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Sociodemographic and psychological determinants of influenza vaccine intention amongst recipients of autologous and allogeneic haematopoietic stem cell transplant: a cross-sectional survey of UK transplant recipients using a modified health belief model.

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Abstract

Objectives: Studies exploring vaccination rates amongst haematopoietic stem cell transplant (HSCT) recipients have focused on physician factors that limit uptake. Understanding the patient factors that determine vaccination intention is crucial to delivering a successful vaccination programme. Using a modified Health Belief Model (mHBM), we conducted a cross-sectional survey with the objective of exploring the sociodemographic and psychological factors that determined autologous and allogeneic HSCT recipients' intention to receive the seasonal inactivated influenza vaccine (SIIV) during the 2015-2016 influenza season.

Setting: The setting of our study was three tertiary-level, UK NHS autologous and allogeneic HSCT centres.

Participants: Eligible patients were aged 16 years or over and recipients of autologous or allogeneic HSCT for any disease indication, with no absolute contraindication to receiving the SIIV during the next influenza season, and having not received the SIIV since transplant. 93 participants from 3 UK NHS HSCT centres completed an anonymous study-specific questionnaire. 78.5% were recipients of allogeneic and 21.5% autologous HSCT.

Results: 23.7% of participants expressed low intent to receive the SIIV. patients aged over 65 (OR 0.02, 95% CI 0.01-0.57, p=0.02) and those who had not received the SIIV prior to HSCT (OR 0.04, 0.02-0.56, p=0.02) were more likely to have low intent. A multivariate logistic regression model incorporating constructs of the mHBM was statistically significant (p<0.001) and explained 74.7% of variation in SIIV intention. More patients felt that a recommendation from their HSCT team than their General Practitioner would prompt them to receive the SIIV, and this was most pronounced in those who had low intent.

Conclusions: The mHBM may provide a useful structure for addressing low vaccine intent amongst HSCT recipients and further interventional studies are warranted. We would encourage HSCT and General practitioners to discuss SIIV intention as a routine part of care.

HRA REC reference 16/WM/0144

Strengths of Study

-To our knowledge this is the first study to explore determinants of influenza vaccine uptake in a population of haematopoietic stem cell transplant recipients

-Participants from 3 geographically dispersed study sites completed anonymous questionnaires

- The questionnaire was based on the established theoretical framework of the Health Belief Model, and questions were specific with regard to vaccine and 2015-2016 season.

Limitations

-The study explored intention to receive the inactivated influenza vaccine during the 2015-2016 influenza season. Uptake was not assessed and may differ from intention rates.

-The study did not include a qualitative component and there may be additional determinants of influenza vaccine intention not captured here.

Introduction

Innate and adaptive immune responses are impaired for months to years following autologous and allogeneic haematopoietic stem cell transplant (HSCT). HSCT recipients are at high risk of morbidity and mortality from influenza viruses[1–3] and guidelines recommend that the seasonal inactivated influenza vaccine (SIIV) is administered annually[4–6]. While the SIIV is recommended by 96% of UK NHS allogeneic HSCT programmes[7], uptake rates of only 60-70% in the first 2 years post HSCT have been reported amongst UK HSCT recipients[8,9].

In both the UK and USA, physicians' familiarity with current guidelines, and perception of graft-versus-host disease (GvHD) as a contraindication to vaccination have been identified as factors limiting vaccine uptake rates[8–10]. No studies to-date have explored the patient factors that influence SIIV hesitancy or intention in an HSCT recipient population.

The Health Belief Model (HBM) is a widely used framework for investigating psychosocial determinants of health behaviours[11] and is recognized as an important predictor of influenza vaccination uptake[12]. The HBM proposes that an individual's engagement in a specific preventative health behaviour is predicated on the following constructs: i) perceived susceptibility to the illness, ii) perceived likelihood of contracting the illness, iii) perceived seriousness of the illness, iv) perceived barriers to engaging in the health behaviour, v) perceived benefits of the health behaviour, vi) cues to engage in the health behaviour such as advice from a healthcare practitioner and, vii) self-efficacy or the individual's perception of their capability to engage or succeed in the behaviour. Additional emotional constructs may modify the HBM. In particular, worry may modify the impact of perceived risk of illness; a patient may perceive themselves to be at risk, but unless this is something that worries them they may not engage in a preventative behaviour[13]. Furthermore, anticipated regret of illness if a health behaviour is not performed is also recognized as a predictor of intent[14].

The objective of this study was to explore the sociodemographic factors, and the vaccine and vaccination-specific health-beliefs that are associated with SIIV intention amongst HSCT recipients, using a HBM modified with the additional

emotional constructs given above (mHBM). A better understanding of such associations may allow development of targeted strategies that address issues specific to this unique and complex patient group, with the aim of increasing influenza vaccine uptake rates.

Participants and Methods

Participants

Patients were screened by HSCT nurse specialists for study eligibility during routine outpatient appointments at 3 study sites in the United Kingdom between June and September 2016. Eligible patients were aged 16 years or over and recipients of autologous or allogeneic HSCT for any disease indication, with no absolute contraindication to receiving the SIIV during the next influenza season, and having not received the SIIV since transplant. All participants gave written informed consent. The study was approved by the Health Research Authority National Research Ethics Committee (Reference 16/WM/0144)

Study Questionnaire and Health Belief Model

Participants completed a study-specific, anonymous, 42-item, paper-based questionnaire.

Questions scoped type of HSCT (autologous or allogeneic), disease indication, time from HSCT, pre-HSCT SIIV receipt, and receipt of non-SIIV vaccines since

HSCT. Sociodemographic questions established age, gender, ethnic background, educational attainment, relationship status and residential circumstances.

Intention to receive the SIIV during the 2016-2017 influenza season, was assessed by 2 statements phrased in the affirmative (I intend to receive the flu vaccine next winter) and negative (I will choose not to receive the flu vaccine next winter). Participants' agreement with each statement was expressed on 5-point Likert scales ranging from strongly disagree to strongly agree.

24 health belief statements were mapped to the mHBM with between 2 and 5 statements clustered around each construct (Table 1). Statements pertaining to the cues to vaccination construct were phrased to explore perception of HSCT team and General Practitioner (GP) knowledge of SIIV in the context of HSCT. Participants' perceived impact of a recommendation to receive the SIIV from their HSCT team or GP was explored. Statements about preferred vaccination location and ease of access to services were also included. Again, participants' agreement with each statement was expressed on 5-point Likert scales ranging from strongly disagree to strongly agree.

Statistical Analysis

Statistical analysis was performed with IBM SPSS version 24.

For the dependent variable vaccination intention, participants' agreement scores were summed and dichotomised to a 'high intent' group (intention score > than neutral value) and a 'low intent' group (intention score ≤ to the neutral value).

Categorical patient characteristics and sociodemographic factors are reported as frequencies and percentages. Associations between these variables and SIIV intention was examined with Pearson's chi-squared test, and Fisher's exact test when expected values were less than 5.

Internal scale reliability for each cluster of mHBM construct statements was assessed using Cronbach's α. A value of >0.6 was considered indicative of

184 *Table 1:Health belief statements grouped by construct with associated Cronbach's Alpha Value*

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Health Belief Model Construct (Cronbach's Alpha)
1.Susceptibility to seasonal influenza (α = 0.83)
Now I have had a stem cell transplant I can catch the seasonal flu more easily than other people my age
Now I have had a stem cell transplant I can catch the seasonal flu more easily than before my transplant
2.Likelihood of catching seasonal influenza (α = 0.91)
My chances of catching seasonal flu next winter will be high if I do not receive the seasonal flu vaccine
I am more likely than other people my age to catch seasonal flu next winter if I do not receive the seasonal flu vaccine
Now I have had a stem cell transplant it is more likely that I will catch seasonal flu next winter if I do not receive the seasonal flu vaccine
3.Severity of seasonal influenza infection (α = 0.91)
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter this would be a serious illness for me
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter this would have a negative impact on my recovery from my stem cell transplant
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter I would become more unwell than other people my age
4.Barriers to vaccination (α = 0.84)
I am worried about side effects of the seasonal flu vaccine
If I receive the seasonal flu vaccine next winter it may make me feel unwell with the flu or a flu-like illness
If I receive the seasonal flu vaccine next winter I am more likely to experience side effects than other people my age
If I receive the seasonal flu vaccine next winter it may have a negative impact on my recovery from my stem cell transplant
Now I have had a stem cell transplant the seasonal flu vaccine may not work as well for me as it does for other people my age
5.Benefits of vaccination (α = 0.66)
If I receive the seasonal flu vaccine next winter it may help to prevent me from catching the seasonal flu
If I receive the seasonal flu vaccine next winter it may help to prevent me from passing the seasonal flu to other people around me
If I receive the seasonal flu vaccine next winter, but still catch the flu, it may help to prevent me from becoming seriously unwell
6.Cues to vaccination (α = 0.76)

If my transplant team advised me to receive the seasonal flu vaccine next winter I would definitely have it
If my GP advised me to receive the seasonal flu vaccine next winter I would definitely have it
My GP understands my condition enough to know if the seasonal flu vaccine is right for me
My transplant team understand my condition enough to know if the seasonal flu vaccine is right for me
7.Worry (α = 0.47)
If I receive the seasonal flu vaccine next winter I will worry less about catching the seasonal flu
The thought of catching seasonal flu next winter worries me
8.Self-efficacy (α = 0.29)
I have enough information and am able to decide whether the seasonal flu vaccine is right for me
I would find it easy to attend my GP surgery next winter to receive the seasonal flu vaccine
9.Anticipated regret (α = 0.15)
I would regret it if I decided not to receive the seasonal flu vaccine next winter and became unwell with seasonal flu
I would regret it if I decided to receive the seasonal flu vaccine next winter and became unwell with side effects

acceptable internal scale reliability [15]. Scale reliability was acceptable for constructs 1-6 (Table 1) and statement scores were summed to give total construct scores for each participant. Scale reliability was unacceptable for constructs 7-9 (Table 1) therefore statements were analysed individually. All construct scores were analysed as continuous scales, with zero representing a neutral response (neither agree nor disagree). Mean agreement scores for low and high intent groups are presented with 95% confidence intervals.

Participants' mean agreement scores for each mHBM construct were compared between SIIV intention groups using Analysis of Variance (ANOVA). Homogeneity of variances was confirmed with Levene's statistic. HSCT team and GP cue scores *within* low and high intent groups were compared with a paired sample T-Test.

The association between sociodemographic variables, health belief constructs and seasonal influenza vaccination intention was examined with hierarchical binary logistic regression. Variables and constructs that were statistically significant in univariate analysis were included as separate regression blocks. Statistically significant variables that improved the predictive value ($p<0.05$ for the regression block) were included in the final model.

The assumption of a linear relationship between each independent variable and log of the outcome variable was tested and confirmed using the Box-Tidwell procedure[16]. Multicollinearity across all constructs was assessed. No variance

inflation factor was greater than 10, and the mean of values was acceptable at 1.92[17].

There were 10 missing data points from 6 participants across the study. These were all responses to mHBM statements from the high intent group. Summed agreement scores were not calculated for that participant for the affected HBM construct only.

Results

Patient Characteristics

Characteristics of 93 study participants are given in Table 2. 78.5% were recipients of allogeneic HSCT and the most frequent disease indication was AML (28.0%). The majority (68.6%) were within the first 6 months post HSCT. 40.9% of participants had received the SIIV before HSCT, and 4.3% had received a non-influenza vaccine since HSCT. 52.7% of participants were male, and most (84.9%) were of a white ethnic group.

SIIV vaccination intention for 2016-2017 influenza season

71 (76.3%) participants expressed high SIIV intent, while 22 (23.7%) expressed low SIIV intent.

*Table 2: Characteristics of n=93 study participants. *Statistically Significant (p<0.05)*

Characteristic, n=93	n(%)	high SIIV Intent (%)	p
Gender			
Male	49 (52.7)	81.6	
Female	44 (47.3)	70.5	0.23
Age group			
16-34	22 (23.7)	68.2	
35-54	36 (38.7)	91.7	
55-64	20 (21.5)	75	
65+	15 (16.1)	53.5	0.02*
HSCT Type			
Allogeneic	73 (78.5)	80	
Autologous	20 (21.5)	75.3	0.78
Disease Indication			
Acute lymphoblastic leukaemia (ALL)	11 (11.8)	72.7	
Acute myeloid leukaemia (AML)	26 (28.0)	76.9	
Aplastic Anaemia (AA)	5 (5.4)	60	
Chronic myeloid leukaemia (CML)	5 (5.4)	100	
Hodgkin Lymphoma	9 (9.7)	88.9	
Myelodysplastic syndrome (MDS)	5 (5.4)	60	
Myelofibrosis (MF)	2 (2.2)	50	
Multiple myeloma (MM)	22 (23.7)	77.3	
Non-Hodgkin Lymphoma (NHL)	8 (8.6)	75	0.79
months from HSCT			
0-6	64 (68.8)	81.3	
>6-12	20 (21.5)	70	
> 12	9 (9.7)	55.6	0.18
SIIV before HSCT			
Yes	38 (40.9)	89.5	
No	55 (59.1)	67.3	0.01*
Any non-SIIV vaccine since HSCT			
Yes	4 (4.3)	100	
No	89 (95.7)	75.3	0.26
Ethnicity			
White	79 (84.9)	77.2	
Asian	8 (8.6)	87.5	
Black	3 (3.2)	66.7	
Mixed	2 (2.2)	50	
Other	1 (1.1)	0	0.32
Educational Background			
Higher Education	30 (32.3)	80	
Secondary Education	49 (52.7)	81.6	

Other	3 (3.2)	66.7	
Prefer not to answer	11 (11.8)	45.5	0.07
Living Circumstances			
Renting	25 (26.9)	76	
Home Owner	54 (58.1)	79.6	
Other	10 (10.8)	70	
Prefer not to answer	4 (4.7)	50	0.56
Relationship Status			
Single	23 (24.7)	78.3	
Married / Cohabiting	56(60.2)	80.4	
Divorced / Separated	10 (10.8)	50	
Prefer not to answer	4 (4.4)	75	0.22

Sociodemographic and Transplant Variables

There was a statistically significant difference in SIIV intention between age groups (p=0.02) (Table 2). Rate of high intent was greatest in the 35-54 age group at 91.7%, and lowest at 53.3% in the 65+ age group. There was no statistically significant difference in gender(p=0.23), ethnicity (p=0.32), educational background (p=0.07), living circumstance (p=0.56), or relationship status (p=0.22) between SIIV intention groups.

There was no difference in type of HSCT (p=0.78) or disease indication (p=0.79) between SIIV intention groups. 81.3% of participants answering within the first 0-6 months post HSCT had high intent, compared with 70% in those answering at 6-12 months, and 55.6% among those answering at >12 months from HSCT, however this finding was not statistically significant (p=0.18). To determine whether there was a difference in health beliefs between participants at different time points post HSCT, mean agreement scores for all constructs were compared.

There was no difference in mean agreement scores between participants at 0-6 and 6-12 and >12 months post HSCT (p>0.05 in all cases).

There was no association between SIIV intention and receipt of any non-influenza vaccine since HSCT (p=0.26). However, of those who had received the SIIV prior to HSCT 81.3% had high intent compared with 67.3% of those who had not (p=0.01)

Health Belief Model Constructs

In univariate analysis, comparing mean construct agreement scores between SIIV intention groups, participants in the high intent group perceived greater susceptibility to influenza (2.09 v 0.05, p<0.001), a greater likelihood of contracting influenza (2.58 v -0.45, p<0.001) and perceived influenza to be a more severe illness (2.65 v 0.77, p=0.002) (Table 3). They also perceived greater potential benefit from vaccination (2.56 v -0.05, p<0.001), and fewer barriers to vaccination (-1.55 v 1.27, p=0.001). Although the two groups expressed similar levels of worry about catching influenza (0.14 v 0.81, p=0.34), participants in the high intent group felt they would worry less about catching influenza if vaccinated compared with the low intent group (0.80 v -0.23, p<0.001). They also expressed greater concern about anticipated regret if they caught influenza having not been vaccinated (1.35 v 0.27, p<0.001). Level of anticipated regret of experiencing side effects if vaccinated was similarly low across the two groups (-0.09 v 0.13, p=0.40). Participants in the high intent group felt more strongly that they had enough information to make decisions about vaccination (0.81 v 0.14,

p=0.007) and that it would be easy to attend their general practice surgery for vaccination (1.10 v 0.32, p<0.001).

Table 3: Mean agreement score values for health belief constructs for low and high SIIV intent groups. [a]*n=68,* [b]*n=69,*[c]*n=70*

Health Belief Model Construct	Low SIIV Intent (n=22)	High SIIV intent (n=71)	p
1.Susceptibility to seasonal influenza	0.05 (-0.70 to 0.70)	2.09 (1.75 to 4.39)	<0.001
2. Likelihood of catching seasonal influenza	-0.45(-1.39 to 0.40)	2.58 (2.00 to 3.18) [b]	<0.001
3. Severity of Seasonal influenza infection	0.77 (-0.17 to 1.72)	2.65 (2.09 to 3.23) [b]	0.002
4. Barriers to vaccination	1.27 (0.11 to 2.44)	-1.55 (-2.34 to -0.80)[a]	0.001
5. Benefits of vaccination	-0.05 (0.00 to 1.78)	2.56 (2.13 to 3.00)	<0.001
6. Cues to Vaccination			
HSCT team understands my condition	1.14 (0.55 to 1.32)	1.63 (1.52 to 1.75)	<0.001
GP understands my condition	-0.32 (0.83 to 0.13)	0.59 (0.55 to0.83)[c]	<0.001
7. Worry			
About catching influenza	0.14 (-0.43 to 0.71)	0.39 (0.17 to -0.63)	0.34
Less about catching influenza if vaccinated	-0.23 (0.60 to 0.07)	0.80 (0.61to 1.00)	<0.001
8. Self-efficacy			
Have enough information to decide about vaccination	0.14 (-0.32 to 0.58)	0.81 (0.61 to 1.00)	0.007
Would find it easy to attend GP for vaccination	0.32 (-0.12 to 1.72)	1.10 (1.89 to 2.00)	<0.001
9. Anticipated regret			
of catching flu if not vaccinated	0.27 (-0.21 to 0.74)	1.35 (1.18-1.52)	<0.001
of side effects if vaccinated	-0.09 (-0.15 to 0.37)	0.13 (-0.12 to 0.39)	0.4

A multivariate regression model (Table 4) was statistically significant when compared with a constant only model ($p<0.001$) indicating that this set of variables and constructs distinguishes reliably between HSCT recipients who express low and high SIIV intent. There was a moderately strong relationship with 74.7% (Nagelkerke R^2) of variation in vaccination intention explained by the overall model. GP ($p=0.24$) and HSCT Team (0.18) cues to vaccination, self-efficacy ($p=0.37$) and anticipated regret ($p=0.78$) constructs did not significantly improve predictive value and so were not included in the final model. Age and pre-HSCT SIIV vaccination receipt remained independent predictors of SIIV intention, with those aged >65 (OR 0.02, 95%CI 0.01-0.57, p=0.02) and those who had not received SIIV before HSCT (OR 00.4, 95%CI 0.02-0.56, p=0.02) more likely to be in the low intent group. A greater perceived benefit of vaccination was the strongest predictor of being in the high intent group (OR 2.96, 95%CI 1.29-6.81, p=0.01). Although the constructs susceptibility to influenza, likelihood of contracting influenza, severity of influenza infection, barriers to vaccination and worry about catching influenza improved the predictive value of the overall multivariate model, they did not independently predict vaccination intention.

*Table 4 Multivariate logistic regression model predicting odds of high SIIV intent. Overall model was statistically significant compared with a constant only model (p<0.001). *Statistically significant independent predictor (p<0.05)*

Variable	Odds Ratio of high SIIV Intent (95% CI)	p
Age >65	0.02 (0.01-0.57)	0.02*
No SIIV before HSCT	0.04 (0.02-0.56)	0.02*
Benefits of vaccination	2.96 (1.29-6.81)	0.01*
Susceptibility to seasonal Influenza	0.96 (0.33-2.78)	0.64
Likelihood of catching seasonal influenza	1.68 (0.86-3.26)	0.13
Severity of seasonal influenza infection	0.69 (0.39-1.21)	0.20
Barriers to vaccination	0.69 (0.57-0.99)	0.05
Worry less about catching seasona infuenza if vaccinated	4.99 (1.01-24.77)	0.05

Cues to Vaccination and Preferred Vaccination Location

Considering their HSCT team and GPs, both high (1.63 v 0.59, p<0.001) and low intent groups (1.14 v -0.32, p<0.001) agreed more strongly with statements that their HSCT team understands their condition enough to know if the influenza vaccine is right for them. Patients were also asked how much they agreed with the statement that they would definitely have the vaccine if their GP or HSCT team recommended it. Agreement scores were dichotomized to low agreement (≤ neutral value) and high agreement (>neutral value). Of those 22 patients with low intent, 90% agreed that they would receive the vaccine if their HSCT Team

recommended it, and only 22.7% if their GP recommended it, compared with 98.6% and 90.0% respectively in the high intent group.

Participant responses to the statement *I would prefer to have the seasonal influenza vaccine next winter at my transplant centre instead of my GP surgery* were categorized into prefers HSCT centre, prefers GP surgery or no preference. Of the low intent group, over half (54.5%) favoured vaccination at their HSCT centre, with only a minority (4.5%) favouring vaccination at their GP surgery. Of those with high intent 43.7% favoured vaccination at their HSCT programme, compared with 29.6% at their GP surgery although these findings did not reach statistical significance (p=0.05).

Discussion

To our knowledge, this is the first study to explore sociodemographic factors and psychological determinants of SIIV intention amongst HSCT recipients. Patients from 3 geographically dispersed study sites completed anonymous questionnaires. We identified low SIIV intent in approximately a quarter of participants. Participants' SIIV uptake during the 2016-2017 UK influenza season was not evaluated, and uptake may not be equivalent to intent rates reported here.

Constructs of a mHBM were significant determinants of SIIV intention. Strategies tailored to a population and their specific concerns are the most effective at improving knowledge and changing attitudes towards vaccination,

and increasing vaccine uptake[18]. Based on our findings, the mHBM may provide a useful framework for structuring strategies to address low SIIV intent in the HSCT population. Exploring HSCT recipients increased risk of influenza, both in terms of susceptibility and severity, discussing the potential benefits of vaccination, and exploring concerns around side effects may help to promote vaccine intent and uptake.

A strong association between past vaccination behaviours and future vaccination intent has been reported[19]. Previous influenza vaccination has been associated with high intent or uptake in all at risk groups [20,21] and cancer patients[22] and our findings accord with this. It may therefore be helpful to explore recipients pre-HSCT SIIV behaviour and discussion rationale for refusal where appropriate.

It was reassuring to find that none of gender, ethnicity, educational background, living circumstances or relationship status were associated with vaccine hesitancy in this study. However, vaccination intention did vary with age. High intent was greatest at 91.7% in the 35-53 age bracket, but of concern, fell in those over 65 to 53.5%, which is below the 2015-2016 uptake rate of 71% in the equivalent UK general population age-group[23]. Older age has been reported as a barrier to vaccination in a cohort of oncology patients, including some with haematological malignancy [22]. However, a French study of patients with secondary immunodeficiency, including haematological disorders, reported higher vaccination rates in those aged over 65 compared with younger patients[24]. In a UK study, older age was found to be a predictor of uptake of the

2009 pandemic influenza A vaccine amongst high-risk adults[25]. A meta-analysis of international studies found inconsistent association between age and vaccination intent and uptake in the general public, older patients, and those with chronic disease [19]. It is not apparent from these studies why age impacts on intent, and there are likely to be a range of social, psychological, financial and healthcare access issues specific to each study population. Our findings highlight a specific age group in whom intent is low and may benefit from targeted intervention. Further evaluation of this finding and exploration of underlying determinants is warranted.

High SIIV intent was greatest in those recipients within the first 0-6 months' post-HSCT (81.3%) and lowest at more than 12 months (55.6%) although this finding was not statistically significant. Longer time from HSCT may be associated with a change in perceived risk of infection, or concern about vaccine side effects or efficacy; however, we did not detect any statistically significant difference in health beliefs at 0-6, 6-12 and > 12 months from HSCT. This finding suggests there is a need for reinforcement of SIIV intent from healthcare professionals throughout and beyond the first-year post HSCT.

In both vaccine intention groups, patients expressed greater confidence in their HSCT team than their GP, with respect to understanding of whether the influenza vaccine is right for them. Fewer patients felt that a recommendation from their GP would prompt them to receive the SIIV compared with if their HSCT Team made the recommendation. This was most marked in the low intent group. These findings suggest that cues from the HSCT team are important in promoting

vaccination amongst HSCT recipients, and particularly for those with low intent. Cues from healthcare providers are considered a key factor in promoting vaccination[19] and a study of Israeli cancer patients identified recommendation from an oncologist as a significant predictor of vaccine uptake [22]. Our findings accord with this, and suggest that HSCT recipients value the advice of their specialist team. This highlights the importance of HSCT specialists engaging in discussion with patients about influenza vaccination. Preference for vaccination at HSCT centres rather than GP surgeries was similar at 43.7% and 54.5% in low and high intent groups respectively. In the high intent group, more patients expressed a preference for vaccination at their GP surgery than in the low intent group. For approximately 50% of those HSCT recipients with both low and high intent, access to an SIIV service at HSCT centres may facilitate vaccination uptake

None of the transplant variables assessed were associated with SIIV intention. Current influenza vaccination guidelines are standardized for all HSCT recipients as evidence is insufficient to recommend modification according to donor type, stem cell source or conditioning[4,5]. Influenza infections are reported to occur with higher frequency in allogeneic compared with autologous HSCT recipients [26,27] and may have a higher associated morbidity and mortality[28] although this latter finding has not been consistently reported[1]. There was no difference in vaccination intention between autologous and allogeneic HSCT recipients. This suggests the unique aspects of allogeneic HSCT, principally GvHD and the need for immunosuppressive therapy, do not contribute to increased influenza vaccination intention in this group compared with autoHSCT recipients.

Conclusion

Our data indicates that the constructs of a mHBM are important determinants of SIIV intention in the HSCT recipient population. These constructs may be used to structure interventions addressing low SIIV intent, and prospective studies are warranted. Those aged over 65, and those who had not received the SIIV prior to HSCT were particularly likely to have low intent and may be target groups. HSCT recipients strongly value the expertise and recommendation of their transplant team, and we would encourage practitioners to discuss SIIV intention with patients as a routine and important aspect of post-transplant care. Local provision of vaccination services at HSCT centres may serve as an additional promoter for a proportion of patients.

Authorship Statement

Paul D E Miller, Alice S Forster, Thushan I de Silva, Karl Peggs, Alejandro Madrigal and John A Snowden made substantial contributions to the conception and design of the work, and to analysis and interpretation of data.

Hayley Leonard, Chloe Anthias, Michaela Mayhew, Matthias Klammer, Susan Paskar and Erin Hurst made substantial contributions to the acquisition of data.

All named authors contributed to the drafting and revising for important intellectual content and gave final of the manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the

accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data sharing statement

The study dataset will be made available via Dryad repository and DOI provided following editorial review

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Sociodemographic and psychological determinants of influenza vaccine intention amongst recipients of autologous and allogeneic haematopoietic stem cell transplant: a cross-sectional survey of UK transplant recipients using a modified health belief model.

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Sociodemographic and psychological determinants of influenza vaccine intention amongst recipients of autologous and allogeneic haematopoietic stem cell transplant: a cross-sectional survey of UK transplant recipients using a modified health belief model.

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Abstract

Objectives: Studies exploring vaccination rates amongst haematopoietic stem cell transplant (HSCT) recipients have focused on physician factors that limit uptake. Understanding the patient factors that determine vaccination intention is crucial to delivering a successful vaccination programme. Using a modified Health Belief Model (mHBM), we conducted a cross-sectional survey with the objective of exploring the sociodemographic and psychological factors that determined autologous and allogeneic HSCT recipients' intention to receive the seasonal inactivated influenza vaccine (SIIV) during the 2015-2016 influenza season.

Setting: The setting of our study was three tertiary-level, UK NHS autologous and allogeneic HSCT centres.

Participants: Eligible patients were aged 16 years or over and recipients of autologous or allogeneic HSCT for any disease indication, with no absolute contraindication to receiving the SIIV during the next influenza season, and having not received the SIIV since transplant. 93 participants from 3 UK NHS HSCT centres completed an anonymous study-specific questionnaire. 78.5% were recipients of allogeneic and 21.5% autologous HSCT.

Results: 23.7% of participants expressed low intent to receive the SIIV. patients aged over 65 (OR 0.02, 95% CI 0.01-0.57, p=0.02) and those who had not received the SIIV prior to HSCT (OR 0.04, 0.02-0.56, p=0.02) were more likely to have low intent. A multivariate logistic regression model incorporating constructs of the mHBM was statistically significant (p<0.001) and explained 74.7% of variation in SIIV intention. More patients felt that a recommendation from their HSCT team than their General Practitioner would prompt them to receive the SIIV, and this was most pronounced in those who had low intent.

Conclusions: The mHBM may provide a useful structure for addressing low vaccine intent amongst HSCT recipients and further interventional studies are warranted. We would encourage HSCT and General practitioners to discuss SIIV intention as a routine part of care.

HRA REC reference 16/WM/0144

Strengths of Study

-To our knowledge this is the first study to explore determinants of influenza vaccine uptake in a population of haematopoietic stem cell transplant recipients

-Participants from 3 geographically dispersed study sites completed anonymous questionnaires

- The questionnaire was based on the established theoretical framework of the Health Belief Model, and questions were specific with regard to vaccine and 2015-2016 season.

Limitations

-The study explored intention to receive the inactivated influenza vaccine during the 2015-2016 influenza season. Uptake was not assessed and may differ from intention rates.

-The number of enrolled participants expressing low vaccination intent was small at 22 (23.7%) and this may bias our data.

Introduction

Innate and adaptive immune responses are impaired for months to years following autologous and allogeneic haematopoietic stem cell transplant (HSCT). HSCT recipients are at high risk of morbidity and mortality from influenza viruses[1–3] and guidelines recommend that the seasonal inactivated influenza vaccine (SIIV) is administered annually starting 4 to 6 months post HSCT [4–6]. While the SIIV is recommended by 96% of UK NHS allogeneic HSCT

programmes[7], uptake rates of only 60-70% in the first 2 years post HSCT have been reported amongst UK HSCT recipients[8,9]. The majority of UK allogeneic HSCT recipients are referred to their General Practitioner (GP) with only 8% of UK adult allogeneic HSCT programmes offering vaccination services. SIIV efficacy of 65.4-80% has been reported in HSCT recipients, although in small cohorts [10,11] In both the UK and USA, physicians' familiarity with current guidelines, and perception of graft-versus-host disease (GvHD) as a contraindication to vaccination have been identified as factors limiting vaccine uptake rates[8,9,12]. No studies to-date have explored the patient factors that influence SIIV hesitancy or intention in an HSCT recipient population.

The Health Belief Model (HBM) is a widely used framework for investigating psychosocial determinants of health behaviours[13] and is recognized as an important predictor of influenza vaccination uptake[14]. The HBM proposes that an individual's engagement in a specific preventative health behaviour is predicated on the following constructs: i) perceived susceptibility to the illness, ii) perceived likelihood of contracting the illness, iii) perceived seriousness of the illness, iv) perceived barriers to engaging in the health behaviour, v) perceived benefits of the health behaviour, vi) cues to engage in the health behaviour such as advice from a healthcare practitioner and, vii) self-efficacy or the individual's perception of their capability to engage or succeed in the behaviour. Additional emotional constructs may modify the HBM. In particular, worry may modify the impact of perceived risk of illness; a patient may perceive themselves to be at risk, but unless this is something that worries them they may not engage in a

preventative behaviour[15]. Furthermore, anticipated regret of illness if a health behaviour is not performed is also recognized as a predictor of intent[16].

The objective of this study was to explore the sociodemographic factors, and the vaccine and vaccination-specific health-beliefs that are associated with SIIV intention amongst HSCT recipients, using a HBM modified with the additional emotional constructs given above (mHBM). A better understanding of such associations may allow development of targeted strategies that address issues specific to this unique and complex patient group, with the aim of increasing influenza vaccine uptake rates.

Participants and Methods

Participants

Patients were screened by HSCT nurse specialists for study eligibility during routine outpatient appointments at 3 study sites in the United Kingdom between June and September 2016. Eligible patients were aged 16 years or over and recipients of autologous or allogeneic HSCT for any disease indication, with no absolute contraindication to receiving the SIIV during the next influenza season, and having not received the SIIV since transplant. All participants gave written informed consent. The study was approved by the Health Research Authority National Research Ethics Committee (Reference 16/WM/0144)

Study Questionnaire and Health Belief Model

Participants completed a study-specific, anonymous, 42-item, paper-based questionnaire.

Questions scoped type of HSCT (autologous or allogeneic), disease indication, time from HSCT, pre-HSCT SIIV receipt, and receipt of non-SIIV vaccines since HSCT. Sociodemographic questions established age, gender, ethnic background, educational attainment, relationship status and residential circumstances.

Intention to receive the SIIV during the 2016-2017 influenza season, was assessed by 2 statements phrased in the affirmative (I intend to receive the flu vaccine next winter) and negative (I will choose not to receive the flu vaccine next winter). Participants' agreement with each statement was expressed on 5-point Likert scales ranging from strongly disagree to strongly agree.

24 health belief statements were mapped to the mHBM with between 2 and 5 statements clustered around each construct (Table 1). Statements pertaining to the cues to vaccination construct were phrased to explore perception of HSCT team and GP knowledge of SIIV in the context of HSCT. Participants' perceived impact of a recommendation to receive the SIIV from their HSCT team or GP was explored. Statements about preferred vaccination location and ease of access to services were also included. Again, participants' agreement with each statement was expressed on 5-point Likert scales ranging from strongly disagree to strongly agree.

Statistical Analysis

Statistical analysis was performed with IBM SPSS version 24.

For the dependent variable vaccination intention, participants' agreement scores were summed and dichotomised to a 'high intent' group (intention score > than neutral value) and a 'low intent' group (intention score ≤ to the neutral value).

Categorical patient characteristics and sociodemographic factors are reported as frequencies and percentages. Associations between these variables and SIIV intention was examined with Pearson's chi-squared test, and Fisher's exact test when expected values were less than 5.

Internal scale reliability for each cluster of mHBM construct statements was assessed using Cronbach's α. A value of >0.6 was considered indicative of

189 *Table 1:Health belief statements grouped by construct with associated Cronbach's Alpha Value*

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Health Belief Model Construct (Cronbach's Alpha)
1.Susceptibility to seasonal influenza (α = 0.83)
Now I have had a stem cell transplant I can catch the seasonal flu more easily than other people my age
Now I have had a stem cell transplant I can catch the seasonal flu more easily than before my transplant
2.Likelihood of catching seasonal influenza (α = 0.91)
My chances of catching seasonal flu next winter will be high if I do not receive the seasonal flu vaccine
I am more likely than other people my age to catch seasonal flu next winter if I do not receive the seasonal flu vaccine
Now I have had a stem cell transplant it is more likely that I will catch seasonal flu next winter if I do not receive the seasonal flu vaccine
3.Severity of seasonal influenza infection (α = 0.91)
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter this would be a serious illness for me
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter this would have a negative impact on my recovery from my stem cell transplant
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter I would become more unwell than other people my age
4.Barriers to vaccination (α = 0.84)
I am worried about side effects of the seasonal flu vaccine
If I receive the seasonal flu vaccine next winter it may make me feel unwell with the flu or a flu-like illness
If I receive the seasonal flu vaccine next winter I am more likely to experience side effects than other people my age
If I receive the seasonal flu vaccine next winter it may have a negative impact on my recovery from my stem cell transplant
Now I have had a stem cell transplant the seasonal flu vaccine may not work as well for me as it does for other people my age
5.Benefits of vaccination (α = 0.66)
If I receive the seasonal flu vaccine next winter it may help to prevent me from catching the seasonal flu
If I receive the seasonal flu vaccine next winter it may help to prevent me from passing the seasonal flu to other people around me
If I receive the seasonal flu vaccine next winter, but still catch the flu, it may help to prevent me from becoming seriously unwell
6.Cues to vaccination (α = 0.76)

If my transplant team advised me to receive the seasonal flu vaccine next winter I would definitely have it
If my GP advised me to receive the seasonal flu vaccine next winter I would definitely have it
My GP understands my condition enough to know if the seasonal flu vaccine is right for me
My transplant team understand my condition enough to know if the seasonal flu vaccine is right for me
7.Worry (α = 0.47)
If I receive the seasonal flu vaccine next winter I will worry less about catching the seasonal flu
The thought of catching seasonal flu next winter worries me
8.Self-efficacy (α = 0.29)
I have enough information and am able to decide whether the seasonal flu vaccine is right for me
I would find it easy to attend my GP surgery next winter to receive the seasonal flu vaccine
9.Anticipated regret (α = 0.15)
I would regret it if I decided not to receive the seasonal flu vaccine next winter and became unwell with seasonal flu
I would regret it if I decided to receive the seasonal flu vaccine next winter and became unwell with side effects

acceptable internal scale reliability [17]. Scale reliability was acceptable for constructs 1-6 (Table 1) and statement scores were summed to give total construct scores for each participant. Scale reliability was unacceptable for constructs 7-9 (Table 1) therefore statements were analysed individually. All construct scores were analysed as continuous scales, with zero representing a neutral response (neither agree nor disagree). Mean agreement scores for low and high intent groups are presented with 95% confidence intervals.

Participants' mean agreement scores for each mHBM construct were compared between SIIV intention groups using Analysis of Variance (ANOVA). Homogeneity of variances was confirmed with Levene's statistic. HSCT team and GP cue scores *within* low and high intent groups were compared with a paired sample T-Test.

The impact of sociodemographic variables andhealth belief constructs on seasonal influenza vaccination intention was examined with hierarchical binary logistic regression. Variables and constructs that were statistically significant in univariate analysis were included as separate regression blocks. Statistically significant variables that improved the predictive value ($p<0.05$ for the regression block) were included in the final model.

The assumption of a linear relationship between each independent variable and log of the outcome variable was tested and confirmed using the Box-Tidwell procedure[18]. Multicollinearity across all constructs was assessed. No variance

inflation factor was greater than 10, and the mean of values was acceptable at 1.92[19].

There were 10 missing data points from 6 participants across the study. These were all responses to mHBM statements from the high intent group. Summed agreement scores were not calculated for that participant for the affected HBM construct only.

Patient and Public Involvement

The study questionnaire was developed with the involvement of volunteers from the Anthony Nolan patients and families panel. Using an initial draft questionnaire, think-aloud sessions were conducted to ensure that the questionnaire was clear, easy to understand, that interpretation of each question was as intended, and that answers were consistent with the question asked. Volunteers were also asked for their overall feedback on the study questionnaire. The revised questionnaire was then piloted with volunteer patients who were asked to complete the questionnaire, keeping note of the time taken, and to highlight any questions that they had difficulty answering or otherwise found problematic. The questionnaires were all completed within 10 minutes and no participants reported difficulty or concerns about the questions. Results will be disseminated to study participants through their transplant teams, and made available to participants through open access publication.

Results

Patient Characteristics

Characteristics of 93 study participants are given in Table 2. 78.5% were recipients of allogeneic HSCT and the most frequent disease indication was acute myeloid leukaemia (AML) (28.0%). The majority (68.6%) were within the first 6 months post HSCT. 40.9% of participants had received the SIIV before HSCT, and 4.3% had received a non-influenza vaccine since HSCT. 52.7% of participants were male, and most (84.9%) were of a white ethnic group.

SIIV vaccination intention for 2016-2017 influenza season

71 (76.3%) participants expressed high SIIV intent, while 22 (23.7%) expressed low SIIV intent.

*Table 2: Characteristics of n=93 study participants. *Statistically Significant (p<0.05)*

Characteristic, n=93	n(%)	high SIIV Intent n(%)	p
Gender			
Male	49 (52.7)	40 (81.6)	
Female	44 (47.3)	31 (70.5)	0.23
Age group			
16-34	22 (23.7)	15 (68.2)	
35-54	36 (38.7)	33 (91.7)	
55-64	20 (21.5)	15 (75)	
65+	15 (16.1)	8 (53.5)	0.02*

HSCT Type			
Allogeneic	73 (78.5)	59 (80.8)	
Autologous	20 (21.5)	15 (75)	0.78
Disease Indication			
Acute lymphoblastic leukaemia (ALL)	11 (11.8)	8(72.7)	
Acute myeloid leukaemia (AML)	26 (28.0)	20 (76.9)	
Aplastic Anaemia (AA)	5 (5.4)	3 (60)	
Chronic myeloid leukaemia (CML)	5 (5.4)	5 (100)	
Hodgkin Lymphoma	9 (9.7)	9 (88.9)	
Myelodysplastic syndrome (MDS)	5 (5.4)	3 (60)	
Myelofibrosis (MF)	2 (2.2)	1 (50)	
Multiple myeloma (MM)	22 (23.7)	17 (77.3)	
Non-Hodgkin Lymphoma (NHL)	8 (8.6)	6 (75)	0.79
months from HSCT			
0-6	64 (68.8)	52 (81.3)	
>6-12	20 (21.5)	14 (70)	
> 12	9 (9.7)	5 (55.6)	0.18
SIIV before HSCT			
Yes	38 (40.9)	34(89.5)	
No	55 (59.1)	37 (67.3)	0.01*
Any non-SIIV vaccine since HSCT			
Yes	4 (4.3)	4 (100)	
No	89 (95.7)	67 (75.3)	0.26
Ethnicity			
White	79 (84.9)	69 (77.2)	
Asian	8 (8.6)	7 (87.5)	
Black	3 (3.2)	2 (66.7)	
Mixed	2 (2.2)	1 (50)	
Other	1 (1.1)	0 (0)	0.32
Educational Background			
Higher Education	30 (32.3)	24 (80)	
Secondary Education	49 (52.7)	40 (81.6)	
Other	3 (3.2)	2 (66.7)	
Prefer not to answer	11 (11.8)	5 (45.5)	0.07
Living Circumstances			
Renting	25 (26.9)	33 (76)	
Home Owner	54 (58.1)	43 (79.6)	
Other	10 (10.8)	7(70)	
Prefer not to answer	4 (4.7)	2 (50)	0.56
Relationship Status			
Single	23 (24.7)	18 (78.3)	
Married / Cohabiting	56(60.2)	45 (80.4)	
Divorced / Separated	10 (10.8)	5 (50)	
Prefer not to answer	4 (4.4)	3 (75)	0.22

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Sociodemographic and Transplant Variables

There was a statistically significant difference in SIIV intention between age groups (Table 2). Rate of high intent was greatest in the 35-54 age group at 91.7%, and lowest at 53.3% in the 65+ age group. There was no statistically significant difference in gender, ethnicity, educational background, living circumstance, or relationship status between SIIV intention groups.

There was no difference in type of HSCT or disease indication between SIIV intention groups. 81.3% of participants answering within the first 0-6 months post HSCT had high intent, compared with 70% in those answering at 6-12 months, and 55.6% among those answering at >12 months from HSCT, however this finding was not statistically significant. To determine whether there was a difference in health beliefs between participants at different time points post HSCT, mean agreement scores for all constructs were compared. There was no difference in mean agreement scores between participants at 0-6 and 6-12 and >12 months post HSCT.

There was no association between SIIV intention and receipt of any non-influenza vaccine since HSCT. However, of those who had received the SIIV prior to HSCT 81.3% had high intent compared with 67.3% of those who had not .

Health Belief Model Constructs

In univariate analysis, comparing mean construct agreement scores between SIIV intention groups, participants in the high intent group perceived greater susceptibility to influenza, a greater likelihood of contracting influenza and perceived influenza to be a more severe illness (Table 3). They also perceived greater potential benefit from vaccination, and fewer barriers to vaccination. Although the two groups expressed similar levels of worry about catching influenza, participants in the high intent group felt they would worry less about catching influenza if vaccinated compared with the low intent group. They also expressed greater concern about anticipated regret if they caught influenza having not been vaccinated. Level of anticipated regret of experiencing side effects if vaccinated was similarly low across the two groups. Participants in the high intent group felt more strongly that they had enough information to make decisions about vaccination and that it would be easy to attend their general practice surgery for vaccination.

Table 3: Mean agreement score values for health belief constructs for low and high SIIV intent groups. [a]*n=68,* [b]*n=69,* [c]*n=70*

Health Belief Model Construct	Low SIIV Intent (n=22)	High SIIV intent (n=71)	p
1.Susceptibility to seasonal influenza	0.05 (-0.70 to 0.70)	2.09 (1.75 to 4.39)	<0.001
2. Likelihood of catching seasonal influenza	-0.45(-1.39 to 0.40)	2.58 (2.00 to 3.18) [b]	<0.001
3. Severity of Seasonal influenza infection	0.77 (-0.17 to 1.72)	2.65 (2.09 to 3.23) [b]	0.002
4. Barriers to vaccination	1.27 (0.11 to 2.44)	-1.55 (-2.34 to -0.80)[a]	0.001
5. Benefits of vaccination	-0.05 (0.00 to 1.78)	2.56 (2.13 to 3.00)	<0.001
6. Cues to Vaccination			
HSCT team understands my condition	1.14 (0.55 to 1.32)	1.63 (1.52 to 1.75)	<0.001

	GP understands my condition	-0.32 (0.83 to 0.13)	0.59 (0.55 to0.83)[c]	<0.001
7. Worry				
	About catching influenza	0.14 (-0.43 to 0.71)	0.39 (0.17 to -0.63)	0.34
	Less about catching influenza if vaccinated	-0.23 (0.60 to 0.07)	0.80 (0.61to 1.00)	<0.001
8. Self-efficacy				
	Have enough information to decide about vaccination	0.14 (-0.32 to 0.58)	0.81 (0.61 to 1.00)	0.007
	Would find it easy to attend GP for vaccination	0.32 (-0.12 to 1.72)	1.10 (1.89 to 2.00)	<0.001
9. Anticipated regret				
	of catching flu if not vaccinated	0.27 (-0.21 to 0.74)	1.35 (1.18-1.52)	<0.001
	of side effects if vaccinated	-0.09 (-0.15 to 0.37)	0.13 (-0.12 to 0.39)	0.4

A multivariate regression model (Table 4) was statistically significant when compared with a constant only model indicating that this set of variables and constructs distinguishes reliably between HSCT recipients who express low and high SIIV intent. There was a moderately strong relationship with 74.7% (Nagelkerke R^2) of variation in vaccination intention explained by the overall model. GP and HSCT Team cues to vaccination, self-efficacy and anticipated regret constructs did not significantly improve predictive value and so were not included in the final model. Age and pre-HSCT SIIV vaccination receipt remained independent predictors of SIIV intention, with those aged >65 and those who had not received SIIV before HSCT more likely to be in the low intent group. A greater perceived benefit of vaccination was the strongest predictor of being in the high intent group. Although the constructs susceptibility to influenza,

likelihood of contracting influenza, severity of influenza infection, barriers to vaccination and worry about catching influenza improved the predictive value of the overall multivariate model, they did not independently predict vaccination intention.

*Table 4 Multivariate logistic regression model predicting odds of high SIIV intent. Overall model was statistically significant compared with a constant only model (p<0.001). *Statistically significant independent predictor (p<0.05)*

Variable	Odds Ratio of high SIIV Intent (95% CI)	p
Age >65	0.02 (0.01-0.57)	0.02*
No SIIV before HSCT	0.04 (0.02-0.56)	0.02*
Benefits of vaccination	2.96 (1.29-6.81)	0.01*
Susceptibility to seasonal Influenza	0.96 (0.33-2.78)	0.64
Likelihood of catching seasonal influenza	1.68 (0.86-3.26)	0.13
Severity of seasonal influenza infection	0.69 (0.39-1.21)	0.20
Barriers to vaccination	0.69 (0.57-0.99)	0.05
Worry less about catching seasona infuenza if vaccinated	4.99 (1.01-24.77)	0.05

Cues to Vaccination and Preferred Vaccination Location

Considering their HSCT team and GPs, both high and low intent groups agreed more strongly with statements that their HSCT team understands their condition enough to know if the influenza vaccine is right for them. Patients were also asked how much they agreed with the statement that they would definitely have the vaccine if their GP or HSCT team recommended it. Agreement scores were dichotomized to low agreement (≤ neutral value) and high agreement (>neutral value). Of those 22 patients with low intent, 90% agreed that they would receive the vaccine if their HSCT Team recommended it, and only 22.7% if their GP recommended it, compared with 98.6% and 90.0% respectively in the high intent group.

Participant responses to the statement *I would prefer to have the seasonal influenza vaccine next winter at my transplant centre instead of my GP surgery* were categorized into prefers HSCT centre, prefers GP surgery or no preference. Of the low intent group, over half (54.5%) favoured vaccination at their HSCT centre, with only a minority (4.5%) favouring vaccination at their GP surgery. Of those with high intent 43.7% favoured vaccination at their HSCT programme, compared with 29.6% at their GP surgery although these findings did not reach statistical significance (p=0.05).

Discussion

To our knowledge, this is the first study to explore sociodemographic factors and psychological determinants of SIIV intention amongst HSCT recipients. Patients from 3 geographically dispersed study sites completed anonymous questionnaires. Approximately a quarter of participants expressed low SIIV intent. While this is in keeping with previously reported SIIV uptake rates of 60-70% [8,9], the small absolute number of participants expressing low SIIV intent in our study may bias our data. Participants' SIIV uptake during the 2016-2017 UK influenza season was not evaluated, and uptake in this cohort may not be equivalent to intent rates reported here.

Constructs of a mHBM were significant determinants of SIIV intention. Strategies tailored to a population and their specific concerns are the most effective at improving knowledge and changing attitudes towards vaccination, and increasing vaccine uptake[20]. Based on our findings, the mHBM may provide a useful framework for structuring strategies to address low SIIV intent in the HSCT population. Exploring HSCT recipients increased risk of influenza, both in terms of susceptibility and severity, discussing the potential benefits of vaccination, and exploring concerns around side effects may help to promote vaccine intent and uptake.

A strong association between past vaccination behaviours and future vaccination intent has been reported[21]. Previous influenza vaccination has been associated with high intent or uptake in all at risk groups [22,23] and cancer patients[24] and our findings accord with this. It may therefore be helpful to

explore recipients pre-HSCT SIIV behaviour and discussion rationale for refusal where appropriate.

It was reassuring to find that none of gender, ethnicity, educational background, living circumstances or relationship status were associated with vaccine hesitancy in this study. However, vaccination intention did vary with age. High intent was greatest at 91.7% in the 35-53 age bracket, but of concern, fell in those over 65 to 53.5%, which is below the 2015-2016 uptake rate of 71% in the equivalent UK general population age-group[25]. Older age has been reported as a barrier to vaccination in a cohort of oncology patients, including some with haematological malignancy [24]. However, a French study of patients with secondary immunodeficiency, including haematological disorders, reported higher vaccination rates in those aged over 65 compared with younger patients[26]. In a UK study, older age was found to be a predictor of uptake of the 2009 pandemic influenza A vaccine amongst high-risk adults[27]. A meta-analysis of international studies found inconsistent association between age and vaccination intent and uptake in the general public, older patients, and those with chronic disease [21]. It is not apparent from these studies why age impacts on intent, and there are likely to be a range of social, psychological, financial and healthcare access issues specific to each study population. Our findings highlight a specific age group in whom intent is low and may benefit from targeted intervention. Further evaluation of this finding and exploration of underlying determinants is warranted.

High SIIV intent was greatest in those recipients within the first 0-6 months' post-HSCT (81.3%) and lowest at more than 12 months (55.6%) although this finding was not statistically significant. Longer time from HSCT may be associated with a change in perceived risk of infection, or concern about vaccine side effects or efficacy; however, we did not detect any statistically significant difference in health beliefs at 0-6, 6-12 and > 12 months from HSCT. This finding suggests there is a need for reinforcement of SIIV intent from healthcare professionals throughout and beyond the first-year post HSCT.

In both vaccine intention groups, patients expressed greater confidence in their HSCT team than their GP, with respect to understanding of whether the influenza vaccine is right for them. Fewer patients felt that a recommendation from their GP would prompt them to receive the SIIV compared with if their HSCT Team made the recommendation. This was most marked in the low intent group. These findings suggest that cues from the HSCT team are important in promoting vaccination amongst HSCT recipients, and particularly for those with low intent. Cues from healthcare providers are considered a key factor in promoting vaccination[21] and a study of Israeli cancer patients identified recommendation from an oncologist as a significant predictor of vaccine uptake [24]. Our findings accord with this, and suggest that HSCT recipients value the advice of their specialist team. This highlights the importance of HSCT specialists engaging in discussion with patients about influenza vaccination. Preference for vaccination at HSCT centres rather than GP surgeries was similar at 43.7% and 54.5% in low and high intent groups respectively. In the high intent group, more patients expressed a preference for vaccination at their GP surgery than in the low intent

group. For approximately 50% of those HSCT recipients with both low and high intent, access to an SIIV service at HSCT centres may facilitate vaccination uptake

None of the transplant variables assessed were associated with SIIV intention. Current influenza vaccination guidelines are standardized for all HSCT recipients as evidence is insufficient to recommend modification according to donor type, stem cell source or conditioning[4,5]. Influenza infections are reported to occur with higher frequency in allogeneic compared with autologous HSCT recipients [28,29] and may have a higher associated morbidity and mortality[30] although this latter finding has not been consistently reported[1]. There was no difference in vaccination intention between autologous and allogeneic HSCT recipients. This suggests the unique aspects of allogeneic HSCT, principally GvHD and the need for immunosuppressive therapy, do not contribute to increased influenza vaccination intention in this group compared with autoHSCT recipients.

Conclusion

Our data indicate that the constructs of a mHBM are important determinants of SIIV intention in the HSCT recipient population. These constructs may be used to develop interventions addressing low SIIV intent For example, SIIV uptake amongst HSCT recipients may be promoted by public health authorities and patient support groups with messages adapted from our findings. Future prospective studies to investigate the efficacy of such intervention are warranted. HSCT recipients strongly value the expertise and recommendation of their transplant team, and we would encourage practitioners to discuss SIIV intention

with all patients as a routine and important aspect of post-transplant care. Furthermore, those aged over 65, and those who had not received the SIIV prior to HSCT were particularly likely to have low intent and may be target groups. Local provision of vaccination services at HSCT centres may serve as an additional promoter for a proportion of patients and this would require allocation of resources from health commissioners.

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Authorship Statement

Paul D E Miller, Alice S Forster, Thushan I de Silva, Karl Peggs, Alejandro Madrigal and John A Snowden all contributed substantially to the design, analysis, and interpretation of data. Hayley Leonard, Chloe Anthias, Michaela Mayhew, Matthias Klammer, Erin Hurst and Susan Paskar all contributed substantially to the acquisition of data. All authors contributed to drafting the work and/or revising it critically for intellectual content. All authors gave final approval of the version to be published.

Data sharing statement

The study dataset will be made available via Dryad repository and DOI provided following editorial review

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Sociodemographic and psychological determinants of influenza vaccine intention amongst recipients of autologous and allogeneic haematopoietic stem cell transplant: a cross-sectional survey of UK transplant recipients using a modified health belief model.

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Sociodemographic and psychological determinants of influenza vaccine intention amongst recipients of autologous and allogeneic haematopoietic stem cell transplant: a cross-sectional survey of UK transplant recipients using a modified health belief model.

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Abstract

Objectives: Studies exploring vaccination rates amongst haematopoietic stem cell transplant (HSCT) recipients have focused on physician factors that limit uptake. Understanding the patient factors that determine vaccination intention is crucial to delivering a successful vaccination programme. Using a modified Health Belief Model (mHBM), we conducted a cross-sectional survey with the objective of exploring the sociodemographic and psychological factors that determined autologous and allogeneic HSCT recipients' intention to receive the seasonal inactivated influenza vaccine (SIIV) during the 2015-2016 influenza season.

Setting: The setting of our study was three tertiary-level, UK NHS autologous and allogeneic HSCT centres.

Participants: Eligible patients were aged 16 years or over and recipients of autologous or allogeneic HSCT for any disease indication, with no absolute contraindication to receiving the SIIV during the next influenza season, and having not received the SIIV since transplant. 93 participants from 3 UK NHS HSCT centres completed an anonymous study-specific questionnaire. 78.5% were recipients of allogeneic and 21.5% autologous HSCT.

Results: 23.7% of participants expressed low intent to receive the SIIV. patients aged over 65 (OR 0.02, 95% CI 0.01-0.57, p=0.02) and those who had not received the SIIV prior to HSCT (OR 0.04, 0.02-0.56, p=0.02) were less likely to have high intent. A multivariate logistic regression model incorporating constructs of the mHBM was statistically significant (p<0.001) and explained 74.7% of variation in SIIV intention. More patients felt that a recommendation from their HSCT team than their General Practitioner would prompt them to receive the SIIV, and this was most pronounced in those who had low intent.

Conclusions: The mHBM may provide a useful structure for addressing low vaccine intent amongst HSCT recipients and further interventional studies are warranted. We would encourage HSCT and General practitioners to discuss SIIV intention as a routine part of care.

HRA REC reference 16/WM/0144

Strengths of Study

- The study questionnaire was based on the established theoretical framework of the Health Belief Model, and questions were specific with regard to vaccine and 2015-2016 season.

-Participants from 3 geographically dispersed study sites completed anonymous questionnaires

Limitations

-The study explored intention to receive the inactivated influenza vaccine during the 2015-2016 influenza season. Uptake was not assessed and may differ from intention rates.

-The number of enrolled participants expressing low vaccination intent was small at 22 (23.7%) and this may bias our data.

-The study did not include a qualitative component and there may be additional determinants of influenza vaccine intention not captured here.

Introduction

Innate and adaptive immune responses are impaired for months to years following autologous and allogeneic haematopoietic stem cell transplant (HSCT). Immune impairment following autologous HSCT is secondary to the administration of immunosuppressive conditioning regimens. In the setting of allogeneic HSCT, chronic graft versus host disease (GvHD) may also contribute to immune impairment and dysfunction through thymic atrophy [1,2] and functional hyposplenism [3], and the mainstay of GvHD treatment is immunosuppressive therapy. Infection is therefore an important complication of both autologous and allogeneic HSCT, and recipients are at high risk of morbidity and mortality from influenza viruses[4–6]. Guidelines recommend that the seasonal inactivated influenza vaccine (SIIV) is administered annually starting 4 to 6 months post HSCT [7,8], including patients with GvHD[9] While the SIIV is recommended by 96% of UK NHS allogeneic HSCT programmes[8], uptake rates of only 60-70% in the first 2 years post HSCT have been reported amongst UK HSCT recipients[10,11]. The majority of UK allogeneic HSCT recipients are referred to their General Practitioner (GP) with only 8% of UK adult allogeneic HSCT programmes offering vaccination services. SIIV efficacy of 65.4-80% has been reported in HSCT recipients, although in small cohorts [12,13] In both the UK and USA, physicians' familiarity with current guidelines, and perception of GvHD as a contraindication to vaccination have been identified as factors limiting vaccine uptake rates[10,11,14]. No studies to-date have explored the patient factors that influence SIIV hesitancy or intention in an HSCT recipient population.

The Health Belief Model (HBM) is a widely used framework for investigating psychosocial determinants of health behaviours[15] and is recognized as an

important predictor of influenza vaccination uptake[16]. The HBM proposes that an individual's engagement in a specific preventative health behaviour is predicated on the following constructs: i) perceived susceptibility to the illness, ii) perceived likelihood of contracting the illness, iii) perceived seriousness of the illness, iv) perceived barriers to engaging in the health behaviour, v) perceived benefits of the health behaviour, vi) cues to engage in the health behaviour such as advice from a healthcare practitioner and, vii) self-efficacy or the individual's perception of their capability to engage or succeed in the behaviour. Additional emotional constructs may modify the HBM. In particular, worry may modify the impact of perceived risk of illness; a patient may perceive themselves to be at risk, but unless this is something that worries them they may not engage in a preventative behaviour[17]. Furthermore, anticipated regret of illness if a health behaviour is not performed is also recognized as a predictor of intent[18].

The objective of this study was to explore the sociodemographic factors, and the vaccine and vaccination-specific health-beliefs that are associated with SIIV intention amongst HSCT recipients, using a HBM modified with the additional emotional constructs given above (mHBM). A better understanding of such associations may allow development of targeted strategies that address issues specific to this unique and complex patient group, with the aim of increasing influenza vaccine uptake rates.

Participants and Methods

Participants

Patients were screened by HSCT nurse specialists for study eligibility during routine outpatient appointments between June and September 2016. Participants were recruited from 3 study sites to reduce geographical bias. Eligible patients were aged 16 years or over and recipients of autologous or allogeneic HSCT for any disease indication, with no absolute contraindication to receiving the SIIV during the next influenza season, and having not received the SIIV since transplant. All participants gave written informed consent. The study was approved by the Health Research Authority National Research Ethics Committee (Reference 16/WM/0144)

Study Questionnaire and Health Belief Model

Participants completed a study-specific, 42-item, paper-based questionnaire. The questionnaire was completed anonymously and returned in sealed envelopes, so participants felt free to express their belief without influence from their healthcare team.

Questions scoped type of HSCT (autologous or allogeneic), disease indication, time from HSCT, pre-HSCT SIIV receipt, and receipt of non-SIIV vaccines since HSCT. Sociodemographic questions established age, gender, ethnic background, educational attainment, relationship status and residential circumstances.

Intention to receive the SIIV during the 2016-2017 influenza season, was assessed by 2 statements phrased in the affirmative (I intend to receive the flu vaccine next winter) and negative (I will choose not to receive the flu vaccine next winter). Participants' agreement with each statement was expressed on 5-point Likert scales ranging from strongly disagree to strongly agree.

24 health belief statements were mapped to the mHBM with between 2 and 5 statements clustered around each construct (Table 1). Statements pertaining to the cues to vaccination construct were phrased to explore perception of HSCT team and GP knowledge of SIIV in the context of HSCT. Participants' perceived impact of a recommendation to receive the SIIV from their HSCT team or GP was explored. Statements about preferred vaccination location and ease of access to services were also included. Again, participants' agreement with each statement was expressed on 5-point Likert scales ranging from strongly disagree to strongly agree.

Statistical Analysis

Statistical analysis was performed with IBM SPSS version 24.

For the dependent variable vaccination intention, participants' agreement scores were summed and dichotomised to a 'high intent' group (intention score > than neutral value) and a 'low intent' group (intention score ≤ to the neutral value).

Categorical patient characteristics and sociodemographic factors are reported as frequencies and percentages. Associations between these variables and SIIV intention was examined with Pearson's chi-squared test, and Fisher's exact test when expected values were less than 5.

Internal scale reliability for each cluster of mHBM construct statements was assessed using Cronbach's α. A value of >0.6 was considered indicative of

197 *Table 1:Health belief statements grouped by construct with associated Cronbach's Alpha Value*

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Health Belief Model Construct (Cronbach's Alpha)
1.Susceptibility to seasonal influenza (α = 0.83)
Now I have had a stem cell transplant I can catch the seasonal flu more easily than other people my age
Now I have had a stem cell transplant I can catch the seasonal flu more easily than before my transplant
2.Likelihood of catching seasonal influenza (α = 0.91)
My chances of catching seasonal flu next winter will be high if I do not receive the seasonal flu vaccine
I am more likely than other people my age to catch seasonal flu next winter if I do not receive the seasonal flu vaccine
Now I have had a stem cell transplant it is more likely that I will catch seasonal flu next winter if I do not receive the seasonal flu vaccine
3.Severity of seasonal influenza infection (α = 0.91)
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter this would be a serious illness for me
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter this would have a negative impact on my recovery from my stem cell transplant
If I do not receive the seasonal flu vaccine and caught the seasonal flu next winter I would become more unwell than other people my age
4.Barriers to vaccination (α = 0.84)
I am worried about side effects of the seasonal flu vaccine
If I receive the seasonal flu vaccine next winter it may make me feel unwell with the flu or a flu-like illness
If I receive the seasonal flu vaccine next winter I am more likely to experience side effects than other people my age
If I receive the seasonal flu vaccine next winter it may have a negative impact on my recovery from my stem cell transplant
Now I have had a stem cell transplant the seasonal flu vaccine may not work as well for me as it does for other people my age
5.Benefits of vaccination (α = 0.66)
If I receive the seasonal flu vaccine next winter it may help to prevent me from catching the seasonal flu
If I receive the seasonal flu vaccine next winter it may help to prevent me from passing the seasonal flu to other people around me
If I receive the seasonal flu vaccine next winter, but still catch the flu, it may help to prevent me from becoming seriously unwell
6.Cues to vaccination (α = 0.76)

If my transplant team advised me to receive the seasonal flu vaccine next winter I would definitely have it
If my GP advised me to receive the seasonal flu vaccine next winter I would definitely have it
My GP understands my condition enough to know if the seasonal flu vaccine is right for me
My transplant team understand my condition enough to know if the seasonal flu vaccine is right for me
7.Worry (α = 0.47)
If I receive the seasonal flu vaccine next winter I will worry less about catching the seasonal flu
The thought of catching seasonal flu next winter worries me
8.Self-efficacy (α = 0.29)
I have enough information and am able to decide whether the seasonal flu vaccine is right for me
I would find it easy to attend my GP surgery next winter to receive the seasonal flu vaccine
9.Anticipated regret (α = 0.15)
I would regret it if I decided not to receive the seasonal flu vaccine next winter and became unwell with seasonal flu
I would regret it if I decided to receive the seasonal flu vaccine next winter and became unwell with side effects

acceptable internal scale reliability [19]. Scale reliability was acceptable for constructs 1-6 (Table 1) and statement scores were summed to give total construct scores for each participant. Scale reliability was unacceptable for constructs 7-9 (Table 1) therefore statements were analysed individually. All construct scores were analysed as continuous scales, with zero representing a neutral response (neither agree nor disagree). Mean agreement scores for low and high intent groups are presented with 95% confidence intervals.

Participants' mean agreement scores for each mHBM construct were compared between SIIV intention groups using Analysis of Variance (ANOVA). Homogeneity of variances was confirmed with Levene's statistic. HSCT team and GP cue scores *within* low and high intent groups were compared with a paired sample T-Test.

The impact of sociodemographic variables and health belief constructs on seasonal influenza vaccination intention was examined with hierarchical binary logistic regression. Variables and constructs that were statistically significant in univariate analysis were included as separate regression blocks. Statistically significant variables that improved the predictive value ($p<0.05$ for the regression block) were included in the final model.

The assumption of a linear relationship between each independent variable and log of the outcome variable was tested and confirmed using the Box-Tidwell procedure[20]. Multicollinearity across all constructs was assessed. No variance

inflation factor was greater than 10, and the mean of values was acceptable at 1.92[21].

There were 10 missing data points from 6 participants across the study. These were all responses to mHBM statements from the high intent group. Summed agreement scores were not calculated for that participant for the affected HBM construct only.

Patient and Public Involvement

The study questionnaire was developed with the involvement of volunteers from the Anthony Nolan patients and families panel. Using an initial draft questionnaire, think-aloud sessions were conducted to ensure that the questionnaire was clear, easy to understand, that interpretation of each question was as intended, and that answers were consistent with the question asked. Volunteers were also asked for their overall feedback on the study questionnaire. The revised questionnaire was then piloted with volunteer patients who were asked to complete the questionnaire, keeping note of the time taken, and to highlight any questions that they had difficulty answering or otherwise found problematic. The questionnaires were all completed within 10 minutes and no participants reported difficulty or concerns about the questions. Results will be disseminated to study participants through their transplant teams, and made available to participants through open access publication.

Results

Patient Characteristics

Characteristics of 93 study participants are given in Table 2. 78.5% were recipients of allogeneic HSCT and the most frequent disease indication was acute myeloid leukaemia (AML) (28.0%). The majority (68.6%) were within the first 6 months post HSCT. 40.9% of participants had received the SIIV before HSCT, and 4.3% had received a non-influenza vaccine since HSCT. 52.7% of participants were male, and most (84.9%) were of a white ethnic group.

SIIV vaccination intention for 2016-2017 influenza season

71 (76.3%) participants expressed high SIIV intent, while 22 (23.7%) expressed low SIIV intent.

*Table 2: Characteristics of n=93 study participants. *Statistically Significant (p<0.05)*

Characteristic, n=93	n(%)	high SIIV Intent n(%)	p
Gender			
Male	49 (52.7)	40 (81.6)	
Female	44 (47.3)	31 (70.5)	0.23
Age group			
16-34	22 (23.7)	15 (68.2)	

35-54	36 (38.7)	33 (91.7)	
55-64	20 (21.5)	15 (75)	
65+	15 (16.1)	8 (53.5)	0.02*
HSCT Type			
Allogeneic	73 (78.5)	59 (80.8)	
Autologous	20 (21.5)	15 (75)	0.78
Disease Indication			
Acute lymphoblastic leukaemia (ALL)	11 (11.8)	8(72.7)	
Acute myeloid leukaemia (AML)	26 (28.0)	20 (76.9)	
Aplastic Anaemia (AA)	5 (5.4)	3 (60)	
Chronic myeloid leukaemia (CML)	5 (5.4)	5 (100)	
Hodgkin Lymphoma	9 (9.7)	9 (88.9)	
Myelodysplastic syndrome (MDS)	5 (5.4)	3 (60)	
Myelofibrosis (MF)	2 (2.2)	1 (50)	
Multiple myeloma (MM)	22 (23.7)	17 (77.3)	
Non-Hodgkin Lymphoma (NHL)	8 (8.6)	6 (75)	0.79
months from HSCT			
0-6	64 (68.8)	52 (81.3)	
>6-12	20 (21.5)	14 (70)	
> 12	9 (9.7)	5 (55.6)	0.18
SIIV before HSCT			
Yes	38 (40.9)	34(89.5)	
No	55 (59.1)	37 (67.3)	0.01*
Any non-SIIV vaccine since HSCT			
Yes	4 (4.3)	4 (100)	
No	89 (95.7)	67 (75.3)	0.26
Ethnicity			
White	79 (84.9)	69 (77.2)	
Asian	8 (8.6)	7 (87.5)	
Black	3 (3.2)	2 (66.7)	
Mixed	2 (2.2)	1 (50)	
Other	1 (1.1)	0 (0)	0.32
Educational Background			
Higher Education	30 (32.3)	24 (80)	
Secondary Education	49 (52.7)	40 (81.6)	
Other	3 (3.2)	2 (66.7)	
Prefer not to answer	11 (11.8)	5 (45.5)	0.07
Living Circumstances			
Renting	25 (26.9)	33 (76)	
Home Owner	54 (58.1)	43 (79.6)	
Other	10 (10.8)	7(70)	
Prefer not to answer	4 (4.7)	2 (50)	0.56
Relationship Status			
Single	23 (24.7)	18 (78.3)	
Married / Cohabiting	56(60.2)	45 (80.4)	
Divorced / Separated	10 (10.8)	5 (50)	

Prefer not to answer	4 (4.4)	3 (75)	0.22

Sociodemographic and Transplant Variables

There was a statistically significant difference in SIIV intention between age groups (Table 2). Rate of high intent was greatest in the 35-54 age group at 91.7%, and lowest at 53.3% in the 65+ age group. There was no statistically significant difference in gender, ethnicity, educational background, living circumstance, or relationship status between SIIV intention groups.

There was no difference in type of HSCT or disease indication between SIIV intention groups. 81.3% of participants answering within the first 0-6 months post HSCT had high intent, compared with 70% in those answering at 6-12 months, and 55.6% among those answering at >12 months from HSCT, however this finding was not statistically significant. To determine whether there was a difference in health beliefs between participants at different time points post HSCT, mean agreement scores for all constructs were compared. There was no difference in mean agreement scores between participants at 0-6 and 6-12 and >12 months post HSCT.

There was no association between SIIV intention and receipt of any non-influenza vaccine since HSCT. However, of those who had received the SIIV prior to HSCT 81.3% had high intent compared with 67.3% of those who had not .

Health Belief Model Constructs

In univariate analysis, comparing mean construct agreement scores between SIIV intention groups, participants in the high intent group perceived greater susceptibility to influenza, a greater likelihood of contracting influenza and perceived influenza to be a more severe illness (Table 3). They also perceived greater potential benefit from vaccination, and fewer barriers to vaccination. Although the two groups expressed similar levels of worry about catching influenza, participants in the high intent group felt they would worry less about catching influenza if vaccinated compared with the low intent group. They also expressed greater concern about anticipated regret if they caught influenza having not been vaccinated. Level of anticipated regret of experiencing side effects if vaccinated was similarly low across the two groups. Participants in the high intent group felt more strongly that they had enough information to make decisions about vaccination and that it would be easy to attend their general practice surgery for vaccination.

Table 3: Mean agreement score values for health belief constructs for low and high SIIV intent groups. [a]*n=68,* [b]*n=69,* [c]*n=70*

Health Belief Model Construct		Low SIIV Intent (n=22)	High SIIV intent (n=71)	p
1.Susceptibility to seasonal influenza		0.05 (-0.70 to 0.70)	2.09 (1.75 to 4.39)	<0.001
2. Likelihood of catching seasonal influenza		-0.45(-1.39 to 0.40)	2.58 (2.00 to 3.18) [b]	<0.001
3. Severity of Seasonal influenza infection		0.77 (-0.17 to 1.72)	2.65 (2.09 to 3.23) [b]	0.002
4. Barriers to vaccination		1.27 (0.11 to 2.44)	-1.55 (-2.34 to -0.80)[a]	0.001
5. Benefits of vaccination		-0.05 (0.00 to 1.78)	2.56 (2.13 to 3.00)	<0.001
6. Cues to Vaccination				
	HSCT team understands my condition	1.14 (0.55 to 1.32)	1.63 (1.52 to 1.75)	<0.001
	GP understands my condition	-0.32 (0.83 to 0.13)	0.59 (0.55 to0.83)[c]	<0.001
7. Worry				
	About catching influenza	0.14 (-0.43 to 0.71)	0.39 (0.17 to -0.63)	0.34
	Less about catching influenza if vaccinated	-0.23 (0.60 to 0.07)	0.80 (0.61to 1.00)	<0.001
8. Self-efficacy				
	Have enough information to decide about vaccination	0.14 (-0.32 to 0.58)	0.81 (0.61 to 1.00)	0.007
	Would find it easy to attend GP for vaccination	0.32 (-0.12 to 1.72)	1.10 (1.89 to 2.00)	<0.001
9. Anticipated regret				
	of catching flu if not vaccinated	0.27 (-0.21 to 0.74)	1.35 (1.18-1.52)	<0.001
	of side effects if vaccinated	-0.09 (-0.15 to 0.37)	0.13 (-0.12 to 0.39)	0.4

A multivariate regression model (Table 4) was statistically significant when compared with a constant only model indicating that this set of variables and constructs distinguishes reliably between HSCT recipients who express low and high SIIV intent. There was a moderately strong relationship with 74.7% (Nagelkerke R^2) of variation in vaccination intention explained by the overall model. GP and HSCT Team cues to

vaccination, self-efficacy and anticipated regret constructs did not significantly improve predictive value and so were not included in the final model. Age and pre-HSCT SIIV vaccination receipt remained independent predictors of SIIV intention, with those aged >65 and those who had not received SIIV before HSCT more likely to be in the low intent group. A greater perceived benefit of vaccination was the strongest predictor of being in the high intent group. Although the constructs susceptibility to influenza, likelihood of contracting influenza, severity of influenza infection, barriers to vaccination and worry about catching influenza improved the predictive value of the overall multivariate model, they did not independently predict vaccination intention.

*Table 4 Multivariate logistic regression model predicting odds of high SIIV intent. Overall model was statistically significant compared with a constant only model (p<0.001). *Statistically significant independent predictor (p<0.05)*

Variable	Odds Ratio of high SIIV Intent (95% CI)	p
Age >65	0.02 (0.01-0.57)	0.02*
No SIIV before HSCT	0.04 (0.02-0.56)	0.02*
Benefits of vaccination	2.96 (1.29-6.81)	0.01*
Susceptibility to seasonal Influenza	0.96 (0.33-2.78)	0.64
Likelihood of catching seasonal influenza	1.68 (0.86-3.26)	0.13
Severity of seasonal influenza infection	0.69 (0.39-1.21)	0.20
Barriers to vaccination	0.69 (0.57-0.99)	0.05
Worry less about catching seasonal influenza if vaccinated	4.99 (1.01-24.77)	0.05

Cues to Vaccination and Preferred Vaccination Location

Considering their HSCT team and GPs, both high and low intent groups agreed more strongly with statements that their HSCT team understands their condition enough to know if the influenza vaccine is right for them. Patients were also asked how much they agreed with the statement that they would definitely have the vaccine if their GP or HSCT team recommended it. Agreement scores were dichotomized to low agreement (≤ neutral value) and high agreement (>neutral value). Of those 22 patients with low intent, 90% agreed that they would receive the vaccine if their HSCT Team recommended it, and only 22.7% if their GP recommended it, compared with 98.6% and 90.0% respectively in the high intent group.

Participant responses to the statement *I would prefer to have the seasonal influenza vaccine next winter at my transplant centre instead of my GP surgery* were categorized into prefers HSCT centre, prefers GP surgery or no preference. Of the low intent group, over half (54.5%) favoured vaccination at their HSCT centre, with only a minority (4.5%) favouring vaccination at their GP surgery. Of those with high intent 43.7% favoured vaccination at their HSCT programme, compared with 29.6% at their GP surgery although these findings did not reach statistical significance (p=0.05).

Discussion

This is the first study to explore sociodemographic factors and psychological determinants of SIIV intention amongst HSCT recipients Approximately a quarter of participants expressed low SIIV intent which is in keeping with previously reported SIIV uptake rates of 60-70% [10,11] Participants' SIIV uptake during the 2016-2017 UK influenza season was not evaluated, and uptake in this cohort may not be equivalent to intent rates reported here.

Constructs of a mHBM were significant determinants of SIIV intention. Strategies tailored to a population and their specific concerns are the most effective at improving knowledge and changing attitudes towards vaccination, and increasing vaccine uptake[22]. Based on our findings, the mHBM may provide a useful framework for structuring strategies to address low SIIV intent in the HSCT population. Exploring HSCT recipients increased risk of influenza, both in terms of

susceptibility and severity, discussing the potential benefits of vaccination, and exploring concerns around side effects may help to promote vaccine intent and uptake.

A strong association between past vaccination behaviours and future vaccination intent has been reported[23]. Previous influenza vaccination has been associated with high intent or uptake in all at risk groups [24,25] and cancer patients[26] and our findings accord with this. It may therefore be helpful to explore recipients pre-HSCT SIIV behaviour and discussion rationale for refusal where appropriate.

It was reassuring to find that none of gender, ethnicity, educational background, living circumstances or relationship status were associated with vaccine hesitancy in this study. However, vaccination intention did vary with age. High intent was greatest at 91.7% in the 35-53 age bracket, but of concern, fell in those over 65 to 53.5%, which is below the 2015-2016 uptake rate of 71% in the equivalent UK general population age-group[27]. Older age has been reported as a barrier to vaccination in a cohort of oncology patients, including some with haematological malignancy [26]. However, a French study of patients with secondary immunodeficiency, including haematological disorders, reported higher vaccination rates in those aged over 65 compared with younger patients[28]. In a UK study, older age was found to be a predictor of uptake of the 2009 pandemic influenza A vaccine amongst high-risk adults[29]. A meta-analysis of international studies found inconsistent association between age and vaccination intent and uptake in the general public, older patients, and those with chronic disease [23]. It is not apparent

from these studies why age impacts on intent, and there are likely to be a range of social, psychological, financial and healthcare access issues specific to each study population. Our findings highlight a specific age group in whom intent is low and may benefit from targeted intervention. Further evaluation of this finding and exploration of underlying determinants is warranted.

High SIIV intent was greatest in those recipients within the first 0-6 months' post-HSCT (81.3%) and lowest at more than 12 months (55.6%) although this finding was not statistically significant. Longer time from HSCT may be associated with a change in perceived risk of infection, or concern about vaccine side effects or efficacy; however, we did not detect any statistically significant difference in health beliefs at 0-6, 6-12 and > 12 months from HSCT. This finding suggests there is a need for reinforcement of SIIV intent from healthcare professionals throughout and beyond the first-year post HSCT.

In both vaccine intention groups, patients expressed greater confidence in their HSCT team than their GP, with respect to understanding of whether the influenza vaccine is right for them. Fewer patients felt that a recommendation from their GP would prompt them to receive the SIIV compared with if their HSCT Team made the recommendation. This was most marked in the low intent group. These findings suggest that cues from the HSCT team are important in promoting vaccination amongst HSCT recipients, and particularly for those with low intent. Cues from healthcare providers are considered a key factor in promoting vaccination[23] and a study of Israeli cancer patients identified recommendation from an oncologist as a

significant predictor of vaccine uptake [26]. Our findings accord with this, and suggest that HSCT recipients value the advice of their specialist team. This highlights the importance of HSCT specialists engaging in discussion with patients about influenza vaccination. Preference for vaccination at HSCT centre rather than GP surgery was similar at 43.7% and 54.5% in low and high intent groups respectively. In the high intent group, more patients expressed a preference for vaccination at their GP surgery than in the low intent group. For approximately 50% of those HSCT recipients with both low and high intent, access to an SIIV service at HSCT centres may facilitate vaccination uptake

None of the transplant variables assessed were associated with SIIV intention. Current influenza vaccination guidelines are standardized for all HSCT recipients as evidence is insufficient to recommend modification according to donor type, stem cell source or conditioning[7,30]. Influenza infections are reported to occur with higher frequency in allogeneic compared with autologous HSCT recipients [31,32] and may have a higher associated morbidity and mortality[33] although this latter finding has not been consistently reported[4]. There was no difference in vaccination intention between autologous and allogeneic HSCT recipients. This suggests the unique aspects of allogeneic HSCT, principally GvHD and the need for immunosuppressive therapy, do not contribute to increased influenza vaccination intention in this group compared with autoHSCT recipients.

Strength and Weaknesses of the Study

Our study was developed from an established theoretical framework for exploring health beliefs. Think-aloud sessions and a pilot exercise ensured that the questionnaire was easy to understand and acceptable to participants. By completing the questionnaire anonymously, participants were encouraged to respond according to their own beliefs without influence by their healthcare team. By recruiting from 3 study sites we sought to capture the beliefs of participants with different experiences of post HSCT care, reduce the impact of geographical bias and render our results more generalizable to the UK HSCT population. The study did not include a qualitative component and there may be additional determinants of influenza vaccine intention not captured here. Data on non-responders was not captured and therefore we cannot exclude a participation bias. The small absolute number of participants expressing low SIIV intent in our study may bias our data.

Conclusion

Our data indicate that the constructs of a mHBM are important determinants of SIIV intention in the HSCT recipient population. These constructs may be used to develop interventions addressing low SIIV intent, for example, SIIV uptake amongst HSCT recipients may be promoted by public health authorities and patient support groups with messages adapted from our findings. Future prospective studies to investigate the efficacy of such intervention are warranted. HSCT recipients strongly value the expertise and recommendation of their transplant team, and we would encourage practitioners to discuss SIIV intention with all patients as a routine and

important aspect of post-transplant care. Furthermore, those aged over 65, and those who had not received the SIIV prior to HSCT were particularly likely to have low intent and may be target groups. Local provision of vaccination services at HSCT centres may serve as an additional promoter for a proportion of patients and this would require allocation of resources from health commissioners.

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Authorship Statement

Paul D E Miller, Alice S Forster, Thushan I de Silva, Karl Peggs, Alejandro Madrigal and John A Snowden all contributed substantially to the design, analysis, and interpretation of data. Hayley Leonard, Chloe Anthias, Michaela Mayhew, Matthias Klammer, Erin Hurst and Susan Paskar all contributed substantially to the acquisition of data. All authors contributed to drafting the work and/or revising it critically for intellectual content. All authors gave final approval of the version to be published.

Data sharing statement

No additional data available

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Abstract line 41-43
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Abstract line 36-71
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Introduction Line 103-141
Objectives	3	State specific objectives, including any prespecified hypotheses Introduction line 143-146
Methods		
Study design	4	Present key elements of study design early in the paper Method Section
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection line 155-162
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants line 157-160
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Line 169-188
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Line 169-188
Bias	9	Describe any efforts to address potential sources of bias lines 157-158 and 168-170
Study size	10	Explain how the study size was arrived at N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why. Lines 197-199, 213-216
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding lines 218-229
		(*b*) Describe any methods used to examine subgroups and interactions N/A
		(*c*) Explain how missing data were addressed Lines 237-240
		(*d*) If applicable,describe analytical methods taking account of sampling strategy N/A
		(*e*) Describe any sensitivity analyses N/A
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Line 264
		(b) Give reasons for non-participation at each stage N/A
		(c) Consider use of a flow diagram N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Table 2
		(b) Indicate number of participants with missing data for each variable of interest Table 3
Outcome data	15*	Report numbers of outcome events or summary measures line 273-274
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included Table 3 and Table 4
		(*b*) Report category boundaries when continuous variables were categorized Table 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses N/A
Discussion		
Key results	18	Summarise key results with reference to study objectives Line 380-382
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. Lines 385-393
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence . Line 387-463
Generalisability	21	Discuss the generalisability (external validity) of the study results Line 486-489
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based – line 30-32

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.