



# Tobacco & Behavioral Health : A State Approach-Kansas

Friday December 4, 2020

## Tobacco Treatment & Biochemical Quantification of Tobacco Consumption

Adapted from the Society for Research in Nicotine & Tobacco  
Annual Conference 2019 Presentation  
Hilton San Francisco Union Square  
Feb 22, 2019



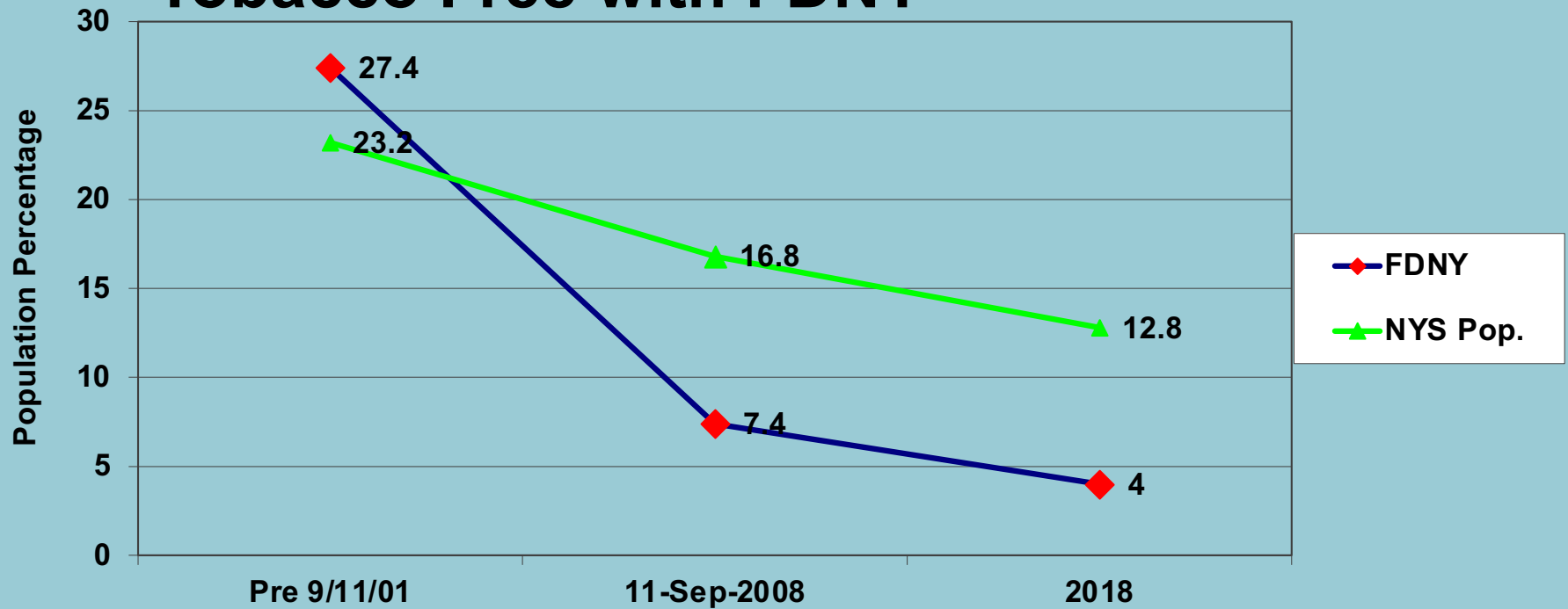


## Objectives

- Review the pharmacology of nicotine and carbon monoxide delivery via tobacco products
- Review tobacco treatment medications (This ain't your grandfather's SmokEnders)
- Biochemical assessment of nicotine (TNEs) and carbon monoxide (EtCO) to personalize tobacco treatments, quantify therapeutic progress and abstinence, dramatically reducing individual morbidity and mortality and bending the arc of population health



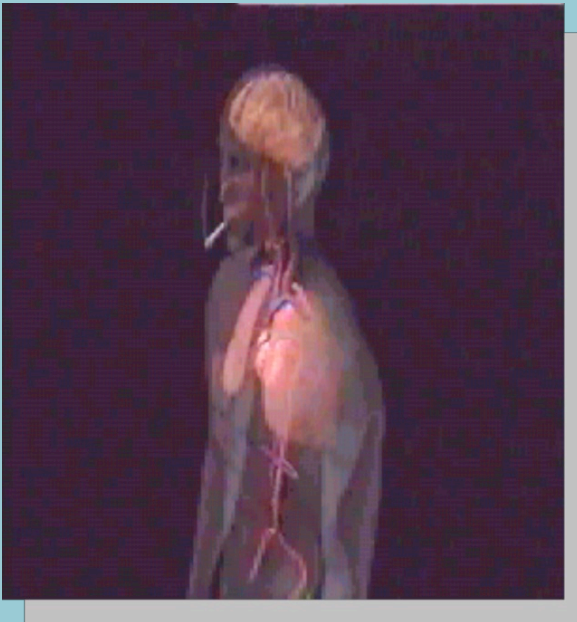
## Tobacco Free with FDNY



[https://nccd.cdc.gov/STATESystem/rdPage.aspx?rdReport=OSH\\_STATE.Highlights&rdRequestForwarding=Form](https://nccd.cdc.gov/STATESystem/rdPage.aspx?rdReport=OSH_STATE.Highlights&rdRequestForwarding=Form)  
Lung Function in Rescue Workers at the World Trade Center after 7 Years N Engl J Med 2010; 362:1263-1272  
<http://www.nejm.org/doi/full/10.1056/NEJMoa0910087>  
[www.health.state.ny.us/nysdoh/tobacco/reports/brfss2001.htm](http://www.health.state.ny.us/nysdoh/tobacco/reports/brfss2001.htm)  
[http://online.wsj.com/public/resources/documents/st\\_SMOKE\\_20091113.html](http://online.wsj.com/public/resources/documents/st_SMOKE_20091113.html)



## Pulmonary drug delivery



The most rapid drug delivery is via inhalation

Nicotine, carried on “tar” particles and in gaseous phase, enters the pulmonary circulation and the CNS in 7 seconds. The gas phase also includes carbon monoxide (CO), a signal for the intensity of tobacco consumption.



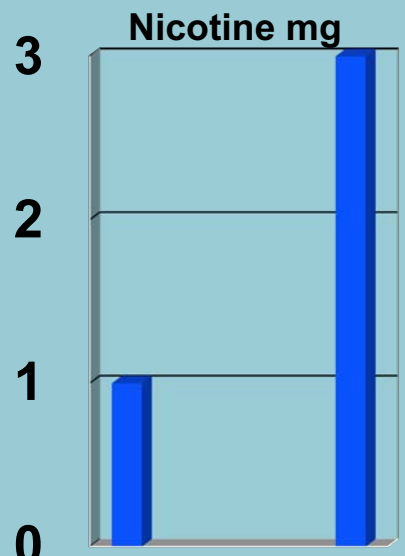
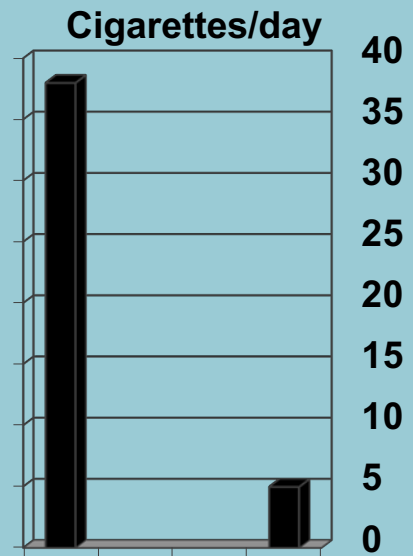


# Counting cigarettes is inadequate & biochemically inaccurate

Smokers average ~1 mg of nicotine/ cigarette  
 Nicotine consumption is extremely variable  $\geq \Delta 300\%$

Tremendous bioavailable variability

↓ cigarettes/d    ↑ nicotine/cigarette



Average CPD Forced Reduction

Average CPD Forced Reduction

Benowitz NL, Kuyt F, Jacob P III, Kozlowski LT, Yu L. Influence of smoking fewer cigarettes on exposure to tar, nicotine, and carbon monoxide. N Engl J Med 1986; 315:1310-3

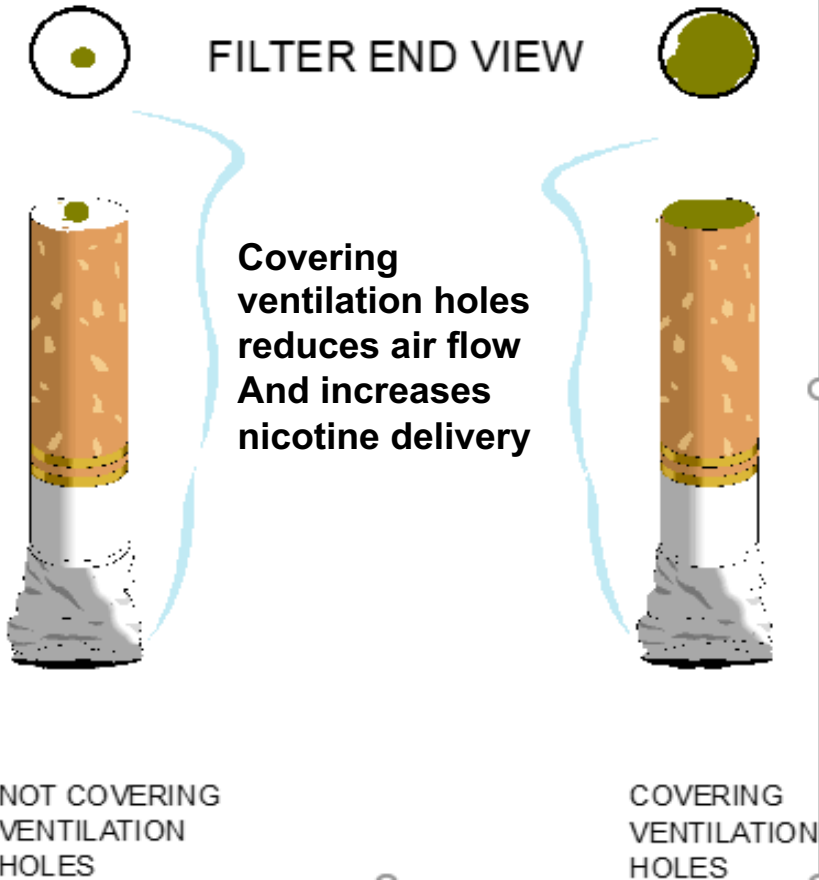
Benowitz, NL., Jacob, P., III. Daily intake of nicotine during cigarette smoking. Clinical Pharmacology and Therapeutics 35(4):499-504, 1984





# Compensatory smoking

When is a light cigarette NOT a light cigarette?

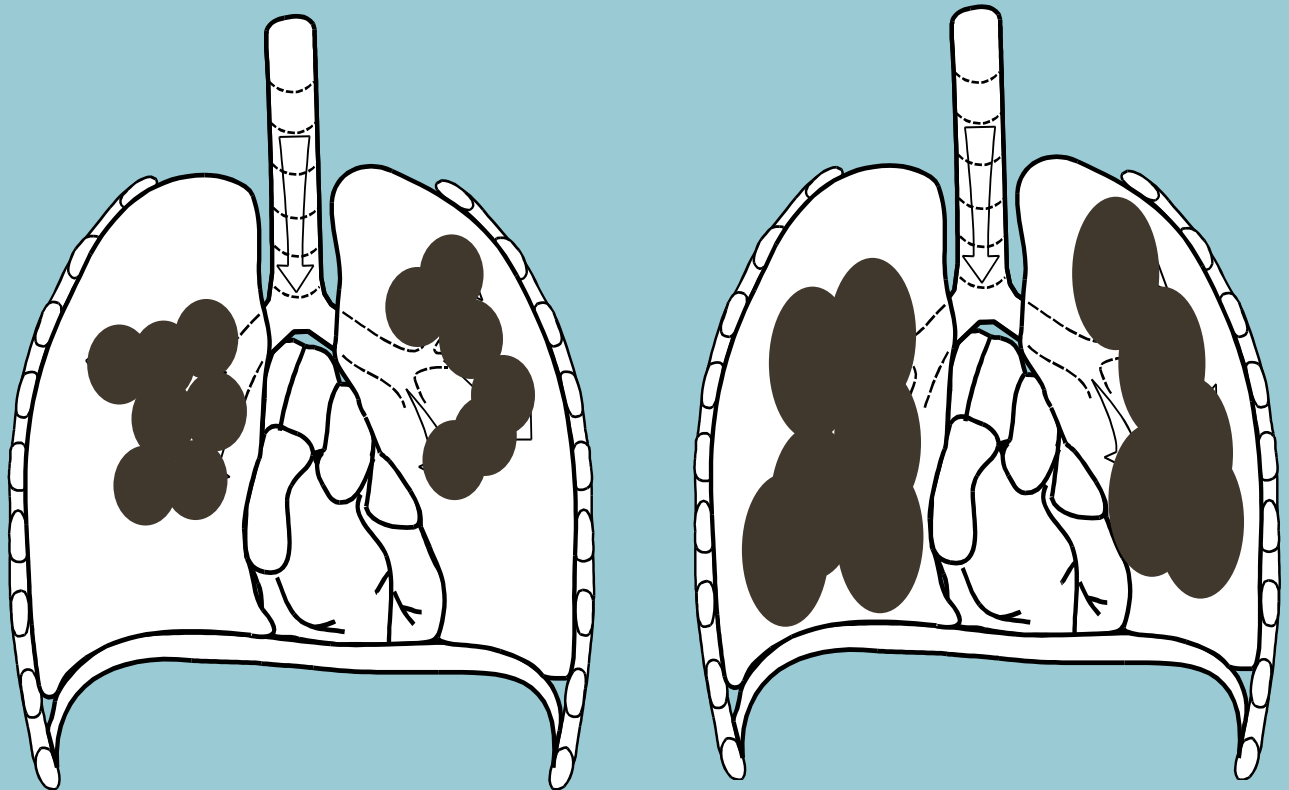


Courtesy RD Hurt, MD,  
 Mayo Tobacco  
 Dependence Center



## Compensatory smoking typography

- ✓ Puffs/ cigarette
- ✓ Puffs/ minute
- ✓ Inspiratory volume & time
- ✓ Breath hold (secs)
- ✓ Peak inspiratory flow (L/min)





Pharmacotherapy	Estimated Odds Ratio Compared to Placebo
<b>Nicotine Polacrilex Gum</b>	<b>1.5</b>
<b>Transdermal Nicotine Patch</b>	<b>1.9</b>
<b>Nicotrol Nicotine Nasal Spray</b>	<b>2.7</b>
<b>Nicotrol Inhaler</b>	<b>2.5</b>
<b>Bupropion SR</b>	<b>2.1</b>
<b>Commit Lozenge</b>	<b>2.1 to 2.7</b>
<b>Chantix (Varenicline)</b>	<b>3.1</b>





## Pharmacotherapies





- 70% of smokers want to stop = 73,000 / day.
- Only 8% to 12% of smokers prefer abrupt quit interventions (quitting now).
- More smokers prefer RTC.
- Both cessation strategies will engage the most smokers.

Moore D, Aveyard P, Connock M, et al. Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis: BMJ 2009;338:b1024

Wewers ME, Stillman FA, Hartman AM, Shopland DR. Distribution of daily smokers by stage of change: Current Population Survey results. Prev Med.2003;36(6):710-720.



Almost half of those planning to quit in the next 12 months (44%) prefer to quit via gradual cessation and most (68%) would use a reduction product or medication.

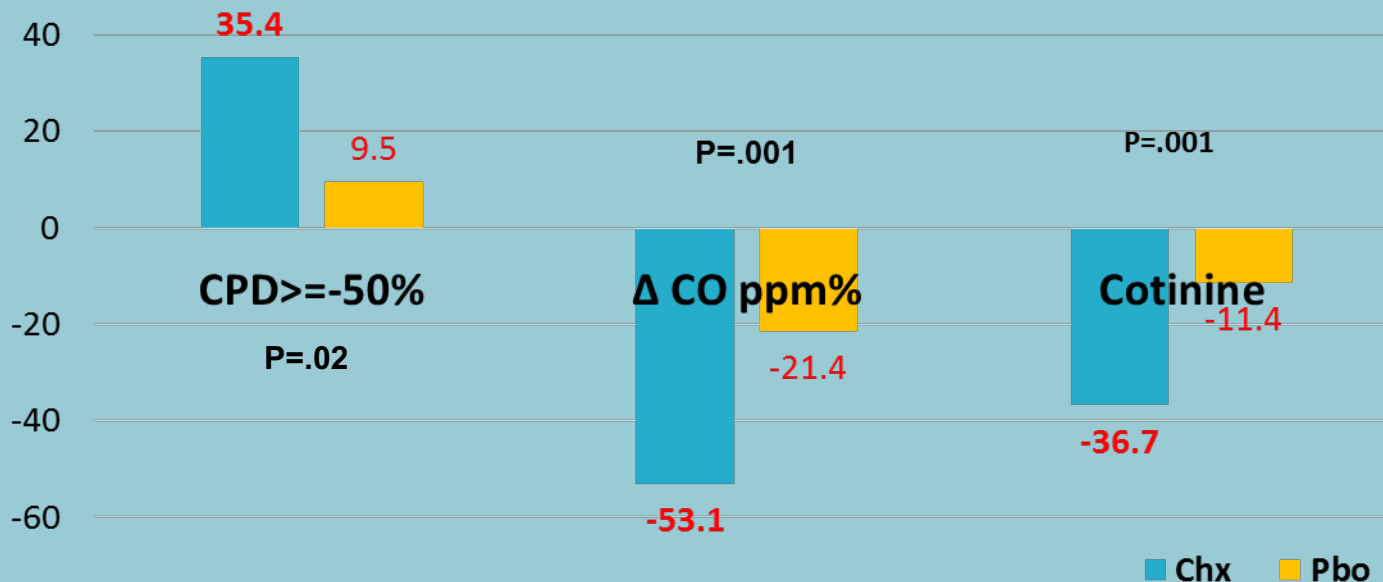
CPD↑    Addiction↑    RTC↑

Most smokers (57%) report previously trying to reduce their smoking.



## Varenicline preloading leads to decreased tobacco consumption

### Reductions at 3 wks post intake

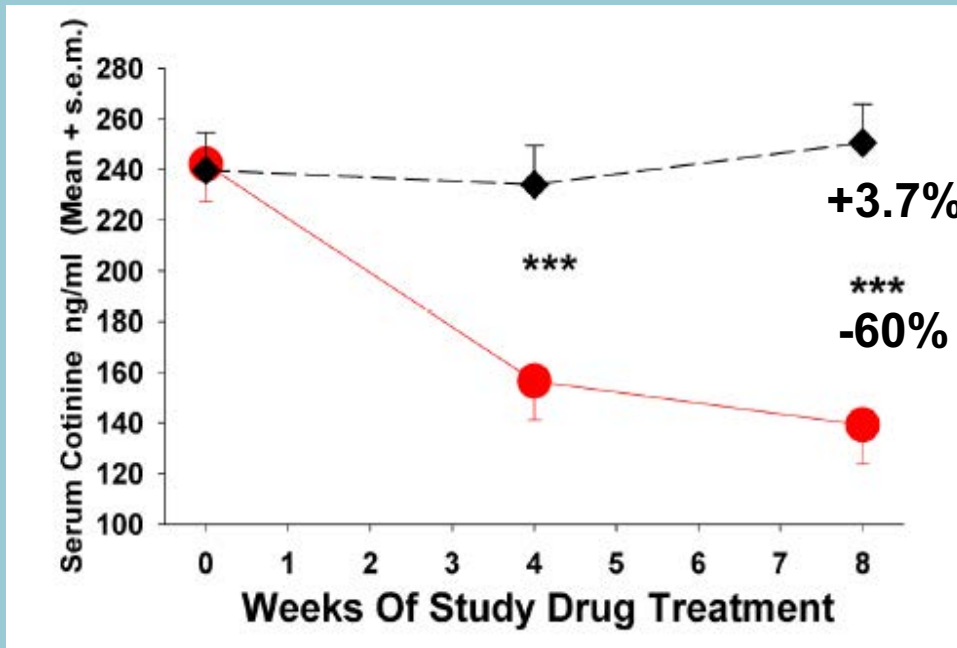


Hajek P, McRobbie HJ, Myers KE, Stapleton J, Dhanji AR. Use of Varenicline for 4 weeks before quitting smoking: decrease in ad lib smoking and increase in smoking cessation rates. Arch Intern Med. 2011 Apr 25;171(8):770-7. doi: 10.1001/archinternmed.2011.138.





## Varenicline reduced cotinine in unmotivated schizophrenic smokers. Cotinine assays guide successful treatment



\*\*\* P<.001

Smith RC, Amiaz R, Si T-M, Maayan L, Jin H, Boules S, et al. (2016) Varenicline Effects on Smoking, Cognition, and Psychiatric Symptoms in Schizophrenia: A Double-Blind Randomized Trial. PLoS ONE 11(1): e0143490. doi:10.1371/journal.pone.0143490



**Better Nicotine Replacement Therapy (NRT) dose matching has been accomplished by measuring baseline cotinine levels while smoking and titrating NRT to this baseline intake and/or subsequent levels.**

**Studies show % replacement of nicotine is inversely correlated with withdrawal symptoms and positively correlated with quit rates.**

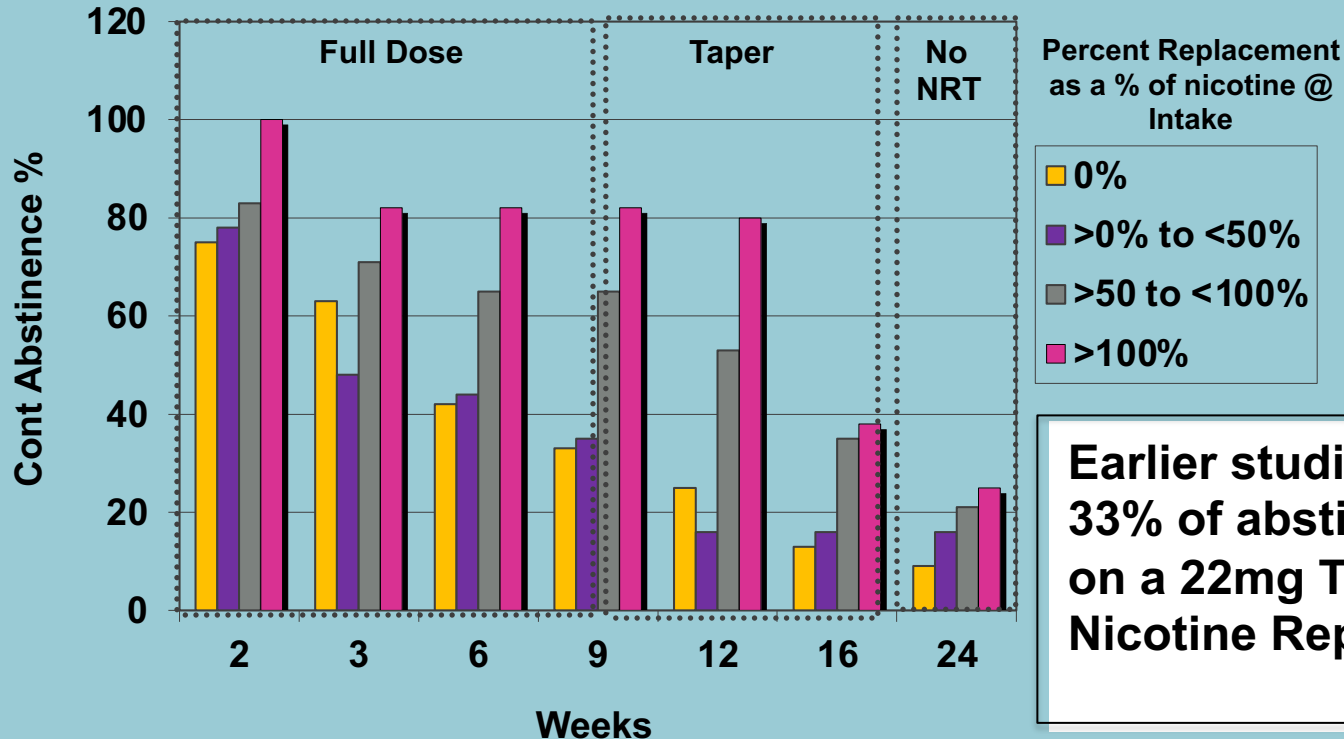
Hurt RD, Dale LC, Offord KP, Croghan IT, Hays JT, Gomez-Dahl L. Nicotine patch therapy for smoking cessation in recovering alcoholics. *Addiction*. 1995 Nov;90(11):1541-6. PubMed PMID: 8528039.

Lawson GM, Hurt RD, Dale LC, Offord KP, Croghan IT, Schroeder DR, Jiang NS. Application of serum nicotine and plasma cotinine concentrations to assessment of nicotine replacement in light, moderate, and heavy smokers undergoing transdermal therapy. *J Clin Pharmacol*. 1998 Jun;38(6):502-9. PubMed PMID: 9650539.



# Cotinine assays guide successful treatment

## Increasing nicotine replacement increases treatment success

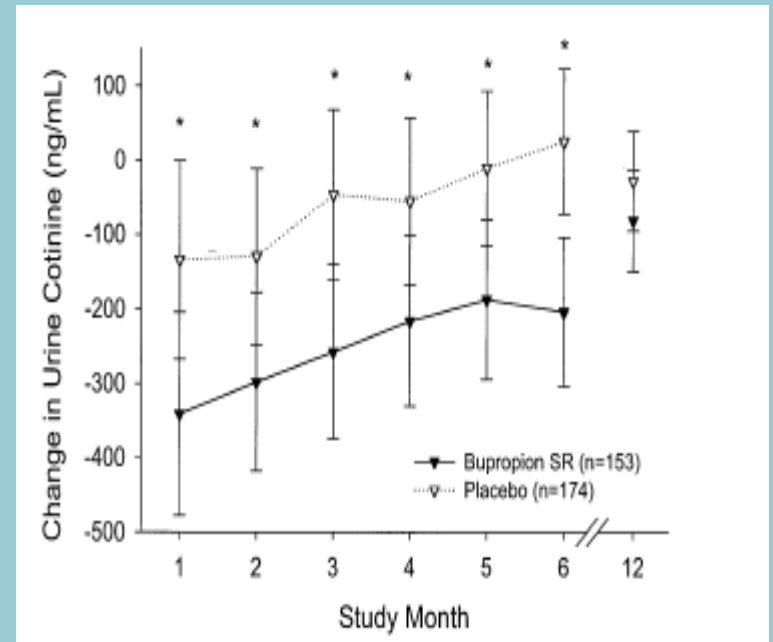
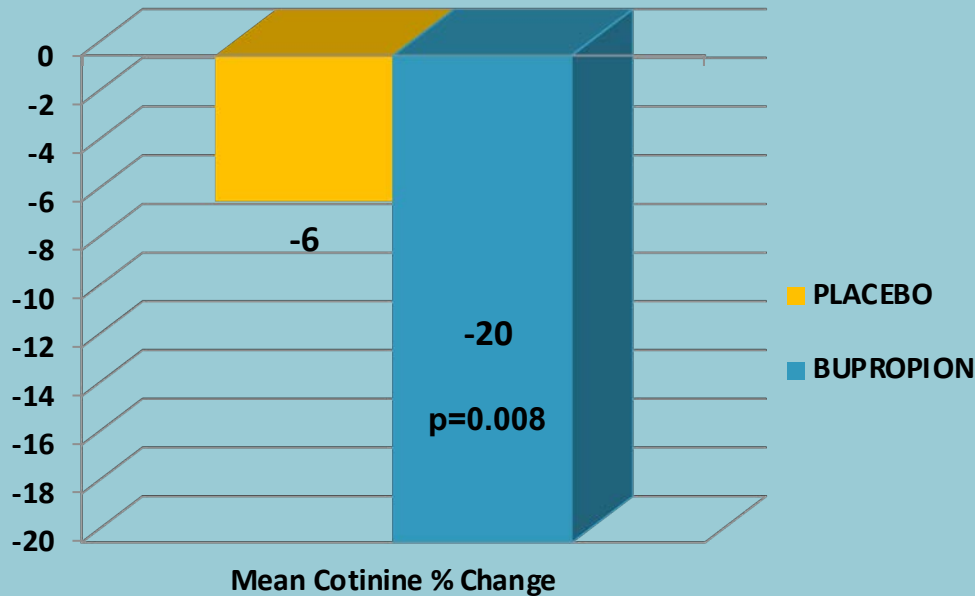


**Earlier studies found only 33% of abstinent smokers on a 22mg TNP had  $\geq 100\%$  Nicotine Replacement**



# Cotinine assays guide successful treatment

## Bupropion helps smokers cut down biochemically before quitting



Effects of sustained-release bupropion among persons interested in reducing but not quitting smoking Hatsukami D.K., Rennard S., Patel MK., Kotlyar M., Malcolm R., Nides MA., Dozier G., Bars, MP., Jamerson BD. (2004) American Journal of Medicine, 116 (3) , pp. 151-157





**Total Nicotine Equivalents (TNEs) can aid treatment planning & medication titration while assessing biochemical reduction in consumption and abstinence.**

Lawson GM, Hurt RD, Dale LC, Offord KP, Croghan IT, Schroeder DR, Jiang NS. Application of serum nicotine and plasma cotinine concentrations to assessment of nicotine replacement in light, moderate, and heavy smokers undergoing transdermal therapy. *J Clin Pharmacol.* 1998 Jun;38(6):502-9. PubMed PMID: 9650539.

Effects of sustained-release bupropion among persons interested in reducing but not quitting smoking Hatsukami D.K., Rennard S., Patel MK., Kotlyar M., Malcolm R., Nides MA., Dozier G., Bars, MP., Jamerson BD. (2004) *American Journal of Medicine*, 116 (3) , pp. 151-157



**Carboximetry levels are directly related to number of cigarettes smoked and how long CO levels remain elevated is a function of number of cigarettes smoked.**

Ringold, A., Goldsmith, JR., Helwig, HI., Finn, R. & Schuette, F. Estimating recent carbon monoxide exposures. Archives of Environmental Health, 1962,5, 308-318.

Rea, JH., Tyrer, PJ., Kasap, HS. & Beresford, AA. Expired air carbon monoxide, smoking, and other variables. British Journal of Preventive Social Medicine, 1973, 27, 114-120.

Vogt, TM., Selvin, S., Widdowson, G. & Hully, SB. Expired air carbon monoxide and serum thiocyanate as objective measures of cigarette exposure. American Journal of Public Health, 1977,67, 545-548.

Horan, JJ., Hackett, G. & Linberg, SE. Factors to consider when using expired air carbon monoxide in smoking assessment. Addictive Behaviors, 1978, 3, 25-28.

Henningfield, JE, Stitzer ML, Griffiths, RR. Expired air carbon monoxide accumulation and elimination as a function of number of cigarettes smoked. Addict Behav. 1980;5(3):265-72.



**Expired end-tidal breath CO (EtCO) and TNE assays are powerful tools to assess both tobacco dependence and therapeutic progress regarding all tobacco product use.**

**After baseline measurements, adaptive treatment protocols can be implemented based on changing clinical findings, patient preferences, and clinician input over the course of the treatment.**



## End tidal expired breath carbon monoxide/ carboxyhemoglobin measurement (EtCO)







**Generally, if the tobacco dependent patient is prescribed a non-nicotine medication (e.g. Varenicline), frequent EtCO and TNE measurements should both decrease over time with corresponding decreases in combustible tobacco and nicotine consumption towards tobacco abstinence.**

**In contrast, successful administration of NRTs or successful combination pharmacotherapies {NRT(s) plus Varenicline &/or Bupropion} would result in a relatively rapid decrease in EtCO due to a reduction in combustible tobacco while TNEs would remain relatively constant due to the additional nicotine from NRTs.**



- **With NRTs, after initial high % replacement as treatment continues, TNE assays begin to decrease during downward titration of NRT towards abstinence.**
- **This reflects decreases in both combustible and non-combustible tobacco use.**
- **EtCO and TNEs enable personalized tobacco treatment and the titration of medications towards optimal efficacy.**



## Adaptive treatment protocols on follow-up

- ✓ Quantify  $\Delta$  consumption via  $\Delta$  TNEs,  $\Delta$  EtCO,  $\Delta$  CPD secondary to treatment plans
- ✓ Medication(s) specifics
- ✓  $\Delta$ TWS &  $\Delta$  ADEs
- ✓ Idiosyncratic responses (e.g. tobacco dysgeusia)
  - ↓ cpd
  - ↓ puffs/ cig or e-cig
  - ↓ tobacco anhedonia
  - ↓ inhalation depth
  - ↓ cp2AMh
  - ↑ motivation to quit
  - ↑ AM latency(TTFC, “forgetting to smoke”)

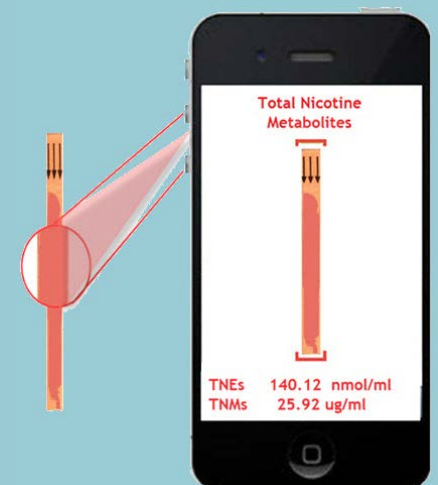


As one example, even with smokers with no desire to quit or reduce their smoking, nicotine replacement therapy suppressed nicotine intake from cigarettes in a dose dependent manner up to as much as 40%. Cigarettes, nicotine intake and carbon monoxide decreased by 26.3%, 36%, and 28%, respectively.



**Until recently nicotine and related metabolite assays were expensive, inconvenient and time-consuming rendering point of care testing (POCT) impractical.**

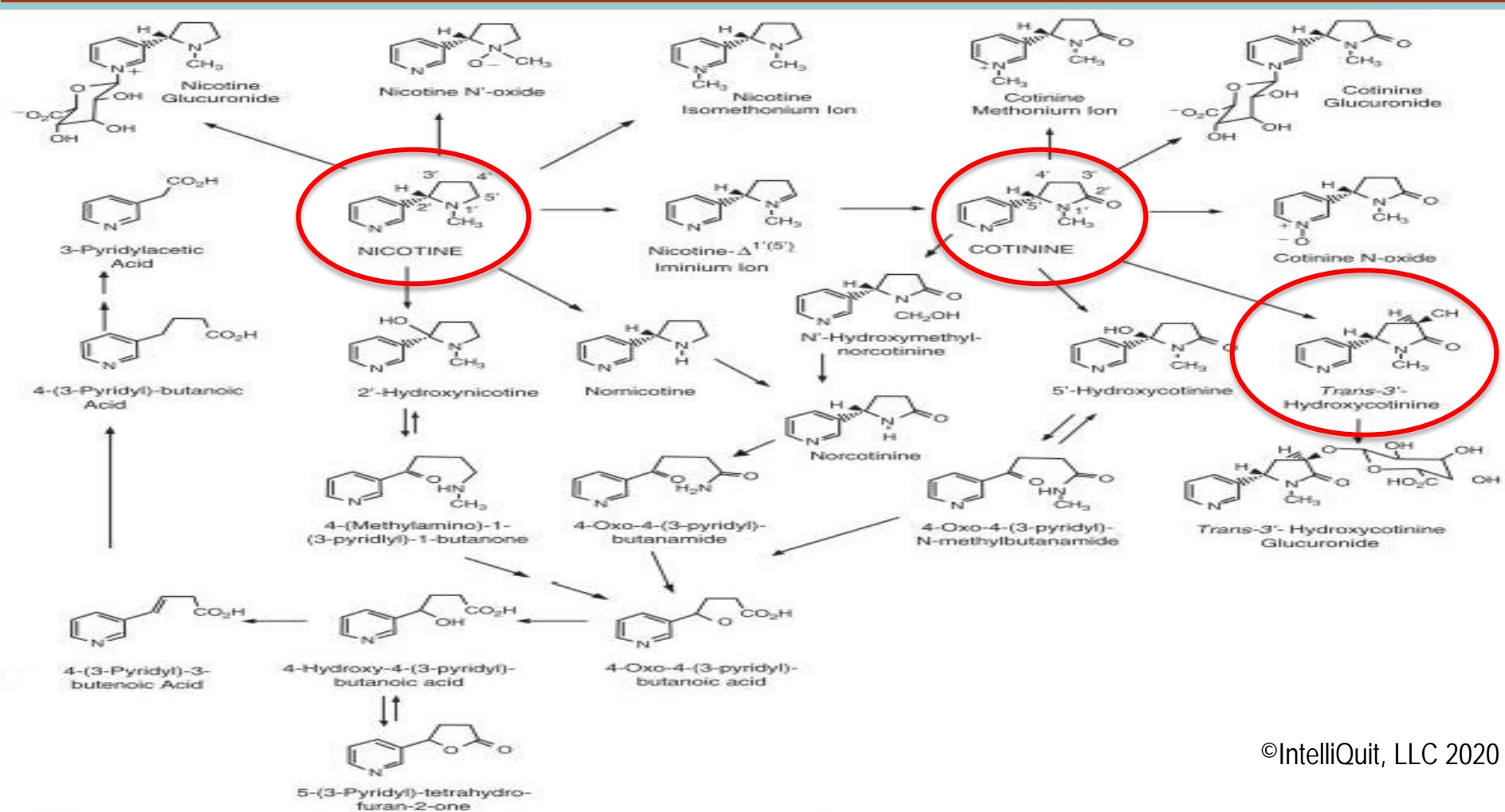
**These barriers have been overcome with the IntelliQuit mobile app.**





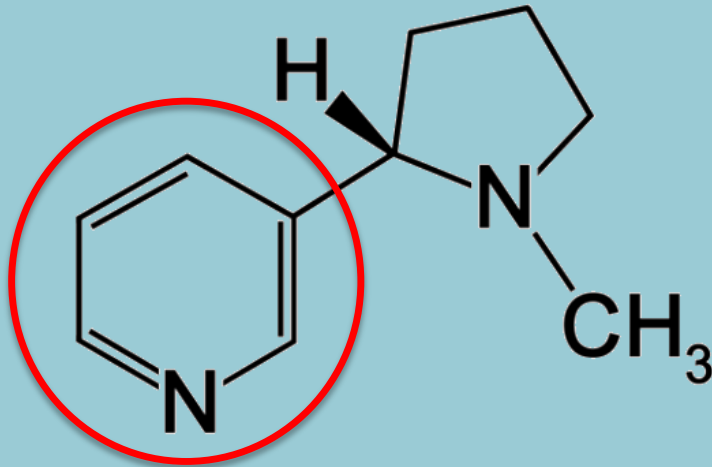


# Nicotine Metabolism



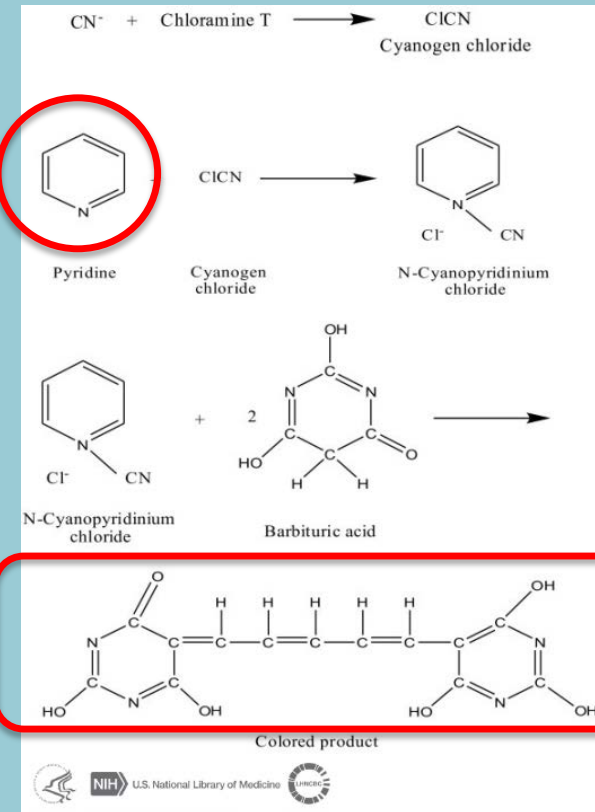


# Nicotine & metabolite chemistry & the Konig reaction



Nicotine and all metabolites have the ubiquitous pyridine ring

**Konig reaction**  
**Reddish-pink color**

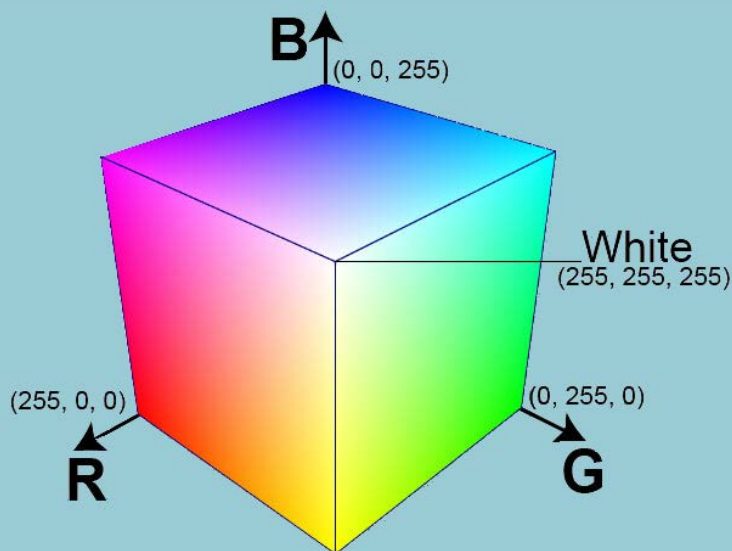


Hukkanen J, Jacob P, Benowitz NL. Metabolism and Disposition Kinetics of Nicotine  
 Pharmacological Reviews March 2005, 57 (1) 79-115; DOI: <https://doi.org/10.1124/pr.57.1.3>

[https://openi.nlm.nih.gov/detailedresult.php?img=PMC3475106\\_1476-511X-11-74-4&req=4](https://openi.nlm.nih.gov/detailedresult.php?img=PMC3475106_1476-511X-11-74-4&req=4)



**Increased pyridine deepens reddish-pink colors**  
**Red-Green-Blue color mapping generates ~17 million colors**



**Computer vision (CV)**  
**enables high-level**  
**understanding from digital**  
**images and**  
**the precise color mapping**  
**of the Konig reaction**



## BioStrip test system



**FDA cleared, CLIA waived**

**All sources of nicotine contribute to the resulting König colormap- Combustible tobacco, Juul, e-cigs, HNB, NRTs, smokeless tobacco**





**Neural networks are a set of algorithms, modeled after the human brain, that are designed to recognize clusters of data and data patterns.**

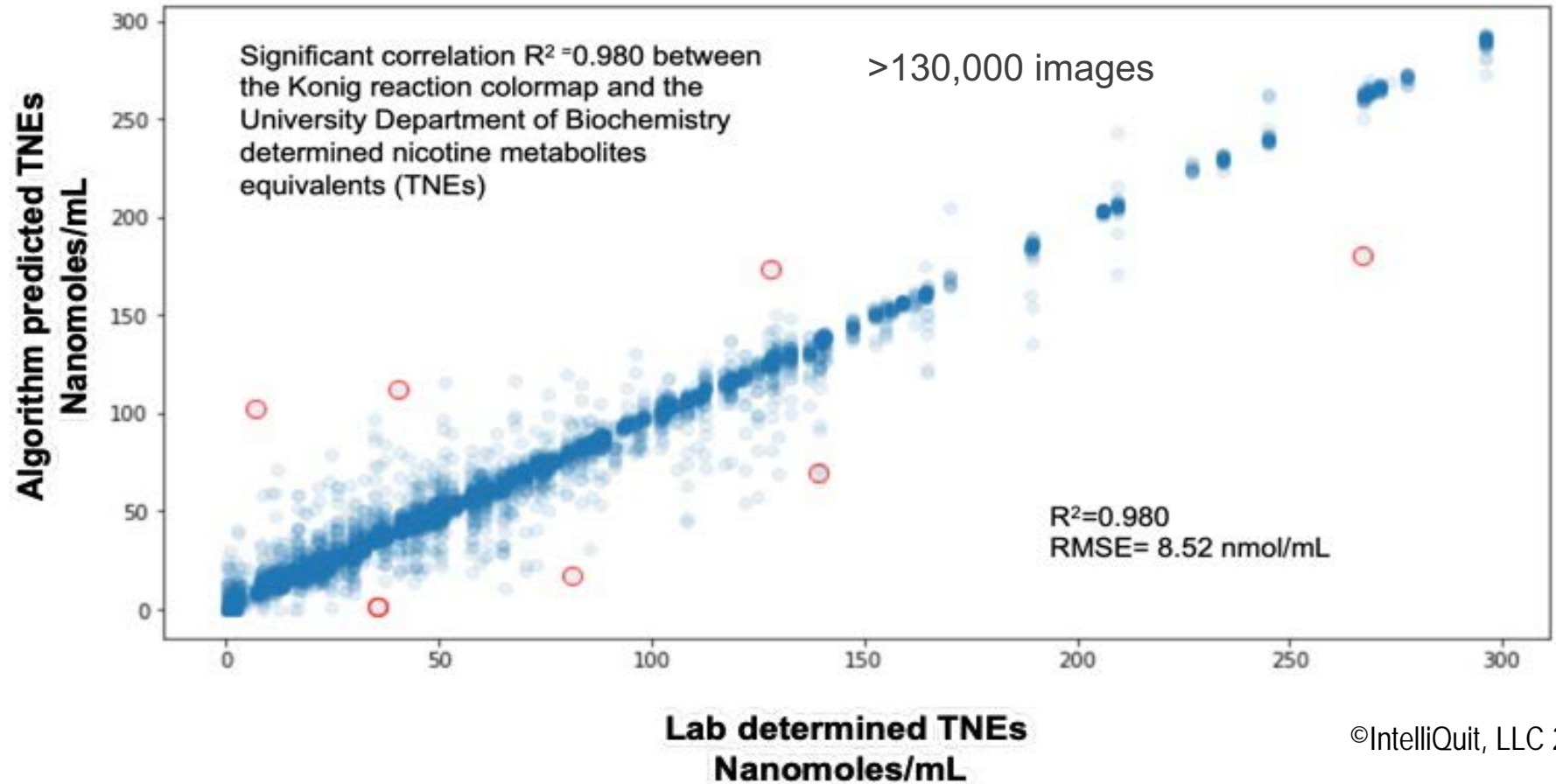
**CV color mapping and neural network architecture define a significant quantitative relationship between the University Department of Biochemistry reference laboratory nicotine metabolite assays and the Konig reaction color.**

**IntelliQuit mobile app algorithm >1000 data clusters**





**Model 2020-10**





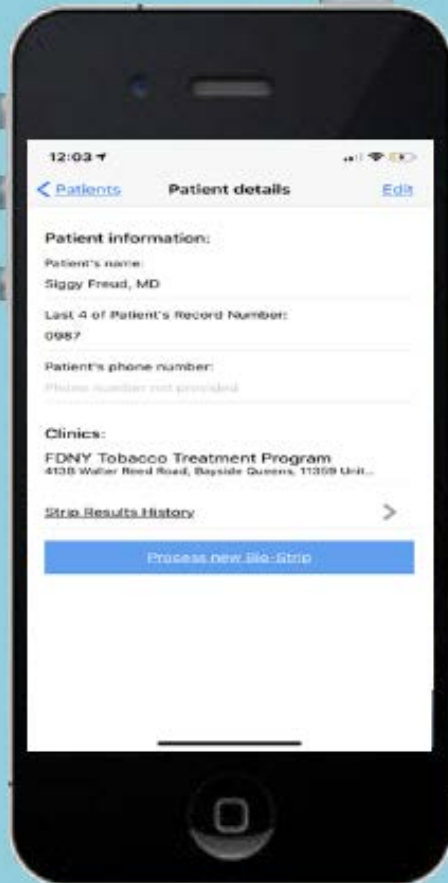
## FDA Cleared & CLIA waived



Computer vision and neural network architecture enables precise quantification of nicotine metabolites @ point of care (POC) within 15 minutes

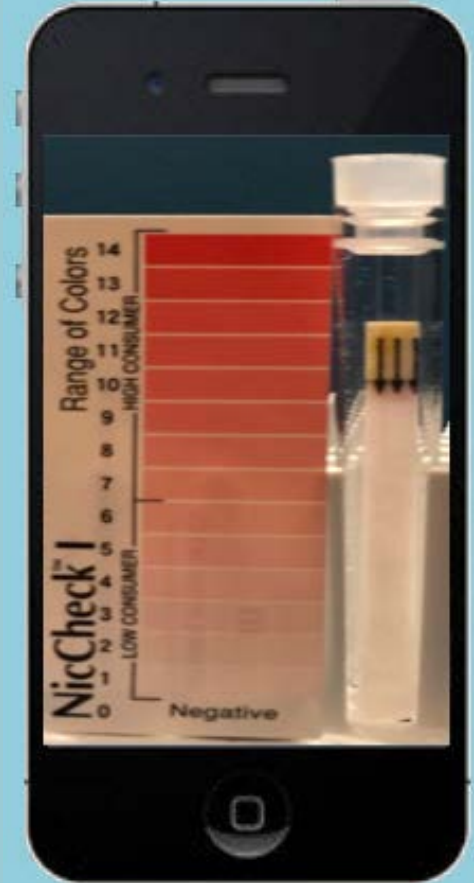


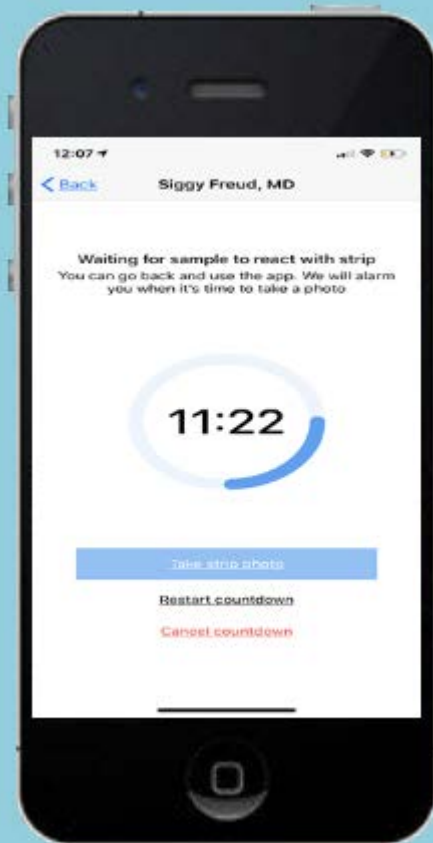
## Simple POCT procedure



Deposit 0.5 - 1.0 ml  
unprocessed urine in  
13 x 100 mm test tube  
oriented to the right in  
peg rack with color chart  
oriented to the left

**Add Biostrip**





**Timer-based functionality prompts user to auto-capture image when bio-strip reaction is complete**







## Telehealth functionality increases clinical utility



**Personal remote patient monitoring (RPM) test tube rack and single-use nicotine biostrips**

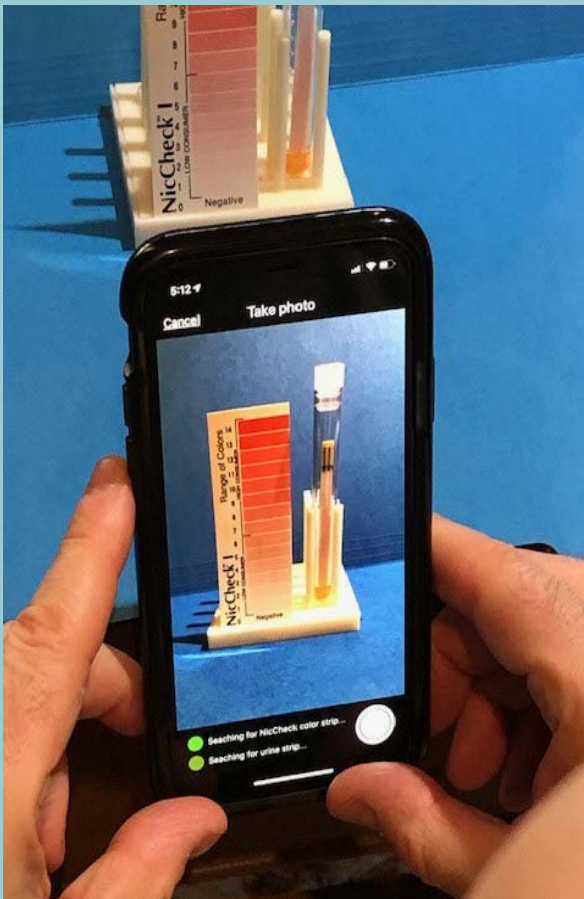
- ✓ **Lightweight**
- ✓ **Mailable**





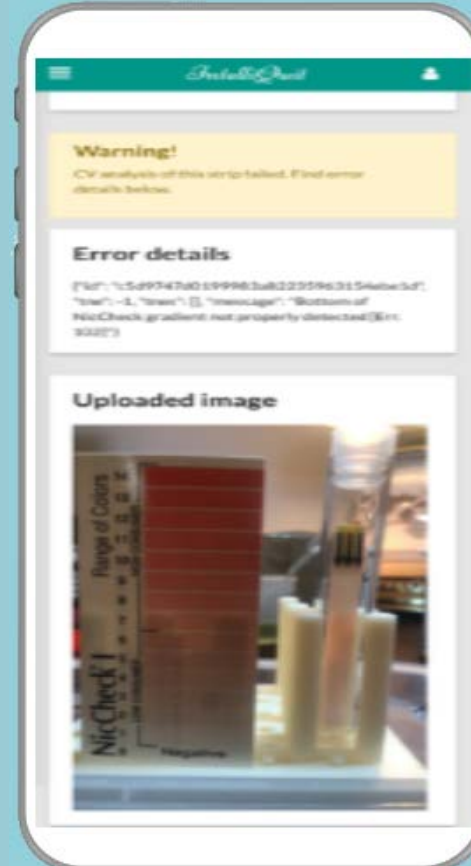
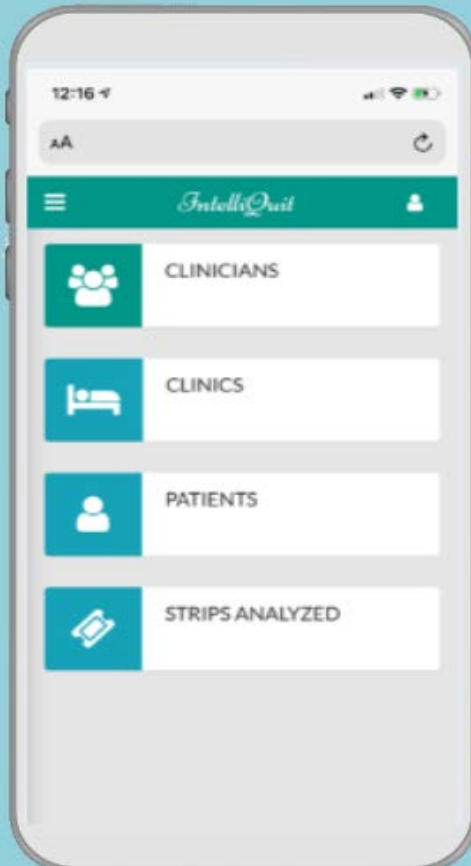
## Take strip photo

Two indicator lights turn **Green** when the orientation is correct. In the correct orientation ( Range of Color chart to the left & test tube to the right) photo can be captured either automatically or manually by pressing the camera button.





## Back office support





## In summary:

- All tobacco users can be treated regardless of readiness (unwilling or unable)
- POCT (in-office & RPM) biochemical quantification of tobacco consumption to titrate tx  
and
- Individualized titrated use cases using all 7 FDA approved medications  
will

Dramatically bend the curve towards reduced individual morbidity and mortality and improved population health.





# Freedom from tobacco - Yearning to breath free

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