

Table S1: Questionnaire used

Demographic Section 1	
1. Do you have a diagnosis of the following?	Tick Boxes: <ul style="list-style-type: none"> • Vitamin B12 Deficiency • Pernicious Anaemia • Neither of the above (told ineligible for study)
2. What is your age?	Tick boxes: <ul style="list-style-type: none"> • 18-24 years old. • 25-34 years old. • 35-44 years old. • 45-54 years old. • 55-64 years old. • 65-74 years old. • 75 years and older
3. What is your gender?	Tick boxes: <ul style="list-style-type: none"> • Male • Female • Other (please state)
4. What is your education level?	Tick boxes: <ul style="list-style-type: none"> • Primary school • Secondary school up to 16 years • Higher or secondary or further education (A-levels, BTEC, etc.) • College or university • Post-graduate degree • Prefer not to say
5. What is your employment status?	Tick boxes: <ul style="list-style-type: none"> • Employee or self-employed • Student • Full time caring responsibilities at home • Unemployed • Other (please state)
6. Which region do you live in?	Tick boxes: <ul style="list-style-type: none"> • East of England • East Midlands • London • North East • North West • Northern Ireland

	<ul style="list-style-type: none"> • Scotland • South East • South West • Wales • West Midlands • Yorkshire / Humberside
7. 'How often do you need to have someone help you when you read instructions, pamphlets, or other written material from your doctor or pharmacy? (SILS one item)	Likert Scale 1. Never 2. Rarely 3. Sometimes 4. Often 5. Always
6. How would you rate your overall health?	Tick box: <ul style="list-style-type: none"> • poor • fair • good • excellent
Section 2: Patient Safety in Primary Care	
1. What treatment do you currently receive from your GP for your B12 deficiency/pernicious anaemia	Free Text
2. How often do you receive this treatment?	Free Text
3. How has Covid-19 impacted the treatment of your B12 Deficiency or Pernicious Anaemia in primary care?	Free Text
Insert Validated PCPMOS 28-item measure. Responses on 5 point Likert Scale, Strongly Agree to Strongly Disagree	
I was always treated with dignity and respect.	
The doctor always considered what I want for my care.	
The doctor did not have the skills, experience or knowledge to correctly manage my health condition.	
The doctor always seemed to have the right information after I received treatment elsewhere.	
The doctor was interrupted during my consultation.	
Other health professionals at this practice did not have the skills, experience or knowledge to correctly manage my health condition.	
I got answers to all the questions I had regarding my care.	
I was able to make an appointment with a health professional of my choice.	
I understood what staff were explaining to me about my care	
Information about me that my health care team needed was always available e.g. discharge summary, referral letters, test results.	
Staff always knew everything they needed to know to care for me. e.g. allergies, other conditions, medical history, medications.	

The cost of medications prevented me from filling a script when I needed medication.	
I was able to access the after hours service when needed.	
I had enough time during the consultation with a health care professional.	
I knew who to go to in the practice if I needed to ask a question.	
If I was referred important information about my care was passed on / made available.	
Equipment needed for my care was always working properly.	
I was involved in all the decisions about my care.	
The practice was very clean.	
The cost of seeing a doctor, nurse or other health professional at the practice prevented me from seeking care when I needed it.	
I was able to make an appointment at a time that suited me.	
My test results were always available when required e.g. scans, blood tests, x-rays.	
I always felt that staff listened to me about my concerns.	
Where necessary my doctor, nurse or other health professional regularly monitors/reviews my health condition.	
Seeing the same doctor, nurse or other health professional is important to me.	
Administration staff interacted with me in a manner I found acceptable.	
My referrals have always been appropriate.	
I was always given enough information that I could understand about my care and treatment.	
Section 3: Self Medication	
1. In general apart from treatments prescribed by your doctor do you sometimes take medications on your own to treat your B12 deficiency?	Yes/No (No, end of survey)
2. If yes, which of the following do you take?	1. Self-injection (in addition to anything prescribed by GP) 2. Oral medication in tablet form (in addition to anything prescribed by GP) 3. Oral medication in liquid form (in addition to anything prescribed by the GP) Other (please state)
3. For what reasons do you self-medicate? (please tick all that apply)	Tick box: 1. Unsatisfied with prescribed treatment effect 2. Unsatisfied with prescribed treatment frequency 3. Suboptimal relationships with healthcare professionals 4. Unsatisfied with current policy and practice 5. To improve quality of life

	6. Lack of trust in knowledge and judgement of healthcare professionals 7. Healthcare professionals are over-reliant on tests and not symptoms or patient experience 8. No time to visit physician 9. Emergency use 10. Familiar with treatment 11. Financial reasons 4. Other _____
4. What are your sources of information for self-medication? (please select all that apply)	1. Previous experience 2. Family 3. Friends 4. Advertisements 5. Websites 6. Instagram 7. Twitter 8. Facebook (friends list) 9. Facebook (closed support group) 10. Other social media 11. Charities 12. Books Other _____
5. To what extent to do agree self-medication is safe?	Five point Likert scale: Strongly disagree to strongly agree.
6. Do you have any concerns about safety and self-medication?	1. Free text
7. Are any healthcare professionals aware that you self-medicate?	1. General practitioner 2. Nurse 3. Other (please state) 2. None
8. Have you ever experienced side effects or complications after treating yourself?	4. Yes (please state) 5. No
9. Do you chose to self-medicate to improve one particular symptom of your condition (more than others)?	1. Fatigue 2. Mental Health (depression, anxiety etc.) 3. Concentration/brain fog 4. Pins and needles 5. Digestive issues 6. Leg cramps 7. Balance 8. Blurred vision 9. Hair loss 6. Other (please state)

Table S2: Responses to Self-medication questionnaire

Item	Percentage	N (805, 62%)
Method of self-medication		
Self-injection	63%	510
Solid oral medication usage	26%	210
Liquid oral medication usage	14%	116
Other (patches, sublingual's, sprays)	18%	144
Reasons for self-medicating		
Unsatisfied with prescribed treatment	42%	341
Unsatisfied with prescribed treatment frequency	68%	545
Suboptimal relationship with healthcare professional	20%	164
Unsatisfied with current policy and practice	47%	379
To improve quality of life	80%	644
Lack of trust in knowledge and judgement of health professionals	45%	366
Healthcare professionals are over-reliant on tests	53%	429
No time to visit physician	3%	23
Emergency use	4%	29
Familiar with treatment	9%	69
Financial reasons	1%	8
Sources of knowledge for self-medication		
Previous experience	27%	218
Family	11%	87
Friends	12%	94
Advertisement	1%	5
Websites	44%	355
Instagram	0%	1
Twitter	1%	5
Facebook friends list	3%	21
Facebook closed support group	72%	577
Charities	19%	154
Books	21%	169
Healthcare professional aware about self-medication		
General Practitioner	30%	241
Nurse	19%	155
None	54%	437
Have you experienced any side effects of self-medicating?		
Yes	0%	0
No	100%	805
Does self-medicating improve specific symptoms?		

Fatigue	95%	762
Mental health	66%	530
Concentration/Brain fog	87%	697
Pins and needles	78%	629
Digestive issues	54%	433
Leg cramps	50%	405
Balance	58%	470
Blurred	52%	420
Hair loss	32%	261

To what extent do you agree self-medication (via injection) is safe?

Agree	79%	634
Neutral	14%	111
Disagree	6%	47
No response	2%	13

Table S3: Comparison of validation study mean scores on each domain with current study

PCPMOS Domain	Greater Manchester Mean Domain Score from Validation Study (n=490)	Vitamin B12 Deficiency Mean Domain Score, Current Study (n=1297)
Access	3.49	2.65
Communication	4.11	2.82
External policy	3.57	3.14
Information flow	3.81	2.56
Organisation care planning	3.91	2.29
Patient-related factors	4.24	2.73
Physical environment	4.15	3.36
Referrals	3.83	2.82
Task performance	3.71	2.56
Total PMOS score	3.87	2.74

Table S4: Responses to individual PMOS items

	Agree (n)	Agree (%)	Neutral (n)	Neutral (%)	Disagree (n)	Disagree (%)	N/A (n)
I was always treated with dignity and respect.	649	50%	229	18%	409	32%	10
The doctor always considered what I want for my care.	387	30%	256	20%	640	49%	14

The doctor did not have the skills, experience or knowledge to correctly manage my health condition.	282	22%	201	15%	762	59%	52
The doctor always seemed to have the right information after I received treatment elsewhere.	163	13%	365	28%	391	30%	378
The doctor was not interrupted during my consultation.	811	63%	110	8%	83	6%	293
Other health professionals at this practice did not have the skills, experience or knowledge to correctly manage my health condition.	218	17%	207	16%	741	57%	131
I got answers to all the questions I had regarding my care.	231	18%	178	14%	864	67%	24
I was able to make an appointment with a health professional of my choice.	478	37%	157	12%	614	47%	48
I understood what staff were explaining to me about my care	796	61%	208	16%	228	18%	65
Information about me that my health care team needed was always available e.g. discharge summary, referral letters, test results.	517	40%	207	16%	418	32%	155
Staff always knew everything they needed to know to care for me. e.g. allergies, other conditions, medical history, medications.	407	31%	192	15%	628	48%	70
The cost of medications did not prevent me from filling a script when I needed medication.	689	53%	93	7%	101	8%	414
I was able to access the after hours service when needed.	440	34%	156	12%	142	11%	559
I had enough time during the consultation with a health care professional.	562	43%	186	14%	514	40%	35
I knew who to go to in the practice if I needed to ask a question.	535	41%	185	14%	513	40%	64
If I was referred important information about my care was passed on / made available.	361	28%	241	19%	347	27%	348
Equipment needed for my care was always working properly.	638	49%	139	11%	93	7%	427
I was involved in all the decisions about my care.	423	33%	226	17%	573	44%	75
The practice was very clean.	1165	90%	82	6%	28	2%	22
The cost of seeing a doctor, nurse or other health professional at the practice did not prevent me from seeking care when I needed it.	490	38%	63	5%	25	2%	719
I was able to make an appointment at a time that suited me.	583	45%	181	14%	512	39%	21
My test results were always available when required e.g. scans, blood tests, x-rays.	634	49%	175	13%	392	30%	96
I always felt that staff listened to me about my concerns.	348	27%	207	16%	725	56%	17

Where necessary my doctor, nurse or other health professional regularly monitors/reviews my health condition.	312	24%	167	13%	776	60%	42
Seeing the same doctor, nurse or other health professional is important to me.	1061	82%	139	11%	78	6%	19
Administration staff interacted with me in a manner I found acceptable.	744	57%	220	17%	316	24%	17
My referrals have always been appropriate.	612	47%	232	18%	239	18%	214
I was always given enough information that I could understand about my care and treatment.	476	37%	235	18%	549	42%	37

Table S5: Logistic regression analysis to assess association of key variables with self-medication via injection

Variable	OR	SE	95% CI	P-value
<i>Self-medicated:</i>				
- No	1	NA	NA	NA
- Yes	5.413	2.047	1.516, 8.712	0.967
PMOs total	0.977	1.003	0.971, 0.984	<0.0001
DOM1: Patient related factors	0.753	1.028	0.712, 0.794	<0.0001
DOM2: Task performance	0.857	1.020	0.824, 0.890	<0.0001
DOM3: Quality of communication	0.912	1.012	0.890, 0.933	<0.0001
DOM4: Access	0.942	1.016	0.913, 0.972	0.0002
DOM5: Information Flow	0.960	1.016	0.931, 0.989	0.0079
DOM6: external policy context	1.044	1.017	1.011, 1.078	0.0085
DOM7: Organisation and care planning	0.935	1.018	0.902, 0.968	0.0002
DOM8: referrals	0.939	1.021	0.901, 0.979	0.0032
DOM9: Physical environment	0.903	1.026	0.858, 0.950	<0.0001
<i>Diagnosis:</i>				
- B12	1	NA	NA	NA
- B12 & PA	0.759	1.121	0.606, 0.949	0.016
<i>Health status:</i>				
- Good/Excellent	1	NA	NA	NA
- Fair/Poor	1.459	1.136	1.139, 1.876	0.003
<i>Health literacy:</i>				
- Always/Often	1	NA	NA	NA
- Sometimes	1.475	1.437	0.733, 3.063	0.284
- Rarely	1.226	1.439	0.607, 2.550	0.576
- Never	1.230	1.384	0.661, 2.383	0.524
<i>Education level:</i>				
- College or university	1	NA	NA	NA
- Higher or secondary	0.879	1.167	0.648, 1.189	0.405

- Post-graduate	1.170	1.170	0.858, 1.592	0.319
- Prefer not to say	0.777	1.390	0.398, 1.460	0.444
- Primary/ Secondary school	0.824	1.190	0.584, 1.154	0.264
<i>Age:</i>				
- 18 to 34 yrs.	1	NA	NA	NA
- 35 to 44 yrs.	1.330	1.203	0.928, 1.916	0.123
- 45 to 54 yrs.	1.660	1.193	1.179, 2.354	0.004
- 55 to 64 yrs.	1.799	1.220	1.221, 2.664	0.003
- 65 yrs. And older	2.112	1.295	1.272, 3.514	0.004
<i>Gender:</i>				
- Female	1	NA	NA	NA
- Male	0.933	1.311	0.542, 1.573	0.797
- NR	0.308	2.995	0.016, 1.919	0.283
<i>Country:</i>				
Other	1	NA	NA	NA
England/Wales	1.203	1.154	0.911, 1.596	0.196

Table S6: Multivariable logistic regression model for factors associated with patients who self-inject

Variable	OR	2.50%	97.50%	P-value	VIF*
(Intercept)	2.329	1.158	4.709	0.0180	-
Total PMOS score	0.957	0.888	1.030	0.2409	4.165
DOM1: Patient related factors	0.821	0.734	0.918	0.0006	2.005
DOM2: Task performance	0.947	0.869	1.032	0.2141	2.093
DOM3: Quality of communication	1.025	0.933	1.126	0.6105	3.835
DOM4: Access	1.078	0.991	1.174	0.0817	2.499
DOM5: Information Flow	1.108	1.016	1.210	0.0216	2.656
DOM6: external policy context	1.100	1.016	1.192	0.0194	2.314
DOM7: Organisation and care planning	0.985	0.931	1.043	0.6045	1.490
DOM8: referrals	1.061	0.964	1.168	0.2264	2.119
DOM9: Physical environment	1.030	0.930	1.140	0.5696	1.859
PA vs. B12 diagnosis	0.802	0.629	1.021	0.0738	1.010
Fair/Poor vs. Good/Excellent Health Overall	1.154	0.877	1.522	0.3085	1.035
Age [35–44 years old. vs. < 34]	1.490	1.012	2.203	0.0444	1.019
Age [45–54 years old. vs. < 34]	2.064	1.423	3.017	0.0002	-
Age [55–64 years old. vs. < 34]	2.310	1.511	3.552	0.0001	-

Age [75 years and older vs. < 34]	2.803	1.607	4.909	0.0003	-
Final model fit statistics:	AIC=1589.8; R ² =13%; χ^2 (8) = 4.666, P=0.793				

*VIF: variance inflation factor estimated using 'regclass' package in R and is interpreted as:

- 1= not correlated
- Between 1 and 5 = moderately correlated
- Greater than 5 = highly correlated.

Table S7: Summary of Thematic Synthesis

Concerns about self-medication (responses from n=638/805)	Summary	Key themes within the responses and example quotes
Not Concerned (n=386)	Over 50% of the participants stated that they were not concerned about safety and self-medication.	<ol style="list-style-type: none"> 1) Experience: Patients reported having experience with needles and self-medicating. For example, many patients who were diabetic, qualified healthcare professionals or taught by a qualified healthcare professional (which makes the transition to self-medication easier). Also many patients reported that they were confident about self-medicating because they have done sufficient research. <i>'No I'm a registered nurse'</i> 2) Lack of trust in GPs: Lack of trust led to many patients conducting research into B12 deficiency independently and they feel as they know more than GPs when it comes to managing B12 deficiency. Many patients reported the lack of trust due to misdiagnosis, lack of curiosity from the GPs or financial issues related to visiting the GP regularly. <i>'I would prefer medical supervision, but feel doctors don't have enough knowledge to treat me properly.'</i> 3) Improved Quality of Life: Many patients reported that they have found a much better quality of life once they started self-medicating and this forms part of the reason why they are confident as they have seen results. <i>'No as my life it's gone back to almost normal. I was super ill before I started to self-inject.'</i> 4) Adherence to guidelines: Some patients were not worried about over-medicating because they mentioned that they follow BSH or NICE guidelines on the maximum doses. Other patients were under the conception over medication has no side effects. <i>'No because you cannot over dose on B12'</i> 5) Credibility of sources: Some patients mentioned that they were not worried because they purchase the B12

		from credible sources or go privately for B12. <i>'No if sourced from a well-known pharmacy supplier'</i>
Mixed/Indifferent (n=60)*	This group was largely categorised by patients who were initially concerned but were no longer concerned	<p>1) Overcame initial concerns: Patients reported initial worries with regards to self-medicating, however once the benefits from self-medicating were experienced their concerns alleviated or disappeared. <i>'I did at first but not now'</i></p> <p>2) Social Support: Others mentioned they would be worried however, they have a good support circle around them which includes online forum groups. <i>'If I didn't have the online support group I had with the plethora of knowledge they share I definitely wouldn't have been able to self-inject safely.'</i></p> <p>3) Type of Injection: Patients have mixed feelings to self-medicating used subcutaneous injections and intramuscular <i>'I used to do subcutaneous injections into my belly and have always feared that somehow I would hit something I am not supposed to hit, e.g. an organ, or that I wasn 't injecting it at the right angle or depth and the B12 would just sit under my skin without ever dissolving and eventually make me sick. I have since switched to my thigh and am no longer worried.'</i></p>
Concerned (n=192)	Most patients who were concerned, would have preferred treatment administered via medical professionals but felt they had no other choice to improve their quality of life.	<p>1) Preference of health professional administration: they would much rather prefer a healthcare professional to administer the B12 injections, rather than self-inject <i>'Yes. I would prefer a health care professional to administer.'</i></p> <p>2) No other choice: Patients reported worries about self-medicating but they continue because they 'have no choice'. <i>'I don't feel safe self-injecting, but I don't have any other choice'</i></p> <p>3) Complications: Patients are worried about hitting a vessel or nerve, because it is an intramuscular injection, or they previously experienced such complications <i>'Worry about hitting a nerve!'</i></p> <p>4) Storage and Disposal: Patient reported concerns over storage and disposal of the B12 and needles <i>'I have no way to dispose of needles unless I register as a drug addict.'</i></p> <p>5) Financial and Credibility Concerns: Some patients reports financial concerns over self-medicating, many patients purchasing the medication abroad and they are worried about the reliability of the medication. <i>'I'm a little dubious about what I could be buying online to inject into myself'</i></p>

*The patients categorised as mixed/indifferent were hard to categorise objectively, 167 participants did not respond to this question

Effect of Covid-19 on treatment		
Not Affected (n=495)	Many reported not being affected and this was because they self-medicate	<ol style="list-style-type: none"> 1. Self-Medication: Many self-medicate therefore felt this question was not applicable to them. 2. Proactive GP: GP has been proactive and been consistent with following up with them, 3. Proactive Patient: Patients feel they have to pester the GP to obtain their injection, 4. Receiving Treatment in Car: Some reported that they couldn't go into the GP but they would receive the injections in the car during the pandemic, 5. Alternative treatment sufficient: Some patients were offered alternatives such as oral tablets of B12 and some patients felt they were more sustainable than injections and worked for them 6. Direct contact with nurse practitioner: Those who directly liaised with nurse practitioners to get the B12 appointments did not seem to miss any injections 7. Location: There was a tendency in the data for those in England, Wales and Scotland to report more effects than other countries, as those from other countries did not report any disturbance.
Affected (n=749)	The main reported problem in this group was termination of regular injections.	<ol style="list-style-type: none"> 1. Appointment difficulties: COVID-19 made it much harder for patients to get an appointment with the doctor 2. Treatment stopped or cancelled: Many patients reported poor experiences with the GP during COVID and got their appointments/treatments cancelled or refused. They were told that they were 'not priority' and one patient reported that their appointment was cancelled without their acknowledgement. 3. Monitoring and diagnosis stopped: Many patients could not get an appointment to monitor their B12 deficiency or pernicious anaemia as they were refused blood tests. 4. Alternative treatments not effective: Patients with pernicious anaemia were more effected by COVID-19 as oral tablets are not effective on them so they became more difficult to manage remotely. Many patients reported that they were given

		<p>alternatives to help ease the transition to remote care during the pandemic.</p> <p>5. Delayed/Reduced Frequency of Injections: Some patients still gotten their injections, however, they were delayed or given at a slower rate.</p> <p>6. Effect on Daily Activities: Patients that were effected heavily reported severe symptoms of fatigue and pain; this resulted in them not being able to carry out their daily activities.</p>
--	--	---

*51 patients gave a not applicable answer, primarily because they no longer sought primary care provision due to dissatisfaction