

Animal Table

Reference	Experimental Design	Species	Sample Size	Age	Inhaled Nicotine Product	Nicotine content	Outcome measures	Biochemical Analyses of Nicotine
(Shao et al., 2019)	Passive whole body exposure	mice	5 per group	Adult (8-12 weeks)	bluCig PLUS e-cig	2.4%	Food intake, locomotion, body weight	plasma nicotine/cotinine
(Javadipaydar et al., 2019)	Passive exposure	rats	8	Adult (10-11 weeks)	e-cig cartridges (protank 3 atomizer, MT32 coil)	0, 1, 10, 30 mg/mL	body temperature, locomotor activity	Plasma nicotine and cotinine
(Shao et al., 2017)	passive nose-only exposure	rats	n/a	adult	3-jet Collison nebulizer	1%	Uterine artery blood flow, arterial blood pressure, ECG	plasma nicotine/cotinine
(Ahmad et al., 2019)	Passive nose only exposure	rats	6	Adult (275-300 g)	Bioaerosol Nebulizer Generator	0/5/10%	Toxicity markers	n/a
(Nabavizadeh et al., 2018)	Passive nose-only	rats	60	Adult 8-10 weeks	IQOS	aerosol particle phase: 0.67 ± 0.02	Arterial flow-mediated dilation,	serum nicotine/cotinine
(Titz et al., 2018)	Passive nose-only exposure	rats	83	Adult, 6-8 weeks old	CHTP1.2,	15, 23, 50 ug/L	System toxicology results	n/a
(Lefever et al., 2017)	Passive exposure	mice	8/sex/group	adult	modified e-cig (iStick 30W CE5-S tank)	0, 12, 24, 30 mg/ml	Hypothermia, locomotor suppression	Plasma and brain nicotine/cotinine
(Espinoza-derout et al., 2019)	passive exposure	mice	5 per group	Adult (8 weeks)	e-cigs, bluCig PLUS	0%, 2.4%	Echo, Ventricular transcriptomic analysis, Transmission electron microscopy	plasma cotinine
(Orzabal et al., 2019)	passive exposure	rats	37	adult	nicotine aerosol	50, 100 mg/mL	maternal and fetal vascular hemodynamics, growth deficits	n/a
(Shi et al., 2019)	whole body exposure	mice	3-5 per group	Adult (2-3 months)	nicotine aerosol	24 mg/ml	Echo	plasma cotinine
(Wetendorf et al., 2019)	whole body passive exposure	mice	5 per group	Adult	Joyetech eVic VTC Mini with a 0.15-V e-cig	24mg/ml	embryo implantation, RNA microarray, weight	n/a

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(Laube et al., 2017)	whole-body passive exposure	mice	45	Adult (10.5 weeks)	Joytech 510-T@ e-cig	0,2,4%	mucociliary clearance in lungs	serum cotinine
(Madison et al., 2019)	passive exposure	mice	n/a	Adult (two months)	Zeus e-cig (5 V, 1300-mAh capacity, and cartomizer with a 2.5- Ω coil)	33mg/ml	inflammation emphysema	n/a
(Crotty Alexander et al., 2018)	nose only exposure	mice	6	Adult (6-8 weeks)	e-cig (1.8 Ω) lithium ion battery (3.4 V)	24mg/ml	HR, BP, inflammatory markers	serum cotinine
(Alasmar i et al., 2017)	passive nose only exposure	mice	4-5 per group	Adult (6-week-old)	nicotine aerosol	24 mg/mL	α -7 anchor, GLT-1, xCT, GLAST and GAPDH in FC, STR and HIP changes	brain nicotine/cotinine
(Lee et al., 2019)	passive nose-only exposure	mice	3-15 per group	Adult (10 weeks)	MarkTenVR e-cig	4%	terminal organ weights, lung transcriptomics and proteomics	n/a
(Wang et al., 2019)	passive exposure	mice	6 per group	Adult	e Joytech eVIC VTC mini e-cig [atomizer/coil (0.15 Ω)]	25 mg/mL	inflammatory markers	n/a
(Alasmar i et al., 2019)	passive exposure	mice	5 per group	Adult (6-8 weeks)	e-cig cartomizers (tanks; 2.4 Ω)	24 mg/ml	neurotransmitters in frontal cortex and striatum	n/a
(Lefever et al., 2019)	Passive exposure	mice	6-8 per sex	adult	modified e-cig (iStick 30W CE5-S tank)	12,18,24, 30mg/ml	Nicotine discrimination	plasma and brain nicotine
(Montana ri et al., 2019)	passive exposure	rats	6 per group	Adult (~250 g)	e-cig (Protank II Atomizer, MT32 coil operating at 2.2 Ω)	20, 40, 80 mg/mL	somatic withdrawal signs	plasma nicotine/cotinine
(Phillips et al., 2018)	Passive nose-only exposure	rats	284	Adult (6-8 weeks)	CHTP1.2	15,23, 50 μ g /L,	nasal epithelium changes	Plasma nicotine/cotinine
(Phillips et al., 2017)	Passive nose-only exposure	rats	208	Adult (6 weeks)	6-jet Collison nebulizer	.023mg/L	toxicological endpoints	plasma nicotine/cotinine levels
(Qasim et al., 2018)	Passive whole body exposure	mice	5-8 per group	Adult (10 weeks)	e-cig: SMOK TFV4 Mini Tanks (5 V, 0.4 Ω)	18mg/ml	Thrombotic events	Plasma cotinine
(Ha et al., 2019)	Passive whole body exposure	mice	24	n/a	Nicotine vapor	n/a	Larynx inflammation	n/a

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(Olfert et al., 2018)	Passive whole body exposure	mice	45	Adult (13-14 weeks)	tank e-cig (eGrip OLED, Joyetech)	18mg/ml	aortic arterial stiffness,	Urine cotinine
(Phillips et al., 2019)	passive whole-body exposure	mice	882	Adult (8-10 weeks)	CHTP 1.2, THS 2.2,	28 µg/L	lung function, lung volume, inflammation, oxidative stress	plasma nicotine/cotinine
(Glynos et al., 2018)	passive whole-body exposure	mice	5-10 per group	Adult (8-12 weeks)	e-cig vapors	18 mg/ml	Lung inflammation; lung mechanics	n/a

e-cig=e-cigarette; ECG=electrocardiogram; CHTP 1.2=carbon heated tobacco product 1.2; THS 2.2=tobacco heating system 2.2; $\alpha 7$ = $\alpha 7$ nicotinic acetylcholine receptor; GLT-1=glutamate transporter 1; xCT=cystine–glutamate antiporter; GLAST=glutamate and aspartate transporter; GAPDH=Glyceraldehyde 3-phosphate dehydrogenase; FC=frontal cortex; STR=striatum; HIP=hippocampus; HR=heart rate; BP=blood pressure; echo=echocardiography; Ω =ohms; V=volts

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Reference	Experimental Design	Subjects	Sample Size	Age (Years M(SD))	Inhaled Nicotine Product	Nicotine content	Flavors	Outcome measures	Biochemical Analyses of Nicotine
(Staudt et al., 2018)	directed e-cig puffing session	Self-reported never-smokers	10	40.2 ± 9.7	Blu brand e-cig	n/a	n/a	endothelial microparticles, transcriptome of small airway epithelium, alveolar macrophages	n/a
(Caponnetto et al., 2018)	directed e-cig puffing session	smoking ≥10 CPD for at least 5 years	12	28.6	Heated tobacco products (iQOS, GLO)	n/a	n/a	Carbon monoxide	n/a
(Leventhal et al., 2019)	directed e-cig puffing session	current e-cig user (>1 day/week for >1 month), use e-cigs with nicotine	100	25.4 (4.4)	Joyetech Delta 23 Atomizer tank with eVic Supreme battery e-cig	6 mg/mL, 0 mg/mL	9 flavors; 5 Fruit, 2 menthol, 2 tobacco	Subjective effects	n/a
(Devito et al., 2019)	directed e-cig puffing and ad-lib session	≥5 CPD for past year; lifetime e-cig use	32	32.5 (7.8)	eVic Supreme e-cigs (Joyetech) (9W)	0 mg/mL, 24 mg/mL	unflavored, menthol, fruit-flavored	Subjective effects, number of puffs	plasma nicotine, cotinine, 3-hydroxycotinine
(St. Helen et al., 2017)	Directed e-cig puffing and ad-lib session	e-cig users (used at least 25 days for 3 months) or dual users (e-cig and cig users who smoked <5 CPD)	14	32.3 (13.8)	KangerTech mini ProTank 3 e-cig	19.9mg/mL, 19.3 mg/mL, 7.4 ± 3.4 mg/mL	strawberry, tobacco, users' own	subjective effects HR, pH	plasma nicotine
(Spindle et al., 2018)	directed e-cig puffing sessions	smoke <5 CPD, use ≥ 1 mL ECIG liquid daily for ≥ 3 months	30	26.9 (7.1)	eGO' battery with dual-coil, 510 cartomizer e-cig	18 mg/ml	tobacco	subjective effects, HR, puff topography	plasma nicotine
(Hiler et al., 2017)	directed e-cig puffing sessions	e-cig experienced users: e-cig use for ≥ 3 months, ≥ 1 ml e-cig solution daily currently smoking ≤5 CPD. E-cig naïve cigarette smokers: ≥ 10 CPD, < 5 e-cig uses lifetime	64	30.6 (9.1)	3.3 V eGo battery with 1.5 Ω cartomizer e-cig	0, 8, 18, or 36 mg/ml	Tobacco or menthol	puff topography, Subjective effects, HR	plasma nicotine

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(Pullicin et al., 2019)	directed e-cig puffing session	e-cig use with nicotine for ≥ 1 month	19	24.5	V2 Ex Blank Cartridge and a V2 Standard 79-mm E-cig Battery (4.2 V)	0,6,12mg/ml	cherry flavor (4.7% or 9.3%)	subjective effects	n/a
(Voos et al., 2019b)	directed e-cig puffing and ad-lib session	smoked ≥ 5 CPD	18	44.1(7.0)	SuperCig Automatic eGo 510 Battery 910mAh (4.1V, 3.0 Ω)	24mg/ml	cherry, tobacco, espresso, menthol, and vanilla	puffing topography, subjective effects	plasma nicotine
(Voos et al., 2019a)	directed e-cig puffing and ad-lib session	smoked ≥ 10 CPD	18	41.3(9.7)	disposable; rechargeable; eGO; mod; e-Cigar; and e-Pipe	11.7mg/ml, 19.4mg/ml, 29.9mg/ml, 15.5 mg/ml, 29.9mg/ml	tobacco	subjective effects	plasma nicotine
(Wagener et al., 2017)	directed e-cig puffing and ad-lib session	e-cig users used e-cig for 3 months, smokers used cig for 3 months	30	33.8(10.9)	own G2, G3 e-cig device	preferred nicotine concentration	preferred flavor	subjective effects	plasma nicotine
(Maloney et al., 2019)	directed e-cig puffing and ad-lib session	smoked ≥ 10 CPD for at least a year	24	30.9 (9.5)	nicotine inhaler, eGo 3.3 V, 1000 mAh e-cig battery with a 1.5 Ω , dual-coil, 510-style cartomizer	nicotine inhaler 10mg, 36mg/ml e-liquid	preferred flavor tobacco or menthol	multiple-choice procedure, subjective effects	plasma nicotine
(Antoniwicz et al., 2019)	directed e-cig puffing session	occasional cig users (max ten cigarettes/month)	15	26 (3)	variable mod e-cig (32 W, 0.20 Ω).	0,19mg/ml	n/a	BP, HR, arterial stiffness, dynamic spirometry and impulse oscillometry	n/a
(Hiler et al., 2019)	directed e-cig puffing and ad-lib session	smoke <5 CPD, use ≥ 1 mL e-cig liquid daily for ≥ 3 months	32	25.6(7.1)	4.5-V Kanger SUBOX e-cig	3, 8mg/ml	Honeydew Pear	HR, subjective effects, puff topography, and e-liquid consumption	plasma nicotine
(Yingst et al., 2019b)	directed e-cig puffing session	pod-based ENDS users	6	37.8 (15.8)	own pod-based e-cig	59mg/mL	Users' own	subjective effects	Serum nicotine, cotinine, and 3-hydroxycotinine

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(St. Helen et al., 2019)	directed e-cig puffing session	smoked ≥ 5 CPD past month, use same e-cig device at least 15/30 past days	36	35.4 (11.7)	Users' own e-cig	Users' own	Users' own	subjective effects	plasma nicotine
(Harvanko et al., 2019)	Cig and e-cig ad-lib session	smoked ≥ 5 CPD past month, use same e-cig device at least 15/30 past days	36	35.4 (11.7)	own e-cig	Users' own e-liquid and cig	Users' own	subjective effects	plasma nicotine/cotinine
(Spindle et al., 2017)	directed e-cig puffing and ad-lib session	smoke < 5 CPD, use ≥ 1 mL e-cig liquid daily for ≥ 3 months	29	29.6 (7.7)	preferred e-cig battery	Users' own	n/a	HR, subjective effects	plasma nicotine
(Perry et al., 2019)	directed puffing session	daily smokers	26	32.7 (11.5)	nicotine inhaler	10mg/4 mg deliverable	citrus or mint	MRI Resting state functional connectivity between insula, dorsal anterior cingulate cortex and nucleus accumbens	n/a
(Teichert et al., 2018)	directed puffing session	smoked cigs for ≥ 3 years	14	39.8(13.8)	Nicotine inhaler, P3L system	P3L(50, 80, and 150 $\mu\text{g}/\text{puff}$), Nicotine Inhaler (15 mg)	n/a	subjective effects, tolerability	plasma nicotine
(De La Garza et al., 2019)	directed e-cig puffing session	smoke ≥ 10 CPD for a year	15	50.6 (7.6)	eGo e-cig devices (3.3V battery and 1.5 Ω dual coil cartomizer)	0, 18, 36mg/ml in e-liquids	tobacco	subjective effects	n/a
(Baldassari et al., 2018)	directed e-cig puffing session	daily e-cig use for at least 1 month; cig smokers-or smoked > 10 CPD for the past year	7	26 (4)	Go e-cig devices (3.3V battery and 1.5 Ω dual coil cartomizer)	0, 8, and 36 mg/ml nicotine	tobacco	PET scan, $\beta 2^*$ -nAChRs receptor occupancy	plasma nicotine
(Breland et al., 2019)	directed e-cig puffing session	smoke < 5 CPD, use ≥ 1 mL e-liquid daily for ≥ 3 months	24	28.6(7.4)	user own e-cig, an eGo e-cig, nicotine inhaler	used own	used own	multiple-choice procedure, subjective effects	plasma nicotine
(Smith et al., 2019)	directed e-cig puffing session	smoked ≥ 5 non-menthol CPD past year, < 5 e-cig use	30	43.7 (12.4)	ego e-cig-T 1100 mAh battery, cartomizers (510 Smoketech, 1.5- Ω dual coil)	18mg/ml,	tobacco	subjective effects, Reinforcement value	n/a

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(Krishnan-Sarin et al., 2017)	directed e-cig puffing and ad-lib session	use e-cig 10/past 30 with nicotine	60	18.82 (0.77)	V2 Cigs (e-cig)	0 mg/ml, 6 mg/ml, 12 mg/ml	Menthol: 0%, 0.5%, 3.5%	subjective effects	saliva nicotine
(Cobb et al., 2019)	directed e-cig puffing session	smoked \geq 5 CPD past 3 months	20	19.9 (1.1)	e-cig device (eGo 3.3–4.1 V, 1100 mAh battery and a 1.5- Ω dual-coil, 510-style cartomizer (SmokTech))	0, 36mg/ml	tobacco/menthol, tropical fruit, cream	HR, BP, subjective effects	n/a
(O'Connell et al., 2019)	directed e-cig puffing session	smoked \geq 10 CPD at least one year	15	42.3 (12.41)	Myblu pod system, blu PRO open system e-cig	25mg, 16mg, 40mg, 48mg	tobacco	subjective effects	plasma nicotine
(Yingst et al., 2019a)	Directed e-cig puffing session	use e-cig for at least 30 days in life, use e-cig for 20/28 past days	14	34.3 (10.8)	User own e-cig (first-generation or advanced)	Used own	Used own	Subjective effects	Serum nicotine
(Franzen et al., 2018)	Directed e-cig puffing session	cig smokers	15	22.9 (3.5)	e-cig (eGO-T CE4 vaporizer 3.3 V, 1.5 Ω , 7.26 W)	0, 24 mg/mL	tobacco	arterial stiffness, blood pressure	n/a
(Hajek et al., 2017)	Ad-lib session	Dual users (currently smoking and vaping)	11	34.1 (12.0)	first generation, second generation and third generation e-cigs	16–48mg/ml	tobacco	Subjective effects	Plasma nicotine
(Chaumont et al., 2018)	Directed e-cig puffing session	occasional tobacco smokers	25	23 (0.4)	e-cig [60 W (0.4 Ω dual coils)]	0.3mg/ml	n/a	microcirculatory function, arterial stiffness, hemodynamic parameters, oxidative stress.	
(Rüther et al., 2018)	Directed e-cig puffing session	e-cig users: use e-cig over 3 months. Cig user: use cigs over 3 years	20	28.5 (8.9)	disposable cigalikes, a tank model e-cigs, cig	~18mg/ml	tank model=strawberry/mint	subjective effects, heart rate	n/a
(Farsalinos et al., 2018)	Ad-libitum	former daily smokers who used nicotine-containing e-cigs daily for at least 1	21	31(8)	e-cig: battery (EVIC Supreme, Joyetech) 2600 mAh, 30 W	Used own	Used own	Puff topography, subjective effects.	Plasma nicotine

Human Table

		month			atomizer				
(Van Heel et al., 2017)	Ad-lib session	Smoke 10 CPD in past 3 years, no vaping experience	81	29.8(13.2)	White Cloud disposable e-cig	0% ,3.6% nicotine	Apple, tobacco	Subjective effects	n/a
(Hobkirk et al., 2018)	Directed puffing bout	used e-cig at least 20/28 last days	9	35.1(12.3)	Used own e-cig	Used own	Used own	Subjective effects. Resting state functional brain connectivity	n/a
(Kerr et al., 2019)	Directed puffing bout	habitual smoker at least 1 CPD	20	31.6(10.5)	e-cig: 1300mAh, tank and atomizer (SmokeMax; Groove Trading Ltd)	18mg/ml	tobacco	Respiratory function, cardiovascular function	Blood nicotine
(Hajek et al., 2018)	Ad-lib session	Dual users (vaping and smoking), past smoking history	15	36.3 (11.2)	'cig-a-like', refillable products, variable voltage and own e-cig	6-48mg/ml	tobacco	Subjective effects	n/a
(Adriaens et al., 2018)	Ad-lib session	smoke for at least 3 years, 10 CPD	30	22(3.1)	e-cig: Eleaf iStick Power 5000 mAh battery, 8 W, with an Aspire Nautilus 2 tank, IQOS	18 mg/mL	Tobacco	Subjective effects	Blood nicotine

Notes: e-cig=e-cigarette; CPD=cigarettes per day; HR=heart rate; BP=blood pressure; MRI=magnetic resonance imaging; PET=positron emission tomography; nAChRs=nicotinic acetylcholine receptors; ENDS=electronic nicotine delivery system; W=watts; Ω =ohms; V=volts; mAh= milliamp Hour;

Baseline assessments of nicotine/cotinine for inclusion criteria for studies were not included in table.

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