**Abstract S79 Table 1**

| NICE recommendation | eCBD responses | | | |
|---|---|---|---|---|
| **Is combination nicotine replacement therapy (NRT) safe and effective?** | | | | |
| **Yes** - *"offer licensed NRT (usually a combination of patches with a fast-acting product…) to all people who smoke"* | **Yes** | **No** | **Don't know** | **Maybe for certain patients** |
| | 37% | 23% | 40% | - |
| **Would you recommend e-cigarettes for smoking cessation?** | | | | |
| **No** - *"Encourage people who are already using…electronic cigarettes to switch to a licensed product"* | 10% | 20% | 23% | 47% |
| **Would you offer NRT to help cut-down on smoking?** | | | | |
| **Yes** - *"Offer all types of licensed NRT to people who smoke, as part of a harm-reduction strategy"* | 77% | 0% | 23% | - |


## REFERENCES

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2 National Institute for Health and Clinical Excellence. *Smoking cessation in secondary care: acute, maternity and mental health services.* PH48. London: NICE, 2013


## S80 GAME ON? THE GAMIFICATION OF MHEALTH APPS IN THE CONTEXT OF SMOKING CESSATION

M Ahmed, Y Sherwani, M Muntasir, A El-Hilly, S Iqbal, S Siddiqui, Z Al-Fagih, O Usmani, A Eisingerich. *Imperial College London, London, UK*

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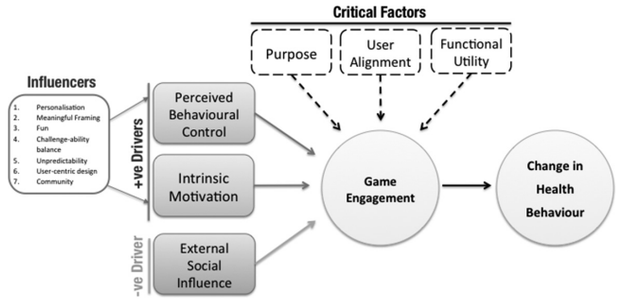
**Introduction and objectives** Increasing emphasis has been placed on behavioural therapy in smoking cessation efforts. mHealth aims to join today's arsenal of smoking cessation techniques. Many apps are utilising 'gamification' (the use of game design elements in non-game contexts) as a tool to drive positive behaviour change. However, a significant knowledge gap currently remains regarding how gamification can affect health behaviour. Our study seeked to elucidate the motivational mechanisms exploited by gamification in promoting positive health behaviours in the context of smoking cessation, with a view to generating recommendations on how to create effective gamified mHealth interventions.

**Methods** We conducted a qualitative longitudinal study using a sample of 16 smokers divided into two cohorts. The first cohort used a non-gamified mHealth intervention, whilst the second used a gamified mHealth intervention. The added game components allowed us to isolate the effects of gamification. Each participant underwent 4 one-on-one, semi-structured interviews over a period of 5 weeks. Interviews were transcribed verbatim after which thematic analysis was undertaken.

**Results** We observed that perceived behavioural control and intrinsic motivation acted as positive drivers to game engagement and consequently positive health behaviour. Importantly, external social influences exerted a negative effect. We identified three critical factors, whose presence was necessary for game engagement; purpose (explicit purpose known by the user), user alignment (congruency of game and user objectives), functional utility (a well-designed game). We summarise these findings in a framework (Figure 1), which we propose to guide the development of gamified mHealth interventions.




**Abstract S80 Figure 1** A framework proposing effective use of gamification to promote positive health behaviour

**Conclusions** Our framework outlines the characteristics critical to consider when developing any gamified mHealth intervention to promote a particular health behaviour. Gamification holds the potential for low-cost, highly effective mHealth solutions that may replace or supplement the behavioural support component found in current smoking cessation programmes. Our proposed framework has been built on evidence specific to smoking cessation, but is versatile and can be extended to health interventions in other disease categories. Future research is now required to evaluate the effectiveness of the above framework directly against current behavioural support therapy interventions in smoking cessation.

## S81 FEASIBILITY AND UPTAKE OF ENHANCED SMOKING CESSATION SERVICES WITHIN AMBULATORY HIV CARE

[1]C Kyriacou, [1]N Stewart, [1]A Melville, [1]J Brown, [1]K Edwards, [1]R Lloyd, [1]M Johnson, [1]J Flint, [2]A Rodger, [1]M Lipman. *[1]Royal Free London NHS Trust, London, UK; [2]Department of Infection and Population Health, University College London, London, UK*

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**Background** HIV infected individuals are at increased risk of smoking-related illness and smoking rates amongst populations with HIV are often significantly higher than the general population. Interventions that reduce the prevalence of smoking in this population are urgently required.

**Aims** We sought to establish the impact of initiating regular smoking screening and advice by healthcare assistants (HCAs) or nurses as part of routine care appointments in a HIV ambulatory care service.

**Methods** Individuals attending for ambulatory HIV care appointments were asked brief screening questions regarding cigarette smoking by Healthcare Assistants (HCAs) or nurses. This was completed whilst clinical observations were performed, allowing this intervention to be delivered as part of routine care. Those who were current smokers were given Very Brief Advice (VBA) regarding smoking cessation and offered referral to smoking cessation services. The number of referrals to smoking cessation services was compared to the six months prior to the introduction of the enhanced service.

**Results** 1,031 individuals were screened between October 2014 and March 2015: 262 (25%) reported that they were current smokers. 248 (93%) of these smokers were provided with VBA and the opportunity of referral to smoking cessation services. Of these, 103 (38%) accepted referral compared to 6 referrals from the HIV outpatient service in the preceding 6 months.

**Conclusions** An intervention to ask service users about smoking and provide smoking cessation advice can be undertaken as part

of routine care in an ambulatory HIV care service and is effective in identifying smokers and increasing referrals to smoking cessation services. Further work will evaluate the impact of this intervention in HIV positive subjects.

## Lung infection mechanisms

### S82 'THE KISS OF DEATH' – CALCINEURIN INHIBITORS PREVENT ACTIN-DEPENDENT LATERAL TRANSFER OF ASPERGILLUS FUMIGATUS IN NECROPTOTIC HUMAN MACROPHAGES

[1]A Shah, [1]S Kannambath, [1]S Herbst, [2]A Rogers, [2]M Carby, [2]A Reed, [1]S Mostowy, [1]S Shaunak, [1]D Armstrong-James. *[1]Imperial College, London, UK; [2]Royal Brompton and Harefield NHS Foundation Trust, London, UK*

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Invasive fungal infections are a major cause of mortality in solid-organ transplantation where steroids and calcineurin inhibitors form the core of immunosuppression. Our group has previously shown in established hydrocortisone-based mouse models of invasive aspergillosis that calcineurin inhibitors increase mortality through effects on the innate immune response.[1] As alveolar macrophages present the primary resident innate immune cell in the airways responsible for fungal clearance, we perform a detailed study of the role of the calcineurin pathway in the human macrophage response to *A. fumigatus* (AF).

We show that the calcineurin-NFAT pathway is highly activated in the human lung transplant alveolar macrophage response to AF with inhibition resulting in impaired fungal clearance. Calcineurin inhibition leads to delayed phagocytosis, reduction in reactive-oxygen species production and an impairment of a novel actin-dependent process of lateral transfer of swollen AF conidia between human macrophages. Further characterisation reveals that transfer of AF occurs during macrophage necroptosis with subsequently around 50% control of germination in the receiving macrophage. To understand the calcineurin-dependent mechanism, next generation RNA sequencing was performed which confirms that calcineurin inhibition impairs the macrophage programmed cell death immune response. Utilising phosphoproteomics we additionally show that calcineurin inhibition impairs dephosphorylation of vasodilator-stimulated phosphoprotein (VASP), an important actin regulatory protein which promotes actin filament formation. High-resolution confocal microscopy confirms that VASP strongly co-localises to AF conidial phagocytosis and facilitates lateral transfer through tunnel-like structures. Lastly, we utilise a zebrafish model of invasive aspergillosis to confirm the in-vivo relevance of AF macrophage lateral transfer.

In conclusion our data shows the importance of the calcineurin pathway in the macrophage innate immune response to AF and highlights a novel calcineurin-actin dependent host defense mechanism which may have significant implications on persistence and dissemination within solid organ transplantation. To our knowledge this is the first report of a host-mediated cell-cell transfer mechanism for any pathogen.

#### REFERENCE

1 Herbst S, Shah A, Mazon Moya M, Marzola V, Jensen B, Reed A, *et al*. Phagocytosis-dependent activation of a TLR9-BTK-calcineurin-NFAT pathway co-ordinates innate immunity to Aspergillus fumigatus. *EMBO Mol Med*. 2015;**7**(3):240–58

### S83 CALCINEURIN INHIBITION IMPAIRS PHENOTYPIC MATURATION OF DENDRITIC CELLS IN A *IN VITRO* MODEL OF INVASIVE ASPERGILLOSIS IN LUNG TRANSPLANT RECIPIENTS

[1]AG Adlakha, [2]DPH Armstrong-James, [1]B Lenhard. *[1]MRC Clinical Sciences Centre, Imperial College, London, UK; [2]National Heart and Lung Institute, Imperial College, London, UK*

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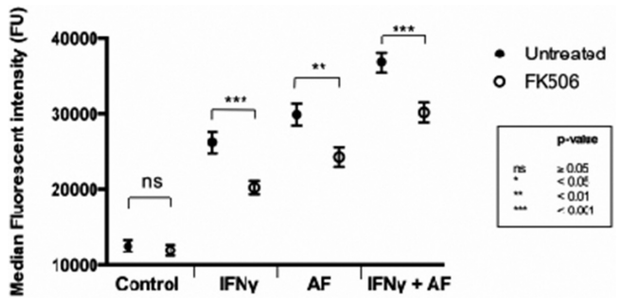
**Introduction** Invasive aspergillosis in lung transplant recipients on immunosuppression is associated with high morbidity and mortality. The calcineurin inhibitor tacrolimus (FK506) inhibits the calcineurin-NFAT axis, which impairs the innate response to fungal infection.[1] Dendritic cells (DC's) play a pivotal role in signalling to the adaptive immune system in infection – immature DC's phagocytose antigen, leading to maturation into DC's capable of stimulating T-cells. We investigated the effect of FK506 on DC function in invasive aspergillosis by assessing phenotypic maturation of DC's in response to *Aspergillus fumigatus* (AF) infection.

**Methods** Healthy volunteer PBMC's negatively isolated by Ficoll® gradient were differentiated into DC's with GM-CSF and IL-4. Day 5 cells were matured with IFN-γ. Day 7 cells were treated with FK506 and/or inoculated with swollen conidia of *A.fumigatus* (MOI 1:1). Cells were then stained with PE-bound anti-CD83 (a late maturation marker) and PerCP-Cy5.5-bound anti-CD-209 (a DC-specific marker) and analysed by the ImageStream® imaging flow cytometer. Statistical analysis was performed with Graphpad Prism v6.0, using unpaired t-tests with Welch correction.

**Results** 5000 cells/condition were analysed. DC's were subsetted by gating for CD-209 positivity. FK506 was not toxic to cells (similar cell viability between groups).

We demonstrated up-regulation of CD83 (measured by mean fluorescent intensity) with IFN-γ stimulation of DC's (12534 ± 799.3 vs. 26228 ± 1462, $p < 0.0001$; mean fluorescent units +/-SEM), AF infection of unstimulated DC's (12534 ± 799.3 vs. 29888 ± 1393, $p < 0.0001$) and for AF infection of IFN-γ-stimulated DC's (26228 ± 1462 vs. 36778 ± 1356, $p < 0.0001$).




**Abstract S83 Figure 1**

CD83 mean fluorescent intensity was reduced with FK506 treatment of IFN-γ-stimulated DC's (26228 ± 1462, vs. 20219 ± 846.0, $p = 0.0004$), AF-infected unstimulated DC's (29888 ± 1393 vs. 24289 ± 1253, $p = 0.0028$), and AF-infected, IFN-γ-stimulated DC's (36778 ± 1356 vs. 30159 ± 1279, $p = 0.0004$), but unchanged for unstimulated, un-infected DC's (12534 ± 799.3, vs. 11942 ± 762.5, $p = 0.5921$).

**Conclusion** Both *A.fumigatus* infection and IFN-γ stimulation promote phenotypic maturation of DC's *in vitro*, and treatment