Camden and Islington NHS
NHS Foundation Trust

NEW MEDICINE REVIEW

Meeting:	**Drugs and Therapeutics Group**
Date:	**6th November 2014**

Title: **Unlicenced electronic nicotine delivery systems "e-cigarettes".**

Summary:

The Trust currently has no policy on the use of electronic-cigarettes (e-cigarettes), though staff and service users are currently using them. This paper should be read in conjunction with the evidence presented in the systematic review conducted by Hajek et al. (2014), the Public Health England report on e-cigarettes (Britton, 2014), and the actions required in Department of Health (DH) Alerts EFA/2014/002 and DH/2014/002.

Preliminary action advising of restrictions on charging electronic-cigarettes were issued to all staff on 9th September 2014, and preliminary actions against DH/2014/002 were completed by 29th September 2014

This paper describes the options available to the Trust, and makes a recommendation for the preferred option. This paper does not propose for the Trust to recommend the use of e-cigarettes as a smoking cessation aid, but to consider the evidence base, which suggests that fully prohibiting their use would be disproportionate to their risks, and would introduce additional risks and dis-benefits.

Action required:

The group is requested to:

- Review the risks associated with e-cigarettes in comparison with the risks associated with prohibiting e-cigarette use
- Review the policy options available and agree a position
- Agree the actions detailed in the summary below
- Note the risk implications of not undertaking this decision

The Drugs and Therapeutics Group is asked to consider the best available evidence re: safety, and not to seek to prohibit service users to using self-purchased e-cigarettes on Trust premises.

Report from: Simon Bristow – Matron for Smoking Cessation

Compliance with statute, directions, policy, guidance	**Reference:**
Lead: Lucy Reeves, Chief Pharmacist.	

Unlicenced electronic nicotine delivery systems - "e-cigarettes"	
Compliance with Care Quality Commission Regulations / Outcomes Lead: Lucy Reeves, Chief Pharmacist.	**Reference:**

Product details

Un-licenced electronic nicotine delivery systems - "e-cigarettes"

National guidelines on e-cigarettes

In the recent Public Health England Report on e-cigarettes Britton (2014) states

"The option of switching to electronic cigarettes as an alternative and much safer source of nicotine, as a personal lifestyle choice rather than medical service, has enormous potential to reach smokers currently refractory to existing approaches. The emergence of electronic cigarettes and the likely arrival of more effective nicotine-containing devices currently in development provides a radical alternative to tobacco, and evidence to date suggests that smokers are willing to use these products in substantial numbers.

Electronic cigarettes, and other nicotine devices, therefore offer vast potential health benefits, but maximising those benefits while minimising harms and risks to society requires appropriate regulation, careful monitoring, and risk management. However the opportunity to harness this potential into public health policy, complementing existing comprehensive tobacco control policies, should not be missed."

NICE guidelines (2013) PH48 'Smoking cessation in secondary care: acute, maternity and mental health services' state:

"Although unlicensed and of variable quality, safety and effectiveness, these products are expected to be less harmful than smoking. Therefore whilst not actively endorsing the use of unlicensed products, the PDG recognised that some people may find these helpful, either alone or in combination with licensed nicotine-containing products, to support abstinence from smoking."

The Royal Pharmaceutical Society published a position statement regarding the use of e-cigarettes in February 2014.

It states:

- As of yet there have been limited rigorous peer reviewed studies to support their use as safe and effective NRT products. E-cigarettes are currently unlicensed products with no standardisation of safety, quality or efficacy. As such, they should not be sold or advertised from pharmacies.
- We support the original June 2013 intention of The Medicines and Healthcare products Regulatory Agency to regulate e-cigarettes as medicinal products as an aid to smoking cessation only. The licensing process would align e-cigarettes with other NRT products and assure the public and patients of their safety and efficacy.
- If an NRT product is considered the best option for a person attempting to quit or reduce their smoking then pharmacists should encourage the use of licensed NRT products.

Licensed Indications:

In 2013, after a consultation process that began in 2010, the UK MHRA announced that from 2016, it intended to regulate electronic cigarettes and other nicotine-containing products as medicines by function, and thus require manufacture to medicinal purity and delivery standards, and proactive controls on advertising.

Proposed indication under review

N/A

Introduction

Electronic cigarettes are devices that deliver nicotine by heating and vapourising a solution that typically contains nicotine, propylene glycol and/or glycerol, and flavourings

Current treatment options

The following medicines are included in the Trust formulary:

- Nicotine Transdermal Patches
- Nicotine Inhalation Cartridge for Oromucosal use
- Nicotine Lozenge
- Nicotine Nasal Spray
- Nicotine Oral Spray

Service users are also currently using highly harmful, unlicenced nicotine delivery systems in the form of smoked tobacco.

Efficacy Data

Due to the lack of medicinal regulation around e-cigarettes and their relatively recent development, there is a lack of large RCT studies, which would be regarded as providing 'conclusive' evidence of their efficacy as a smoking cessation tool. The best available evidence therefore comes from studies of moderate academic strength such as small RCT's, cohort studies and survey data.

However, it should be noted that the Public Health England Report on e-cigarettes Britton (2014) states:

"There is questionable value in clinical trials of these products relative to NRT or placebo, if they are shown to deliver nicotine. There is a mass of evidence demonstrating that products that deliver nicotine help people stop smoking, which is why the MHRA, in its proposal for medicines licensing, does not require trial information. Requiring suppliers to demonstrate nicotine delivery and uptake will therefore obviate the need for placebo-controlled trials."

This report also states that one of the key research priorities should be methods of integrating electronic cigarette or other nicotine devices into health services, in general and particularly in mental health settings, where conventional approaches have failed.

The best available evidence suggests that e-cigarettes are likely to be as effective as a smoking cessation aid as other forms of nicotine delivery (Bullen et al., 2010) (Bullen et al., 2013) (Dawkins et al., 2013), and are more effective for achieving smoking cessation in people not intending to quit (Polosa et al., 2011) (Polosa et al., 2014) (CaponnettoCampagna et al., 2013). This is likely linked to their replication of the sensorimotor aspects of smoking, which can be valued over the delivery of nicotine in dependent persons (Rose et al., 2010)

Their success and popularity has not excluded mental health service users. Anecdotally, every service user group met during the engagement process of the better nicotine management project has had representatives who have successfully used or are currently using e-cigarettes as a smoking cessation aid. Permitting their use has been strongly advocated for by all service users groups, and also by staff during the recent 'staff views on smoking and smokefree services survey'. A recent observational study over one year found that e-cigarettes use by smokers with schizophrenia had a quit rate of 14% which is comparable with the outcomes

from our specialist Assertive Smoking Cessation Outreach Team (CaponnettoAuditore et al., 2013) who have a quit rate of 16%.

Best evidence suggests approximately 60% of smokers with mental health problems want to quit (Siru et al., 2009). Therefore, 40% of smokers who do not wish to quit will be required to abstain while using our services. This group are arguably most likely to benefit from the use of an acceptable alternative to smoking, and identification of a device which can replicate and replace the experience of smoking in an acceptable way would deliver health benefits and increase quit rates for this group.

Safety

Nicotine does not cause serious adverse health effects such as acute cardiac events, coronary heart disease or cerebrovascular disease, and is not carcinogenic. The doses of nicotine delivered by electronic cigarettes are therefore extremely unlikely to cause significant short or long-term adverse events. (Britton, 2014)

Nicotine Replacement Therapy is a safe and effective treatment for the management of nicotine dependence, and overdose is rare in nicotine dependent patients (Cahill et al., 2013), there is little reason to consider e-cigarettes will be much different.

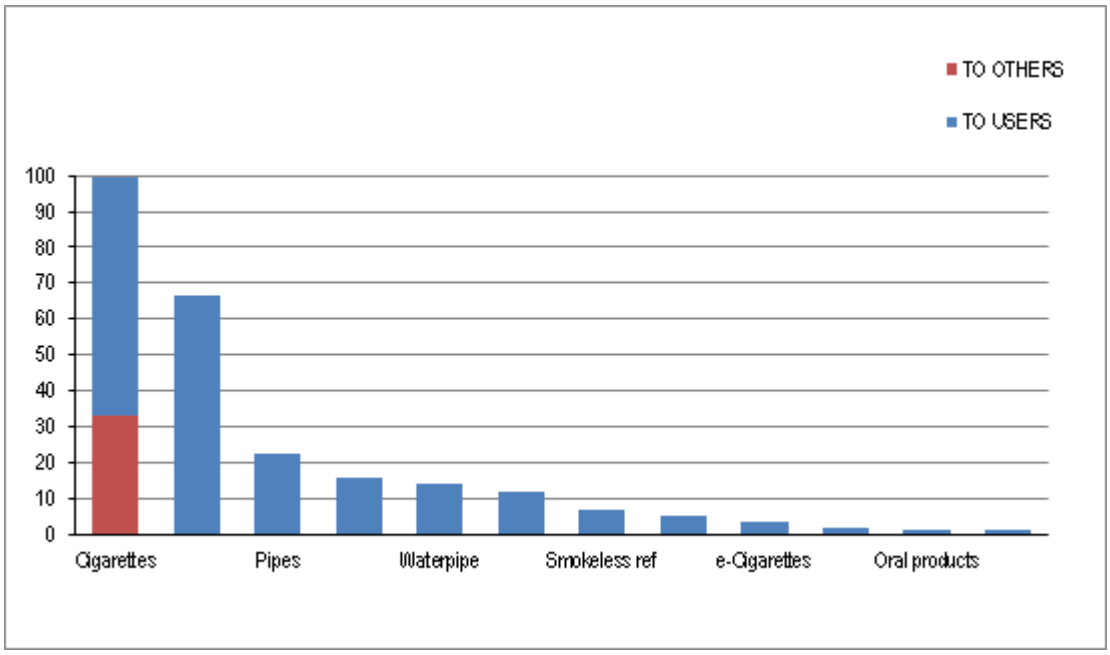
Recent systematic review of the contents of e-cigarettes aerosol by (Burstyn, 2014) concluded that:

"Current state of knowledge about chemistry of liquids and aerosols associated with electronic cigarettes indicates that there is no evidence that vaping produces inhalable exposures to contaminants of the aerosol that would warrant health concerns by the standards that are used to ensure safety of workplaces. However, the aerosol generated during vaping as a whole (contaminants plus declared ingredients) creates personal exposures that would justify surveillance of health among exposed persons in conjunction with investigation of means to keep any adverse health effects as low as reasonably achievable. Exposures of bystanders are likely to be orders of magnitude less, and thus pose no apparent concern."

Other reviews have also found no evidence of risk associated with exposure to passive vapour (Hajek et al.), with (Callahan-Lyon, 2014) finding exhaled airborne contaminants to be equal with licenced nicotine inhalers.

There have been no SAEs reported in any clinical trials of e-cigarettes (Gualano et al., 2014) AE's include dry mouth, cough and shortness of breath.

Nutt et al. (2014) ranks their level of harm to users as significantly lower than all forms of tobacco use.



There is a chance there may be subtle, currently unforeseen long term health risks with e-cigarette use, however as 50% of lifetime smokers die of a disease caused by smoking (Doll et al., 2004), on balance the risks are likely to be a fraction of conventional cigarettes, and therefore smokers will see health benefits from switching (Farsalinos et al., 2014).

Therefore to decline access to e-cigarettes pending long term effect studies of 10-20+ years would potentially deny access to health benefits from the use of e-cigarettes as a harm minimisation tool. Current e-cigarette users would also be denied access to their preferred form of nicotine dependence management.

1. **Charging and fires**

DH Alert EFA/2014/002 states:

'A number of incidents have been reported across the UK involving rechargeable e-cigarettes that have exploded or ignited to cause a fire during the charging process. A number of different brands of e-cigarette have been implicated within these incidents.
Incidents have occurred in both premises and vehicles. Recharging modes included connection to a computer USB port, car cigarette lighter/accessory socket, and connection to a mains recharger.

It is possible some rechargeable devices do not have adequate over-charge safeguards. Some e-cigarettes may incorporate a high level of over-charge protection using fuses or intrinsically safe batteries for example. However, it is difficult to readily identify or distinguish these products from those with less protection or possibly no over-charge protection.'

Similar risks may also occur with the use of non-standard mobile phone chargers and/or batteries. Risk management protocols to mitigate fire and ligature risks associated with mobile phone charging involves nursing staff retaining charging apparatus and charging devices on patients behalf in the nursing station. This could be a possible mechanism to mitigate the risk associated with e-cigarettes.

e-cigarettes and e-cigarette chargers must not be used in oxygen rich environments in line with DH alert EFA/2014/002. A briefing has been circulated to all staff, and this should be reflected in the revised policy.

Overdose:

Cigarettes offer greater yields of nicotine to users than e-cigarettes and NRT. The risk of accidental nicotine overdose is low even with multiple forms of administration, ie: 'dual use'. Nicotine consumption tends to be self-limiting even in heavily dependent smokers due to nausea/vomiting induced by low levels of overdose, and the short half-life of nicotine in the body.

The minimum lethal dose of nicotine in a non-tolerant man has long been reported to be 40 to 60mg. However recent review of the evidence have traced this assertion back to Victorian-era self experiments of little scientific validity (Mayer, 2014), and that all evidence indicates at least 500mg of oral nicotine would be required to kill an adult.

Nicotine liquid could theoretically be used as a tool for self-harm, however the review by Hajek et al. (2014) notes cases of the consumption of high doses (1500mg) in a self-harm attempt causing vomiting and no lasting adverse effects.

Instructions for extracting nicotine from tobacco using water and has been used in successful, and unsuccessful suicide attempts in the general population (Schneider et al., 2010) (Corkery et al., 2010)

Symptoms of overdose are those of acute nicotine poisoning and include nausea, vomiting, increased salivation, abdominal pain, diarrhoea, sweating, headache, dizziness, disturbed hearing and marked weakness. At high doses, these symptoms may be followed by hypotension, rapid or weak or irregular pulse, breathing difficulties, prostration, circulatory collapse and general convulsions.

Management of an overdose: All nicotine intake should stop immediately and the patient should be treated symptomatically. Artificial respiration should be instituted if necessary. Activated charcoal reduces the gastro-intestinal absorption of nicotine.

Vehicles for other substances:
Liquid refillable devices can and have been used as vehicles for consumption of illicit substances or 'legal highs'. Refillable cartridge type, and disposable type do not have this risk.

Risks of discouraging/preventing e-cigarette use

Prohibiting e-cigarette use in inpatient units would extremely difficult to police. The vapour is odourless and colourless, and therefore service users using them in their bedrooms would be almost impossible to detect. This would undermine efforts to enforce a ban, and would potentially lead to concealed charger units and increased risk of fires.

1. **Policy breaches and relapse to smoking**

Prohibiting the use of e-cigarettes may encourage relapse to smoking, and policy compliance breaches by nicotine dependent service users. For example, the revised smoking policy will need to place cigarettes on the list of prohibited items on inpatient units. If a service user who is dissatisfied with the sensorimotor aspects of receiving nicotine by NRT leaves the ward, they may purchase a packet of cigarettes and attempt to smuggle the remaining cigarettes into the unit.

2. **Illicit smoking, secondhand smoke exposure and fires**

Illicit smoking poses a health and safety risk, and the Trust suffered 13 fires related to smoking in bedroom in 2013-2014. Acceptable replication of the smoking experience through e-cigarettes may reduce these events in this sub-population of smokers.

Illicit smoking from heavily dependent inpatients will increase the risk of future legal action from staff or service users exposed to secondhand smoke (Zellers et al., 2007). Legal firms, including the firm representing

UNISON members, currently offer to pursue negligence/industrial injury cases on behalf of individuals who fall ill as a result of exposure to second-hand smoke at work.

Pharmacodynamics:

Newer, 2nd generation devices are much more efficient than first-generation devices, however still not as efficient as cigarettes. It is not yet clear whether electronic cigarettes produce vapour that is sufficiently fine to reach the alveoli, but available pharmacokinetic data suggests that absorption is primarily from the upper airway, that is, slower than a cigarette, and achieving systemic venous blood levels of similar order of magnitude to a conventional NRT inhalator. (Farsalinos et al., 2014)

Interactions:

Tobacco smoke speeds up the metabolism of some antipsychotic medications, as well as some antidepressants and benzodiazepines, by inducing certain liver enzymes (CYP450 1A2 isoenzyme). This effect is not caused by nicotine but is secondary to the polycyclic aromatic hydrocarbons from the tar in tobacco smoke.

A consequence of speeding up the metabolism of some medicines, is that smokers need higher doses of some psychotropic medicines compared to non-smokers. Blood levels of medication will be affected by many things such as age, gender and how well they adhere to their prescribed treatment. Stopping smoking can result in an increase in blood levels of some medicines; these are likely to increase within seven days of quitting. Because this could potentially lead to toxicity, doses of affected psychotropic medicines may need to be reduced by 25–50% once someone stops smoking.

Blood levels, clinical symptoms and any changes in the frequency and severity of side effects all need to be closely monitored when cigarette consumption is reduced or stopped, but also for a few weeks after patients are discharged, as they may start smoking again. Blood levels of clozapine may still be altered for up to six months after stopping smoking.

Currently there are no published guidelines about the effect of cutting down the amount of cigarettes smoked on the metabolism of psychotropic medication, therefore it may be wise to be led by symptoms and side effects and still take plasma levels, particularly for clozapine.

(NCSCT, 2014)

Contraindications

N/A

Cautions

Any risks that may be associated with e-cigarettes are substantially outweighed by the well-established dangers of continued smoking.

- *Transferred dependence:* e-cigarette use appears to decrease over time, suggesting limitation to any transfer dependence (Lechner et al., 2014). Transferred dependence is less harmful than smoking dependence.
- *Stopping smoking:* Polycyclic aromatic hydrocarbons in tobacco smoke induce the metabolism of drugs metabolised by CYP 1A2 (and possibly by CYP 1A1). When a smoker stops smoking, this may result in slower metabolism and a consequent rise in blood levels of such drugs. This is of potential clinical importance for products with a narrow therapeutic window, e.g. theophylline, clozapine and ropinirole.

Convenience

E-cigarettes are perceived as much more acceptable to users than NRT (Steinberg et al., 2014) and are the preferred option for quit attempts for many people. A survey published by Action on Smoking and Health (ASH, 2014) showed that 2.1 million people in Great Britain are using e-cigarettes and around one third are now ex-smokers. To affect the immediate welfare and long-term health outlook of 700,000 people is an achievement, requiring no NHS resources or public spending. (Britton, 2014)

User acceptability is the greatest strength of e-cigarettes, the benefits of which should not be underestimated. We are on the verge implementing a revolutionary new approach to the management of nicotine dependence, which requires a significant culture shift for staff and service users, who, despite its potential to deliver exponential health benefits to both groups, have expressed active resistance.

At all service user forums attended during the better nicotine management project engagement exercise, service users expressed a desire to have e-cigarette use permitted on inpatient units, as an alternative to smoking for service users who do not wish to quit. At almost every group there was at least one representative who cited their experience of quitting solely using e-cigarettes, and expressed concern that prohibition of their use in Trust sites would result in users who have previously quit smoking having their preferred, safer method of consuming nicotine withdrawn. Allowing the use of a highly acceptable form of nicotine delivery to the sub-population of service users who do not wish to quit could play a valuable role in a successful implementation strategy, as acceptable replacement for smoking will promote good service user experience of the policy, and would therefore give less motivation to attempt to illicitly procure and consume cigarettes. To prevent access to them would potentially increase patient safety incidents and risk to staff posed by illicit smoking.

Cost-effectiveness

N/A

Summary

The toxicant levels contained in e-cigarettes appear to be sub-clinical significance. No significant adverse effects have been reported in any existing clinical trials, and their relative risk of harm to users is low, and there is no evidence of passive vapour risk. The long term effects of use are unknown, but are likely to be exponentially less harmful than smoking.

Risks in the use of e-cigarettes exist in the form of:

- Fires from chargers
- Ingestion of liquid

Risks in the prohibition of e-cigarettes exist in

- Highly difficult to enforce e-cigarette ban
- Increased illicit smoking – increased risk of fire and secondhand smoke exposure
- Increased relapse to smoking risk for e-cigarette users

Proposed Place in Therapy:

The Trust would continue to recommend evidence based treatments in the form of licenced NRT products to all service users, in line with (NICE, 2013) guidelines and the Royal Pharmaceutical Society Guidelines. However would acknowledge the evidence base, and expressions of patient choice in the method of obtaining nicotine, and would not prohibit the use of e-cigarettes in Trust sites.

Available options

Permit use of e-cigarettes with restrictions.

Current approach of CNWL, Kent and Medway, and Devon Partnership Trust
Permitted for use only in bed areas to eliminate re-normalisation/social triggers to smoke for those attempting quitters
Restricting the type of e-cigarettes permitted to cartridge rather than liquid to mitigate the limited overdose risk
Restricting access to chargers to supervised charging in nursing base only, or restricting use to non-rechargeable e-cigarettes

Permit sale of e-cigarettes
Currently approach used by SLaM and ELFT
Bulk purchase makes them potentially more cost effective than NRT
Restrictions could be applied as described above to manage charging risks

Prohibit e-cigarette use
Current approach of BEH
Eliminates charging risk
Likely to increase relapse to smoking and policy breaches
Likely to damage engagement with service user groups

Should supervised charging e-cigarettes be permitted, the additional actions specified in DH/2014/002 must be followed.

Conclusion & Recommendation

There is a chance there may be subtle, currently unforeseen long term health risks with e-cigarette use, however as 50% of lifetime smokers die of a disease caused by smoking (Doll et al., 2004), on balance the risks are likely to be a fraction of conventional cigarettes, and therefore smokers will see health benefits from switching (Farsalinos et al., 2014).

This paper does not propose for the Trust to recommend the use of e-cigarettes as a smoking cessation aid, but to consider the evidence base, which suggests that fully prohibiting their use would be disproportionate to the risks, and would introduce additional risks and dis-benefits.

NICE (2013) guidelines PH48 state:

“Although unlicensed and of variable quality, safety and effectiveness, these products are expected to be less harmful than smoking. Therefore whilst not actively endorsing the use of unlicensed products, the PDG recognised that some people may find these helpful, either alone or in combination with licensed nicotine-containing products, to support abstinence from smoking.

The Quality Committee has recently adopted the ‘nicotine management strategy 2014-2016’ as a framework for the Trust to implement revised NICE Guidelines (2013) PH48 smoking cessation in secondary care: acute, maternity and mental health services. The evidence of risk to users and others from e-cigarettes is limited, and is significantly lower than continued smoking. Use of e-cigarettes with appropriate safeguards could be a valuable component of a harm minimisation strategy to improve health outcomes for service users.

The recommendation to the group is to permit use of patient purchased e-cigarettes with a restriction to:

- Supervised charging arrangements to eliminate risk from charging
- Cartridge type only to reduce limited risk from consumption of nicotine liquid.
- Restrictions on use in oxygen rich environments

Actions

- Matron for Smoking Cessation to provide an update to interim briefing on the use of e-cigarettes and charging prior to development of the nicotine management policy
- Agreed position to be discussed at other relevant groups/committees and incorporated in to the nicotine management policy

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