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

©IntelliQuit, LLC 2020
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

- Pre 9/11/01: 27.4%
- 11-Sep-2008: 23.2%
- 2018: 7.4%

FDNY

- Pre 9/11/01: 16.8%
- 11-Sep-2008: 12.8%
- 2018: 4%

NYS Pop.

Source:
- Lung Function in Rescue Workers at the World Trade Center after 7 Years N Engl J Med 2010; 362:1263-1272
- www.health.state.ny.us/nysdoh/tobacco/reports/brfss2001.htm

©IntelliQuit, LLC 2020
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 ≥ Δ300%

Tremendous bioavailable variability

Compensatory smoking
When is a light cigarette NOT a light cigarette?

Covering ventilation holes reduces air flow
And increases nicotine delivery

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

- CVS Health Nicotine Gum
- NicoDerm CO Clear Patch Extended Release
- Walgreens Nicotine Mini Lozenge
- Nicotrol Inhaler
- Nicotrol NS (nicotine nasal spray)
- ZYBAN
- CHANTIX (varenicline tablets)
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.


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.

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

Varenicline preloading leads to decreased tobacco consumption

Reductions at 3 wks post intake

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.


Cotinine assays guide successful treatment
Increasing nicotine replacement increases treatment success

Earlier studies found only 33% of abstinent smokers on a 22mg TNP had ≥ 100% Nicotine Replacement

Cotinine assays guide successful treatment
Bupropion helps smokers cut down biochemically before quitting

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


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.


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 Δ consumption via Δ TNEs, Δ EtCO, Δ CPD secondary to treatment plans
- Medication(s) specifics
- ΔTWS & Δ 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 rending point of care testing (POCT) impractical.

These barriers have been overcome with the IntelliQuit mobile app.
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


©IntelliQuit, LLC 2020
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 Konig 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

Significant correlation $R^2 = 0.980$ between the Konig reaction colormap and the University Department of Biochemistry determined nicotine metabolites equivalents (TNEs).

Algorithm predicted TNEs
Nanomoles/mL

Lab determined TNEs
Nanomoles/mL

$R^2 = 0.980$
RMSE = 8.52 nmol/mL

>130,000 images

©IntelliQuit, LLC 2020
FDA Cleared & CLIA waived

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

Matthew Bars, MS, CTTS, NCTTP
(m) 201-960-9906
Tollfree 800-45-SMOKE
matt@IntelliQuit.org