High exposure to nicotine among adolescents who use Juul and other vape pod systems (‘pods’)

INTRODUCTION
Although e-cigarette use among US youth decreased in 2016 for the first time since 2011,12 with the introduction of the new generation of nicotine vapourisers, ‘pods,’ this trend may not continue. Pods are compact, lightweight, ultraportable and easy to use inconspicuously. Popularity of these devices has increased in the past year, most notably, one brand, Juul. Use of Juul and similar products (‘Juuling’) among youth has parents, teachers and the lay public appropriately concerned. However, to date, there are no data on nicotine exposure among youth who use pod systems.

METHODS
Survey
To characterise the use of pods among adolescents, we surveyed patients 12–21 years seen at three Stony Brook Children’s Hospital outpatient clinics (Long Island, New York) from April 2017 to April 2018. All participants/parents provided written consent. Participants completed a 60-item anonymous questionnaire about personal use of e-cigarettes, including specific product types and brands, and provided a spot urine sample.

Product analysis
Using previously described analytical methods,3 we measured total nicotine concentration in pod products, purchased online, that were popular among our participants. We also measured total nicotine yields in aerosols generated from these products using a smoking machine and standardised laboratory puffing protocol (70mL puff volume, 2s puff duration and puff intervals of 10s).3 We used gas chromatography-mass spectroscopy to identify type of nicotine salt used in pod products.4

RESULTS
Survey results
A total of 506 patients were consented for the study, and all completed administered questionnaires. Based on product brand names reported by study participants, we estimated that, among 506 surveyed, 7.9% (n=38) reported current daily or some day use of pods. The most popular brands of pod systems used by our patients in the past 30 days were Juul (79.7% of pod users), Bo (36.4%), Phix (18.2%) and Sourin (12.1%)(multiple answers allowed). Preferred flavours in our participants were menthol/mint (24.2%), fruit (21.2%) and candy, desserts or other sweets (18.2%).

Biomarker analysis
We estimated nicotine exposure in our participants who reported exclusive use of pods (ie, no combusted tobacco use) by measuring cotinine, a major metabolite of nicotine in collected urine samples.5 Non-smoking status reported by our participants was verified by measuring urinary levels of tobacco-specific biomarker 4-(methylamino)no-1-(3-pyridyl)-1-butanol (NNAL).5 Due to urine cotinine’s short elimination half-life, we restricted analysis to 22 subjects who used pods within 7 days prior to the clinic visit. Of the 22 participants included in the urine analysis, average age was 16.8±1.8 (mean±SD; range 13–21 years).

RESULTS of product testing
All tested products contained high nicotine concentrations, from 21.8 mg/mL to 56.2 mg/mL in a form of salt with benzoic acid (nicotine benzoate) or levulinic acid (nicotine levulinate) dissolved in a mixture of propylene glycol and vegetable glycerin (Table 1). We estimated that users of prefilled pod systems (Juul, Bo and Phix) may inhale with 10 puffs from 0.77 to 0.85 mg of nicotine (Table 1), considerably higher than previously reported in older generations of e-cigarettes (0.02–0.51 mg/10 puffs).3

Biomarker data
The median urinary cotinine concentration measured in our participants who used pods was 244.8 ng/mL (IQR 8.4–1255.8), higher than 155.2 ng/mL (IQR: 68.8–579.2) reported by Benowitz et al in 55 adolescents (ages 13–19 years) who regularly smoked conventional tobacco cigarettes.6 All analysed samples had either undetectable or very low levels of the urinary tobacco-specific biomarker, NNAL, confirming lack of exposure to tobacco smoke.

DISCUSSION
Product testing results and participants’ high urinary cotinine levels provide physiologic evidence for significant nicotine exposure among pod users. Indeed, such high cotinine levels raise concerns about the potential for earlier and more significant nicotine addiction in teens. Although the exact physiological mechanisms of nicotine salts are not well studied, these compounds are believed to increase the amount and rate of nicotine uptake in e-cigarette users.7 Potential health risks of repeated inhalation of high doses of nicotine salts are unknown.

Study limitations include small sample size and a convenience sample of adolescents presenting to clinics in suburban Long Island, New York. These findings are not representative of the entire population of US adolescents and may not be generalisable to other e-cigarette user groups. Additionally, survey response to self-reported pod use in the past 7 days may introduce recall bias.

Table 1 Nicotine levels in the pod products and urine cotinine concentrations detected in 22 surveyed patients (aged 13–21 years) who reported pods use within 7 days prior to the clinic visit

<table>
<thead>
<tr>
<th>Brand name of pod system</th>
<th>Number of patients who reported using the pod product (single brand/in combination with other pod products)</th>
<th>Nicotine concentration in a pod (mg/mL)</th>
<th>Nicotine yields in 10 puffs (mg)</th>
<th>Type of nicotine salt</th>
<th>Median urinary cotinine concentration in exclusive users (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juul</td>
<td>10/6</td>
<td>56.2</td>
<td>0.83</td>
<td>Benzoate</td>
<td>135.1</td>
</tr>
<tr>
<td>Bo</td>
<td>3/6</td>
<td>37.9</td>
<td>0.85</td>
<td>Levulinate</td>
<td>508.4</td>
</tr>
<tr>
<td>Phix</td>
<td>2/3</td>
<td>48.0</td>
<td>0.77</td>
<td>Benzoate</td>
<td>906.4</td>
</tr>
<tr>
<td>Sourin (refilled with BlowSauce e-liquid)</td>
<td>0/2</td>
<td>21.8</td>
<td>0.26</td>
<td>Benzoate</td>
<td>N/A*</td>
</tr>
</tbody>
</table>

* All users of Sourin brand reported using multiple products.
Clinicians must be aware of and educate their patients about the potential for long-term sequelae of using e-cigarettes, especially pods. Public health advocates and regulatory agencies must act now to restrict youth access to e-cigarettes before decades of progress in tobacco control is undone. On 24 April 2018, Food and Drug Administration announced several enforcement actions as part of a new Youth Tobacco Prevention Plan to stop youth use of and access to Juul and other e-cigarettes. Additionally, raising the legal age to 21 years (“Tobacco 21”) to purchase tobacco products has gained traction as an evidenced-based measure to prevent teen access to all tobacco products, including e-cigarettes.

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Acknowledgements The authors would like to thank Liam-Gavin Dell, Noel Leigh, Mary Palumbo and Taylor Vanderbush from Roswell Park Comprehensive Cancer Center for assistance with product and biomarker testing.

Contributors RB and MLG conceptualised and designed the study, drafted the initial manuscript and reviewed and revised the manuscript. CRM, AE and JT collected data, carried out the initial analyses and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding This study was funded by an Intramural Research Grant Award to RB from Department of Pediatrics, Stony Brook University School of Medicine and Stony Brook Children’s Hospital, New York. Laboratory testing of nicotine products was supported by NIH grant NCI P30CA16056.

Disclaimer The policy implications written in this manuscript are the views of the authors and do not necessarily represent the views of the other members of the Committee, the NASEM or the FDA.

Competing interests MLG has received fees for serving on an advisory board to Johnson & Johnson and research grant support from Pfizer. MLG was a member of the National Academies of Science, Engineering and Medicine (NASEM) Committee on the Review of the Health Effects of Electronic Nicotine Delivery Systems and contributed to the writing of the NASEM report.

Patient consent Not required.

Ethics approval The study was approved by Stony Brook University IRB.

Provenance and peer review Not commissioned; externally peer reviewed.

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Received 13 June 2018
Revised 13 August 2018
Accepted 14 August 2018
Published Online First 7 September 2018

doi:10.1136/tobaccocontrol-2018-054565

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