

CoaguCarnet®: A Structured Paper Booklet to Improve Vitamin K Antagonist Monitoring—Protocol for an Ambispective Comparative Cohort Study in Côte d'Ivoire

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Abstract

Background: Vitamin K antagonist (VKA) therapy requires reliable documentation of international normalised ratio (INR) measurements, prescribed doses, clinical decisions and next review. At the SSRCV, a conventional folded monitoring sheet has limited longitudinal space. A locally developed 31-page paper booklet, CoaguCarnet®, aims to improve the traceability of monitoring and facilitate continuity of care. **Methods:** This single-centre, non-randomised, ambispective comparative cohort study will identify exhaustively eligible historical patients with an index INR follow-up encounter between 1 January and 31 March 2026 and reconstruct individual six-month observation from the index date, ending no later than 30 September 2026. All eligible historical patients will be retained; the prospective CoaguCarnet® cohort will target 75 consecutively recruited patients from 15 October 2026, subject to operational authorisation, with six-month individual follow-up. This target is feasibility-based, not yet supported by a formal power calculation. The primary outcome is the patient-level mean five-item Clinical Traceability Index (CTI; 0 - 5), based strictly on the original monitoring support. Source retrieval, a common-item score, temporal changes, baseline differences and missingness will be analysed explicitly. We will also assess whether patients' INR monitoring history can be reliably reconstructed and whether the available INR results are sufficient to calculate time in therapeutic range (TTR). In the CoaguCarnet® group, we will explore patients' understanding of their anticoagulant treatment, their experience using the booklet, and their satisfaction with it. **Discussion:** This

study will assess whether CoaguCarnet® improves the quality of anticoagulation records. It is not designed to determine whether the booklet reduces bleeding or thrombotic events. Because the two groups will be drawn from different periods, differences in patient characteristics and documentation practices may influence the findings, even after statistical adjustment. Results will therefore be interpreted as associations.

Keywords

Vitamin K Antagonists, Anticoagulation, Patient-Held Records, Historical Cohort, Côte d'Ivoire

1. Background and Rationale

Patients receiving vitamin K antagonists (VKAs), particularly those with mechanical heart valves, need an individual INR target, regular dose review and clear communication between caregivers and clinicians. Current guidelines emphasise the importance of well-managed anticoagulation [1]. A systematic review has shown that maintaining INR within the therapeutic range remains difficult in sub-Saharan Africa [2]. This supports closer examination of how treatment is monitored in routine practice. Our study will assess whether CoaguCarnet® is associated with more complete documentation and continuity of follow-up.

At the SSRVCV, patients taking VKAs have traditionally used a folded sheet to record their INR results and dose changes. Space for documenting successive visits is limited. CoaguCarnet® was developed as a 31-page booklet containing INR results, prescribed doses, appointment dates, consultation notes, practical advice and contact details. It drew on French patient-education and VKA monitoring booklets, adapted to how anticoagulation care is organised in our service. The original documents and their conditions of reuse still need to be confirmed. The booklet is being studied as an organisational intervention informed by the Medical Research Council framework [3]. Previous research on anticoagulation education provides a rationale for evaluating patient-facing tools, although findings from other settings may not apply directly here [4] [5].

2. Objectives and Estimands

Primary objective. To estimate the adjusted difference between cohorts in the mean patient-level Clinical Traceability Index (CTI; 0 - 5) over six months from each patient's index visit. The CTI will be scored only from the original monitoring document. This outcome measures the quality of the record, not the effect of the booklet on bleeding, thrombosis or other clinical outcomes.

Secondary comparative objectives. To examine the availability and completeness of the original monitoring records, including longitudinal INR results, prescribed doses and documented medical follow-up. We will assess whether the available INR measurements allow calculation of time in therapeutic range (TTR)

according to predefined rules. Recorded bleeding, thrombotic events and other complications will be reviewed only where the information is sufficiently comparable between cohorts.

Prospective-only objectives. Among patients using CoaguCarnet®, we will assess understanding of anticoagulant treatment, satisfaction with the booklet, its use during follow-up and whether patients bring it to appointments. We will also record how well the booklet holds up over time, gather healthcare professionals' impressions of it, and time how long it takes to review a patient's treatment history. Medication adherence will be measured only if a validated French-language questionnaire is available. The Adherence to Refills and Medications Scale (ARMS) is one candidate [6], though its use here depends on confirming a suitable French-language version and its conditions of use.

3. Design, Setting and Calendar

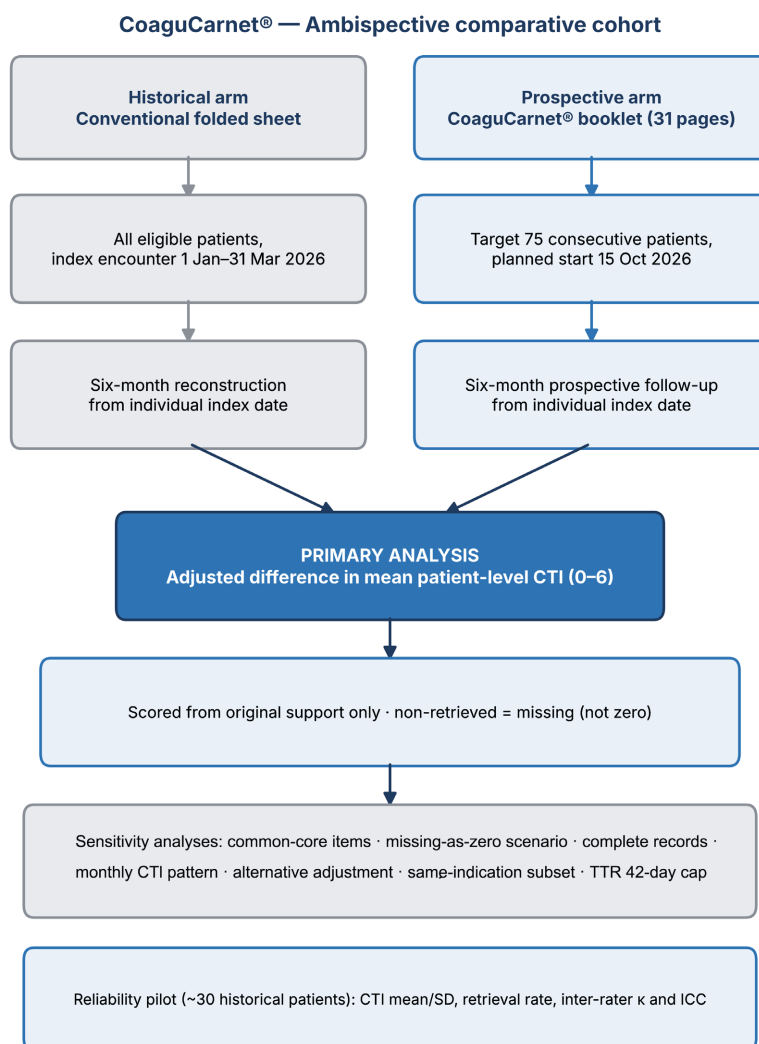
This single-centre ambispective study will compare a historical cohort using the conventional sheet with a prospective cohort using CoaguCarnet®. All eligible historical patients whose first qualifying visit occurred between 1 January and 31 March 2026 will be included. Prospective recruitment will aim for 75 consecutive patients from 15 October 2026, subject to institutional activation. Patients will not be randomly assigned to either group. For each patient, follow-up will begin at the first eligible INR monitoring visit during the recruitment period; those attending more than once will be included only once. Both cohorts will be followed or reconstructed for six months from that date (Table 1, Figure 1).

Because the two recruitment periods are separate, the same person may be eligible in both. Such a patient may contribute one observation to each cohort, but only once within each period. A stable study identifier will flag anyone re-enrolling across cohorts. In the primary patient-level regression, two observations from the same person will be treated as correlated, with Huber-White standard errors clustered by patient identifier. A sensitivity analysis restricted to patients in only one cohort will also be reported.

The historical observation period will end before the new booklet is introduced. We will document staffing changes, interruptions in INR reagent supply, laboratory procedures, clinic schedules, educational activities and other changes to routine care during both periods.

Table 1. Ambispective design: cohort identification and observation windows.

Cohort	Identification/entry	Observation
Historical	All eligible individuals with index encounter, 1 Jan-31 Mar 2026	Six calendar months from individual index date (latest allowable endpoint 30 Sep 2026)
Prospective	Target: 75 consecutive eligible patients from planned 15 Oct 2026, after institutional activation	Six calendar months from individual index date; subsequent recruitment close and study end to be recorded



Ethics approval obtained (July 2026) within the CoaguloCare decentralised-INR programme; scope covers retrospective record use.

Figure 1. Ambispective study flow. The historical conventional-sheet cohort comprises all eligible patients with index encounters from 1 January to 31 March 2026; the prospective CoaguCarnet® cohort targets 75 consecutive patients, with a planned start on 15 October 2026. Observation lasts six months from each patient's index date. Non-retrieved original supports are missing, not zero, in the primary analysis. The schematic contains placeholders for actual screening and analysis counts; these must be completed when available. The July 2026 institutional authorisation covers the retrospective records used here.

4. Eligibility, Recruitment and Selection

Common eligibility criteria. age ≥ 18 years on index date; documented VKA prescription and indication; participation in SSRCV INR follow-up; an identifiable index encounter; and sufficient unique identifiers in the source system to deduplicate records. For the historical cohort, we will include all eligible patients, including those who have died, stopped attending follow-up visits, or have incomplete records. Patients will not need to have undergone a minimum number of INR tests after inclusion. In the prospective cohort, patients will be informed about the study and asked to provide their consent before enrolment, following

the approved study procedures.

Historical identification. We will review the anticoagulation follow-up register for January to March 2026 to identify all patients who meet the study criteria. Patients who attended more than once during this period will be counted only once. We will record the number of patients screened, how many met the eligibility criteria, and the reasons why some were not included.

Prospective identification. We will record all patients considered for the prospective cohort, including those who decline to participate or are not enrolled for other reasons. Cohort assignment will be based on the monitoring document used at the first eligible visit. Patients who do not complete the six-month follow-up will remain in the cohort, and the reasons for incomplete follow-up will be recorded whenever available. Death, transfer, a change of anticoagulant or loss to follow-up will not be used to exclude patients retrospectively.

5. Intervention and Usual Care

Historical standard care. the conventional folded VKA monitoring sheet, with usual prescribing and INR assessment.

Prospective intervention. Each participant will receive a 31-page CoaguCarnet® booklet, accompanied by a brief standard explanation and demonstration of an INR entry. Patients will be encouraged to bring it to their appointments. Anticoagulant dosing and other clinical decisions will remain with the treating clinicians. Training time and any additional education will be recorded. To describe implementation, we will document booklet distribution, availability at visits, staff orientation and the use of designated sections. Copies of both monitoring supports and the teaching materials will be retained as study materials, subject to clarification of reproduction rights. Staff instructions will not suggest that one support is superior.

6. Outcomes and Source Hierarchy

6.1. Primary CTI

For every eligible INR encounter with a retrieved original support, we will award one point for each legible, interpretable and visit-attributable component: 1) sampling/control date, 2) numerical INR result, 3) prescribed VKA dose schedule, 4) identifiable prescriber, and 5) next scheduled INR date. The CTI score ranges from 0 to 5. When an INR visit appears in the clinical register but the original monitoring sheet is unavailable, we will treat the CTI score as missing, not as zero. We will make this distinction in the main analysis to avoid confusing missing records with poorly documented care. Each patient's primary CTI is the arithmetic mean of scored encounters within their six-month window, regardless of number of visits. The number of retrieved and non-retrieved supports will be reported by group.

Primary analysis population. The primary CTI analysis includes cohort-period observations from patients with at least one INR encounter whose original

support is retrieved and whose five CTI items can each be judged present or absent. Patients with no scorable encounter have a missing primary CTI and do not enter the primary regression, but remain in the eligible cohort denominator for recruitment, source-retrieval and missingness reporting. The primary adjusted analysis will therefore include only patients with at least one original monitoring record available for scoring, rather than all eligible patients. To assess the possible impact of missing records, we will repeat the analysis under two conditions: assigning a score of zero to visits for which the original document could not be retrieved, and restricting the analysis to patients with complete monitoring records.

CTI construction and scoring rationale. The CTI includes five components that reflect the information routinely needed to monitor patients receiving VKA treatment. All five can be assessed from the original monitoring documents used in both cohorts. The control date and INR value show when the test was performed and the result obtained. The prescribed dose schedule indicates the treatment prescribed, while prescriber identification shows who was responsible for that decision. The date of the next INR test indicates when follow-up is planned.

Each component is worth one point, giving a total score ranging from 0 to 5. We chose this simple scoring system to assess how completely monitoring information is recorded, rather than to evaluate clinical risk. The physician's signature or visa was excluded because it is not consistently available on the documents used in either cohort. Its absence will therefore not affect the CTI score.

We will report the findings for each component alongside the overall CTI score. Although all five components receive one point, this does not mean they are equally important in clinical practice.

For the INR component, one point is given when a numerical INR result is recorded and can be tied to the visit; both decimal-point and decimal-comma notation count. A qualitative note such as "therapeutic", with no number, scores zero.

All five components are assessed at every eligible visit, so the CTI reaches at most five points. The NA-RULE code is not used in the primary analysis. When an assessor marks a component as non-applicable, the case is reviewed before the database is locked, and the CTI stays missing until that review concludes. If it confirms that the visit cannot be scored on the five components, the visit is dropped from the primary analysis and the reason noted. The same rules apply to both cohorts. The full coding and audit form is provided in **Appendix A**.

Because the booklet gives more room and structure, one sensitivity analysis will keep only the items that could plausibly be recorded on either support. Another will score zero for every visit whose original document cannot be found; this is a deliberately harsh assumption about missing paperwork, not a conclusion that the care itself was poorly recorded. In neither analysis will gaps in the original-support CTI be filled from the clinical register.

6.2. TTR and Other Outcomes

Time in therapeutic range (TTR) will be calculated from the INR results recorded

during follow-up and each patient's target range, drawn from clinical records separately from the documents used to score the CTI. The Rosendaal method applies when at least two dated INR results and a known target range are available [7]. Interpolation runs from the first eligible INR measurement in the six-month window to the last; days before the first and after the last are left out of the denominator. Intervals of 56 days or less with an unchanged target are interpolated to daily INR values, while intervals longer than 56 days are dropped from both the numerator and the denominator. When the target range or the anticoagulation management changes, the periods are kept separate and only the eligible sub-intervals contribute. TTR is then $100 \times (\text{interpolated eligible days within the patient's target range} / \text{total interpolated eligible days})$. For each patient we will also report coverage, the number of denominator days divided by the total days in the six-month window. Because two measurements alone may not reflect six-month control, the number of INR tests and the coverage will be given alongside the estimate. A sensitivity analysis repeats the calculation with a 42-day maximum interval; these gap limits are study-specific and not part of the original Rosendaal method [7].

Clinical events. Major and minor bleeding, thrombotic complications, related hospital admissions and deaths will be recorded from the available clinical notes, including event dates where documented. Major bleeding will be classified using International Society on Thrombosis and Haemostasis (ISTH) criteria when enough information is available [8]. Events that cannot be classified reliably will be labelled unclassifiable. Clinical events may be more thoroughly captured during prospective follow-up, so comparisons between cohorts will be exploratory and will not be used to claim a reduction in complications.

Other variables. For each patient, we will record the VKA used, indication for anticoagulation, target INR range, age, sex and treatment duration. Comorbidities will be included where recorded comparably in both groups, together with INR testing dates and frequency. Staffing changes and interruptions to routine services will also be noted, as these may have affected care across the two periods. Satisfaction, knowledge, adherence, booklet durability and usability will not be compared with the historical cohort when equivalent historical measurements are unavailable.

7. Measurement Schedule

The schedule of measurements for each cohort is summarised in **Table 2**.

Table 2. Measurement schedule by cohort and time point.

Measurement	Historical cohort	Prospective cohort
Baseline/index	Register + archived record	Interview + clinical record
Each INR encounter	Original support scored from archive; separate register extraction	Original booklet scored; separate routine register extraction

Continued

Monthly pattern	Retrospective months 1 - 6 as available	Months 1 - 6; evaluate waning completeness
Month 3	Retrospective data status only	CTI, fidelity, adverse events, usability
Month 6	Retrospective endpoint, censoring and completeness	CTI, TTR eligibility, adverse events, satisfaction, physical durability, feasibility
Patient knowledge/adherence	Not compared; generally unavailable	Baseline/follow-up only with suitable instruments

8. Bias Minimisation and Quality Assurance

Selection bias. The historical register will be reviewed exhaustively, while prospective patients will be recruited consecutively. Completion of six-month follow-up will not be a condition for remaining in either cohort.

Period effects. Staffing, INR testing procedures, supply availability and the organisation of care will be reviewed for changes between the two periods. Other developments that could have affected follow-up will also be noted. Where the information permits, these factors will be considered in the analysis, although adjustment cannot fully separate the booklet from changes over time.

Hawthorne effect. Healthcare professionals will know that CoaguCarnet® is being evaluated. CTI scores will therefore not be shared with the care team during follow-up, and staff will receive the same instructions for using the booklet. Monthly CTI patterns will be examined to see whether documentation changes over the six months. This cannot rule out the influence of being observed on routine recording practices.

Information bias. Both cohorts will be assessed using the same scoring rules. Copies of original monitoring documents will be anonymised and presented to reviewers in random order. Patient identities and clinical outcomes will be concealed from the reviewers where possible, although the layout of each document may reveal the group. Retrieval rates will be reported separately, and a second reviewer will verify data extracted from the anticoagulation register against the source records.

Confounding. Baseline adjustment variables will be taken from information available before or at the index visit in both cohorts: age in years; sex; VKA indication (mechanical heart valve versus other); VKA treatment duration at index in months; prior anticoagulation control, defined as the proportion of INR results within the patient's target range in the 90 days before index, with a separate indicator for patients having no pre-index INR; and prior monitoring frequency, the number of INR visits in that same 90-day window. Variables that may have shifted as a result of CoaguCarnet® use will not be used for baseline adjustment. Period-level service changes will be described and considered only in prespecified sensitivity analyses, since they may be incompletely measured. A bias and missingness

audit checklist is provided in **Appendix B**.

9. Sample Size and Reliability Pilot

We plan to recruit 75 patients into the prospective cohort during routine follow-up visits. This number reflects the number of patients we expect to enrol at our service, rather than a formal sample-size calculation. In the historical cohort, all eligible patients identified in the register between 1 January and 31 March 2026 will be included, each counted once. We will not reduce that group to match the prospective target. After the record review, both the total number eligible and the number with sufficient data for CTI analysis will be reported.

Before analysis of the prospective data, a pilot review of approximately 30 historical patients selected across January, February and March 2026 will estimate the mean patient-level CTI, its standard deviation and distribution, the retrieval rate of original sheets, and the number of INR visits per patient. These estimates will inform a sensitivity-based assessment of power and precision using a two-sided alpha of 0.05, 80% target power (with a 90% scenario), the historical cohort size and unequal allocation. A difference of one CTI point out of five is a provisional operational threshold that must be justified before prospective outcomes are inspected. The calculations will account for the expected proportion of evaluable prospective records. If 75 patients do not offer adequate power or precision, the study will emphasise adjusted differences and 95% confidence intervals rather than claims of superiority or equivalence. The pilot will not be used to select an effect size that favours a particular result.

Two reviewers will independently score at least 20 historical sheets and 20 CoaguCarnet® booklets, including records with differing levels of completeness where possible. Agreement on each CTI item will be reported as a percentage and with Cohen's kappa, interpreted in light of item prevalence. For the total score, we will calculate an absolute-agreement intraclass correlation coefficient (ICC) with a 95% confidence interval. Differences will be discussed after independent scoring, and any clarification of the rules will be made before the main dataset is locked. This pilot will show how consistently reviewers apply the CTI scoring criteria, although it will not establish the clinical validity of the score.

10. Statistical Analysis Plan

Patient characteristics will be described separately for each cohort. We will use descriptive statistics and standardised differences to assess how the groups compare at baseline, without relying solely on p-values. We will report numbers screened and enrolled, index visits, original documents retrieved, INR visits with a CTI score, follow-up person-time and reasons for missing data. Patient-level CTI will be described using means and standard deviations, medians and inter-quartile ranges, and the proportions with a mean score of exactly 0 or 5.

Primary analysis

The primary comparison uses ordinary least-squares linear regression, with

each cohort-period patient's mean CTI across scored visits as the outcome. The model includes study group (prospective CoaguCarnet® versus historical conventional sheet) and the prespecified baseline covariates: age in years, sex, VKA indication (mechanical heart valve versus other), VKA treatment duration in months, the proportion of INR results within target in the 90 days before index plus an indicator for no pre-index INR, and the number of INR visits in that same 90-day window. Standard errors will be clustered by patient identifier (Huber-White), so that someone appearing in both cohorts is not counted as two independent observations. The effect measure is the adjusted mean difference in CTI (prospective minus historical), with a 95% confidence interval and p-value. The regression uses observations with a non-missing CTI and the required covariates; the amount and pattern of covariate missingness will be reported, and multiple imputation examined in sensitivity analysis if its assumptions hold. Residuals and influential observations will be checked; if linear-model assumptions are materially inadequate, patient-level bootstrap confidence intervals will be reported as a sensitivity analysis. A supplementary visit-level mixed-effects model with a patient random intercept will account for repeated visits within patients.

Sensitivity analyses

Sensitivity analyses will test whether findings depend on the scoring rules or on record availability: a score restricted to items recordable on both supports, a scenario assigning zero to visits without a retrieved original (not read as evidence of poor care), and an analysis restricted to patients with complete records. We will also examine the monthly CTI pattern during prospective follow-up, try alternative baseline adjustments, and repeat the comparison among patients with similar VKA indications. For TTR, a separate analysis applies a 42-day maximum interval between INR measurements. We will also repeat the primary comparison after excluding patients who contributed to both cohort periods.

Missing data and secondary outcomes

Missing information will be classified as never recorded, illegible, original support not found, clinically unavailable, or not applicable for non-CTI variables. For the primary CTI, all five items are applicable by definition; a non-retrieved original is coded as missing source rather than zero, and a patient with no scorable encounter has a missing patient-level CTI. We will describe the extent and reasons for missing data in each cohort. Because records may be less complete or harder to retrieve in one group than the other, a complete-record analysis alone could bias the result. Multiple imputation will be considered for missing covariates when the data, sample size and assumptions allow; the primary CTI itself will not be imputed from the clinical register.

We will also compare how many patients have enough information to calculate TTR, reporting the risk difference with a 95% confidence interval. These figures will be read together with the frequency of INR testing and the share of follow-up covered by interpolation.

Bleeding, thrombotic events, related hospitalisations and deaths will be given

as event counts and as rates per observed person-time. Since these events may have been recorded differently in the historical and prospective periods, the comparisons will stay exploratory. Knowledge, adherence (where a validated questionnaire is available), satisfaction and booklet durability will be described within the prospective cohort. Time taken to reconstruct treatment history will be compared between cohorts only if an equivalent timed assessment can be applied, with reviewers blinded wherever feasible.

11. Data Governance, Ethics and Participant Safety

The Direction Médicale et Scientifique (DMS) of the Institut de Cardiologie d'Abidjan (ICA) granted institutional approval in July 2026 within the CoaguloCare programme, according to the study's institutional record. This is a non-invasive documentation intervention and does not require protocol-directed changes in VKA treatment. This approval covers the use of retrospective monitoring records and the applicable consent requirements. Prospective participants will receive information about the study and give informed consent before enrolment, in line with the approved procedures. Each patient will be given a study code, and the file linking these codes to patients will be kept separately, with access restricted to authorised members of the research team. Any current anticoagulation safety concern identified during follow-up will be referred to the treating clinicians.

12. Reporting, Dissemination and Intellectual Property

This is a protocol of a non-randomised observational comparison, not a randomised trial. STROBE will guide reporting of the completed cohort results [9], RECORD will supplement reporting of routinely recorded retrospective data [10], and the Medical Research Council framework will inform description and evaluation of the complex intervention [3]. SQUIRE 2.0 may further inform description of the local service-improvement context [11], without being treated as the governing protocol standard. The booklet's French educational antecedents will be acknowledged, and any third-party copyrighted materials will be reproduced only where rights permit. No clinical efficacy claim will be made from documentation outcomes alone.

13. Study Limitations Specified in Advance

The comparison has several limitations. Patients come from different periods, healthcare professionals cannot be blinded to the booklet, and the CTI is a new score whose validity has not been established. Some original monitoring records may be missing, and bleeding or thrombotic events may have been captured unevenly across the two cohorts, which could affect the results. The study will test whether CoaguCarnet® is associated with more complete documentation of anticoagulation care in our setting; any gain seen, however, may also come from shifts in routine practice rather than from the booklet alone. A higher CTI score cannot be taken as evidence of fewer bleeding or thrombotic events.

Ethics Approval

Approved by the Direction Médicale et Scientifique, Institut de Cardiologie d'Abidjan, in July 2026, within the CoaguloCare programme; see Section 11 for scope and consent procedures.

Author Contributions

Boka BC conceived and designed the study, designed the statistical analysis plan and drafted the manuscript. Coffie P, Hauhouot M-L and Ekou KA supervised the work. Flainde LD and Yeo A were responsible for data collection. Oga S contributed to supervision and critical revision. All authors reviewed and approved the final manuscript.

Data Availability

No study results are reported in this protocol. Access conditions for future de-identified study data will follow institutional approvals.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Appendix A: CTI Coding and Audit Form

Item	1 (present)	0 (absent/invalid)
Control date	Valid encounter-specific date	Missing, unreadable or cannot link to INR
INR value	Clearly numerical INR result attributable to the encounter (decimal point or comma accepted)	Missing, unreadable, qualitative-only notation, or no encounter attribution
VKA dosing schedule	Interpretable prescribed regimen for next dosing interval	Medication name alone; unreadable or absent schedule
Prescriber ID	Named, numbered or otherwise attributable qualified prescriber	Unidentifiable author or blank
Next INR control	Explicit next control date	Generic advice without date or blank

Rules. Score the CTI from the original paper support only. A zero is not the same as “source not retrieved,” coded separately as NA-SOURCE. All five items apply to every eligible INR encounter, so NA-RULE is not used in the primary score and the denominator stays five. If an assessor considers an item genuinely non-applicable, the encounter is flagged for adjudication and its total CTI stays missing until the decision is resolved. The INR item needs a numerical value; decimal-point and decimal-comma notation are accepted, qualitative-only terms are not. For each control, record source retrieval, the five-item CTI vector, total score, assessor ID and adjudication status. Keep an item-level scoring log and a prespecified random reassessment sample.

Appendix B: Bias and Missingness Audit Checklist

- ☐ Historical register denominator and unique-patient deduplication verified
- ☐ Original folded sheets retrievable for each scheduled/recorded INR encounter
- ☐ Same index definition and six-month follow-up anchor applied to both groups
- ☐ Staffing, testing capacity, INR reagent supply and workflow change log collected
- ☐ Baseline covariates measured in both cohorts and overlap checked
- ☐ Inter-rater reliability pilot completed without exposure to group-level results
- ☐ Primary versus common-core and missing-source sensitivity analyses locked
- ☐ Prospective training script and monthly fidelity monitoring archived
- ☐ Prospective consent and historical-record ethics decision documented
- ☐ Data sources and clinical-event ascertainment limitations reported