

Adjunctive Nabilone
in Cancer
Pain & Symptom Management

Vincent Maida

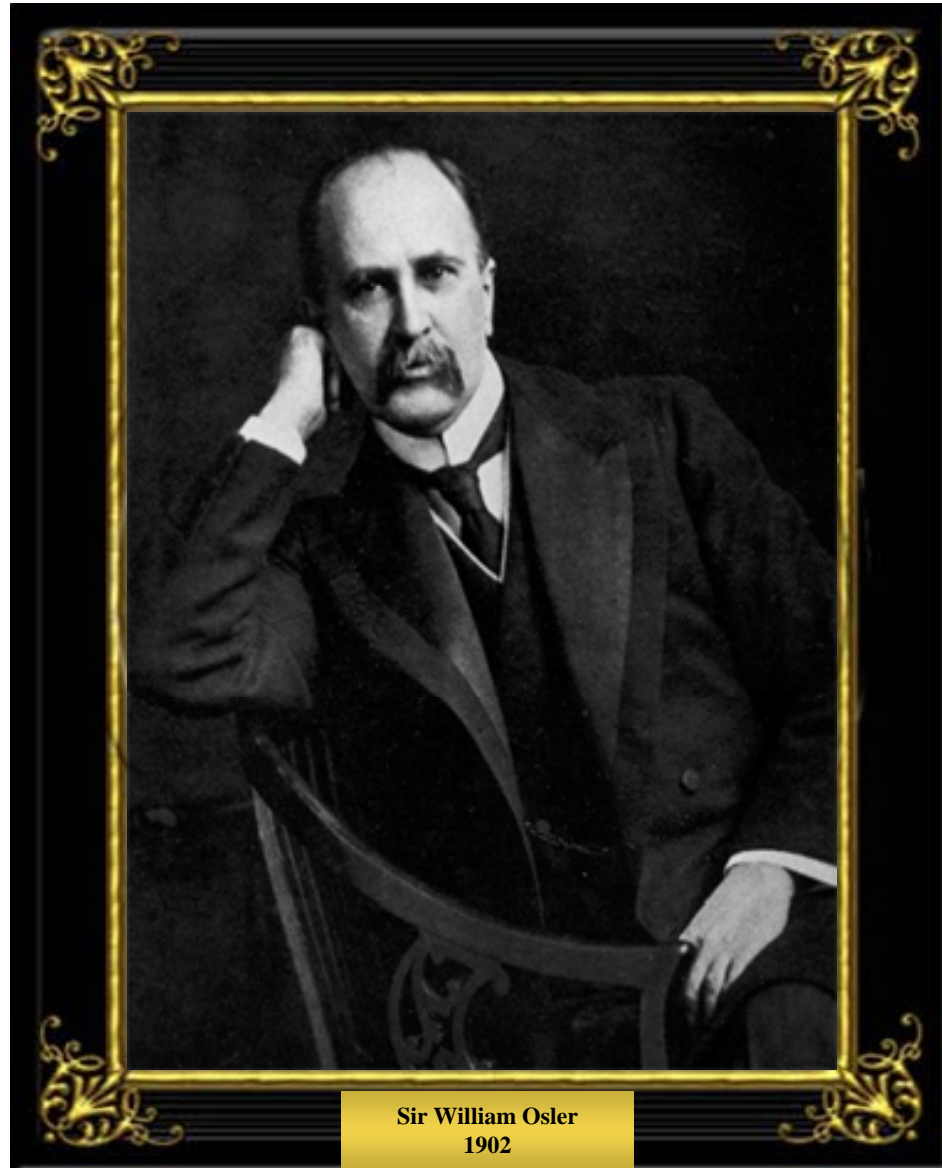
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Disclosure

Advisory Board & Speaker Bureau Membership

- Bayer { International }
- SYSTAGENICS Wound Management
- KCI
- Pfizer
- Pharmascience
- Purdue
- Smith & Nephew { International }
- Valeant { International }
- Wyeth
- Coloplast
- EUROMED { International }
- MEDA Pharma { International }





Sir William Osler
1902

Cannabinoids

◆ Botanical

- Marijuana
- Hashish

◆ Endogenous

- Anandamide
- 2-AG
- PEA

◆ Pharmaceutical

- Cesamet ®
- Marinol ®
- Sativex ®

TABLE 2. Localisation and characteristics of CB1 and CB2 receptors^{19,23}

	neuronal	non-neuronal
G-protein-coupled receptor	CB1	CB2
location	CNS >> periphery basal ganglia hippocampus cerebral cortex cerebellum spinal cord afferent nociceptors	periphery >> CNS spleen tonsils mast cells macrophages lymphocytes microglia
function	neuromodulatory	immunomodulatory
endogenous agonist	anandamide 2-arachidonoylglycerol (2-AG)	palmitoyl-ethanolamide (PEA)
exogenous agonist	THC	THC, CBD
antagonist	SR141716 (rimonabant)	SR144528

CBD = cannabidiol; THC = delta-9-tetrahydrocannabinol

Goals of Observational Study

◆ Primary

- Effect of Nabilone on pains scores
- Effect of Nabilone on Opioid and adjuvant utilization

◆ Secondary

- Effect of Nabilone on other ESAS parameters
- Effect of Nabilone on other drug utilization

Methods to reduce Selection Bias & Confounding

- ◆ Propensity scoring
- ◆ Multivariable regression modeling
- ◆ Instrumental variables

Propensity scoring

- ◆ One of many techniques used to analyze observational data.
- ◆ Method for adjusting for confounding factors in non-randomized observational studies.
- ◆ Involves logistic regression analysis.
- ◆ A collection of covariates is replaced by a single covariate.

Evidence-Based Medicine

- ◆ Level I Evidence from at least one properly designed RCT.
- ◆ Level IIa Evidence from well designed controlled studies without randomization.
- ◆ Level IIb Evidence from well designed cohort or case control analytical studies, preferably more than one centre or research group.
- ◆ Level IIc Evidence from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this level of evidence.
- ◆ Level III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Baseline Features

	Nabilone n=47	Non-nabilone N=65	<i>P</i> -value
Age (mean)	67.0	71.6	0.054 ¹
Gender (male/female)	29/18	36/29	0.56 ²
Race (Caucasian/Non)	45/2	59/6	0.46 ²
PPSv2	56.0	56.2	0.93 ¹
# Co-morbidities	7.6	8.7	0.08 ¹

1 Independent samples t-test

2 Pearson χ^2 test with continuity adjustment

Primary Diagnosis at Baseline

Primary Diagnosis	Nabilone n=47 No. (%)	Non-nabilone N=65 No. (%)
GI	13 (27.7)	15 (23.1)
Lung	10 (21.3)	20 (30.7)
GU	7 (14.9)	7 (10.8)
Breast	3 (6.4)	5 (7.6)
H + N	1 (2.1)	1 (1.5)
GYN	2 (4.3)	4 (6.1)
Haem/Lymphatic	2 (4.3)	4.5 (7.6)
Other	9 (19.1)	8 (12.3)

$P=0.8733$ (Fisher test)



**Edmonton Symptom Assessment System:
Numerical Scale**
Regional Palliative Care Program

Please circle the number that best describes:

No pain	0	1	2	3	4	5	6	7	8	9	10	Worst possible pain
Not tired	0	1	2	3	4	5	6	7	8	9	10	Worst possible tiredness
Not nauseated	0	1	2	3	4	5	6	7	8	9	10	Worst possible nausea
Not depressed	0	1	2	3	4	5	6	7	8	9	10	Worst possible depression
Not anxious	0	1	2	3	4	5	6	7	8	9	10	Worst possible anxiety
Not drowsy	0	1	2	3	4	5	6	7	8	9	10	Worst possible drowsiness
Best appetite	0	1	2	3	4	5	6	7	8	9	10	Worst possible appetite
Best feeling of wellbeing	0	1	2	3	4	5	6	7	8	9	10	Worst possible feeling of wellbeing
No shortness of breath	0	1	2	3	4	5	6	7	8	9	10	Worst possible shortness of breath
Other problem	0	1	2	3	4	5	6	7	8	9	10	

Patient's Name _____

Date _____ Time _____

Complete by (*check one*)

- Patient
- Caregiver
- Caregiver assisted

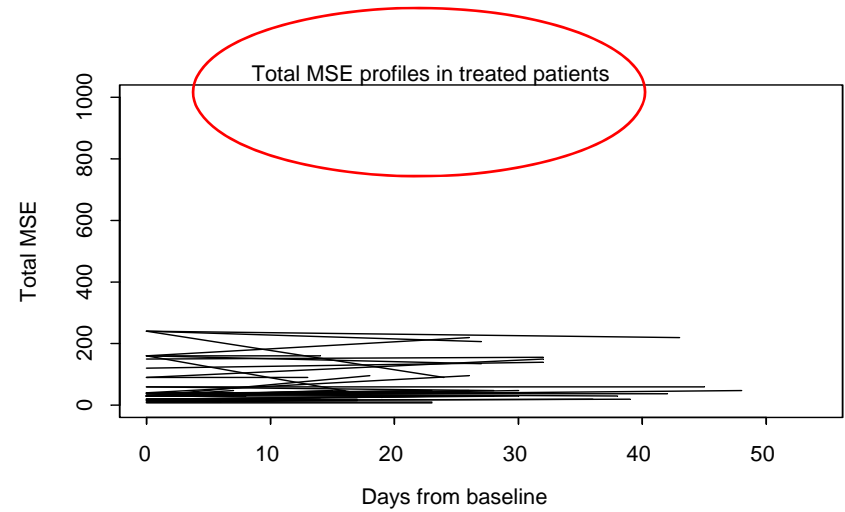
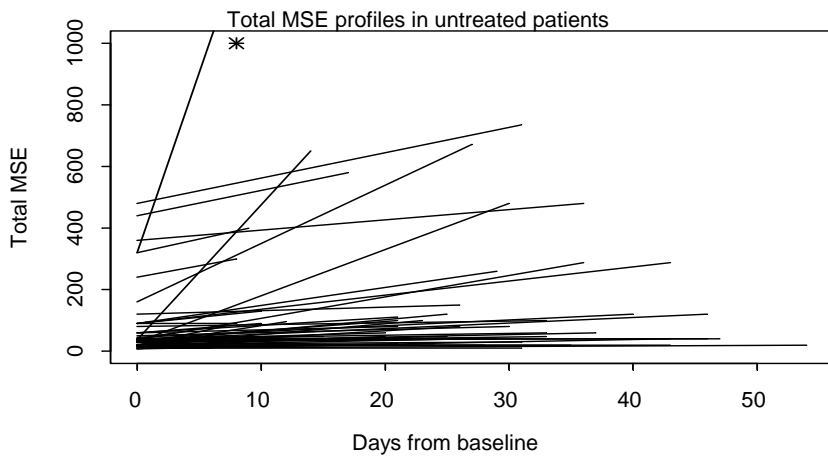
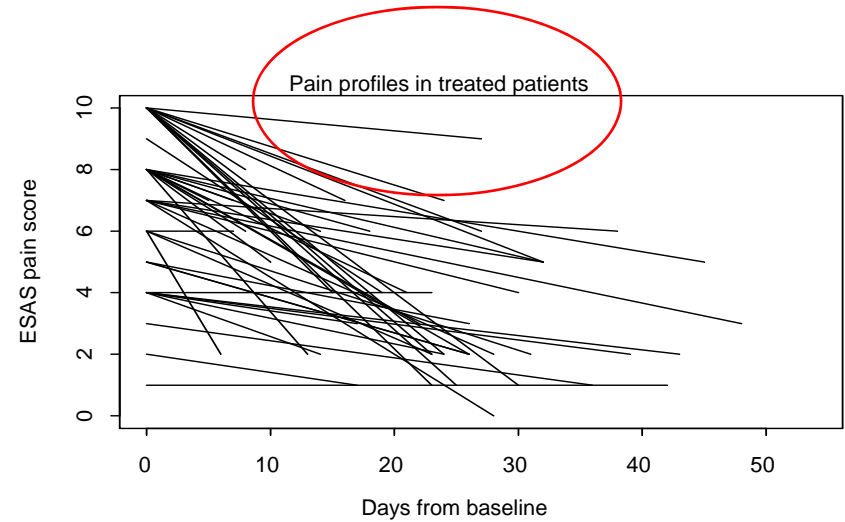
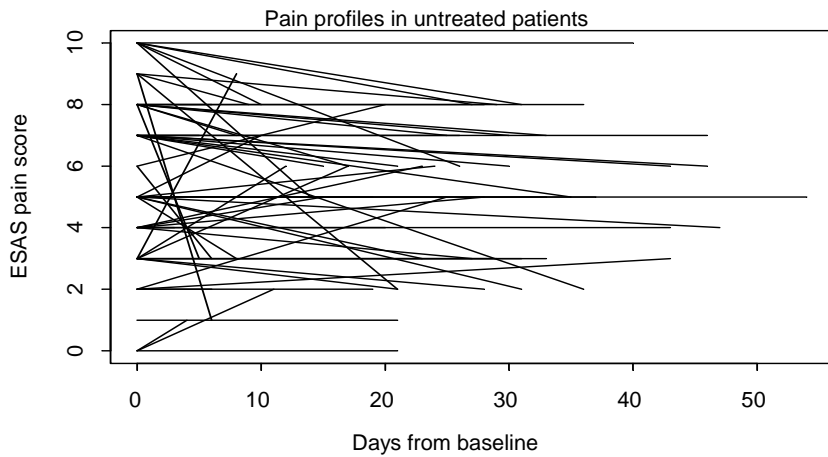
Baseline ESAS Scores

	Nabilone N=47	Non-nabilone N=65	<i>P</i> -value*
Pain	7.1	5.6	0.0029
Tiredness	5.7	4.8	0.0109
Nausea	4.7	3.4	0.0024
Depression	5.1	3.5	0.0003
Anxiety	5.2	4.0	0.0038
Drowsiness	4.4	3.4	0.0041
Appetite	6.0	4.8	0.0113
Well-being	5.7	4.3	0.0010
Shortness of Breath	2.8	3.2	0.2765
Total Distress	46.7	37.1	0.0002

* t-test

Follow-up

	Nabilone Treated N=47	Non-nabilone treated N=65
Mean (days)	23.8	23.2
Median (days)	24	23
Quartile 1 (days)	16.5	12
Quartile 3 (days)	30	31



Pain

	Baseline (first and third QTL)	Fitted for Nabilone patients	Fitted for Non-nabilone patients	Difference	Propensity adjusted P- value for difference
Pain				-2.5	<0.0001
	4	2.0	4.5		
	8	3.7	6.2		
Total MSE's					
	20	23.5	42.2	-18.7	
	60	63.3	113.4	-50.4	
Log (Total MSE's)				-0.58	<0.0001
	3	3.2	3.7		
	4.09	4.1	4.7		

Propensity Adjusted Data

ESAS Parameter	Baseline	Fitted* follow-up Nabilone N=47	Fitted* follow-up Non-nabilone N=65	Difference	Propensity adjusted P-value
Pain	6.3	3.0	5.5	-2.5	<0.0001
Tiredness	5.2	6.1	6.1	0.0	0.9782
Nausea	3.9	2.0	3.8	-1.8	<0.0001
Depression	4.2	3.7	4.0	-0.3	0.4110
Anxiety	4.5	3.6	4.5	-0.9	0.0284
Drowsiness	3.8	5.2	5.1	0.1	0.8553
Appetite	5.3	5.1	6.1	-1.0	0.0512
Well-being	4.9	6.0	5.5	0.5	0.2417
Shortness of breath	3.0	3.6	3.2	0.4	0.2479
Total distress	41.1	38.1	43.8	-5.7	0.0208

*According to multiple regression model with treatment status, baseline status, and propensity scores as predictors.

Primary Drug Utilization

Drug	Baseline Dosage (mg/day)	Follow-up Nabilone treated (mg/day) n=47	Follow-up Non-nabilone treated (mg/day) n=65	<i>P</i> -value (propensity adjusted)
Nabilone	0	1.79	0	
Total MSE's	38.2	42.2	75.6	
Log (Total MSE's)	3.6	3.7	4.3	<0.0001

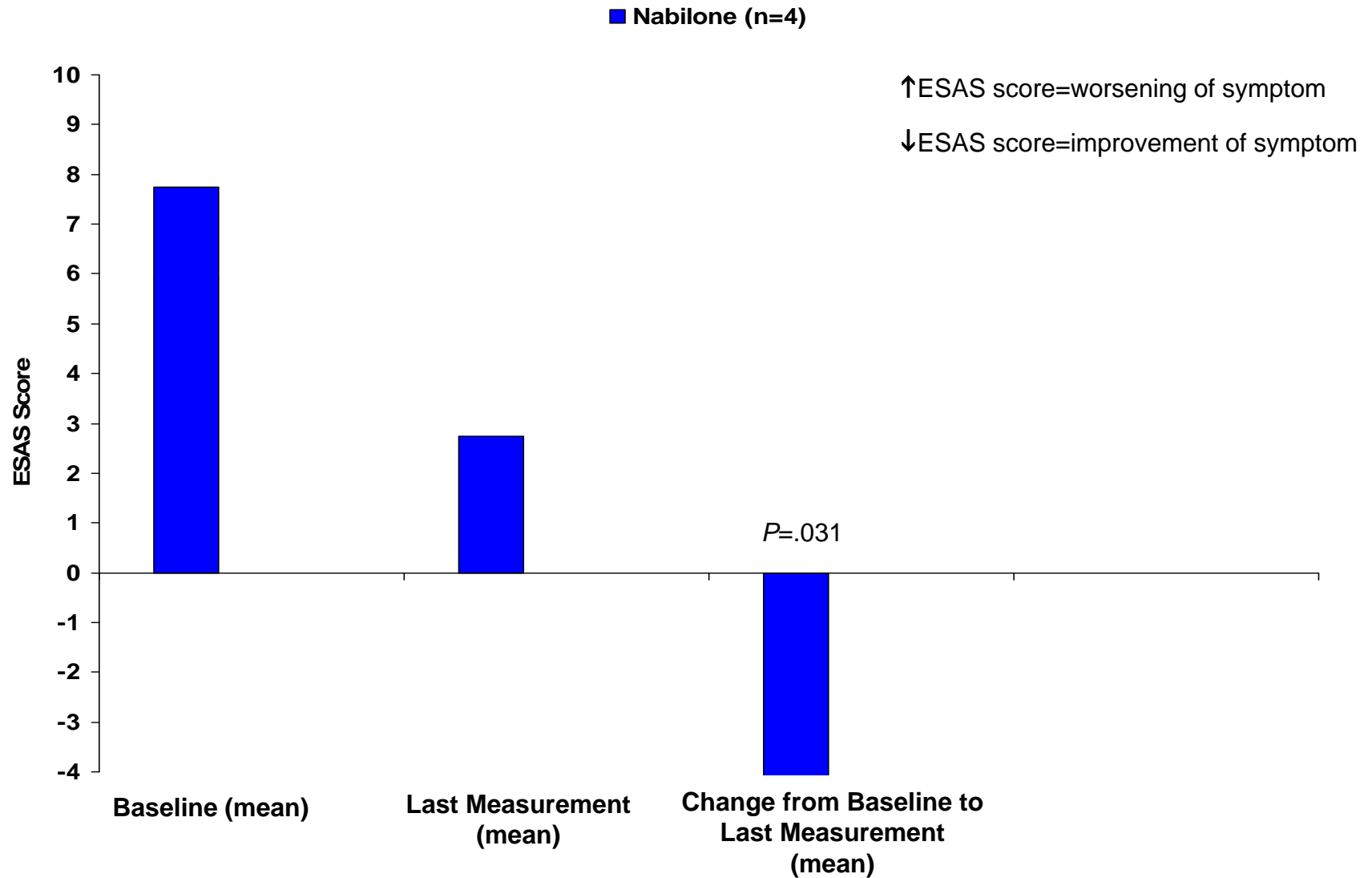
Secondary Drug Utilization

Drug	Baseline	Nabilone treated using drug at F/U Proportion(%)	Non-nabilone using drug at F/U Proportion(%)	P-value (propensity adjusted)
NSAID				<0.0001
	No	0/28 (0)	2/45 (4.4)	
	Yes	0/19 (0)	20/20 (100)	
TCA				<0.0001
	No	0/37 (0)	3/50 (6.0)	
	Yes	1/10 (10)	15/15 (100)	
Gabapentin				0.0008
	No	0/38 (0)	8/58 (13.8)	
	Yes	9/9 (100)	7/7 (100)	

Secondary Drug Utilization

Drug	Baseline	Nabilone treated using drug at F/U Proportion(%)	Non-nabilone using drug at F/U Proportion(%)	P-value (propensity adjusted)
Dexamethasone				0.0005
	No	0/28 (0)	11/49 (22.4)	
	Yes	14/19 (73.7)	16/16 (100)	
Metoclopramide				0.0070
	No	0/20 (0)	4/25 (16.0)	
	Yes	25/27 (92.6)	40/40 (100)	
Ondansetron				0.0011
	No	0/43 (0)	0/60 (0)	
	Yes	0/4 (0)	5/5 (100)	

Paraneoplastic Night Sweats



Summary

**“BROAD SPECTRUM OPTIMIZER
OF
PAIN & SYMPTOM MANAGEMENT”**

Summary

- ◆ Nabilone usage associated with greater improvement in pain scores.
- ◆ Nabilone usage associated with improvements in nausea, anxiety, and overall distress.
- ◆ Nabilone usage associated with lower utilization of opioids.
- ◆ Nabilone usage associated with lower utilization of adjuvant analgesics (NSAID's, TCA's, and Gabapentin).



