Tabagisme, vapotage, sevrage et risques cardio-vasculaire et rénal

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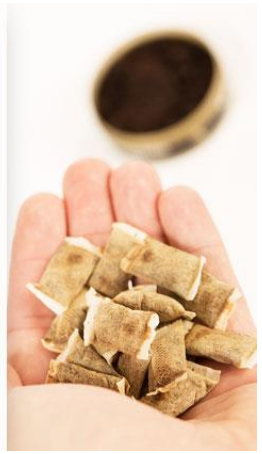
Pneumologie et Addictologie

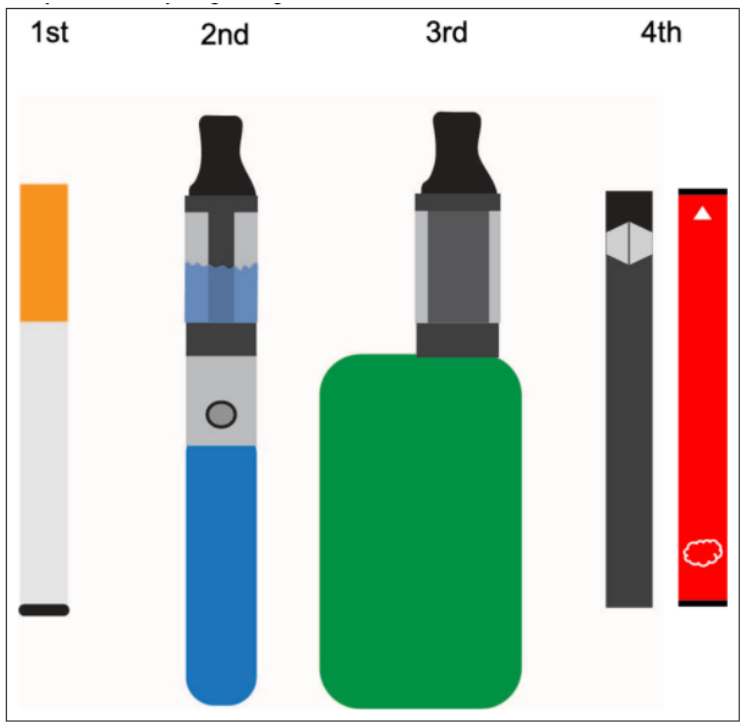
PhyMedExp INSERM U1046

CHU Arnaud de Villeneuve Montpellier

PLAN

- **Tabagisme, vapotage, et risques CV et rénal**
- **Sevrage / Réduction et risques CV et rénal**
- **Les outils du sevrage**

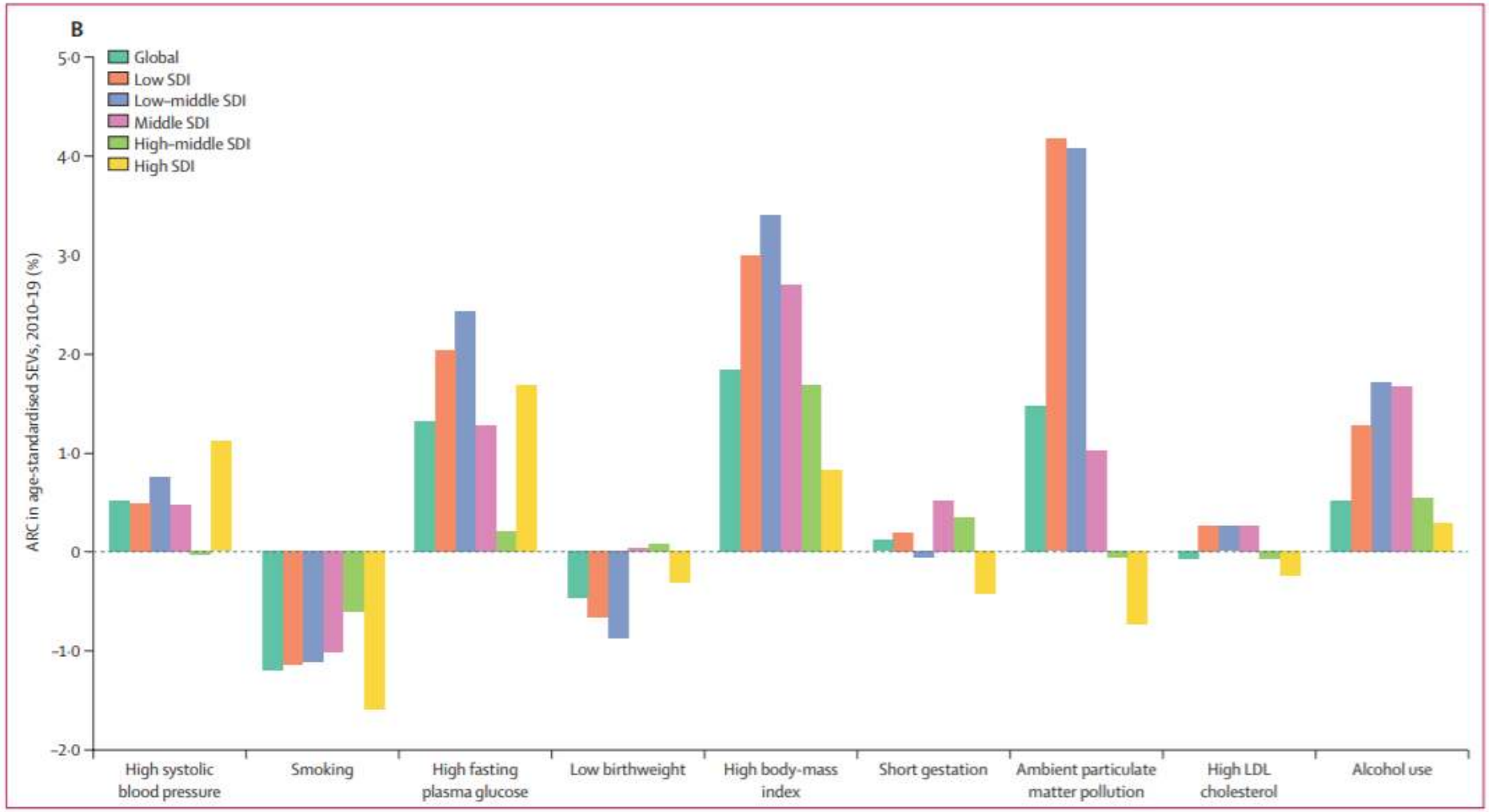



1st
2nd
3rd
4th

PLAN

- **Tabagisme, vapotage, et risques CV et rénal**
- **Sevrage, Réduction et risques CV et rénal**
- **Les outils du sevrage**

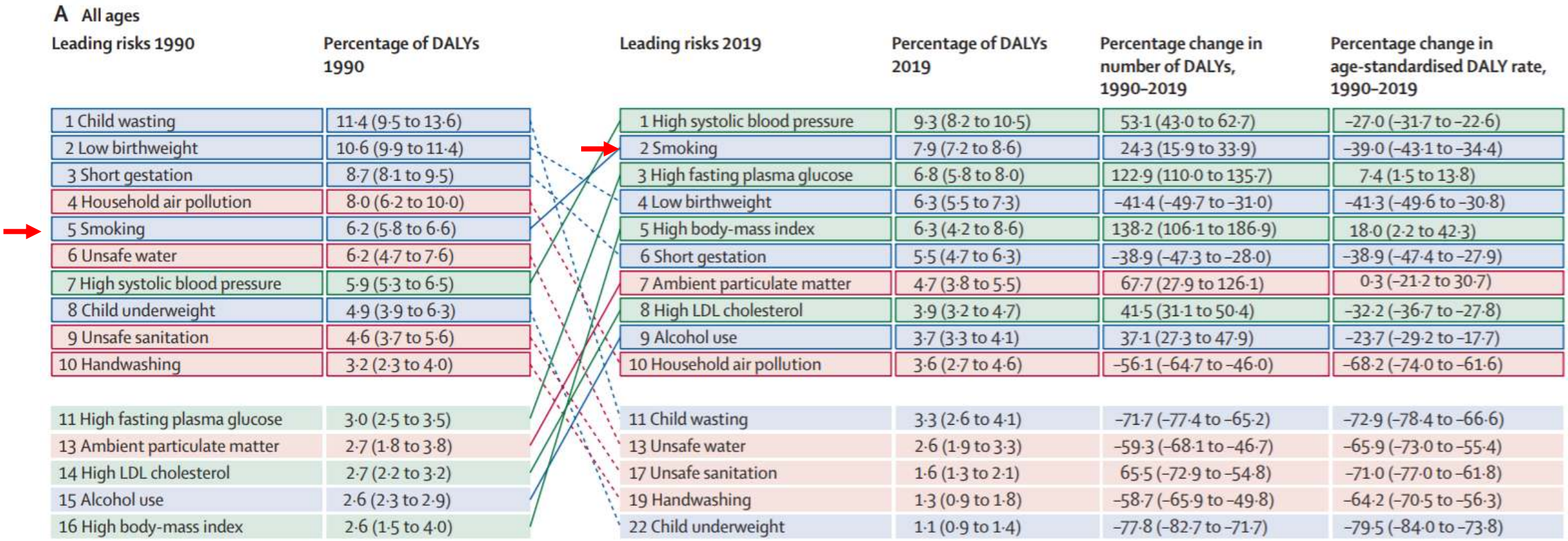
Tabagisme, vapotage et « risque »



Efforts pour réduire « l'exposition » de la population au risque …

GBD 2019 Risk Factors Collaborators, Lancet 2020; 396: 1223–49

Tabagisme, vapotage et « risque »



A All ages

Leading risks 1990	Percentage of DALYs 1990	Leading risks 2019	Percentage of DALYs 2019	Percentage change in number of DALYs, 1990–2019	Percentage change in age-standardised DALY rate, 1990–2019
1 Child wasting	11·4 (9·5 to 13·6)	1 High systolic blood pressure	9·3 (8·2 to 10·5)	53·1 (43·0 to 62·7)	−27·0 (−31·7 to −22·6)
2 Low birthweight	10·6 (9·9 to 11·4)	2 Smoking	7·9 (7·2 to 8·6)	24·3 (15·9 to 33·9)	−39·0 (−43·1 to −34·4)
3 Short gestation	8·7 (8·1 to 9·5)	3 High fasting plasma glucose	6·8 (5·8 to 8·0)	122·9 (110·0 to 135·7)	7·4 (1·5 to 13·8)
4 Household air pollution	8·0 (6·2 to 10·0)	4 Low birthweight	6·3 (5·5 to 7·3)	−41·4 (−49·7 to −31·0)	−41·3 (−49·6 to −30·8)
5 Smoking	6·2 (5·8 to 6·6)	5 High body-mass index	6·3 (4·2 to 8·6)	138·2 (106·1 to 186·9)	18·0 (2·2 to 42·3)
6 Unsafe water	6·2 (4·7 to 7·6)	6 Short gestation	5·5 (4·7 to 6·3)	−38·9 (−47·3 to −28·0)	−38·9 (−47·4 to −27·9)
7 High systolic blood pressure	5·9 (5·3 to 6·5)	7 Ambient particulate matter	4·7 (3·8 to 5·5)	67·7 (27·9 to 126·1)	0·3 (−21·2 to 30·7)
8 Child underweight	4·9 (3·9 to 6·3)	8 High LDL cholesterol	3·9 (3·2 to 4·7)	41·5 (31·1 to 50·4)	−32·2 (−36·7 to −27·8)
9 Unsafe sanitation	4·6 (3·7 to 5·6)	9 Alcohol use	3·7 (3·3 to 4·1)	37·1 (27·3 to 47·9)	−23·7 (−29·2 to −17·7)
10 Handwashing	3·2 (2·3 to 4·0)	10 Household air pollution	3·6 (2·7 to 4·6)	−56·1 (−64·7 to −46·0)	−68·2 (−74·0 to −61·6)
11 High fasting plasma glucose	3·0 (2·5 to 3·5)	11 Child wasting	3·3 (2·6 to 4·1)	−71·7 (−77·4 to −65·2)	−72·9 (−78·4 to −66·6)
13 Ambient particulate matter	2·7 (1·8 to 3·8)	13 Unsafe water	2·6 (1·9 to 3·3)	−59·3 (−68·1 to −46·7)	−65·9 (−73·0 to −55·4)
14 High LDL cholesterol	2·7 (2·2 to 3·2)	17 Unsafe sanitation	1·6 (1·3 to 2·1)	65·5 (−72·9 to −54·8)	−71·0 (−77·0 to −61·8)
15 Alcohol use	2·6 (2·3 to 2·9)	19 Handwashing	1·3 (0·9 to 1·8)	−58·7 (−65·9 to −49·8)	−64·2 (−70·5 to −56·3)
16 High body-mass index	2·6 (1·5 to 4·0)	22 Child underweight	1·1 (0·9 to 1·4)	−77·8 (−82·7 to −71·7)	−79·5 (−84·0 to −73·8)

..mais tabagisme reste 1er FdR évitable en terme de DALYs

Pas d'amélioration en terme de fardeau attribuable au tabagisme

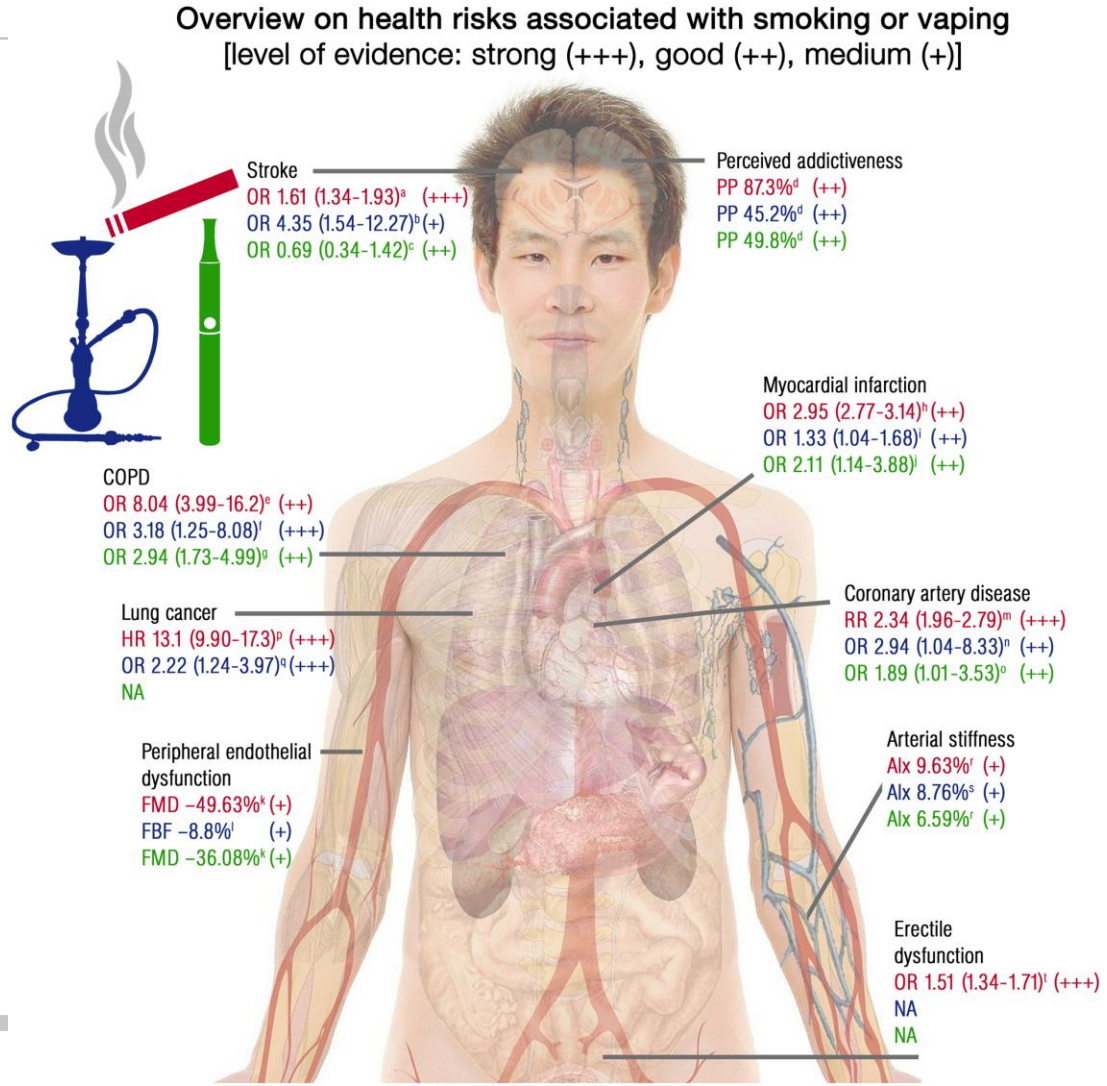
GBD 2019 Risk Factors Collaborators, Lancet 2020; 396: 1223–49

Website Altria

Tabagisme, vapotage et risque cardiovasculaire

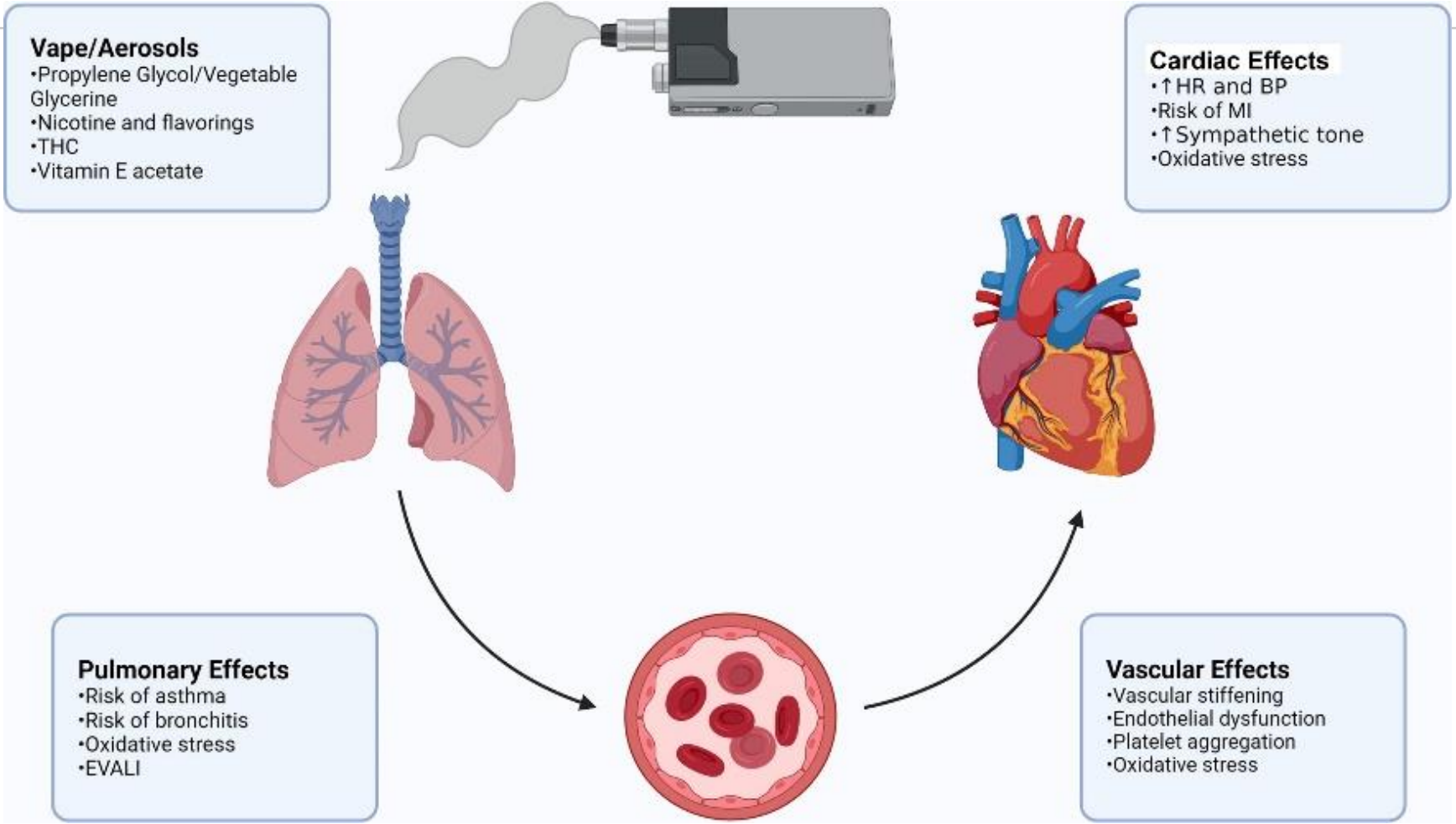
- **Cardiopathie ischémique**
- **AOMI**
- **~AVC**

Cigarettes « standards »…ET électroniques



Münzel et al, June 2020, European Heart Journal, ehaa460, https://doi.org/10.1093/eurheartj/ehaa460

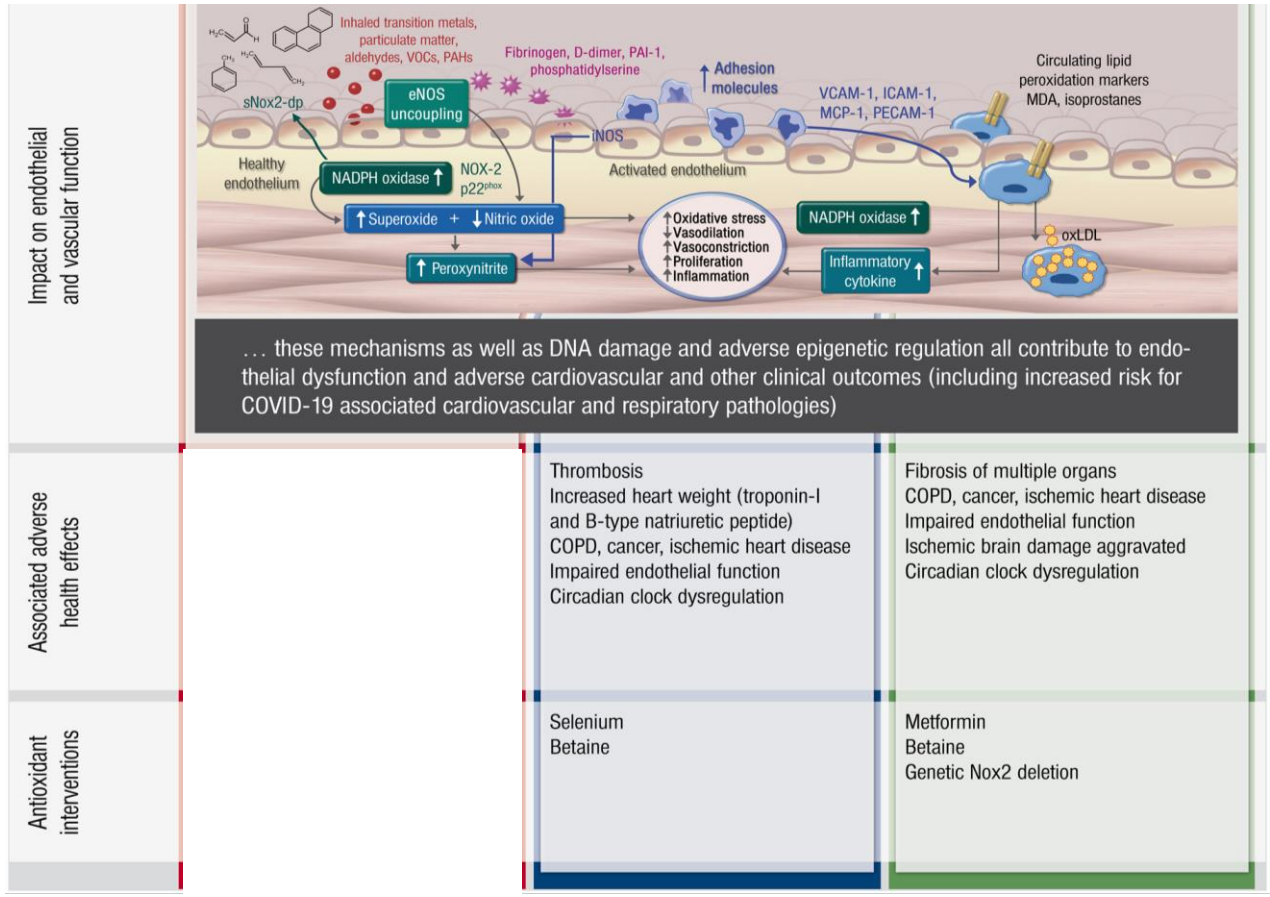
Tabagisme, vapotage et risque cardiovasculaire



https://doi.org/10.1161/CIRCULATIONAHA.121.056777Circulation. 2022;145:219–232

Tabagisme, vapotage et risque cardiovasculaire

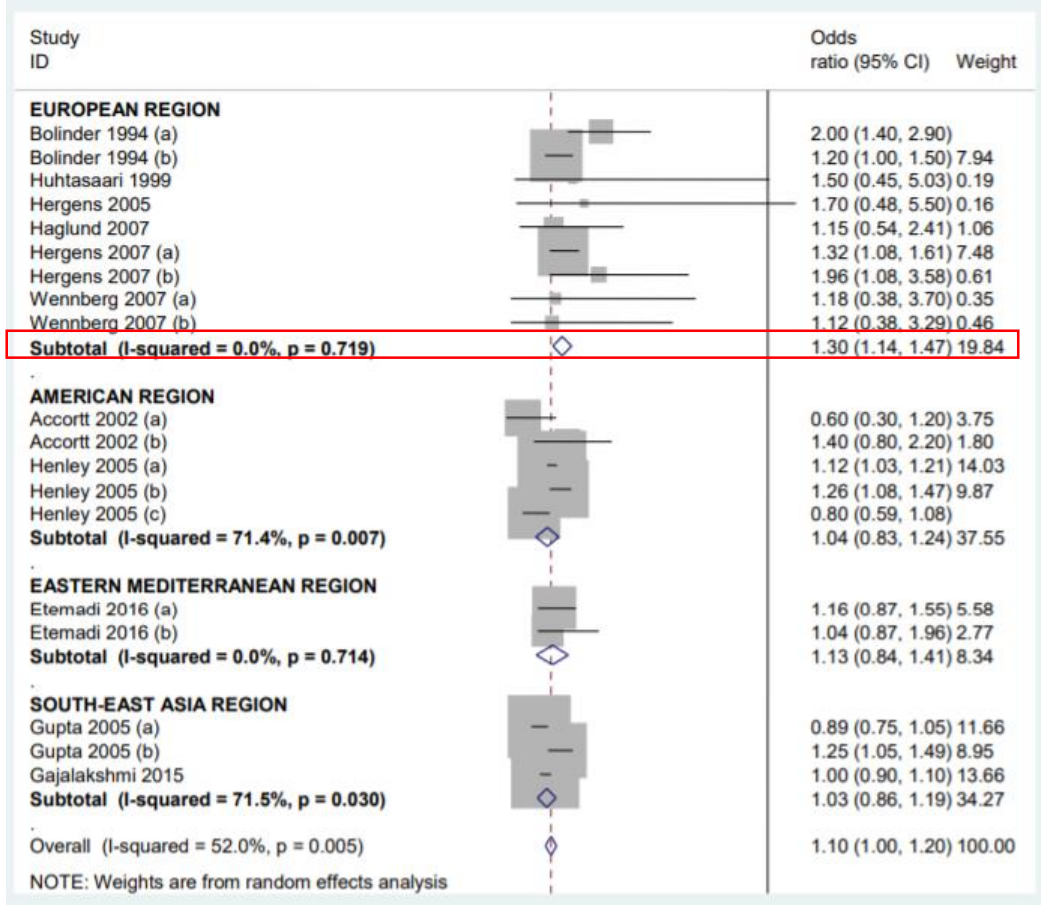
	Transition metals Carbon monoxide Aldehydes Nicotine N-nitrosamines Solid particulate matter VOCs, PAHs	Transition metals Aldehydes Nicotine N-nitrosamines VOCs
Oxidative stress:	MDA in lung ↑ TBARs in heart ↑ SOD, GPx-1, catalase in lung ↓ Plasma vitamin C, GSH reductase ↓ Lipid peroxidation ↑ urinary isoprostane	Soluble NOX2-derived peptide ↑ NO ↓ isoprostane ↑ Plasma vitamin E ↓ oxLDL ↑ Aortic NOX-2 ↑, ROS ↑ eNOS uncoupling
Inflammation:	IL-1β, IL-6, IL-8, TNF-α, CRP, WBCs ↑ iNOS and NO in lung ↑ MMP-9, MPO activity ↑ ICAM-1, PGE2	IL-1β, IL-6, IL-8, interferon-γ, MMP-9 ↑ ICAM-1, PECAM-1, VCAM-1 ↑ angiopoietin-1, epidermal growth factor, IL-8
Thrombosis:	Fibrinogen, PAI-1 ↑	integrin, phosphatidylserine ↑ Platelet activation, tail bleeding time ↑
DNA damage:	DNA repair genes OGG1 and XRCC1 ↓ DNA stand breaks ↑ 8-hydroxy-2'-deoxyguanosine ↑	O^6-methyldeoxyguanosine ↑ DNA repair genes ↓ γ-hydroxy-1,N^2-propano-deoxyguanosine ↑ 8-hydroxy-2'-deoxyguanosine ↑



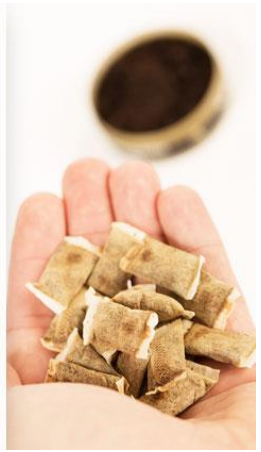
Associated adverse health effects	Thrombosis Increased heart weight (troponin-I and B-type natriuretic peptide) COPD, cancer, ischemic heart disease Impaired endothelial function Circadian clock dysregulation	Fibrosis of multiple organs COPD, cancer, ischemic heart disease Impaired endothelial function Ischemic brain damage aggravated Circadian clock dysregulation
Antioxidant interventions	Selenium Betaine	Metformin Betaine Genetic Nox2 deletion

Münzel et al, June 2020, European Heart Journal, ehaa460, https://doi.org/10.1093/eurheartj/ehaa460

Tabagisme, vapotage et risque cardiovasculaire



- Risque de CMI fatale
- Ajustement strict sur tabagisme « inhalé»
- Données à consolider



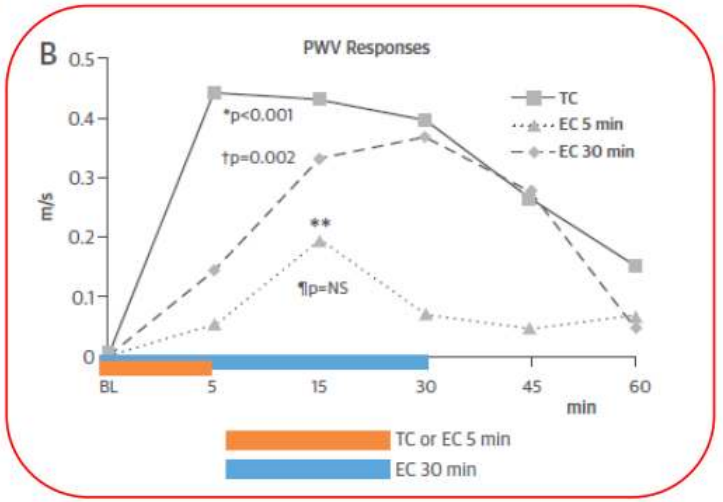
« Smokeless tobacco product »

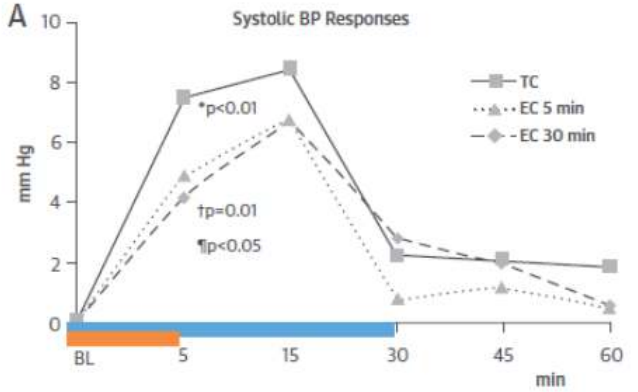
Gupta R et al. Nicotine Tob Res. 2019 Jan 1;21(1):25-31. doi: 10.1093/ntr/nty002. PMID: 29325111

Tabagisme, vapotage et HTA

Tabagisme, vapotage et HTA

- Rationnel (dysfonction endothéliale, athéroscolérose etc…)
- Effet aigu
  - Activation système sympathique/nicotine, adrénergique
  - Augmentation FC, Tas, Rigidité paroi aortique
- Effet chronique ?
- Relation dose-effet ?





Vlachopoulos C et al. JACC 2016; 67:2802-3

Tabagisme, vapotage et HTA

Un rationnel, mais quid des données épidémiologiques ?

TABLE 4. Mean SBP and DBP Adjusted for Age, BMI, Alcohol Intake, and Social Class

BP by Age and Gender, mm Hg	Smoking Status				
	Never	Ex	1–9 cigarettes/d	10–19 cigarettes/d	20+ cigarettes/d
Mean SBP					
Men, y					
16–44	131.8	130.9†	131.3	131.4	131.5
45+	142.6	142.4	145.0*	145.2†	145.4†
Women, y					
16–44	123.3	122.9	122.5	123.3	123.1
45+	142.7	141.8	141.1	143.6	143.7
Mean DBP					
Men, y					
16–44	72.1	71.1‡	71.1	71.2*	71.5
45+	82.2	81.3†	82.2	82.1	81.8
Women, y					
16–44	69.2	68.6*	67.8‡	68.7	69.2
45+	76.9	76.4	76.0	77.6	77.6

*$P<0.05$.
†$P<0.01$.
‡$P<0.001$.

Table 2 Hazard Ratios (95% Confidence Intervals) From Cox Proportional Hazards Survival Models of Incident Hypertension, According to Baseline Cigarette Smoking Status Among 28,236 Participants

	Baseline Smoking Status				Higher Categories	
	Never	Former	1 to 14/day	≥15/day	15 to 24/day	≥25/day
n	14,377	10,115	1,409	2,335	1,633	702
Person-yrs	117,020	81,898	11,523	18,491	13,120	5,371
Cases	4,273	3,150	417	731	493	238
Crude	1.00 (ref)	1.06 (1.01–1.11)	0.99 (0.90–1.10)	1.08 (1.00–1.17)	1.03 (0.94–1.13)	1.20 (1.06–1.37)
Age-adjusted	1.00 (ref)	1.04 (0.99–1.09)	1.00 (0.90–1.10)	1.10 (1.01–1.19)	1.05 (0.95–1.15)	1.22 (1.07–1.39)
Multivariable*	1.00 (ref)	1.03 (0.98–1.08)	1.02 (0.92–1.13)	1.11 (1.03–1.21)	1.07 (0.97–1.18)	1.21 (1.06–1.39)
Multivariable+systolic and diastolic blood pressure	1.00 (ref)	1.05 (1.00–1.10)	1.09 (0.98–1.21)	1.11 (1.02–1.20)	1.08 (0.98–1.18)	1.18 (1.03–1.35)

*Adjusted for age, body mass index, exercise level, alcohol use, parental history of myocardial infarction before age 60 years, diabetes and high cholesterol (self-reported history or current treatment), and intake of energy-adjusted dietary factors (fruits and vegetables, saturated fat, sodium, and potassium). Note: The further consideration of randomized treatment assignment (aspirin, beta-carotene, vitamin E) in the multivariable model did not change the hazard ratios for smoking status.

- Rationnel « logique » pour lien tabac-HTA mais données parfois contradictoires
- Qualité des données et analyses statistiques ?
- Forte interdépendance des variables ?

Primatesta et al. Hypertension 2001 Feb;37(2):187-93.

Bowman et al. JACC, 2007 Nov 20;50(21):2085-92.

Tabagisme, vapotage et HTA

Table 2.—Office and Ambulatory Blood Pressures (BP) and Heart Rates (HR) of Smokers and Nonsmokers: (Means ± SDs)*

	All Ages		Age <50 y		Age ≥50 y	
	Smokers	Nonsmokers	Smokers	Nonsmokers	Smokers	Nonsmokers
Age, y	45.0 ± 11.5 (59)	51.0 ± 13.6 (118)	37.4 ± 6.7 (36)	38.7 ± 7.6 (52)	56.8 ± 6.1 (23)	60.6 ± 8.5 (66)
Sex, M/F	33/26	67/51	20/16	29/23	13/10	38/28
Race, W/B	50/9	102/13	29/7	42/9	21/2	60/4
Office BP, mm Hg	140.9 ± 19.5 (54) 93.4 ± 11.8	142.2 ± 21.0 (105) 92.6 ± 10.8	139.3 ± 18.6 (35) 92.9 ± 12.8	141.0 ± 19.1 (45) 94.6 ± 10.4	143.9 ± 21.2 (19) 94.4 ± 9.9	143.0 ± 21.0 (60) 91.1 ± 10.9
Awake BP, mm Hg	145.0 ± 22.2 (58)† 92.7 ± 10.1	140.4 ± 16.4 (118) 91.3 ± 11.2	139.9 ± 18.6 (35) 91.9 ± 11.6	138.6 ± 14.4 (52) 93.4 ± 9.6	152.8 ± 25.1 (23)‡ 93.8 ± 7.4	141.9 ± 17.8 (66) 89.6 ± 12.1
Sleep BP, mm Hg	120.9 ± 19.5 (44) 76.0 ± 10.8	123.3 ± 19.3 (97) 77.0 ± 11.9	117.2 ± 16.1 (26) 74.0 ± 10.5	121.4 ± 16.7 (47) 77.8 ± 11.4	126.2 ± 23.0 (18) 78.9 ± 10.9	125.1 ± 21.5 (50) 76.2 ± 12.5
Awake-sleep BP difference	23.4 ± 12.2 (43)‡ 16.5 ± 7.4	17.3 ± 11.0 (97) 14.2 ± 7.7	19.4 ± 11.0 (25) 17.1 ± 6.3	17.6 ± 9.3 (47) 15.8 ± 8.2	28.9 ± 12.0 (18)‡ 15.7 ± 8.8	17.1 ± 12.5 (50) 12.7 ± 7.0
Awake HR, beats/min	84 ± 14 (22)	80 ± 12 (75)	85 ± 16 (12)	84 ± 12 (35)	83 ± 13 (10)	77 ± 11 (40)
Sleep HR, beats/min	74 ± 11 (22)	67 ± 11 (75)	74 ± 11 (13)	67 ± 11 (35)	72 ± 12 (10)	67 ± 11 (40)

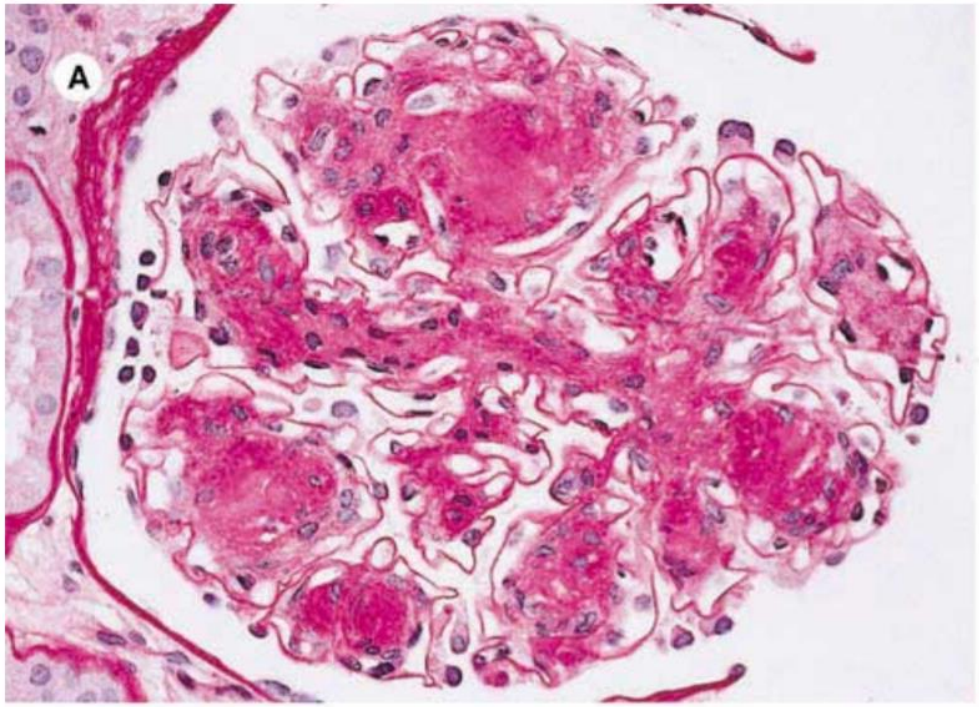
*Numbers of patients are given in parentheses.
†$P \leq .05$, smokers vs nonsmokers.
‡$P \leq .01$, smokers vs nonsmokers.

- Ambulatoire versus cabinet

Samuel J. Mann et al. *JAMA.* 1991;265(17):2226-2228. doi:10.1001/jama.1991.03460170080037

Tabagisme, vapotage et Risque rénal

Tabagisme, vapotage et Risque rénal



Glen S Markowitz, 2002, Human Pathologyn PMID: 12203216

Idiopathic nodular glomerulopathy

- Similarités entre histologie néphropathie diabétique, glomérulopathie de l'obèse et lésions liées au tabac = trajectoire similaire ?
- Hypothèse: Hyperfiltration et protéinurie dans maladie rénale PRECOCE ?
- Etude prospective avec évaluation à 6 ans

Isseki Maeda, Clinical journal of the American Society of Nephrology : CJASN 6: 2462-2469, 2011.

Tabagisme, vapotage et Risque rénal

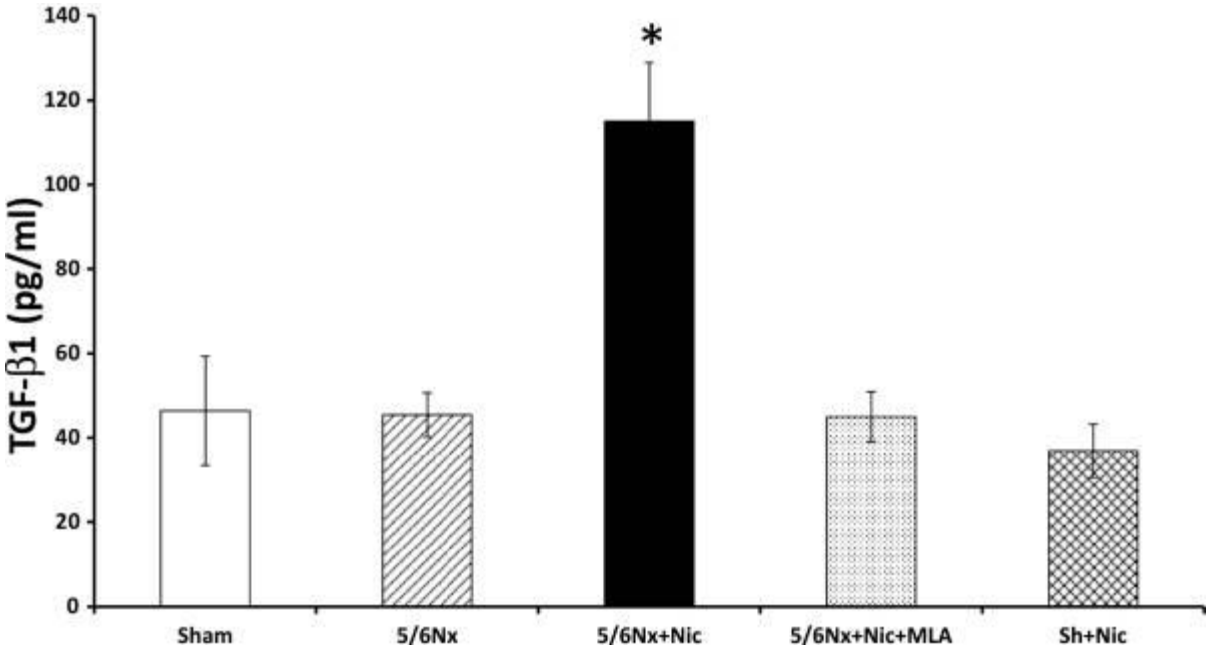
Table 2. Association Between Smoking and Rapid Decline in Renal Function >30% From Visit 1 to Visit 3

Model	Smoking Status, Incidence Rate Ratio (95% CI); *P* Value			
	Past vs Never Smokers	Current vs Never Smokers	Current (1–19 Cigarettes per Day) vs Never Smokers	Current (≥20 Cigarettes per Day) vs Never Smokers
Model 1, unadjusted	1.53 (1.21–1.94); <0.001	1.51 (1.14–1.99); 0.004	1.35 (0.95–1.91); 0.095	1.82 (1.21–2.75); 0.004
Model 2, adjusted for age, sex and body mass index	1.26 (0.99–1.61); 0.059	1.90 (1.43–2.54); <0.001	1.67 (1.17–2.39); 0.005	2.31 (1.50–3.53); <0.001
Model 3, includes model 2 plus diabetes, hypertension, total cholesterol	1.21 (0.94–1.57); 0.147	1.86 (1.35–2.56); <0.001	1.73 (1.18–2.54); 0.005	2.03 (1.23–3.35); 0.005
Model 4, includes model 3 plus education, physical activity, prevalent cardiovascular disease, and alcohol consumption in the past 12 months	1.20 (0.92–1.56); 0.172	1.83 (1.31–2.56); <0.001	1.75 (1.18–2.59); 0.006	1.97 (1.17–3.31); 0.011

- Relation dose-effet entre intensité tabagisme et rapidité du déclin de la fonction rénale

Hall ME et al. Journal of the American Heart Association 2016https://doi.org/10.1161/JAHA.116.003280

Tabagisme, vapotage et Risque rénal



Quid E-cig ?

- Nicotine hautement concentrée dans les reins
- Filtration glomérulaire et sécrétion tubulaire
- Induction de marqueurs pro-inflammatoires et pro-fibrosants dans cortex rénal

Gabriel Rezonzew et al. Am J Physiol Renal Physiol. 2012 Jul 15; 303(2): F304–F312

Tabagisme, vapotage et Risque rénal

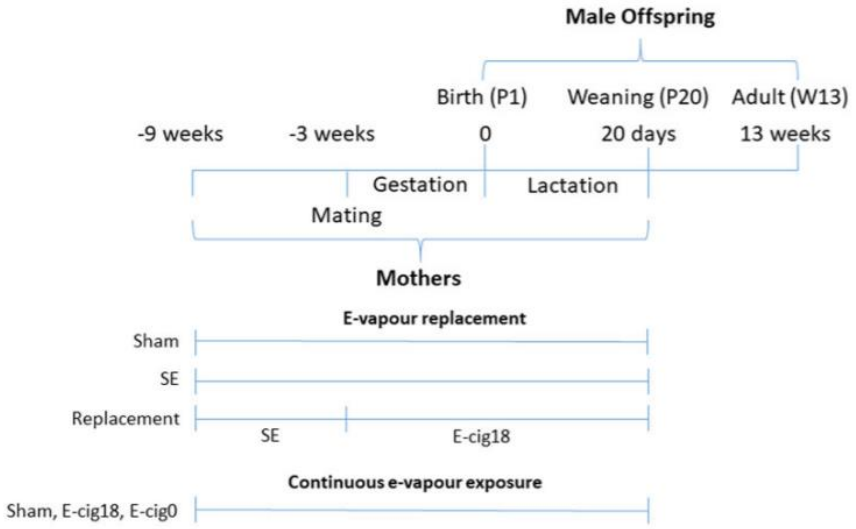
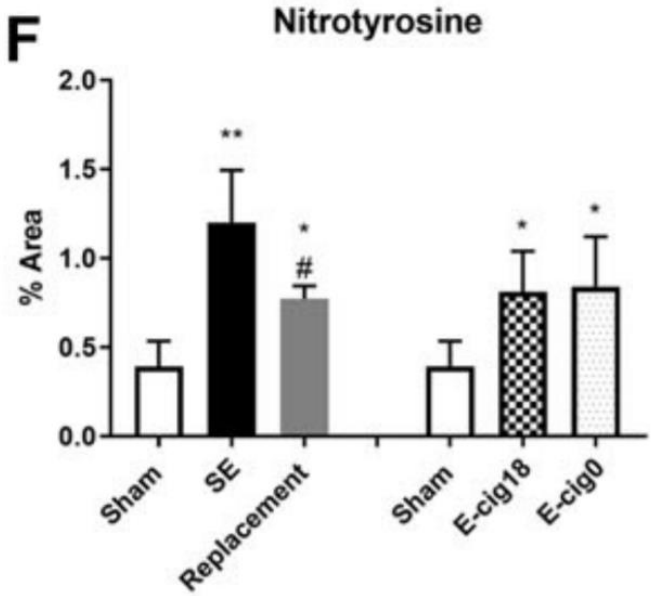


Figure 1. Schematic presentation of the study design. SE, cigarette smoke exposure; replacement, e-vapor replacing SE during gestation; E-cig18, exposure to nicotine-containing e-vapor; E-cig0, exposure to nicotine-free e-vapor.



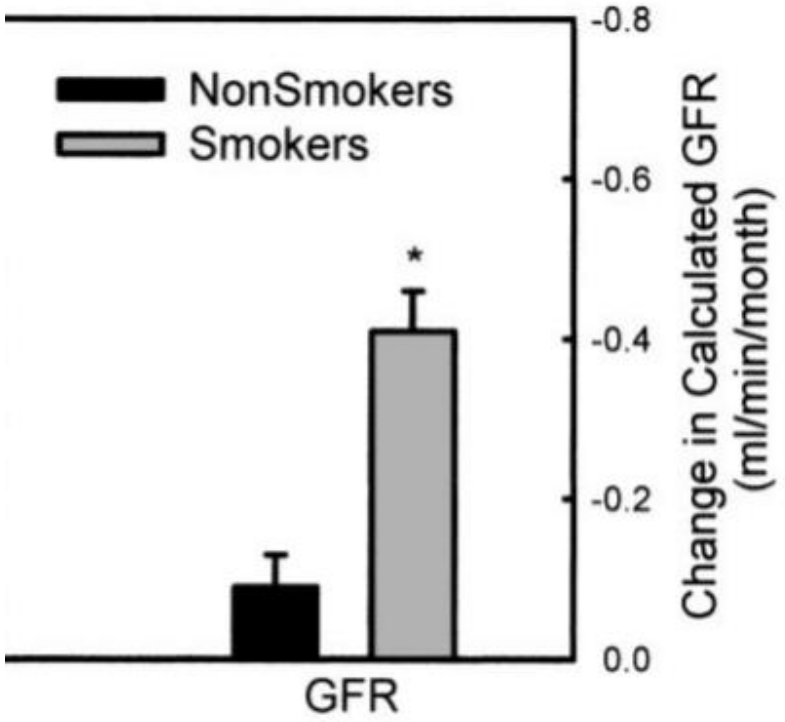
Quid E-cig ?

- Souris exposées sham vs. cig standard vs. e-cig en remplacement ou en continu
- Développement rénal sham > e-cig continue > cigarette standard
- Augmentation marqueurs stress oxydant indépendamment taux nicotine => pas seule molécule en jeu

Gerard Li et al. doi: 10.1111/nyas.14174 Ann. N.Y. Acad. Sci. xxxx (2019) 1–13 © 2019 New York Academy of Sciences.

. 2000 Apr;35(4):687-94. doi: 10.1016/s0272-6386(00)70017-5

Tabagisme, vapotage et Risque rénal



Effet cumulatif Tabac + HTA sur déclin fonction rénale

M Regalado[1], S Yang, D E Wesson Am Jounral Kidney 2000 DOI: 10.1016/s0272-6386(00)70017-5

PLAN

- Tabagisme, vapotage, et risques CV et rénal
- **Sevrage, Réduction et risques CV et rénal**
- Les outils du sevrage

Sevrage, Réduction et risques CV et rénal

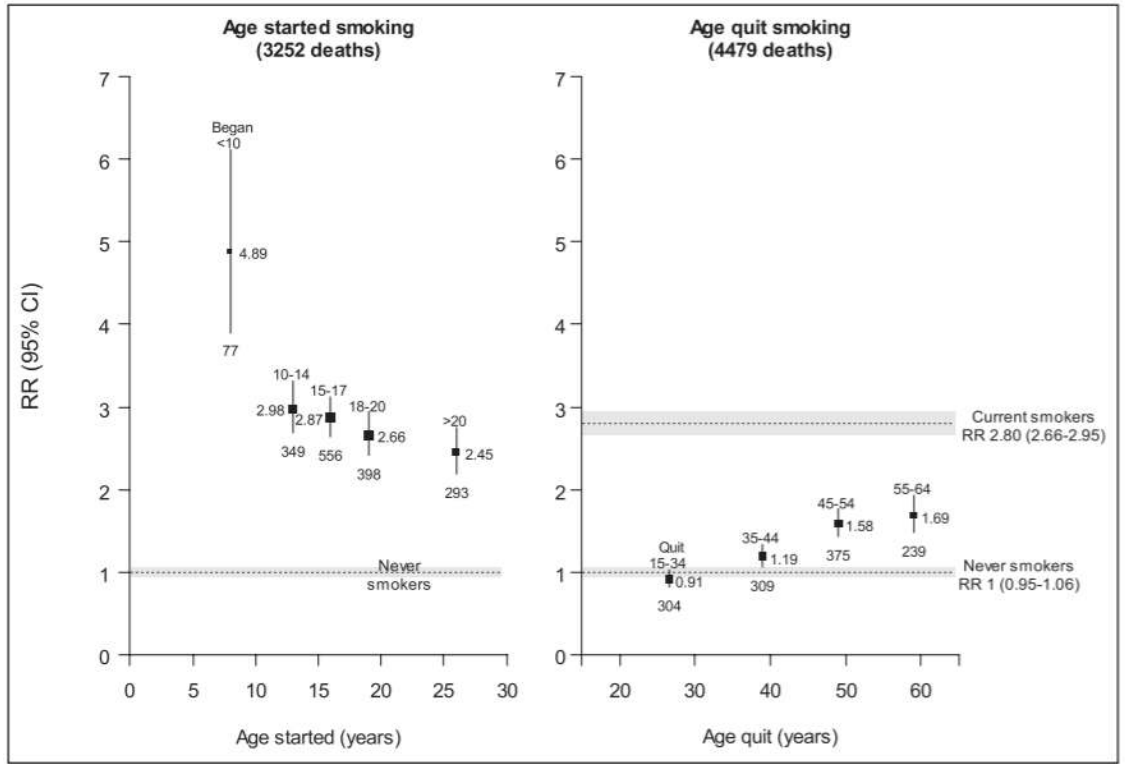


Figure 1. Cardiovascular mortality RRs by age started smoking among current smokers, and age quit smoking among ex-smokers, compared with never smokers, age at risk 25 to 74 years.
Shaded areas and error bars indicate 95% CI. Box area is inversely proportional to the variance of the log risk. Number below box indicates deaths in that category. NHIS data include waves 1997–2014 followed through December 31, 2015. Adjusted for age at risk, sex, education, alcohol consumption, race, and region. NHIS indicates National Health Interview Surveys; and RR, rate ratio.

- Sevrage
- Mortalité par événement CV diminuée à tout âge d'arrêt
- Risque davantage diminué si arrêt précoce
- Impact de l'âge de début du tabagisme

Blake Thomson et al. JAHA Oct 2020 https://doi.org/10.1161/JAHA.120.018431

Sevrage, Réduction et risques CV et rénal

TABLE 2. Changes From Baseline in SBP and DBP With Respect to Smoking Habit During the Follow-Up Periods Among 8170 Male Workers

	Smoking Habit (sample size)						
	Current Smoker (n=5372)	Current Nonsmoker (n=2090)	Quitter (n=708)				
			<1 y (n=210)	1–3 y (n=374)	≥3 y (n=124)	P*	Adjusted R^2
Crude							
SBP	3.9 (3.6–4.2)	4.4 (3.9–4.8)	4.4 (2.8–5.9)	6.2† (5.1–7.4)	6.1 (4.1–8.2)	<0.000	...
DBP	3.1 (2.9–3.3)	3.3 (3.0–3.6)	3.7 (2.7–4.7)	4.8† (3.9–5.7)	4.1 (2.6–5.6)	<0.000	...
Adjusted‡							
SBP	3.8 (3.5–4.0)	4.9† (4.4–5.3)	3.6 (2.3–4.8)	5.2† (4.3–6.2)	5.6 (3.9–7.2)	<0.000	28.9%
DBP	2.9 (2.7–3.1)	3.8† (3.5–4.2)	3.1 (2.2–4.1)	4.1† (3.4–4.8)	4.2 (2.9–5.4)	<0.000	22.7%

*P values were based on 1-way ANOVA or ANCOVA.

†Statistically significant ($P<0.05$) compared with the current smokers by Tukey's multiple comparison.

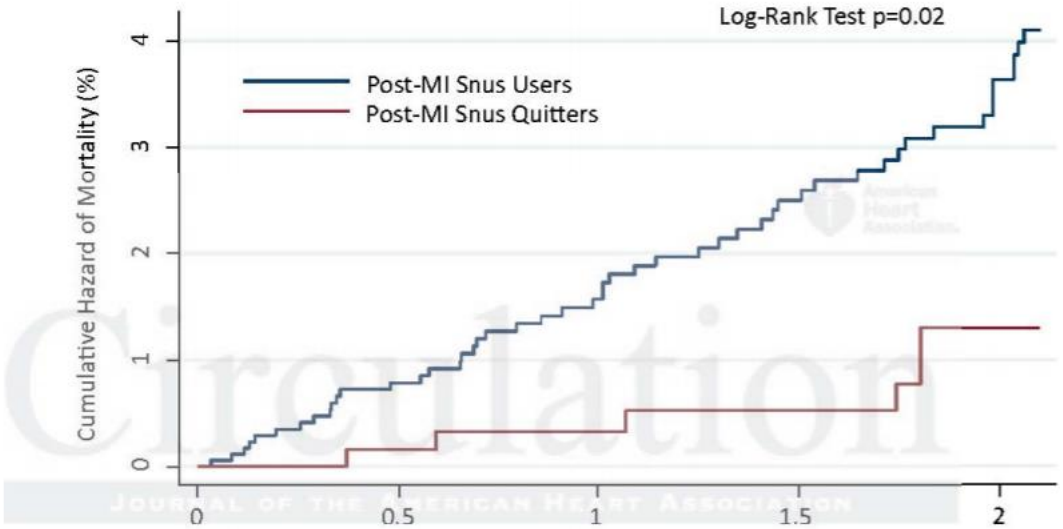
‡Adjusted for the baseline age, BMI, smoking (pack-y), alcohol consumption (g/wk), exercise (times/wk), family history of hypertension, SBP or DBP (baseline for the dependent variable), and changes in BMI and alcohol consumption during the follow-up period.

Values are mean (95% CI).

- Augmentation BP après arrêt
- Idem après ajustement sur prise (ou non) de poids
- Autres effets environnementaux concomitants non pris en compte ?

Duk-Hee Lee et al. Feb 2001https://doi.org/10.1161/01.HYP.37.2.194Hypertension. 2001;37:194–198

Sevrage, Réduction et risques CV et rénal



Number at Risk

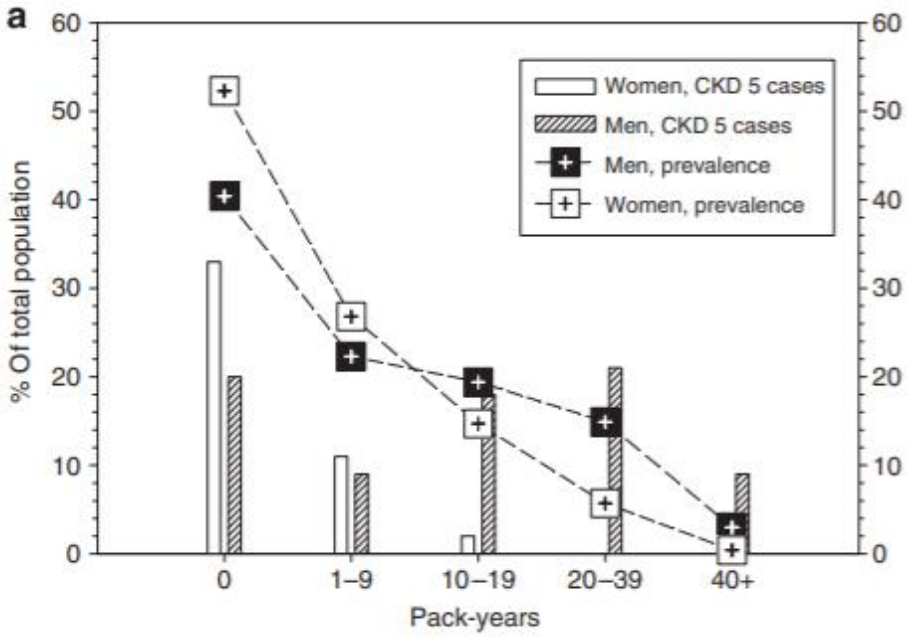
Post-MI Snus Users	1771	1534	1278	1083	873
Post-MI Snus Quitters	672	615	517	445	344

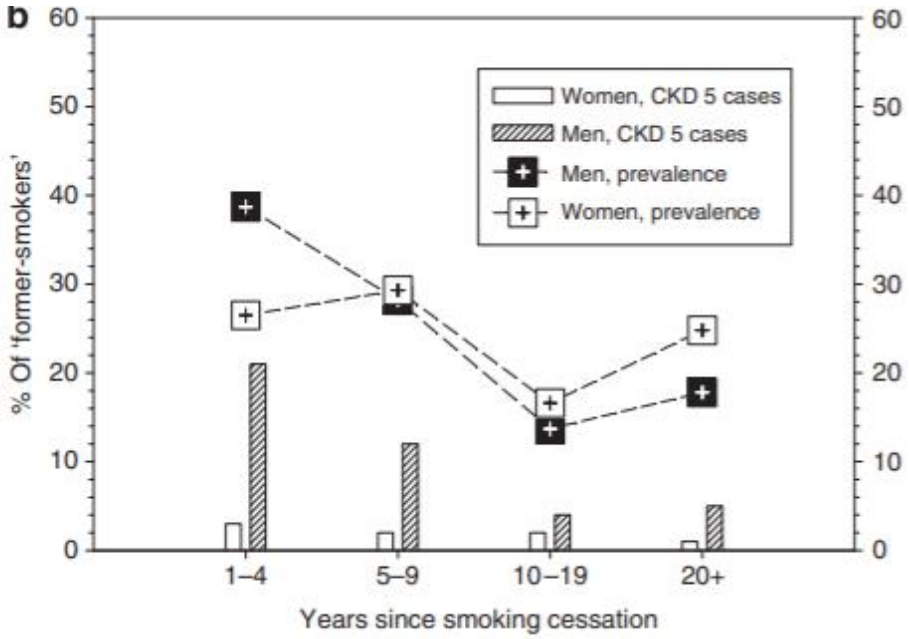
Mortalité par IDM à 2 ans réduite de moitié chez personnes ayant arrêté snus

« Smokeless tobacco product »

Arefalk G et al. Circulation. 2014 Jul 22;130(4):325-32. doi: 10.1161/CIRCULATIONAHA.113.007252. Epub 2014 Jun 23. PMID: 24958793.

Sevrage, Réduction et risques CV et rénal





- Diminution de la prévalence de maladie rénale chronique après arrêt tabac

Hallan, et al.2011 Sep;80(5):516-23. doi: 10.1038/ki.2011.157. Epub 2011 Jun 15. x

Sevrage, Réduction et risques CV et rénal

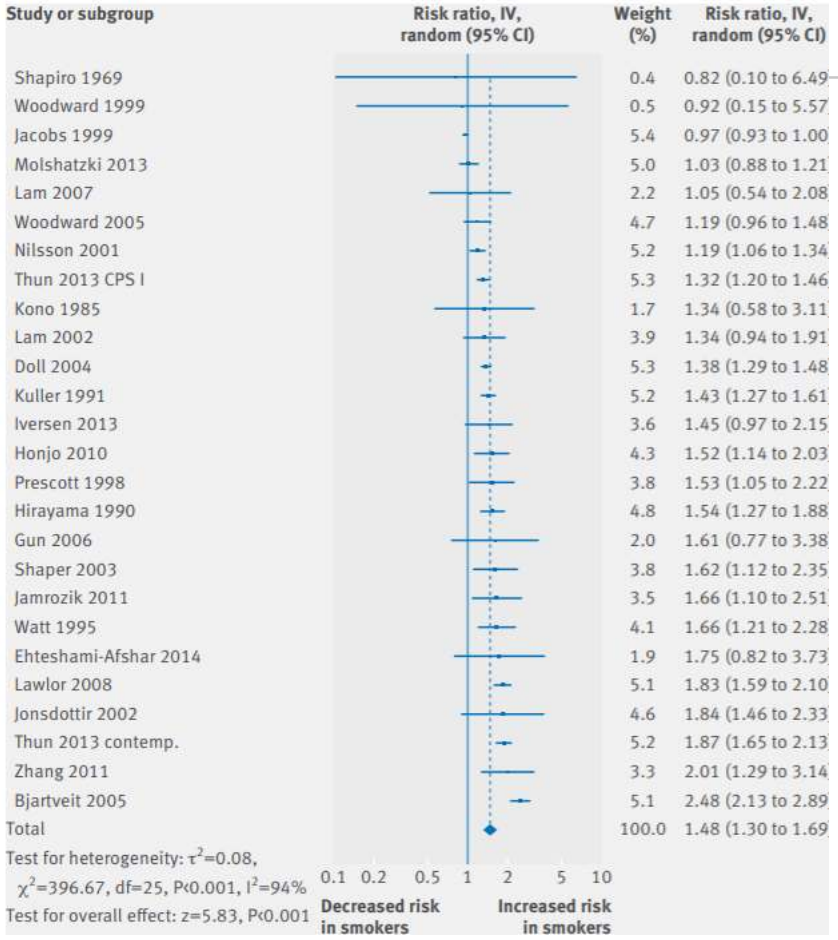
Réduction de la consommation

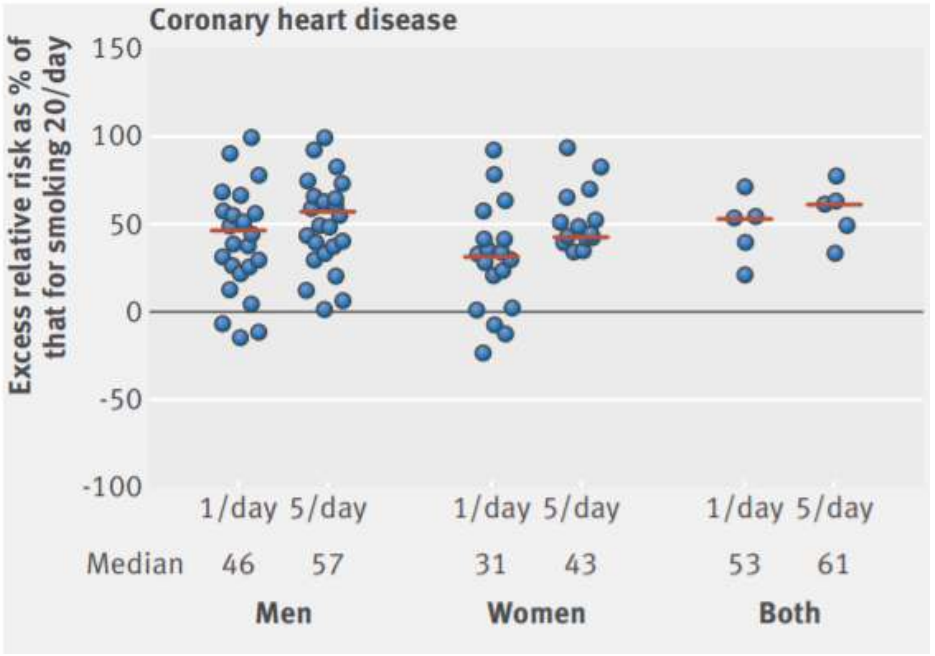
=

Réduction du risque

?

Sevrage, Réduction et risques CV et rénal





- Risque CV dès 1 cigarette par jour
- Pas de réduction du risque de MORTALITE CV

Excès de risque environ 50% pour 1-5 cigarettes/j chez les hommes fumeurs

Hackshaw A et al. BMJ. 2018 Jan 24;360:j5855. doi: 10.1136/bmj.j5855

Sevrage, Réduction et risques CV et rénal

Table 2. Point-prevalence abstinence in studies testing a reduction intervention.[a]

Study	Sample size	Follow-up (months)	Point-prevalence abstinence		Odds ratio for increased cessation in active group
			Active	Control	
Nicotine gum					
Batra et al., 2005	*364*	*13*	*12%*	*5%*	2.6[a*]
Haustein et al., 2003	*192*	*12*	*11%*	*8%*	1.4[a]
Wennike et al., 2003	411	24	9%	3%	2.9[b*]
Nicotine inhaler					
Bolliger et al., 2000	400	24	11%	9%	1.3[c]
Rennard et al., 2002	*429*	*15*	*8%*	*2%*	4.3[a]
Multiple NRTs					
Etter et al., 2004	923	26	12%	12%[d]	1.0[a]
Joseph et al., 2005	*152*	*6*	*8%*	*7%*	1.2[a]
Kralikova et al., 2002	*314*	*12*	*19%[d]*	*9%[d]*	2.4[a]

Note. Unpublished studies in italics. NRT, nicotine replacement therapy. [a]Calculated from abstinence rates. [b]Adjusted odds ratio from text. [c]Sustained abstinence, not point-prevalence abstinence. [d]Two control groups. *$p \leqslant .05$; otherwise, $p > .05$ or not reported.

- Stratégie de réduction augmente la probabilité d'être abstinent
- Problème de la définition de l'abstinence (6mois sur 7j, dosage cotinine, CO…)

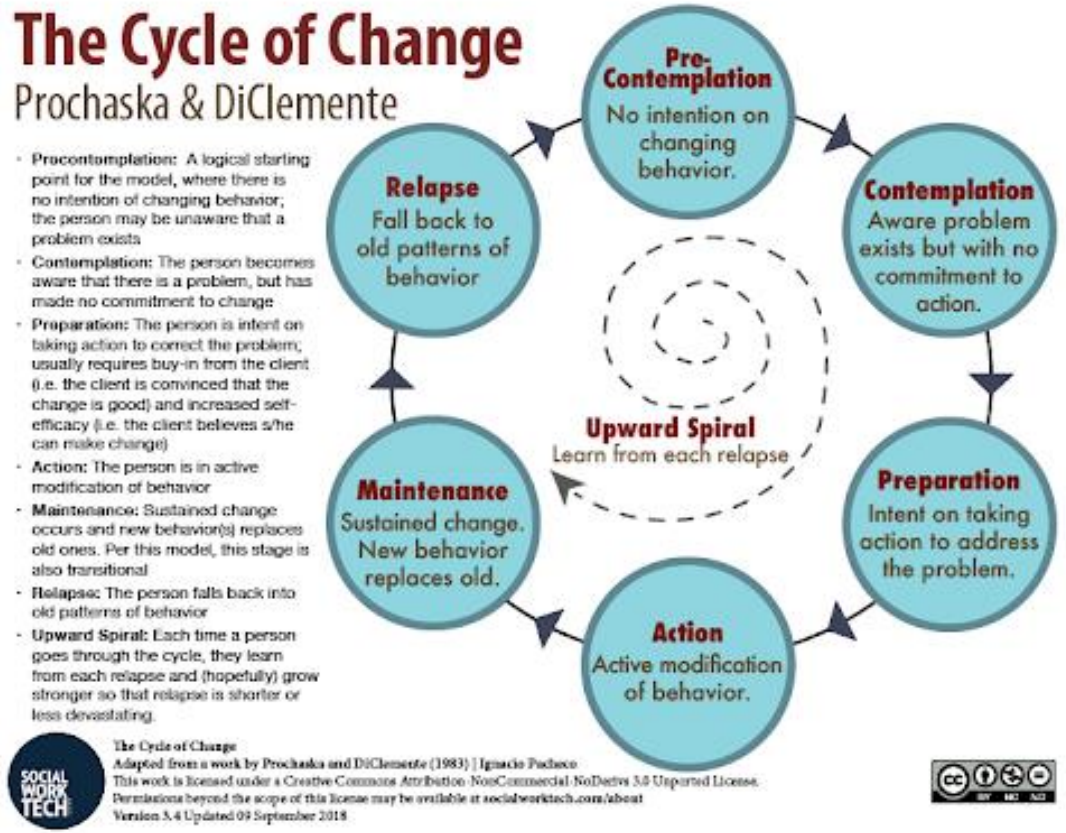
Hughes JR, Carpenter MJ. Nicotine Tob Res. 2006 Dec;8(6):739-49. doi: 10.1080/14622200600789726. PMID:

PLAN

- Tabagisme, vapotage, et risques CV et rénal
- Sevrage, Réduction et risques CV et rénal
- **Les outils du sevrage**

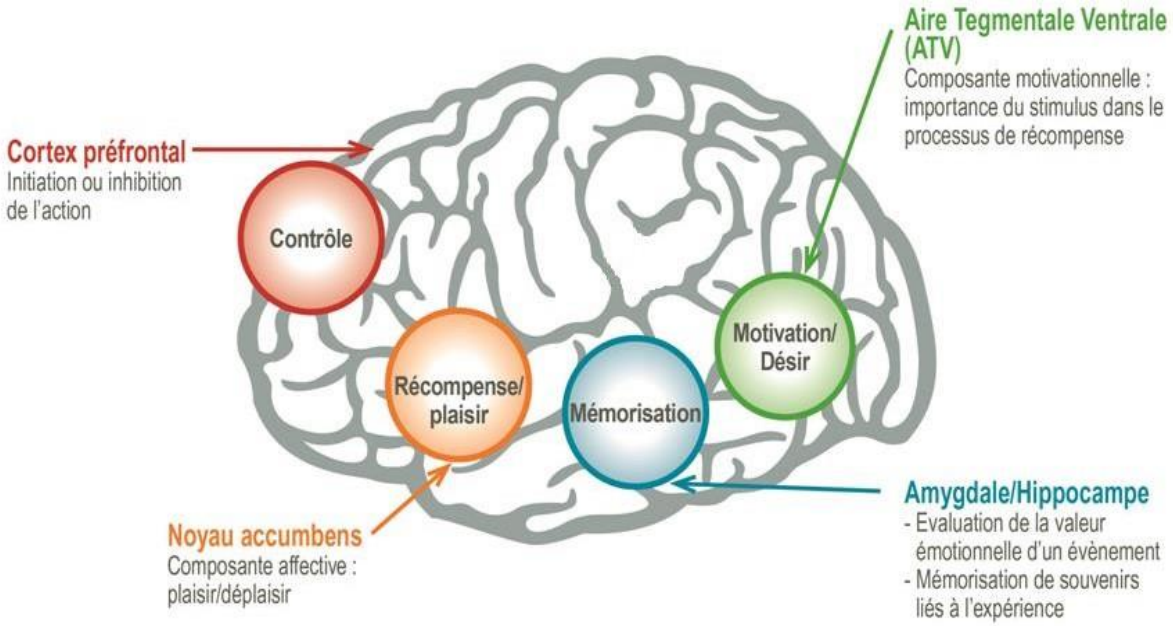
Les outils du sevrage

- **Evaluer la motivation / la renforcer**
- **Evaluer LES dépendances**
- **Evaluer le craving**
- ***Traiter l'addiction comme n'importe quelle autre maladie (peu importe la motivation….?)***

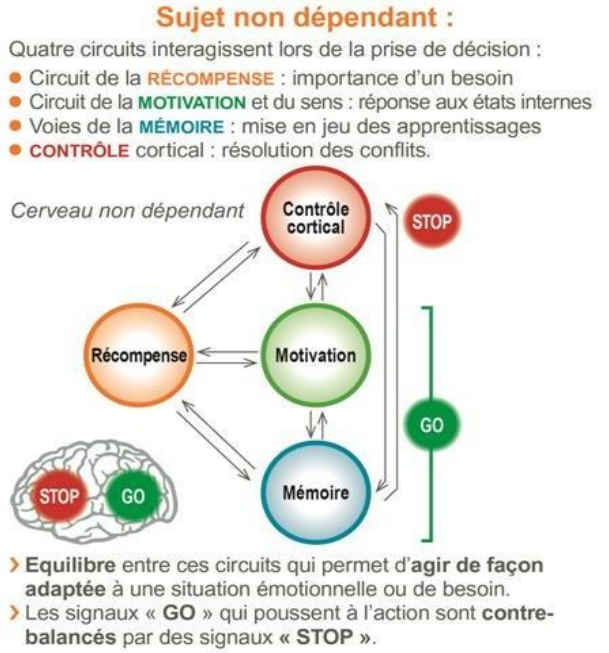


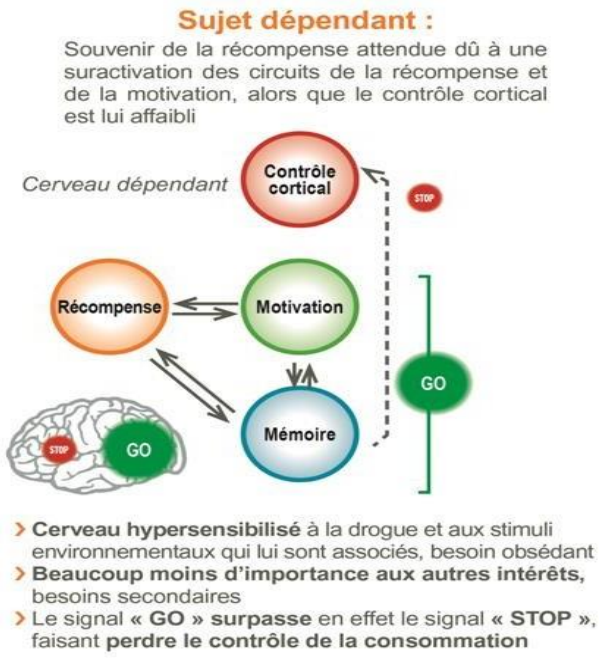
Nicotine

Circuit de la récompense

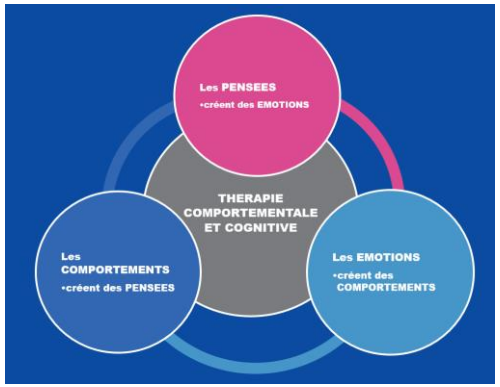


Perte contrôle cortical





Les outils du sevrage



Nicotine

Titration

T1/2 = 2h
Steady State = 10h

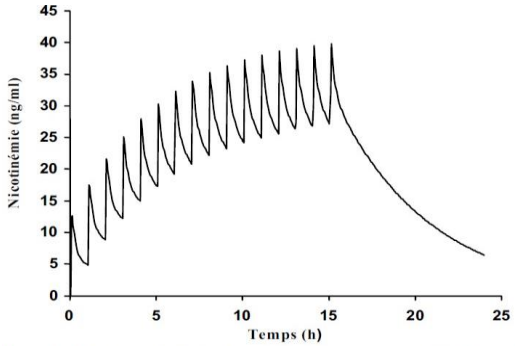
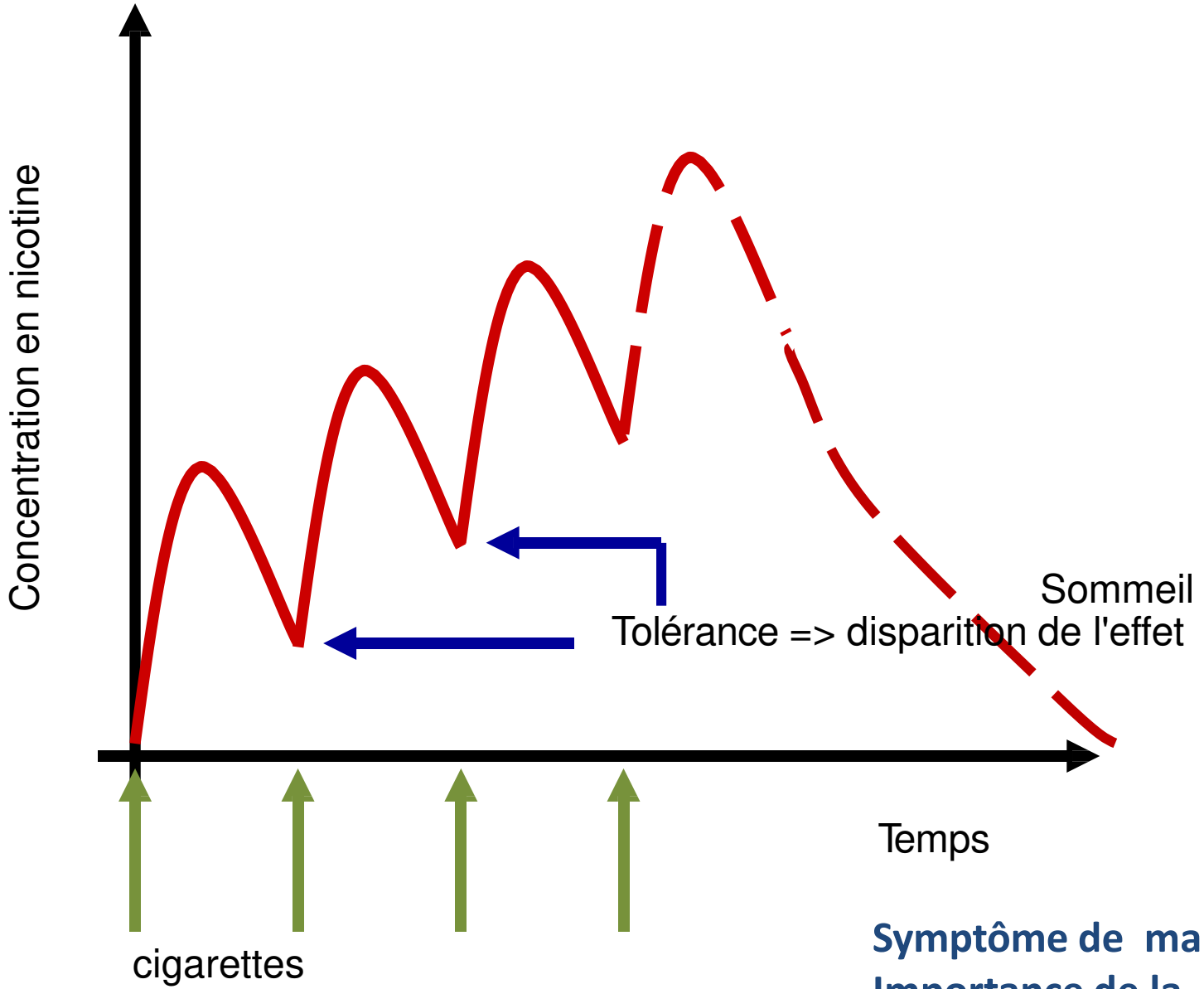


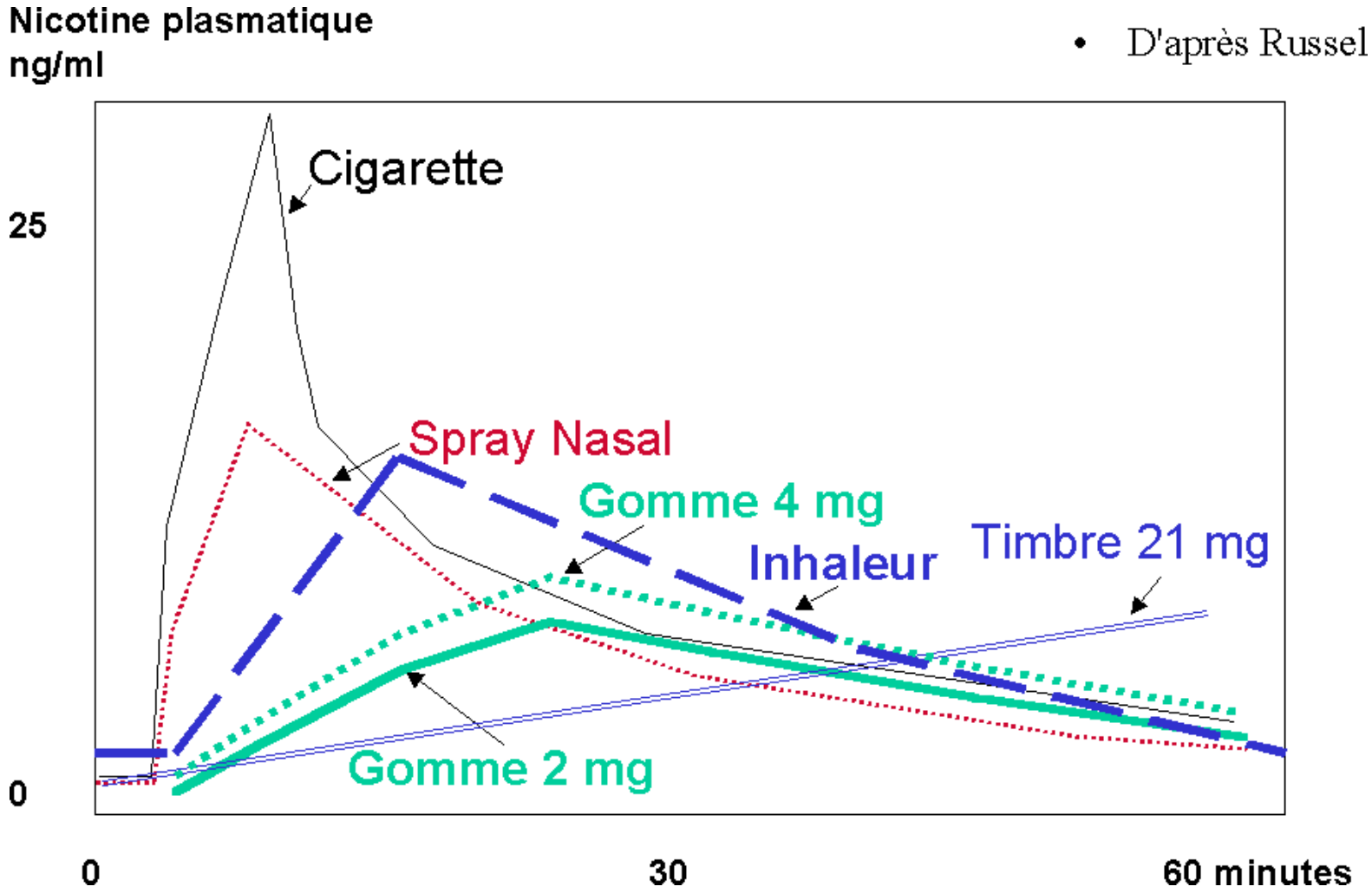
Figure 3.5 : Simulation de la nicotinémie d'un fumeur au cours de la journée basée sur des données pharmacocinétiques moyennes (une cigarette par heure pendant 16 heures)



Symptôme de manque du matin
Importance de la 1ère cigarette

Nicotine

Traitements Substitutifs Nicotiniques



Nicotine

Traitements Substitutifs Nicotiniques

Cochrane Library — Trusted evidence. Informed decisions. Better health.

Cochrane Database of Systematic Reviews

Comparison 1. Any type of NRT versus placebo/no NRT control

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Smoking cessation at 6+ months follow up	133	64640	Risk Ratio (M-H, Fixed, 95% CI)	1.55 [1.49, 1.61]
1.1 Gum	56	22581	Risk Ratio (M-H, Fixed, 95% CI)	1.49 [1.40, 1.60]
1.2 Patch	51	25754	Risk Ratio (M-H, Fixed, 95% CI)	1.64 [1.53, 1.75]
1.3 Inhalator	4	976	Risk Ratio (M-H, Fixed, 95% CI)	1.90 [1.36, 2.67]
1.4 Intranasal spray	4	887	Risk Ratio (M-H, Fixed, 95% CI)	2.02 [1.49, 2.73]
1.5 Tablets/lozenges	8	4439	Risk Ratio (M-H, Fixed, 95% CI)	1.52 [1.32, 1.74]
1.6 Oral spray	1	479	Risk Ratio (M-H, Fixed, 95% CI)	2.48 [1.24, 4.94]
1.7 Choice of NRT product	7	8288	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [1.25, 1.52]
1.8 Patch and inhalator	1	245	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.57, 1.99]
1.9 Patch and lozenge	1	308	Risk Ratio (M-H, Fixed, 95% CI)	1.83 [1.01, 3.31]
1.10 Patch and gum	2	259	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.64, 2.06]
1.11 Patch, gum and lozenge	1	424	Risk Ratio (M-H, Fixed, 95% CI)	15.0 [2.00, 112.54]

Hartmann-Boyce Cochrane 2018

Efficacité TSN quelque soit niveau de « support » non pharmacologique

Nicotine

Traitements Substitutifs Nicotiniques

RESEARCH PAPER

Use of nicotine replacement therapy and the risk of acute myocardial infarction, stroke, and death

R Hubbard, S Lewis, C Smith, C Godfrey, L Smeeth, P Farrington, J Britton

Tobacco Control 2005;**14**:416–421. doi: 10.1136/tc.2005.011387

See end of article for authors' affiliations

Correspondence to: Dr Richard Hubbard, Clinical Sciences Building, City Hospital, Hucknall Road, Nottingham NG5 1PB, UK; Richard.Hubbard@Nottingham.ac.uk

Received 1 February 2005
Accepted 8 June 2005

Objective: To determine whether nicotine replacement therapy (NRT) is associated with an increased risk of acute myocardial infarction, acute stroke, or death.
Design: Self control case series analysis of data from The Health Improvement Network (THIN) to estimate the relative incidence of myocardial infarction and stroke in four 14 day periods before and after the first prescription for NRT.
Setting: THIN is a computerised general practice database.
Subjects: Patients contributing data to THIN.
Interventions: Observational study of NRT.
Main outcomes: Acute myocardial infarction, acute stroke, and death.
Results: 33 247 individuals had been prescribed NRT, of whom 861 had had a myocardial infarction and 506 a stroke. There was a progressive increase in the incidence of first myocardial infarction in the 56 days leading up to the first NRT prescription (overall incidence ratio 5.55, 95% confidence interval (CI) 4.42 to 6.98), but the incidence fell after this time and was not increased in the 56 days after starting NRT (incidence ratio 1.27, 95% CI 0.82 to 1.97). The results were similar for second myocardial infarction and stroke, and for subgroups of people with pre-existing angina and hypertension. There were 960 deaths in our cohort during a mean follow up period of 2.6 years after starting NRT, with no evidence of an increased mortality in the 56 days after the NRT prescription (incidence ratio 0.86, 95% CI 0.60 to 1.23).
Conclusions: The use of NRT is not associated with any increase in the risk of myocardial infarction, stroke, or death.

- Bon profil de sécurité des TSN même en aigu

Nicotine

Traitements Substitutifs Nicotiniques – quelques « règles »

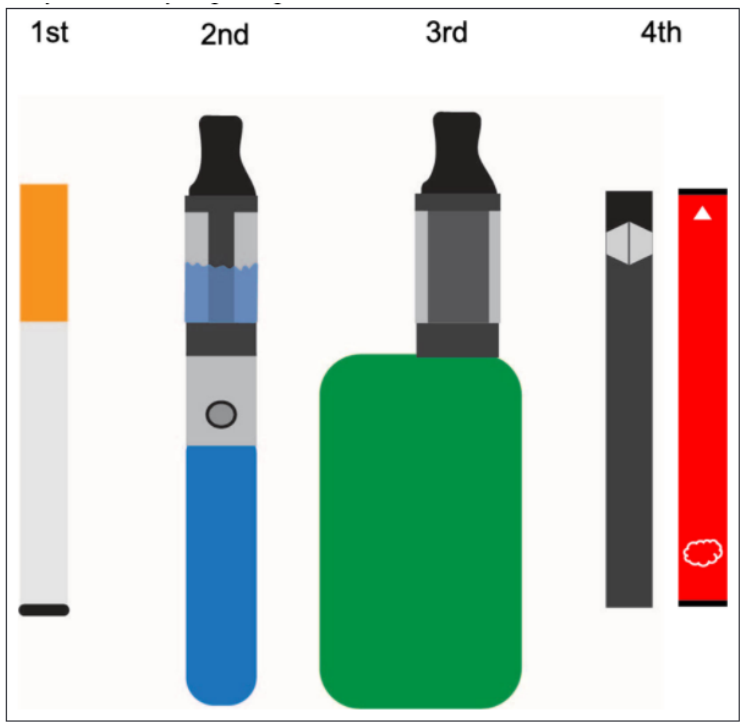
- Associer les galénique: TSN transdermique + « oral »

(si stratégie réduction, TSN oraux exclusifs OK)

- Fortes doses nicotine souvent nécessaires (2, voire 3…voire 4+ patchs)
- Adapter régulièrement posologie (Plan d'action personnalisé!) en fonction signes sous/sur-dosage
- Pas d'allergie à la nicotine…mais à la colle

Les outils du sevrage

VS

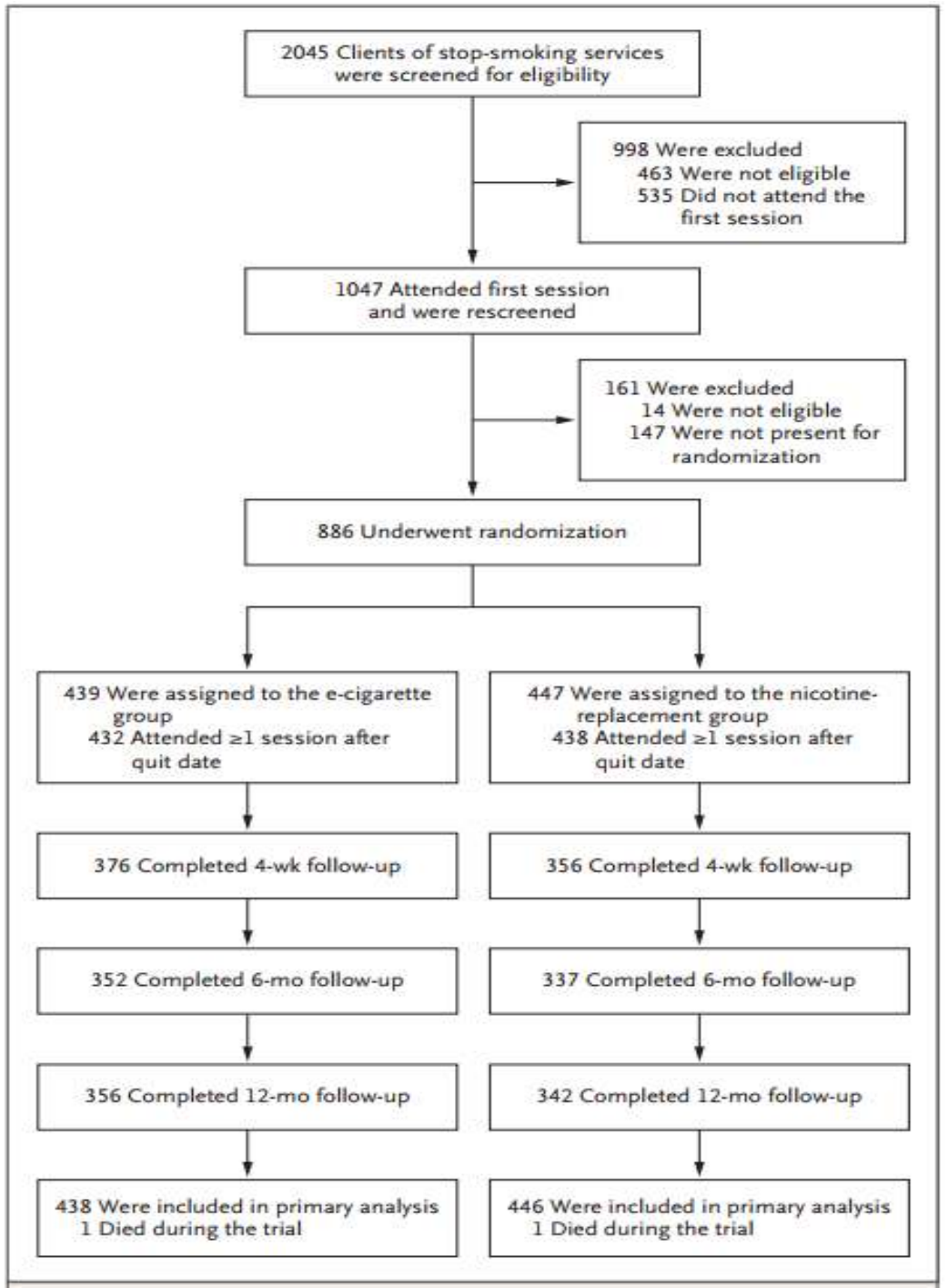


ORIGINAL ARTICLE

A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy

Peter Hajek, Ph.D., Anna Phillips-Waller, B.Sc., Dunja Przulj, Ph.D., Francesca Pesola, Ph.D., Katie Myers Smith, D.Psych., Natalie Bisal, M.Sc., Jinshuo Li, M.Phil., Steve Parrott, M.Sc., Peter Sasieni, Ph.D., Lynne Dawkins, Ph.D., Louise Ross, Maciej Goniewicz, Ph.D., Pharm.D., Qi Wu, M.Sc., and Hayden J. McRobbie, Ph.D.

- E-cigarette (starter kit,) vs. TSN (+/- combinaisons, gratuit 3 mois)
- « Smoking support » 1 fois par semaine
- Pas de changement de bras pendant 4 semaines



2019

Table 2. Abstinence Rates at Different Time Points and Smoking Reduction at 52 Weeks.*

Outcome	E-Cigarettes (N=438)	Nicotine Replacement (N=446)	Primary Analysis: Relative Risk (95% CI)†	Sensitivity Analysis: Adjusted Relative Risk (95% CI)
Primary outcome: abstinence at 52 wk — no. (%)	79 (18.0)	44 (9.9)	1.83 (1.30–2.58)	1.75 (1.24–2.46)‡
Secondary outcomes				
Abstinence between wk 26 and wk 52 — no. (%)	93 (21.2)	53 (11.9)	1.79 (1.32–2.44)	1.82 (1.34–2.47)§
Abstinence at 4 wk after target quit date — no. (%)	192 (43.8)	134 (30.0)	1.45 (1.22–1.74)	1.43 (1.20–1.71)¶
Abstinence at 26 wk after target quit date — no. (%)	155 (35.4)	112 (25.1)	1.40 (1.14–1.72)	1.36 (1.15–1.67)‡
Carbon monoxide–validated reduction in smoking of ≥50% in participants without abstinence between wk 26 and wk 52 — no./total no. (%)	44/345 (12.8)	29/393 (7.4)	1.75 (1.12–2.72)	1.73 (1.11–2.69)‖

- CJP: Abstinence déclarative à 52 semaines = pas plus de 5 cigarettes, CO expiré < 8

- 1.75 fois plus de chances d'arrêter de fumer avec e-cig que TSN ? …

Table 1. Characteristics of the Participants at Baseline.*

Characteristic	E-Cigarettes (N=438)	Nicotine Replacement (N=446)	Total (N=884)
Median age (IQR) — yr	41 (33–53)	41 (33–51)	41 (33–52)
Female sex — no. (%)	211 (48.2)	213 (47.8)	424 (48.0)
Employed — no. (%)	299 (68.3)	316 (70.9)	615 (69.6)
Entitled to free prescriptions — no. (%)	181 (41.3)	179 (40.1)	360 (40.7)
Median no. of cigarettes per day (IQR)	15 (10–20)	15 (10–20)	15 (10–20)
Median expired carbon monoxide level (IQR) — ppm	20 (13–27)	21 (13–28)	20 (13–28)
Score on the Fagerström Test for Cigarette Dependence†	4.5±2.5	4.6±2.4	4.6±2.4
Past use of nicotine replacement — no. (%)	328 (74.9)	334 (74.9)	662 (74.9)
Past use of e-cigarettes — no. (%)	186 (42.5)	181 (40.6)	367 (41.5)

- **Parmi la population étudiée, 75% d'atcd d'échecs TSN à l'inclusion (contre 40% pour e-cig)**

⇒ *Taux de succès des TSN: moitié de ceux habituellement observés (9.9% contre 15-20% habituellement*

- Parmi abstinents à 1 an: 80% groupe e-cig. continuaient à vaper / 9% groupe TSN les poursuivaient

- 25% des participants du groupe e-cigarette sont devenus des « **dual-users** » => davantage de « dual users » que de « quitters » (*cf. Nicotine Tob Res. 2017 Feb;19(2):183-189. doi: 10.1093/ntr/ntw218. Epub 2016 Aug 31.*)

Nicotine patches used in combination with e-cigarettes (with and without nicotine) for smoking cessation: a pragmatic, randomised trial

Natalie Walker, Varsha Parag, Marjolein Verbiest, George Laking, Murray Laugesen, Christopher Bullen

Summary

Background Combination nicotine replacement therapy shows additive cessation benefits. We aime effectiveness of combining nicotine patches with an e-cigarette (with and without nicotine) on six- abstinence.

- Stratégie patchs + e-cig avec nicotine plus efficace que patchs + e-cig sans nicotine (mais 7% abstinence à 6 mois sur données brutes)

- Pas de différence significative pour Patchs seuls vs. Patchs + e-cig nicotine (manque de puissance)

	Patches plus nicotine e-cigarette (n=500)	Patches plus nicotine-free e-cigarette* (n=499)	Relative risk (95% CI)	Risk difference (95% CI)	p value
Continuous abstinence					
Self-reported quit rate at 1 month	189 (38%)	147 (30%)	1·28 (1·08 to 1·53)	8·34 (2·50 to 14·18)	0·005
Self-reported quit rate at 3 months	117 (23%)	69 (14%)	1·69 (1·29 to 2·22)	9·57 (4·78 to 14·36)	<0·001
Self-reported quit rate at 6 months	89 (18%)	53 (11%)	1·68 (1·22 to 2·30)	7·18 (2·87 to 11·49)	0·001
CO-verified quit rate at 6 months (primary outcome)	35 (7%)	20 (4%)	1·75 (1·02 to 2·98)	2·99 (0·17 to 5·81)	0·038
Sensitivity analyses					
Extrapolated adjustment for CO-verification†	85 (17%)	50 (10%)	1·70 (1·22 to 2·35)	6·98 (2·76 to 11·20)	0·001
Complete cases analysis‡	35/330 (11%)	20/328 (6%)	1·74 (1·03 to 2·95)	4·51 (0·30 to 8·72)	0·037

	Patches plus nicotine e-cigarette (n=500)	Patches only* (n=125)	Relative risk (95% CI)	Risk difference (95% CI)	p value
Continuous abstinence					
Self-reported quit rate at 1 month	189 (38%)	21 (17%)	2·25 (1·50 to 3·30)	21·0 (13·19 to 28·81)	<0·001
Self-reported quit rate at 3 months	117 (23%)	13 (10%)	2·25 (1·31 to 3·86)	13·00 (6·49 to 19·51)	<0·001
Self-reported quit rate at 6 months	89 (18%)	10 (8%)	2·23 (1·19 to 4·15)	9·80 (3·98 to 15·62)	0·007
CO-verified quit rate at 6 months (primary outcome)	35 (7%)	3 (2%)	2·92 (0·91 to 9·33)	4·60 (1·11 to 8·09)	0·05
Sensitivity analyses					
Extrapolated adjustment for CO-verification†	85 (17%)	9 (7%)	2·36 (1·22 to 4·56)	9·80 (4·20 to 15·40)	0·006
Complete cases analysis‡	35/330 (11%)	3/61 (5%)	2·16 (0·68 to 6·79)	5·69 (-0·67 to 12·05)	0·17

Cigarette électronique

Est-ce toxique ?

Est-ce une stratégie de « Réduction de risque » acceptable ?

ERS Position Paper on Tobacco Harm Reduction

A statement by the ERS Tobacco Control Committee

The ERS Tobacco Control Committee (TCC) published the position paper on tobacco harm reduction in May 2019.

The ERS TCC believe that current strategies which support the use of alternative nicotine delivery products for smoking cessation are not effective as they are based upon incorrect assumptions and undocumented claims about the safety and effectiveness of alternative nicotine delivery products for smoking cessation.

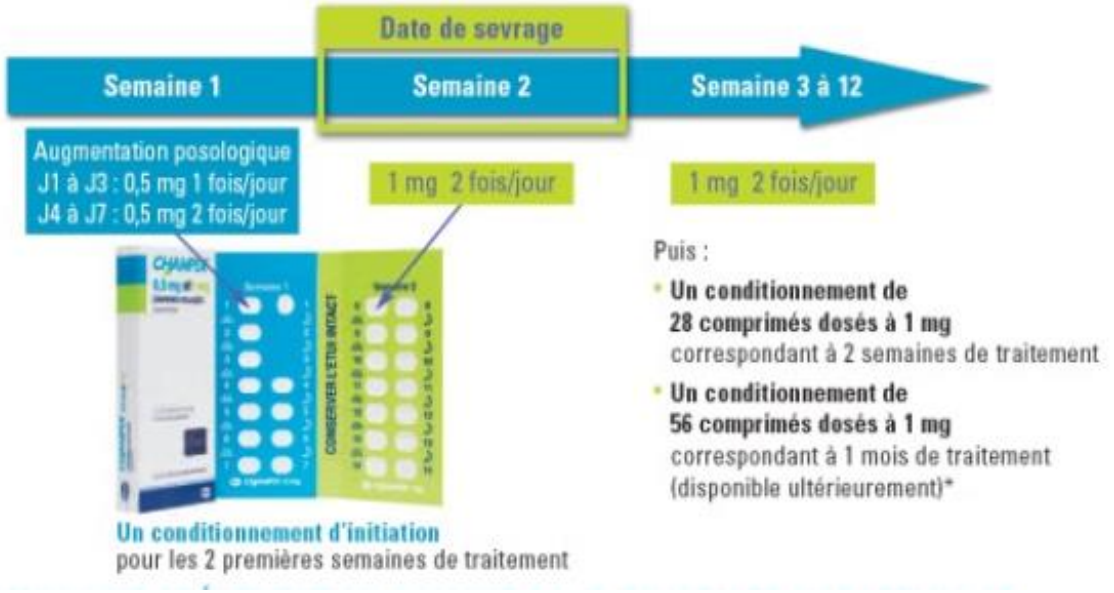
Therefore, the statement brings together scientifically-backed arguments for why a tobacco harm reduction strategy should not be used as a population-based strategy in tobacco control, including that harm reduction arguments are:

- Based on incorrect claims that smokers cannot or will not quit smoking
- Reliant upon undocumented assumptions that alternative nicotine delivery products are highly effective as a smoking cessation aid
- Built on incorrect assumptions that smokers will replace conventional cigarettes with alternative nicotine delivery products
- Ignorant to the lack of evidence to show that alternative nicotine delivery products are safe for human health

Les outils du sevrage

Varéniciline

- Traitement de 2è intention
- 12 semaines renouvelable 1 fois (ou davantage…)
- Agoniste partiel sélectif des récepteurs nicotiniques (dont alpha4bêta2)
- Effet **agoniste partiel**: réduit le besoin impérieux de fumer et les symptômes de manque
- Effet **antagoniste**: réduit les effets de récompense et de renforcement du tabagisme

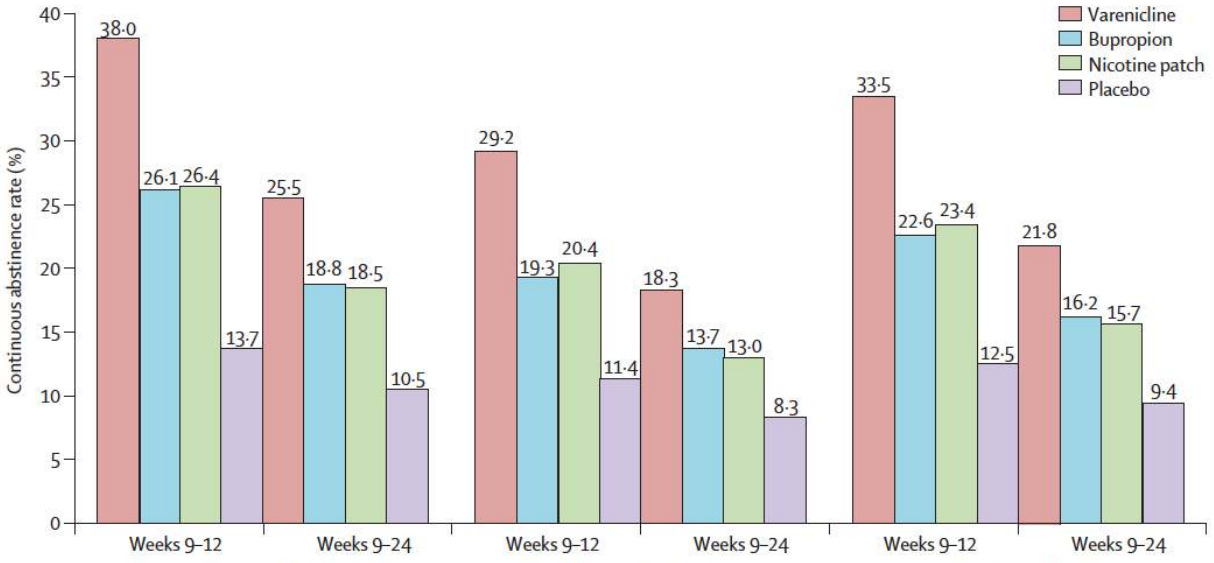


Les outils du sevrage

Varéniciline

- Effets indésirables:
  - ✓ Céphalées
  - ✓ Nausées (prise pendant repas, ajust. poso)
  - ✓ Rêves « anormaux » (délires oniriques)
  - ✓ Insomnies

Les outils du sevrage



OR (95% CI) p value	Weeks 9–12	Weeks 9–24	Weeks 9–12	Weeks 9–24	Weeks 9–12	Weeks 9–24
Primary comparisons						
Varenicline *vs* placebo	4·00 (3·20–5·00) p<0·0001	2·99 (2·33–3·83) p<0·0001	3·24 (2·56–4·11) p<0·0001	2·50 (1·90–3·29) p<0·0001	3·61 (3·07–4·24) p<0·0001	2·74 (2·28–3·30) p<0·0001
Bupropion *vs* placebo	2·26 (1·80–2·85) p<0·0001	2·00 (1·54–2·59) p<0·0001	1·87 (1·46–2·39) p<0·0001	1·77 (1·33–2·36) p<0·0001	2·07 (1·75–2·45) p<0·0001	1·89 (1·56–2·29) p<0·0001
Secondary comparisons						
Nicotine patch *vs* placebo	2·30 (1·83–2·90) p<0·0001	1·96 (1·51–2·54) p<0·0001	2·00 (1·56–2·55) p<0·0001	1·65 (1·24–2·20) p=0·0007	2·15 (1·82–2·54) p<0·0001	1·81 (1·49–2·19) p<0·0001
Varenicline *vs* nicotine patch	1·74 (1·43–2·10) p<0·0001	1·52 (1·23–1·89) p=0·0001	1·62 (1·32–1·99) p<0·0001	1·51 (1·19–1·93) p=0·0008	1·68 (1·46–1·93) p<0·0001	1·52 (1·29–1·78) p<0·0001
Bupropion *vs* nicotine patch	0·98 (0·80–1·20) p=0·8701	1·02 (0·81–1·28) p=0·8645	0·94 (0·75–1·16) p=0·5467	1·07 (0·83–1·39) p=0·5824	0·96 (0·83–1·11) p=0·5797	1·04 (0·88–1·24) p=0·6002
Varenicline *vs* bupropion	1·77 (1·46–2·14) p<0·0001	1·49 (1·20–1·85) p=0·0003	1·74 (1·41–2·14) p<0·0001	1·41 (1·11–1·79) p=0·0047	1·75 (1·52–2·01) p<0·0001	1·45 (1·24–1·70) p<0·0001

Figure 3: **Continuous abstinence rates for weeks 9–12 and 9–24**
Analyses based on the all-randomised population. OR=odds ratio.

EAGLES, Anthenelli et al, Lancet 2016

Les outils du sevrage

	Non-psychiatric cohort* (n=3984)				Psychiatric cohort* (n=4074)			
	Varenicline (n=990)	Bupropion (n=989)	Nicotine patch (n=1006)	Placebo (n=999)	Varenicline (n=1026)	Bupropion (n=1017)	Nicotine patch (n=1016)	Placebo (n=1015)
Primary composite neuropsychiatric endpoint	13 (1·3%)	22 (2·2%)	25 (2·5%)	24 (2·4%)	67 (6·5%)	68 (6·7%)	53 (5·2%)†	50 (4·9%)
Estimated primary composite neuropsychiatric adverse events (% [95% CI])	1·25% (0·60 to 1·90)	2·44% (1·52 to 3·36)	2·31% (1·37 to 3·25)	2·52% (1·58 to 3·46)	6·42% (4·91 to 7·93)	6·62% (5·09 to 8·15)	5·20% (3·84 to 6·56)	4·83% (3·51 to 6·16)
Difference in risk of composite primary endpoint (RD% [95% CI])								
Versus placebo	−1·28 (−2·40 to −0·15)	−0·08 (−1·37 to 1·21)	−0·21 (−1·54 to 1·12)	..	1·59 (−0·42 to 3·59)	1·78 (−0·24 to 3·81)	0·37 (−1·53 to 2·26)	..
Versus nicotine patch	−1·07 (−2·21 to 0·08)	0·13 (−1·19 to 1·45)	..	..	1·22 (−0·81 to 3·25)	1·42 (−0·63 to 3·46)	..	..
Versus bupropion	−1·19 (−2·30 to −0·09)	..	..	..	−0·20 (−2·34 to 1·95)	..	..	..
Components of primary neuropsychiatric composite endpoint								
Anxiety‡	0	1 (0·1%)	0	3 (0·3%)	5 (0·5%)	4 (0·4%)	6 (0·6%)	2 (0·2%)
Depression‡	1 (0·1%)	0	0	0	6 (0·6%)	4 (0·4%)	7 (0·7%)	6 (0·6%)
Feeling abnormal‡	0	0	0	0	0	1 (0·1%)	0	0
Hostility‡	0	1 (0·1%)	1 (0·1%)	0	0	0	0	0
Agitation§	10 (1·0%)	11 (1·1%)	19 (1·9%)	11 (1·1%)	25 (2·4%)	29 (2·9%)	21 (2·1%)	22 (2·2%)
Aggression§	3 (0·3%)	3 (0·3%)	2 (0·2%)	3 (0·3%)	14 (1·4%)	9 (0·9%)	7 (0·7%)	8 (0·8%)
Delusions§	0	0	1 (0·1%)	0	1 (0·1%)	1 (0·1%)	1 (0·1%)	0
Hallucinations§	1 (0·1%)	0	0	0	5 (0·5%)	4 (0·4%)	2 (0·2%)	2 (0·2%)
Homicidal ideation§	0	0	1 (0·1%)	0	0	0	0	0
Mania§	0	1 (0·1%)	2 (0·2%)	2 (0·2%)	7 (0·7%)	9 (0·9%)	3 (0·3%)	6 (0·6%)
Panic§	0	4 (0·4%)	1 (0·1%)	3 (0·3%)	7 (0·7%)	16 (1·6%)	13 (1·3%)	7 (0·7%)
Paranoia§	0	1 (0·1%)	0	0	1 (0·1%)	0	0	2 (0·2%)
Psychosis§	0	0	1 (0·1%)	0	4 (0·4%)	2 (0·2%)	3 (0·3%)	1 (0·1%)
Suicidal behaviour§	0	1 (1·0%)	1 (0·1%)	0	1 (0·1%)	1 (0·1%)	0	1 (0·1%)
Suicidal ideation§	0	1 (0·1%)	2 (0·2%)	3 (0·3%)	5 (0·5%)	2 (0·2%)	3 (0·3%)†	2 (0·2%)
Completed suicide§	0	0	0	1 (0·1%)	0	0	0	0

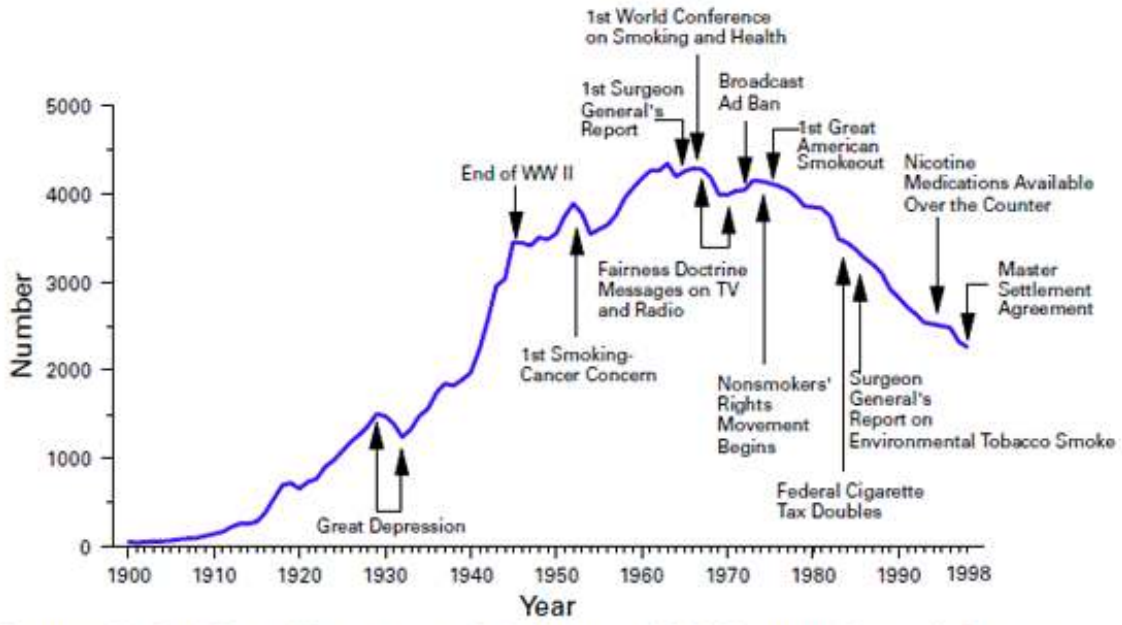
(Table 2 continues on next page)

EAGLES, Anthenelli et al, Lancet 2016

Les outils du sevrage

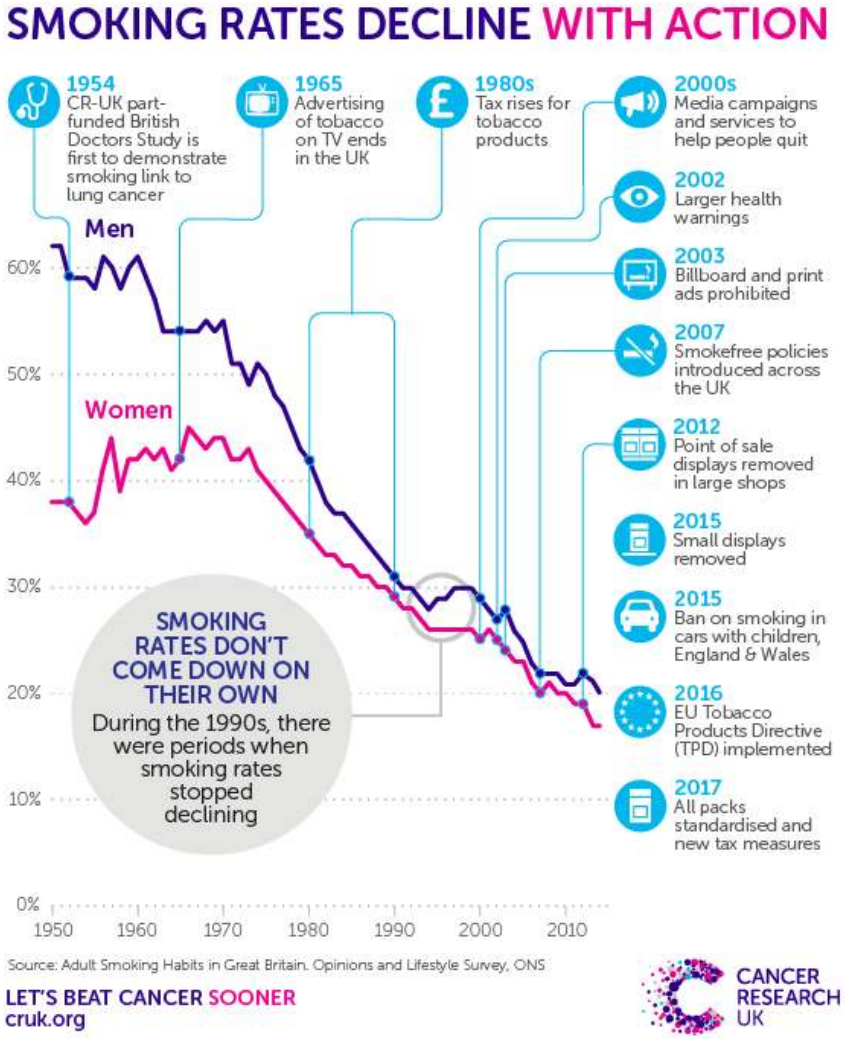
Tabac et politique: Monde

FIGURE 1. Annual adult per capita cigarette consumption and major smoking and health events — United States, 1900–1998



Sources: United States Department of Agriculture; 1986 Surgeon General's Report.

USA



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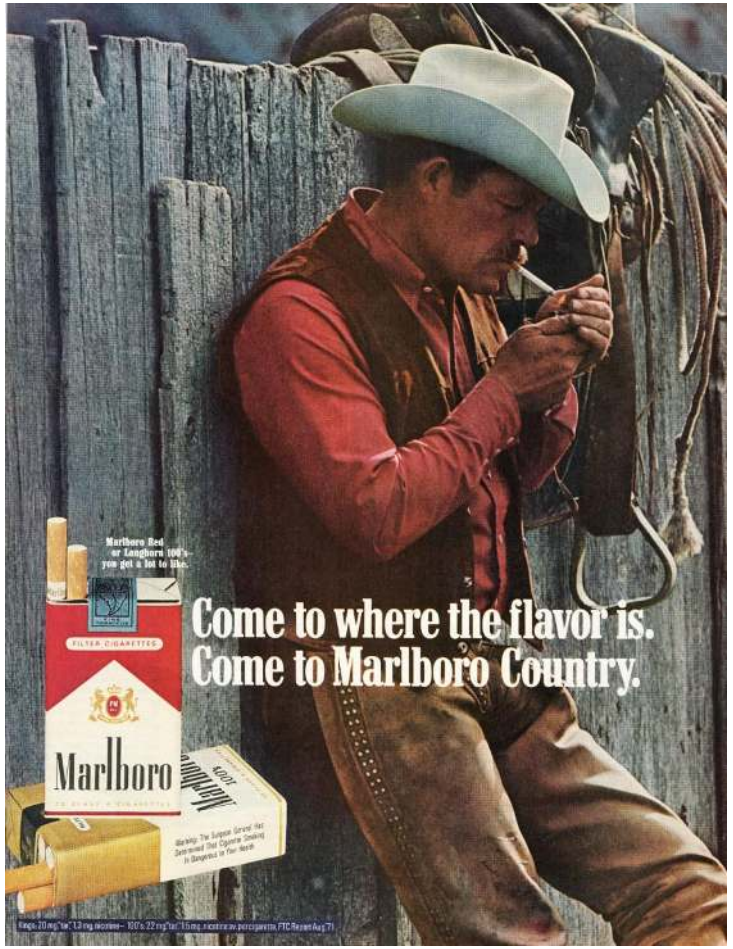
Les outils du sevrage



1955

2020

Take Home Message

- Tabagisme ET vapotage = FdR CV et (respi.!)
- « smokeless tobacco product »: FdR, données à consolider
- Réduction de la consommation ≠ Réduction du risque (ou presque)
  mais augmente chances de sevrage
- La dépendance à la nicotine est une maladie
- Nombreux outils de sevrage EFFICACES et sans risques…si bien utilisés
  + suivi rapproché
- *Dura lex, sed lex !*

Merci de votre attention

Dr Jérémy Charriot

Pneumologie et Addictologie

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