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At-Home Racemic Ketamine Treatment: A Structured Framework for Preparation, Route-Specific Dosing, Monitoring, Rescue, Recovery, and Follow-Up

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Abstract

Ketamine is increasingly used in psychiatric and psychotherapeutic treatment through intravenous, intranasal, sublingual or buccal, and subcutaneous administration. Its therapeutic applications extend beyond formally diagnosed psychiatric disorders and include existential anxiety, persistent emotional distress, trauma-related suffering, psychological responses to serious illness or major life events, fear of mortality, loss of meaning, demoralization, and psychospiritual distress. Nonintravenous racemic ketamine is particularly suited to prescriber-directed treatment outside conventional infusion clinics because formulation, route, dose, treatment frequency, and degree of external support can be individualized. Large real-world cohorts already demonstrate structured at-home treatment through sublingual and subcutaneous administration. This paper develops a structured framework for at-home racemic ketamine treatment based on route-specific pharmacology, body-weight-normalized dose interpretation, patient-specific pharmaceutical preparation, initial treatment selection, standardized administration, pre-session physiological assessment, set and setting, route-specific monitoring, psychological and cardiovascular escalation criteria, management of nausea, predefined rescue procedures, functional recovery, post-session care, and systematic measurement of therapeutic outcome. The framework follows one operational principle: every clinically relevant decision that can be made before ketamine takes effect should be made before ketamine takes effect. Dose, formulation, maximum session exposure, timing, physiological thresholds, rescue medication, treatment environment, escalation criteria, and follow-up are therefore predetermined. This minimizes calculation, interpretation, and improvisation during the psychoactive period and converts home administration into a reproducible therapeutic process.

Keywords: Racemic ketamine, At-home treatment, Intranasal ketamine, Sublingual ketamine, Subcutaneous ketamine, Ketamine-assisted psychotherapy, Treatment-resistant depression, Existential distress, Cardiovascular monitoring, Ketamine safety.

1. Introduction

Ketamine has developed from an anesthetic agent into a rapidly acting therapeutic compound used across psychiatry, psychotherapy, palliative care, and related clinical fields. Its best-established psychiatric application is the treatment of major depression and treatment-resistant depression, but contemporary therapeutic use extends considerably beyond diagnostic symptom reduction. Ketamine and ketamine-assisted psychotherapy are used in work involving anxiety, trauma-related distress, serious illness, existential anxiety, fear of mortality, demoralization, loss of meaning, emotional burden, and psychospiritual distress [1].

This broader therapeutic field is now measurable rather than merely descriptive. In 2026, an intranasal racemic-ketamine study in patients with advanced cancer documented substantial improvement in death-and-dying distress, quality of life, anxiety, and existential well-being. Fifteen participants received three ketamine treatments. Improvement on the Death and Dying Distress Scale reached an effect size of $d = 0.91$, while improvement in existential well-being on the McGill Quality of Life Questionnaire reached $d = 1.02$. Changes in these existential outcomes were not significantly correlated with changes in depression severity, supporting existential distress as a therapeutic outcome domain that is not adequately represented by depression severity alone [2].

A real-world academic palliative-care program published in the same year similarly described ketamine-assisted psychotherapy as treatment addressing anxiety, depression, demoralization, loss of meaning, existential distress, and related psychospiritual suffering [3]. These developments are relevant to home treatment because the therapeutic objective of ketamine is not always reduction of a diagnostic score. In some patients, the principal target is emotional processing, fear of mortality, psychological rigidity, persistent distress following major life events, or a disturbed relationship to meaning and mortality.

The expansion of therapeutic aims has been accompanied by diversification of administration routes. Intravenous racemic ketamine generated much of the early psychiatric evidence, followed by intranasal esketamine and increasing clinical use of nonintravenous racemic ketamine. Intranasal, sublingual or buccal, and subcutaneous

administration make treatment possible without intravenous infusion and have enabled structured prescriber-directed treatment in the home.

The acute medical safety profile of subanesthetic ketamine supports this development. A systematic review covering 93 studies and 3,756 adults exposed to subanesthetic ketamine for psychiatric treatment identified medically serious adverse events in approximately 0.1% of treated participants. The reported events resolved without lasting sequelae, and no serious cardiac adverse event or death occurred in the reviewed population [4].

At-home treatment is already represented by substantial clinical populations. A prospective telehealth-supported study included 1,247 patients receiving sublingual ketamine at home and demonstrated substantial reductions in depression and anxiety [5]. A later longitudinal analysis included 11,441 patients receiving at-home ketamine and documented reported adverse events in approximately 3.0–4.8% of participants [6].

The 2026 U.S. subcutaneous home-treatment cohort further demonstrates how structured treatment can operate outside a clinic. A total of 3,870 patients were approved for treatment, 3,567 completed at least one session, and 3,041 entered the principal analysis. Treatment combined clinician-directed weight-based dosing, remote physiological screening, home blood-pressure monitoring, standardized injection materials, symptom measurement, and mandatory peer monitoring [7]. At the three principal assessment waves, reported side effects were approximately 2.8–3.2%. Across the wider 22-month safety-reporting population, three serious adverse events were recorded among 3,943 treated patients, corresponding to 0.08% [7].

The scientific task is therefore no longer to establish that structured home administration occurs. The task is to organize it more precisely. Dose, formulation, administration, physiological thresholds, psychological escalation criteria, rescue, recovery, and therapeutic follow-up can all be defined before the psychoactive state begins.

2. Framework Development

The framework integrates controlled clinical studies, pharmacokinetic investigations, large real-world home-treatment cohorts, interdisciplinary consensus recommendations, operational ketamine-treatment protocols, and contemporary route-specific best-practice recommendations.

The central method is direct translation of established clinical variables into predefined home-treatment decisions. Pharmacokinetic findings determine route-specific timing. Clinical treatment studies establish therapeutic dose ranges. Home cohorts establish practical entry criteria and treatment logistics. Operational ketamine protocols provide direct models for management of marked cardiovascular and behavioral responses. These elements are combined into a unified structure in which treatment decisions are made in advance and expressed through dose, time, physiological measurements, observable behavior, and predetermined actions.

The purpose of this construction is not to reproduce an infusion clinic in the home. It is to identify those variables that materially affect home treatment and can be standardized without unnecessary complexity.

3. Scope and Initial Treatment Selection

This framework concerns adult, prescriber-directed, subanesthetic racemic ketamine treatment conducted in the home through intranasal, sublingual or buccal, or subcutaneous administration. Subanesthetic treatment refers here to dosing intended to produce therapeutic psychological and neuropsychiatric effects without general anesthesia.

The therapeutic indication can include major depression, treatment-resistant depression, anxiety-related conditions, trauma-related distress, existential anxiety, fear of mortality, demoralization, persistent emotional burden, psychospiritual distress, and other forms of psychological suffering for which ketamine is used within a structured therapeutic context.

Home treatment occurs with varying levels of remote and in-person support. The strongest contemporary home datasets describe structured models in which prescribing, screening, treatment preparation, dosing, symptom measurement, and follow-up remain clinician-directed even though administration occurs in the patient's home [5–7].

Initial selection is part of the protocol itself. The largest subcutaneous home cohort used medical and psychiatric history, medication reconciliation, physiological screening, assessment of the treatment environment, and confirmation of a trusted adult treatment monitor before home administration began [7].

3.1. At-Home Treatment Exclusion Criteria

The threshold for home treatment is narrower than the threshold for ketamine treatment in a monitored medical environment. The relevant question is whether the patient's anticipated response can be managed predictably within the resources of the home framework.

Published home-treatment criteria provide a direct model. Conditions incompatible with the at-home setting include active psychotic or manic symptoms, a primary psychotic disorder with current instability, active suicidal intent or planning, a recent serious suicide attempt requiring a higher level of observation, uncontrolled hypertension, unstable or substantially impaired cardiac status, severe poorly controlled respiratory disease, active ketamine use disorder, hypersensitivity to ketamine, and other acute medical or psychiatric states requiring continuous clinical supervision [7].

Untreated hyperthyroid states producing substantial cardiovascular activation, markedly elevated intraocular pressure, and other conditions specifically identified during prescriber assessment can likewise shift treatment from the home environment to a more closely monitored setting [7].

These are at-home exclusion criteria rather than universal prohibitions against ketamine. A condition that makes independent or lightly supported home administration inappropriate can still be compatible with treatment in a setting providing the required level of medical monitoring.

Serious illness by itself does not determine treatment suitability. Suitability is determined by current physiological stability, medication profile, expected ketamine response, treatment environment, and the level of support available in the intended setting.

Previous ketamine exposure strengthens this assessment because it provides direct information about the patient's actual cardiovascular response, nausea tendency, dissociative intensity, behavioral response, and recovery pattern.

4. Off-Label Racemic Ketamine, Compounding, Dispensing, and Storage

In the United States, an approved medication can be prescribed by an appropriately licensed clinician for an unapproved indication, dose, or route when that use is medically appropriate [8]. This established off-label pathway gives racemic ketamine substantial clinical flexibility.

Patient-specific compounding extends this flexibility. Under Section 503A of the U.S. Federal Food, Drug, and Cosmetic Act, compounded medication can be prepared pursuant to a valid prescription for an identified individual patient [9]. In home ketamine treatment, pharmaceutical preparation therefore becomes part of treatment design.

A nasal formulation can be prepared so that each actuation contains a defined quantity of racemic ketamine. Sublingual or buccal preparations can be supplied in predefined treatment units. Subcutaneous formulations can be prepared at concentrations that permit the prescribed dose to be administered without complex calculation.

This matters because ketamine progressively alters attention, coordination, working memory, time perception, and judgment. Calculation therefore belongs before treatment. A patient should not have to divide powder, convert milligrams into milliliters, calculate concentrations, or decide on additional dosing while ketamine is active.

For staged intranasal treatment, the same principle applies to each actuation. Milligrams per spray, interval between sprays, and maximum number of sprays are determined before the session begins. Metered-dose preparations are particularly suitable because dose per actuation and maximum session exposure remain explicit.

This structure differs from the U.S. pathway for intranasal esketamine. Spravato is supplied as a proprietary standardized formulation and operates under a product-specific Risk Evaluation and Mitigation Strategy requiring administration in a certified healthcare setting under direct observation [10]. Racemic ketamine follows a different prescribing pathway and allows individualized home formulations where permitted.

The quantity dispensed should correspond to the prescribed treatment interval. Concentration, treatment units, storage conditions, dose log, maximum session dose, and refill schedule are established in advance. Secure storage and controlled quantities preserve pharmaceutical integrity and maintain treatment within the prescribed dose structure. Contemporary best-practice recommendations for nonintravenous racemic ketamine similarly emphasize predefined dose escalation, controlled dispensing, secure storage, dose records, and fixed refill procedures [11].

5. Route-Specific Pharmacology

Intranasal, sublingual or buccal, and subcutaneous ketamine cannot be compared milligram for milligram because systemic availability, absorption, metabolite exposure, and timing differ substantially between routes.

Comparative pharmacokinetic work reported intranasal ketamine bioavailability of approximately 45% and sublingual bioavailability around 30% [12]. A dedicated sublingual study reported median absolute bioavailability of approximately 29% and a median time to maximum plasma concentration of approximately 45 minutes [13].

Sublingual and buccal administration also produces a different relationship between ketamine and metabolites because a portion of the administered material is swallowed and undergoes gastrointestinal absorption followed by hepatic first-pass metabolism. Contact time, saliva handling, and whether remaining material is swallowed or expelled therefore materially affect exposure.

Swallowing a larger fraction increases gastrointestinal absorption and hepatic first-pass metabolism and consequently increases relative exposure to norketamine and downstream metabolites [12,13]. These metabolites contribute to the overall pharmacodynamic profile and can extend the period during which ketamine-related subjective effects remain present. The swallow-or-expel procedure therefore affects not only the quantity of parent ketamine reaching systemic circulation but also the temporal profile of the session and recovery.

Subcutaneous estimates vary with pharmacokinetic model and study design. Population pharmacokinetic and pharmacodynamic modelling in treatment-refractory depression estimated absolute subcutaneous/intramuscular bioavailability at approximately 64.4%, with an absorption terminal half-life of approximately 6.4 minutes [14]. The large 2026 home-SC study described the subcutaneous route using an assumed bioavailability of approximately 93% [7]. Clinical dose selection is therefore anchored primarily in observed route-specific treatment data rather than derived from a single theoretical bioavailability conversion.

Body weight materially changes dose exposure. A fixed 50 mg dose represents 1.0 mg/kg in a 50 kg patient and 0.5 mg/kg in a 100 kg patient. Every treatment record should therefore contain both total milligrams and milligrams per kilogram. Total milligrams define what was administered; milligrams per kilogram permit meaningful comparison across body sizes and treatment sessions.

This dual documentation is particularly useful when fixed-dose nasal or sublingual treatment is used. It preserves the simplicity of a fixed pharmaceutical unit while capturing the substantial weight-normalized exposure difference between patients receiving the same nominal dose.

6. Route-Specific Dosing

6.1. Intranasal Racemic Ketamine

A randomized controlled trial demonstrated antidepressant activity after 50 mg of intranasal racemic ketamine [15]. Contemporary best-practice recommendations for compounded racemic intranasal ketamine describe approximately 25–50 mg as an initial observed dose, with clinically justified titration toward approximately 50–100 mg according to response and tolerability [11].

This range avoids treating 1 mg/kg intranasally as a universal starting point. A 50 kg patient receiving 50 mg already receives 1.0 mg/kg, whereas the same fixed dose corresponds to 0.5 mg/kg in a 100 kg patient. At 70 kg, 50 mg corresponds to approximately 0.71 mg/kg; at 80 kg, approximately 0.63 mg/kg.

Clinical maintenance experience demonstrates that intranasal dosing can also be divided into predefined portions. A naturalistic maintenance series used 50 mg intranasal administrations at five-minute intervals in patients already established on ketamine treatment [16]. The practical value of staged administration is that subsequent portions remain controllable while earlier portions are still being absorbed.

Intranasal treatment should therefore begin with a predefined total dose rather than open-ended subjective titration. Early subjective weakness does not justify spontaneous escalation because previously administered ketamine has not yet reached full effect.

Intranasal administration also depends on technique. Spray concentration, amount per actuation, spray device, nasal condition, volume per spray, runoff into the throat, and consistency of administration can all influence systemic exposure. Standardization of technique therefore belongs to dosing itself.

The evidence hierarchy among nonintravenous racemic routes is route-specific. Subcutaneous ketamine has coherent randomized short-term dose-ranging evidence, whereas compounded intranasal racemic ketamine has more heterogeneous exposure and dosing data [11]. Structured intranasal home treatment therefore depends particularly on metered formulations, observed initiation, documented individual tolerability, reproducible administration technique, and controlled dispensing.

6.2. Sublingual and Buccal Ketamine

Sublingual and buccal administration requires higher nominal doses because systemic availability is lower and the amount entering systemic circulation depends strongly on administration technique.

Large home-treatment programs have used rapid-dissolve formulations in the several-hundred-milligram range, with protocols specifying mucosal contact time and whether residual material is swallowed or expelled [6,17].

The nominal dose therefore has meaning only together with formulation and technique. Contact time, placement in the mouth, saliva handling, swallowing, and first-pass metabolism determine the resulting exposure. A patient who holds the medication against the oral mucosa for a defined period and then expels the remaining material receives a different pharmacokinetic profile from a patient who swallows the preparation.

Swallowing increases the fraction entering gastrointestinal and hepatic first-pass metabolism and thereby increases relative exposure to norketamine and other metabolites. This changes both the composition and duration of the resulting pharmacological exposure. The swallow-or-expel procedure must therefore remain consistent between sessions when treatment response and recovery time are being compared.

Sublingual or buccal treatment should specify the dose in milligrams, the corresponding milligrams per kilogram, formulation, contact time, and swallow-or-expel procedure. A change in technique can function pharmacologically like a change in dose.

6.3. Subcutaneous Ketamine

Subcutaneous treatment provides the clearest weight-based nonintravenous model. Earlier controlled dose-titration research demonstrated antidepressant activity across subcutaneous doses from 0.1 to 0.5 mg/kg [18].

The phase III Ketamine for Adult Depression Study provides the strongest short-term primary evidence for flexible subcutaneous dosing. Participants received treatment twice weekly for four weeks. The flexible-dose cohort began at 0.5 mg/kg and used response-guided dosing up to 0.9 mg/kg. Remission at the end of week four occurred in 19.6% of ketamine-treated participants compared with 2.0% receiving midazolam, whereas the earlier fixed-dose 0.5 mg/kg cohort did not separate from the active comparator [19].

The large 2026 home-treatment cohort likewise began subcutaneous treatment at 0.5 mg/kg and adjusted later sessions according to therapeutic response, tolerability, and subjective treatment intensity [7]. Contemporary best-practice recommendations therefore use approximately 0.5 mg/kg as the practical starting point and response-guided increments of about 0.1 mg/kg toward approximately 0.9 mg/kg [11].

Subcutaneous administration differs from staged intranasal treatment in one fundamental respect. Once the injection has been given, the administered dose cannot be withdrawn. The full dose is therefore determined before injection.

Subcutaneous home administration also requires standardized equipment and technique. The prescribed concentration, dose, syringe or delivery device, injection-site procedure, skin preparation, injection volume, and sharps disposal method are established before the first home session and reproduced consistently thereafter.

Across all routes, the governing dose principle is the lowest therapeutically effective dose. This is not synonymous with the lowest perceptible dose. A patient can clearly feel ketamine while remaining below an effective therapeutic exposure. Conversely, pronounced dissociation is not required for meaningful therapeutic response.

Therapeutic improvement, duration of benefit, tolerability, route, body weight, and acute treatment intensity determine subsequent dosing. Subjective intensity informs dosing; it does not define therapeutic success.

6.4. Route-Specific Maximum Session Dose

Every home prescription defines a maximum session dose before treatment begins. The maximum is route- and formulation-specific rather than a single absolute milligram ceiling applied across all forms of ketamine.

For compounded intranasal racemic ketamine, the present short-term framework uses approximately 100 mg as the upper end of the contemporary titration range described in best-practice recommendations [11]. A lower individual maximum remains appropriate when therapeutic response is achieved below that level.

For subcutaneous treatment, controlled short-term evidence and contemporary recommendations extend the titration range to approximately 0.9 mg/kg [11,19]. The predetermined individual maximum therefore remains expressed in milligrams per kilogram as well as absolute milligrams.

Sublingual and buccal formulations require higher nominal milligram doses because bioavailability and administration technique differ substantially. Their maximum session dose is consequently defined by the

prescribed formulation, contact method, swallow-or-expel procedure, prior individual response, and treatment-unit design rather than by an absolute cross-route milligram ceiling.

The prescribed maximum is not exceeded during the session because early subjective intensity or apparent weakness does not reliably predict the final exposure.

7. Transition from Observed Initiation to Home Treatment

The transition from initial treatment to home administration is strongest when the patient's individual response is established before the same regimen is reproduced at home.

For ketamine-naive patients and after substantial dose escalation, observed administration establishes the magnitude of cardiovascular response, dissociative intensity, nausea susceptibility, behavioral response, recovery time, and the patient's ability to follow the intended administration technique. Contemporary best-practice recommendations similarly place initial doses and dose increases under direct observation before less-supervised continuation [11].

The home phase then reproduces an already characterized treatment rather than introducing an unknown exposure. Formulation, total dose, administration technique, treatment environment, and monitoring sequence remain consistent with the established response.

This principle is particularly important for compounded intranasal ketamine because absorption and dose delivery depend on device and technique. It is equally useful for subcutaneous treatment, where the full dose becomes committed at the moment of injection.

Previous supervised intravenous, intramuscular, intranasal, sublingual, or subcutaneous ketamine exposure can provide the same type of individualized information when route differences are taken into account.

8. Treatment Rhythm

Ketamine can produce meaningful therapeutic change after a single administration, but repeated treatment substantially increases the proportion of patients who respond.

One established intravenous induction model uses six treatments over twelve days, commonly administered Monday, Wednesday, and Friday across two consecutive weeks. In a study of 77 patients, response increased from 13.0% after the first infusion to 67.5% after the sixth, while remission increased from 7.8% to 48.1% [20].

A randomized dose-frequency study found comparable antidepressant benefit with twice-weekly and three-times-weekly intravenous treatment [21]. The initial treatment rhythm is therefore determined by route and treatment model rather than by one universal schedule.

The phase III subcutaneous KADS protocol used twice-weekly treatment for four weeks [19]. Current route-specific recommendations likewise describe subcutaneous treatment twice weekly during an initial course, while compounded intranasal racemic ketamine can be given once or twice weekly during a short initial trial [11]. Large sublingual home programs have used weekly and more frequent short-course schedules [5–7,17].

The general structure is repeated initial treatment followed by outcome-based reassessment. Four to six sessions provide an appropriate initial treatment window for many protocols, while compounded intranasal treatment can be reassessed after the first two to four administrations [11].

One session therefore often provides insufficient information to judge the full therapeutic value of ketamine. A patient who has not responded substantially after the first treatment can still respond during subsequent administrations. Conversely, treatment should not continue indefinitely merely because the acute experience is strong or subjectively interesting.

Maintenance subsequently moves toward progressively longer intervals as long as therapeutic benefit persists. A patient can move from an initial twice-weekly or weekly phase to every two weeks and then to longer intervals or individual booster sessions.

The appropriate maintenance frequency is the longest interval that preserves the intended therapeutic effect.

9. Preparation on the Treatment Day

Treatment preparation should minimize physiological and practical disruption.

A morning session can occur on an empty stomach. For later treatment, avoiding solid food for approximately two hours and liquids during the final 30 minutes provides a practical preparation interval. These timing rules are established for intranasal esketamine to reduce nausea and vomiting [22] and provide a practical reference for structured nonintravenous treatment.

Fluid timing also has a practical purpose. Large fluid intake during the final one to two hours increases the likelihood of needing to use the bathroom during the acute effect. Ketamine can impair balance, spatial orientation, coordination, and attention. Emptying the bladder immediately before dosing reduces unnecessary movement during the peak while allowing the patient to begin normally hydrated.

The objective is normal hydration rather than dehydration. A large fluid load immediately before dosing is unnecessary.

Normal electrolyte status supports cardiovascular and neuromuscular stability. Potassium, magnesium, sodium, and other electrolytes should remain within the patient's normal physiological range. Potassium is central to cardiac electrical activity, and both insufficient and excessive potassium alter cardiac electrophysiology. Medications affecting potassium handling, including angiotensin-converting-enzyme inhibitors, angiotensin-receptor blockers, potassium-sparing diuretics, and impaired renal function, must therefore be considered when additional potassium is used [23].

An electrolyte drink can be consumed sufficiently before the final fluid interval when appropriate, particularly following fasting, heavy sweating, vomiting, diarrhea, or another source of fluid loss.

Preparation also includes the practical environment. Medication, blood-pressure monitor, timer, emesis bag, prescribed antiemetic, rescue medication when included, music, eye mask when used, drinking water for recovery, and written instructions should all be ready before the first dose.

10. Concomitant Medications and Physiological Modifiers

The current medication and substance profile belongs to the treatment assessment because other compounds can alter the same physiological variables affected by ketamine.

Alcohol increases sedation, dizziness, impaired coordination, and impaired judgment and is therefore excluded from the treatment day.

Benzodiazepines increase sedation and can attenuate antidepressant response at higher concomitant doses. In one clinical analysis, benzodiazepine exposure above approximately 8 mg/day diazepam equivalents distinguished a group with weaker antidepressant response to ketamine, including significantly worse outcomes at days three and seven [24]. Regular benzodiazepine therapy remains clinically managed rather than being abruptly altered for an individual session.

Opioids and other central nervous system depressants increase sedation and respiratory burden. Prescription stimulants, large caffeine intake, and other sympathomimetic substances can raise resting heart rate, blood pressure, and sympathetic activation and therefore alter the patient's baseline before ketamine.

Regular antihypertensive therapy must be distinguished from ketamine rescue medication. Ordinary cardiovascular medication determines baseline physiology. Rescue medication addresses an unusually persistent treatment-associated increase. Both pharmacological effects must be considered together because the rescue drug can remain active after the acute sympathomimetic ketamine effect declines.

Antidepressants are frequently continued during ketamine treatment. Their presence remains relevant because individual agents can influence blood pressure, heart rate, sedation, gastrointestinal function, and other treatment variables.

The same principle applies to sleep medication, sedating antihistamines, cannabis, psychedelics, stimulants, and other psychoactive substances. Unplanned combinations reduce reproducibility by introducing additional pharmacological variables.

10.1. GLP-1, GIP, and Related Metabolic Medication

GLP-1 receptor agonists, dual GLP-1/GIP compounds, and related metabolic medications are increasingly relevant to ketamine treatment.

These agents slow gastric emptying and gastrointestinal motility [25], modestly increase resting heart rate, and commonly produce nausea during initiation or dose escalation. A 2026 meta-analysis found an average increase in resting heart rate of approximately 3.5 beats per minute across GLP-1-based therapies, with variation among individual compounds [26].

The treatment record should therefore contain the measured pre-session heart rate together with the patient's established resting range under the current medication regimen. The current metabolic medication, dose, recent dose changes, nausea, fullness, vomiting, constipation, and hydration status define the physiological context in which the ketamine session begins.

This matters particularly when interpreting a heart-rate threshold such as 100 beats per minute. A patient whose established resting rate under current treatment is 90–95 beats per minute has a different baseline from a patient whose usual resting pulse is 60 and who unexpectedly presents at 95.

The gastrointestinal effect is equally relevant. Delayed gastric emptying and medication-related nausea increase the importance of last-meal size, current fullness, antiemetic preparation, and treatment-day gastrointestinal symptoms.

10.2. Off-Label Peptides and Hormone-Like Compounds

The same principle applies to off-label peptides and hormone-like compounds.

"Peptide" does not define one pharmacological action. Individual compounds can alter sympathetic activity, metabolic rate, resting heart rate, blood pressure, thermoregulation, gastrointestinal function, appetite, hydration, or electrolyte balance.

Their relevance is therefore determined by actual physiological action. A compound that raises metabolic rate or resting pulse changes the cardiovascular baseline against which ketamine is interpreted. A compound that alters gastrointestinal function changes the baseline nausea and absorption environment. A compound affecting fluid balance changes hydration and electrolyte status.

Recent initiation or dose escalation deserves particular attention because the patient's established physiological baseline may be changing.

11. Adjunctive Pre-Session Preparation

Mild non-sedating adjuncts can be used when a patient benefits from reduced pre-session tension. L-theanine reaches peak plasma concentration at approximately 0.8 hours after oral administration [27], and a randomized placebo-controlled crossover study using 200 mg demonstrated modulation of acute stress-related measures [28]. Administration approximately one to two hours before ketamine therefore corresponds to its pharmacokinetic profile.

Taurine influences autonomic and cardiovascular regulation and has produced modest average reductions in resting blood pressure in human meta-analysis [29]. Magnesium supports normal neuronal, muscular, and cardiac physiology and can form part of ordinary nutritional and electrolyte preparation.

These adjuncts remain secondary to the principal determinants of treatment: dose, route, physiological state, medication profile, set, setting, and previous individual response.

New supplements should not be introduced on the day of the first ketamine administration or simultaneously with a substantial ketamine dose increase. Establishing the initial ketamine response under otherwise familiar physiological conditions allows cardiovascular response, nausea, dissociative intensity, behavioral response, and recovery time to be attributed to the ketamine session itself rather than to several newly introduced variables.

Once the individual ketamine baseline is established, an adjunct can be added separately when it serves a defined purpose. Reproducibility is strongest when one material treatment variable is changed at a time.

12. Set and Setting

The psychological state preceding treatment should be understood in relation to the therapeutic objective. Depression, anxiety, trauma-related distress, existential fear, grief, emotional tension, and difficult thoughts may themselves constitute the material being treated.

Preparation therefore reduces unnecessary additional activation rather than requiring emotional normality. Several minutes of quiet sitting or lying down, slow rhythmic breathing, closed eyes, a brief relaxation practice, and calming music create a more regulated transition into treatment.

The physical environment should be familiar, quiet, comfortable, safe, and free from unnecessary interruption. Calls, messages, visitors, work obligations, appointments, and other external demands should be removed from the treatment period. Everything required during the session should already be within reach.

The phone should preferably be switched off or placed in Do Not Disturb mode. The patient should not be expected to answer messages, navigate social media, perform work, or make practical decisions during the acute state.

A reclining or lying position is appropriate when substantial dissociation is expected. Showering, bathing, cooking, unnecessary use of stairs, standing at heights, and use of potentially dangerous tools wait until normal coordination has returned.

A randomized controlled study of a combined intervention incorporating mindfulness, music, and visual occlusion found comparable antidepressant improvement to ketamine alone while producing a more immersive, focused, and emotionally meaningful acute experience for many participants [30].

Music can therefore be selected deliberately according to therapeutic purpose and individual preference. Classical, neoclassical, ambient, instrumental, relaxation-oriented, and specifically curated ketamine- or psychedelic-therapy playlists can all provide a useful treatment environment.

A playlist can begin quietly, increase gradually in emotional intensity, and return toward calmer material during recovery. Music should be selected before dosing so the patient does not need to search, skip tracks, or manipulate a phone after dissociation develops.

An eye mask can reduce external visual stimulation and support inward attention. It remains optional and can be removed whenever the patient prefers greater orientation to the external environment.

13. The Sober Support Person

A patient can be entirely capable of measuring baseline blood pressure, preparing medication, and beginning treatment independently. That capacity can change rapidly once ketamine becomes active. Attention, fine coordination, working memory, time perception, and judgment become less reliable as dissociation increases.

A sober trusted person therefore becomes increasingly important with stronger treatment intensity.

The support person's role is operational rather than diagnostic. The person tracks time, performs scheduled measurements, records values, withholds later staged doses when a predefined threshold is reached, follows the written rescue protocol, provides calm reassurance, reminds the patient to breathe slowly during transient anxiety, observes changes in behavior and orientation, and helps maintain the prepared environment.

The largest published subcutaneous home-treatment program required a trusted adult peer monitor during every home session [7]. This demonstrates that practical home observation can be performed by a nonmedical support person when the relevant decisions have already been converted into objective instructions.

The value of such support rises with treatment intensity. A patient receiving a mild dose can remain capable of self-monitoring throughout much of the session. A patient entering pronounced dissociation may no longer be able to apply a blood-pressure cuff correctly, read a timer, or decide whether another nasal portion should be taken.

The support person is therefore particularly valuable when stronger dissociation, staged administration, cardiovascular rescue, or psychological escalation criteria form part of the treatment plan.

14. Previous Ketamine Exposure and Individual Response

Previous ketamine treatment provides direct individual information about the patient's response.

A person who has already completed supervised sessions has generated an observed cardiovascular and experiential profile. Blood-pressure increase, heart-rate response, nausea tendency, dissociative intensity, behavioral response, and recovery time become known variables.

The large home subcutaneous program explicitly incorporated prior intravenous or intramuscular dose, session intensity, therapeutic response, and side-effect profile when selecting the initial home dose [7].

A ketamine-naive patient therefore begins with an unknown individual acute response, while a previously treated patient begins with documented response information.

Repeated uncomplicated sessions progressively refine the individualized treatment profile. If a patient repeatedly experiences a predictable rise in blood pressure, a consistent degree of dissociation, minimal nausea, an organized psychological response, and a similar recovery time, subsequent sessions can be interpreted against that established pattern.

The value lies in direct observation rather than an assumption that cardiovascular or psychological tolerance develops. The patient's actual response has been measured.

15. Pre-Session Physiological Assessment

Blood pressure and heart rate provide the principal objective pre-session variables for home treatment.

A 2026 interdisciplinary consensus identifies persistent pre-treatment systolic blood pressure above 150 mmHg, diastolic pressure above 100 mmHg, and heart rate above 100 beats per minute as clinically relevant physiological abnormalities [31]. The large 2026 home subcutaneous program likewise required blood pressure below 150/100 mmHg and heart rate below 100 beats per minute before treatment began [7].

Blood pressure should be measured after several minutes of quiet rest. An initial measurement at or above 150/100 mmHg leads to another five to ten minutes of rest followed by repeat measurement. Persistent elevation at or above this level means the session does not begin.

This is distinct from post-dose rescue. Before ketamine has been administered, there is no ketamine-induced hypertensive response to treat. The correct pre-session action is simply not to administer ketamine when the baseline remains above the predefined limit.

Heart rate is interpreted against the patient's established resting range. A stable pulse of 95 beats per minute in a patient whose current medication regimen routinely produces a resting rate between 90 and 95 carries different information from an abrupt increase to 95 in a patient whose normal resting rate is 60.

The treatment record should therefore contain both the measured heart rate and the patient's established resting range under the current medication regimen.

Baseline measurement also provides the reference against which later changes are interpreted. A rise from 118/74 to 155/92 has a different physiological context from a rise from 148/96 to 155/100 even though the final values are similar.

16. Standardized Administration and Timing

The same nominal dose produces more reproducible exposure when administration technique remains consistent.

Intranasal documentation should contain formulation concentration, milligrams per actuation, number and timing of sprays, total dose, first-dose time, and last-dose time.

Sublingual or buccal documentation should contain formulation, total dose, dose per kilogram, mucosal contact time, placement in the mouth, and whether residual material is swallowed or expelled.

Subcutaneous documentation should contain concentration, total dose, dose per kilogram, injection volume, injection site, device or syringe, skin-preparation procedure, injection time, and disposal of used sharps.

Intranasal administration offers a particular practical advantage because the total dose can be divided into predefined portions. Clinical intranasal protocols have used five-minute intervals between administrations [16]. This limits nasal volume at one time, creates gradual delivery, and allows subsequent portions to be withheld.

Each preceding portion continues to absorb while later portions are administered. A mild effect at five or ten minutes therefore does not predict the final intensity of the planned total dose. The maximum planned dose remains fixed once the session begins.

The time of the first dose and the time of the last dose should both be recorded.

This distinction becomes particularly important when administration extends over 20 or 30 minutes. A measurement 40 minutes after the first dose can occur only 10 or 20 minutes after the last dose. Once dosing is complete, post-dose monitoring is therefore pharmacologically more meaningful when anchored primarily to the final administration.

17. Route-Specific Monitoring

Monitoring follows the expected pharmacokinetic course of the selected route.

Intranasal ketamine develops relatively rapidly and can be administered in stages. A practical sequence includes baseline measurement, observation during dose build-up when appropriate, and post-dose measurements around 20, 40, and 60 minutes after the last administration, with a later measurement around 90 minutes when significant effects remain. An intranasal ketamine research protocol used cardiovascular assessments at 15, 30, 45, 60, 90, and 120 minutes [32].

During staged intranasal dosing, blood pressure can also be measured before subsequent portions when treatment intensity or previous cardiovascular response makes this useful. This creates a practical hold point while part of the planned dose remains unadministered.

Sublingual or buccal ketamine rises more slowly. Its median Tmax of approximately 45 minutes [13] supports a first post-dose assessment around 30–45 minutes, followed by reassessment around 60 minutes and later when substantial effects remain.

Subcutaneous ketamine is absorbed rapidly. Pharmacokinetic modelling demonstrates a short absorption half-life [14], so monitoring concentrates on the early acute period and continues until cardiovascular values and functional recovery move clearly toward baseline.

The objective is targeted observation of the period in which clinically relevant physiological changes are expected.

Monitoring can become simpler after repeated sessions establish a consistent individual response pattern. Patient-specific data progressively replace unnecessary repetition of measurements that have ceased to add useful information.

18. Cardiovascular Response and Rescue

18.1. Physiological Response and Persistence Criterion

Temporary increases in systolic pressure, diastolic pressure, and heart rate are characteristic sympathomimetic effects of ketamine. Home monitoring therefore distinguishes an expected transient rise from a persistent severe elevation.

A moderate increase during the acute effect is observed rather than automatically treated.

During staged intranasal dosing, a marked increase first leads to withholding remaining ketamine portions and repeating blood pressure after rest. This is the principal advantage of staged dosing: part of the planned exposure can still be prevented.

Once the complete dose has already been administered, the relevant task is observation of the subsequent trajectory.

A systolic value of 180 mmHg or a diastolic value of 110 mmHg provides the severe-elevation threshold because ketamine treatment protocols already use these values. An intranasal ketamine research protocol specified treatment readiness for values above 180/110 mmHg when they did not resolve spontaneously within a short period and measured cardiovascular values at 15-minute intervals [32].

The present framework converts this clinical principle into a home persistence criterion. Because the source protocol uses short repeated measurement intervals and distinguishes spontaneous resolution from sustained elevation, persistence is operationalized as approximately 15–20 minutes across repeated measurements.

When the first reading reaches or exceeds 180 systolic or 110 diastolic, remaining staged ketamine is withheld and the patient rests quietly for approximately five minutes. Blood pressure is then repeated. If the value remains at or above the threshold, rest continues and another measurement follows approximately ten to fifteen minutes later. Persistence across these measurements activates the predetermined rescue pathway.

The trigger therefore consists of three variables: magnitude, repeated confirmation, and persistence. This distinguishes a short sympathetic peak from sustained severe elevation and converts the decision into an objective sequence.

18.2. Pharmacological Blood-Pressure Rescue

An operational ketamine-assisted psychotherapy study protocol specifies oral clonidine 0.1 mg when blood pressure exceeds 180/110 mmHg, followed by reassessment, providing a concrete clinical model for pharmacological management of marked ketamine-associated hypertension [33].

Clonidine directly addresses sympathetic activation through reduction of central sympathetic outflow.

When clonidine forms part of an individual home plan, the prescriber defines the rescue medication, single dose, reassessment interval, any permitted repeat dose, and the endpoint of the home pathway before the ketamine session begins.

The patient therefore does not choose an antihypertensive medication while dissociated and does not calculate a dose during the acute treatment state.

The purpose of rescue is not to force blood pressure rapidly back to baseline. It is to address an unusually persistent severe ketamine-associated elevation after spontaneous resolution has failed to occur.

A major new neurological deficit, substantial acute chest symptoms, pronounced breathing difficulty, or marked alteration of consciousness supersedes the timed numerical pathway because these findings represent a different clinical state from an isolated ketamine-associated blood-pressure rise.

19. Psychological and Behavioral Escalation Criteria

Ketamine can produce intense perceptual alteration, temporary disorientation, fear, crying, emotional release, unusual thoughts, depersonalization, derealization, and profound dissociation. These effects can remain fully compatible with an organized ketamine experience.

The role of the support person is therefore not to terminate a session merely because the experience becomes emotionally intense. Anxiety, transient fear, crying, or temporary confusion can first be managed through calm reassurance, reduction of external stimulation, comfortable positioning, and slow breathing.

The relevant distinction is between an intense but organized ketamine state and a psychological or behavioral state that is progressively losing safety and organization.

During staged intranasal administration, remaining portions are withheld when psychological distress becomes progressively more severe rather than stabilizing, when the patient repeatedly requests that no further dose be administered, or when behavior becomes sufficiently disorganized that continued dosing is no longer compatible with the predefined treatment plan.

Acute psychotic or manic behavior, delirium-like confusion extending beyond the expected dissociative state, severe agitation creating physical danger, suicidal behavior, violent behavior, inability to maintain basic physical safety, or a marked and unexpected deterioration in responsiveness activates the predefined escalation pathway [7,11].

After subcutaneous injection or completion of a mucosal dose, the already administered ketamine cannot pharmacologically be withdrawn. At that point the objective changes from continuation of the therapeutic session to protection of physical safety, reduction of stimulation, observation, and escalation to medical assistance when the behavioral state exceeds the boundaries of the home protocol.

The psychological pathway therefore follows the same structural principle as the cardiovascular pathway: ordinary expected treatment phenomena are distinguished from a persistent or qualitatively different state that requires a change in management.

20. Nausea and Gastrointestinal Management

Nausea is predictable and can be prepared for in advance.

Ondansetron is particularly useful because it controls nausea without materially increasing sedation. The 2026 subcutaneous home-treatment cohort supplied ondansetron 8 mg as an orally disintegrating tablet to be taken approximately one hour before ketamine unless contraindicated [7].

Patients with a consistent history of ketamine-associated nausea can therefore use prophylactic ondansetron according to the prescribed treatment plan. Patients who experience nausea only occasionally can keep the prescribed antiemetic immediately available for rescue.

An emesis bag or container should be within reach before dosing so that pronounced dissociation does not require unnecessary standing or movement.

The growing prevalence of GLP-1/GIP treatment increases the importance of gastrointestinal preparation because nausea, delayed gastric emptying, fullness, vomiting, or constipation can already be present before ketamine is administered.

Last-meal size, current gastrointestinal symptoms, GLP-1/GIP dose changes, previous ketamine-associated nausea, and fasting interval should therefore be considered together.

21. The Home Treatment and Rescue Kit

The home kit should remain deliberately small.

A validated automatic upper-arm blood-pressure monitor, timer, individually prescribed blood-pressure rescue medication when included in the treatment plan, prescribed antiemetic, emesis bag, and concise written protocol cover the central practical requirements of ordinary home treatment.

Water for the recovery period can also be prepared before the session so the patient does not need to leave the treatment environment while coordination remains impaired.

The purpose of the kit is immediate availability of the few interventions that can realistically become necessary during a session.

Home treatment becomes more reliable through preparation and predefined decisions, not through accumulation of hospital equipment.

The written protocol should contain the patient's established baseline, pre-session blood-pressure criterion, severe post-dose threshold, timing of repeat measurements, rescue medication and dose when prescribed, psychological and behavioral escalation criteria, reassessment intervals, and endpoint of the home pathway.

22. Measuring Therapeutic Effect

Acute ketamine intensity is not an adequate measure of treatment success. The actual therapeutic target must be measured.

For depression, anxiety, and post-traumatic stress, the PHQ-9, GAD-7, and PCL-5 provide established longitudinal measures and have already been used successfully in large home-treatment cohorts [5–7].

Baseline measurement followed by reassessment during the treatment series creates a quantitative record of cumulative change. Measurement before the initial course and again after selected sessions such as the second, fourth, and sixth treatments provides a practical structure.

A broader therapeutic scope requires broader outcome measures.

Existential anxiety, fear of mortality, loss of meaning, and psychospiritual distress are not adequately represented by depression scores alone. The 2026 intranasal study in advanced cancer used the Death and Dying Distress Scale together with the McGill Quality of Life Questionnaire and specifically quantified existential well-being [2]. Large improvements occurred in these domains, while their changes were not significantly correlated with the change in depression severity.

Outcome measurement should therefore match the actual therapeutic objective.

A treatment directed primarily toward depression can use depression measures. A treatment addressing existential distress can incorporate death-and-dying distress, existential well-being, quality of life, demoralization, and structured psychotherapeutic evaluation.

Emotional processing, reduced fear of mortality, increased acceptance, changes in perspective, and changes in the relationship to meaning can therefore be evaluated alongside conventional symptom measures when they constitute the actual purpose of treatment.

Therapeutic outcome directly guides dose and frequency.

A patient whose symptoms, functioning, or existential distress improve substantially does not need a stronger acute experience simply because the session felt comparatively mild.

Repeated intense sessions without meaningful subsequent change do not constitute therapeutic success.

23. Nonresponse and Reassessment

A single treatment does not define the full response trajectory.

Repeated-treatment data demonstrate that response accumulates across sessions [20].

Reassessment should therefore occur according to route and treatment rhythm. Contemporary intranasal recommendations use early evaluation after approximately two to four administrations, while broader short-course ketamine protocols commonly reassess after approximately four to six treatments [11].

At reassessment, the clinically relevant questions are whether exposure was sufficient, whether technique remained consistent, whether the chosen route was appropriate, whether the therapeutic target changed, and whether objective outcome measures demonstrate meaningful benefit.

A sublingual treatment that was inconsistently held in the mouth, an intranasal spray with substantial runoff, or a subcutaneous dose that remained below the therapeutic range should not be interpreted identically to a consistently delivered treatment series.

Treatment frequency and dose then follow the observed response rather than a predetermined indefinite schedule.

24. Maintenance and Long-Term Observation

Following successful initial treatment, maintenance moves toward progressively longer intervals.

The objective is the lowest treatment frequency that preserves the desired therapeutic effect.

A patient can move from an initial twice-weekly or weekly treatment rhythm toward every two weeks, monthly treatment, or individual booster sessions according to the duration of benefit.

The timing should be guided by the patient's actual return of symptoms or decline in therapeutic benefit rather than by continuation of induction frequency indefinitely.

Long-term treatment also includes simple observation of urinary symptoms.

High-frequency nonmedical ketamine exposure is associated with urinary toxicity, making urinary frequency, burning, pain, hematuria, and bladder or lower abdominal discomfort relevant longitudinal variables.

A 2025 systematic review of psychiatric ketamine treatment reported urinary symptoms across studies ranging from 0 to 24.5%, predominantly mild or moderate [34].

Within a continuing maintenance program, the present framework uses a brief monthly urinary-symptom check as a practical longitudinal interval. This creates a regular record of frequency, dysuria, pain, hematuria, and

bladder or lower abdominal discomfort without turning each treatment session into an extensive medical assessment.

25. Recovery

Recovery is determined by actual function rather than by a fixed number of minutes.

The acute treatment period ends when orientation, communication, balance, coordination, and dissociation return sufficiently toward baseline and cardiovascular measurements show a stable or declining trajectory.

The patient should be able to communicate normally, understand the environment, sit and stand without marked disequilibrium, and move without substantial dizziness before ordinary activity resumes.

Blood pressure and heart rate should show a stable or declining pattern rather than continuing to rise.

Normal fluid intake resumes once substantial nausea and dissociation have subsided. A light meal can follow according to appetite.

For sublingual or buccal treatment, recovery time should be interpreted together with the swallow-or-expel procedure because swallowing increases gastrointestinal and first-pass metabolite exposure and can alter the duration of the overall pharmacological profile.

Recovery can take longer after stronger treatment, higher exposure, a larger swallowed fraction of a mucosal dose, or a route producing prolonged absorption. Individual treatment records make this duration increasingly predictable over time.

26. Driving, Machinery, and Activities Requiring Full Coordination

The principal psychoactive effects usually resolve within hours, while subtler after-effects can persist through the remainder of the day and into the following day.

Fatigue, mild dizziness, altered concentration, slower reaction time, residual disequilibrium, and emotional sensitivity can remain after the central dissociative state has ended.

Intranasal esketamine instructions prohibit driving and operation of machinery until the following day after restful sleep [22].

The same practical standard applies to home racemic ketamine.

Driving, dangerous machinery, work at height, and activities requiring unimpaired coordination and reaction remain deferred for the remainder of the treatment day and until the following day after restorative sleep and return of normal function.

This does not mean that the intense ketamine effect itself lasts until the next day. It means that subtle residual impairment can outlast the principal psychoactive state.

If residual impairment remains after sleep, driving or other high-coordination activity waits until normal function has returned.

27. Emotional Sensitivity and the Post-Treatment Period

The emotional recovery period deserves deliberate protection.

Ketamine can be followed by increased emotional openness and sensitivity. For several hours, and sometimes into the following day, a patient can be more receptive to environmental and interpersonal input.

This period can be therapeutically valuable, particularly when the session involves emotional processing, existential work, grief, fear of mortality, or personally significant psychological material.

Heavy traffic, turbulent surroundings, large crowds, conflict-heavy conversations, stressful appointments, and excessive digital stimulation can therefore be reduced during this period.

Rest, restorative sleep, calm music, quiet surroundings, time for reflection, journaling when desired, and gentle activity after coordination has returned provide an appropriate transition from the treatment state.

The post-treatment period therefore forms part of the therapeutic process in patients for whom emotional integration and changes in perspective are central treatment aims.

28. Session Documentation

Each session should generate a concise structured record.

The record should contain the date, body weight, administration route, formulation, total dose in milligrams, dose in milligrams per kilogram, predefined maximum session dose, first-dose time, last-dose time, baseline blood pressure, baseline heart rate, relevant measurements during treatment, maximum blood pressure, maximum heart rate, approximate subjective onset, approximate peak, psychological or behavioral escalation when present, nausea or vomiting, other significant acute effects, rescue intervention when used, recovery time, and therapeutic response over subsequent days.

For intranasal treatment, the number of actuations, milligrams per actuation, dosing interval, and whether the planned dose was completed or stopped early should be recorded.

For sublingual or buccal treatment, mucosal contact time and whether residual material was swallowed or expelled should be recorded.

For subcutaneous treatment, concentration, injection volume, injection site, device, and exact mg/kg dose should be documented.

Repeated documentation creates an individualized dose-response profile, cardiovascular profile, psychological-response profile, tolerability profile, and therapeutic-response profile.

This progressively shifts treatment from population averages toward observed individual data.

A patient whose blood pressure repeatedly rises from approximately 120/75 mmHg to 145/90 mmHg has established an individual cardiovascular pattern. A later measurement far outside that trajectory becomes more informative because the prior response is known.

A patient who consistently experiences therapeutic benefit for ten days after a particular dose likewise provides direct information for maintenance scheduling.

Documentation therefore serves physiological management, psychological characterization, and therapeutic optimization.

29. Discussion

At-home racemic ketamine treatment is already a clinical reality across several administration routes. Large home cohorts demonstrate that structured treatment can combine prescriber-directed dosing, home physiological measurements, standardized pharmaceutical units, validated outcome measures, and nonmedical support persons while maintaining a low incidence of medically serious complications [5–7].

The next stage is standardization.

Pharmaceutical standardization moves dose calculation out of the psychoactive period. Patient-specific compounding allows the clinician and pharmacy to define the treatment unit before the patient begins. Controlled dispensing, metered formulations, secure storage, predefined maximum session exposure, and predetermined refill intervals keep prescribed treatment stable over time [11].

Route specificity then determines dose and timing. Intranasal, sublingual or buccal, and subcutaneous ketamine differ in absorption, systemic availability, metabolism, dose, and the ability to interrupt further exposure. A common home architecture becomes scientifically coherent when these route-specific differences remain explicit.

The strength and type of evidence also differ by route. Subcutaneous racemic ketamine has the clearest randomized short-term dose-ranging evidence among the nonintravenous racemic routes, while compounded intranasal treatment is characterized by greater variability in formulation and exposure [11,19]. This difference directly determines the structure of the home framework: intranasal treatment depends particularly on metered delivery, observed initiation, documented individual response, and controlled dispensing.

A universal absolute milligram ceiling would ignore these route differences. The appropriate maximum is therefore predefined separately for each route and formulation. Intranasal treatment can use a fixed milligram ceiling, subcutaneous treatment is naturally bounded in mg/kg, and sublingual or buccal treatment requires limits tied to formulation and mucosal technique.

Body weight further improves interpretation. The same fixed intranasal dose can represent a twofold mg/kg difference between patients of substantially different body size. Recording both total milligrams and milligrams per kilogram therefore preserves the simplicity of fixed pharmaceutical units while adding an important normalization variable.

Observed initiation provides the bridge into home treatment. Initial administration or a substantial dose increase establishes the patient's cardiovascular response, nausea susceptibility, dissociative intensity, behavioral response, recovery time, and ability to use the prescribed administration technique. Home treatment then reproduces a characterized exposure rather than introducing an unknown one.

Physiological simplicity converts monitoring into action. Blood pressure and heart rate can be measured easily and tied to predefined decisions. Persistent pre-session blood pressure at or above 150/100 mmHg prevents treatment from beginning. During treatment, severe elevation around 180/110 mmHg is interpreted through repeated measurement and persistence rather than through a single isolated reading.

The persistence criterion is central because transient sympathetic peaks are part of ketamine pharmacology. Published intranasal protocols distinguish spontaneously resolving severe numerical elevations from sustained hypertension through repeated measurements over short intervals [32]. The 15–20-minute rule translates that clinical principle into a home sequence defined by magnitude, confirmation, and time.

The psychological pathway follows the same architecture. Intense fear, emotional release, dissociation, or temporary disorientation can remain within the expected treatment state and are first managed by reassurance, reduction of stimulation, and environmental support. Acute mania, psychotic behavior, dangerous agitation, suicidal behavior, or loss of basic physical safety represent qualitatively different states and activate the predetermined escalation pathway.

The same logic governs rescue medication. The patient does not choose an antihypertensive agent during dissociation. When clonidine forms part of the prescribed plan, it is selected beforehand, the dose is predetermined, and reassessment follows a written protocol. Operational ketamine protocols already use oral clonidine 0.1 mg for marked treatment-associated hypertension [33].

Nausea is managed in the same manner. Ondansetron or another prescribed antiemetic is prepared before the session and used according to a predetermined plan.

The home kit therefore remains deliberately small. Blood-pressure measurement, timing, antiemetic treatment, predetermined cardiovascular rescue, psychological escalation criteria, and clear written instructions address the practical variables that can realistically be managed in the home without recreating a hospital environment.

Set and setting extend standardization beyond pharmacology. A quiet environment, protected time, preselected music, comfortable positioning, optional visual occlusion, and an appropriate sober support person reduce environmental variability and eliminate avoidable decisions during the psychoactive period.

Modern medication use further strengthens the need for individualized baselines. GLP-1/GIP medications, stimulants, metabolic drugs, peptides, and hormone-like compounds can alter resting pulse, blood pressure, gastrointestinal function, appetite, fluid balance, and nausea. A measured value becomes clinically meaningful when interpreted against the individual's established baseline under the current medication regimen.

The same experimental logic applies to adjuncts. Introducing a new supplement during the first ketamine session obscures attribution of cardiovascular, gastrointestinal, and psychological effects. Establishing ketamine alone under otherwise familiar conditions creates a cleaner individual baseline, after which additional variables can be introduced separately.

Previous ketamine treatment adds another layer of individualization. Once several sessions have been documented, the patient's actual cardiovascular response, nausea tendency, dissociation intensity, psychological response, recovery time, and duration of therapeutic benefit become known variables.

The distinction between first dose and last dose is particularly important for staged intranasal administration. When dosing extends over 20 or 30 minutes, the final portion is pharmacologically much younger than the first.

Monitoring anchored only to the beginning of the session can therefore misrepresent the period of greatest combined exposure. Recording both times creates a more accurate physiological timeline.

For sublingual and buccal administration, an analogous principle applies to technique. Swallowing a larger fraction increases first-pass metabolism and metabolite exposure, changing the temporal profile of the session. Contact time and swallow-or-expel procedure therefore belong to the pharmacological record rather than being treated as minor procedural details.

Treatment frequency also becomes increasingly individualized. An initial repeated-treatment phase establishes response; maintenance then expands intervals according to duration of benefit. The goal is not continuation of an induction schedule indefinitely but preservation of therapeutic effect with the lowest necessary frequency.

Finally, home treatment remains a therapeutic process rather than a monitoring exercise. Depression, anxiety, trauma-related distress, existential anxiety, mortality-related fear, quality of life, loss of meaning, emotional processing, and functional improvement require outcome measures matched to the actual purpose of treatment.

The strongest home protocol is therefore not the one containing the most equipment. It is the one in which the fewest clinically important decisions remain unresolved once ketamine alters perception and judgment.

30. Conclusion

At-home racemic ketamine treatment can be organized as a reproducible therapeutic model across intranasal, sublingual or buccal, and subcutaneous administration. Route determines dose, absorption, timing, metabolite profile, maximum session exposure, and opportunities for staged administration, while the overall treatment architecture remains consistent.

A robust home framework begins with appropriate patient selection, explicit at-home exclusion criteria, observed characterization of the initial response, a predefined therapeutic dose, a route-specific maximum session dose, standardized pharmaceutical preparation, controlled dispensing, and documentation of both total milligrams and milligrams per kilogram. Medications, metabolic agents, peptides, hydration, electrolyte status, set, setting, and support are addressed before treatment begins.

Blood pressure and heart rate provide objective pre-session criteria. Route-specific monitoring follows the expected pharmacokinetic course. Staged intranasal administration permits later portions to be withheld. Severe treatment-associated hypertension is defined through magnitude, repeated confirmation, and persistence, distinguishing a transient sympathetic peak from sustained marked elevation. A prescriber-defined rescue medication then follows a written protocol.

The psychological framework follows the same logic. Expected dissociation, fear, emotional release, and temporary disorientation are distinguished from acute mania, psychotic behavior, delirium-like disorganization, dangerous agitation, suicidal behavior, or loss of basic physical safety. The latter activate a predefined escalation pathway rather than leaving the support person to improvise during the session.

Antiemetic preparation addresses predictable treatment-associated nausea. Sublingual and buccal treatment additionally requires consistent documentation of mucosal contact time and swallowing because first-pass metabolism and norketamine exposure alter the resulting pharmacological profile and recovery period.

The treatment environment is prepared in advance. Music, visual reduction, comfortable positioning, absence of interruption, and a sober support person when treatment intensity warrants one reduce practical and psychological variability during the acute state.

New supplements are not introduced during the first ketamine administration or simultaneously with a substantial dose increase. Establishing the initial ketamine response under familiar physiological conditions creates a clean individual baseline against which later changes can be interpreted.

Previous ketamine exposure and repeated documentation progressively transform treatment from population-based estimation toward individual response data. Blood-pressure response, nausea, psychological response, dissociation, recovery time, therapeutic duration, and optimal maintenance interval become increasingly predictable.

Recovery is defined by return of orientation, communication, balance, coordination, and a stable physiological trajectory. Driving and activities requiring full coordination remain deferred until the following day after restorative sleep and normal functional recovery. The post-treatment period is deliberately kept relatively calm when emotional sensitivity or openness remains.

Therapeutic outcome is measured according to the actual purpose of treatment. Depression, anxiety, trauma-related symptoms, existential distress, fear of mortality, quality of life, and meaning-related suffering each require measures appropriate to their domain. Treatment frequency subsequently follows observed benefit, while repeated documentation builds an increasingly precise individual profile of dose, physiological response, psychological response, subjective effect, tolerability, and therapeutic outcome.

The governing principle is straightforward: every relevant decision that can be made before ketamine takes effect should be made before ketamine takes effect. This converts home ketamine administration from an improvised act into a structured, reproducible therapeutic process.

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The author confirms sole responsibility for the conception, theoretical development, literature synthesis, writing, and revision of this manuscript.

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