

1 **Anti-Hepatitis C (HCV) test positivity and new HCV diagnoses among women tested in**
2 **antenatal services in England between 2015-2019**

3

4 **Objective**

5 To determine associations with hepatitis C virus (HCV) positivity, new HCV diagnoses and
6 subsequent linkage to HCV treatment services among pregnant women in England.

7 **Method**

8 A retrospective cohort using routine laboratory tests for HCV-specific antibody (anti-HCV)
9 and HCV-RNA undertaken during antenatal attendances England. All women receiving at
10 least one anti-HCV test during an antenatal clinic attendance between 2015-2019 were
11 included. Multivariable logistic regression was used to investigate sociodemographic
12 associations with anti-HCV test positivity among pregnant women who did (PWIDs) and did
13 not (non-PWIDs) inject drugs, as well as to identify sociodemographic factors associated
14 with being newly diagnosed during pregnancy. Linkage to antiviral treatment services and
15 treatment outcomes were determined for those women who tested HCV-RNA positive.

16 **Results**

17 32,088 women (median age 32 years, 19,664 (61%) UK-born, 337 (1.1%) PWID) received an
18 anti-HCV test among whom 814 (2.5%) had a positive anti-HCV test (95% confidence
19 interval [2.4-2.7%]). Anti-HCV test positivity was 2.1% [2.0-2.3%] among non-PWIDs and
20 40% [35-46%] among PWIDs. In multivariable analyses among non-PWIDs, anti-HCV test
21 positivity was associated with older age, living in more deprived areas, and varied by
22 ethnicity and country of birth. Among PWIDs, anti-HCV test positivity was associated with
23 older age only. Three hundred and twenty (39%) of the women testing anti-HCV positive
24 were new diagnoses; those who were newly diagnosed were younger and lived in less
25 deprived than those with a prior diagnosis whereas PWIDs were less likely to be newly
26 diagnosed. HCV-RNA positivity was 52% (n=330/640, 95%CI[47.6-55.5%]) among those
27 with an HCV-RNA test within 30 days, and 75% (n=220/293, 95%CI[69.7-79.9%]) of those
28 eligible for treatment had engaged in HCV treatment services after antenatal testing.

29 **Conclusions**

30 Antenatal testing for HCV provides an opportunity for new case findings and engagement
31 with treatment services where needed. Therefore, universal opt-out testing for HCV
32 antenatally should be reconsidered.

33

34 **Keywords:** Hepatitis C virus, antenatal testing, linkage to treatment

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38 **Introduction**

39 In 2016, the World Health Organization (WHO) released a strategy that aimed to eliminate
40 viral hepatitis as a public health threat by the year 2030, as well as reduce the incidence of,
41 and death from, chronic hepatitis (World Health Organization, 2016). It is estimated that
42 internationally 95% of deaths from viral hepatitis are attributable to hepatitis B (HBV) and C
43 (HCV) viruses (World Health Organization, 2016). England has committed to the WHO
44 strategy to eliminate viral hepatitis as a public health threat (The UK Health Security Agency,
45 2022a). In 2020, it was estimated that there were 81,000 people living with chronic HCV
46 infection in England (The UK Health Security Agency, 2022a), the majority of whom either
47 had no history of injecting (n=8,700) or a previous injecting risk only (n=50,200) meaning
48 that they were unlikely to be identified through routine testing in drug and alcohol services.
49 Furthermore, only 30% of people who inject drugs (PWID) sampled in a cross-sectional
50 survey in the UK were aware of their current chronic HCV infection (The UK Health
51 Security Agency, 2022b).

52 HCV has a long progression time, remaining asymptomatic and often undetected for decades
53 before liver cirrhosis may develop (Sweeting et al., 2006). People with HCV in England tend
54 to have a late presentation, with an estimated around half of those with liver cirrhosis being
55 diagnosed in the previous two years (The UK Health Security Agency, 2022a), and 17% of
56 those with HCV-associated end-stage liver disease (ESLD) presenting with this prior to HCV
57 diagnosis (Ireland et al., 2020). Therefore, to prevent future disease burden and transmission
58 of HCV it is important to diagnose promptly with early linkage to care and treatment. New
59 approaches to increase testing coverage outside traditional testing services, such as opt-out
60 screening in accident and emergency departments or antenatal services, are needed to
61 improve treatment coverage and reduce HCV morbidity and mortality (Evans et al., 2018;
62 Selvapatt et al., 2015).

63 Antenatal screening in the UK routinely offers syphilis, HIV and HBV testing (Public Health
64 England, 2020). These are usually done by 10 weeks gestation at an appointment with a
65 midwife in the community or at a hospital ([https://www.nhs.uk/pregnancy/your-pregnancy-
66 care/screening-for-hepatitis-b-hiv-and-syphilis/](https://www.nhs.uk/pregnancy/your-pregnancy-care/screening-for-hepatitis-b-hiv-and-syphilis/)). Acceptance of antenatal HBV screening in
67 2019/20 was 99.8% (657,375 women screened) with a test positivity rate of 3.77 per 1,000
68 women tested and a new diagnosis rate of 0.86 per 1,000 women tested (Public Health
69 England, 2021). In contrast, routine universal HCV testing is not currently recommended as
70 part of antenatal screening, due to a low risk of infant acquisition following childbirth, lack of
71 trial evidence on the efficacy of treatment for HCV in pregnancy, and uncertainty about the
72 prevalence of HCV infection among pregnant women (Solutions for Public Health, 2018).
73 However, national guidance recommends opportunistic risk-based HCV testing within
74 antenatal services for women with risk factors for HCV, such as injecting drug use or being
75 from a country with a high HCV prevalence (National Institute for Health and Care
76 Excellence, 2012). These recommendations are supported by findings from a cross-sectional
77 survey of maternity service providers in England, where the majority of service providers
78 (87%) offered HCV testing to pregnant women with risk factors, which was mostly done via
79 a routine risk assessment; most common risk factors considered were a history of injecting
80 drugs, or a previous diagnosis of hepatitis B or HIV (Vusirikala et al., 2022). Half of those
81 surveyed indicated that where official local guidance for discussing blood-borne virus testing
82 was in place, this guidance did not include guidance on HCV (Vusirikala et al., 2022).

83 Previous research in London found that when adopting a universal HCV testing service, most
84 (73%) of those newly diagnosed would not have been identified through risk-based screening
85 (Ward et al., 2000). More recent research has found a higher prevalence of HCV among
86 women tested antenatally who were born in Eastern Europe, who may not have met routine
87 risk assessment criteria (Cortina-Borja, Williams, Peckham, Bailey, & Thorne, 2016),

88 depending on how the national guidance for testing of people born in countries of
89 intermediate or high prevalence had been implemented at a local level (National Institute for
90 Health and Care Excellence, 2012). In one antenatal clinic in London that has adopted opt-out
91 anti-HCV testing, the test positivity was similar to that of antenatal HBV testing (3.85 per
92 1,000 women tested) (Selvapatt et al., 2015).

93 An international systematic review for HCV case-finding and linkage to care found mixed
94 evidence for the cost-effectiveness of antenatal screening which depended upon the
95 prevalence in the population and successful linkage to HIV services (Public Health England,
96 2019). Antenatal screening for HCV has been demonstrated to be cost-effective in certain
97 areas of the UK, such as London (Selvapatt et al., 2015), although screening was also
98 modelled to be cost-effective in areas of lower HCV prevalence, which may apply to the UK
99 more widely. Given the new era of HCV treatment, where direct-acting antivirals (DAAs)
100 offer a highly effective and tolerable treatment compared to previous interferon treatments
101 (Dore & Feld, 2015; Martin et al., 2013), antiviral treatment for those who are HCV-RNA
102 positive at antenatal screening may not only improve the health of pregnant women, their
103 partners, and their children, but also prevent onwards transmission (Orkin, Jeffery-Smith,
104 Foster, & Tong, 2016). However, treatment for HCV is not currently recommended whilst
105 pregnant and breastfeeding given the lack of large scale studies on safety in pregnancy
106 (Chappell et al., 2020), although longitudinal trials are ongoing (Gupta, Hiebert, Armstrong,
107 Wester, & Ward, 2022). This may act as a barrier to treatment and increase the number of
108 women who do not return for HCV care, particularly women from under-served and
109 marginalised groups like PWIDs (Krans et al., 2016).

110 Using data from the sentinel surveillance of blood borne virus testing (SSBBV) conducted
111 between 2015 and 2019, we investigated HCV testing in antenatal services, and the
112 subsequent linkage into HCV treatment services for those found to be HCV positive. In this

113 article, we investigate sociodemographic factors associated with hepatitis C-specific antibody
114 (anti-HCV) test positivity among women tested as part of antenatal care and factors
115 associated with a new HCV diagnosis among those testing positive. Using data collected
116 through the HCV treatment database we identified those who were referred for treatment, and
117 their corresponding treatment outcome.

118

119 **Methods**

120 The SSBBV in England was established in 2002 (Public Health England, 2020) and captures
121 testing conducted at any one of 23 sentinel laboratories across England. Participating
122 laboratories are estimated to cover approximately 40% of the English population and are
123 broadly representative of most laboratories providing HCV testing. Data collection methods
124 for SSBBV have been described previously (Brant et al., 2007). Demographic and testing
125 data were extracted for females aged 12-49 years tested antenatally for anti-HCV, indicative
126 of current or cleared HCV, from 2015-2019. The test request location and clinical details
127 accompanying the test request were used to distinguish women assumed to be tested for HCV
128 as part of routine antenatal screening from those tested in other settings and for other reasons.
129 For those with multiple tests in the study period, the first antenatal anti-HCV test was used in
130 analyses. Where possible, the date of first HCV infection diagnosis in SSBBV was updated
131 by the routine laboratory reports of HCV. The routine laboratory reports of HCV were linked
132 to SSBBV using full name, NHS (National Health Service) number (a unique identifier used
133 when accessing healthcare across England) and date of birth. Injecting drug use was
134 determined by the reporting of injecting drug use through SSBBV or from information on a
135 previous test for blood borne viruses in a drug service.

136 Deprivation of residence was ascertained using the participant's postcode with indices of
137 deprivation grouped at a small local level (Lower-layer Super Output Areas) into deciles
138 (Ministry of Housing Communities & Local Government, 2019). Deprivation decile of
139 residence was then used as a continuous variable where higher deprivation decile indicated
140 lower deprivation.

141 Among those who were anti-HCV positive, participants who had a positive test in SSBBV or
142 from laboratory reports prior to the antenatal test date were considered to be previously
143 diagnosed, with all remaining participants who tested anti-HCV positive considered to be
144 newly diagnosed with HCV.

145 HCV-RNA testing data from SSBBV were used to identify those with treatment needs among
146 those testing anti-HCV positive (antiviral treatment for HCV is provided to those who are
147 HCV-RNA positive). Linkage to treatment services was determined for all of those with a
148 positive HCV-RNA test within (+/-) 30 days of their anti-HCV positive antenatal test date.
149 Whether treatment had resulted in a sustained virological response (SVR; treatment
150 completion and clearance of HCV) was determined from clinical reporting of treatment
151 outcomes.. To do this, data from SSBBV was linked to the HCV treatment database (2015-
152 2021) by a combination of NHS number, soundex (a coded version of a person's surname),
153 date of birth and gender. Where SVR was not recorded, a negative HCV-RNA test between
154 12 and 52 weeks was used as a proxy for SVR achievement. These analyses were restricted to
155 those who started treatment from 2015-2020 due to reporting delay of SVR for women
156 starting treatment in 2021.

157 *Linkage to live births*

158 Data were linked to the Office of National Statistics registry of live births, a dataset of all
159 women who gave birth in England between 2015-2020, to obtain the mother's country of
160 birth, using a combination of mother's surname, soundex and mother's date of birth.

161 *Public engagement*

162 The findings of the study were presented to a public engagement group to receive feedback
163 and to discuss implications for antenatal care in relation to their own antenatal experiences, as
164 well as potential implications to a change in HCV antenatal testing policy. The group
165 consisted of women who had engaged in antenatal care in the past three years recruited from
166 antenatal services and personal networks.

167 *Ethics*

168 Laboratory diagnosis data are collated and processed by X as part of surveillance of HCV
169 infection and disease. These data collections are covered by Health Service (Control of
170 Patient Information) Regulations 2002 (regulation 3) which makes provisions for the
171 recognition, control and prevention of communicable diseases and other risks to public
172 health. Caldicott approval, an approval process that ensures national guidance of anonymity
173 of healthcare data is upheld, was obtained for the linkage between laboratory reports and the
174 live births dataset.

175 *Statistical Analysis*

176 Statistical analysis was carried out in STATA (version 17). Univariable and multivariable
177 logistic regression analyses were used to investigate sociodemographic factors associated
178 with (i) anti-HCV test positivity among women tested antenatally and (ii) being newly
179 diagnosed among those with a positive anti-HCV test. Due to difference in sociodemographic
180 risk factors for HCV between people who do not inject drugs (non-PWIDs) and PWIDs,

181 regression analyses for the first outcome were stratified by PWID status. Factors where
182 global p-values were <0.1 in univariable analyses were included in the multivariable model.
183 A Kaplan-Meier curve was produced to display the cumulative time to treatment initiation for
184 those who were HCV-RNA positive, stratified by antenatal or prior diagnosis, using R
185 (version 4.1.0). For women who were HCV-RNA positive but not linked to treatment
186 services, follow-up was right-censored on the end date of 31st December 2021. Chi-squared
187 tests were used to compare linkage to treatment, treatment initiation and SVR achievement
188 between women newly diagnosed antenatally and women previously diagnosed.

189

190 **Results**

191 Between 2015-2019, 32,088 females aged 12-49 years received an anti-HCV test within an
192 antenatal service. The median age of women tested was 32 years (range 13-49 years), 61%
193 (n=19,664) were born in the UK and 337 (xx.x%) were PWIDs. Anti-HCV test positivity was
194 2.5% (n=814, 95% confidence interval (95%CI) 2.4-2.7%). Test positivity steadily decreased
195 over the five years from 3.1% in 2015 to 1.8% in 2019.

196 Table 1 displays the results of analyses of sociodemographic factors associated with anti-
197 HCV test positivity among non-PWIDs and PWIDs. Among non-PWIDs, anti-HCV test
198 positivity was 2.1% (n=678/31,751, 95%CI 2.0-2.3%). In the multivariable logistic
199 regression among non-PWIDs increases in age were associated with increased odds of anti-
200 HCV test positivity. Anti-HCV positivity varied by ethnicity whereby being of Asian
201 Bangladeshi, Black or Chinese ethnicity was associated with reduced odds of anti-HCV
202 positivity compared to White British and Irish ethnicity and being of Asian Pakistani
203 ethnicity was associated with increased odds of anti-HCV positivity. Anti-HCV positivity
204 also varied by region of birth where a country of birth in Asia, or Western and Eastern

205 Europe was associated with increased odds of anti-HCV positivity compared to birth in the
206 UK, and an African country of birth was associated with reduced odds of anti-HCV
207 positivity. Additionally, a higher deprivation of residence decile, which indicates residing in a
208 less deprived area, was associated with reduced odds of anti-HCV positivity.

209 Among PWIDs, anti-HCV test positivity was 40% (n=136/337, 95%CI 35-46%). Older age
210 was the only factor significantly associated with an increased odds of anti-HCV test positivity
211 in univariable analyses (Table 1).

212 *New diagnoses*

213 Among those who tested anti-HCV positive, 39% (n=320, 95%CI 36.0-42.8%) had no
214 previous diagnosis in SSBBV or through routine laboratory reports of hepatitis C and were
215 considered to be newly diagnosed. Table 2 displays the associations of sociodemographic
216 factors with a new HCV diagnosis among those testing positive. Due to substantial
217 collinearity between ethnicity and region of birth, only region of birth was entered into the
218 multivariable model. In multivariable logistic regression analyses, being older and being a
219 PWID were associated with reduced odds of the antenatal positive test being a new diagnosis.
220 Being born in Eastern Europe compared to being born in the UK and residing in a less
221 deprived area were associated with increased odds of being a new diagnosis.

222 *HCV-RNA positivity*

223 Among those that tested anti-HCV positive, 79% (n=640/814) of women had had an RNA
224 test within 30 days (71% (n=581/814) within 7 days). There was no significant difference in
225 age (p=0.225), being a PWID (p=0.635), being newly diagnosed with HCV antenatally
226 (p=0.674) and country of birth (p=0.836) between women who received an RNA test within
227 30 days and those who did not, although women who received a test within 30 days were
228 more likely to be of White ethnicity than those who were not tested within 30 days (64% vs.

229 53%, $p < 0.05$). Among women receiving a test within 30 days, 52% ($n = 330/640$, 95%CI 47.6-
230 55.5%) tested HCV-RNA positive. The median age of women testing HCV-RNA positive
231 was 33 years (range 18-49), 63% ($n = 209/330$) were White British and nearly one fifth (18%,
232 $n = 61/330$) were PWID. Overall, 45% ($n = 148/330$) of those who were HCV-RNA positive
233 were newly diagnosed, but among PWIDs, this was only 18% ($n = 11/61$).

234 *Linkage to HCV treatment services*

235 Thirty-six women had already been linked to treatment services prior to testing HCV-RNA
236 positive in their antenatal clinic. Three of these women had received treatment prior to this
237 test, two of whom tested in an antenatal setting within five months of first starting HCV
238 treatment and one who was lost to follow-up from HCV treatment services.

239 There were 293 women eligible for postnatal HCV treatment as 37 women experienced
240 spontaneous clearance of HCV-RNA after antenatal testing (i.e. they tested HCV-RNA
241 negative without treatment), and thus treatment was not required. Of those with a positive
242 HCV-RNA test, 75% ($n = 220/293$, 95%CI 69.7-79.9%) were linked to treatment services after
243 antenatal testing and 71% ($n = 207/293$, 95%CI 65.1-75.8%) had started HCV treatment.

244 Linkage to treatment services was similar ($p = 0.662$) for those who were previously diagnosed
245 (76%, $n = 121/159$) and for those newly diagnosed (74%, $n = 99/159$), with treatment initiation
246 also being similar between the two groups (72%, $n = 114/159$ and 69%, $n = 93/134$, respectively,
247 $p = 0.667$). The median duration between antenatal anti-HCV testing and treatment was 2.3
248 years overall, with no significant difference between those newly diagnosed or previously
249 diagnosed (2.2 vs 2.3 years, $p = 0.52$, log-rank test, Figure 1).

250 Of those that were treated and who received treatment from 2015-2020, the rate of SVR was
251 74% overall ($n = 144/194$, 95%CI 67.5-80.2%), and in those with (78% $n = 69/88$) and without
252 (71%, $n = 75/106$) a new diagnosis ($p = 0.225$).

253

254 **Discussion**

255 This study aimed to investigate HCV antenatal testing in England which is currently not
256 recommended as a universal programme. We found a relatively high test positivity in
257 comparison to HBV antenatal screening (2.5% vs. 0.4%) (Public Health England, 2021),
258 which is not unexpected since risk-based testing was being conducted in the majority of
259 antenatal services. Similarly, the test positivity rate observed in this study was higher
260 compared to an antenatal service offering opt-out HCV testing in London (2.5% vs. 0.4%)
261 (Selvapatt et al., 2015). Over half of those who tested anti-HCV positive also tested HCV-
262 RNA positive, highlighting a need for linkage to care for treatment and partner
263 notification/testing of other children. Given late diagnosis of people with HCV (Ireland et al.,
264 2020; Sweeting et al., 2006; The UK Health Security Agency, 2022a), a large proportion of
265 these women could have been diagnosed earlier, at the time of pregnancy, if opt-out antenatal
266 testing for HCV was in place. Additionally, women born in certain regions that are at
267 increased risk of HCV should have met the inclusion criteria for risk-based screening based
268 on current guidelines (National Institute for Health and Care Excellence, 2012). Therefore, if
269 risk-based screening is to continue in certain regions of England, it is possible that training on
270 at-risk populations may be needed.

271 PWID had a high rate of anti-HCV test positivity (40%) but many of these women had
272 previously received a diagnosis of HCV, and thus this was associated with reduced odds of
273 being newly diagnosed in antenatal settings. However, several women testing HCV-RNA
274 positive were PWID who had been diagnosed previously. Therefore, testing PWIDs for
275 HCV-RNA in antenatal clinics provides an opportunity to support women to re-engage with
276 HCV treatment and care services. Despite the challenges in achieving this (Krans et al.,

277 2016), our study found that two-thirds of women were linked to postnatal HCV treatment, a
278 higher rate than that found in other settings such as emergency departments (Parry et al.,
279 2018).

280 Anti-HCV positivity also varied by ethnicity and country of birth. Similar to previous
281 research in England, being from Eastern Europe was associated with anti-HCV positivity and
282 being newly diagnosed among non-PWID women (Cortina-Borja et al., 2016). Antenatal
283 testing for HCV among women who were born outside the UK can provide an opportunity to
284 diagnose women earlier and to engage in healthcare and treatment, as well as providing an
285 opportunity to reengage in treatment services for those previously diagnosed. Women who
286 had an Asian ethnicity as well as women born in Asia also had increased odds of anti-HCV
287 positivity. It is recommended that these women are screened for HCV antenatally (National
288 Institute for Health and Care Excellence, 2012), but it is unclear how well this guidance is
289 implemented (Vusirikala et al., 2022). Given the complexities of targeting people based on
290 ethnicity and migration status, such as missed (or fewer) opportunities for testing or being
291 perceived as discriminatory or stigmatising, even if antenatal screening is not adopted across
292 England, opt-out testing in more diverse regions could be more appropriate as an alternative
293 to risk-based testing. Additionally, for services that do not adopt opt-out testing, training for
294 midwives may be needed to ensure that populations which may benefit from HCV antenatal
295 testing in addition to PWID are provided with appropriate care.

296 Residing in a more deprived area was associated with an increased likelihood of anti-HCV
297 positivity and a reduced likelihood of a new HCV diagnosis. Utilising HCV antenatal testing
298 in more deprived regions only may result in more anti-HCV test positivity but may fail to
299 diagnose some people with HCV residing in less deprived regions. Therefore, providing opt-
300 out testing regardless of the local level of deprivation would provide an opportunity to
301 support women to access care and treatment services in deprived areas, regardless of their

302 HCV status, and increase the number of women in areas of less deprivation who are aware of
303 their HCV status.

304 Linkage to HCV treatment services was sub-optimal among women testing in antenatal
305 settings, however this may be partially explained by the fact that treatment is not
306 recommended whilst pregnant and breastfeeding (Chappell et al., 2020). This may also
307 contribute to the long period of time between antenatal testing and treatment start. Therefore,
308 ongoing work is needed to ensure women who receive a positive HCV-RNA test in antenatal
309 services are supported to remain in care throughout pregnancy and childbirth, and to have the
310 opportunity for treatment as soon as possible. Whether midwives could play a greater role in
311 terms of ensuring initial engagement with treatment services, regardless of when treatment
312 can be initiated, and helping women to remain engaged with treatment services should be
313 considered. Improving linkage to treatment should be a priority for service providers if HCV
314 antenatal testing is to be cost-effective (Public Health England, 2019). The proportion of
315 those achieving an SVR was similar to that previously reported for England (The UK Health
316 Security Agency, 2022a), which demonstrates a high likelihood of treatment success when
317 women who are diagnosed with HCV antenatally start treatment.

318 We have identified several limitations. The period of 2015-2019 was chosen as 2015 is the
319 baseline year for benchmarking WHO elimination progress and 2020 was excluded to
320 minimize the potential effect of the COVID-19 pandemic and social distancing restrictions on
321 the provision of antenatal testing (Mitchell et al., 2022). However, a limitation of this analysis
322 is that data were linked to the treatment database including during the pandemic (2015-2021).
323 This was reasonable given the median duration between diagnosis and treatment, however,
324 the linkage to care estimate may have been affected by disruption to healthcare services
325 caused by the COVID-19 pandemic. Additionally, the categorisation of a person with a
326 positive HCV test as a new diagnosis and identifying the proportion linked to treatment

327 services were both partly reliant on linkage between databases and therefore true matches
328 may have been missed if data on identifiers or test results were missing or incomplete. The
329 majority of PWID were White British, and therefore our ability to identify risk factors
330 relating to ethnicity and country of birth were limited. Furthermore, as SSBBV is a database
331 of approximately 40% of HCV testing in England, testing conducted outside of these centres
332 and timeframe would not be included in analyses. Despite these limitations, this is a
333 comprehensive analysis of HCV antenatal testing using available surveillance data in
334 England, with important implications for policy.

335 In conclusion, given the new era of DAA treatment for HCV, antenatal testing provides a
336 great opportunity for new case finding and linkage to treatment for women newly and
337 previously diagnosed, as they are engaged in a managed care pathway with follow-up post-
338 partum. We found that while well-known risk factors for HCV, such as injection drug use,
339 were associated with anti-HCV positivity, a risk-based testing approach may miss women
340 with less-frequently considered characteristics indicative of a high risk of HCV infection,
341 such as an endemic region of birth and ethnicity, which are also challenging to assess. Given
342 that around two-thirds of the population that are undiagnosed with HCV in England are not
343 current drug users, antenatal testing may provide an additional method for case finding
344 among a group that is not routinely offered testing (The UK Health Security Agency, 2022a).
345 Additionally, if England is to achieve the WHO targets of reducing morbidity and mortality
346 from HCV, new strategies for case finding and linkage to treatment, like opt-out antenatal
347 testing, should be considered as this will provide not only an opportunity to treat the women
348 tested antenatally, but also their partners and other children who may also require treatment.
349 Modelling studies may help to understand the most effective and cost-effective combination
350 of risk-based and universal screening options to achieve and sustain targets to eliminate HCV
351 as a public health threat.

352

353

Table 1. Univariable and multivariable logistic regression analyses for factors associated with anti-HCV positivity among women tested in antenatal settings.

	People who do not inject drugs (N=31,751)						People who inject drugs (N=337)				
	Anti-HCV negative N=31,073 <i>Mean (SD)</i>	Anti-HCV positive N=678 Row % <i>Mean</i> (<i>SD</i>)	OR (95% CI)	p-value	aOR (95% CI)	p-value	Anti-HCV negative N=201 <i>Mean (SD)</i>	Anti-HCV positive N=136 Row % <i>Mean</i> (<i>SD</i>)	OR (95% CI)	p-value	
Age	32 (6.4)	33.6 (5.9)	1.04 (1.03, 1.05)	<0.0001	1.05 (1.04, 1.06)	<0.0001	32.8 (5.5)	34.4 (5.4)	1.06 (1.01, 1.10)	0.008	
Ethnicity				<0.0001		<0.0001				0.907	
White British/Irish	19,372	378 (1.9%)	ref.		ref.		178	125 (41%)	ref.		
White Other	3,662	144 (3.8%)	2.02 (1.66, 2.45)		1.13 (0.89, 1.44)		9	5 (36%)	0.79 (0.26, 2.42)		
Asian Indian	830	16 (1.9%)	0.99 (0.60, 1.64)		0.85 (0.50, 1.44)		1	0 (0%)	-		
Asian Pakistani	1,549	67 (4.1%)	2.22 (1.70, 2.89)		1.62 (1.19, 2.20)		3	0 (0%)	-		
Asian Bangladeshi	465	5 (1.1%)	0.55 (0.53, 1.34)		0.37 (0.15, 0.92)		2	0 (0%)	-		
Asian Other	1,028	24 (2.3%)	1.20 (0.79, 2.89)		0.89 (0.56, 1.39)		2	0 (0%)	-		
Black Caribbean /African/Other	1,482	6 (0.4%)	0.21 (0.09, 0.47)		0.20 (0.09, 0.45)		1	1 (50%)	1.42 (0.09, 22.98)		
Chinese	507	4 (0.8%)	0.40 (0.15, 1.09)		0.30 (0.11, 0.83)		0	0	-		
Other/unknown	2,178	34 (1.5%)	0.80 (0.56, 1.14)		0.62 (0.42, 0.99)		5	5 (50%)	1.42 (0.40, 5.02)		
Region of birth				<0.0001		<0.0001				0.956	
UK	19,062	323 (1.7%)	ref.		ref.		170	111 (40%)	ref.		
Western and Southern Europe	1,494	63 (4.0%)	2.49 (1.89, 3.28)		2.35 (1.75, 3.16)		7	7 (50%)	1.53 (0.52, 4.49)		
Eastern Europe	2,081	109 (5.0%)	3.09 (2.48, 3.86)		2.80 (2.15, 3.64)		4	2 (33%)	0.77 (0.13, 4.25)		
Africa	2,546	25 (1.0%)	0.58 (0.38, 0.87)		0.63 (0.41, 0.97)		3	3 (50%)	1.53 (0.30, 7.72)		
Asia	3,497	100 (2.8%)	1.69 (1.34, 2.11)		1.58 (1.19, 2.10)		7	3 (30%)	0.66 (0.17, 2.59)		
Central and Southern America	402	8 (2.0%)	1.17 (0.58, 2.38)		0.99 (0.49, 2.04)		2	2 (50%)	1.53 (0.21, 11.03)		
North America	232	2 (0.9%)	0.51 (0.13, 2.06)		0.49 (0.12, 1.98)		2	1 (33%)	0.77 (0.07, 8.55)		
Oceania	160	1 (0.6%)	0.36 (0.05, 2.64)		0.34 (0.05, 2.45)		1	1 (50%)	1.53 (0.09, 24.74)		
Unknown	1,599	47 (2.9%)	1.73 (1.27, 2.37)		1.23 (0.85, 1.78)		5	6 (55%)	1.84 (0.55, 6.17)		
Deprivation Decile	4.6 (2.9)	3.8 (2.7)	0.90 (0.87, 0.93)	<0.0001	0.88 (0.86, 0.91)	<0.0001	3.3 (2.6)	3.1 (2.6)	0.98 (0.90, 1.06)	0.562	

Table 2. Univariable and multivariable logistic regression analyses for a new diagnosis among women tested anti-HCV positive in antenatal settings.

	Previously diagnosed N=494 <i>Mean (SD)</i>	Newly diagnosed (N=320), Row % <i>Mean (SD)</i>	OR (95% CI)	p-value	aOR (95% CI)	p-value
Age	34.2 (5.7)	32.9 (6.0)	0.96 (0.94, 0.99)	0.0023	0.96 (0.94, 0.99)	0.0064
Ethnicity				0.0049		
White British/Irish	329	174 (35%)	ref.		-	
White Other	67	82 (55%)	2.31 (1.60, 3.35)		-	
Asian Indian	9	7 (44%)	1.47 (0.54, 4.02)		-	
Asian Pakistani	44	23 (34%)	0.99 (0.58, 1.69)		-	
Asian Bangladeshi	2	3 (60%)	2.84 (0.47, 17.13)		-	
Asian Other	15	9 (38%)	1.13 (0.49, 2.65)		-	
Black						
Caribbean/African/Other	4	3 (43%)	1.42 (0.31, 6.41)		-	
Chinese	2	2 (50%)	1.89 (0.26, 13.54)		-	
Other/unknown	22	17 (44%)	1.46 (0.76, 2.82)		-	
Region of birth				0.0047		0.0199
UK	288	146 (34%)	ref.		ref.	
Western and Southern Europe	37	33 (47%)	1.76 (1.06, 2.93)		1.40 (0.82, 2.39)	
Eastern Europe	49	62 (56%)	2.50 (1.63, 3.81)		1.84 (1.18, 2.87)	
Africa	16	12 (43%)	1.48 (0.68, 3.21)		1.41 (0.64, 3.14)	
Asia	66	37 (36%)	1.11 (0.71, 1.73)		0.92 (0.58, 1.47)	
Central and Southern America	6	4 (40%)	1.32 (0.37, 4.73)		1.29 (0.34, 4.87)	
North America	1	2 (67%)	3.95 (0.35, 43.87)		5.65 (0.42, 76.81)	
Oceania	1	1 (50%)	1.97 (0.12, 31.76)		4.15 (0.22, 78.05)	
Unknown	30	23 (43%)	1.51 (0.85, 2.70)		1.37 (0.68, 2.75)	
Person who injects drugs				<0.0001		<0.0001
No	378	300 (44%)	ref.		ref.	
Yes	116	20 (15%)	0.22 (0.13, 0.36)		0.23 (0.14, 0.40)	
Deprivation Decile	3.4 (2.5)	4.1 (2.9)	1.11 (1.05, 1.16)	0.0002	1.10 (1.04, 1.16)	0.0009

Figure 1. Kaplan-Meier curve showing the cumulative time to treatment initiation after a positive HCV-RNA test, stratified by whether the HCV diagnosis was a new or pre-existing diagnosis.

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