

This is a “preproof” accepted article for *Journal of Clinical and Translational Science*.

This version may be subject to change during the production process.

10.1017/cts.2024.656

## **A scoping review of Adrenal Vein Sampling in practice settings: Applying an implementation science lens**

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## **Abstract**

Adrenal Vein Sampling (AVS) is a complicated procedure requiring clinical expertise, collaboration, and patient involvement to ensure it occurs successfully. Implementation science offers unique insights into the barriers and enablers of service delivery of AVS.

The primary aim of this review was to identify implementation components as described within clinical studies, that contribute to a successful AVS procedure. The secondary aim was to inform practice considerations to support the scale-up of AVS.

A scoping review of clinical papers that discussed factors contributing to effective AVS implementation were included. A phased approach was employed to extract implementation science data from clinical studies. Implementation strategies were named and defined, allowing for implementation learnings to be synthesised, in the absence of dedicated research examining implementation process and findings only.

Ten implementation components reported as contributing to a successful AVS procedure were identified. These components were categorised according to actions required pre-AVS, during AVS and post-AVS.

Using an implementation science approach, the findings of this review and analysis provide practical considerations to facilitate AVS service delivery design. Extracting implementation science information from clinical research has provided a mechanism that accelerates the translation of evidence into practice where implementation research is not yet available.

## Introduction

Primary aldosteronism (PA) is a common and potentially curable form of secondary hypertension, associated with increased cardiovascular morbidity when compared to essential hypertension.<sup>1-3</sup> PA results from aldosterone overproduction from either one or both adrenal glands, with differentiation being important as the former may be cured by surgery while the latter requires long-term medical treatment.<sup>2</sup> PA was historically considered rare, however, more recent studies have identified its prevalence to be up to 14% in primary care, and close to 30% in referral centres.<sup>4-6</sup> As more clinicians screen for PA, there will be an increase in the demand for diagnostic tests, including a confirmatory test to demonstrate autonomous aldosterone production and adrenal vein sampling (AVS) to subtype PA as either unilateral (and curable with adrenal surgery) or bilateral (requiring lifelong medical therapy).<sup>2</sup>

AVS is currently the gold standard investigation to subtype PA and identify surgically curable disease<sup>2</sup> as CT imaging alone has low diagnostic accuracy.<sup>7</sup> AVS is an invasive, highly technical and resource-intensive procedure, involving cannulation of bilateral adrenal veins most often through the femoral vein(s) in the groin for blood sampling to measure aldosterone and cortisol concentrations. Radiologist expertise and patient anatomy impact the duration of procedure and risk of complications such as bleeding, infection and adrenal vein haemorrhage. There is also the risk of inconclusive results or procedural failure. There are strategies that have been associated with improved AVS success, defined by the ability to cannulate both adrenal veins and interpret the results for the assessment of aldosterone lateralisation. These include having dedicated radiologists and using specific imaging and point-of-care assays to confirm adrenal vein cannulation success during the procedure.<sup>8-10</sup> The clinician performing AVS, often a radiologist, requires training, sufficient referrals for experience, and hospital resources including equipment, room availability and support staff. Guidelines and protocols can offer support to clinicians performing AVS, however, there is a lack of consensus on the optimal methods for performing and interpreting AVS. AVS is available in limited tertiary referral centres and with few dedicated clinicians who perform the procedure, waiting lists can be long, thereby delaying the diagnosis and treatment of unilateral PA.

The issues described above outline the pre-, during and post-AVS components that constitute the definition of a successful AVS procedure, each of which do not exist in isolation and are sequentially connected. However, these components, or barriers (or

enablers) should be viewed as opportunities to generate change for which the field of implementation science has developed guidance (theories, models, and frameworks) and strategies to support this. Implementation science literature outlines antecedent factors to progress the introduction of a new practice, drug, or facility, as well as detailing processes for successful implementation. Using an implementation science approach to the problems seen with AVS allows for the characterisation of what is needed to establish AVS successfully in a new setting and/or evaluate a current setting that is conducting AVS to determine if the ingredients for success are evident. This is a critical step as increased awareness of, and screening for PA will spur the uptake of AVS at scale, growing patients, clinicians, and hospitals that encounter the procedure. Currently there is no implementation research around AVS, and the need to ‘raise the bar’ through implementation science research in cardiology has been mentioned<sup>11</sup>. Hence, the primary aim of this research was to conduct a scoping review of studies that examined the conduct of AVS and implementation information that contributed to successful procedures. The secondary aim was to articulate considerations that support future scale-up.

## **Materials and Methods**

### ***Design and Approach***

A scoping review of studies that described factors and processes involved in implementing and delivering AVS, in accordance with the established methodology<sup>12</sup> was conducted as a paucity of dedicated implementation research on AVS delivery was evident. In a novel approach that authors HM and AM devised, the review extracted information about implementation processes from clinical research papers that discussed AVS but did not explicitly investigate implementation concepts — a process termed by the authors as ‘implementation science gymnastics’. This process involved 4 phases, see Figure 1, and reflects an overarching principle of applying implementation science thinking to unlock implementation information about supporting AVS.

### ***Apply implementation science thinking to the clinical issue***

An implementation science lens was applied to the examination of clinical studies. As a four phased approach, the intention here was not to describe the clinical elements of AVS such as procedural details or result interpretation. These details are available in the guidelines and in published reviews<sup>2,15-17</sup>. Rather, the implementation specialists on the authorship team [HM, AM and HS] examined clinical AVS studies that identify critical features of a

successful procedure which may inform the implementation processes. The authors' knowledge of implementation informing this lens included frameworks such as the Consolidated Framework for Implementation Research (CFIR)<sup>2,18</sup>, strategy lists such as Expert Recommendations for Implementing Change (ERIC)<sup>13</sup>, competencies<sup>19</sup>, drivers and timeframes<sup>20</sup>. This approach was applied when reading clinical papers specifically to determine if any implementation knowledge was embedded such as barriers or enablers to a successful AVS outcome. This process was conducted in conjunction with clinicians who have expertise in AVS [Authors JY, WC, EN]. Although a complex activity, it was achievable by recruiting this competency and engaging with an implementation specialist into a specific research team.

### **Phase 1 – Consider clinical area: Search strategy to identify AVS-related research**

Phase 1 identified the clinical area where implementation information was needed. This involved a search of the literature using a systematic methodology. Three databases, PubMed, Ovid Medline and CINAHL, were searched with no date limit until January 2023. The search strategy for Ovid Medline is detailed in Table 1 and was translated for the other databases included. The inclusion criteria are also outlined further in Table 1. Abstracts were excluded if: 1) they were not relevant to AVS delivery including its use and success (e.g. focused on other procedures associated with PA or screening programs); and 2) there was no description of implementation strategies used to support an effective AVS procedure. Papers were included if they described both the study of AVS use and an implementation factor that impacted its success, which may be a clinical tool or method (such as CT imaging) or process related (such as training<sup>13</sup>). One hundred percent agreement was obtained between authors via discussion and consensus as to the papers included in the review for data extraction.

A systematic quality assessment was not conducted. Given the main objective was to understand implementation factors described in the successful delivery of AVS, rather than seeking confidence in AVS itself, individual study quality was not considered of relevance to this review. Existing systematic reviews have confirmed the efficacy of AVS in determining the laterality of disease<sup>14,15</sup>.

### **Phase 2 – Describe implementation themes (Data Extraction from clinical studies)**

Implementation information that emerged from the studies were grouped into themes. These themes were categorised by consensus between data extractors authors HM and AM and labelled implementation components, and later confirmed by clinicians and authors [EN,

JY]. They were then mapped using Proctor et al.'s (2013) framework for specifying and reporting implementation strategies<sup>21</sup>, where the themes were named, defined and specified. To specify the components the following information was extracted: The actors who enacts the component, e.g., clinicians involved in undertaking the clinical procedure or supporting the delivery of a service; The action - the specific actions, steps, or processes, e.g., the clinical techniques applied; The action target, the unit of analysis for measuring implementation outcomes, e.g., completion of a task or procedure ; Temporality, when the strategy is used, e.g., timing of when to undertake a task or procedure; Dose, e.g., how many procedures must be undertaken at any one point or the number of procedures to undertaken per clinician, frequency of use; Implementation outcome affected (Appropriateness, Adoption, Acceptability, Feasibility, Fidelity, Cost, Penetration, and Sustainability); and its Justification. Extracting data using this framework enabled a clear description of aspects needed to adopt AVS into new locations and sustain it within existing settings<sup>21</sup>.

### **Phase 3 - Categorise details to facilitate real-world implementation**

The data from the implementation components were then selected for their alignment with the Expert Recommendations for Implementing Change (ERIC) taxonomy (Powell 2015). These are 73 discrete evidence-based strategies that promote the replication and advancement of implementation science, to strengthen the scale-up and translation of evidence into practice<sup>13</sup> (Nathan 2022). This phase enabled the articulation of implementation components presently used in the successful completion of AVS. The consistent and established taxonomy facilitated the considerations for implementation planning needed for phase 4.

### **Phase 4 - Present information for implementation planning**

A set of considerations were devised through thematic evidence synthesis of the extracted data, using the Proctor Framework (Proctor 2013). These considerations enable decision making with the right information, invite the system to think about the actors vital for effective AVS completion, support cost factors that impact effective implementation, and will provide practical insights for future implementation planning.

## **Results**

The search returned 1316 articles, of which 20 were included in the final review<sup>22-41</sup> published from 2009 to 2023. Authors AM and HM each screened 50% of the abstracts and 100% of the full text papers. One paper was originally published in Chinese (the abstract was

published in English) and translation software was used<sup>30</sup>. No other paper was originally published in another language other than English that we found. In the second phase authors HM and AM were the most flexible in their ‘implementation science gymnastics’. There was much discussion, interpretation and (re)examination of the literature between authors as it was believed that this approach would enable the collection of best available evidence. Particularly in light of the fact that no implementation studies exist about AVS. By applying an implementation science lens to clinical research about successful AVS procedures, a compilation of issues, barriers and enablers were identified. Those that play a specific role in the success or failure of the procedure were identified, along with solutions and suggestions for the better implementation of AVS in existing or new service.

Data were thematically grouped to form ten implementation components that aligned with before, during and after AVS. Figure 2 presents a conceptual model of these components and how they are related.

### **Conduct of AVS and Implementation Information**

The Proctor 2013 framework was used to guide data extracted (see Supplementary Table 1) that are described below. This framework was developed in response to the need for clarity around specific details implementation strategies. Here we present the detail about implementation information that contributed to successful AVS procedures. Whilst the implementation components identified were not strategies per say, the framework provided a structure to unpack the details including the justification for the component.

#### **Pre-AVS**

**Developing technical skill:** The learning curve for AVS proficiency is approximately 20-30 procedures per radiologist,<sup>22,27,30</sup> and to maintain this skill, a minimum of 15-20 procedures annually has been suggested<sup>22,34</sup>. In light of these numbers, hospitals over the last decade have altered their approach to upskilling practitioners doing AVS: 1) by narrowing the number of clinicians to one or two people<sup>26,27,34-37,39,40</sup>; or 2) referring patients to a larger centre with more expertise<sup>24,37</sup>. These measures enhance the procedure’s fidelity and sustainability.

**Protocol:** Papers included in this scoping review noted that operation protocols need to exist at the hospital level. One paper suggested that the endocrine society guidelines should instruct decisions about lateralisation<sup>36</sup> and another referred to a patient’s clinical

characteristics for the need for AVS at all<sup>25</sup>. Apart from these studies, there was a lack of clarity about the inclusion of evidence-based guidelines into hospital level protocols. There was a widely-held view however, that a hospital guideline should be written collaboratively<sup>24</sup>, with representatives from many departments<sup>24,37,40 29,40</sup>. This may enhance the speed of the protocol's penetration throughout the relevant departments. The protocol may include specific instructions about staff and hospital procedures to restrict operator error or confusion<sup>24</sup>. Collaboration with the referring physician was noted by So (2021) as important in two ways: 1) to support the referral pathways, preparation and results interpretation; and 2) to support the inexperienced referring physician in preparing the patient correctly (such as avoiding some medications)<sup>34</sup>.

***AVS suitability and procedure preparation:*** There was little consensus about preparation and confirmatory tests for AVS. The literature is clear on the inadequacy of imaging alone in determining the likelihood of unilateral PA and therefore the need for AVS<sup>22</sup> with discordance between imaging and AVS results being as high as 73%<sup>37</sup>. An update of the Endocrine Society's guidelines in 2016 included many factors around confirmatory testing and work-up. New parameters exist which, if met, could facilitate referral for AVS without confirmatory testing<sup>38</sup>, however the appropriateness of this needs to be considered. A recent multicentre study involving 435 people found that 40.7% (n=177) of patients did not need confirmatory testing according to the guideline, but only 18.9% (n=49) of patients that needed testing actually completed it<sup>38</sup>. This suggests that the guideline is not being followed for confirmatory testing and decisions about what tests to do and when, are largely based on the clinicians choice<sup>38</sup>. The risk of overlooking evidence-based guidelines is an unnecessary AVS procedure which is a concern given cost implications for hospitals and the risk of procedural complications for patients<sup>32,38</sup>. Indeed the age<sup>24</sup> or comorbidities<sup>29</sup> of some patients may contribute to a clinician's decision about undergoing AVS or a surgical treatment option at all. Recent studies suggest that variance in confirmatory testing remains an issue to this day<sup>17,42</sup>.

***Patient voice and informed choice:*** Patients play a significant role in the conduct of AVS, with a recent study finding the main reason for not performing AVS on a patient was their refusal to participate<sup>22</sup>. When considering the option of doing AVS, studies agreed it should only be done on patients who want a surgical cure<sup>29,40</sup>, with one study revealing the main reason for refusing surgery post AVS was a change of mind<sup>29</sup>. This suggests that better preparation is needed to support patients prior to doing AVS about what come afterwards.



Cost and time may be saved through enhanced knowledge provision to the patient about the procedure<sup>22</sup>, outcomes, complications<sup>38</sup> and effectiveness including the potential for repeating AVS should it fail<sup>34</sup>. Patients should feel supported to make an informed decision about undergoing AVS<sup>22</sup>, having a surgical cure post procedure, and know that long term medicinal treatment is an option<sup>29</sup>.

**Imaging:** Imaging, including MRI and CT, was considered by the included studies as an important part of the pre-AVS phase, however is not appropriate as the only test for. Whilst current guidelines recommend imaging to rule out adrenocortical carcinoma<sup>26,27</sup>, it is most frequently conducted to provide anatomical information to the radiologist about the right adrenal vein<sup>27,30-32,35,37</sup>. One study reported that use of pre-AVS contrast-enhanced CT scan enabled operators to visualise the left adrenal vein in 98% of cases and the right in 95% of cases, contributing to technical success<sup>31</sup> and procedural fidelity. Another study that described the learning curve required to perform AVS without use of prior imaging indicated that a clinician who had completed between 50-60 procedures could do this adequately<sup>27</sup>.

## **During AVS**

**Procedural Support:** For clinicians training to perform AVS, having access to support during a procedure is critical to the timeliness of the learning curve, and enhances fidelity to the procedure. This support may be in the form of mentoring and/or technological supports, such as Rapid Cortisol Testing and Cone beam CT discussed below. Support during the procedure by a skilled clinician with technical expertise was recognised by several studies as an important contributor to procedural success, attributable in part to support with planning, guidance with adrenal vein cannulation, and moral support<sup>24,26,31</sup>. Having a system of support may increase the adoption of the procedure within a new service and support the sustainability of the program.

**Rapid Cortisol Testing:** Eight studies referred to the use of rapid cortisol assay (RCA) (Serum/plasma or point of care) as an important tool for the confirmation of adrenal vein cannulation<sup>24,26,30,33,35-37,39</sup>, contributing to a reduction in failed cannulation during the training phase<sup>24</sup>. Timing can become an issue. Point of care RCA can be done within a few minutes at the bedside while laboratory based RCA requires different preparation<sup>35</sup>, and the proximity of the lab means the results can take up to 30-60 minutes to return<sup>24</sup>. One study suggested that lower income countries such as China may find it difficult to employ this test due to the number of institutions with RCA capacity<sup>30</sup>.

**Cone Beam Computer Tomography (CBCT):** The use of CBCT during the procedure was only mentioned in two papers<sup>30,35</sup>. One paper proposed it could serve as an alternative for low resource hospitals that do not have access to RCAs<sup>30</sup>. Clinicians would need to consider the appropriateness or feasibility of this test for use during AVS when RCA is available.

**Communication and Collaboration:** A number of communication and collaboration systems need to be in place to ensure that AVS occurs effectively and with the least avoidable errors. Papers identified specimen handling protocols<sup>34</sup> or safeguards<sup>40</sup> for test tube labelling including the use of printed labels to avoid mistakes<sup>35</sup>. Also mentioned was a collaborative approach needed for reporting preferences, such as in absolute values<sup>35</sup> or in a particular table<sup>28</sup>. An acceptable and communicated agreement between departments and clinicians about processes is needed to reduce avoidable errors and increase adoption.

## **Post AVS**

**Results interpretation:** Once AVS has been conducted, biochemical results are analysed to determine the success of cannulation (using the selectivity index) and if the source of PA is on one side or both (lateralisation index). While the Endocrine Society guidelines offer advice for selectivity and lateralisation indices, one study noted that hospitals use their own guidelines and criteria<sup>32</sup> with an overall lack of consensus on how AVS should be interpreted<sup>22</sup>. In fact, it has been noted that recommendations for AVS or adrenalectomy are at times, not made using the guidelines<sup>23</sup>. The reasons for this remain unclear. Perhaps it is because a clinician must combine several pieces of information including imaging and biochemistry results, patient demographics and comorbidities, along with the AVS outcome to make a decision about appropriate treatment options for the patient<sup>28,34</sup>. These factors become quite important as being more liberal or restrictive with a selectivity index or lateralisation index can change the success rate and lateralisation rate of AVS markedly<sup>37</sup>.

## **Implementation strategies and considerations for practice**

The Expert Recommendations for Implementing Change (ERIC) strategies employed by different hospitals and clinicians as they undertook the implementation components are spelled out in Supplementary Table 2. ERIC strategies are effective in improving the implementation of a clinical intervention<sup>13</sup>. Embedded within the clinical research papers were 13 different methods that had been employed by hospitals or clinicians as they implemented AVS for success. In particular these methods focus on knowledge translation (such as ‘capture and share local knowledge’) and development (such as, ‘prepare

patients/consumers to be active participants'). Other strategies may have been used that were not reported in the literature, which contributed to change. Using the data presented in the scoping review, and clinical expertise from our authorship team, a list of considerations ('what' needs to be implemented and 'how') for each implementation component was produced to support the decision-making of hospitals or centres who are considering the introduction, modification or upscale of an AVS service, see Table 2.

## **Discussion**

This scoping review has detailed implementation components that support the successful completion of AVS while also providing considerations for healthcare policy makers and administrators. The fact there are several components, aligns with Tan (2022) who note that multiple efforts to improve AVS success was what worked and not 'one' thing<sup>35</sup>. The Proctor (2013) framework requiring researchers to name, define and specify the implementation components was utilised, which were then graphically represented in a conceptual model (see Figure 2). There was a clear volume of evidence about the pre-AVS implementation components such as developing technical skill, use of CT imaging and having a local AVS hospital protocol lead to increased AVS success. These, in conjunction with procedural support and communication during AVS minimises avoidable mistakes and enhances operator skill. There was further evidence to support the need for in procedure support by an expert for clinicians on a learning journey. In addition, the use of rapid cortisol testing to confirm the correct cannulation of the adrenal veins offers a clear avenue for reduced AVS failure and repetition. Together these components increase the chances of successful completion of AVS. Evidence for the best way to use other implementation components, (patient voice and choice; AVS suitability and procedure preparation; CBCT; results interpretation) which are needed for procedure preparation and outcome analysis, which was less clear. This was due many factors including the natural variability in patients and their comorbidities; clinicians' use of evidence-based guidelines in concert with their practice-based expertise; views from multi-disciplinary colleagues to inform decision-making; and imaging equipment availability within the hospital setting. This suggests that more information is needed to inform the 'how' of best implementation when variability is unavoidable.

A marked increase in AVS success was demonstrated when hospitals actively minimised the number of interventional radiologists doing AVS to one or two clinicians, due to the volume of procedures required to be proficient<sup>26,32,34</sup>. Since few procedures are done per month even in high volume centres, and maintenance of expertise requires 15<sup>22</sup> -20<sup>26</sup> procedures annually, the decision to consolidate expertise into one or two highly skilled operators was logical. Conversely only one study noted that multiple surgeons should be involved to ensure that expertise is developed across their staff<sup>33</sup>. As it may take 2-3 years to reach 30 procedures (the learning curve for AVS) depending on hospital volume, referral rates and other factors, there must be systems of support, training, and feedback in place to ensure staff can develop and/or maintain the AVS learning curve<sup>43</sup>. While this requires a long-term focus from hospital administrators, it will strengthen the fidelity of the procedure and potentially minimise costs from failed procedures.

The success of AVS is essentially based on the selectivity index which tells us whether the catheter was in the adrenal vein. Hence, factors which confound the selectivity index, such as concurrent autonomous cortisol secretion<sup>44</sup>, the use of adrenocorticotrophic hormone (ACTH) during AVS<sup>45,46</sup> or the use of sedation<sup>47</sup>, may cause an apparent failure of cannulation. As new information emerges around the AVS procedure and outcomes<sup>48,49</sup>, there will continue to be variation across hospitals and centres about the indices that are used (as opposed to recommended). It therefore becomes important for clear justifications of clinical decisions made, with regular reviews of new evidence and where relevant, and updating local hospital protocols to ensure that implementation is based on the best evidence.

As centres initiate and optimise patient engagement in research and quality improvement initiatives related to AVS delivery, there is much to learn from an implementation perspective so that AVS can be an acceptable, cost-effective and feasible procedure. Little discussion in the identified papers was about the patient as an active participant in their AVS experience. Understandably the patient was not the focus of the papers and any note of their participation was related to the procedure itself (such as, timing of the day<sup>34</sup> or adjustments to medications prior to<sup>22</sup>) or their interest in surgery post AVS. In one study patient refusal was the major reason for not doing surgery<sup>29</sup>, and since the rationale for doing AVS is a surgical cure, engaging the patient early and often about their choices is a vital part. Yet, little research on patient views, experiences or engagement with PA or AVS is available to inform how best to support clinicians in their care. One study found patient knowledge of the

condition and the procedure is inadequate, and their journey towards a PA diagnosis being a major barrier to treatment<sup>50</sup>.

### **Implementation components and considerations for future implementation and scale up**

This review outlined implementation components that service providers can utilise in their establishment of AVS in a new service, to monitor and assess the progress of their AVS implementation. The ERIC strategies described in the reviewed literature frequently referenced readiness, training, supervision and assistance, and harnessing local knowledge, likely due to AVS being a complicated procedure. Future implementation research into the scale up of AVS should investigate the ERIC strategies more deeply to identify other strategies that may generate a greater implementation effect.

Working with the named components from Figure 2, the practical aspects drawn from clinical research for scaling or implementing successful AVS were studied. From this, considerations for future AVS implementation and scale up were developed to support hospital administrators and policy makers. Indeed, a crucial factor is to have the radiologists, biochemists and endocrinologists review the evidence and decide collaboratively what is possible to adopt in their own service. These considerations are by no means complete and should prompt challenging conversations with multi-disciplinary voices including patients to enhance the chances of success. As this review points out, there are many factors that contribute to AVS success and while certainly there will be failures, the findings of this review offer ways to mitigate and strengthen the factors that contribute to its success. These considerations should be examined in the light of the local context and adaptations based on the availability or constraints of human, equipment and financial resources should be clearly justified, but also revisited as systems and resources change.

### **Strengths and Limitations**

The approach of extracting implementation science information from clinical research is a mechanism to accelerate the translation of evidence into practice where implementation research is not yet available. This method, though likened to 'implementation science gymnastics' due to the extensive discussion, application, translation, and thoughtful engagement with the literature it required, provided an opportunity to explore the translational potential of clinical research. It could inform future implementation research in a more directed and focused manner. Additionally, it leveraged the knowledge from existing

implementation science frameworks as a foundation. Expanding implementation science use within the clinical setting and promoting high quality reporting of clinical research<sup>6 51</sup>, can only hasten the translation of knowledge into practice. Of note, a prerequisite for enabling our approach was the considerable information about implementation activities present in the clinical literature on delivering AVS. However, there are limitations to translating clinical information into implementation science concepts. Potential issues include misunderstanding or misattribution, overlooking important factors, and author bias. To mitigate these risks, regular multidisciplinary meetings with context experts and authors JY, EN and WC were instituted.

Our search strategy initially included the acronym 'AVS' as a search term. Its high frequency of use in the literature (see for example, automated vehicles, atrial ventricular syncope) tripled the number of results to screen. Thus, to narrow the scope of our search this was omitted, however it is possible papers were missed due to this approach. Of the studies found, all but one (a randomised study<sup>39</sup>) were retrospective in nature. The retrospective study design comes with serious biases that affect the reliability of study findings<sup>52</sup>. Across the included retrospective studies, we observed selection bias with patients included in the retrospective studies which was acknowledged by the authors. The lack of prospective design means that information biases can affect the measurement of clinical outcomes which are based on existing records in the retrospective studies. In addition, the implementation evidence was based on the experiences of others and only of those that were described. It is likely that other effective methods were utilised to enhance AVS success but not published.

## **Conclusion**

This scoping review examined the implementation components found in clinical research papers that support the successful conduct of AVS. Using a novel approach of data extraction informed by implementation science frameworks, components that support successful AVS procedures were named, defined and specified. In contrast to guidelines that report evidence to support best practice, the rationale and implementation of these practices is often unreported, yet this information is necessary to enhance AVS scale up. The findings provide practical insights and recommendations to facilitate service delivery and design. This will enhance the effectiveness of a health service providing AVS, potential saving resources whilst improving patient outcomes.

### **Authors Contribution**

HM and AM: Contributed to the conceptualization, methodology, literature search and screening, synthesis and analysis, investigation and co-writing (original draft, review and editing). EG, HS, WC and JY: Contributed to conceptualization, clinical content and sense-making of clinical implementation context. They were also involved in co-writing (review and editing). HS and JY: provided oversight and leadership responsibility for the research activity planning and execution.

### **Competing interests**

All authors have no issues relating to journal policies; we have no potential competing interests to declare.

### **Funding**

The research was funded by the Australian Medical Research Future Fund (MRFAR000172)

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**Table 1.** Search terms and inclusion criteria for the scoping review

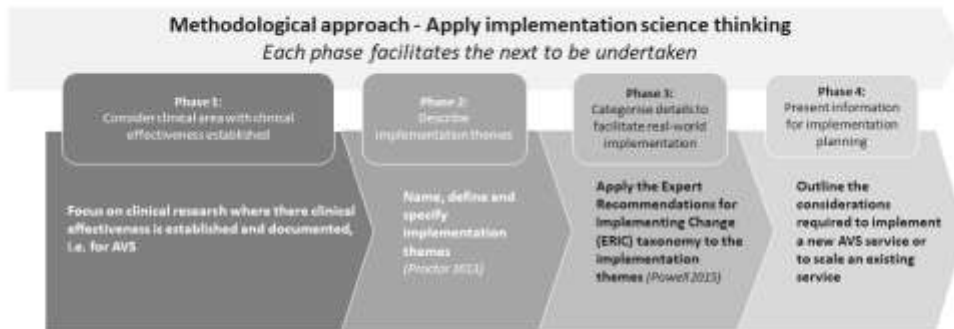
<i>Search terms</i> (Ovid Medline)	Hospital <b>OR</b> Centre <b>OR</b> Center <b>OR</b> healthcare <b>OR</b> service <b>OR</b> clinician <b>OR</b> doctor <b>OR</b> radiologist <b>OR</b> tertiary <b>AND</b> “Adrenal Vein Sampling” <b>OR</b> “adrenal venous sampling”
<i>Inclusion</i>	<ul style="list-style-type: none"><li>• Investigation of adrenal vein sampling (AVS) use <b>AND</b> description of at least one implementation factor impacting the success of AVS</li><li>• Any study design</li><li>• No study date limit</li><li>• AVS delivered in hospital setting (low or high -volume centres)</li><li>• Clinical outcomes about AVS techniques reported</li></ul>

**Table 2.** Considerations to support decision making around adrenal vein sampling (AVS)

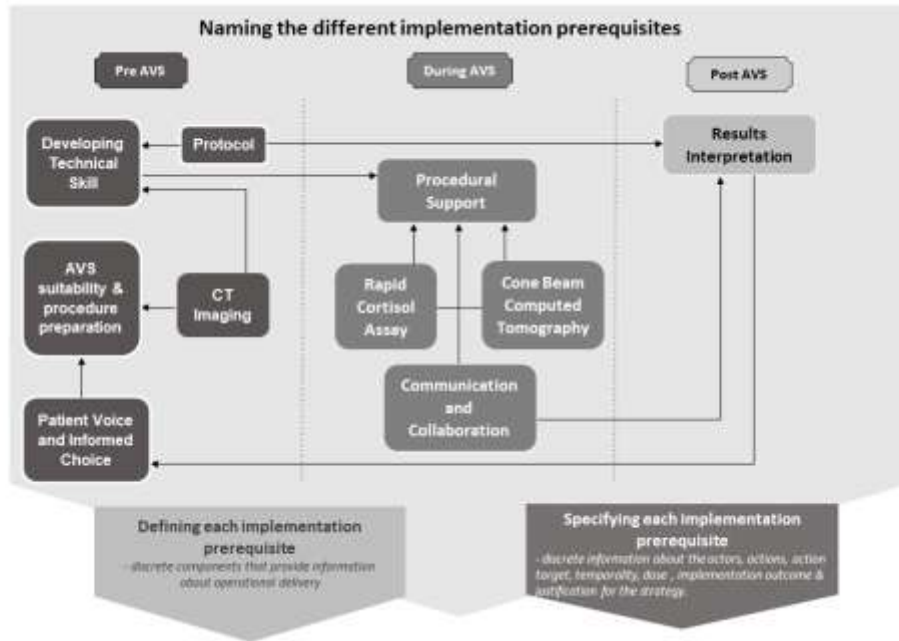
<b>Implementation Component</b> <b>- what needs to be implemented</b>	<b>Considerations to support decision making for future implementation and scale up</b> <b>- how the component needs to be implemented</b>
<b>Pre-AVS</b> Developing technical skill	<ul style="list-style-type: none"> <li>• Select interventional radiologists doing AVS to one or two clinicians</li> <li>• Consider mitigation strategies to prevent or minimise the failure rate as operators develop new skills, such as having a specialised interventional radiologist available during the procedure to support new operators</li> <li>• Consider leveraging existing staff and specialties that can do this procedure</li> <li>• Offer training, support and technologies to increase the rate of AVS success</li> <li>• Develop or strengthen referral pathways to ensure the annual, minimum number of procedures required for an interventional radiologist to maintain their skills</li> </ul>
<b>Pre-AVS</b> CT imaging	<ul style="list-style-type: none"> <li>• Ensure CT scan access for patients in hospital/centre</li> <li>• Consider a high-quality imaging scanner to strengthen the success of our AVS procedures</li> <li>• Consider not using imaging as a diagnostic tool in isolation of other tests</li> </ul>
<b>Pre-AVS</b> Patient voice and informed choice	<ul style="list-style-type: none"> <li>• To ensure patients understand the AVS procedure, patients need information and explanations including detail about possible surgical cure               <ul style="list-style-type: none"> <li>○ The most appropriate content, context and format of this information needs to be considered for patients</li> </ul> </li> <li>• Patient preferences and perspectives should be recognised and considered in information provision and decision making about undertaking AVS</li> </ul>
<b>Pre-AVS</b> Work-up preparations and decisions	<ul style="list-style-type: none"> <li>• Develop a local protocol about the confirmatory tests that are in use at a local site (hospital/centre)               <ul style="list-style-type: none"> <li>○ Include details about the guidelines or published protocols that have informed the decision-making process and rationale for using the selected confirmatory tests</li> </ul> </li> <li>• Develop a version (of this local procedure) for patients to understand the work-up preparations needed before AVS</li> </ul>

<p><b>Pre-AVS</b> Protocols (as opposed to guidelines) for AVS</p>	<ul style="list-style-type: none"> <li>• Ensure local protocols about the whole AVS procedure are disseminated, referred to and updated regularly</li> <li>• Appoint a champion to develop a new protocol who can initiate a multi-department collaboration <ul style="list-style-type: none"> <li>○ Consult with a multi-disciplinary clinician group during the process</li> </ul> </li> <li>• Audit the current protocol's use and investigate the barriers to its uptake in practice <ul style="list-style-type: none"> <li>○ Use this information to develop a local implementation plan</li> </ul> </li> </ul>
<p><b>During AVS</b> Rapid Cortisol Testing</p>	<ul style="list-style-type: none"> <li>• Consider whether 'point of care' rapid cortisol testing can be undertaken in local sites (hospital/centre)</li> <li>• Understand the structural barriers (such as physical location of the lab) that can be overcome to improve outcomes</li> <li>• Establish a collaborative and equitable working relationship between the lab and theatre to ensure efficient conduct of rapid cortisol testing</li> </ul>
<p><b>During AVS</b> Cone-beam Computerised Tomography (CBCT)</p>	<ul style="list-style-type: none"> <li>• Investigate how a local site (hospital/centre) can conduct CBCT in the context of 'in procedure' testing.</li> <li>• Understand the barriers to CBCT access and use at a local site (hospital) and establish strategies to improve or overcome these.</li> </ul>
<p><b>During AVS</b> Communication and collaboration</p>	<ul style="list-style-type: none"> <li>• Understand the process and impact of current communication methods between all staff, within departments and between clinicians at a local site.</li> <li>• Understand and use preferred presentation styles and formatting of information that enhance rapid communication of data.</li> </ul>
<p><b>During AVS</b> Procedural support</p>	<ul style="list-style-type: none"> <li>• Establish or link into an organisational learning/training system that will support learners of new procedures.</li> <li>• Include provisions for technical assistance during a procedure training and incorporate feedback loops that informs learners when they have achieved a sufficient skill level.</li> </ul>
<p><b>Post AVS</b> Results interpretation</p>	<ul style="list-style-type: none"> <li>• For local protocol development, include the expertise required for decision-making for AVS results. <ul style="list-style-type: none"> <li>○ Include details about decision support mechanisms for clinicians to improve accuracy of result interpretation.</li> </ul> </li> <li>• Consider how to engage referring clinicians in results interpretation</li> </ul>





**Figure 1.** Methodology used to extract implementation information from clinical research to inform new or scale-up of adrenal vein sampling (AVS) services



**Figure 2.** Conceptual model for successful adrenal vein sampling (AVS)