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Longitudinal evaluation of whole blood viscosity for evidence-based pathology in cardiovascular medicine: Study protocol

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Top End AOD services pr…

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We are still developing and optimizing this protocol

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Abstract

Background: Mental and work-related stress is a significant global concern with huge social and economic impacts. To date, there has been a plethora of tools for assessing the risk of stress, but not for diagnosis and this is a limitation in service delivery for mental health. However, evidence has continued to grow that extrapolated whole blood viscosity (eWBV) is associated with stress and mental health conditions.

Objectives: The main objective is to evaluate patients changes in WBV among mental health clients from a nursing perspective. Four specific objectives would be investigated.

Methods: This would be a clinical observational mixed-method study using a longitudinal audit of medical record files in the outpatient setting. Measurables would include routine laboratory data to generate eWBV as well as other clinical profiles. The mixed-method statistical analyses for the hypothesis are descriptive and comparative. First two objectives would be based on baseline cross-sectional dataset, while the third and fourth objectives are going to be on outcome measures of cohort data.

Expected outcome and Significance: The findings will indicate whether eWBV as a laboratory tool would be a good and informed evidence that can be used to convey the effectiveness of management regimen in mental health and Alcohol & other Drugs services. It is conceivable that a biomarker would be an added advantage in evaluating and evidencing effectiveness of clinical management.

Introduction

1 Whole blood viscosity (WBV) is a laboratory test in medical practice. Currently WBV testing for stasis (how the thinness or thickness of the blood may be affecting its flow or pooling) is mainly restricted to the management of diseases associated with too much protein (hyperproteinaemia), too many red blood cells (polycythaemia) and problems of blood flow to the eye (retinal occlusion). However, WBV is a factor in diabetes and related diseases; hence it can be used to assess the efficacy of blood-thinning medications (**Rigotti & Clair, 2013**). Further, the test can demonstrate the risk of cigarette-induced blood pooling among smokers (**de Simone et al., 2005**).

WBV can also be used to assess mental stress (**Reims et al., 2005**). Limited access to pathology services that routinely provide WBV testing has resulted in the under-utilisation of this important diagnostic test (**Celik et al., 2016**). Current testing provides a valid result only if immediate access to pathology services is available (transporting the sample for any distance results in the deterioration of the sample). A newly-developed process for estimating WBV using the results from routine blood tests (haematocrit and total serum protein) offers ready access to this important measure of WBV (**de Simone et al., 2005**; **Nwose, 2010**).

Work-related stress has been a significant global concern with huge economic impacts, especially for health insurance companies. To date, there has been a plethora of tools for assessing the risk of stress, but not for diagnosis (**Jeon & Kim, 2018**). In particular, there has yet to be a laboratory biomarker established for clinical diagnosis. Yet, evidence has continued to grow that WBV is associated with acute psychological stress and more chronic mental health conditions such as depression (**Kalelioglu et al., 2018**; **Muldoon et al., 1995**). It is conceivable that a biomarker would be an added advantage in identifying and treating mental stress. Figure 1a presents the summarizing graphical concept, while figure 1b presents the perspective of what is known versus unknown.

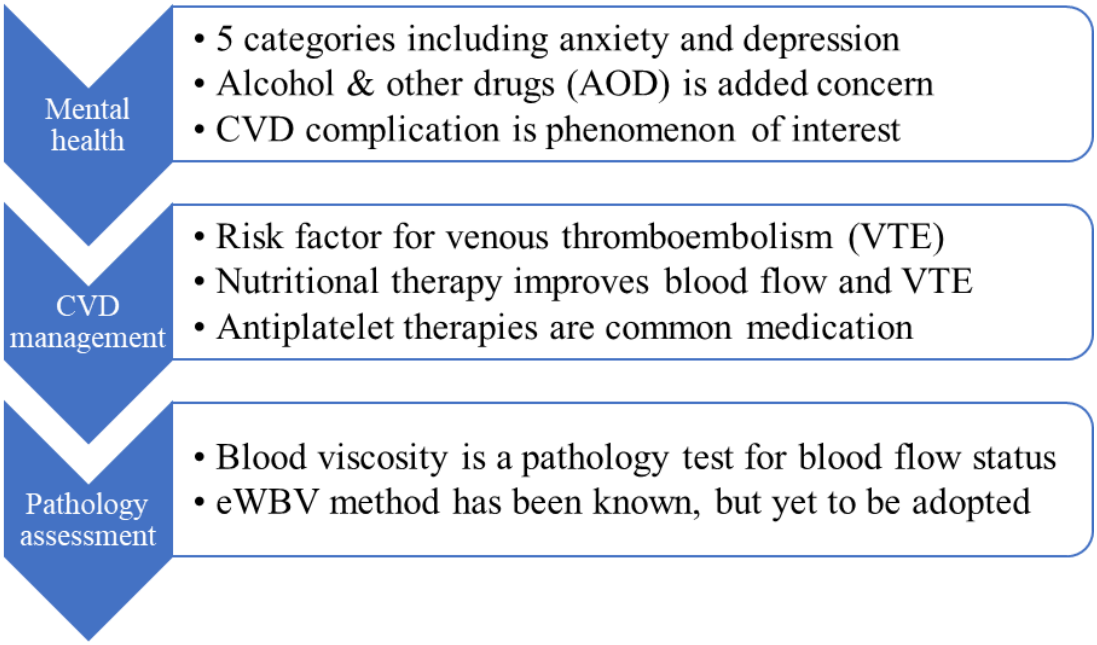

Fig 1a: Graphical summary of the research concept

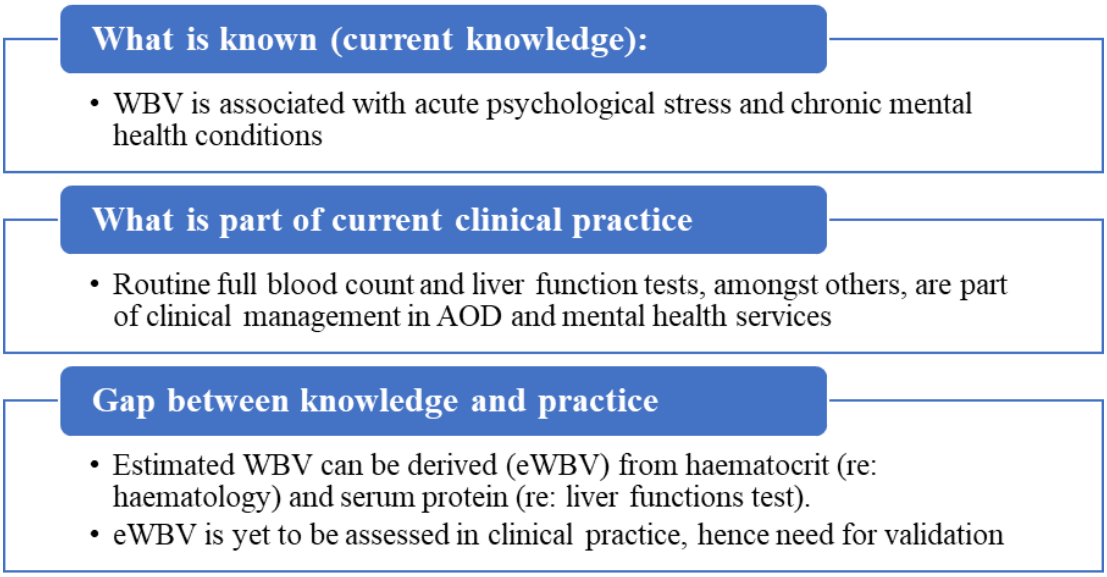

Fig 1b: What is known vs unknown

The study objectives

2 ***Broad objective***

Broad objective is to evaluate patients changes in WBV over 6 – 9 months period from a nursing perspective.

Specific objectives include evaluation of:

1. Protocol for assessing laboratory results of eWBV parameters in care management, if assessment is more among mental stress and AOD clients with known co-morbidities.
2. Difference in blood pooling/viscosity (indicated by eWBV method) levels between sub-groups of clients attending mental health facility.
3. Changes in eWBV levels among cases that have received some form of treatment – re: post-intervention assessment of effect of clinical management on eWBV.
4. To identify the impact of changes to sleeping and weight patterns on eWBV.

Hypothesis: Table 1. The hypotheses for all four specific research objectives

Research objectives	Research hypothesis
Protocol for assessing laboratory results of eWBV parameters in care management, if assessment is more among mental stress and AOD clients with known co-morbidities.	Assessment of laboratory indices for eWBV is significantly more among 'mental stress and AOD clients' with known co-morbidities than those without comorbidity.
Difference in blood pooling/viscosity (indicated by eWBV method) levels between sub-groups of clients attending mental health facility.	There is significant difference in blood pooling/viscosity (indicated by eWBV method) levels between sub-groups of clients attending mental health facility.
Changes in eWBV levels among cases that have received some form of treatment – re: post-intervention assessment of effect of clinical management on eWBV.	There are significant changes in eWBV levels among cases that have received some form of treatment – re: post-intervention assessment of effect of clinical management on eWBV.
To identify the impact of changes to sleeping and weight patterns on eWBV.	There are significant identifiable impacts of changes to sleeping and weight patterns on eWBV.

The Protocol

3 ***Research design***:

This study is planned to follow a clinical observational approach including mixed methods in statistical evaluations.

Setting:

Outpatient Mental Health and AOD Services at Royal Darwin Hospital (RDH). Outpatients in RDH are independently funded by the government under the same umbrella with Mental Health services. Clients include both men and women. About 10 new clients per week, and up to 115 clients on record for AOD services and up to 150 for combined services.

Study participants:

De-identified cases who meet inclusion criteria. Incidental cases of co-morbidities would include pregnant women, diabetes, cardiometabolic syndrome as well as eating and sleeping patterns. Details are as outlined in tables 2 and 3.

Table 2: Proposed subgroups for the 1st and 2nd objectives

SN	Target subpopulation	Subgroups	Audit date	FBC†	LFT†	eWBV*
1	Pregnant vs. non-pregnant **women**	Pregnant				
		Non-pregnant				
2	Diabetes vs. non-diabetes patients	Diabetes				
		Non-diabetes				
3	Hypertension vs. non-hypertensive	Hypertensive				
		Non-hypertensive				
4	Obese vs. non-obese	Obese				
		Non-obese				
5	Asthma vs. non-asthmatic	Asthmatic				
		Non-asthmatic				
6	Men and non-pregnant women	Men				
		Women				

†Independent variables, *Dependent variable

Table 3. Subgroups for 3rd and 4th research objectives

Research objectives	*Subpopulations*
Objective 3	AOD clients on drug*† withdrawal – changes in eWBV
	MH‡ clients on drug treatments – changes in eWBV
	MH‡ clients on drugs & nutritional management - changes in eWBV
Objective 4	Insomnia with weight gain
	Insomnia without weight gain
	Weight gain without insomnia
	Weight loss without insomnia

Keys: *Opioids including met, heroin, cocaine, and other substances such as cannabis, nicotine & alcohol, ‡Blood test is: monthly if on depo injection, or 3-monhtly if regular medication, †OPP: opioid pharmaceutical program - involve urine & blood test (esp cardiac + LFT & RFT) to screen for cardiac issues.

Data resources:
Laboratory and other clinical data on clients' file. Laboratory data will be routine haematology and liver function tests. Clinical data would include medication, medical history, lifestyle factors (weight, sleeping & eating patterns), sociodemographic status, and vital signs. The process of data collection is graphically outlined in figure 2.

The Process

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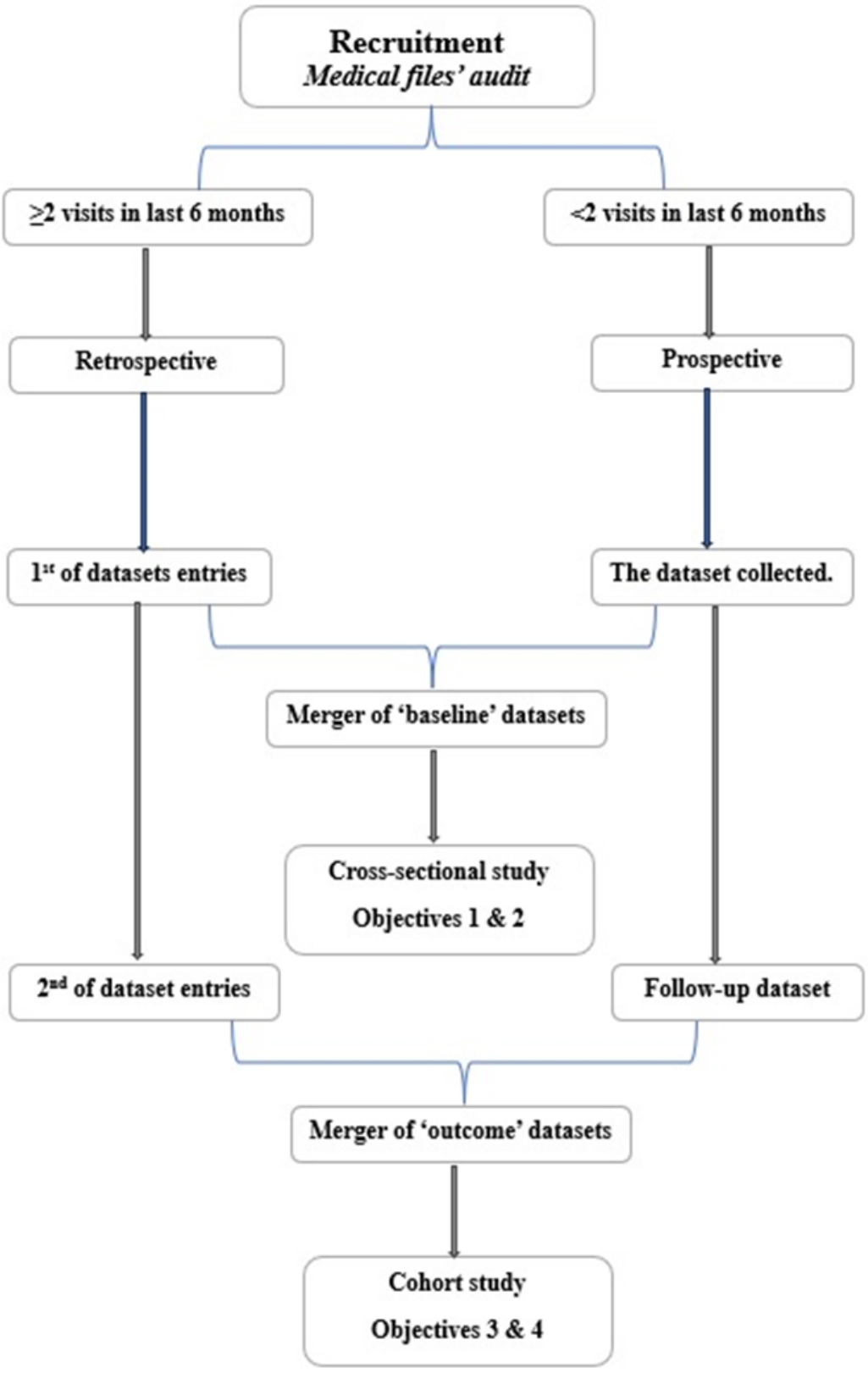

Fig 2: Graphical flow chart of the data collection process

Ethical clearance

This study is subject to ethics clearance and clinicians' support, especially as access to clients' medical records is required. Hence application for ethics approval has been submitted to Top End AOD and Mental Health Services of Royal Darwin Hospital

Statistical analysis

5 **Statistical analyses**

Descriptive frequency analysis, comparative analysis including Student's t-test, ANOVA, and MANOVA with post-hoc test will be performed using Statistical Package for the Social Sciences (SPSS version 28). Nursing care case reports would also be performed. Specifically, the objectives involve mixed methods descriptive frequency statistics, and clinical case review as well as cohort, cross-sectional approaches (Table 4).

Table 4: Overview of statistical methods for the various research objectives

SN	Research hypothesis	Data	Statistics
1	Assessment of laboratory indices for eWBV is significantly more among 'mental stress and AOD clients' with known co-morbidities than those without comorbidity.	Numbers of those with lab tests vs those without lab test	Descriptive frequency comparison
2	There is significant difference in blood pooling/viscosity (indicated by eWBV method) levels between sub-groups of clients attending mental health facility.	Among those with lab test, derive eWBV values and compare between subgroups	T-test, ANOVA & MANOVA
3	There are significant changes in eWBV levels among cases that have received some form of treatment – re: post-intervention assessment of effect of clinical management on eWBV.	Non-experimental intervention study (including vital signs)	Outcome comparisons; after intervention
4	There are significant identifiable impacts of changes to sleeping and weight patterns on eWBV.	Cohort study (lifestyle and sociodemographic factors)	Outcome comparisons; linear regression

Conclusion: Expected results and significance

6 **Expected results:**

In accordance with the hypotheses, the results would provide evidence of potential usefulness of eWBV evaluation in mental health, including pregnant women living with diabetes and AOD issues. This new process for assessing WBV using results from routine blood tests (haematocrit and total serum protein) can be accessed without using advanced

testing. This means it can be used in various common diseases that are reported to be associated with changes in WBV, such as stress, with outpatient mental health and AOD services at RDH, diabetes mellitus, cardiovascular and kidney diseases.

Significance of study:

This study would make a creditable contribution towards assessment and monitoring, identifying different strategies, techniques, and methods of preserving Mental health, AOD, diabetes mellitus, cardiovascular, and kidney diseases clients. This medical assessment does not require clients to be hospital inpatients or to travel to any reference facility at certain geographical locations. For instance, requisition of WBV (for a mental health client's evaluation of stress levels or for an individual living with diabetes to monitor for antiplatelet therapy) can be done by a GP, who would then collaborate with other healthcare professionals and specialists – without the client needing to travel.

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