Beginning at the bottom of page 5 the author asks, "Are there other factors [other than fibrosis stage] we should be "looking at as well, such as autoimmune responses, mental health, or extrahepatic manifestations?"

My questions are as follows:

1. Is there a particular HCV patient population, e.g. those co-infected with HIV, the author has in mind when she refers to "autoimmune responses"?

No. The relationship between HCV and autoimmune triggers is based on genetic factors.

The HCV alone causes autoimmune responses in people. It does not occur only in those co-infected with HIV.

The page from World Health Organization has a section with refs.

http://www.who.int/csr/disease/hepatitis/whocdscsrlyo2003/en/index3.html#extrahepatic

Quote from WHO link above:

"Extrahepatic manifestations of HCV infection (known autoimmune examples in red)

Damage to the bile ducts, lymphoid aggregates or <u>follicles</u>, and <u>microvesicular</u> steatosis are some characteristic findings associated with HCV infection. $\frac{41}{52}$

Manifestations of HCV infection are primarily nonhepatic, and include <u>membranoproliferative</u> glomerulonephritis and <u>necrotizing</u> vasculitis of the skin. 39, 41, 52, 53, 97

No unique histopathologic findings that allow specific histopathologic diagnosis are associated with HCV infection. 41

Hepatitis C may be associated with autoimmune diseases such as <u>Sjögren's syndrome</u> and <u>sialadenitis</u>, <u>idiopathic pulmonary fibrosis</u>, <u>polyarteritis nodosa</u>, <u>porphyria cutanea tarda</u>, and a variant of autoimmune hepatitis associated with the presence of anti-kidney and liver microsomal auto<u>antibodies</u>. ³⁹, ⁴¹, ⁵², ⁵³

Antiviral treatment should be considered for hepatitis C patients manifesting extrahepatic complications. 53"

2. The group's submission mentions that many people with HCV are depressed. Is depression what she has in mind when referring to "mental health" or is she thinking of different degrees of anxiety and frustration that patients (especially those who think they are being "warehoused") are experiencing?

There is a known correlation between HCV and depression which is compounded by the psychological stress of having the disease, such as treatment issues, fear of death. The activity of the virus itself can trigger depression. http://hcvadvocate.org/hepatitis/factsheets_pdf/MH_HCV_and_Depression.pdf

From Peppermint Patti's FAQs, Section II.9.7:

Once hepatitis C has progressed to cirrhosis, sometimes even before, the patient can find himself or herself confused and unable to focus. This "brain fog" eventually can progress to full-blown Hepatic Encephalopathy, which is caused by the liver being unable to remove poisons from the blood such as ammonia. "A patient with chronic hepatic encephalopathy may develop progressive loss of memory, disorientation, untidiness, and muscular tremors, leading to a form of chronic dementia." NOTE: Controlling this (preventable and often reversible if caught in time) disease generally involves intensive care, expensive drugs and hospitalization.

3. What "extrahepatic manifestations" other than impaired renal function does the author have in mind?

Cancer other than liver cancer is one of the major manifestations: "Re searchers have long known that patients with hepatitis C are at increased risk of liver cancer. But a new study recently presented at the **European Association for the Study of the Liver's 50th International Liver Congress in Vienna, Austria**, finds hepatitis C may also raise the risk of developing other cancers." And "The researchers found that, compared with patients without HCV, patients with HCV are not only at increased risk of liver cancer but of other cancers, including non-Hodgkin lymphoma and prostate and renal cancers." And "Based on their findings, the researchers calculated that patients with HCV were 2.5 times more likely than non-HCV patients to be diagnosed with cancer, including liver cancer. When liver cancer was excluded, cancer risk was still almost two times higher for patients with HCV, according to the study." (http://www.medicalnewstoday.com/articles/293082.php)

See attached Cdn Assn for the Study of the Liver 2015 Guidelines for the Treatment of Viral Hepatitis (**Can J Gastroenterol Hepatol Vol29 No 1 January/February 2015. PAGE 21**: "Patients with extrahepatic manifestations of CHC including cryoglobulinemic vasculitis, porphyria cutanea tarda and glomerulonephritis should be considered for treatment regardless of their underlying liver disease severity because these conditions typically respond to viral eradication (30)." and "(Recommendation # 6) Patients with extrahepatic manifestations of HCV should be considered for antiviral therapy (Class 1, Level A).

Also see WHO article referenced in point 1.

A wide variety of extrahepatic manifestations (cardiac function, neuropathic, vascular, dermatological) can be triggered by hepatitis C.

http://hcvadvocate.org/hepatitis/factsheets_pdf/Extrahepatic.pdf

More on extrahepatic.. Another study that shows a clear relationship between chronic HCV and heart disease Article: Chronic Hepatitis C Virus Infection Is Associated with Subclinical Coronary Atherosclerosis in the Multicenter AIDS Cohort Study (MACS): a Cross-Sectional Study—RA McKibben et al.

Source: J Infect Dis. 2015 Jul 27. pii: jiv396. [Epub ahead of print]

Hep C is not just a liver disease. It affects ALL the body organs. See list below (from HepCBC's "Peppermint Patti's FAQs") which references:

The publication Hepatitis C: management guide а (Aust Family Physician 1999;28 SI:27-31) recently listed a range of HCV extrahepatic conditions (below). ED30, Review, September 2000, by Dr Bryan Speed 12), Dr Tony Jones (page Dr Ed Gane (page 30) and Tina Pirola (page 34).

Arthralgia
Cyroglobulinaemia
Diabetes melitis
Glomerulonephritis
Lichen planus
Non-Hodgkin's lymphoma
Peripheral neuropathy
Porphyria cutanea tarda
Sicca syndrome
Sjogren's syndrome
Thrombocytopaenia
Thyroid disorders
Vasculitis