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**EATING DISORDERS****Binge-eating disorder is associated with an unfavourable body mass composition in patients with Non-alcoholic fatty liver disease**

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Manuscripts

**Binge-eating disorder is associated with an unfavorable body mass composition in patients with non-alcoholic fatty liver disease (Binge-eating disorder in NAFLD)**

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8 CH wrote the first draft and carried out the data collection and analysis. BMH, PM and MRT edited  
9 the manuscript. All authors read and approved the final draft submitted.

## ABSTRACT

The interaction between eating disorders and non-alcoholic fatty liver disease (NAFLD) remains unexplored, especially with regards to binge-eating disorder (BED). Our team conducted a service evaluation project in order to assess risk factors for the presence of BED among patients with NAFLD and the impact of BED on body mass composition. The overall prevalence of patients screening positive to BED Screener-7 (BEDS-7) was 28.4%, while a previous diagnosis of depression and marital status (as single or separated) were independently associated with positive BED. Furthermore, patients with positive BEDS-7 had higher BMI, with greater visceral component and overall lower muscle mass. There was no difference in terms of liver disease severity as assessed by non-invasive markers of fibrosis. However, as body mass composition and sarcopenia have been shown to be associated to disease progression in patients with NAFLD, further studies are required to ascertain the long-term impact of BED in these patients. Moreover, further work is warranted to identify to implement multidisciplinary approach within clinical psychology for the management of patients with BED, who may be particularly challenging in terms of achieving lifestyle modifications. As a hepatology community, we should address NAFLD with a more holistic approach.

**Keywords:** non-alcoholic fatty liver disease, binge-eating disorder, visceral obesity, sarcopenia, depression

## 1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is considered the hepatic manifestation of metabolic syndrome and a leading cause of liver disease worldwide (Younossi, Marchesini, Pinto-Cortez, & Petta, 2019). As there is still no licensed drug for treating NAFLD, long-term weight control and other lifestyle interventions stand as the mainstay of the management of the disease (European Association for the Study of the, European Association for the Study of, & European Association for the Study of, 2016). The decline in lean body mass, namely sarcopenia, has been recognised as one of the comorbidities associated with chronic liver diseases, including NAFLD (Bhanji, Carey, Yang, & Watt, 2017). Risk factors for sarcopenia in patients with type 2 diabetes mellitus (a central condition within the metabolic syndrome) include biological factors (including age, disease duration and glycaemic control), and lifestyle factors, with poor nutrition amongst the most contributory of this latter group (Izzo, Massimino, Riccardi, & Della Pepa, 2021). Moreover, sarcopenia in patients with NAFLD is associated with more severe forms of the condition, including non-alcoholic steatohepatitis (NASH) or advanced fibrosis (Yu, Shi, Liu, & Chen, 2018). Furthermore, reducing fat to muscle mass ratio may improve liver disease in diabetics with NAFLD (Osaka et al., 2019).

Notably, patients with NAFLD also report high prevalence of psychiatric disorders (Weinstein et al., 2011). However, there has been little exploration as to whether patients with NAFLD have higher rates of disordered eating patterns, and their implication in clinical practice if so. More specifically, if present, such abnormal eating patterns may impact upon nutritional status (including calorie intake and/or relative intake of macro- and micronutrients), which may contribute to sarcopenic obesity and associated changes in body composition that characterise the condition. A close interaction between socio-economic status, quality of diet and NAFLD has been suggested before, which may also be contributory to the nutritional status of NAFLD patients (Alkerwi, Vernier, Sauvageot, Crichton, & Elias, 2015; Frohme & Tacke, 2020).

Binge-eating disorder (BED) represents the commonest eating disorder in Western countries with an estimated prevalence of 1.4% in the general population (Kessler et al., 2013). Patients with BED have recurrent episodes of binge eating, which occur on average at least once a week for three months and are associated with marked distress (Battle, 2013). Unlike other eating disorders, individuals with BED do not often develop compensatory behaviours such as inducing vomiting or starvation. Subsequently, over 40% of patients with BED experience obesity and carry an increased risk of developing metabolic syndrome (Hudson et al., 2010) (Mathisen et al., 2018).

However, the interactions between eating disorders or BED, body mass composition and the overall clinical impact in NAFLD has remained poorly-explored. A relationship between BED and these other factors could give further insight into the pathology of NAFLD, and might inform novel, psychological approaches for management of the condition.

**2. A PRELIMINARY INVESTIGATION**

Our team conducted a service evaluation project to assess the prevalence of binge-eating disorders and ascertain risk factors for BED among patients with NAFLD. Furthermore, the impact of BED on body mass composition was also assessed in this population. All new referrals with a diagnosis of NAFLD followed-up at Imperial College Healthcare NHS Trust (London, UK) were included in the analysis. Patients were asked to complete a 7-items Binge-Eating Disorder Screener (BEDS-7) which is a brief, patient-reported screener for BED , with an overall 100% sensitivity and 38.7% specificity for diagnosing BED (Herman et al., 2016). The screener begins with a single yes/no question related to excessive overeating in the last three months. If individuals answer affirmatively, they answer six more psychometric questions that align with DSM-5 criteria for diagnosing BED. In this second part, patients are asked to report previous episodes of lack of control, episodes of guilt, embarrassment and, finally, self-induced vomiting due to the binge eating. Other data recorded from patients included the severity of their NAFLD, their self-reported physical activity levels, and demographics (including socio-economic status, based on index of multiple deprivation); full details of this are provided within **Supplementary Materials**. In addition, sample size effects were estimated using d Cohen or number needed to treat/take (NNT) as appropriate (**Supplementary Materials and Table 1**).

Between March 2019 and February 2020, a total of 81 patients were included in the study, 25 (28.4%) of whom screened positive for BED. Overall, those who screened positive for BED were significantly younger (52 vs 59 years,  $p=0.03$ ;  $d$  Cohen 0.38) and more frequently single or separated (61.5% vs 20.8%,  $p=0.013$ ; NNT 2.4) compared to BEDS-7 negative ( $n=58$ ) (**Table 1**). Furthermore, patients with positive BEDS-7 suffered more frequently from depression compared with non-BED (34.8% vs 12.1%,  $p=0.017$ ; NNT 4.4) and were more frequently on anti-depressant medications (31.5% vs 10.2%,  $p=0.02$ ; NNT 3.5). Of note, none of the patients was treated with weight-gain inducing medications, such as olanzapine, risperidone, quetiapine or clozapine. In terms of socio-economic status, 49 patients were classified as living in the most socially deprived areas (Index of

Multiple Deprivation, IMD tertile 1), while 11 were living in the least deprived areas (IMD tertile 3). When looking into whether deprivation status had an impact on screening positive for BED, there was no difference in terms of overall IMD rank as well as single domain ranks between those who screened positive for BED vs those who did not (**Supplementary material**).

In terms of risk factors, a previous diagnosis of depression (aOR 2.5, 95% CI 1.1-7.2, SE 0.53, Wald 2.3,  $p=0.015$ ) and marital status (as single or separated) (aOR 4.2, 95% CI 1.09-10.8, SE 0.67, Wald 5.9,  $p=0.0001$ ) were independently associated with screening positive for BEDS-7, after adjusting for age, female gender and socioeconomic status (IMD). The Hosmer and Lemeshow test was 0.87, showing that the model fits the population well.

Given the importance of body mass composition in this population, when we had a closer look into anthropometric parameters as well as into body mass composition. Overall, patients who screened positive for BED had significantly larger waist (111.5 vs 103 cm,  $p=0.03$ ;  $d$  Cohen -0.5) and hip circumferences (111.5 vs 103 cm,  $p=0.01$ ;  $d$  Cohen -0.39) compared to those who did not (**Table 1**). Moreover, median BMI was also significantly higher among those who tested positive for BED (33.8 vs 29.6 kg/m<sup>2</sup>;  $d$  Cohen -0.37). Interestingly, muscle mass was significantly lower in those with positive BEDS-7 (56.7% vs 65.1%,  $p=0.001$ ;  $d$  Cohen 0.79) while fat mass was significantly higher (37.1% vs 31.4%,  $p=0.002$ ;  $d$  Cohen -0.06) compared to those with negative BEDS-7. These results suggest a more enhanced tendency towards sarcopenic obesity in those who screened positive for BEDS-7.

As fibrosis stage represents the main prognostic factors in patients with NAFLD (Ekstedt et al., 2015), we explored whether there was any difference in terms of non invasive markers of fibrosis between the two groups stratified for BEDS-7 results. There was no difference in terms of Fibrosis score-4 FIB-4 (non invasive markers based on blood tests) as well as in terms of transient elastography (non invasive marker based on shear wave propagation) (Wang et al., 2015) (**Table 1**). These findings suggest that patients who screened positive for BED do not present more advanced liver disease compared to those who screened negative. These observations are in line with previously published data (Canivet et al., 2020). However, longitudinal studies are required to ascertain the long-term impact of BED on liver disease progression in NAFLD.

**3. MORE RESEARCH IS NEEDED**

There remain significant gaps in elucidating the association between NAFLD and BED. More importantly, there is an increasing need for raising the awareness of psychiatric disorders and BED in the hepatology community. In this setting, we have highlighted those we think are the key priorities for future research in the field.

**3.1 Improvement of the diagnosis of BED in NAFLD**

One limitation of this project was a small sample size; however, reassuringly, the d Cohen suggested a moderate to small effect of the sample size on most variables. A further limitation of this work was the use of a screener rather than a diagnostic interview for identifying patients susceptible for BED. Other works in the field have also employed screeners for BED in a similar fashion, such as the Binge Eating Scale (BES) (Zhang et al., 2017) or the Bulimia-test revised (Canivet et al., 2020). These studies had similarities and differences in design to our work but found comparable outcomes, noting the high prevalence of BED in a NAFLD population (Zhang et al., 2017) and no clear association with NAFLD disease severity. Being shorter but showing similar sensitivity, the BEDS-7 may prove advantageous for screening for BED in the context of a time-limited clinical appointment. There is, however, a specific need for studies including a two-steps approach, i.e involving a specialist interview after the screener. This will allow firstly for true prevalence of the BED, secondly for a more comprehensive evaluation of these patients. An input from a psychiatric perspective will also shed light on possible therapeutical options for the management of BED in this population.

**3.2 A tailored approach to patients with BED and NAFLD**

As there is no licensed medication to treat NAFLD, weight loss remains the mainstay of treatment of the disease. However, lifestyle changes are not easy to obtain in clinical practice, as most patients complain a long series of dieting and weight cycling. In this sense, patients with BED may prove particularly difficult to manage, as they may show peculiar dietary features, such as greater frequency of snacks, morning under-eating or eating double meals (Carrard, Crepin, Ceschi, Golay, & Van der Linden, 2012; Masheb, Grilo, & White, 2011). Moreover, there is evidence suggesting that dietary restraint may perpetuate BED rather than control it in these patients (Carrard

et al., 2012). As such, further studies are needed to explore the application of tailored care beyond weight-reducing regimes specifically in patients with BED and NAFLD.

Behavioural intervention/psychological support for patients has now become well-embedded in other chronic conditions with behavioural contributions, including other liver diseases (i.e. alcohol-related liver disease (Mullish, Kabir, Thursz, & Dhar, 2014)) and in bariatric surgery pre-assessment (Ratcliffe et al., 2014); based on this precedent and the results of our current study, we are in the process of introducing a clinical psychologist into our NAFLD multidisciplinary team.

### 3.3 Long-term effects of BED on NAFLD

Body mass composition plays a crucial role in the development and progression of NAFLD (De Fre et al., 2019). Sarcopenic obesity *per se* is considered a strong driver of advanced fibrosis in NAFLD, regardless of the other components of metabolic syndrome (Merli & Dasarathy, 2015). Our preliminary findings suggest that patients who screened positive for BED show an unfavourable body mass composition compared to those negative for BED, i.e. an overall greater fat mass and lower muscle mass. Also, literature suggests that patients with BED frequently suffer from malnutrition and vitamin deficiency compared to healthy controls (Bahat, Reisler, Brandriss, Bar-Chaim, & Goldman, 2020) and this may act as an accelerator for the development of sarcopenia. Collectively, these results demand *ad-hoc*, prospective studies to investigate the progression of liver disease in this population, as they may be more susceptible to advanced fibrosis in the long-term.

#### 4. CONCLUSION

In conclusion, we found that 28.4% of patients with NAFLD screened positive for BEDs-7 in a tertiary care centre. A previous diagnosis of depression and marital status are independently associated with a positive BEDs-7. In terms of body mass composition, screening positive for BED is associated with increased visceral adiposity and an overall reduced muscle mass. However, our findings suggest that patients who screened positive for BED do not present more advanced liver disease compared to those who screened negative. Tackling obesity and metabolic diseases required a holistic approach. As a hepatology community, we should not overlook mental health in NAFLD patients, and should focus more on assessment and modification of eating behaviour.

For Review Only

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6. FIGURE LEGEND

Figure 1: Fat and muscle mass as percentage of total body weight in patients who screened positive for BED (Blue) vs those who did not (Yellow).

**Binge-eating disorder is associated with an unfavourable body mass composition in patients  
with Non-alcoholic fatty liver disease  
(Binge-eating disorder in NAFLD)**

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8 CH wrote the first draft and carried out the data collection and analysis. BMH, PM and MRT edited  
9 the manuscript. All authors read and approved the final draft submitted.

**ABSTRACT (178 words)**

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**Keywords:** nNon-alcoholic fatty liver disease, bBinge-eEating dDisorder, Visceral obesity, sarcopenia, depression

## 1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is considered the hepatic manifestation of metabolic syndrome and a leading cause of liver disease worldwide (Younossi, Marchesini, Pinto-Cortez, & Petta, 2019). As there is still no licensed drug for treating NAFLD, long-term weight control and other lifestyle interventions stand as the mainstay of the management of the disease (European Association for the Study of the, European Association for the Study of, & European Association for the Study of, 2016). The decline in lean body mass, namely sarcopenia, has been recognised as one of the comorbidities associated with chronic liver diseases, including NAFLD (Bhanji, Carey, Yang, & Watt, 2017). Risk factors for sarcopenia in patients with type 2 diabetes mellitus (a central condition within the metabolic syndrome) include biological factors (including age, disease duration and glycaemic control), and lifestyle factors, with poor nutrition amongst the most contributory of this latter group (Izzo, Massimino, Riccardi, & Della Pepa, 2021). Moreover, sarcopenia in patients with NAFLD is associated with more severe forms of the condition, including non-alcoholic steatohepatitis (NASH) or advanced fibrosis (Yu, Shi, Liu, & Chen, 2018). Furthermore, reducing fat to muscle mass ratio may improve liver disease in diabetics with NAFLD (Osaka et al., 2019).

Notably, patients with NAFLD also report high prevalence of psychiatric disorders (Weinstein et al., 2011). However, there has been little exploration as to whether patients with NAFLD have higher rates of disordered eating patterns, and their implication in clinical practice if so. More specifically, if present, such abnormal eating patterns may impact upon nutritional status (including calorie intake and/or relative intake of macro- and micronutrients), which may contribute to sarcopenic obesity and associated changes in body composition that characterise the condition. A close interaction between socio-economic status, quality of diet and NAFLD has been suggested before, which may also be contributory to the nutritional status of NAFLD patients (Alkerwi, Vernier, Sauvageot, Crichton, & Elias, 2015; Frohme & Tacke, 2020).

Binge-eating disorder (BED) represents the commonest eating disorder in Western countries with an estimated prevalence of 1.4% in the general population (Kessler et al., 2013). Patients with BED have recurrent episodes of binge eating, which occur on average at least once a week for three months and are associated with marked distress (Battle, 2013). Unlike other eating disorders, individuals with BED do not often develop compensatory behaviours such as inducing vomiting or starvation. Subsequently, over 40% of patients with BED experience obesity and carry an increased risk of developing metabolic syndrome (Hudson et al., 2010) (Mathisen et al., 2018).

1           However, the interactions between eating disorders or BED, body mass composition and the  
2 overall clinical impact in NAFLD has remained poorly-explored. A relationship between BED and  
3 these other factors could give further insight into the pathology of NAFLD, and might inform novel,  
4 psychological approaches for management of the condition.

7   **2. A PRELIMINARY INVESTIGATION**

8           Our team conducted a service evaluation project to assess the prevalence of ~~B~~binge-e Eating  
9 ~~d~~Disorders and ascertain risk factors for BED among patients with NAFLD. Furthermore, the impact  
10 of BED on body mass composition was also assessed in this population. All new referrals with a  
11 diagnosis of NAFLD followed-up at Imperial College Healthcare NHS Trust (London, UK) were  
12 included in the analysis. Patients were asked to complete a 7-items Binge-E-eating ~~D~~isorder  
13 ~~S~~creener (BEDS-7) which is a brief, patient-reported screener for BED , with an overall 100%  
14 sensitivity and 38.7% specificity for diagnosing BED (Herman et al., 2016). The screener begins with a  
15 single yes/no question related to excessive overeating in the last three months. If individuals answer  
16 affirmatively, they answer six more psychometric questions that align with DSM-5 criteria for  
17 diagnosing BED. In this second part, patients are asked to report previous episodes of lack of control,  
18 episodes of guilt, embarrassment and, finally, self-induced vomiting due to the binge eating. Other  
19 data recorded from patients included the severity of their NAFLD, their self-reported physical activity  
20 levels, and demographics (including socio-economic status, based on index of multiple deprivation);  
21 full details of this are provided within **Supplementary Materials**. In addition, sample size effects  
22 were estimated using d Cohen or number needed to treat/take (NNT) as appropriate  
23 (Supplementary Materials and Table 1).

24           Between March 2019 and February 2020, a total of 81 patients were included in the study,  
25 25 (28.4%) of whom screened positive for BED. ~~The answers from those who screened positive for~~  
26 ~~BED are shown in Table 1.~~ Overall, those who screened positive for BED were significantly younger  
27 (52 vs 59 years,  $p=0.03$ ; d Cohen 0.38) and more frequently single or separated (61.5% vs 20.8%,  
28  $p=0.013$ ; NNT 2.4) compared to BEDS-7 negative (n=58) (Table 1). Furthermore, patients with  
29 positive BEDS-7 suffered more frequently from depression compared with non-BED (34.8% vs 12.1%,  
30  $p=0.017$ ; NNT 4.4) and were more frequently on anti-depressant medications (31.5% vs 10.2%,  
31  $p=0.02$ ; NNT 3.5). Of note, none of the patients was treated with weight-gain inducing medications,  
32 such as olanzapine, risperidone, quetiapine or clozapine. In terms of socio-economic status, 49

patients were classified as living in the most socially deprived areas (Index of Multiple Deprivation, IMD tertile 1), while 11 were living in the least deprived areas (IMD tertile 3). When looking into whether deprivation status had an impact on screening positive for BED, there was no difference in terms of overall IMD rank as well as single domain ranks between those who screened positive for BED vs those who did not (**Supplementary material**).

In terms of risk factors, a previous diagnosis of depression (aOR 2.5, 95% CI 1.1-7.2, SE 0.53, Wald 2.3,  $p=0.015$ ) and marital status (as single or separated) (aOR 4.2, 95% CI 1.09-10.8, SE 0.67, Wald 5.9,  $p=0.0001$ ) were independently associated with screening positive for BEDS-7, after adjusting for age, female gender and socioeconomic status (IMD). The Hosmer and Lemeshow test was 0.87, showing that the model fits the population well.

Given the importance of body mass composition in this population, when we had a closer look into anthropometric parameters as well as into body mass composition. Overall, patients who screened positive for BED had significantly larger waist (111.5 vs 103 cm,  $p=0.03$ ; *d Cohen -0.5*) and hip circumferences (111.5 vs 103 cm,  $p=0.01$ ; *d Cohen -0.39*) compared to those who did not (**Table 1**). Moreover, median BMI was also significantly higher among those who tested positive for BED (33.8 vs 29.6 kg/m<sup>2</sup>; *d Cohen -0.37*). Interestingly, muscle mass was significantly lower in those with positive BEDS-7 (56.7% vs 65.1%,  $p=0.001$ ; *d Cohen 0.79*) while fat mass was significantly higher (37.1% vs 31.4%,  $p=0.002$ ; *d Cohen -0.06*) compared to those with negative BEDS-7. These results suggest a more enhanced tendency towards sarcopenic obesity in those who screened positive for BEDS-7.

As fibrosis stage represents the main prognostic factors in patients with NAFLD (Ekstedt et al., 2015), we explored whether there was any difference in terms of non invasive markers of fibrosis between the two groups stratified for BEDS-7 results. There was no difference in terms of Fibrosis score-4 FIB-4 (non invasive markers based on blood tests) as well as in terms of transient elastography (non invasive marker based on shear wave propagation) (Wang et al., 2015) (**Table 1**). These findings suggest that patients who screened positive for BED do not present more advanced liver disease compared to those who screened negative. These observations are in line with previously published data (Canivet et al., 2020). However, longitudinal studies are required to ascertain the long-term impact of BED on liver disease progression in NAFLD.

**3. MORE RESEARCH IS NEEDED**

There remain significant gaps in elucidating the association between NAFLD and BED. More importantly, there is an increasing need for raising the awareness of psychiatric disorders and BED in the hepatology community. In this setting, we have highlighted those we think are the key priorities for future research in the field.

**3.1 Improvement of the diagnosis of BED in NAFLD**

One limitation of this project was a small sample size; however, reassuringly, the Cohen suggested a moderate to small effect of the sample size on most variables. A further limitation of this work was a small size and the use of a screener rather than a diagnostic interview for identifying patients susceptible for BED. Other works in the field have also employed screeners for BED in a similar fashion, such as the Binge Eating Scale (BES) (Zhang et al., 2017) or the Bulimia-test revised (Canivet et al., 2020). These studies had similarities and differences in design to our work but found comparable outcomes, noting the high prevalence of BED in a NAFLD population (Zhang et al., 2017) and no clear association with NAFLD disease severity. Being shorter but showing similar sensitivity, the BEDS-7 may prove advantageous for screening for BED in the context of a time-limited clinical appointment. There is, however, a specific need for studies including a two-steps approach, i.e involving a specialist interview after the screener. This will allow firstly for true prevalence of the BED, secondly for a more comprehensive evaluation of these patients. An input from a psychiatric perspective will also shed light on possible therapeutical options for the management of BED in this population.

**3.2 A tailored approach to patients with BED and NAFLD**

As there is no licensed medication to treat NAFLD, weight loss remains the mainstay of treatment of the disease. However, lifestyle changes are not easy to obtain in clinical practice, as most patients complain a long series of dieting and weight cycling. In this sense, patients with BED may prove particularly difficult to manage, as they may show peculiar dietary features, such as greater frequency of snacks, morning under-eating or eating double meals (Carrard, Crepin, Ceschi, Golay, & Van der Linden, 2012; Masheb, Grilo, & White, 2011). Moreover, there is evidence suggesting that dietary restraint may perpetuate BED rather than control it in these patients (Carrard

et al., 2012). As such, further studies are needed to explore the application of tailored care beyond weight-reducing regimes specifically in patients with BED and NAFLD.

Behavioural intervention/psychological support for patients has now become well-embedded in other chronic conditions with behavioural contributions, including other liver diseases (i.e. alcohol-related liver disease (Mullish, Kabir, Thursz, & Dhar, 2014)) and in bariatric surgery pre-assessment (Ratcliffe et al., 2014); based on this precedent and the results of our current study, we are in the process of introducing a clinical psychologist into our NAFLD multidisciplinary team.

### 3.3 Long-term effects of BED on NAFLD

Body mass composition plays a crucial role in the development and progression of NAFLD (De Fre et al., 2019). Sarcopenic obesity *per se* is considered a strong driver of advanced fibrosis in NAFLD, regardless of the other components of metabolic syndrome (Merli & Dasarathy, 2015). Our preliminary findings suggest that patients who screened positive for BED show an unfavourable body mass composition compared to those negative for BED, i.e. an overall greater fat mass and lower muscle mass. Also, literature suggests that patients with BED frequently suffer from malnutrition and vitamin deficiency compared to healthy controls (Bahat, Reisler, Brandriss, Bar-Chaim, & Goldman, 2020) and this may act as an accelerator for the development of sarcopenia. Collectively, these results demand *ad-hoc*, prospective studies to investigate the progression of liver disease in this population, as they may be more susceptible to advanced fibrosis in the long-term.

#### 1 4. CONCLUSION

2 In conclusion, we found that 28.4% of patients with NAFLD screened positive for BEDs-7 in a  
3 tertiary care centre. A previous diagnosis of depression and marital status are independently  
4 associated with a positive BEDs-7. In terms of body mass composition, screening positive for BED is  
5 associated with increased visceral adiposity and an overall reduced muscle mass. However, our  
6 findings suggest that patients who screened positive for BED do not present more advanced liver  
7 disease compared to those who screened negative. Tackling obesity and metabolic diseases required  
8 a holistic approach. As a hepatology community, we should not overlook mental health in NAFLD  
9 patients, and should focus more on assessment and modification of eating behaviour.

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6. FIGURE LEGEND

Figure 1: Fat and muscle mass as percentage of total body weight in patients who screened positive for BED (Blue) vs those who did not (Yellow).

## **SUPPLEMENTARY MATERIAL**

### **1. METHODS**

#### **1.1 Study population**

At baseline, a full range of clinical parameters were recorded: demographic, anthropometric and biochemical data. Based upon baseline blood tests, Fibrosis-4 (FIB-4) score was also calculated following the published formula. Cut-offs of FIB-4 were applied to stratify the patients into low, intermediate and high risk respectively for liver fibrosis (Vallet-Pichard, Mallet, & Pol, 2006). Comorbidities were recorded based upon past medical history. This included a specific focus upon psychological/ psychiatric conditions in the medical history, given the potential interplay between such disorders (in particular, depression) and NAFLD (Izzo, Massimino, Riccardi, & Della Pepa, 2021).

Physical activity levels were measured against the current recommendations (Department of Health, 2004). Patients were therefore stratified into sedentary, minimally active and moderately active.

#### **1.2 Index of multiple deprivation**

There is a well-established interaction between socio-economic status and quality of diet (Alkerwi, Vernier, Sauvageot, Crichton, & Elias, 2015), as well as an association between 'food insecurity' and NAFLD (Frohme & Tacke, 2020). To explore the relationship between socio-economic status and screening positive for BED, patients' postcodes were used to assign a deprivation rank derived by the English Index of Multiple Deprivation (IMD). In the UK, IMD scores represent a measure of the socioeconomic status of a patient, based on the income, employment, disability, educational attainment and other attributes. IMD also provides a breakdown of single deprivation domains such as income, employment, education, living environment, crime and health and disability.

#### **1.3 Body mass composition and FibroScan**

Body mass composition was analysed at baseline, using a bioelectrical impedance analysis (BIA). On a BIA measurement, muscle mass and fat mass were expressed as relative percentage (%) over the total body mass. Furthermore, patients received a fasting Fibroscan, which reports a liver stiffness measurement (LSM) and a controlled attenuation parameter (CAP) score. Specifically, liver stiffness is estimated based on the velocity of low-frequency elastic shear wave propagating through the liver and is an established proxy of hepatic fibrosis; in contrast, CAP is a marker of hepatic

1     steatosis (European Association for Study of & Asociacion Latinoamericana para el Estudio del,  
2     2015).  
3             Clinical parameters as well as BIA and transient elastography were recorded at the routine 6-  
4     months follow-up visit.  
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#### 1.4 Ethics

This study was considered a service evaluation project, using routinely collected patient data, therefore no ethical approval was required under the UK policy framework for health and social care.

#### 1.5 Statistical analysis

As per the Shapiro-Wilk test, data were non-normally distributed. Continuous variables were expressed as medians and interquartile range (IQR), while categorical variables were expressed as relative frequencies and percentages (%). The difference between the groups was explored using Mann-Whitney for continuous variables and Chi square for categorical variables. To minimise the effect of sample size bias, we calculated *d* Cohen as an effect size metric for continuous and categorical data. For dichotomous data, numbers-needed-to-treat/take (NNT) was also calculated.

Significant variables were carried forward to multivariate analysis with logistic regression to identify the odds ratio (OR) of the variables independently associated with outcomes. OR were adjusted for confounding factors and reported with 95% confidence interval (95% CI). Hosmer and Lemeshow test was calculated to assess the goodness of fit of the logistic regression model. All tests were considered significant with a p-value=0.05 was considered significant. Statistical analysis was performed using SPSS© (version 23.0; SPSS Inc. Chicago, IL).

**TABLE 1. Differences in Index of multiple deprivation and single domains between those with positive BEDS-7 and negative BED-7.**

|                                   | <b>BEDS-7 positive</b> | <b>BEDS-7 negative</b> | <b>P-value</b> | <b><u>d Cohen</u></b><br><b><u>(95%CI)</u></b> |
|-----------------------------------|------------------------|------------------------|----------------|------------------------------------------------|
|                                   | <b>N=23</b>            | <b>N=58</b>            |                |                                                |
|                                   | <b>Median (IQR)</b>    | <b>Median (IQR)</b>    |                |                                                |
| <b>IMD</b>                        | 10706<br>(7079-17746)  | 12986<br>(7082-20610)  | 0.52           | <u>0.45</u><br><u>(-0.02-0.94)</u>             |
| <b>Income rank</b>                | 9875<br>(6640-16906)   | 13348<br>(5782-21306)  | 0.53           | <u>0.55</u><br><u>(0.06-1.05)</u>              |
| <b>Employment Rank</b>            | 12046<br>(9004-20239)  | 13283<br>(6849-25523)  | 0.48           | <u>0.2</u><br><u>(-0.27-0.68)</u>              |
| <b>Education and skills rank</b>  | 22462<br>(17558-27020) | 22032<br>(16517-27434) | 0.96           | <u>-0.07</u><br><u>(-0.55-0.41)</u>            |
| <b>Health and disability rank</b> | 18838<br>(14341-24511) | 20486<br>(15003-26164) | 0.59           | <u>0.27</u><br><u>(-0.2-0.7)</u>               |
| <b>Crime rank</b>                 | 10824<br>(4251-17080)  | 10599<br>(6405-18730)  | 0.91           | <u>-0.03</u><br><u>(-0.52-0.44)</u>            |
| <b>Barriers rank</b>              | 4597<br>(3485-9112)    | 6683<br>(2521-11126)   | 0.76           | <u>0.34</u><br><u>(-0.13-0.83)</u>             |
| <b>Living environment rank</b>    | 5448<br>(3036-7849)    | 6743<br>(4614-9373)    | 0.38           | <u>0.21</u><br><u>(-0.26-0.7)</u>              |

\* indicates a significant difference between the two groups to a p value <0.05.

1 *IMD: index of multiple deprivation.*

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- 3
- 4 Alkerwi, A., Vernier, C., Sauvageot, N., Crichton, G. E., & Elias, M. F. (2015). Demographic and  
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- 20

**Table 1: Characteristics of the study population stratified according to BEDS-7 results.** In addition, sample size effect is reported as *d* Cohen for continuous variables and number-needed-to-treat/take (NNT) for categorical variables.

|                                    | <b>BEDS-7<br/>positive<br/>N=23</b> | <b>BEDS-7<br/>negative<br/>N=58</b> | <b>P-value</b> | <b><i>d</i> Cohen<br/>(95%CI)</b> |
|------------------------------------|-------------------------------------|-------------------------------------|----------------|-----------------------------------|
|                                    | <b>Median (IQR)</b>                 | <b>Median (IQR)</b>                 |                |                                   |
| <b>Age, yrs</b>                    | <b>52<br/>(45-57.5)</b>             | <b>59<br/>(49-63)</b>               | <b>0.03*</b>   | 0.38<br>(-0.1-0.8)                |
| <b>BMI, kg/m<sup>2</sup></b>       | <b>33.8<br/>(32.4-35.6)</b>         | <b>29.6 (26.0-34.6)</b>             | <b>0.01*</b>   | -0.37<br>(-0.86-0.11)             |
| <b>Waist<br/>circumference, cm</b> | <b>111.5<br/>(102-120)</b>          | <b>103<br/>(95-113)</b>             | <b>0.03*</b>   | -0.5<br>(-0.99- -0.017)           |
| <b>Hip circumference,<br/>cm</b>   | <b>111.5<br/>(105-118)</b>          | <b>103<br/>(100-113)</b>            | <b>0.01*</b>   | -0.39<br>(-0.88- 0.08)            |
| <b>Waist-hip ratio</b>             | 0.98<br>(0.96-1.06)                 | 0.97<br>(0.94-0.99)                 | 0.24           | -0.34<br>(-0.83-0.13)             |
| <b>Fat mass, % of BW</b>           | <b>37.1<br/>(32.15-42.58)</b>       | <b>31.4<br/>(22.97-36.36)</b>       | <b>0.002*</b>  | -0.06<br>(-0.54-0.42)             |
| <b>Muscle mass, % of<br/>BW</b>    | <b>56.7<br/>(52.57-63.17)</b>       | <b>65.1<br/>(60.31-72.79)</b>       | <b>0.001*</b>  | 0.79<br>(0.2-1.2)                 |
| <b>Fat: muscle mass<br/>ratio</b>  | <b>0.62<br/>(0.50-0.78)</b>         | <b>0.48<br/>(0.31-0.57)</b>         | <b>0.002*</b>  | -0.9<br>(-1.49- -0.47)            |
| <b>LSM, kPa</b>                    | 7.8<br>(5.35-12.95)                 | 6.55<br>(5.5-9.0)                   | 0.28           | -0.5<br>(-1.04-0-0.06)            |
| <b>CAP score, dB/m</b>             | <b>331<br/>(292-372.5)</b>          | <b>299<br/>(249-342)</b>            | <b>0.041*</b>  | -0.5<br>(-0.99- -0.01)            |
| <b>Delta LSM,<br/>kPa/month</b>    | -0.063<br>(-0.24- +0.07)            | -0.081<br>(-0.32 - +0.001)          | 0.28           | 0.08<br>(-0.4-0.56)               |
| <b>ALT, IU/L</b>                   | 55                                  | 46                                  | 0.99           | 0.08                              |

|                                  |                     |                     |                |                      |
|----------------------------------|---------------------|---------------------|----------------|----------------------|
|                                  | (34-73)             | (37-75)             |                | (-0.39-0.56)         |
| <b>AST, IU/L</b>                 | 33<br>(28-47)       | 37<br>(30.5-52.5)   | 0.28           | 0.22<br>(-0.25-0.7)  |
| <b>GGT, IU/L</b>                 | 41.5<br>(32-79)     | 43<br>(29-75)       | 0.9            | 0.2<br>(-0.27-0.69)  |
| <b>Total Cholesterol, mmol/L</b> | 4.1<br>(3.7-5)      | 4.3<br>(3.4-5.6)    | 0.99           | 0.07<br>(-0.4-0.5)   |
| <b>Triglycerides, mmol/L</b>     | 1.82<br>(1.18-2.85) | 1.66<br>(1.21-2.51) | 0.38           | -0.27<br>(-0.75-0.2) |
| <b>HDL, mmol/L</b>               | 1.10<br>(0.80-1.31) | 1.04<br>(0.89-1.41) | 0.65           | 0.06<br>(-0.41-0.54) |
| <b>LDL, mmol/L</b>               | 2.16<br>(1.70-3.07) | 2.31<br>(1.69-3.56) | 0.68           | 0.08<br>(-0.39-0.5)  |
| <b>HbA1c, mmol/mol</b>           | 52<br>(42-66)       | 44.5<br>(38-57)     | 0.13           | -0.12<br>(-0.6-0.3)  |
| <b>Ferritin, µg/L</b>            | 74.5<br>(44-136)    | 161<br>(64.5-250.5) | 0.09           | 0.37<br>(-0.11-0.8)  |
| <b>FIB-4 score</b>               | 1.13<br>(0.71-1.83) | 1.29<br>(0.90-1.89) | 0.43           | 0.37<br>(-0.11-0.8)  |
|                                  | <b>N (%)</b>        | <b>N (%)</b>        | <b>P-value</b> | <b>NNT</b>           |
| <b>Male gender</b>               | 10 (56.5)           | 21 (67.2)           | 0.36           | 13.7                 |
| <b>Active smoker</b>             | 3 (15)              | 7 (11.8)            | 0.73           | 102.6                |
| <b>Physically inactive</b>       | 10 (45.5)           | 15 (26.4)           | 0.10           | 5.6                  |
| <b>In employment</b>             | 8 (68.4)            | 50 (86.2)           | 0.14           | -1.9                 |
| <b>Single/ separated</b>         | <b>14 (61.5)</b>    | <b>12 (20.8)</b>    | <b>0.013*</b>  | 2.4                  |
| <b>T2DM</b>                      | 18 (78)             | 35 (60)             | 0.12           | 5                    |
| <b>HTN</b>                       | 11 (48)             | 25 (43)             | 0.69           | 21.1                 |
| <b>Dyslipidemia</b>              | 13 (57)             | 29 (50)             | 0.59           | 15.3                 |
| <b>Thyroid disorder</b>          | 2 (8.7)             | 5 (8.6)             | 0.99           | 1334                 |
| <b>Psychiatric comorbidity</b>   | 8 (34.8)            | 9 (15.5)            | 0.054          | 5.1                  |
| <b>Depression</b>                | <b>8 (34.8)</b>     | <b>7 (12.1)</b>     | <b>0.017*</b>  | 4.4                  |

\* indicates a significant difference between the two groups to a p value <0.05.

*BMI: body mass index. BW: body weight. LSM: liver stiffness measurement. CAP score: controlled attenuation parameter. ALT: alanine aminotransferase. AST: aspartate aminotransferase. ALP: alkaline phosphatase. GGT: gamma-glutamyl transferase. HDL: high density lipoprotein. LDL: low density lipoprotein. T2DM: type 2 diabetes mellitus. HTN: hypertension. 95%CI: 95% confidence interval. NNT: number needed to treat/take*

For Review Only

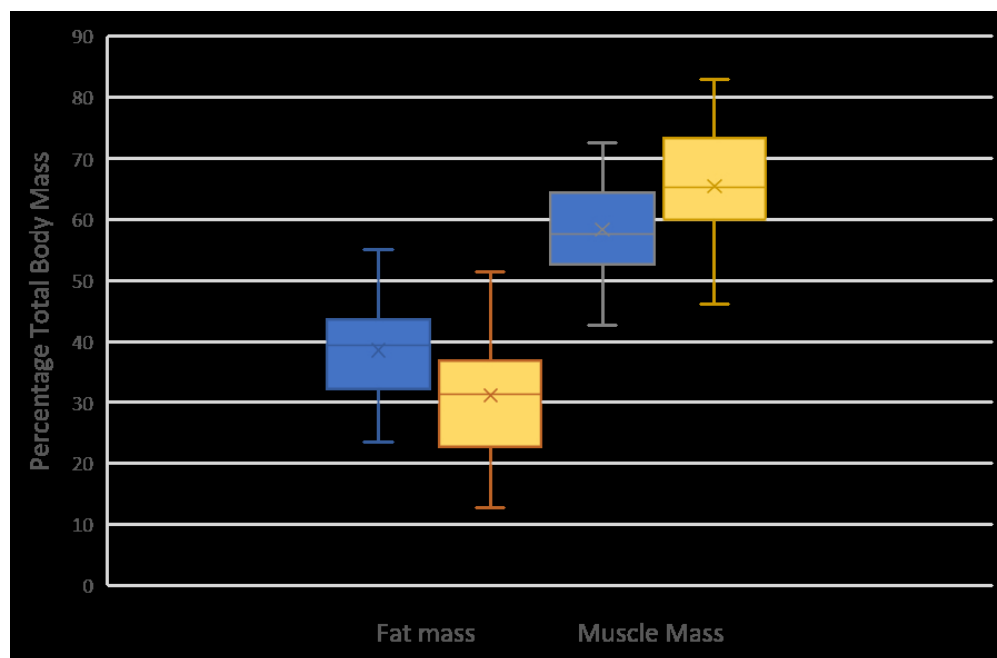


Figure 1: Fat and muscle mass as percentage of total body weight in BED and non-BED patients.  
Blue: BED positive. Yellow: BED negative

152x99mm (150 x 150 DPI)