Supplemental File to

Wastewater-based epidemiology (WBE): Potential application for assessing the use of conventional and new generation tobacco and nicotine products

Gerhard Scherer[1*], Nikola Pluym[1], Max Scherer[1]

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Table S1: Studies considered in the systematic review on WBE and the use of tobacco/nicotine products (alphabetically ordered to the first authors)

1	2	3	4	5
Authors, year (reference) Subcategories (I – V)	**Locations of WW sample collection and populations covered**	**Time and WW sampling**	**Biomarkers used**	**Results**
Alygizakis et al., 2021 (1) **II**	Greece: -Athens -1WWTP (~4 million people covered)	2019-2020: -2019: Mar 13-19 (non-COVID-19) -2020: Mar 25-Apr 8 (COVID-19, full lockdown)	Cot, OH-Cot: -LC-MS/MS -CF(Cot)=3.4 -CF(OH-Cot)=1.9 -Nic dose absorbed: 1.25 mg/cig (2)	-Population-normalized nicotine dose (mg/d/1000p): --2019, Cot-based: 3800; OH-Cot-based: 3472 --2020, Cot-based: 2347; OH-Cot-based: 2809 -Decrease in tobacco consumption during pandemic: 33% -Other WW changes during COVID-19: Surfactants: +331%, biocides: +196%, industrial chemicals: -52% (reduced business)
Asicioglu et al., 2021 (3) **I, II**	Turkey: -Istanbul (14 WWTPs, 20 Million) -Census-based, 15-64 years old	2019: -Mar, Jun, Sep, Dec -7 consecutive days	Cot: -LC-MS/MS -UER=30 % (corrected to nicotine equivalents (4) -CF=3.33 (ditto)	-Nicotine consumption (mg/d/1000p): --Mar: 4294.86 ± 2110.00 --Jun: 4366.31 ± 4114.44 --Sep: 7055.72 ± 4692.81 and --Dec: 6313.47 ± 2553.32 --Mean: 5507.59 ± 1392.77 -No significant seasonal changes -No significant differences between workdays and weekends -No conventional prevalence data for tobacco, therefore no comparison with WBE possible -Tobacco consumption higher in Oslo and Zurich than in Istanbul
Bade et al, 2020 (5) **I, III**	Australia: City in Southern Australia (4 WWTPs, 1.1 million people covered)	2015 - 2019 -Oct 2015 – Feb 2019 -Every 2 months -24j-composite WW samples -7 consecutive days in each month	Cotinine, AB, AT:: -LC-MS/MS	-Mass load ranges over the study period: --Cot (mg/d/1000 p): 1549-1935 (21 single values) --AB (mg/d/1000 p): 2.3-4.4 (21 single values) --AT (mg/d/1000 p): 4.2-76.2 (21 single values) -Cot mass load in WW samples decreased by 3.3 % over the study period -For AB the change was 30 % -Reasons: Most probably the increasing use of NRT products (ECs did not play a significant role in Australia at that time -AB is a suitable WW marker for tobacco use -Use of AB as BM in WW is preferable compared to AT, due to less variability of content in tobacco
Baz-Lomba et al., 2016 (6) **IV**	Norway, Belgium UK, Netherlands, Italy, Switzerland, Denmark:	2015: -Mar -7 consecutive days	Cot + OH-Cot: -LC-MS/MS -Not provided	-Nicotine consumption (mg/d/1000p), based on Cot+OH-Cot: --Oslo: 6700 --Castellon: 5200 --Bruessel: 5300

	-Oslo, Brussels, Bristol, Utrecht, Milan, Zurich, Copenhagen -WWTP-based, normalized to 15+ years old population -In total about 5 Million people were covered in the 8 cities		-UER:30 % for Cot, 44 % for OH-Cot (corrected to nicotine equivalents (4) -CF=1.35	--Bristol: 3400 --Utrecht: 2100 --Milan: 2600 --Zurich: 6000 --Copenhagen: 2100 -Comparisons with cigarette sales: no good agreement --Comparisons based on cigarette sales between cities are problematic (e.g. high use of snus in Oslo)
Boogaerts, 2021 (7) **I, IV**	Lithuania: -3 cities (Vilnius, Kaunas, Klaipeda) --Vilnius: 10.2% of 536631=103033 --Kaunas: 10.5% of 288363=30278 --Klaipeda: 5.9% of 164038=9678	2018/2019: -IWW 24h-composite samples -collected on 7 consecutive days	Cot + OH-Cot -LC-MS/MS -CF for Cot: 3.13 (UER = 32 %) -CF for OH-Cot: 2.31 (UER = 43%) -0.9 mg nic/cig (for calc. of cigarette dose)	-WBE-derived cig consumption: 3.5 -10.5 cig/d/p (15+), similar to results in other European cities -In 2018: no sign. diff. between 3 cities -In 2019: sign. lower (by ~25%) in Kaunas compared to 2018 (as yet no explanation) -WBE-derived cig consumption higher (by ~35%) than cig. sales data (including roll-your-own), discussed reasons: --Sales data were from 2016 --Other Nic sources could have contributed (NRT products, ECs, water pipe etc.) --Illegal tobacco products --Disposed cig butts (conversion to Cot, OH-Cot) -No effect of weekends reported for nic consumption
Campo et al., 2023 (8) **I,II**	Spain: -Valencia -3 WWTPs (together 1.5 million inhabitants covered)	2011-2020 -Tobacco/Nic only determined in WW in 2018 and 2020* -24h-composite samples (time-proportional) over 1 or 2 weeks -21 WW samples in each 2018 and 2020	Cot: -LC-MS/MS -UER: 10-15% (no deconjugation in WW considered!?) CF=8.33 (ditto) (9)	-Nicotine consumption, means (ranges) (mg/d/1000p): --2018: 5486 (3059-9526) --2020: 1893 (1370-2606) -Significant difference between 2018 and 2020 not explained or discussed -Nic consumption stable throughout the week *Contradictory statements in the article: on other pages it is stated that cotinine was measured in the period 2014-2017!
Castiglioni, 2015 (4) **II, IV**	Italy: -8 cities (population >14y served): --Milan (960300) --Como (79926) --Bologna (470640) --Turin (1201490) --Rome (1107699) --Naples (549250) --Bari (296922) --Palermo (223254)	2012 (Oct): -IWW 24h-composite samples -one week collection	Cot + OH-Cot -LC-MS/MS -UER (%*) --Nic: 13% --Cot: 30% --OH-Cot: 44% *: free + conjugated, data based on Byrd et al. (10)	-Nic abs/d/1000p15+ (mg/d) / Diff. in cig-number survey vs. WBE --Milan: 2209 / +30% --Como: 3015 / +4% --Bologna: 2840 / +8% --Turin: 3958 / -26% --Rome: 3371 / +4% --Naples: 4537 / -16% --Bari: 3624 / +7% --Palermo: 4291 / -10% -Nic consumption was clearly higher in Southern compare to Northern Italy -Nic absorbed and found in WW was stable over workdays and weekends -In the authors' opinion, the WW data on number of cigarettes match those from survey data!?

				-Other sources (NRT products, ECs) for absorbed nic (reflected in WW samples) were of minor importance at that time (0.4 % of market share in 2010) at that time
Centazzo, 2019 (11) **II**	USA: -New York City (6 WWTPs): --Manhattan --The Bronx --Queens --Brooklyn	2016: -8 Time-points --before/after major holidays --Special holidays: 4th of July, Labor Day, New Year -48 one-time grab WW samples	Cot -LC-MS/MS -All concentrations normalized for creatinine -CF or UER applied	-Cot in WW (ranges ng/mg creatinine) by WWTP (8 samples per plant): --Hunts Point: 507.0–2075.1 --North River: 187.6–449.6 --Tallman: 394.2–2027.9 --Jamaica: 395.1–1210.4 --North Creek (Brooklyn/Queens): 248.1–944.7 --North Creek (Manhattan): 200.1–495.4 -Differences to WWTP locations (cotinine highest in The Bronx) -No effects due to holidays
Chen, 2019 (12) **IV**	USA: -3 Communities in the USA (A, B, C) -Population: total/15+/18+ smokers: --A: 125000/100000/19950 --B: 44000/35200/6988 --C: 53000/42400/6211	2015/2016 -1x/month, over 11 months -samplings only on weekdays	Cot, OH-Cot, Nic* -LC-MS/MS -UER for Cot+OH-Cot: 74%, CF=1.35 (4) -Nic absorbed/cig: 1.25mg (4) -*Nic/Cot (‘ideal’ ratio: 0.6), observed 0.6-9.2 (reason: disposal in WW through cig butts and ash)	-WW concentrations (µg/L), all locations: --Nic: 0.6–26.7, Cot: 0.2–3.8, OH-Cot: 0.3–3.8 --14.2 cig/d/smoker (18+) -Nicotine consumption (mg/d/p), WW-based: --Population: Total / 15+ / smoker 18+ --A: 2.7 ± 0.6 / 3.4 ± 0.7 / 17.2 ± 3.7 --B: 2.4 ± 1.2 / 3.0 ± 1.4 / 15.3 ± 7.3 --C: 2.6 ± 0.5 / 3.3 ± 0.6 / 22.5 ± 3.9 Weighted ave.: 2.7 / 3.3 / 17.8 -No influence of weekend suggested for Nic consumption (13), not investigated in this study -WW-based cigarette consumption was found to be similar (A), lower (B) or higher (C) than in national or state surveys --The higher WW-based value could be explained by unassessed nicotine sources in surveys (NRT products, other tobacco products, NGPs, illegal cig imports, under-reporting of cig consumption etc. --Reasons for the lower WW-based values are less straight forward
Do et al., 2023 (14) **II, IV**	Vietnam: -Ho Chi Minh City --1 Urban WWTP, population: 637080; 78% were assumed to be 15+ years old --1 W University town WWTP, pop: 16287	2023: -Urban: 2-15 Apr 2023, 24 samples -University: 11-22 May 2023, 28 samples -Pump station collection (auto-sampler --day: 8am – 6pm --night: 6pm – 8am	Cot: -LC-MS/MS -UER: 32.3% (15, 16) -Nic absorbed: 1.25 mg/cig	-Nic consumption (mg/d/p(15+): --Urban residents: 4.34±0.60 --Students: 1.2±0.2 (slightly (sign.) higher in night samples -13.9 cig/d/smoker (close to survey data for Vietnam) -Slightly higher at weekends (urban pop.)
Driver et al., 2020 (17) **II, IV**	USA: -university campus -~60000 students -Population was normalized by HIAA, enterolactane and	2017/2018: -sampling on7 consecutive days -10 months (Aug to May), 1 week per month -2 collection points -autosampler, 24h-composite samples	Cot + OH-Cot -LC-MS/MS -UER=74%, CF=1.35 (4)	-Nicotine consumption (µg/d/p): --WW: 627±219 --Survey: 927±243 (the authors discuss possible demographic differences between US students in general and the actual study college students) -Nic (and alcohol, but not caffeine) consumption was lower (p<0.01) on workdays than on weekends (Sat, Sun). -Correlations (WW data):

	average water consumption/p			--Nic vs alcohol: r=0.71 (p<0.01) --Nic vs caffeine: r=0.59 (p<0.01)
Driver et al., 2022 (18) **-**	USA: -American Indian Reservations (feasibility study) -6 Locations -Number of WWTPs and pop. size provided in the Suppl. data	2018: -the week of 23 Jul -24h-composite samples (3 locations) -Grab samples (3 locations)	Cot+OH-Cot: -LC-MS/MS -UER=74% CF=1.35 (4) -Various other drugs	-Mean (range) of Nic consumption (g/d/1000p): --3.2 (0.78-4.63) -Implementation of WBE in American Indian Reservations is feasible
Duan et al., 2022 (19) **II**	China: -Beijing, 1 WWTP -Population estimates (PE) can be based on COD, NH_4-N, TN, TP (NH_4-N most suitable, used here)	2018-2019: -one normal and 2 weeks with holidays (New Year, Labor Day) -24h-composite samples (auto-sampler)	Cot: -LC-MS/MS -CF=(MWnic/MWcot) /UER = 2.88 (15) -UER=32%, MW ratio=0.92	-Nic consumption (mg/d/p): --Mean: 1.4, range: 0.3-5.4, median: 1.2 -Cotinine load in WW lower on weekends in normal weeks (probable reason: commuting)
Estevez-Danta, 2022 (20) **II, IV**	-Spain/Portugal: 4 areas: --Bilbao (pop served: 860237), Vitora-Gasteiz (255052), Castellon (179661), Santiago de Compostella (136500) -Portugal, 2 areas: --Porto (150000), Vila do Conde (80000) (Source for population size not reported)	2019 – 2020: -2019 (Apr toMay, normal, for reference) -2020 (Mar – July), during COVID-19 lockdown -24h-composite raw influent WW samples (time-proportional mode sampling) -6 WWTP	Cot, OH-Cot: -LC-MS/MS -CF (Cot)=3.41 (equivalent to 29.3% UER) -CR (OH-Cot)=1.90 (UER: 52.6%) (2)	-Nic cons based on average of Cot+OH-Cot (mg/d/1000p): --Bilbao: 2019: - 2020: 1674±672 --Castellon: 2019: 1949±580 2020: 1497±594 --Santiago de Comp.: 2019: 1393±190 2020: 1659±663 --Vitoria-Gasteiz: 2019: - 2020: 2654±1421 --Porto: 2019: - 2020: 1501±204 --Vila de Conde: 2019: - 2020: 1391±514 --Only minor impact of lockdown (trend to decrease) on WW-based Nic consumption, different to alcohol (trend to increase) --Cig sales data show decrease during lockdown --Detailed data in supplemental file (20)
Fallati et al. 2020 (21) **-**	Maldives: -Malé (capital) -153940 inhabitants (2016) -9 Pumping stations (over all the city)	2015: -12h-composite samples (day/night) -2 samples/d -9 consecutive days	Cot, OH-Cot -LC-MS/MS -CF=1.35 -Nic abs/cig=1.25 mg (4)	Nic and cig consumption: -Nic: 2.6 g/d/1000p -Cig: 2048/d/1000p -Cot and OH-Cot mass loads slightly higher in 'night' WW samples -No other information for Nic/tobacco (influence of weekends, association with surveys or sales) provided
Gao, 2020 (15) **I, IV**	China (cities): -2014: 29 WWTPs, 17 cities, 53 WW samples -2016: 19 WWTPs, 16 cities, 45 WW samples -Population size obtained from the	2014 / 2016 -24h-composite samples (auto-sampler)	Cot, OH-Cot -LC-MS/MS -UER(Cot): 32.3% -UER(OH-Cot): 43.4%	Per capita consumption was calculated on Cot data -2014: --Cot: 1.6 µg/L; ratio Cot/OH-Cot: 0.8; 1.6±0.9 mg Nic/d/p(15+); CPD: 3.1 cig/d/p(15+) -2016: --Cot:2.4 µg/L; ratio Cot/OH-Cot: 0.5; 1.9±1.1 mg Nic/d/p(15+), CPD: 3.7 cig/d/p(15+) -Increase in CPD from 2014 to 2016 not sign. -Good agreement with WHO survey data and sales -Consumption of NRT products and ECs is negligible in China

	National Bureau of Statistics -Average % of 15+ pop: 86% (Suppl)			-The authors do not discuss the change in the Cot/OH-Cot ratio from 2014 to 2016 (0.8 to 0.5)
Genc, 2021 (22) **II**	Turkey: -6 cities (Antalya, Aydın, Bursa, Denizli, İzmir and Samsun) -17 WWTPs -census data were used for pop.	2019: -4 periods (March, June, Sep, Dec) -7 consecutive days per period, special event days were avoided -24h-composite, time-proportional samples (in total 476 WW samples)	Cot: -LC-MS/MS -CF=3.33 (UER: 30 %) (4)	-Range of mass load of cotinine (mg/d/1000p) and (in paratheses) mean±SD nicotine consumption (mg/d/1000p(15-64y): --Antalya: 604-2082 (5375±2272) --Aydin: 1047-6337 (8792±8362) --Bursa: 1028-2561 (5145±2322) --Denizli: 215-753 (1856±786) --Izmir: 892-2130 (4355±1859) --Samsun: 571-3394 (4763±4436) -High tobacco (and alcohol) use compared to other European cities -No sign. daily and seasonal differences observed -Nic consumption in September is strikingly high in Aydin, Bursa, Izmir and Samsun compared to the other months (no obvious reason for this can be seen, underestimated pop? unannounced special events?). -No influence of weekends
Gracia-Lor 2020 (23) **I, II, IV**	Italy: -16 cities (6 in the north, 6 in the center, 4 in the south) -Population served by the WWTP: --5.8 million p --5.4 million p (15+)	2013 - 2015 -24h-composite inlet samples (auto-sampler) -7 consecutive days	Cot + OH-Cot -LC-MS/MS -UER(Cot+OH-Cot)=74% -CF=1.35 (4) -Nic absorbed/cig: 1.25 mg	-Nicotine consumption, back-calc. with sum of Cot+OH-Cot (see Excel Suppl) -cig/d/smoker (survey data), using the local smoking prevalences: --North: 13.3 (12.8) --Center: 10.1 (14.8) --South: 12.6 (13.4) -- similar on each day, except Milan on Sundays (commuters) --Decrease from 2013 to 2015 --Other nicotine sources (snus, NRT, ECs) were considered to be insignificant in Italy by the authors -Sign..correlation between daily nicotine and caffeine consumption -mostly in agreement with survey data for consumption (r=0.79)
Guzel et al., 2021 (24) **II, IV**	Turkey: -11 cities -18 WWTPs -Population: from census 2019	2019: -Mar-Dec (spring, summer, autumn, winter)	Cot: -LC-MS/MS after LLE -UER=32.3% -Nic abs/cig: 1 mg	-Nic consumption (mg/d/1000 p(15-64): --Average (all cities): 2930±1600 --Range: 987-4283 --No influence of season or weekends -CPD: WW-based higher than national statistics (2.9 vs 2.1 cig/d) -Deviations from market data may be caused by illegal tobacco products -Comparison of Nic consumption in other countries: similar (differences in back-calculation, Table S2)
Guzel et al., 2022 (25) **II**	Turkey: -Amada province -WWTP served pop.: 1.1 million -For back-calculation, the pop. was adjusted to the age group 15-64	2019: -Ramadan (May 6 to June 3) and normal periods -1 week during Ramadan and 1 week after Ramadan -24h-composite influent samples (auto-sampler)	Cot: -LC-MS/MS -CF=3.3 (UER: 30 %) (4) -Nic absorbed/cig: 1 mg	-Nic cnonsumption (mg/d/1000p): --Normal week: 2811±257 --Ramadan: 2119±310 -There was a sign. decrease in nicotine use during Ramadan (similar to alcohol and some illicit drugs) - Friday is different for nicotine (and alcohol): lower during Ramadan, higher during normal week. (Friday is a holy day for Muslims)

	y (Turkish Statistical Institute)			
Hahn et al., 2022 (26) **II**	Brazil: -Small urban comm. 'Novo Hamburgo' -1179 inh. -PE based on BOD	2020/2021: -18 Mar 2020 to 3 Mar 2021 (during limitations due to COVID-19 pandemic) -POCIS sampling at the inlet of a WWTP -24 periods of 14 d samplings	Cot: -LC-MS/MS -UER=30% -MW ratio=0.92 -CF=3.1 (4)	-Nic consumption (mg/d/1000p): --Whole period: 162 ± 65 --Limitations: 119.7 ± 28 --After re-flexibilization: 194.3 ± 67 -Negative correlation between mobility (measure by cellular phone) and Nic consumption (similar to alcohol, caffeine, illicit drugs) -'Stay-at-home' recommendation is associated with lower consumption
Kasprzyk-Hordern et al., 2023 (27) **II**	England: -10 cities -11WWTPs (repres. 7 million people) -PE provided by WWTP -PE also based on patient numbers	2021: -4-5 d very week (including weekends) -24h-composite samples	Cot, Nic -No conversion to consumption data -Other WW BMs: --Caffeine --Pharmaceuticals --Industrial chemicals --Endogenous BM: creatinine, HNE-MA, 2-deoxyguanosine	-Population normalized daily loads (PNDL), mg/d/1000p.: --Cot: 400 – 1200 (from 11 WWTPs, Figure 5) --Nic: 50 – 550 (from 11 WWTPs, Figure 5) -Cot and Nic showed strong correlation (r>0.9) with PE (population estimate or equivalent), indicating low variability over time (would be suitable PE markers)
Kumar et al., 2019 (28) **II, V (heavy rainfall)**	New Zealand: -1 Urban WWTP (catchment: ~100000 people) -Used for PE: BOD, COD, TKN, TP, NH_4-N, Nic metabolites	2016/2017: -1-week sampling in Oct 2016, Jan 2017, May 2017, Jul 2017 -4 days sampling in Apr 2017 during heavy rainfalls -24h-composite samples (auto-sampler, time-proportional)	Cot, OH-Cot: -LC-MS/MS -CF=1.35 -1.25 mg Nic abs./cig (4) -Additional BMs in WW for alcohol, 17 IDs	Nic cons. (mg/d/1000p) in Spring/Summer/Autumn/Winter/Rainfalls (calculated from mass loads): -Cot-based: 1288±80 / 1316±113 / 1248±43 / 1199±64 / 1267±120 -OH-Cot-based: 2132±27 / 2115±71 / 2157±27 / 2190±38 / 2146±74 -Nic consumption was consistent over the weeks (other than alcohol, which was increased on weekends) -There was no sign influence of seasons on Nic consumption -During heavy rainfall, WW concentrations of all BMs were sign. lower, however, Nic consumption data were consistent
Kumar et al., 2022 (29) **III, V (MAs in WW)**	USA: -Community 1: 25000p, closer to VOC emitters -Community 2: 32000p, cleaner air than Comm. 1	2021: -4d in Max 2021 -24h-composite samples -n = 8 WW samples	Cot, OH-Cot, Nic, AB, AT -LC-MS/MS -Metaboites of 35 VOCs (mostly mercapturic acids)	-Comm 1 showed higher mass loads for VOC metabolites -After normalization with Cot, levels were no longer systematically higher in Comm.1 compared to Comm. 2 -Cot-normalized CEMA was equal in Comm. 1 and 2 -Cot-normalized 3-HPMA and HMPMA were slightly higher in Comm.1 -Smoking rates were higher in Comm. 1 -Results suggest that smoking is associated with many of the VOC metabolites in WW
Lai et al., 2017 (30) **II, III**	Belgium: -2 cities (Geraardsbergen, Ninove) --GER: 29000 p served --NIV: 36000 p served	2014/2015 -Nivenone: March 2014 -Geraardsbergen: March 2015 -24h-composite raw WW samples (time-proportional) -8 consecutive days	Cot + OH-Cot -LC-MS/MS - AB -AT -NAB -NAT -NNN -NNK: NNAL (N- and O-ß-glucuronides)	Pop-normalized mass loads (mg/d/1000p). GER / NIV (AB, AT, NAT, NAB: µg/d/1000p) -Cot: 693-828 / 393-721 -OH-Cot: 1350-1610 / 822-2100 -AT: 7.86-10.9 / 7.28-12.8 -AB: 3.39-4.55 / 2.31-5.03 -NAT: 0.13-0.41 / 0.11-0.12 (6 of 8 samples <LOQ) -NAB, NNN, NNK, NNAL: <LOD -Stable tobacco use over the week -Ratio OH-Cot/Cot: 1.9 (Spain: 1.8, China:1.2, urine: 1.5

				-Ratio AT/AB: 2.5 (similar to Australia) -All analytes sufficiently stable over 24h at 4 and 20 °C
Lai, 2018 (31) **II, IV**	Australia: --18 WWTPs across 5 states (approximately 45 % of the Australian population (24 million) covered) --164 WW samples --catchment population provided by the WWTP personnel	2014-2015: -1-week samplings (special events avoided) -modest sampling uncertainty of 5-20%	Cot, OH-Cot: -LC-MS/MS -UER(Cot)=28.05% -UER(OH-Cot)=45.23% -Nic/cig: 0.9 mg (for CPD calculation) (4, 32)	-Nationwide consumption of nicotine: mg Nic/d/p(15-79) cig/d/p(15-79) --based on WW Cot: 2.23 2.52 --based on WW OH-Cot: 2.10 2.37 --Cig sales data of 2015: - 2.48 -Consumption of Nic and alcohol about 3-4 times higher in rural than urban communities -Spatial consumption was consistent -Nicotine metabolites decreased by 14-25% over time in some WWTPs, not sign. for rural locations (11% reduction) -Weekday dependence for alc. but not Nic -Elevated consumption (Nic and alcohol) during one large event observed -WW data close to sales data
Lai, 2018 (33) **II, III, IV**	Greece (Athens), Switzerland (Geneva), Belgium (Geraardsbergen, Ninove): catchment population: -Athens: 3700000 -Geneva: 600000 -Geraardsbergen: 29100 -Ninove: 36200	2014-2017: -24h-composite influent WW -7 consecutive days -particular events avoided	Cot, OH-Cot -LC-MS/MS -AB, AT, NNK --NNK analyzed after enzymatic deconjugation	Pop-normalized mass loads, medians (mg/d/1000p): Athens Geneva Geraards. Ninove -Cot: 1160 520 740 640 -OH-Cot : 1960 1010 1470 1250 -AB: 5.4 6.7 4.2 2.9 -AT: 11 15 9.1 7.7 -NNK: 1.5 1.0 0.5 0.5 -From relationship of markers: substantial use of non-Tob Nic can be deduced from the (e.g.) AB/Cot ratio in Greece and Belgium (4.5-5.7), but not in Switzerland (12.9), corresponds very well with the EC use prevalence in Greece (3%), Belgium (4%) and Switzerland (0.3%), as cited by the authors. -No distinct weekly pattern for any of the WW biomarkers -NNK indicates third-hand smoke exposure (observed particularly in Athens) -Third-hand smoke exposure conclusions are doubtful -Monte Carlo estimates included the following uncertainties: chem. analyses: 10%, WW sampling: 10%, WW flow rate: 20%, catchment population: 15%
Lopes et al., 2014 (34) **II, IV**	Portugal: -Lisbon -Major WWTP (serving 756000 p) -Various parameters for PE proposed (P, N, BOD, COD)	2011; -Tuesdays and Thursdays on 4 weeks in Oct/Nov 2011 -24h-composite smples	Cot: -LC-MS/MS -UER=14.1% (free Cot?) -12-17% excreted as glucuronide (35) -0.8 mg Nic/cig -85% absorbed	-Nic consumption (mg/d/1000p): 5.860 g -Nic consumption consistent over working days, increase on a holiday -Significant correlation between Nic and cocaine consumption -Consumer (smoker) percentage estimate based on WW Nic: 36.6-66.6% (Survey: 23%) -Consumer overestimation due to low UER?
Mackie, 2019 (36)	Australia:	2010 – 2017:	Cot, OH-Cot -LC-MS/MS	-Average WW-based nic consumption from 2010 to 2017, only deducible from graphs (mg/d/1000p): 3000 (Cot-based)

I, II, IV	-city in South-East Queensland with 110000 inhabitants -population size calculated from census data 2011/2016	-Feb 2010 to Oct 2017, every 2nd month -7 consecutive days, avoiding major events -42 weeks, 291 WW samples -24h-composite samples (auto-sampler, flow-proportional)	-UER (Cot): 32% (from various studies) -CF (Cot): 3.125 -Nic absorbed (mg/cig): 1±0.36 (35)	-25 % reduction in Nic consumption from 2010 to 2017, 3 %/a -Good agreement with sales and survey data (5 and 4 %/a, respectively) -WW-based cig consumption compared with: --National survey: 37-69% higher --Local sales: 16-40% higher --Legal and illicit consumption data: 11-29% higher ---Discussed reasons: (i) self-report bias (lower cons. stated), (ii) illicit tobacco use not or incompletely assessed in surveys, (iii) other Nic sources (EC; NRT) not considered as important -The authors conclude that WBE is suitable approach for long-term nicotine consumption assessment
Mackul'ak et al. 2015 (37) **IV**	Czech and Slovak Republic (CR, SR): -CR: 2 cities, 1.4 million inh., 2 WWTPs -SR: 5 cities, 0.9 million inh., 5 WWTPs -PE considered: COD, BOD, N, P (6.2-12.5% RSD during the study)	2014: -11-18 Mar 2014 -24h-composite WW samples	Cot: -LC-HRMS -UER:14.1% -MW ratio=0.92 -85% Nic absorbed (35) -CF: considers time of Cot in WW (0.45 x t) (38)	-Nicotine consumption (g/d/1000p) --SR: Bratislava: 4.2; Petrzalka: 5.1; Kosice: 2.4, Nitra: 8.0, Piestany: 2.2 --CR: Prag: 4.3; Budweis: 3.6 -Cigarette per year and person: --SR: 2362 (99% conformity with national statistics) --CR: 2088 (96% conformity with national statistics)
Mackul'ak et al, 2015, (39) **II, IV**	Czech and Slovak Republic (CR, SR): -3 cities, 5 WWTPs -70000 usual inh. -80000 participants in 4 music festivals -PE considered: COD, BOD, N, P (6.0-12.1% RSD during the study)	2014: -Jun to Sep 2014 (during 4 music festivals) -24h-composite WW samples	Cot: -as in (37)	-Significant increase in Nic consumption during festivals -Rock/metal music festival: 8 g/d/1000p (compared to 4 g/d/1000p non-festival value) -No significant increase during country and folk festival -Good agreement with official statistics for cigarette consumption
Montes, 2020 (2) **II, IV**	Spain: -7 regions -17 WWTPs -6 million p. covered (=12.8% of total Spain)	2018: -24h-composite samples -1-week daily sampling (no coincidence with local festivities or special events) -112 WW samples in total	Cot, OH-Cot -LC-MS/MS with prior enzymatic deconjugation -UER(Cot): 27% -UER(OH-Cot): 44.5% (35, 40)	-Strong correlation between Cot and OH-Cot in WW (r=0.96) -Average Nic consumption: 2.2±0.7 g/d/1000p -No dependence on weekday -Good agreement with sales and less so with survey data -Of interest is that sales correlated better than survey data -Regional differences: Basque Country and Catalonia highest, Galicia lowest -No conclusive correlation with health data -Sign. negative correlation with education level
Nguyen et al., 2018 (41) **-**	Vietnam: -Ho Chi Minh City -2 WWTPs (A, B) --A: 425830 p served	2015: -Dec 8–14, 2015 (WWTP A) -Dec 20-22, 2015 (WWTP B) -Grab WW samples every 6 h (n=80)	Cot, OH-Cot, Nic: -LC-MS/MS -UER (Cot/OH-Cot/Nic): 30/44/13 % (10)	-Nicotine consumption, based on Cot and OH-Cot in WW (g/d/1000p): --WWTP A: 1.1 ± 0.25 --WWTP B: 1.3 ± 0.26 -Load or Cot, OH-Cot and Nic are lower than in European cities

	--B: 120000 p served		-In addition: Caffeine, alcohol, IDs, artificial sweeteners, PPCP (pharmaceuticals and personal care products)	
Oertel et al., 2023 (42) **II**	Germany: -15 WWTPs (all over Germany) -Urban, small-town, rural locations -Pop. served: 3000-671800p) -Pop estimated by PEs	2020/2021: -Apr 2020 to Dec 2021 at various restriction phases of the COVID-19 epidemic -24h-composite WW samples (n=860)	Cot: -LC-MS/MS -No further information provided for back-calculation -Various IDs were determined	-Mass load of Cot at 6 locations in Saxon (mg/d/1000p): 286.3 – 843.5 -IDs use (particularly COC, MDMA) were sign. higher at weekends in all lockdown phases# -Cot (and the ß-blocker metoprolol) excretion showed constant loads throughout the seasons and epidemic phases -Both are suitable WBE markers when flow rates and catchment population are unknown
Reinstadler et al., 2021 (43)	Austria: -Innsbruck (132000 inhabitants) -1 WWTP (174000 catchment population) -Considered for PE: COD, BOD, NH_4-N, N, P	2016-2020: -12 Mar – 15 Apr (35d) lockdown due to COVID-19 -Mar 2016 to Jan 2020 (292d), reference period (no lockdown) -24h-composite samples (vol-proportional)	Cot: -LC-MS/MS -CF=7.08 (UER: 15 % ?) -Nic/cig: 1.25 mg (4) -Caffeine, alcohol, IDs, prescribed and non-prescr. Pharmaceuticals	-PNDL for Nic consumption (mg/d/1000p): --2019/2020 (non-pandemic): 604 ± 112 --2020 (during lockdown): 611 ± 84 -No increase on weekends (other than alchol and IDs) -Alcohol id IDs consumption decreased during lockdown -During the whole phase of the study: 3.3 cig/d/p (WW-based) in good agreement with official cig sales in Austria 2014 (3.4 cig/d/p) -Percentage of smokers: 25% (WW-based), 24.5% (Austria statistics)
Rodriguez-Alvarez et al., 2014 (40) **II, IV**	Spain: -Santiago de Compostella -1 WWTP (serving ~130000 inhabitants) -PE was based on house connection (2.5p/house)	2012 – 2014: -24h-composite WW samples (auto-sampler, time-proportional mode) -1 week samplings in each year --Apr 2012 --Mar 2013 --Mar 2014	Cot, OH-Cot: -LC-MS/MS after enzyme. deconjugation -UER(Cot): 22-32 (mean 27) % -UER(OH-Cot): 40-49 (44.5) % (35) -0.8 mg Nic abs./cig	-Nic cons, mean of Cot and OH-Cot (mg/d/p): --2012: 1.7; 2013: 1.9; 2014: 1.8 -No higher Nic consumption on weekends -Comparable to sales data from Galicia 2012/2013/2014: 2.3/1.8/1.9 mg/d/p -Cot higher in WW by ~40% with enzyme. deconjugation -OH-Cot not sign. different with/without enzyme. deconjugation
Rozhanets, 2021 (44) **II, IV**	Russia: -Small community in the Moscow region -1 sewage pump station serving 7600 inhabitants -Population 15+ used for back-calculation	2018-2019: -Mar 2018 (7 d) -Dec 2018-Jan 2019 (40 d (over New Year and Russian Christmas period)	Cot: -LC-MS/MS -WW samples taken after first coarse filter -Collection at 12 noon -UER(Cot): 14.1% (34) would overestimate Nic consump.! -Nic absorbed: 1.28 (?) mg/cig (32, 45)	-Mass load of cotinine: 0.97 ± 0.19 (0.72-5.43) mg/d/p (15+) -Nicotine consumption: 7.83±1.53 mg/d/p(15+) -Nic consumption -Tobacco use was consistent throughout the week and special events (slightly increase in alcohol use) -Tobacco use was consistent with the production data -Calculated cigarette consumption much higher in Russia than in other countries (Table 3, reason: UER?)
Ryu, 2016 (46) **V (BOBE)**	Norway, Switzerland, Belgium, Spain, UK, Denmark:	2014 and 2015:	OH-Cot: -LC-MS/MS	Population-normalized mass loads, estimated with a Monte Carlo approach (mg/d/1000p) -OH-Cot: not reported -8-iso-$PGF_{2\alpha}$: 2.5-9.9 mg/d/1000 p (mean: 4.8)

	-11 Cities (4 in Norway) -Catchment population (as reported earlier, (47, 48))		-4 weekday and 4 weekend samples per city in Norway (2+2 in the other countries) -Main focus of the study was 8-iso-$PGF_{2\alpha}$ (oxidative stress biomarker) in WW	-Strong correlation to per capita load of OH-Cot but not to ES (alcohol) -8-iso-$PGF_{2\alpha}$ showed clear differences between cities correlated to degree of urbanization (in Norway, 4 cities) -8-iso-PGF-2 α is a potential BM for assessment of community public health
Senta et al., 2015 (49) **II, IV**	Italy: -13 Cities in North, Center, South Italy -13 WWTPs (47000 – 1.4 million inhabitants) -BMs for PE: BOD, COD, Cot, OH-Cot	2012: -Spring and autumn of 2012 -24h-composite samples -7 – 28 consecutive days	Cot, OH-Cot: -LC-MS/MS (glucs were considered as split in WW) -UER(Cot)=30% -UER(OH-Cot)=44% (4) -MW ratio (Nic/Cot)=0.92 -MW ratio (Nic/OH-Cot)= 0.84 -1.25 mg Nic abs./cig (35)	Mass loads. (g/d/1000 p): -Cot : North: 0.5±0.1 -OH-Cot: North: 1.4±0.3 Center: 0.4±0.1 Center: 1.1±0.4 South: 0.7±0.2 South: 1.6±0.4 -Nic consumption sign. higher in South compared to North and Center Italy (compares well with smoking prevalences in these areas -No weekly trends Cot and OH-Cot (only slightly lower on Sat and Sum) -Caffeine cons. sign. lower on weekends -Cot- and OH-Cot-based PE agree well with census data (would be well suited for PE) -BOD- and COD-based PE-based PE overestimate the population size
Senta et al, 2023 (50) **II, IV**	Croatia: -City of Split (210000 inhabitants) -2 WWTPs (covering 90% of inh.) -Population size estimates on water consumption, 200L/d)	2016: -3 Periods with weekly WW collections --1. Off-tourist season (Nov) --2. Tourist season, reference (Aug) --3. Tourist season with music festival (Jul) -24h-composite samples (time-proportional) -7 consecutive days	Cot, OH-Cot: -LC-MS/MS -UER(Cor): 27%/MW ratio: 0.92/CR=3.41 -URE (OH-Cot): 44.5%/0.84/1.9 (45) -Ave. cig cons.: 15.9 cig/d (Croatia, 2015) -57 BMs in total (including IDs)	-PNDL (mg/d/1000p): --Cot: 1.: 1034 ± 131; 2.: 1084 ± 118; 3.: 977 ± 41 --OH-Cot: 1.: 1535 ± 189; 2.: 1632 ± 168; 3.: 1490 ± 79 -Nic consumption remained constant over the whole study (IDs and alcohol increased during the festival, MDMA: 30-fold) -No information on the influence of weekends on Nic consumption -Prevalence of smoking, WW-based: 30.6% (national survey: 27.5-31.5%)
Shao et al., 2021 (51) **(comparisons to other studies and countries)**	China: -22 cities (covered all geographic regions in China) -27 WWTPs -Population estimated with $N\text{-}NH_4$ in WW -Total pop: 135,910,000 -WWTP pop: 12,250,000	2018 and 2019: -24h-composite sample, time-proportional (auto-sampler)	Cot: -GC-MS with derivatization after SPE -CF(Cot)=2.85 (UER=35%)(16) -0.9 mg Nic/cig (China) -66% of Nic are absorbed (45)	-Monte Carlo parameters for calculation of consumptions provided -Nicotine consumption based on WW Cot (g/d/1000p): - Average: 0.75±0.09, range: 0.17-1.88 (lower than in many other countries) -Nic consumption was lower than in another Chinese study (15), in Spain (40) and Portugal (34) -Sign correlation with caffeine consumption -Sign. correlation with metformin (drug for diabetes Type 2) -The authors conclude that smoking may play an important role in the induction of Type 2 diabetes
Shao et al., 2022 (52) **-**	China: -33 Cities -38 WWTPs -PE: Model conserving flow, $NH_4\text{-}N$ and Cot	2016-2021: -24h-composite WW samples (time-proportional)	Cot: -LC-MS/MS -UER=30% -CF=3.33 (4)	-Nic consumption (mg/d/p): --0.44 – 2.18 --higher in North than in South China --Significant correlation with sildenafil (r = 0.55)

			-Other BMs in WW: alcohol, opioids, pharmaceuticals (sildenafil)	
Song, 2020 (53) **II**	China: -Yingkou, 1 WWTP -Pop served; 0.51 million (22% of the urban pop of the city) -Population estimated with WW parameters N-NH_4 , chemical oxygen demand (COD) and total phosphorus (TP)	2018/2019: -During 21 holidays (6 major events) and 26 working days -24h-composite samples	Cot: -GC-MS with derivatization after SPE -UER(Cot)=19.4% -Metformin use (treatment drug for Type 2 diabetes), caffeine and MEth was also measured in this study	-Nicotine consumption in the city, mean ± SD (mg/d/1000p): --Weekdays: 0.98±0.23 --Holidays (events): 1.14±0.38 (lower than in other studies (31, 34) -Different patterns on holidays for the various substances were observed -Cot correlates sign. with CAF, metformin and METH -Corr. indicate cross-consumption.of substances -WBE can provide useful information on lifestyle and health control
Subedi et al., 2014 (54) **-**	USA: -Albany area in New York state -2 WWTPs (A, B) -A: ~100000 p -B: ~15000 p	2013: -Jul12 (Fri) – Jul 18 (Thu) -24h-composite WW samples (+ suspended particulate matter, SPM) -No SPM data for Cot reported	Cot: -LC-MS/MS -UER/MW ratio not considered (used for calc in this review: 30%/0.92) (4)	Nic consumption (mg/d/1000 p): -A: 2834 -B: 3649
Thai et al., 2023 (55) **I, II, IV**	Australia: -National WW Drug Monitoring Program (NWDMP) since 2017 -WWTPs cover 56% of population	2017-2020 -bimonthly WW coll. in capital cities -quarterly WW coll. in regional places -7 consecutive days	Cot, OH-Cot: -LC-MS/MS -UER(Cot): 30% 1.25 mg Nic/cig (4)	-Nic consumption (mg/d/p): --2nd half 2019: 1.4 --1st half 2020: 1.8 (COVID-19 restrictions) --2nd half 2020: 1.6 -Nic consumption had decreased from 2017-2019 by 5%/a, but increased in 2020 (discussed reasons: stress, increased smoking/vaping when working at home) -Nic cons (WW-based) 2017-2019, slope: -0.035 (tobacco sales Nic equivalents, slope:-0.12) -NRT cons. (sales-based) increased from 2017 to 2020 -NRT contribute <10% to Nic consumption, ECs of only minor importance in Australia (sales prohibited)
Thanh, 2022 (56) **II, IV**	Vietnam: -Hanoi, 2 sites at the sewage canal, 500 m away from the WWTP --Site 1: 400000 persons served --Site 2: 430000 persons served	2018 – 2020, 3 periods: -Period 1: Sep 2018 -Period 2: Dec 2018-Jan 2019 -Period 3: Dec 2019-Jan 2020 -1-h manual grab samples per day (500 mL)	Cot, OH-Cot -LC-MS/MS -EF=2.96 (=UER=34%) (2, 57) CPD of smokers: 1.05 mg Nic/cig, Pop(15+) times smoking prevalence	-Average Nic consumption: 1.28±0.25 mg/d/p -No trend over the week -Nic consumption in Period 1 lower than in Periods 2 and 3, but no temporal trend (higher in winter than in autumn, as observed in Australia (58 and Turkey {Asicioglu, 2021 #201808) -WW data somewhat lower than in surveys
Tomsone et al., 2022 (59)	Latavia: -Riga	2021: -Dec 2020 to Dec 2021	Cot: -LC-MS/MS	-Nic cons. (mg/d/p15+): mean 5.9 --Winter/Spring/Summer/Autumn: 5.1/5.7/6.8/6.1

II, IV	-1 WWTP (serving 697000 p) -5-HIAA used for population estimate	-24h—composite samples (auto-sampler, flow-prop.: 51 WW samples Mon – Tues) -29 grab morning samples: 6 weeks, Jun 29 to Aug 6, 2021	-UER: 22-32%, 27% used -CF: 0.92 (?) (9) -Also measured in WW: pharmaceuticals, caffeine, alcohol	--Consistent over the weekdays (Mon to Fri) --Higher in May, Jun, Jul --Good agreement with consumption estimates from statistics
Trowsdale, 2021 (60) **II, IV**	New Zealand: -3 Regions -7 WWTPs -Covers 18.3% of NZ population	2018: -1 week (coinciding with the national census on 6 Mar 2018) -24h-composite samples on 7 consecutive days (autosampler)	Cot+ OH-Cot: -LC-MS/MS -CF=1.35 (equiv. to UER=74%) (4) -Nic absorbed: 1.25 mg/cig (4)	Pop-normalized consumption -1528 ± 412 cig/d/1000p, similar to sales and survey data -Nic was consistent during the week, alcohol (ES) peaked on weekends -Nic correlated with neighbourhood-deprivation (measure of socio-economic disadvantage) (alcohol did not) -Inter- and intra-regional differences: Nic consumption was higher outside of the cities -The census night data set helps account for population mobility (including tourists) -Other nicotine products were not mentioned
Tscharke, 2016 (61) **II, III**	Australia: -Adelaide, 1 WWTP -Catchment pop.: 695000 p (provided by the WWTP)	2014 -1 week sampling: 28-09-14 (Sun) to 04-10-14 (Sat)	Cot: -LC-MS/MS -Also determined in WW: --AB, AT, Nic -AB and AT were in the focus of this study as WW markers for tobacco use	-Mass loads, average deduced from Figure 4 (mg/d/1000p): --Cot: ~750 (smokers: 3360±2080 µg/d) (62) --AB: ~4 (smokers: 15.5±11.5 µg/d) " --AT: ~8 (smokers: 24.1±25.3 µg/d) " -Ratios Cot/AB or Cot/AT in WW appear too low compared to smokers (the authors attribute this to the high variability in the smoker study) -All 4 compounds are stable under all conditions -Nic and Cot ~500-1000x higher conc. in WW than AT and AB -No dependency on weekday -AT AB in WW are suitable BMs for tobacco consumption (not including NRT, ECs, etc.)
Van Wel, 2016 (63) **II, IV**	Belgium: -1 mid-size city (Lier) -1 WWTP (capacity: 30600 p) -Census pop 37236 p	2014: -Four 2-week periods form 01.09.14 to 30.11.14 -24h-composite WW samples (time-proportional) -Concurrently with a population (15+) survey on smoking and drinking habits, 1 % response	Cot, + OH-Cot -LC-MS/MS -CF=1.35 (UER=74%) -Nic absorbed: 1.25 mg/cig (4)	-136457 cig/d (equivalent to a 170571 mg Nic/d or 4.58 g Nic/d/1000p -Survey and WBE showed lower consumption of Nic and alcohol (ES) in Lier than in rest of Belgium -Nic (but not ES) showed sign. variations over sampling periods -Nic consumption slightly, alcohol clearly higher on weekends -No correlation between WBE and survey results -According to the authors, missing correlation (WBE vs survey) may be due to small sample size -WBE can identify changed use during major events
Verhagen et al., 2023 (64) **V (Passive WW sampling)** **-**	Australia: -43 with different degrees of remoteness (5 categories) -Pop. sizes: <500 to 150000 p	2019/2020: -Aug/Sep 2019 and Aug/Sep 2020 -Passive WW sampling (Sorbent: sulfonic acid modified poly-divinyl-benzene -Exposure time: 4-14 days	Cot: -LC-MS/MS -No values for UER and CF provided -Additional BMs in WW: cocaine, MDMA, METH, oxycodone	-Nic consumption (mg/d/1000 p): --2019: 560 ± 120 to 17000 ± 1700 --2020: 86 to 9400 ±120 --Spatial trend to higher Nic consumption with remoteness --Comparison with conventional 24h-composite sampling: similar levels and trends -Conclusion: passive sampling is suitable for WBE, if conventional sampling is not available (e.g. in remote places)
Vogel, 2024 (65)	USA -New York state:	2021-2022:	Cot, OH-Cot, (Nic)	-Nic, Cot, OH-Cot detected in 76-100% of WW samples

IV	--10 WWTP with various sewershed characteristics (A-J) --Population catchment: 3076-242377 (from US census data) --WWTPs provided data for flow rates, BOD, TKN, NH_3-N	-24h-composite WW samples, flow-proportional -WWTP provided flow rates, BOD, TKN, NH_3-N -Focus was on psychoactive and life-style compounds used in NY state	LC-HRMS-Orbitrap (online SPE) -targeted quant (39 compounds). -untargeted	-Person loads of Nic were within 30 % of results from other US communities -The Nic/Cot ratio in WW exceeded that in urine (2.4 vs 0.6) -Various normalization factors tested -Importance of parent/metabolite (P/M) ratios stressed -Nic/Cot ratio suggests that non-consumed Nic entered the WW (from butts, ashes, etc.)
Wang et al., 2016 (32) **IV**	China: -City of Dalian -11 WWTPs (serving 2.2 million people, 83% of the city -PE: Statistical data from the government	2015: -Jun 2015 -2 consecutive weeldays -24h-composite samples	Cot, OH-Cot: -LC-MS/MS -UER(Cot): 32.3±8.0% -UER(OH-Cot): 43.4± 13.8% -0.9 mg Nic/cig (Chinese market) -Nic uptake rate: 66±19% (45)	-Nic consumption (mg/d/p): 1.92 (range: 0.25 – 4-22) --Distribution: 10%: 1.56, median: 2.04. 90%: 2.39 -Cig consumption estimated by Monte Carlo simulation (cig/d/smoker): --14.6, range 10-27, median: 16, uncertainty: 2.0 --Sensitivity analysis, contribution to uncertainty: UER(Cot): 52%, UER(OH-Cot): 31%, other factors: <5%
Wang, 2021 (66) **II, IV**	China: -City in Southern China: -Residents: 500000 -24h-composite WW samples, daily 279 WW samples, daily samples -University town: 43 WW samples, weekly -Residents: 200000 (80% students)	2017-2018: -City: Daily samplings Nov 2017 to Oct 2018 -University town: every Wednesday, Nov 2017 to Nov 2018	Cot, OH-Cot: (only Cot was used for back-calc.) -LC-MS/MS -EF=2.85 (UER=35%) (57) -Nic uptake rate from cigs: 66±19%) (45) -0.9 mg Nic/cig (yield)	-City: --1.16 cig/d/p(15+) --slightly increasing trend over the year (consistent with cig sales statistics) --consistent over the week -University town: --0.6 cig/d/p(15+) --stable over the year -Nic/Cot ratio in WW (city): --1.21 (much higher than expected from UER: 0.43) -Cot/OH-Cot ratio in WW (city, univ. town) --0.83, 0.84 (in good agreement with UER: 0.81) -Differences (city/univ. town) may be attributable to demographic factors -Tobacco-free campus policy may be possible reason for lower nic mass load in the University town
Wang, 2024 (67) **I, II, III, IV**	Australia: -Queensland, reginal city --100000 p served --From WWTP operators: flow rate, catchment population --In addition: Census data from 2011, 2016, 2021	2013-2021: -1 week every 2 months -24h-composite samples, flow-proportional -In total 340 WW samples	Cot, OH-Cot, AB: -LC-MS/MS -Nic consumption: --CF(Cot+OH-Cot)=72% (7, 63, 68) --Nic dose: 0.9 mg/cig (7, 35, 51) -Tobacco consumption: --EF(AB)=0.91 µg/cig (68)	-Per capita mass loads (mg/d/1000p): --Cot: 720 ±160 --OHCot: 1300 ±300 --AB: 2.3 ±0.52 -WW-based consumption over time: --Tobacco (AB): First strong (-21%) and then slow (-10%) decrease --Nicotine (Cot+OH-Cot): first slight decrease (-18%) then strong increase (+40%) -WW-based tobacco use higher than sales data suggesting illicit tobacco use -Findings suggest increased use of non-tobacco nicotine products (ECs, NRTs, especially after 2018) -This is one of the first WBE approaches for NGPs

Xu, 2023 (69) **IV**	China: -24 cities (across China) -234 WWTPs	2019: -24h-composite WW samples (auto-sampler) -On sunny/cloudy days (to minimize rainfalls)	Cot: -LC-MS/MS CF(Cot)=MW(Nic)/ MW(Cot)xX(Cot); X(Cot)=UER(Cot) -Nic/cig=0.9 mg -Nic uptake=66% (45) -Metal ions (Na, K, Mg, Ca, Fe, Zn) were used as population BM (PB) to more reliably estimate the population size	-Nic consumption: 1.76±1.19 mg/d/p -Converted to cig/smoker: 13.0±8.76 cig/d/smoker -Kalium-based cig consumption strongly correlate with census data (r = 0.66-0.81) -"Kalium-equivalent population" provides a new method for accurately evaluating spatio-temporal trends in tobacco use among accurate populations -Monte Carlo approach used for Nic consumption (simulation with 100000 'samples', distributions in Table 1)
Zheng et al., (16) **IV, V**	China: -Jilin Province, 8 cities -10 WWTPs (serving 4 million people) -PE based on NH_4-N (compared with WWTP data)	2016: -Aug 2016, 2 consecutive days -24h-composite samples	Cot: -LC-MS/MS -UER: 32.8±8.0% CF=1/0.328 x 0.92 = 2.81 -Nic/cig = 0.9 mg -Nic uptake rate: 66% (45)	-Population-normalized daily nicotine load, PNDL (mg/d/p): --2.39 ± 1.47 -MC simulation for cig cons.: 9.8-31.4 cig/d/smoker (median: 16.9); good agreement with China survey data -NH_4-N-based PE strongly correlated with WWTP-info (r=0.99) -EC and NRT use in C(16)hina <<1% at that time
Zheng et al., 2020 (70) **III**	Australia: -WWTP in South-East Queensland -Catchment population: 100000	2015: -Feb, Apr, Jun, Aug, Oct, Dec -24h-composite WW samples on 7 consecutive days (flow-proportional) -42 WW samples	Cot, OH-Cot, AB, AT, (Nic) -LC-MS/MS (direct-injection):	-Pop-normalized mass load (µg/d/p): --AB: 2.2 --AT: 5.6 --Cot: 200-650 --OH-Cot: 380-1290 -Lower than in Europe (30, 33) (lower smoking prevalence in Australia) -Ratios (AB/AT, AB/Cot, AT/Cot): similar to other studies (30, 61) -AB and AT were less stable than Cot and OH-Cot in sewer reactors -more stable (20% loss/12h) in GS than RMR reactor (-30%/12h) -Nic is degrading to a similar extent -Sign. correlations between all 5 BMs (r=0.67-0.95) -AB and AT in WW can prevent overestimation of tobacco use due to NRT and EC use - Possible degradation should be considered for the estimation of tobacco use in future WBE studies
Zheng, 2020 (58) **I, III, IV**	Australia: -WWTP in South-East Queensland serving ~100000 p -Population size based on census data from 2011 and 2016	2012-2017: -every 2 months (Feb 2012 – Dec 2017), 36 complete weeks -24h-composite WW samples (auto-sampler) -249 WW samples	Cot, OH-Cot, AB, AT -LC-MS/MS	-Mean pop-normalized mass loads: -- AB: 2.2±0.6; AT: 6.3±0.6 µg/d/p -- Cot: 0.53±0.14; OH-Cot: 0.93±0.25 mg/d/p -Annual declines (%): AB (-3.0), AT (-2.7), Cot (-2.4), OH-Cot (-2.1) -Survey: -5% -Taxation: -4% -AB/Cot: -1.2% -AT/Cot: -1.9% -AB/Cot and AT/Cot ratios suggest a relative increase in non-tobacco Nic consumption

				-Nic consumption stable over weeks (no weekend effect) and months (no seasonal effect), other than with alcohol -Nic cons. from patches (% of total) mg/d/p: 2014: 0.013 (0.47), 2015: 0.019 (0.69), 2016: 0.021 (0.78), 2017: 0.024 (0.95) -Estimated contribution of Nic patches: 0.47-0.95% (over the years) -The BM used demonstrate their suitability for monitoring long-term trends
Zheng, 2023 (68) **III, IV**	Australia: -Queensland -2 WWTPs (A and B) -WWTP (A): 28 samples, 2009/2010 -WWTP (B): 249 sampes (see (58)) -Total: 277 WW samples	2009-2019: -277 WW samples -64 Pool urine from 6400 subjects (4 age groups, 15+) collected in 2013, 2015, 2019	Cot, OH-Cot, AB, AT, (Nic) -LC-MS/MS -UER (Cot+OH-Cot): 72% (meta-analysis of 17 studies), EF=1/0.72=1.39 -EF for AB, AT deduced from ratio to Cot in urine	-AB in WW showed similar per person load in pooled urine (2.3±0.3 vs 2.2±0.3 µg/d/p) -AT load in WW was 50% higher than in urine:6.5±0.7 vs 3.1±0.4 µg/d/p (reasons: AT occurs in food such as tomatoes, eggplants, peppers) -AB load by 5% higher than tobacco sales, Cot by 2-28% higher -Study shows concrete evidence that AB in WW is suitable for monitoring tobacco use (as compared to Cot, OH-Cot for Nic consumption) -AB preferable to AT (AT has other sources and is more variable, 20 vs 59%) -Some increase in WW samples after deconjugation with ß-glucuronidase (particularly Cot!)

[1]: Publications were assigned to 5 subcategories: I: time trends were investigated, II: effects of workdays/weekends and special events were studied, III: AB and AT were included in the WW analysis, IV: WBE-derived results were compared to 'classical' methods such as surveys, statistics, sales data, etc., V: other aspects were included such as population size estimates (PE) by special biomarkers, type of WW sampling, biomarkers of biological effects (BOBEs)

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