Supplementary Material

Definitions of variables for difference-in-difference study

Exposures and covariates

This study will be done using the dataset Hospital Episode Statistics. The primary exposure is whether iHOST is implemented at the hospital where the patient was admitted. Covariates (potential confounders) will be:

- Age at last birthday (calculated using ADMIDATE and DOB).
- Sex; male, female, or other (SEX).
- Ethnicity; summarised as (a) White British; (b) white other; (c) Asian or Asian British; (d) Black or Black British; (e) Mixed; (f) other (ETHNOS).
- The primary cause of admission (DIAG_01), defined using the ICD-10 code:

Grouped cause of admission (used in the analysis)	Subgroup 1	Subgroup 2	ICD-10 codes
1. 'Drug-related', including withdrawal, intoxication and overdose	Mental and behavioural disorders	Mental and behavioural disorders due to use of opioids, cannabinoids, sedatives or hypnotics, cocaine, other stimulants, hallucinogens, volatile substances, and multiple/other substances	F11-F16; F18, F19
	Poisoning	Poisoning by drugs, medicaments and biological substances	T35-T50
		Accidental poisoning by and exposure to noxious substances	X40-X49
2. Injecting-related injuries and diseases	Skin and soft tissue infections	Gas gangrene	A48.0
		Cutaneous abscess, furnuncle and carbuncle	L02.X
		Cellulitis	L03.X
		Other specified local infections of skin and subcutaneous tissue	L08.8
		Local infection of skin and subcutaneous tissue, unspecified	L08.9
		Ulcer of lower limb, NEC	L97
		Chronic ulcer of skin, NEC	L98.4
		Other specified disorders of skin and subcutaneous tissue	L98.8
		Disorder of skin and subcutaneous tissue, unspecified	L98.9
		Necrotizing fasciitis	M72.6
		Gangrene, NEC	R02
	Sepsis and bacteraemia	Streptococcal sepsis	A40.X
		Other sepsis	A41.X
		Septic shock	R57.2
		Candidal sepsis	B37.7
	Endocarditis	Candidal endocarditis	B37.6
		Acute and subacute infective endocarditis	I33.0
		Acute endocarditis, unspecified	I33.9
		Mitral (valve) insufficiency	I34.0
		Nonrheumatic mitral (valve) stenosis	I34.2
		Other nonrheumatic mitral valve disorders	I34.8
		Nonrheumatic mitral valve disorder, unspecified	I34.9
		Nonrheumatic aortic valve disorders	I35.X

Grouped cause of admission (used in the analysis)	Subgroup 1	Subgroup 2	ICD-10 codes
		Nonrheumatic tricuspid valve disorders	I36.X
		Pulmonary valve disorders	I37.X
		Endocarditis, valve unspecified	I38
		Endocarditis and heart valve disorders in diseases classified elsewhere	I39.X
		Infection and inflammatory reaction due to cardiac valve prosthesis	T82.6
	Septic arthritis	Pyogenic arthritis	M00.X
	Osteomyelitis & vertebral discitis	Osteomyelitis	M86.X
		Osteomyelitis of vertebra	M46.2
		Infection of intervertebral disc (pyogenic)	M46.3
		Discitis, unspecified	M46.4
		Disorder of bone, unspecified	M89.9
	Central nervous system infections	Intracranial abscess and granuloma	G06.0
		Intraspinal abscess and granuloma	G06.1
		Extradural and subdural abscess, unspecified	G06.2
3. Other bacterial and viral infections		Certain infectious and parasitic diseases	A00-A99, B00-B99, (Excluding codes 2.)
		Acute upper respiratory infections; Influenza and pneumonia	J00-J18
4. Accidents other than drug-related accidents, including self-harm		Injury, poisoning and certain other consequences of external causes, External causes of morbidity and mortality	S00-S99, T00-T99, V00-V99, W00-W99, X00-X99, Y00-Y00 (Excluding codes in 1.)
5. Mental and behavioural disorders		Mental and behavioural disorders	F00-F99 (Excluding codes in 1.)
6. 'Signs and symptoms', which relates to admissions that have recorded symptoms such as abdominal pain or convulsions, but no formal diagnosis		Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	R00-R99
7. Cancers		Neoplasms	C00-C99, D00-D99
8. Other non-communicable diseases		Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	D00-D99
		Endocrine, nutritional and metabolic diseases	E00-E99
		Diseases of the nervous system	G00-G99 (Excluding codes in 2.)
		Diseases of the eye and adnexa	H00-H59
		Diseases of the ear and mastoid process	H60-H99
		Diseases of the circulatory system	I00-I99 (Excluding codes in 2.)
		Diseases of the respiratory system	J00-J99 (Excluding codes in 3.)
		Diseases of the digestive system	K00-K99
		Diseases of the skin and subcutaneous tissue	L00-L99 (Excluding codes in 2.)
		Diseases of the musculoskeletal system and connective tissue	M00-M99 (Excluding codes in 2.)
		Diseases of the genitourinary system	N00-N99
9. Other		Pregnancy, childbirth and the puerperium	O00-O99
		Certain conditions originating in the perinatal period	P00-P99
		Congenital malformations, deformations and chromosomal abnormalities	Q00-Q99

- Comorbidity, defined as the number of unique ICD-10 chapters recorded during the admission, using all diagnosis fields (DIAG_NN).

- Day of the week, time-varying during the admission; Monday-Friday (ADMIDATE and DISDATE).
- Hospital; for list of included acute hospitals (PROCODET / SITETRET – codes at https://github.com/danlewer/ihost/tree/main/hes_study/lookups).
- Proportion of all beds at the hospital that are occupied by patients with COVID-19 (DIAG_01).

Outcomes

The study will have two primary outcomes:

1. Discharge against medical advice, defined as DISMETH = 2.
2. Emergency admission or A&E visit at any hospital within 28 days of discharge.

Limitations for difference-in-difference study

- **Reusing controls**. The effect of iHOST will be estimated for each iHOST site separately, using the same set of control hospitals. Formally, this means that estimated effects for each site are not independent. In this case, the uncertainty is dominated by the intervention/iHOST hospitals rather than the controls because the number of control is much greater than the number of intervention sites.
- **Follow-up duration**. For discharge against medical advice, the duration of admission will differ across patients and therefore the follow-up will differ. We considered offsetting the model by the duration of admission or using a survival model (such as a Cox Proportional Hazards model). These models assume, for example, that patients with a 10-day admission have 10 times the risk of patients with a 1-day admission, which may or may not be true. A simpler logistic model that does not account for follow-up duration would consider the outcome as a binary variable for each hospital stay. We decided this would be a better choice because: (a) we have no strong theory that risk accumulates over time; (2) the duration of follow-up is short; (3) even if risk does vary meaningfully with duration, this is likely to be washed-out in the difference-in-difference analysis so probably would not bias the estimated effect of iHOST.
- **Limitations of linear probability model**. The predicted probabilities for patients might lie outside the range of 0,1; and standard errors could be poorly estimated. We will therefore estimate confidence intervals using a nonparametric bootstrap (i.e., by resampling data).
- **Residual confounding**. This could occur if the characteristics of patients at iHOST sites change between the first and second time period (i.e., before and after iHOST implementation), and this change is unmeasured and different to non-intervention sites. For example, if participants at iHOST sites after iHOST implementation are more likely to be homeless than those before iHOST implementation, while participants at control sites have similar prevalence of homelessness before and after iHOST implementation, this may cause bias in the estimate of the effect of iHOST.

- **Other interventions may be implemented at the same time**, either at iHOST or control sites. This will make it difficult to isolate the effect of iHOST. We are not aware of other interventions aiming to improve OST in hospitals. We will likely be aware of any other interventions at iHOST sites (none are planned) and believe it is unlikely that control sites will have similar interventions at a sufficient scale.

- **Background trends may be different in the iHOST and control groups**. The 'parallel trends' assumption can be explored using trends in outcomes over longer time periods (i.e., longer than the 12 months included in the study) before implementation of iHOST. This can be tested statistically using a regression model with an interaction term between iHOST site and time in the pre-iHOST period. However, in a large dataset this term is likely to be significant even with an unimportant deviation from parallel trends. Therefore, we will use a graphical evaluation of common trends in which we plot the frequency of outcomes over time at iHOST and control sites.

- **Spillover effects** in which learning from iHOST is transferred to control sites could dilute the effect of iHOST in our study. To some extent, spillover effects can be seen if there is an "interruption" in the trend in outcomes in the control group.

- **The study will not capture any effect on patients' propensity to seek treatment**. Part of the rationale for iHOST is that people who are dependent on opioids avoid or delay hospital treatment because they anticipate poor opioid agonist therapy. This study investigates outcomes after admission and will not capture any effect on patients' propensity to seek treatment in hospital. If iHOST leads to more patients seeking hospital care or presenting earlier, this may also cause measurable or residual confounding because patients after implementation will differ from those before.

- **The study will include limited outcome measures** of discharge against medical advice and readmission. These outcomes are based on previous research, patient and public involvement, and the availability of data in Hospital Episode Statistics. Other important outcomes may be affected by iHOST, such as the quality of medical treatment, patient satisfaction, continuation of OAT in the community, and use of illicit drugs. Other parts of the evaluation seek to understand broader outcomes.

- **Not all patients that may benefit from iHOST will be included**. We will use ICD-10 diagnoses of opioid dependence to identify participants. Not all patients with a community prescription of OAT will have this diagnosis. Our research using linked primary care and hospital data suggests that approximately 20% of people with a history of illicit opioid use have a diagnosis of opioid dependence when admitted to hospital, and approximately 60% if the admission is for an injecting-related infection. The sensitivity of ICD-10 codes for identifying hospital patients who are dependent on illicit opioids is likely higher than 20%, because opioid use is time-varying and more likely to be recorded in periods of active drug use.

- **HES does not provide the time of admission**. Availability of OAT is likely to vary by time of day and week, with better availability during 'office hours' (i.e., 9am-5pm Monday-Friday). Those admitted at night or at the weekend may be less likely to get timely OAT, with Friday evening sometimes reported as the worst time because OAT

may be delayed until Monday morning. We will include the day of the week but will not be able to distinguish between admissions at different times of day.

- **COVID-19** may affect both implementation of iHOST and interpretation of the evaluation results. iHOST sites are acute hospitals and may need to change the implementation timetable. COVID-19 may affect hospitals differently, and this may affect the probability of discharge against medical advice and readmission. We will attempt to include these effects in our analysis using the proportion of beds that are occupied by patients with COVID-19 as a site-level covariate, though this may not fully control such effects.
- **No data on OST prescriptions**, either in the community or in hospital. Ideally, our study would include patients who had a community OAT prescription prior to admission. We will not have records of community OAT prescriptions and therefore use patients with a diagnosis of 'opioid dependence' as a group that may benefit from iHOST. This may dilute the effect of iHOST because some participants will not have prescriptions of OAT.