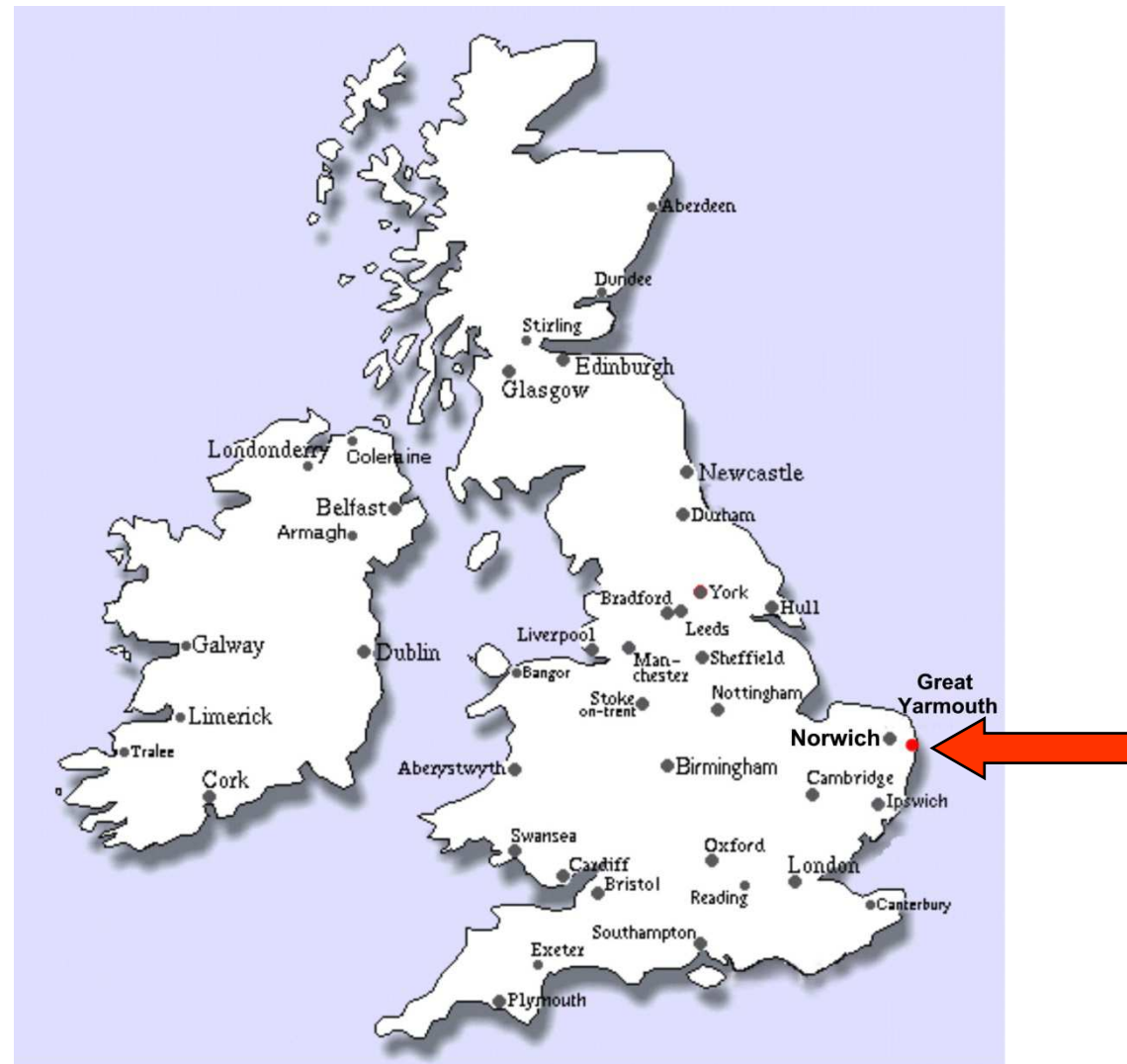


# **The Clinical Management of the Patient using Medicinal Cannabinoids**

El Manejo Clínico Del Paciente Utilizando  
Medicinal Los Cannabinoides

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# My Background

- Specialist in Pain Management (Anaesthetist)
- Started clinical use of Cannabinoids in 1993
- First clinical Trials of Sativex in May 2000
- Treating patients with Cannabinoids since in clinical trials and in ongoing therapy.

# Disclosures

I work for the UK National Health Service

- I am not an employee of any Pharmaceutical company
- I have no stocks or shares in any company
- I have received fees for consultancy and speaking at meetings
- I have taken part in about 20 clinical trials, mostly multicentre for GW Pharma and have been the Chief Investigator on several.
- My research team has been supported by GW Pharma and other pharmaceutical companies

# Program

- Selecting the Patient
- Preparing the Patient
- Managing the Patient
- Problems

# What Are Cannabinoid Medicines?

# Available Cannabinoid Medicines (1)



## NABILONE

THC Alternative  
Oral



## DRONABINOL

THC – Synthetic  
Oral



## SATIVEX

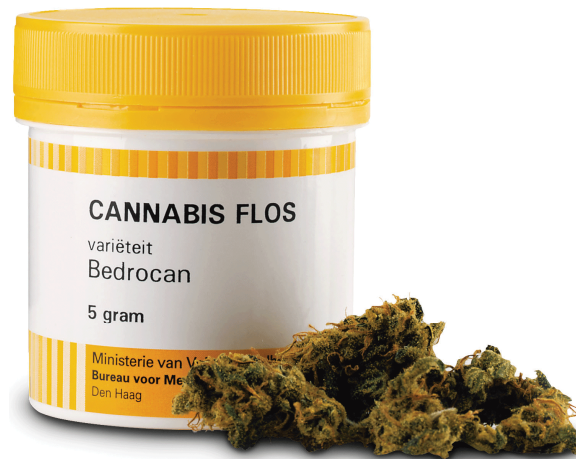
THC/CBD –  
Oro-Mucosal spray

# Available Cannabinoid Medicines (2)



**TINCTURE**

Oral THC



**BEDROCAN**

Herbal Cannabis -  
Standardised



**STREET  
CANNABIS**

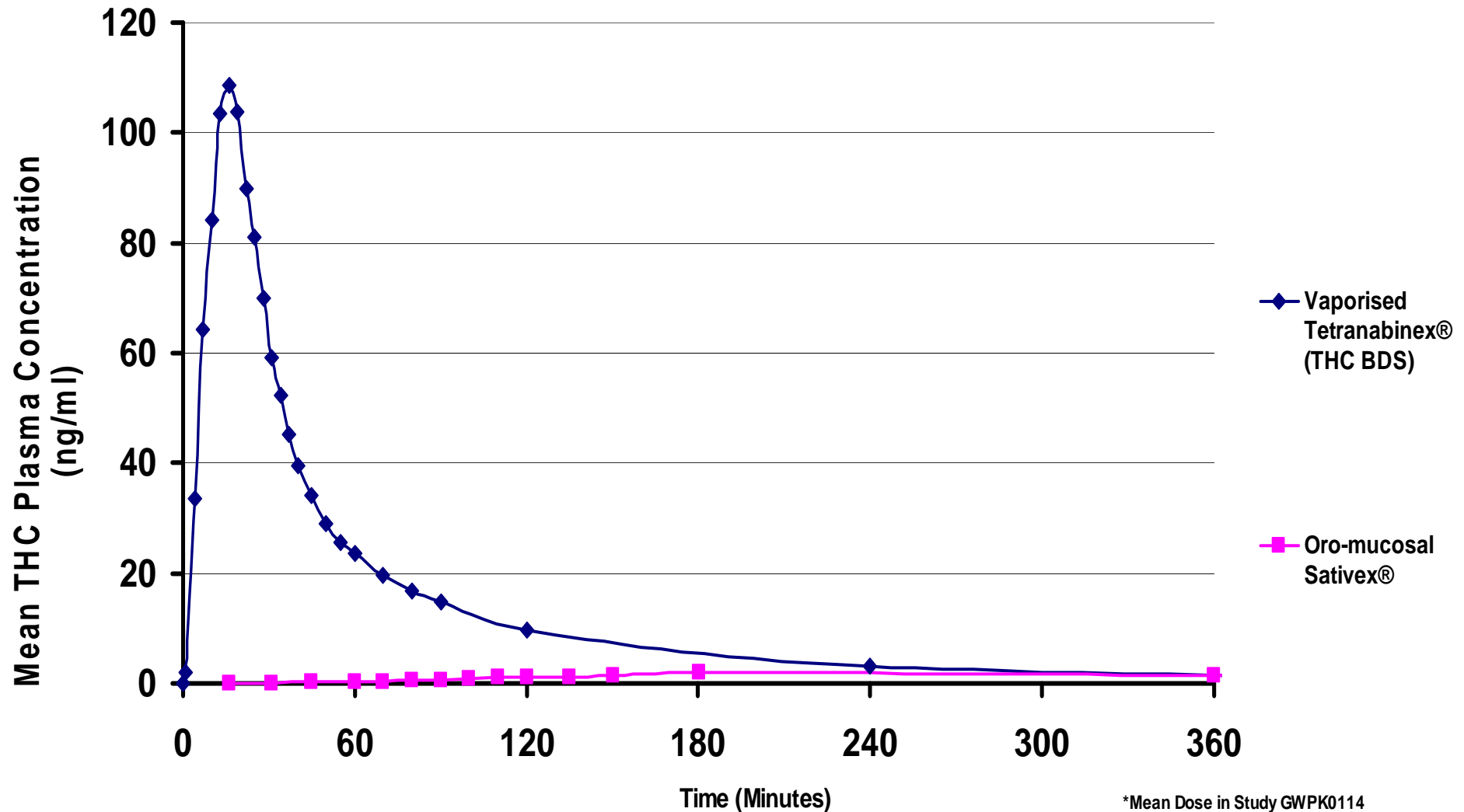
Herbal Cannabis



- Pharmacokinetics
  - What the body does to the drug
    - How high the plasma levels are
- Pharmacodynamics
  - What the drug does to the body
    - Effects and side-effects

# Comparison of THC plasma levels following administration of 6.65mg\* of vaporised THC or 4 sprays of Sativex®

(10.8mg THC & 10mg CBD#)



\*Mean Dose in Study GWPK0114

#Mean Dose in Study GWPK0215

# Will it Work for Me?

# Efficacy - clinical studies

Study Code	Study Details	Key Efficacy Result	P-value	Reference
<b>Phase II (Randomised, Double-Blind, Placebo Controlled Studies)</b>				
<b>GWN19902</b>	Symptoms of MS and other nervous system conditions (n=25)	Improvement in Spasticity (VAS)	<0.05	Wade DT et al. Clin Rehab. 2003
<b>GWMS0001</b>	MS Symptoms (n=160)	Improvement in Spasticity (VAS)	0.001	Wade DT et al. Multiple Sclerosis 2004
<b>Phase III (Randomised, Double-Blind, Placebo Controlled Studies)</b>				
<b>GWCL0403</b>	MS, Spasticity (n=337)	Improvement in Spasticity (NRS)	0.22 0.035 (PP)	Collin C et al. Neurol Res. 2010
<b>GWMS0106</b>	MS, Spasticity (n=189)	Improvement in Spasticity (NRS)	0.048	Collin C et al. Eur J Neurol. 2007
<b>GWSP0604</b>	MS, Spasticity (n= (A) -572, (B) - 241)	Improvement in Spasticity (NRS)	p=0.0002	Novotna J et al. Eur J Neurol 2011
<b>GWSP0702</b>	MS, Spasticity (n=36) <i>Randomised Withdrawal Study Design</i>	Time to treatment failure (NRS)	p=0.013	Notcutt W et al. Multiple Sclerosis 2011
<b>Long Term Extension Studies (Open Label)</b>				
<b>GWMS0001</b>	Open label extension study (n=137)	Long term efficacy(NRS)	N/A	Wade DT et al. Mult Scler 2007
<b>GWEXT0102</b>	Open label extension study (n=507)	Long term efficacy(NRS)	N/A	

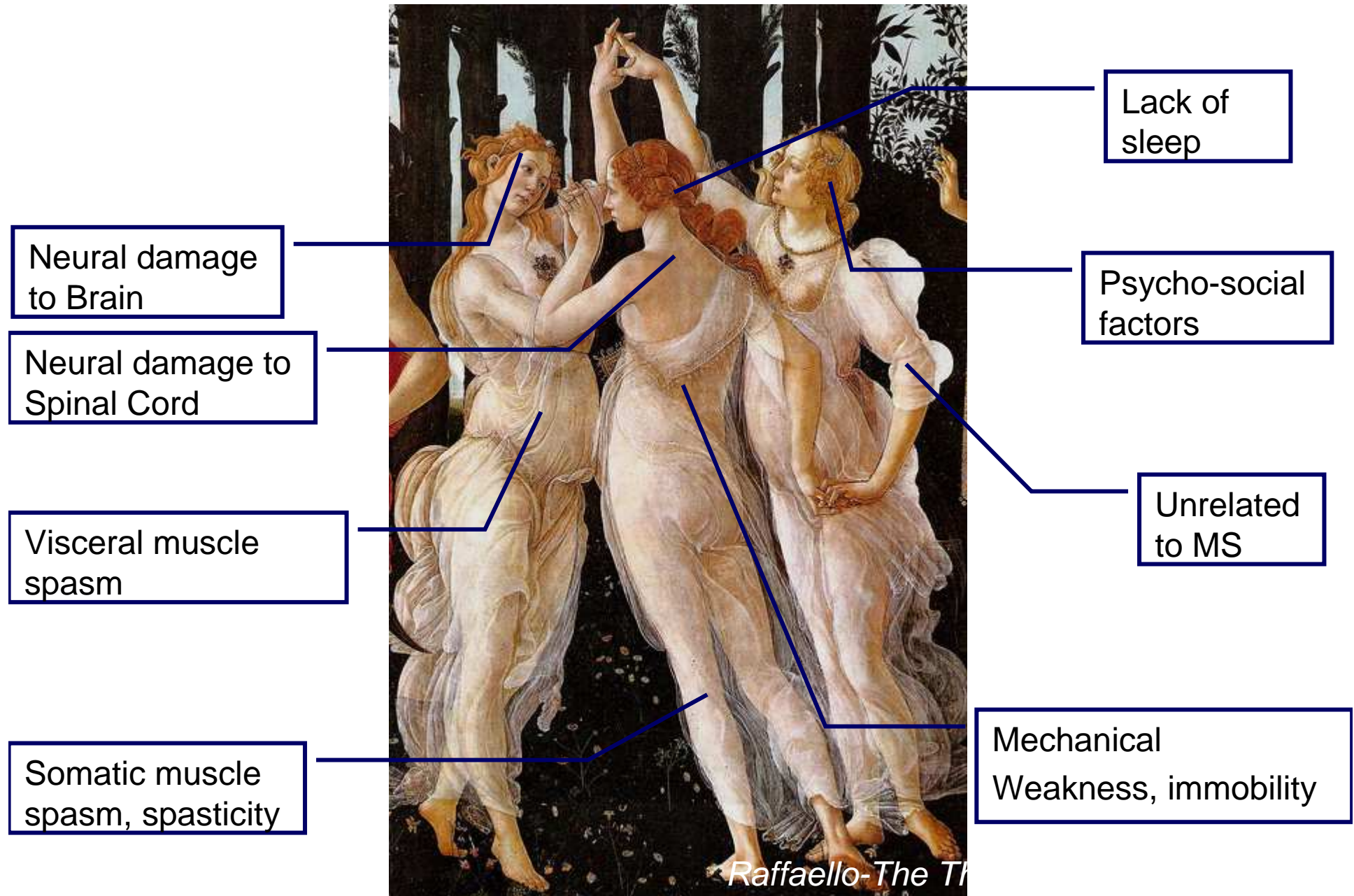
# Pain

- Neuropathic Pain
  - Multiple Sclerosis
  - Brachial Plexus avulsion
  - Trigeminal Neuralgia
- Nociceptive
  - Multiple Sclerosis spasticity and spasms
  - Rheumatoid Arthritis
  - Fibromyalgia - ? Endocannabinoid Deficiency syndrome
- Cancer Pain

# Complex not Simple Problems

- “End-of-the-Road”
  - Add on therapy when all others are ineffective, insufficient or not tolerated (eg. Baclofen, Tizanidine Gabapentin, Opiates)
  - Will try anything for relief

# Origins of Pain in MS



# Am I a Suitable?



# Suitability? : General Factors

- Age
  - >18 years
  - Elderly
- Weight/build
- Frailty
- Pregnancy –No!

# Co-Morbidity: Sensible Cautions

- Cardiovascular Disease
  - Postural Hypotension
  - Arrhythmias
- Respiratory Disease
  - COPD – late stage
- Liver, Kidney
  - Advanced Failure
- No known drug interactions
  - Additive effects

# Co-Morbidity: Psychiatric

- Nervous System
  - Psychosis, Endogenous Depression, Personality disorders
  - Cognitive problems (MS, Dementia etc)
  - Addiction/Abuse/Alcohol problems

# “I have used cannabis before”.

- Previous cannabis use
  - What is acceptable?
    - Occasional recreational use when young
    - Smoking a cannabis cigarette at night to relieve symptoms
  - **No**
    - **Smoking cannabis 6x /day**
    - **Regular recreational use**
    - **Dependency history**

# How do I Use It?

# Using Sativex

- Using Sativex
  - How and where to spray
  - Keep the spray in the mouth for at least 5 minutes

# Dosing → Titration

- **Titrating**
  - 1 spray/day increase

DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14
MORNING	0	0	0	0	1	1	1	2	2	3	3	4	4	5
EVENING	1	1	2	2	2	3	4	4	5	5	6	6	7	7
TOTAL	1	1	2	2	3	4	5	6	7	8	9	10	11	12

– Average Daily Dose →



- **Customising to the pattern of pain/problem**
  - Daytime
  - Night-time
  - 4 hourly interval
  - Break through Pain
- **Maximum Dose**
  - Up to 12 sprays/day. Little benefit from increasing further

# What are the Side Effects?



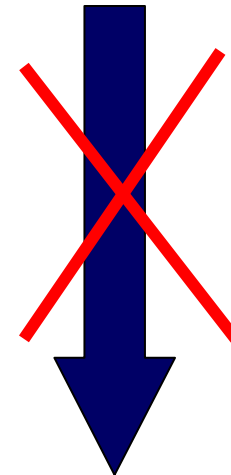
# Side-Effects

- Common CNS Side Effects
  - Drowsy, Dizzy, Light-Headed
    - Likely to have used other Psychoactive drugs and had S/E
  - **Importance of Titration**
  - Too much Sativex
    - Go and lie down
    - Passes off in 2-3 hours

# Unrelieved Symptoms → Side-Effects

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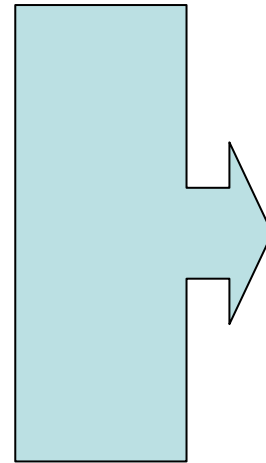
*Immobile from MS*



*Immobile from Treatment*

# No evidence of mood change

- Beck Depression Inventory
- Hospital Anxiety and Depression Scale
- Intoxication VAS
- Anxiety/Depression in EQ-5D
- Cognitive performance



**No difference between  
Sativex/Nabiximols and  
placebo**

Schoedel et al. Human Psychopharmacology: Clinical and Experimental. 2011 26 224–236

Aragona M et al. Clinical Neuropharmacology 2009 32,1 41-47

# Less Common CNS Side Effects

- Less Common Side Effects
  - Panic, anxiety
  - Euphoria
- Other Side Effects
  - Addiction
  - Cognitive Impairment, Memory loss
  - Psychosis
    - Look for infection
  - Increased appetite (Munchies)
    - Aggravated Ataxia

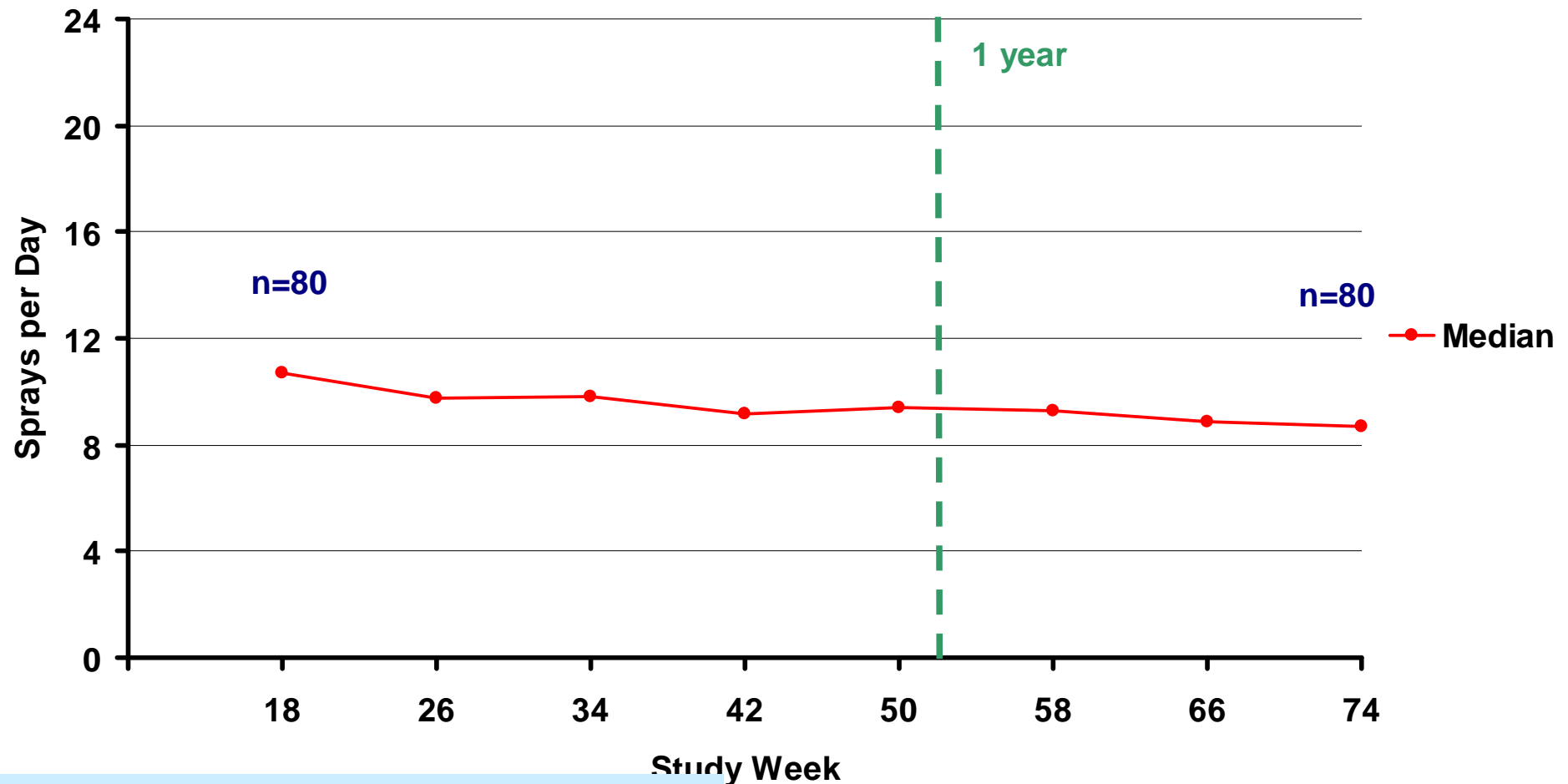


# Using Sativex

- Mouth Problems
  - Unpleasant taste
  - Retching – milk option
  - Dry Mouth
  - Sting, ulcer
  - When to eat or drink
  - High volume of spray



# Sativex: no evidence of tolerance during long-term use



Wade D et al. *Multiple Sclerosis* 2006;12:639-645

# “Can I Drive?”

- The Local Laws
- Other meds
- Distraction by pain, spasms
- Insurance?

# Road Research Laboratory findings

1 “joint” equivalent to get “high”;  
test in a driving simulator:→

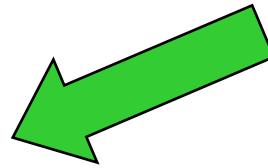
- Reaction times increased slightly
- Tracking tasks are affected
- Aware of impairment,  
therefore drive more slowly  
– unlike alcohol

*UK Transport Research Lab. Report 477,  
2000*



# Influence of Cannabis on Other Activities

- Operating machinery etc.



# Follow up

- How soon?
- Assessment of benefits and side effects
- Long term management
- Other illnesses
- Travelling to other countries

**Re-Assessment: 2-4 weeks**

“It is the small things that make a difference” *JK*

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“Fatigue gone.  
More Energy.  
Only 1 migraine attack.  
Sleep improved.  
Spasms have gone.  
No cramps.  
Nocturia less.  
Balance better.  
Decreased Dysaesthesia.  
Able to move and dress more easily”

# Evaluating Effects

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## Every Patient is Different in Symptoms and Response

- Areas to evaluate:
  - Pattern of Dosing
  - Target and other symptoms
  - Patient Activities of Daily Living
  - Carer Activities of Daily Living
  - Side-Effects
  - Changes to Other Medications
- Consider NRS (Numerical Rating Score 0-10), Verbal Rating Score, or descriptive etc.

# Assessment

- **Target Symptom Assessment:**

- Spasticity
- Spasms
- Pain Problems
- Sleep
- Bladder dysfunction
- Other

- **Patient's Activities**

- Sleep
- Walking
- Transferring
- Dressing
- Washing
- Sex
- Other

NAME Reg. No DoB		Sex M/F	CANNABINOID ASSESSMENT SCHEDULE				
			Titration	Admin	Driving etc.	Travel	Neighbour
			Common S/E	Psychosis	Overload	Allergy	
	<b>CHECK: INFO GIVEN</b>		Item				
	Diagnosis						
	Date						
	Cannabinoid: STVX   Nab						
	Dosing		Morning				
	Pattern of Dosing		Midday				
	Sprays/mg		Evening				
			Night				
			Top-Up				
	<b>Assessment Symptoms</b> Eg. NRS 0-10 or similar						
	Select From:						
	Spasticity						
	Spasms						
	Pain 1						
	Pain 2						
	Dysaesthesia						
	Sleep						
	Distancing						
	Nocturia						
	Other bladder function		Sleep				
	N&V						
	Other						
	<b>Assessment Side Effects</b>						
	Sleepy, Drowsy						
	Dizziness						
Hallucinations,							
Dysphoria							
Oral Mucosa							
Other							
<b>Activities of Daily Living (ADLs)</b>							
Walking							
Transferring							
Standing							
dressing							
Feeding							
<b>Improvements in Carer ADL</b>							
Own Sleep		Sleep					
Transferring							
<b>Changes in Other Medications</b>							
Baclofen, Tizanidine							
Antidepressants							
Gabapentin/Pregabalin/							
Opioids							
Other							
<b>Comments</b>							

- **Pattern of Dosing:**

- Morning Dose
- Midday Dose
- Evening Dose
- Night Dose
- Total/ day (sprays)

- **Carer's ADLs**

- Sleep (carer)
- Dress/ Washing (patient)
- Transferring
- Other

- **Side-Effect Assessment**
- **Medication Changes**

# Carer Fatigue

# Night-time Disturbances for Carers

- Spasms
- Visits to toilet
- Restlessness



# What If...?

- Patient has an injury causing pain
- Patient needs to come into hospital for surgery
- Patient is admitted for a medical emergency
- Patient wants to go abroad on holiday
- Patient wants a break from the medicine

# The Doctors

- Physician issues
  - Helping other prescribers to manage Cannabinoids properly. Problems of bad prescribing as with opiates
  - Problem of status of cannabis in community. Awareness of the local law.
  - Responsibility to advise users of illicit medicinal cannabis
  - Understanding the media and the politicians. Keeping the Medicinal and Recreational apart

# A Long Journey so Far and a Long Way to Go

## Thank You

Further information available from

[willnotcutt@gmail.com](mailto:willnotcutt@gmail.com)