)
- Significant reductions in SOWS scores for all participants (n=14) were also observed acutely after treatment (p=0.015) Patients with partial data (n=4) also showed reductions in ASI-Lite drug use scores and family/social status problems
- One patient enrolled in the study died during treatment

Noller, Frampton & Yazar-Klosinski. (2018). Ibogaine treatment for opioid dependence from a 12-month follow-up observational Study. *American Journal of Drug and Alcohol Abuse*, *44*(1), 37-46

ASI Summary statistics

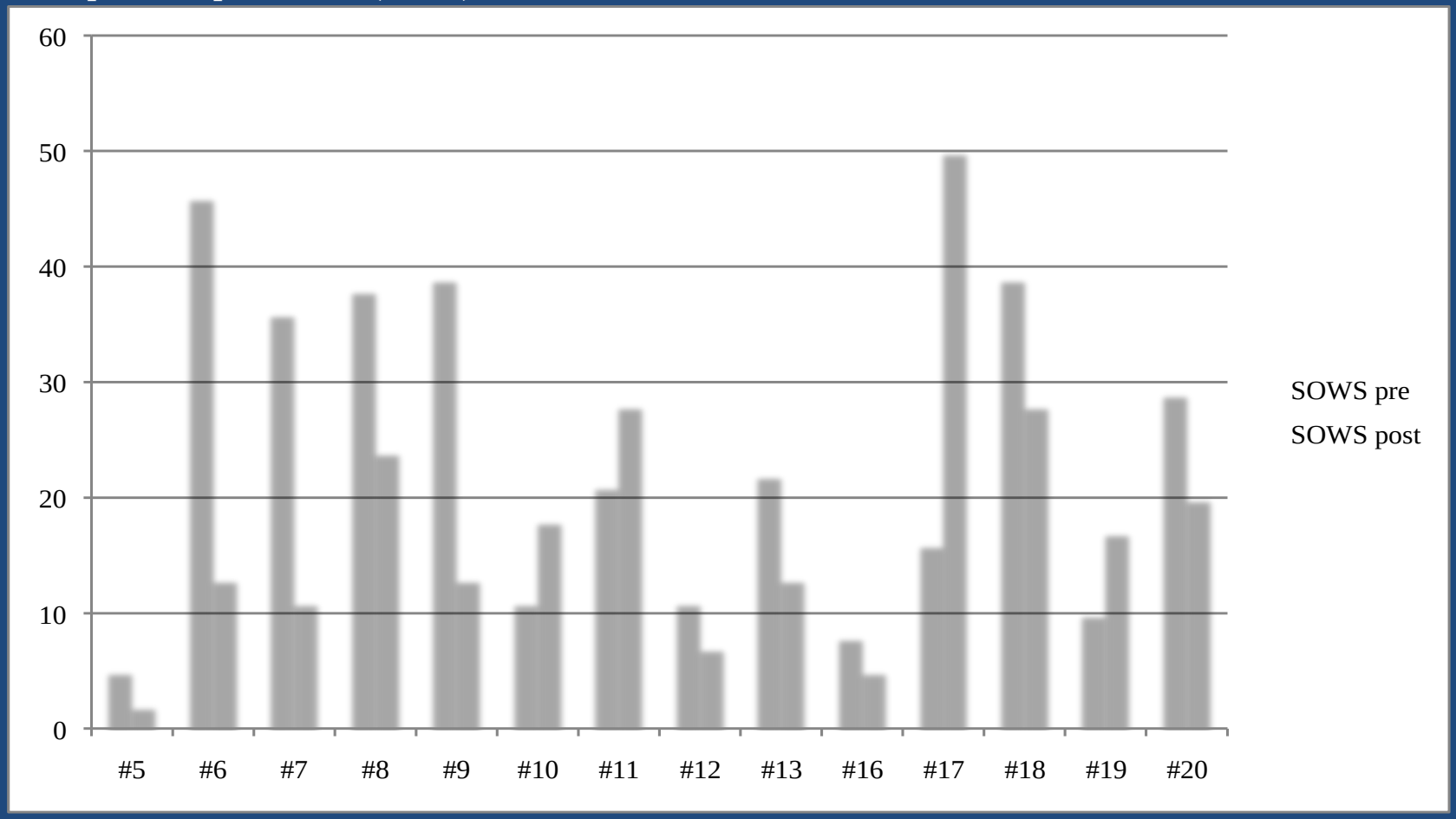
Table 5: ASI summary statistics at baseline and 12-month follow-up.

		Baseline		12-month Follow-up
Average score	N	mean (std)	N	mean (std)
Medical	8	0.00 (0.00)	8	0.34 (0.40)*
Employment	8	0.37 (0.40)	8	0.22 (0.33)
Alcohol	8	0.16 (0.26)	8	0.08 (0.08)
Drug	8	0.32 (0.07)	8	0.06 (0.08)**
Legal	8	0.00 (0.00)	8	0.01 (0.04)
Family/Social	8	0.11 (0.15)	8	0.09 (0.13)
Psychiatric	8	0.11 (0.15)	8	0.05 (0.11)

*$p<0.05$ compared with baseline
**$p<0.01$ compared with baseline

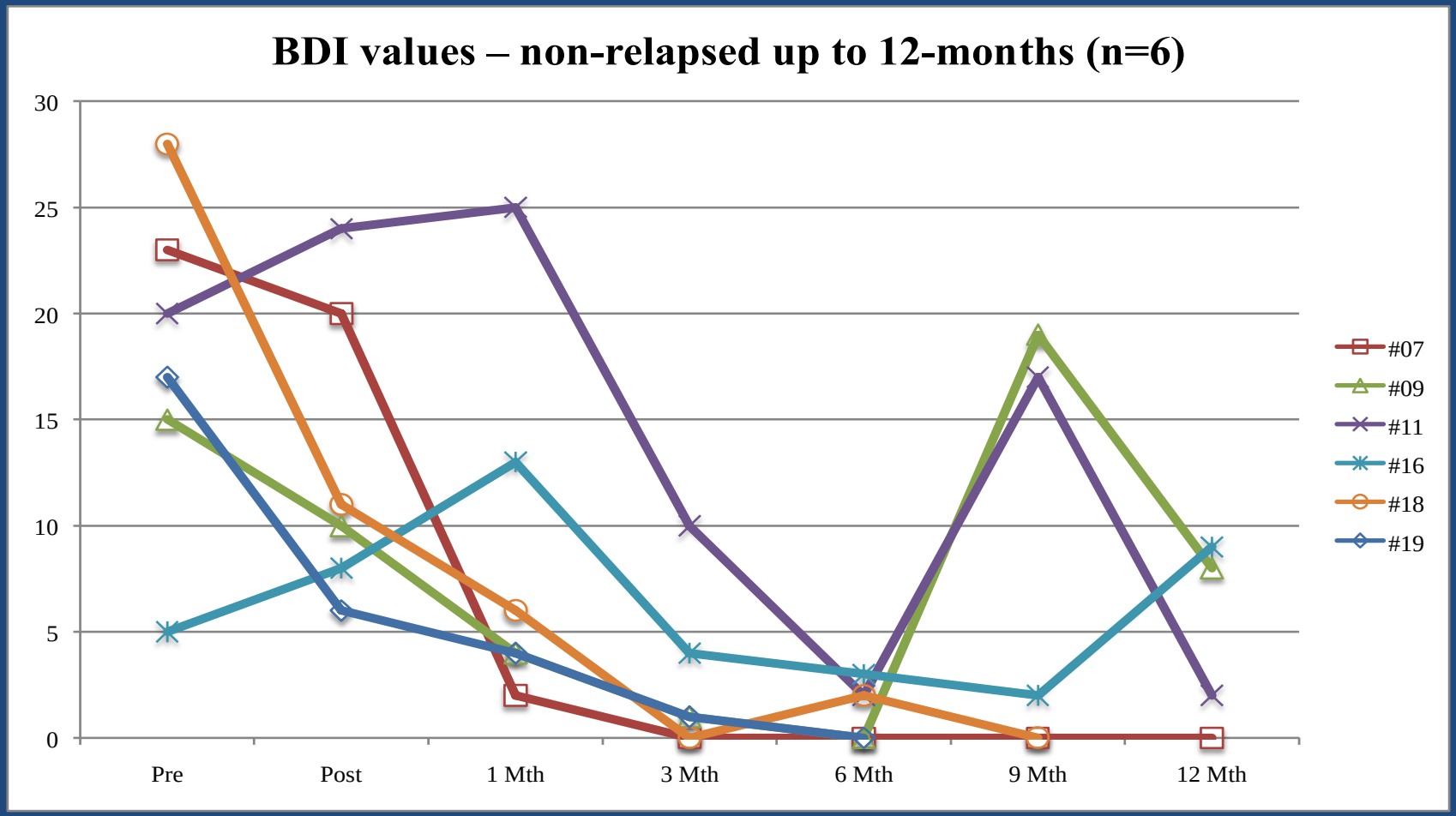
Subjective opioid withdrawal scale (SOWS)

Figure 1: Comparing SOWS scores pre- and post-treatment, of subjects receiving ibogaine for opioid dependence (n=14)



Beck Depression Inventory – BDI-II

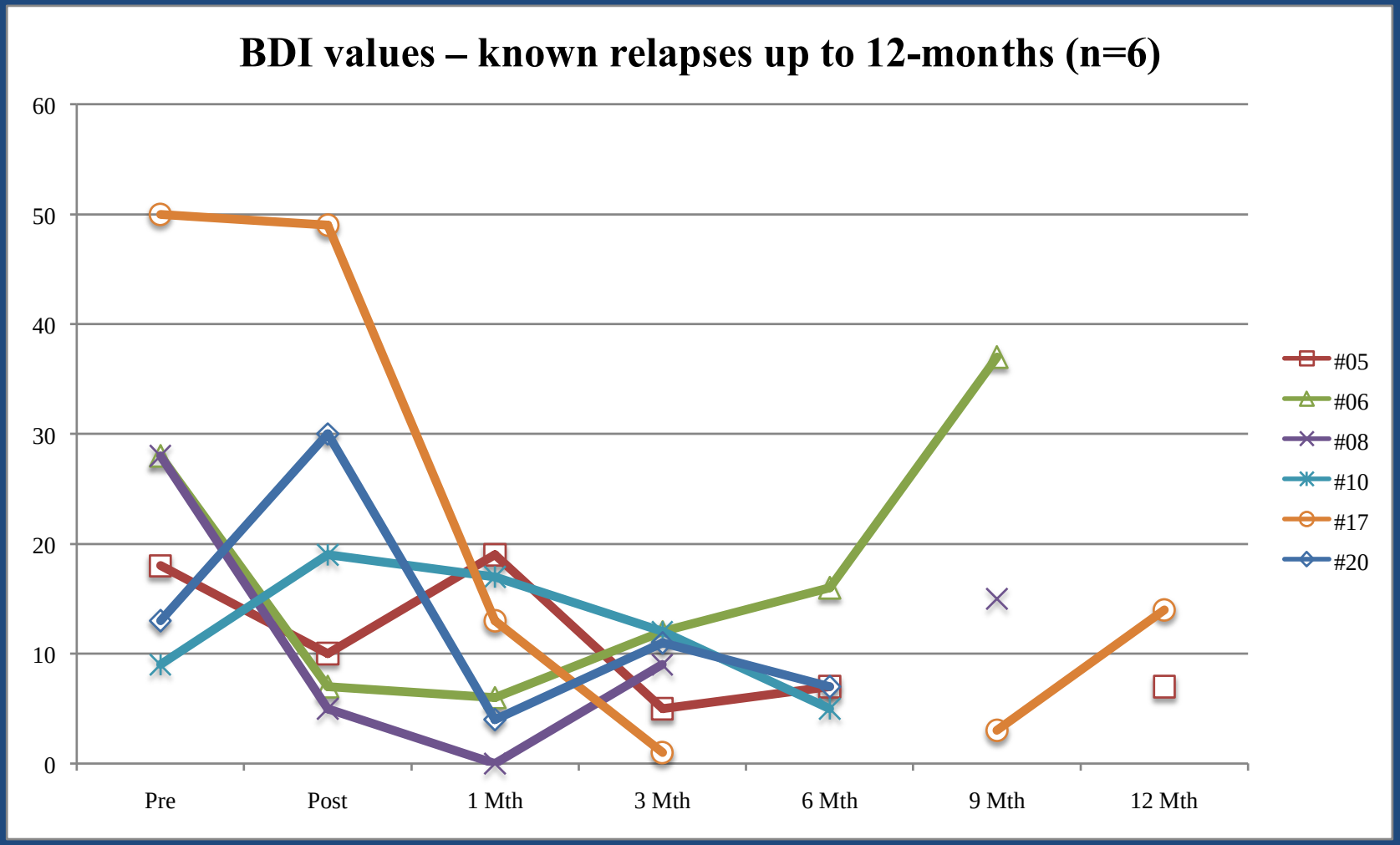
Figure 2: Monthly BDI scores for non-relapsed subjects at 12-months post ibogaine treatment (n=6)



Monthly BDI scores

BDI – Known relapsed subjects

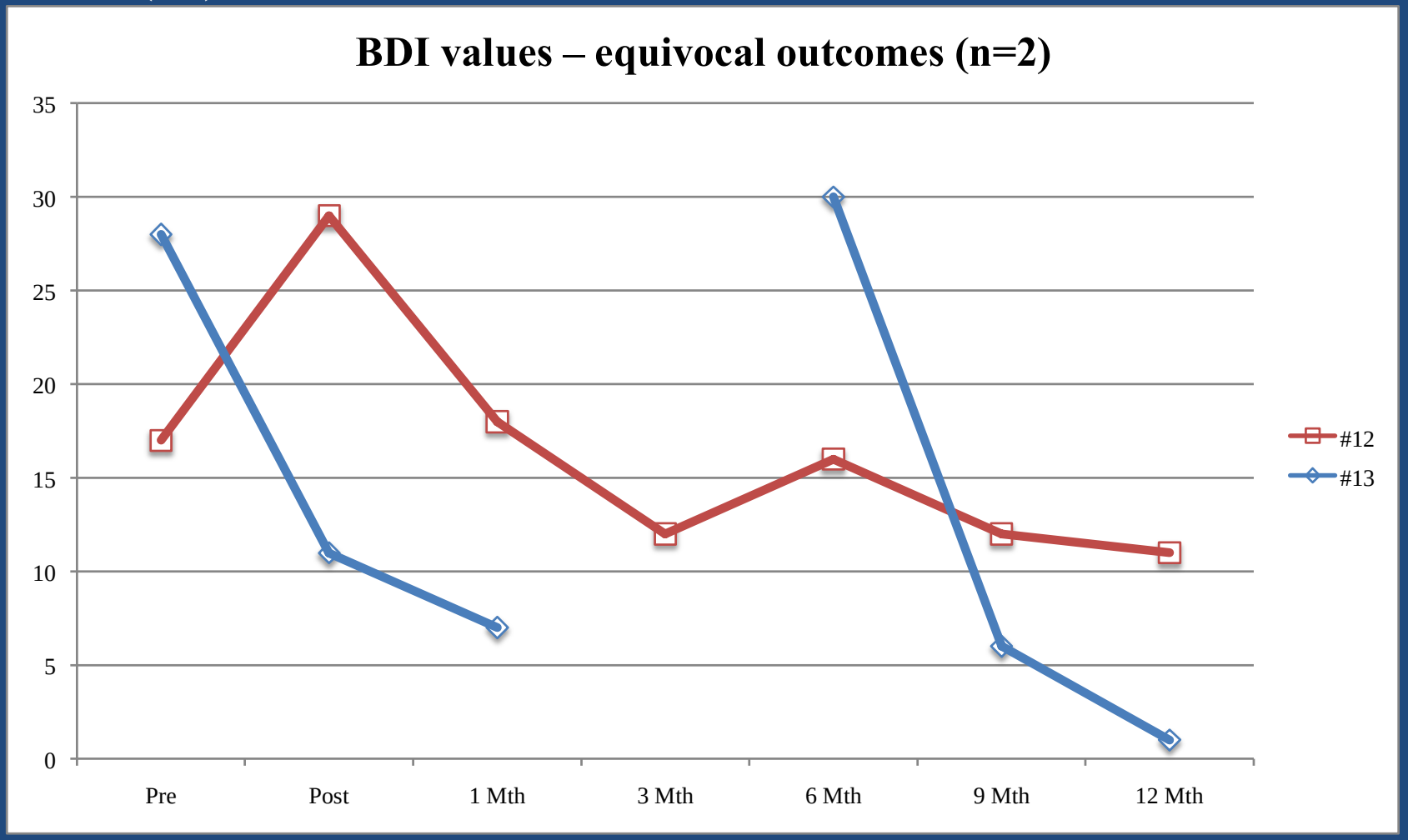
Figure 3: Monthly BDI scores for relapsed subjects at 12-months post ibogaine treatment (n=6)



Monthly BDI scores

BDI – Equivocal results

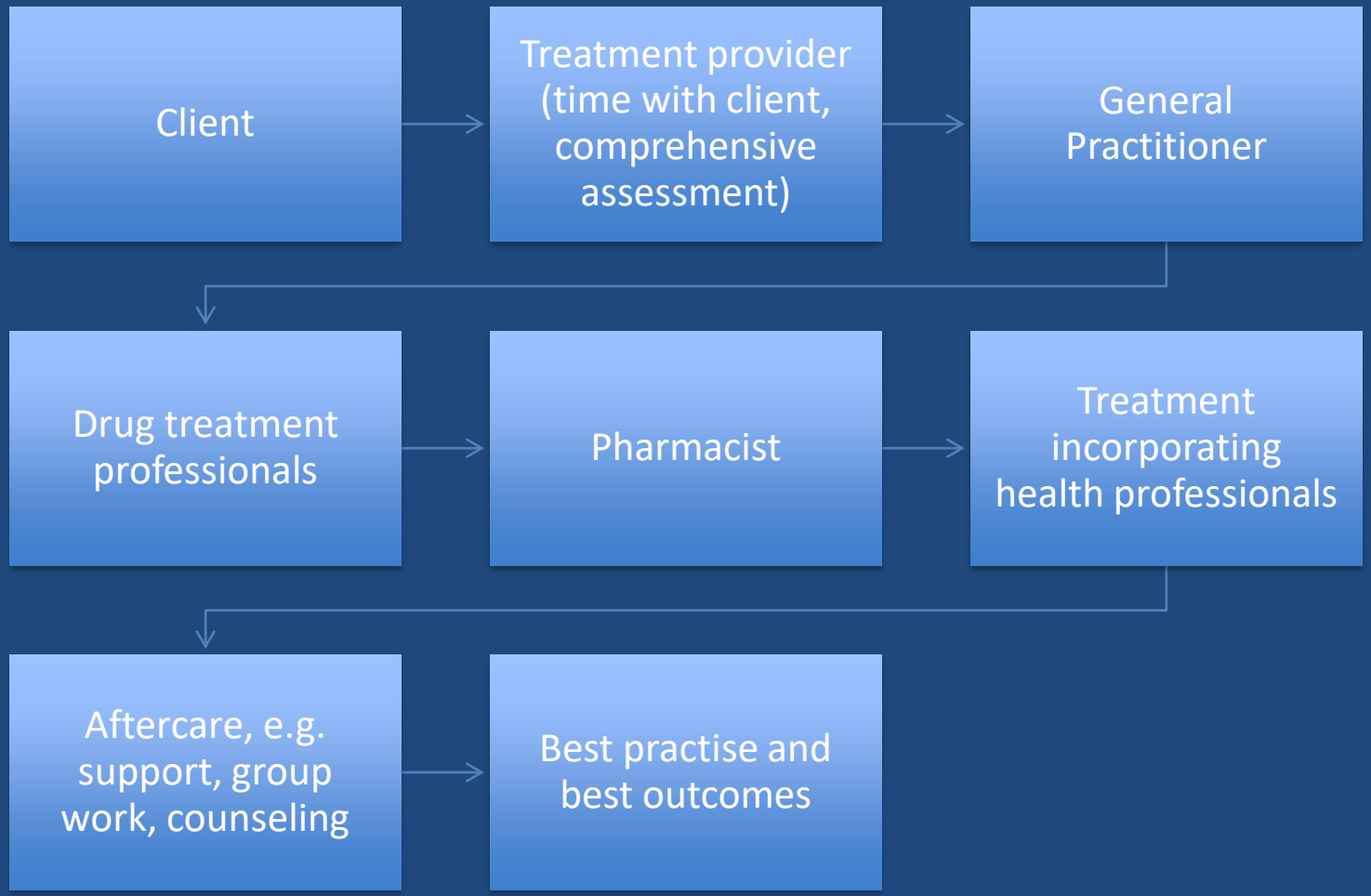
Figure 3: Monthly BDI scores showing equivocal results for subjects at 12-months post ibogaine treatment (n=2)



Monthly BDI scores

Available on Prescription in New Zealand

Promotes integrated care



Therefore, ibogaine treatment outcomes are NOT determined solely by ibogaine and client motivation, but rather reflect the CONTEXT and STYLE of treatment

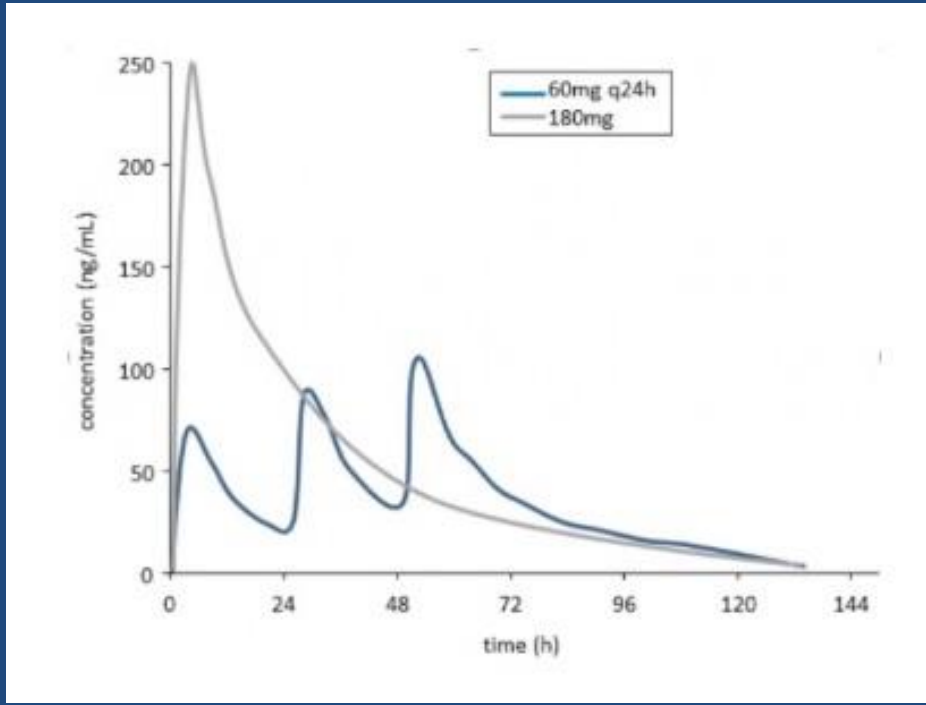
A death in treatment–we know there are risks

- 19 fatalities (1990-2008) temporally associated with ibogaine (Alper et al., 2012)
  - Co-morbidities, e.g. cardio-vascular, seizures associated with alcohol and benzo withrawal
- The NZ case
  - Patient arrives a day for tx heavily drug affected
    - There's a decision to treat
  - In the NZ case the treatment provider (an experienced emergency doctor) was adjudged in breach of his duty of care
  - NZ coroner "strong possibility…cause of death was related to ibogaine ingestion and...cardiac arrhythmia"

Responding to risk

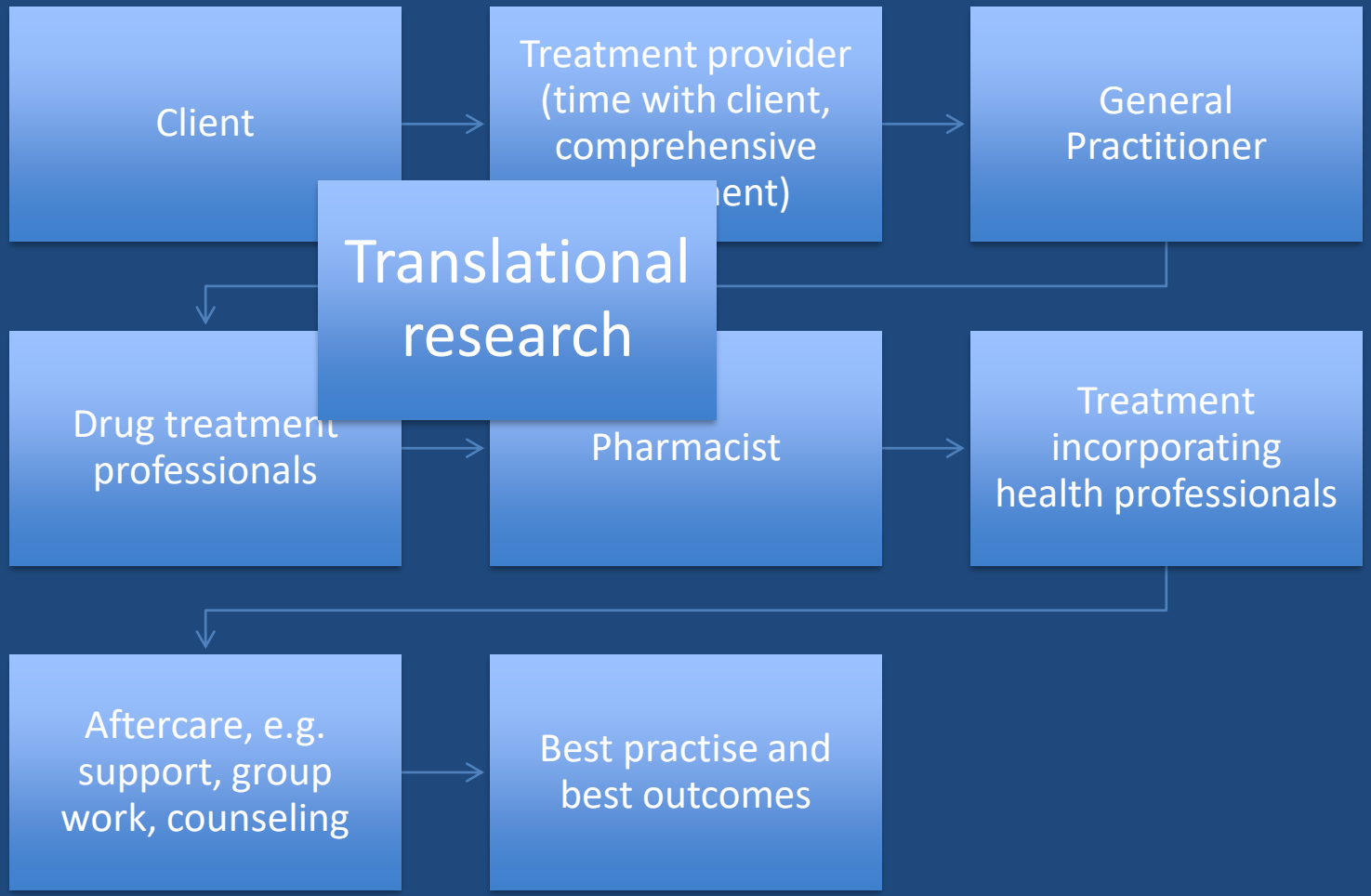
- Jeff Kamlet: “patient selection, patient selection, patient selection”
  - https://www.youtube.com/watch?v=Nd7ljxttGZ8

- Paul Glue and colleagues
  - Ascending dose study (Glue, Winter et al., 2015)
  - CYP2D6 (Glue, Lockhart et al., 2015)



Source: Glue, P. (2017). http://chacruna.net/benefits-risks-potentials-of-mainstreaming-ibogaine-treatment/

Integrated care



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Acknowledgements

The Participants

Sponsors

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