Understanding clinical risk decision making regarding development of depression during interferon-alpha treatment for hepatitis-C: A qualitative interview study

Nilay Hepgul*; Naonori Kodate*; Janet Anderson; Max Henderson; Gopinath Ranjith; Matthew Hotopf; Carmine Pariante (*joint first authors)

Abstract

Background: Hepatitis C virus (HCV) affects 170 million worldwide. Currently, around 30% of patients receiving interferon-alpha (IFN-α) treatment for HCV experience clinically significant depression. Effective and timely detection of depression is crucial to ensuring appropriate treatment and support. However, little is known about how clinical nurse specialists identify patients at risk of developing interferon-alpha-induced depression, and monitor those receiving antiviral treatment for the occurrence of depression.

Objective: This study aimed to gain an in-depth understanding of staff experience of, and attitudes towards, the identification and monitoring of interferon-alpha-induced-depression and the decision-making process concerning the use of liaison psychiatry and other clinical services.

Design: A qualitative interview study was conducted among clinical staff involved in the care of patients with hepatitis C, using the perspective of naturalistic decision making.

Settings: Outpatient liver clinics in three large teaching hospitals in South London, the United Kingdom.
Participants: All clinical nurse specialists from the three outpatient liver clinics were included. All were involved directly in the care of patients receiving interferon-alpha treatment and had at least one year experience (mean 6.4 years, range 1-11 years) in this field.

Methods: Semi-structured face-to-face interviews were conducted between 2010 and 2011. Data collection and analysis were carried out iteratively to ensure the reliability of the analysis using the constant comparison method.

Results: Staff used verbal and non-verbal cues when assessing risks of patients developing depression before and during IFN-α treatment. Major sources of uncertainty were patient engagement and familiarity, referrals to psychiatrists, language barriers, and distinguishing between psychological and physical symptoms. Good rapport with patients and good communication among multidisciplinary professional groups were key strategies identified to reduce uncertainty.

Conclusion: Current methods of identifying vulnerable patients rely on the availability of clinical experts and good communication within a multidisciplinary team. Detection and management of depression in this population is complex, however, various strategies are employed by nurses to overcome difficulties when making decisions regarding patient welfare. Current clinical practices should be taken into account when developing new tools and methods.

Keywords: decision-making; depression; hepatitis C; interferon-alpha; nurse clinicians.
What is already known about the topic?

- There is a vast amount of information about the prevalence of interferon-alpha-induced depression in patients with Hepatitis C treatment. However, there is a lack of information about effective and timely detection of depression and the decisional processes which take place for staff involved in the care of these patients.

What this paper adds?

- Clinical nurse specialists rely mostly on intuitions derived from their own experience and clinical expertise when identifying patients at risk of developing IFN-α-induced depression.

- A decision-making support tool is not commonly applied in any of the three study sites. Instead, other organisational resources, including a multidisciplinary team is utilised where available in order to reduce uncertainty around clinical decisions.

- There is a research gap around how team-based communication works and how best to support specialist nurses’ decision making process in the future.
Introduction

Hepatitis C virus (HCV) infection – the “silent epidemic” – affects between 200 and 400 hundred thousand people (0.5-1% of the population) in England, and 170 million worldwide (Szabo et al., 2003). Combination therapy with pegylated interferon-alpha (IFN-α) and the antiviral agent ribavirin is the treatment of choice for patients with chronic HCV infection and given for 24-48 weeks, clears the virus in 42-80% of cases (Agarwal et al., 2007). Unfortunately, around 30% of patients experience clinically significant depression, and up to 50% experience neuropsychiatric adverse effects (Asnis and De La Garza, 2006). These adverse effects emerge in the early stages of the treatment course, usually in the first 2-3 months (Lotrich et al., 2007, Wichers et al., 2007). The experience of depressive symptoms during the course of antiviral treatment has important negative consequences, such as impairing quality of life, which can reduce compliance and lead to dose reduction or discontinuation of treatment (Asnis and De La Garza, 2006). All of these can compromise the therapeutic response to the treatment. In some cases depression can be so severe that patients experience suicidal ideation, and some published case-reports describe patients who have committed suicide (Ademmer et al., 2001, Dieperink et al., 2004, Fattovich et al., 1996, Fukunishi et al., 1998, Janssen et al., 1994). Effective and timely detection of depression is therefore important to ensure that appropriate treatment and support can be provided.

This qualitative study examined the role of clinical expertise and multidisciplinary teams in identifying patients at risk of developing IFN-α-induced-depression, and in monitoring those receiving antiviral treatment for the occurrence of depression. Making these decisions in the clinical setting is difficult and is often based on incomplete and ambiguous information; symptoms reported and behaviour observed in a brief clinical encounter are not always representative of the patient’s state of mind outside the setting and there is no one-to-one correspondence between a reported symptom and future behaviour. As such, there is
ongoing debate about the most effective tools and methods to use for assessment and monitoring.

Prophylactic treatment with antidepressants is often recommended for those at risk of developing depression. However, few trials of prophylactic antidepressant treatment (Galvao-de Almeida et al., 2010) exist, and these few studies suggest it is not always effective (Morasco et al., 2007, Raison et al., 2007) and can result in dangerous side effects (Weinrieb et al., 2003). Furthermore, many patients are reluctant to take psychoactive medication, particularly given an often prolonged history of drug abuse. Other treatment options include psychiatric interventions which have been suggested to reduce depressive symptoms (Farber et al., 2005, Neri et al., 2010) and cognitive behavioural therapy which has been successfully used to prevent the development of depression during treatment (Ramsey et al., 2011). Given that prophylactic treatment with antidepressants is not an option for all patients and that preventative interventions are not commonly offered, it is important for nursing staff to be able to detect the development of IFN-α-induced-depression in order to provide patients with the correct support.

There is conflicting evidence about what factors are predictive of depressive symptoms during treatment with IFN-α. The factors most often associated with subsequent development of depression are a family history of a mood disorder, a history of two or more psychiatric diagnoses, baseline mood disorder (Dieperink et al., 2003, Fontana et al., 2002) and sleep disorders (Sockalingam et al., 2010). There is some evidence that standardised rating scales to assess depression are effective in detecting those likely to develop depression. For example, both the Beck Depression Inventory (BDI) and the Zung Self Rating Depression Scale have been recommended for assessment and symptom monitoring (Dieperink et al., 2003, Koskinas et al., 2002, Patterson et al., 2011). However, recent studies have raised questions about the validity of rating scales with this group of patients. The Brief
Symptom Inventory was found to be no better than the patient’s answer to one standardised question in predicting the subsequent onset of depression (Fontana et al., 2002). More recently, the BDI was found to have high sensitivity but low specificity with a population of intravenous drug users infected with HCV (Holtzheimer et al., 2010).

Other efforts to increase the accuracy with which vulnerable patients are identified have focused on the development and validation of biological indicators such as measures of sleep disturbance (Franzen et al., 2010), fatigue levels (Hilsabeck et al., 2005) and clinical and genetic indicators and biomarkers (Bull et al., 2009, Pariante et al., 2002, Raison et al., 2005). However, judgements of clinical experts are likely to remain indispensable in identifying vulnerable patients and providing care at least in the short term. Any new tools and methods will have to be integrated with current clinical practices, and so it is important to understand how clinical experts make decisions and how clinical teams co-ordinate their activities to care for patients. In this study we investigated the decision making processes of expert clinicians using the insights of naturalistic decision making (NDM).

Different theoretical perspectives have been used to study health care practitioners’ decision making. Many approaches focus on the factors that determine how the most accurate decisions are made. For example, policy capturing techniques have been used to capture judgements with varying cues (Carroll and Johnson, 1990, Cooksey, 1996). This allows the policy used by the decision maker to be modelled and analysed (Mosier and Fischer, 2010). These models assume a rational systematic process is undertaken whereby the advantages of each option are weighted and the best option is chosen. Emerging studies of how experts make decisions in naturalistic contexts, however, challenged these notions and provided evidence that decisions made outside the laboratory do not involve experts generating and weighting lists of action options. Researchers working in the NDM tradition found that
experts make decisions by recognising patterns and matching these to known courses of action (Hoffman and Millitello, 2009).

The focus of NDM studies of decision making is how experts make decisions in the real world. This perspective assumes that decisions in the real world involve ill-structured problems, uncertainty, time stress, high stakes, multiple actors, organizational goals and action/feedback loops (Zsambok, 1997) and medical decision making shares many of these features. NDM approaches also emphasise the importance of the context in shaping decisions, and focus on the information that is sought and attended to in the assessment of the situation (Hedberg and Satterlund Larsson, 2003).

In this study, we used these insights to frame our approach to the research. We viewed risk assessment in HCV patients as a complex cognitive task which involves on-going decision making about patients’ risk factors and their responses to treatment. Moreover, scientific knowledge about how to predict which patients will develop depression and which will not, is incomplete, and patients are not completely known to clinicians, so clinicians work with ill-defined and incomplete information. In this context, it was inappropriate to take a normative view of decision making and examine, for example, the accuracy of clinicians’ decisions. The NDM perspective was therefore used as a framing perspective for our investigation of decision making in this environment.

The aim of the current study was to gain an in-depth understanding of the staff’s experience of, and attitudes towards, two factors: the identification and monitoring of IFN-α-induced-depression, and decision-making concerning the use of liaison psychiatry and other services. We were interested in the following questions

1. What factors do clinical nurse specialists see as important in determining risk of developing depression, at initial consultation and in ongoing monitoring?
2. What factors do clinical nurse specialists weigh up when deciding on a course of action?

3. What actions do clinical nurse specialists take?

4. What are the sources of uncertainty for clinical nurse specialists and available reduction strategies?

Methods

Participants

Purposive sampling was used to select participants most able to provide information relevant to the study objectives. All clinical nurse specialists (n=9) working in outpatient liver clinics in three large teaching hospitals in South London were approached and agreed to participate. All were involved directly in the care of patients receiving IFN-α treatment and had at least one year experience (mean 6.4 years, range 1-11 years) working in this field but no prior experience of training in mental health. All participants were initially approached via email and subsequently received an information sheet detailing the nature and purpose of the research. The study was approved by the local Ethical Committee, in accordance with the code of ethics of the World Medical Association, and written informed consent was obtained from all participants.

Data Collection

A semi-structured interview guide was developed, and interviews lasting approximately 30 minutes were conducted individually with each member of staff. The interviews were organised into the following sections: background information on training and experience providing HCV care; current clinical practices/protocols for monitoring and identifying depressive symptoms, including referrals to psychiatrists; and personal attitudes
to the use of decision making tools and access to resources. Standard probes, such as verification, were used to clarify fully specific responses. All interviews were conducted jointly by one male and one female, experienced social science interviewers (NK and NH). All interviews were conducted between November 2010 until April 2011 in a private room belonging to the interviewers, and the interviewers took turns in asking the questions. Interviews were tape recorded, transcribed verbatim and then imported into the qualitative data analysis package (QSR NVivo 8.0 data analysis software) to facilitate data handling.

Data Analysis

Data were analysed using thematic framework analysis to identify key themes which were then used to code the interview data (Ritchie and Spencer, 1994). Framework analysis is a method that is particularly suited to studies in which at least some of the themes and concepts can be identified a priori (Dixon-Woods, 2011, Ritchie et al., 2003). Questions of relevance to the researchers are used as an initial thematic framework for the analysis, but the approach also allows for the inductive identification of emergent themes (Dixon-Woods, 2011, Pope et al., 2000). In this study, the initial coding framework was based on the interview schedule. Further themes were then identified as the analysis progressed, and researchers refined the framework iteratively by comparing and discussing interpretations of the data. A final coding framework was developed along with detailed descriptions of each theme to increase the reliability of coding. In order to further ensure the reliability of the analysis, two coders (NH and NK) separately examined portions of the transcripts and resolved any differences. The final coding framework consisted of major factors influencing identification of depression and decision making.

Results
Interviewees from all three sites were asked to describe the standard care processes for providing care for hepatitis C patients. Interviewees described the various stages through which patients’ progress throughout the treatment process and at which clinical decision are required to be made. A simplified flow chart based on the descriptions of all nine clinical nurse specialists is presented in Figure 1.

[Figure I here]

We now illustrate four key themes by providing quotes from the interviews which were assessed by the coders as representative of the responses received.

**Assessing patient risk factors**

The participants discussed factors which they identify when assessing the risk of patients developing depression and when assessing any subsequent development of symptoms during the treatment period. Subsequently, these factors often form the basis for their judgement of both the need and urgency of referring patients to psychiatrists. The same factors were identified by staff as being relevant when assessing both the risk for, and the development of, depression. These have been divided into two categories, psychological and other, and are presented in Tables 1 and 2 respectively.

[Tables I & II here]

**Co-ordinating action**

We also investigated what further actions clinical nurse specialists take when risks are recognised either prior to or during treatment. Four types of actions were identified: involving
patients and/or relatives, referral to liaison psychiatrists, referral to other resources (community services/GPs) and discussion with nursing staff.

First, the staff emphasised that the decision to refer a patient to a psychiatrist or other mental health professional has to be made jointly with patients, as their engagement is the key to successful treatment.

“...we would then make the decision with the patient.” (participant # 1)

“We say that it’s not just one way street, you might come to me and say well I really would like to be referred so it’s not always me who says well we would like you to see somebody.” (participant # 2)

Concerns raised by patient’s relatives can also initiate the referral process.

“We do have relatives who phone us and obviously if they talk to us then we will listen, we might not necessarily comment, but we’ll then act on it nonetheless.” (participant # 2)

Second, in the trusts where liaison psychiatrists are available, their advice is often sought prior to making a formal referral.

“we do work very closely with our liaison consultant psychiatrist, and so if we do feel that we need further advice and we’re not quite sure about something, then we will always have an open discussion with him and he’s very very helpful.” (participant # 2)
“...we already had close contact with his community psychiatrist, our psychiatrist, a haematologist, our consultant, ourselves, the community mental health team...” (participant #2)

“If I think someone is going to need some support during treatment, I will get them referred to the community mental health team...we do find the community mental health team are very good at also assessing patients and supporting them throughout treatment as well. So we’ve got quite a lot of resources open to us.” (participant #4)

“We do sometimes refer patients to the counselling psychotherapy department or recommend that they go to their GP if they are feeling quite low, you know, and start antidepressant treatment, citalopram.” (participant #5)

Additionally, informal discussions about patients take place within the nursing team, when nurses perceive a risk regarding patients’ well-being. This is on a patient by patient basis and serves not only as an information exchange but also as a resource for making decisions.
“We do but we also talk about patients a lot if for example, someone’s come in and there’s been some difficulty, we’ll either email everybody to say can you keep an eye on this patient because at clinic they weren’t quite right so I’ve brought him back sooner. Or we’ll just openly sit and talk about them.” (participant # 4)

“we will also go round and discuss patients within the team “what did you pick up on?” and quite a lot of interesting things come out of that, where we use each other as a resource quite a lot.” (participant # 4)

**Sources of uncertainty regarding decision making and available strategies to reduce them**

Almost all the staff noted that, based on many years of experience, they were confident in their ability to detect signs of psychological deterioration in patients. However, several sources of uncertainty still exist for clinical nurse specialists when making decisions regarding patient welfare. Table 3 shows four main contributing factors to these uncertainties that were identified by staff.

[Table III here]

Developing a good rapport with patients was repeatedly mentioned by nurse specialists as one of the key aspects in the care process, and the key strategy to reduce uncertainty.
“I used to have my own patients in a Monday clinic and I knew them really well and I would know instantly if something was wrong. Now we kind of rotate through the clinics so if you don’t know someone, it might take a couple of times before you can pick up that they’re not quite themselves.” (participant # 4)

However, when asked, they also provided several accounts of very rare, yet unexpected adverse events involving their patients. These illuminate the fact that staff are aware of limitations of the current care process in predicting and preventing such occurrences.

“he went off on his treatment, and about six weeks into treatment he seemed fine but we suddenly got a phone call from his father...umm...who said that he had a locked himself in his room, refused to come out, he wouldn’t eat, you know, really completely out of character and the family were ringing, quite worried obviously about what had gone on. So we stopped his treatment and we got him in and very quickly assessed by the consultant psychiatrist and he had really really deteriorated in his mood and was just not being very lucid basically. He’d kind of just really reacted quite badly and when we talked to him again he’d tried to be, his words, “a bloke about it” and not tell us about what was going on in his head despite the fact that we’d encouraged over and over again. But I had completely missed that because he was so jokey and upbeat and friendly, shaking my hand, and smiley, you know, just did not see that coming.” (participant # 7)

Another uncertainty reduction strategy is good communication among team members and also with the wider multidisciplinary group. Despite all the above-mentioned sources of uncertainty, staff feel that they are generally well supported by their own nursing staff, liaison psychiatrists (if any), and other community teams.
“we’ve got a good relationship between the different doctors and within the team as well so that’s probably helping as well. Supporting each other is very important in these kind of case scenarios because it’s difficult to deal with someone who’s becoming very unwell and knowing that I’ve got the supports from doctors and the other nurses, can make it easier as well.” (participant # 3)

“I think we’re quite good at that, well we’re all in the same office and there’s quite a good relationship, rapport between us all. I mean, if there’s anything that you’ve seen, you know, Mr so and so and you know he seems a bit wound up or emotional, I mean we do tend to sort of tell each other what our observations are.” (participant # 5)

This close knit team allows them to use each other as a source of information to reduce uncertainty about making decisions on the appropriate course of action, as mentioned in the earlier section.

**Suggested areas of improvement**

Interviewees made suggestions for improving their current practice and care processes, including extra time with patients, staff training in mental health, additional support (appointment of liaison psychiatrists and dual qualified nurses, in particular) and the development of a protocol for referrals.

“…discussing things with the consultant psychiatrist, which we do, but, it would be nice to have a little more time to do that and to kind of probably set up a formal meeting with him monthly or something that would be very really useful.” (participant # 1)
“To optimise I could do more training in counselling, I don’t know maybe there are standard questions that we could ask. But maybe more training in counselling would help.” (participant # 5)

“I’ve often wondered if we had a nurse who was dual qualified so had a mental health qualification as well as a general one, whether that would be of any benefit.” (participant # 9)

However, the staff emphasised that they feel confident to overcome these issues, and expressed pride in the way they deliver holistic care for patients through management of psychological, physical and social needs. They were asked whether a decision-making support tool would enhance the accuracy of clinical judgements. Although most respondents agreed that such a tool could be utilised as a back-up for their mostly intuitive ways of assessing risks, or as an effective communication aid when different health care professionals are involved in care processes, they emphasised the importance of their own clinical judgement based on knowledge of the patients.

“I think you’ve always got your own gut instinct, that you will rely on and obviously perhaps you would use a tool as a backup really just to confirm what your hunch is.” (participant # 3)

“I would not solely rely on a tool. I would also communicate with other people about the findings. Yeah, I think it needs both, it’s important to communicate your finding and your feeling about it.” (participant #5)
Discussion

This study investigated how clinical nurse specialists identify and monitor patient risk factors before and during IFN-α treatment, and make decisions on the appropriate course of actions in order to control these risks. It provided valuable insights into the complex clinical processes that take place and also revealed the multifaceted nature of risk factors staff are presented with and must assess within limited resources.

There are two main findings from our study. Firstly, every participant in this study employed a combination of verbal and non-verbal cues to gather information about patients’ status on all psychological, biological and social dimensions. Staff frequently mentioned ‘eye contact’ with patients as a useful indicator, although more subtle and intangible cues including ‘changes in behaviour’ and ‘general demeanour’ were also described as important. Recognition of depressive symptoms is therefore made possible partially by building up familiarity and good rapport with patients over time. The importance of the patient-health professional relationship on both medical and psychosocial outcomes has also been highlighted in a previous qualitative study (Stewart et al., 2011).

Secondly, certain risk factors, for example, past mental history, use of medications/antidepressants, current or past depression and level of available social support are almost unanimously recognised as important. This is in keeping with previous research which has also highlighted the importance of a history of mood disorders (Fontana et al., 2002) and social support (Evon et al., 2011), in vulnerability to IFN-α-induced-depression. Interestingly, the importance of social support is also in keeping with previous research based on patients’ own experiences of Hepatitis C (Erim et al., 2010, Glacken et al., 2001). Other factors, as highlighted by Tables I and II, are also taken into consideration and allow for a
 holistic approach. However, there is variability among nurses in their use of other information and this may in part be due to the current lack of available guidelines.

In accord with NDM studies of experts in other domains, these findings suggest that staff base their judgements and decisions on intuition, drawing on their past experience to recognise patterns and identify risks (Bowers et al., 1990, Klein, 1998). Decisions were not an end point in the process of care, but occurred as an ongoing process of gathering information, planning and taking action as necessary. Staff saw these patterns as subtle and often could not describe precisely how they gathered information or judged a situation as typical. As other studies suggest, intuition can be a highly efficient mode of decision making in limited-resource and time-critical environments (Currey and Botti, 2003, Xiao et al., 1997). However, accounts of adverse events and multiple sources of uncertainty also illuminated the fact that staff recognise the need for further support for enhancing the accuracy of clinical judgements. The lack of guidelines for prioritizing actions in current clinical practice results in uncertainty and means that nurses rely on a combination of knowledge, intuition, experience and team support.

An additional point raised by our study is that organisational and team processes are important in supporting nursing staff’s decision making. This is supported by previous study, which reported significantly greater adherence to antiviral therapy in a clinic based on an integrated mental health and medical approach (Knott et al., 2006). On the other hand, in the two hospitals with liaison psychiatry services, nurses said they had a tendency to over-rely on liaison psychiatrists, which may have exceeded the optimal level of referrals. Development of support aids could improve the accuracy of referrals, and therefore the effectiveness of clinical services for hepatitis C patients receiving IFN-α treatment. Finding the balance between precaution and overreliance on psychiatrists was identified by staff as a potential
area for improvement. To this end, the team-based decision making in this field merits further research in the future.

The major strength of this study is the use of qualitative methods and the NDM perspective, which have elucidated the decision making process of nurse specialists in a naturalistic setting. This study found evidence of how decision making is ongoing throughout the care process, and involves making difficult judgements in uncertain circumstances.

Limitations of this study include the demographic profile of the three metropolitan, teaching hospitals, which may not be representative of other hospitals. Given that all three hospitals are located in London, the issue of language barriers may be particularly prevalent in this study, and not elsewhere. The relatively small number of participants in this study also raises the question of transferability of our findings to other settings. However, given the focus of this study on a relatively homogeneous professional group with special expertise (Guest et al., 2006), it is likely that even with a small sample the most important factors affecting decision making were identified and that the results are generalisable to similar settings in other locations.

**Conclusion**

Our results have highlighted that current methods of identifying vulnerable patients rely on the availability of clinical experts and good communication within a multidisciplinary team. Detection and management of depression in this population is complex, however, various strategies are employed by nurses to overcome difficulties when making decision regarding patient welfare. Our observations may prove useful in the future development of further clinical guidelines.
Acknowledgements

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All authors have no competing interests to report.
References


Table I. Psychological risk factors assessed by nursing staff (n=9)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>n</th>
</tr>
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<tbody>
<tr>
<td><strong>History/diagnosis (verbal)</strong></td>
<td></td>
</tr>
<tr>
<td>Mental health history</td>
<td>9</td>
</tr>
<tr>
<td>Use of medications/anti-depressants</td>
<td>8</td>
</tr>
<tr>
<td>Seen by a psychiatrist and/or mental health team</td>
<td>7</td>
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<tr>
<td>Mental history of family/relatives</td>
<td>4</td>
</tr>
<tr>
<td>Schizophrenia/bipolar</td>
<td>2</td>
</tr>
<tr>
<td>Self-harm</td>
<td>2</td>
</tr>
<tr>
<td><strong>Signs and symptoms (verbal)</strong></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>8</td>
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<tr>
<td>Low mood</td>
<td>6</td>
</tr>
<tr>
<td>Emotional changes and deterioration</td>
<td>6</td>
</tr>
<tr>
<td>Angry/Irritable/Aggressive</td>
<td>5</td>
</tr>
<tr>
<td>Description of ‘how they are feeling’</td>
<td>5</td>
</tr>
<tr>
<td>Suicidal thoughts</td>
<td>3</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2</td>
</tr>
<tr>
<td>Self-harm</td>
<td>2</td>
</tr>
<tr>
<td>Low motivation</td>
<td>1</td>
</tr>
<tr>
<td><strong>Signs and symptoms (non-verbal)</strong></td>
<td></td>
</tr>
<tr>
<td>Eye contact</td>
<td>6</td>
</tr>
<tr>
<td>Tearful</td>
<td>5</td>
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<tr>
<td>Changes in behaviour</td>
<td>4</td>
</tr>
<tr>
<td>Agitation/Fidgety</td>
<td>3</td>
</tr>
<tr>
<td>General demeanour</td>
<td>3</td>
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<tr>
<td>Withdrawn</td>
<td>2</td>
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### Table II. Other factors assessed by nursing staff (n=9)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>n</th>
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<tbody>
<tr>
<td>Family/social support</td>
<td>8</td>
</tr>
<tr>
<td>Sleep pattern/deprivation</td>
<td>7</td>
</tr>
<tr>
<td>Alcohol/drug abuse</td>
<td>6</td>
</tr>
<tr>
<td>Employment</td>
<td>6</td>
</tr>
<tr>
<td>Housing arrangement</td>
<td>4</td>
</tr>
<tr>
<td>Life events (e.g. bereavement)</td>
<td>4</td>
</tr>
<tr>
<td>Medical history</td>
<td>4</td>
</tr>
<tr>
<td>Weight/Diet/Appetite</td>
<td>4</td>
</tr>
<tr>
<td>Medical co-morbidities</td>
<td>4</td>
</tr>
<tr>
<td>Activities/social life</td>
<td>2</td>
</tr>
<tr>
<td>Relationship/marital status</td>
<td>2</td>
</tr>
<tr>
<td>Fatigue/low energy</td>
<td>1</td>
</tr>
</tbody>
</table>
Table III. Main sources of uncertainty

<table>
<thead>
<tr>
<th>Source</th>
<th>Characteristic response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient engagement and familiarity</td>
<td>“I think if it’s the first time you’ve met a patient, its actually quite difficult for me to gauge those things.”</td>
</tr>
<tr>
<td></td>
<td>“It depends what the patient brings to the discussion, so you can asks questions and if they don’t want to talk about it or if they say no everything is fine…”</td>
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<tr>
<td></td>
<td>“I keep in encouraging patients to not keep it in. If there are problems they need to tell us so we can do something about it rather than just sort of suffer quietly.”</td>
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<td></td>
<td>“some people don’t want to always discuss their histories with medical staff as they may have had rather colourful lives and I always say that if there’s any history whether that’s physical or psychological or emotional, the interferon and the ribavirin will expose it.”</td>
</tr>
<tr>
<td>Distinguishing psychological symptoms from others</td>
<td>“Sometimes it’s difficult to separate out which is a physical things and which is related to their psychological health but I think they’re probably all related.”</td>
</tr>
<tr>
<td></td>
<td>“it’s hard to know what’s sort of a physical symptom from treatment or what is actually psychological…”</td>
</tr>
<tr>
<td>Referrals to psychiatrist</td>
<td>“There’s always those more borderline cases where you’re not quite sure; should I refer or shouldn’t I.”</td>
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<tr>
<td></td>
<td>“I feel that somebody may benefit from input from the likes of Dr. XXX (liaison psychiatrist), and yet the individual may not feel that, so that could be a little bit more of a difficult one where I’ve actually gone back and discussed with other staff and said if there were actually concerns.”</td>
</tr>
<tr>
<td>Language barriers</td>
<td>“also, we’re never quite sure that it is translated to...exactly what we want to say is translated to the patient and also the patient, what the patient wants to say to us is translated and I get exactly what they want to say.”</td>
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<td></td>
<td>“some of them will speak English to a limited degree and when you’re chatting to them, after a while, once you’ve heard yes yes yes so many times, you suddenly realise that, or you ask them a question and they give you the wrong answer, I will ask them a question, expecting and knowing what the answer should be and they’ll give me the wrong answer and I’ll know that they’re not understanding.”</td>
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