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Akshay Jain, MD, FRCPC, FACE, CCD, ECNU, DABOM

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About the Author

Akshay Jain, MD, FRCPC, FACE, CCD, ECNU, DABOM

Dr. Akshay Jain is the first Canadian physician to be triple board-certified by the American Boards in Endocrinology, Internal Medicine and Obesity Medicine. He is the only Canadian to have won the AACE Rising Star in Endocrinology Award (2022) and to feature on Medscape's list of 25 Top Rising Stars of Medicine (2020). He practices in Surrey, BC and is a Clinical Instructor in the Division of Endocrinology at the University of British Columbia. He is fluent in 6 languages: English, Hindi, Gujarati, Marathi, Marwari, and Urdu. In 2022, he won the Top 25 Canadian Immigrant Award.

Affiliations: Division of Endocrinology, Department of Medicine, University of British Columbia
TLC Diabetes and Endocrinology, Surrey, BC

Addressing Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in Endocrinology settings in Canada: From Prevalence to Patient-Centered Management

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent in Canadian endocrinology, affecting up to 70% of those with type 2 diabetes and 75% with obesity. Despite this, routine screening is rare, leading to missed detection and intervention. Advanced fibrosis, observed in 15% of cases, increases the risk of liver and cardiovascular complications. This article addresses the burden of MASLD and the need for systemic screening and patient-centred care to improve outcomes and reduce Canada's disease burden.

Introduction

The growing burden of metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), is an escalating concern that increasingly intersects with diabetes and obesity specialties. Yet, routine screening remains uncommon in most Canadian endocrinology practices.[1] Given the scale of undetected disease and its complications, endocrinology must embrace systematic approaches for MASLD detection and risk reduction. This article aims to highlight the epidemiological impact of MASLD and the need for systemic screening and patient-centred care. Recognizing its links to diabetes, obesity, and cardiovascular disease is key to improving outcomes and reducing Canada's growing disease burden.

Epidemiology: MASLD is Widespread in Canadians with Diabetes and Obesity

Approximately 70% of Canadians with type 2 diabetes (T2D) have MASLD, with one third progressing to metabolic dysfunction-associated steatohepatitis (MASH) and up to 15% showing advanced fibrosis.[2] Similarly, nearly 75% of Canadians with overweight/obesity have hepatic steatosis.[2] Patients with both T2D and MASLD face significantly higher risk of cardiovascular disease (CVD), hepatocellular carcinoma (HCC), and overall mortality compared to T2D alone or MASLD without diabetes (**Figure 1**).[3] In Canada, both- population and disease burden are rising, positioning MASLD to become the leading indication for liver transplantation.[2] Importantly, fibrosis—not simple hepatic steatosis—is the strongest predictor of liver-related and extrahepatic complications. Approximately 15% of people with T2D and MASLD develop advanced fibrosis, which directly drives the risk of cirrhosis, HCC, and liver failure, while a much larger proportion are at risk for cardiovascular events, which remain the leading cause of death in MASLD patients.

Under-screening and Missed Opportunities

Despite clear evidence, MASLD remains underdiagnosed in endocrinology and primary care clinics across Canada. In practice, few specialists integrate routine screening or risk stratification for high-risk patients, even though tools such as the fibrosis-4 index (FIB-4) are simple, inexpensive, and validated. Instead, physicians often rely solely on elevation of liver enzyme abnormalities, missing most cases. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) may be normal in up to 15% of those with significant fibrosis. In some regions of Canada, AST testing requires the patient to pay out-of-pocket, which often results in the test not being ordered/performed and, consequently, prevents calculation of the FIB-4 score.

CVD and HCC: Fibrosis Drives Adverse Outcomes

In MASLD, fibrosis stage is the strongest predictor of both liver and non-liver outcomes, including CVD and HCC.[3,4] CVD is the leading cause of death in patients with MASLD, even when liver enzymes are normal and before cirrhosis develops. Among those with advanced fibrosis, the HCC risk increases dramatically, with MASLD becoming a leading indication for HCC-related transplantation in North America.[3,4] Advanced liver fibrosis is associated with a two- to five-fold increase in CVD, cancer risk, and overall mortality.

MASLD Is Underdiagnosed: Screening Gaps in Endocrinology

Despite the elevated risk profile, MASLD remains under detected. More than 85% of Canadian specialists rely solely on liver enzymes to screen for MASLD or fibrosis, with only 17–23% reporting that they find serum biomarkers and transient elastography helpful.[2] Most MASLD patients are managed in primary care or endocrinology clinics where awareness and testing rates are low. Endocrine practices in Canada also face unique barriers: access to AST (needed for FIB-4), limited availability of advanced tests, such as elastography, and uncertainty about referral pathways for patients with higher-risk scores.

FIB-4: A Practical First-Line Tool for Canadian Endocrinology

Why FIB-4?

FIB-4 is the preferred first-line non-invasive test for fibrosis risk, calculated using age, AST, ALT, and platelet count (all routine

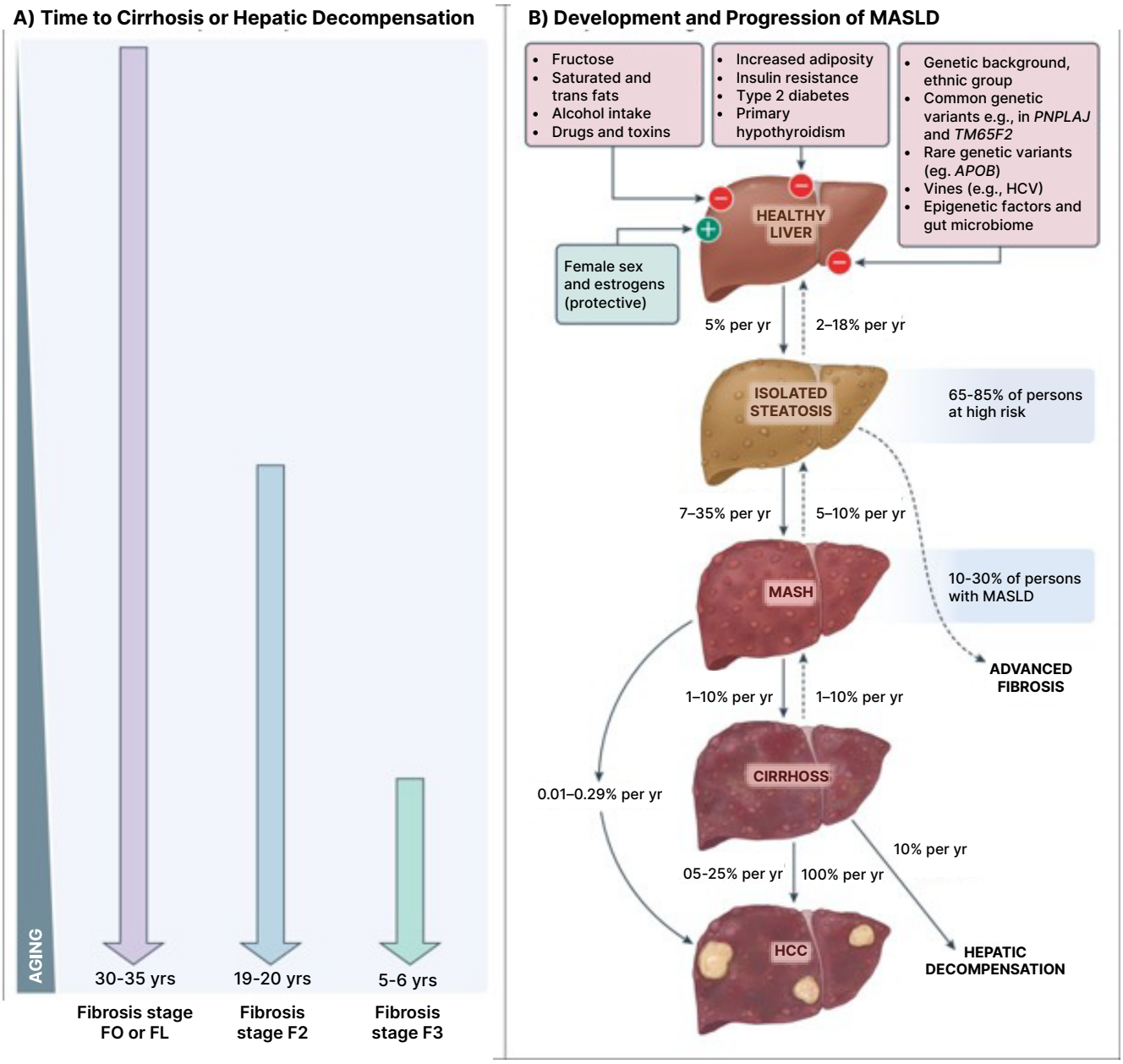

Figure 1. Natural History of Steatotic Liver Disease and MASLD; *used with permission from Targher, G. et al., 2025.*

laboratory values). Free online calculators yield instant results, making this test accessible across Canada. With a very high negative predictive value >90% to rule out advanced fibrosis,[4] it offers strong clinical confidence. FIB-4 can also be integrated into electronic medical records and flagged for annual or biennial screening in those with diabetes, obesity, or other risk factors.

Next Steps: Coordinating Care in Canadian Settings

A summary of FIB-4 score ranges and corresponding clinical actions is provided in **Table 1** and **Figure 2**. For most patients with T2D or obesity (approximately 60–70%) a FIB-4 score of <1.3 indicates low risk, requiring no specialty referral. Management should focus on metabolic risk reduction, weight loss, and retesting every 1–2 years. Those in the indeterminate range (1.3–2.67) need a second tier assessment, such as elastography or enhanced liver fibrosis (ELF) to clarify fibrosis risk, though access to these tests varies by region and may not be freely available. Only those with the highest risk (>2.67) require immediate referral to hepatology, reducing unnecessary referrals.

Pharmacotherapeutic Strategies: Who, When, and How?

Lifestyle Modifications as the Foundation

Behavioural interventions benefit all patients (see **Figure 3**). A weight loss of 5–10% of body weight can reduce steatosis, and losses ~10% may even reverse fibrosis. The Mediterranean diet is preferred, alcohol intake should be limited, and comorbidities such as hypertension, dyslipidemia, and obstructive sleep apnea should be optimized.[1,4] Lifestyle modifications can be initiated for every patient, even high-risk patients that are awaiting assessment by hepatology.

Pharmacotherapy

Several pharmacologic options are available for MASLD with mild, moderate, or advanced fibrosis, offering targeted benefits beyond lifestyle modification (see **Figure 4**).

For patients with T2D or prediabetes who have MASLD and moderate fibrosis (F2–F3), pioglitazone can improve steatohepatitis, and may modestly reduce fibrosis. It is best suited for non-cirrhotic patients and is often combined with a glucagon-like peptide 1 receptor agonist (GLP-1RA) for weight attenuation.[1,4,6] GLP-1-RAs, such as semaglutide (2.4 mg) have demonstrated efficacy in resolving steatohepatitis and reducing liver fat, with emerging evidence for fibrosis improvement in recent randomized controlled trials.[1,3,4] The Phase 3 ESSENCE trial (2025) shows semaglutide's ability to achieve both MASH resolution and fibrosis improvement with no worsening in most participants. Additionally, the dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) agonist tirzepatide has shown promising results in Phase 2 studies and is undergoing further evaluation for this indication. Resmetirom is now FDA-approved for MASH with F2–F3 fibrosis. While not yet approved in Canada, it is recommended in the United States and in global guidelines for eligible patients.[3,4,7] It is important to note that CVD risk reduction is an essential component of MASLD care. Statins are safe for patients with MASLD and should not be withheld in compensated disease. Their use is only contraindicated in cases of decompensated cirrhosis.[1,2,4]

Conclusion

MASLD is a critical, often-overlooked complication of diabetes and obesity. Screening using FIB-4 offers a practical, cost-effective, and immediately actionable approach in most clinical settings.[1,2,4] Management should follow a stepwise, risk-stratified approach, reserving hepatology referral for those with intermediate-to-high FIB-4 or confirmed advanced fibrosis. Pharmacotherapy should be considered for patients with concurrent diabetes or obesity who also show evidence of MASH or advanced fibrosis, particularly leveraging GLP-1RA and pioglitazone as key options. For the majority of patients at lower risk, repeat screening and longitudinal metabolic risk reduction remain the cornerstone of care.

FIB-4 Score	Interpretation and Actions
<1.3	**Low risk:** Manage diabetes/metabolic syndrome; repeat fibrosis-4 index (FIB-4) in 1–2 years
1.3–2.67	**Indeterminate:** Order non-invasive imaging (transient elastography or enhanced liver fibrosis); if unavailable, refer to hepatology for further workup
>2.67	**High risk:** Refer directly to hepatology for evaluation of cirrhosis, advanced fibrosis, and hepatocellular carcinoma surveillance

Table 1. Action Items by Score; *courtesy of Akshay Jain, MD, FRCPC, FACE, CCD, ECNU, DABOM.*

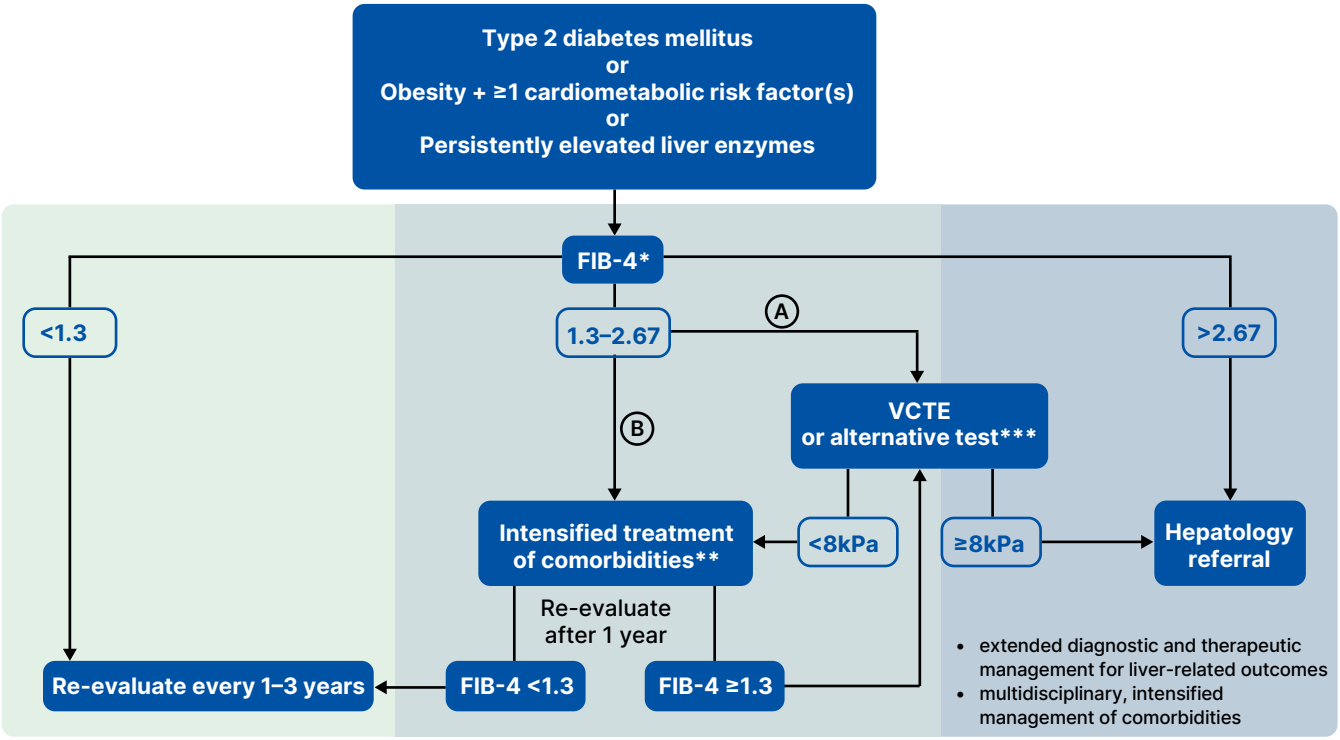

Figure 2. Non-invasive risk stratification of individuals with suspected MASLD; *courtesy of Akshay Jain, MD, FRCPC, FACE, CCD, ECNU, DABOM.*

Algorithm for non-invasive risk stratification of individuals with suspected MASLD (reproduced with modifications from Tacke *et al*[1] under the CC BY-NC license (https://creativecommons.org/licenses/by-nc/4.0/).

*FIB-4 cut-offs are valid for age 65 years (for >65 years, the lower FIB-4 cut-off is 2.0).
**For example, lifestyle interventions, treatment of comorbidities (eg, glucagon-like protein-1 receptor antagonist) and bariatric surgery.
***Alternative test, for example, magnetic resonance elastography (MRF), shear wave elastography (SWE) or enhanced liver fibrosis (ELF) test, with their respective cut-offs. and are options, depending on the disease course, clinical context and local resources.

Abbreviations: FIB-4: fibrosis-4 index; **MASLD:** metabolic dysfunction-associated steatotic liver disease; **VCTE:** vibration-controlled transient elastography.

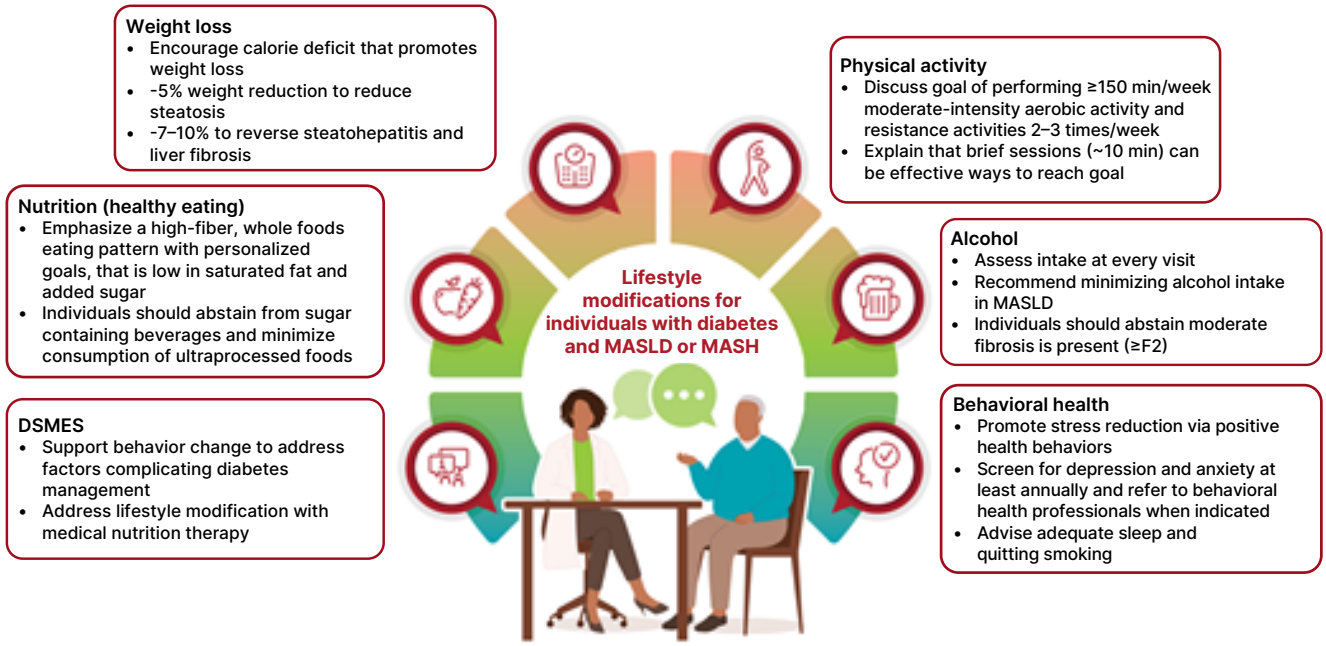

Figure 3. Lifestyle modifications for individuals with diabetes and MASLD or MASH; *used with permission from Cusi, K. et al., 2024.*

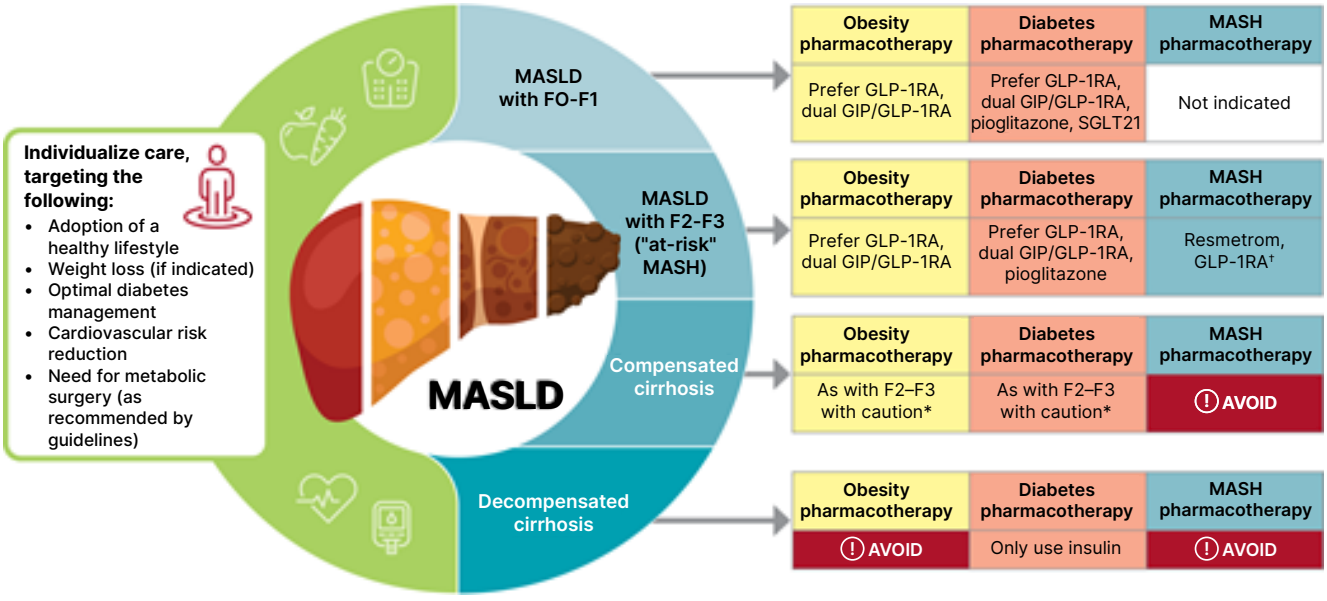

Figure 4. MASLD treatment algorithm for individuals with prediabetes or diabetes; used with permission from Cusi, K. et al., 2024.

Correspondence

Akshay Jain, MD, FRCPC, FACE, CCD, ECNU, DABOM
Email: oxyjain@gmail.com

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