

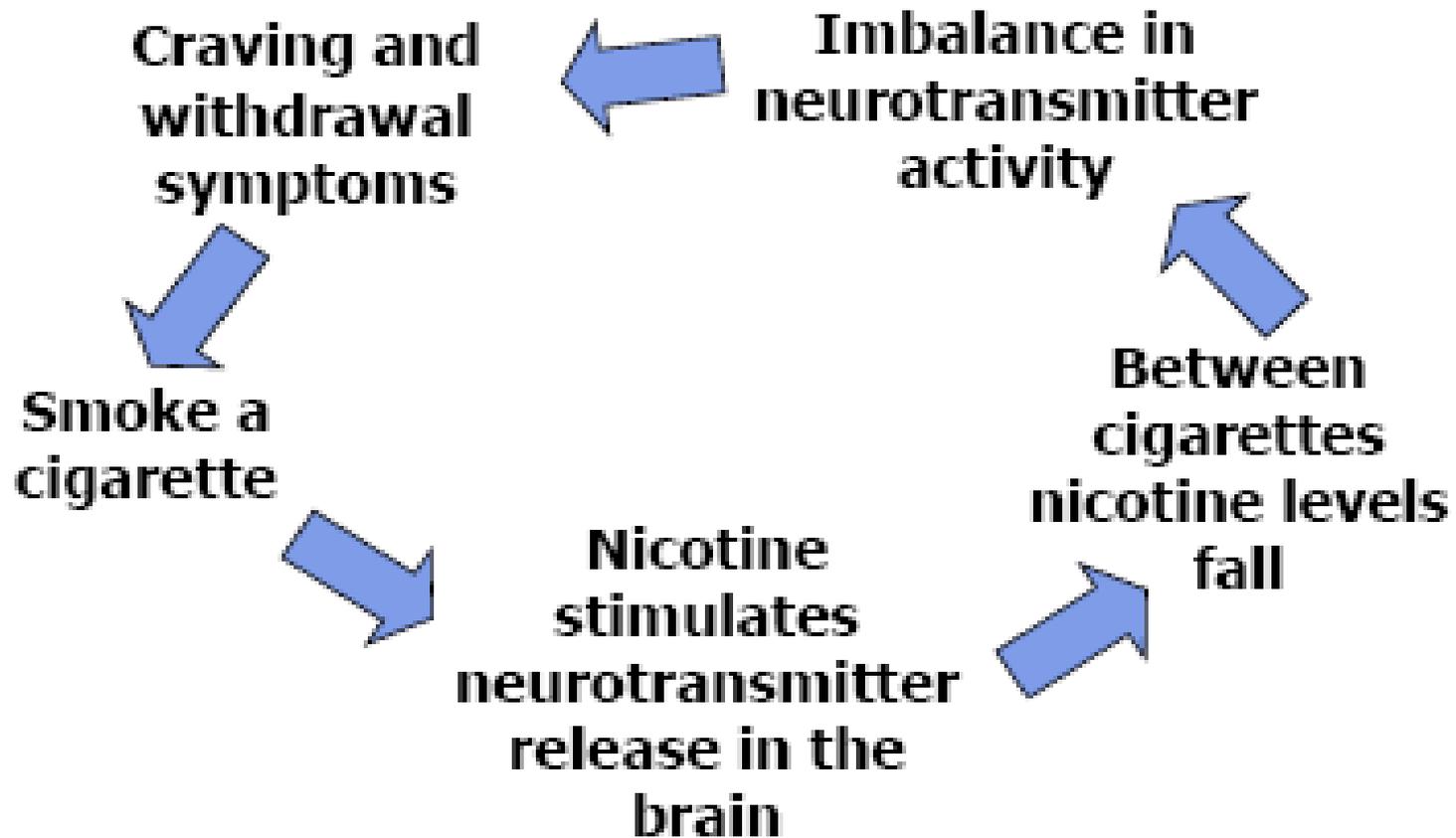
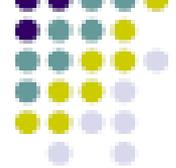
Nicotine replacement therapy

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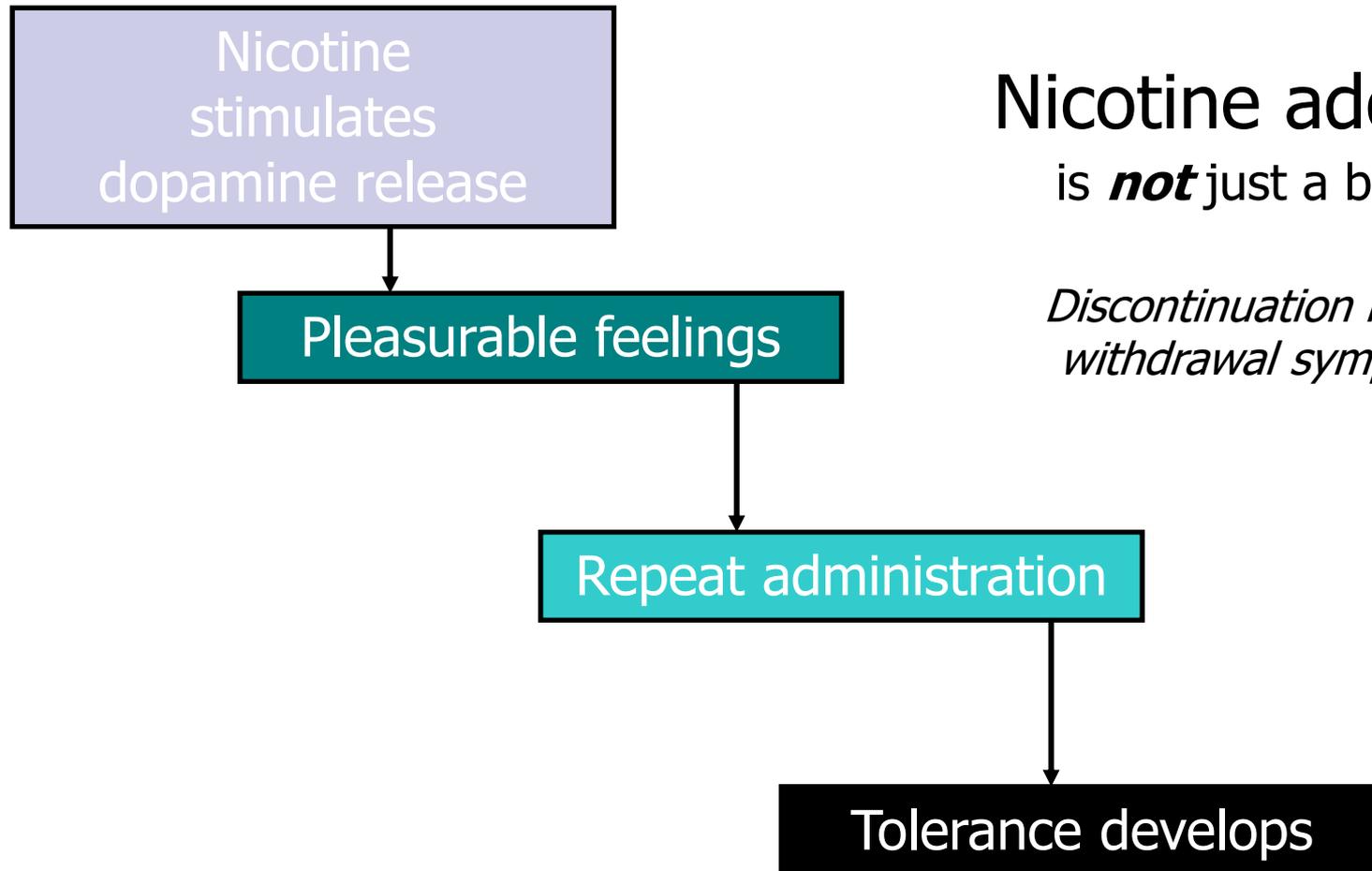
Addiction to nicotine

- An understanding of how nicotine produces addiction and influences smoking behavior provides a necessary basis for smoking cessation therapies.
- Chronic nicotine exposure results in neuroadaptation, that is, the development of tolerance.
- Neuroadaptation is associated with an increased number of brain nicotinic cholinergic receptors.
- Chronic exposure to nicotine also results in changes in gene expression and neural plasticity; which is defined as “ability of the brain to reorganize neural pathways based on new experiences”

Nicotine Addiction



BIOLOGY of NICOTINE ADDICTION: ROLE of DOPAMINE



Nicotine addiction
is ***not*** just a bad habit.

*Discontinuation leads to
withdrawal symptoms.*

DOPAMINE REWARD PATHWAY

Prefrontal cortex

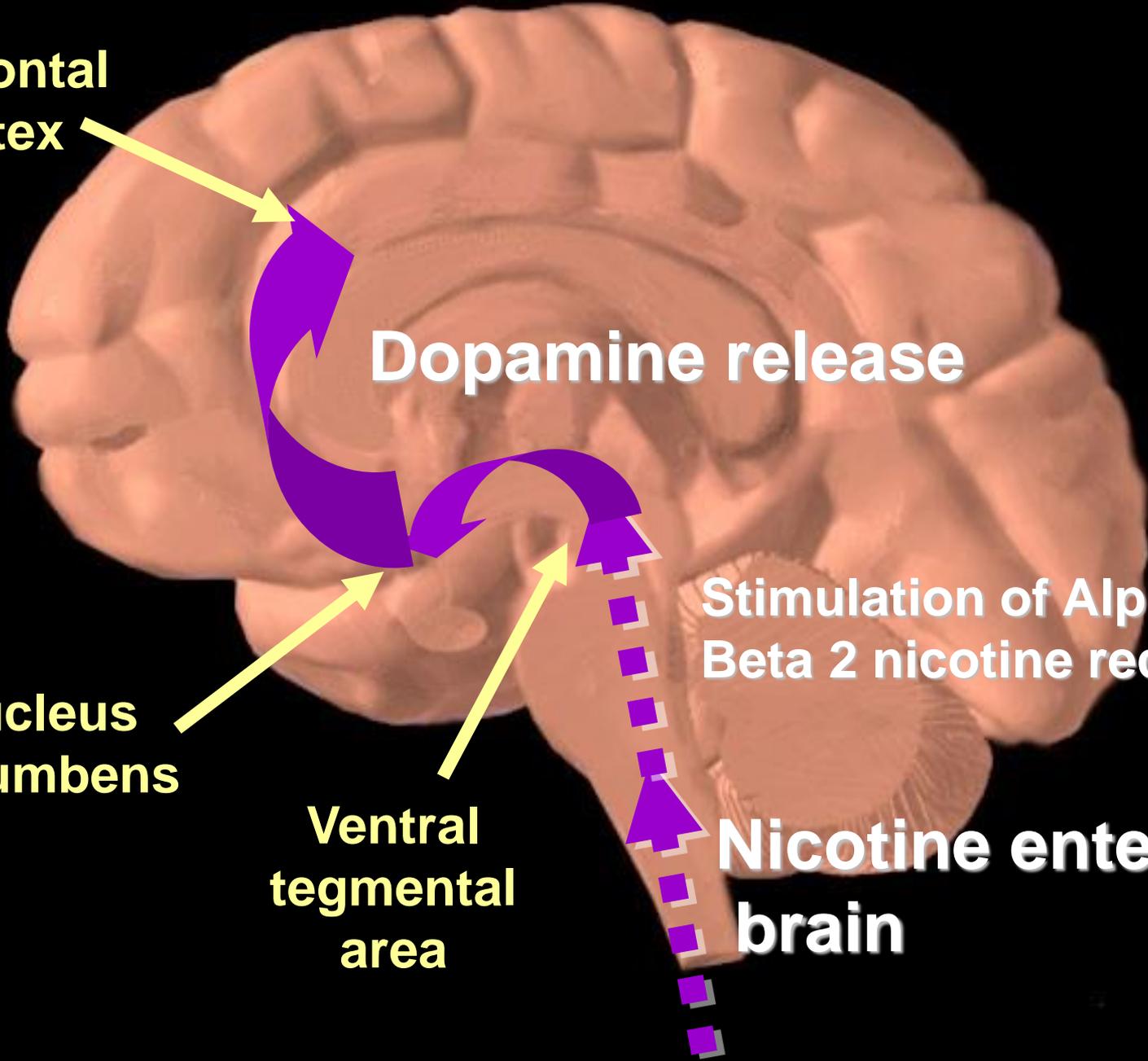
Dopamine release

Nucleus accumbens

Ventral tegmental area

Stimulation of Alpha 4
Beta 2 nicotine receptors

Nicotine enters
brain



Dopamine

- **Dopamine induces feelings of euphoria and pleasure and is responsible for activating the dopamine reward pathway**
- The dopamine reward pathway, as depicted in this simplified diagram, is a network of nervous tissue in the middle of the brain that elicits feelings of pleasure in response to certain stimuli.



Addiction to nicotine

- **Addiction to tobacco is multifactorial:**
- It includes a desire for the direct pharmacologic actions of nicotine, relief of withdrawal symptoms, and learned associations.
- Smokers usually provide different reasons for smoking that could include pleasure, arousal, enhanced vigilance, improved performance, relief of anxiety or depression, reduced hunger, and control of body weight



Addiction to nicotine

- The absence of nicotine due to smoking cessation results in subnormal release of dopamine and other neurotransmitters.
- Nicotine withdrawal results in the state of deficient dopamine responses to novel stimuli in general and a state of malaise and inability to experience pleasure.
- This leads to development of nicotine withdrawal symptoms.

NICOTINE PHARMACODYNAMICS: WITHDRAWAL EFFECTS

- Depression
- Insomnia
- Irritability/frustration/anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Increased appetite/weight gain
- Decreased heart rate
- Cravings*

Most symptoms
peak 24–48 hr
after quitting and
subside within
2–4 weeks.

What are the benefits of stopping smoking?

- It is never too late to stop smoking to gain health benefits.
- For example if the smoker already has a COPD or a heart disease, there would be great improvement in prognosis upon giving up smoking.
- Smoking cessation for smokers with history of ischaemic heart disease is expected to reduce risk of a subsequent fatal heart attack by 25 per cent.

Timeline of health benefits after stopping smoking

Time line (After ...)	Health Benefit
72 hours	Breathing becomes easier. Bronchial tubes begin to relax and energy levels increase.
1 month	Skin appearance improves, owing to improved skin perfusion.
3-9 months	Cough, wheezing, and breathing problems improve and lung function increases by up to 10%.
1 year	Risk of a heart attack falls to about half that of a smoker.
10 years	Risk of lung cancer falls to about half that of a smoker.
15 years	Risk of heart attack falls to the same level as someone who has never smoked.

Source: <http://www.ash.org.uk/stopping-smoking/quitting-smoking>



Management of smoking cessation

Behavioural therapy

and

Nicotine replacement therapy

Or nicotine receptors antagonists

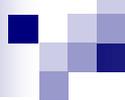
Nicotine replacement therapy (NRT)

- Provides smoker with nicotine without using tobacco, thereby relieving nicotine withdrawal symptoms.
- NRT products differ in the route of delivering nicotine to the circulation.
- Nicotine is absorbed transdermally with the nicotine skin patch, through the nasal mucosa by the nasal spray, or through the oral mucosa with the nicotine chewing gum, nicotine lozenge, or nicotine inhaler.
- Nicotine patches are more tolerated than nasal spray and provides the most continuous delivery of nicotine of nicotine replacement therapies.

Nicotine replacement therapy (NRT)

- Principle:

Many of the difficulties in smoking cessation stems from problems posed by nicotine withdrawal.



Nicotine Replacement Therapy (NRT)

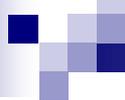
- Reliably attenuates severity of withdrawal, making it easier for would-be ex-smokers to cope with abstinence while unlearning the deeply ingrained habit elements of smoking

Nicotine Replacement Therapy

- First-line pharmacotherapy for smoking cessation
- Indicated for all smokers trying to quit, except in the presence of special circumstances (those with medical contraindications, pregnant and adolescent smokers)

Selected Medication Options: Monotherapy and Combination Therapy

Medication	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Nicotine Patch	32	1.9 (1.7 - 2.2)	23.4% (21.3 - 25.8)
Bupropion SR	26	2.0 (1.8 - 2.2)	24.2% (22.2 - 26.4)
Varenicline	5	3.1 (2.5 - 3.8)	33.2% (28.9 - 37.8)
Patch (>14 wks) + NRT (gum or spray)	3	3.6 (2.5 - 5.2)	36.5% (28.6 - 45.3)
Patch + Bupropion SR	3	2.5 (1.9 - 3.4)	28.9% (23.5 - 35.1)



NRT - Therapeutic Effect

- The primary therapeutic effect of NRT is to reduce the severity of symptoms associated with smoking cessation.
- NRT provides steady levels of nicotine and may reduce the pleasurable effects of tobacco desired by smokers.
- NRT makes it easier to cope in difficult situations.

Nicotine patches

- Transdermal patch (waterproof)
- Nicotine Replacement Therapy (NRT)
- To overcome withdrawal symptoms
- 24-hour patch to deliver constant nicotine levels
- 12 week weaning program that reduces and eliminates body's dependence for nicotine
- Clinically-proven to be better than willpower alone
- **2-4 times the success rate of placebo patches**

Hajek P, West R, Foulds J, Nilsson F, Burrows S, Meadow A. Randomized comparative trial of nicotine polacrilex, a transdermal patch, nasal spray, and an inhaler. *Arch Intern Med.* 1999;159:2033-2038.

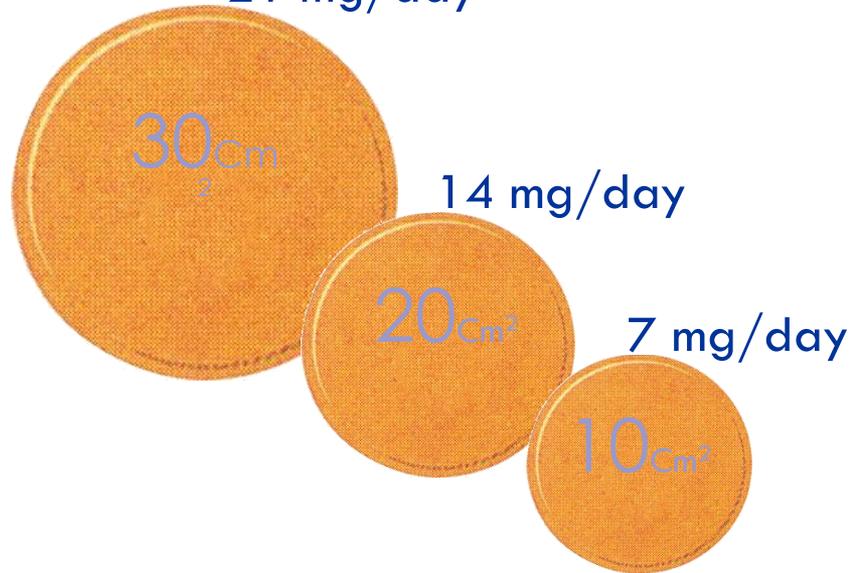
Nicotine patches

21 or 24mg/24hrs, 14mg/24hrs, 7mg/24hrs

21 or 24mg/16hrs, 14mg/16hrs, 7mg/16hrs

15mg/24hrs, 10mg/24hrs, 5mg/24hrs

21 mg/day



Precautions

- ❑ women who are pregnant or breast feeding
- ❑ smokers with cardiovascular conditions

Doctors should weigh risks/vs benefits when prescribing NRT to pregnant women or smokers with cardiovascular conditions.

- ❑ smokers using other nicotine replacement products
- ❑ children
- ❑ non-smokers
- ❑ smokers of fewer than 10 cigarettes a day

Nicotine patches– Application

- Apply to non-hairy, clean, dry skin
- Rotate between sites (this helps to reduce the risk of skin irritation)
- Choose a flat surface
- Avoid joints or skin folds
- Replace the same time everyday



**DO NOT SMOKE WHILE
USING THE PATCH**

Why a 24-hour patch ?

- ▶ Many of the dependent smokers
 - Either smoke just before to go to bed,
 - Or wake up at night for smoking
 - Or wake up early in the morning to have a cigarette

Night smoking is a criteria for strong addiction to nicotine

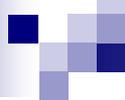
Aubin, H. J. Comparison of the effects of a 24-hour nicotine patch and a 16-hour nicotine patch on smoking urges and sleep. *Nicotine.Tob.Res.* 8.2 (2006): 193-201.

Success rates of nicotine patches as a first line monotherapy

- **Success rate of nicotine patch**
Many studies have been completed on the success rate of nicotine patches.
- **These have found that six weeks after initiating treatment between 23% and 61% of smokers were successful in quitting, while one year after quitting rates ranged from 17%-24 for monotherapy to 28%-34% for combination therapy**
- **The difference in success rates depends largely on the level of motivation and dependency level.**

Nicotine Lozenges

- Nicotine Lozenges are new products that have similar efficacy to nicotine gum but it is easier to use and does not require special technique for optimal use.
- It also delivers more nicotine than equivalent dose of the gum.
- Unlike nicotine gum, smokers with dentures or poor dentition can use Lozenges.

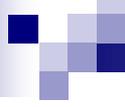


High level of smoking addiction

Combination of behavioural therapy with
nicotine patches and nicotine lozenges
(used for cravings)

Or

Combination of varenicline with behavioural
therapy



For patients with ischaemic heart disease with moderate or high level of addiction:

The best approach is to start with
behavioural therapy

If failed, you can start with nicotine patches

Varenicline (Champix, Chantix)

- a partial agonist at the alpha4beta2 subunit of the nicotinic acetylcholine receptor.
- This drug binds to nicotinic receptors leading to reduction of withdrawal symptoms and decrease rate of cigarettes' nicotine binding to these receptors.

Varenicline (Champix, Chantix)

- This medication has shown a good abstinence rate when compared to nicotine patches, but the difference is small when compared to combined nicotine patches with gum or lozenges.

Varenicline (Champix, Chantix)

- Week 1: Starting dose: 0.5mg once daily for three days, then 0.5mg twice daily for four days.

Smokers have to decide on quit day during this week.

- Then

1mg daily for 8-12 weeks.

For moderate addicts treatment could be shortened into 4 weeks.

Contraindications

- Champix has not been studied in children and should not be taken by young people who are under 18 years of age.
- Breast feeding. Champix may pass into breast milk.

Either use an alternative therapy or follow other ways of feeding the baby may be appropriate if she is currently taking the drug

Precautions for varenicline use

- kidney problems or on dialysis. It may be appropriate for prescribe a lower dose.
- Pregnancy. The effects of Champix on the foetus are not known and it would be better if the lady quits smoking before getting pregnant.



Precautions for varenicline use

- Depression or any psychiatric illnesses in the past.

Varenicline: Side effects

- Vomiting and nausea
- Headaches
- Sleep disturbances and atypical dreams
- Gas (wind)
- Changes in the way food tastes
(Dysgeusia)
- Constipation
- Suicidal thoughts

Bupropion (Zyban)

- Available as an antidepressant in the United States since 1989, is believed to act by enhancing central nervous system noradrenergic and dopaminergic release.
- A sustained-release formulation of the drug is licensed as an aid to smoking cessation (Zyban); it is identical to the antidepressant Wellbutrin SR and is available as a generic drug.



Bupropion (Zyban)

- A meta-analysis of 31 randomized trials of bupropion monotherapy concluded that bupropion SR doubles the likelihood of smoking cessation

Bupropion (Zyban)

- As an example, one multicenter, randomized, double blind trial of 615 patients compared sustained-release [bupropion](#) (150 mg twice daily) with placebo among patients who wished to stop smoking.
- The rates of smoking cessation (confirmed by exhaled carbon monoxide measurements) were significantly greater at the end of a seven-week course of treatment among patients who received bupropion (44 versus 19 percent).

Bupropion (Zyban)

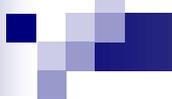
- **Safety** — The most common side effects of [bupropion](#) are insomnia, agitation, dry mouth, and headache.
- A more serious side effect is seizure, which can occur because bupropion reduces the seizure threshold.
- In clinical trials, the risk of seizure was 0.1 percent, and **the drug is contraindicated in patients with a seizure disorder or predisposition to seizure.**

Management plan:

- In the first visit:
- Medical and drug history, smoking pattern and history, nicotine dependence using Fagerstrom Tolerance Questionnaire.
- Counselling on smoking: Motivational interviewing strategies and the “5R’s” for enhancing motivation approaches will be used.
- The first approach is based on the following components: express empathy, develop discrepancy, roll with resistance, support self-efficacy. While the “5R’s” for enhancing motivation includes: Relevance, Risks, Rewards, Roadblocks, Repetition.
- Smokers, who are willing to receive smoking cessation medical therapy, would receive further assessment in order to determine the treatment of choice for their particular condition and to exclude any contraindications for the selected treatments.

استبيان FAGERSTROM للتدخين

كم عدد السجائر التي تدخنها في اليوم الواحد؟
0).....10-1)
1).....20-11)
2).....30-21)
3).....31 أو أكثر)
كم من الوقت تستغرق قبل أن تدخن أول سيجار عند الاستيقاظ من النوم؟
3).....(في غضون خمس دقائق)
2).....(من 6 دقائق إلى 30 دقيقة)
1).....(من 31 دقيقة إلى 60 دقيقة)
0).....(بعد 60 دقيقة)
أي من السجائر التالية يصعب عليك التخلي عنها؟
1).....(السيجار الأول في الصباح)
0).....(كل السجائر الباقية)
أي نوع من السجائر تدخن؟
1).....(السجائر ذات نسبة النيكوتين المنخفضة (0.9 ملغرام أو أقل))
2).....(السجائر ذات نسبة النيكوتين المتوسطة (1 إلى 1.2 ملغرام))
3).....(السجائر ذات نسبة النيكوتين المرتفعة (1.3 ملغرام أو أكثر))
هل في الغالب تقوم باستنشاق دخان السجائر؟
0).....(أبداً)
1).....(في بعض الأحيان)
2).....(دائماً)
هل تقوم بالتدخين أكثر في الساعتين الأولى من اليوم عنه في باقي ساعات اليوم؟
0).....(لا)
1).....(نعم)
هل تجد صعوبة في الامتناع عن التدخين في الأماكن العامة التي يحظر فيها التدخين مثل المباني العامة، أو على متن الطائرات، أو أثناء العمل؟
0).....(لا)
1).....(نعم)
هل ما زلت تمارس التدخين حتى بالرغم من شدة المرض حيث أنك تلازم السرير طوال اليوم؟
0).....(لا)
1).....(نعم)
إجمالي النقاط



1. How many cigarettes a day do you smoke? 1-10.....(0) 11-20..... (1) 21-30.....(2) 31 or more.....(3)	
2. How soon after you wake up do you smoke your first cigarette? Within 5 mins..... (3) 6 to 30 mins.....(2) 31 to 60 mins..... (1) After 60 mins.....(0)	
3. Which cigarette would you hate most to give up? The first one in the morning.....(1) All others.....(0)	
4. What type do you smoke? Low nicotine (0.9mg or less).....(1) Medium nicotine (1 to 1.2mg).....(2) High nicotine (1.3mg or more).....(3)	
5. How often do you inhale the smoke from your cigarette? Never.....(0) Sometimes.....(1) Always.....(2)	
6. Do you smoke more during the first two hours of the day than during the rest of the day? No.....(0) Yes.....(1)	
7. Do you find it difficult to refrain from smoking in places where it is forbidden, such as public buildings, on airplanes, or at work? No.....(0) Yes.....(1)	
8. Do you still smoke even when you are so ill that you are in bed most of the day?	



The Fagerstorm Scoring:

0-5: Low dependence

6-10: Medium dependence

11-15: High dependence

Table 1: Summary of management of smoking using nicotine replacement therapies

Smokes 20 cigarettes or more	A. high dependency	24-hour patches 21mg for 6 weeks plus nicotine gum when craving ↓ 14mg patch for 2 weeks ↓	Assess after one week and assess sleep pattern	Continue with 24 hour patch if no or minor insomnia If moderate to severe insomnia, discontinue 24 hour patches and start with medium dependency plus 2mg nicotine gum at the time of the first cigarette in the morning
	B. Medium dependency	7mg patch for 2 weeks 16-hour 15mg patches plus nicotine gum when craving for 6 weeks ↓ 16-hour 10mg patch for 2 weeks ↓		
	C. low dependency	16-hour 5mg patch for 2 weeks Same as medium dependency but without nicotine gum		
10-19 cigarettes		High dependency Medium dependency	Follow plan B above 10mg/ 16 hour nicotine patch for 6 weeks and nicotine gum when craving ↓	
		Low dependency	5mg/16-hour patch for 4 weeks 10mg/16-hour patches for 6 weeks ↓ 5mg/16-hour patch for 4 weeks	
10 cigarettes or less	Counselling only, if failed 5mg/16-hour patch for 6 weeks			

