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Advances in Anesthetic Drugs: Enhancing Recovery

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Two Patients: Same Surgery. Same Awakening. Different Recovery.

Imagine two patients undergoing the same surgical procedure.

•Both regain consciousness within 10 minutes after surgery.

But there is a difference:

Patient A

•Minimal pain and nausea
•Early mobilization and oral intake
•Clear cognition and rapid return to daily activities

Patient B

•Significant pain and postoperative nausea
•Delayed mobilization and oral intake
•Fatigue and impaired functional recovery

A Question for All of Us:

Have these two patients experienced equally successful anesthesia?

How quickly does the patient recover—not merely wake up?

Complication or adverse outcome	Reported frequency	Evidence
Postoperative nausea and vomiting	**30%** overall; up to **80%** in high-risk patients	Fourth Consensus Guidelines, 2020
Moderate-to-severe pain after discharge	**31–58%**	Systematic review, 27 studies, 22,108 patients, 2023
Postoperative pulmonary complications	**12.6%** after major elective abdominal surgery	Prospective multicenter study, 1,542 patients, 2023
Postoperative delirium	**18%**	Meta-analysis, 8,382 patients, 2023
Postoperative ileus	**9%** after colorectal cancer surgery	Meta-analysis, 30 studies, 73,433 patients, 2026
Chronic postsurgical pain after same-day surgery	**12%** at 90 days	Prospective cohort, 2,054 higher-risk adults, 2024

Emergence, Extubation and Functional Recovery Are Different

Emergence: return of consciousness and responsiveness.

Extubation: readiness for safe removal of the tracheal tube.

Functional recovery: adequate cognitive, respiratory and motor function to resume safe activity.

A patient can be awake yet not be ready for extubation—or extubated yet not be ready for discharge.

The endpoint should be safe functional recovery, not simply the earliest possible emergence.

Do not use “awake,” “extubated” and “recovered” interchangeably.

Recovery Is a Multidimensional Outcome

Predictable emergence and appropriate responsiveness

Restoration of respiratory and neuromuscular function

Effective pain control with minimal adverse effects

Prevention of postoperative nausea and vomiting (PONV)

Hemodynamic stability and safe return to usual function

Recovery begins before induction and continues beyond extubation.

ERAS depends on coordinated preoperative, intraoperative and postoperative care—not one isolated intervention.

Choose a strategy that restores function—completely and safely.

Why haven't we had a new formulation of anesthetic drugs in recent decades?



Challenges in Developing an Ideal Anesthetic

- Hemodynamic Stability
- Rapid Onset and Emergence
- Effective Analgesia
- PONV Control (Postoperative Nausea and Vomiting)
- Preservation of Cognition
- Optimal Functional Recovery
- Minimal Adverse Effects
- Cost
- Environmental Impact

Our Focus Today:

Optimal Recovery

Not just putting the patient to sleep, but helping them:

- Recover better and faster
- with minimal side effects
- in a safe and sustainable way



From a new molecule to a smarter strategy...

Optimizing existing drugs, using novel adjuncts, and advancing perioperative care

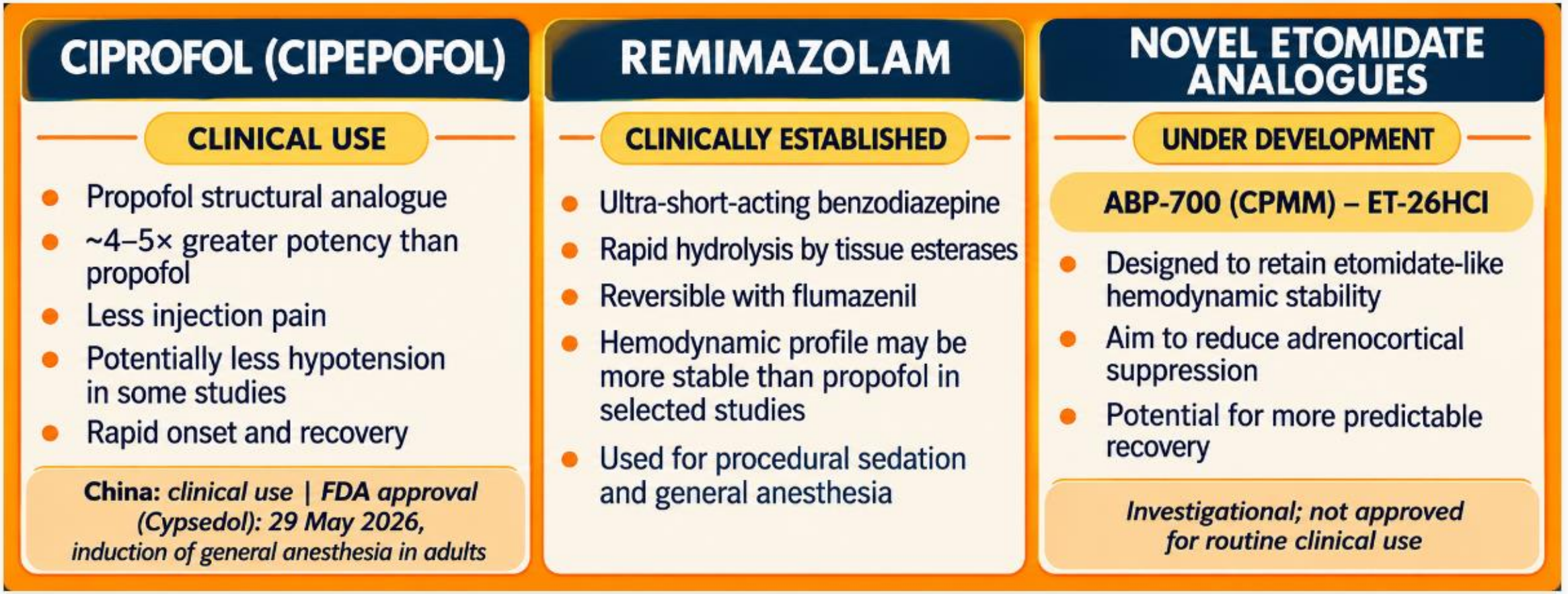
In previous decades, no new inhalational anesthetic has been introduced.

Isoflurane	**Synthesized:** 1965; **Clinical use:** 1981 (FDA approval).
Sevoflurane	**Synthesized:** late 1960s; **Clinical use:** 1990 (Japan); **FDA approval:** 1995 (USA).
Desflurane	**Developed:** 1970s; **Clinical use:** 1992 (USA FDA approval).
Xenon	**Anesthetic activity identified:** 1973; **First clinical trials:** 1977; **Clinical introduction:** 1986 (UK).

No new inhalational anesthetic has been introduced to replace sevoflurane

In recent years

However, advances have been made in the field of intravenous anesthetic agents.



Our Current Best Options

- **Sevoflurane:** A well-established volatile anesthetic with rapid titratability and predictable emergence.
- **Propofol-based TIVA:** Excellent control of anesthetic depth, rapid emergence, and favorable postoperative recovery profile in patients with PONV risk.
- **Remimazolam:** A newer ultra-short-acting benzodiazepine offering rapid recovery and predictable sedation, with potential advantages in selected patient populations.

The Key Message

The goal is not to find one perfect drug, but to select the right drug—or combination of drugs—for the right patient.

Sevoflurane is controllable and clinically valuable—not universally the fastest inhaled agent.

Why Sevoflurane Still Matters

Low blood–gas solubility (approximately 0.65–0.69) supports rapid changes in alveolar and effect-site concentrations.

Allows responsive titration of anesthetic depth and a relatively predictable wash-out after discontinuation.

Can facilitate return of consciousness, response to commands and operating-room extubation in appropriately selected adults.

Emergence is also influenced by anesthetic duration and concentration, alveolar ventilation, age, co-administered drugs, opioid exposure and patient physiology.

Sevoflurane is controllable and clinically valuable—not universally the fastest inhaled agent.

Sevoflurane

Pharmacological profile

- Volatile ether →GABA-A-mediated signaling
- Minimal airway pungency→ suitable for inhalational induction

Potential advantages

- Reliable induction and maintenance of anesthesia
- Rapid adjustment of anesthetic depth
- Has bronchodilatory properties
- Established clinical experience and broad availability

Limitations and adverse effects

- Dose-dependent bradycardia, hypotension and respiratory depression
- PONV
- Pediatric emergence agitation/delirium
- Malignant hyperthermia

➢ Does reliable and rapid emergence translate into superior clinical recovery?

Sevoflurane in Adults: Beyond Pediatric Anesthesia

Its role in adults extends to fast-track anesthesia and ERAS pathways.

Relatively low airway irritation and bronchodilatory properties may be useful in patients with asthma, COPD or airway hyperreactivity.

Can be used across different induction and maintenance techniques.

Offers a practical balance of titratability, clinical familiarity and acceptable recovery in many adult procedures.

Its value lies in controllability and fit with the overall anesthetic plan.

Cardiovascular Considerations in Adult: Potential Benefits of Sevoflur

Sevoflurane, has been investigated for potential myocardial protection through preconditioning and postconditioning pathways.

Potential effects include reduced systemic vascular resistance and afterload, and modulation of myocardial oxygen demand.

In patients with coronary disease, left ventricular dysfunction or valvular disease, gradual titration may support controlled anesthetic maintenance.

Balance afterload reduction against dose-dependent negative inotropy; excessive concentrations may impair cardiac output.

Potential cardioprotection is plausible; a definitive outcome advantage remains unproven.

Sevoflurane vs TIVA: Does it Change Recovery?

VITAL Trial — JAMA 2026

- Multicenter pragmatic RCT; 2,508 patients, ≥50 years.
- 49 UK hospitals; major elective noncardiac surgery.

Outcomes

- No significant differences in delirium, major complications, or mortality.
- TIVA reduced selected symptoms, including nausea and vomiting.

2026 Ambulatory Surgery Meta-analysis

- 15 RCTs; 1,345 patients.
- TIVA reduced PONV: RR 0.67 (95% CI 0.47–0.96).
- No significant difference in pooled PACU length of stay.

❖ Neither strategy demonstrates superiority in better recovery; anesthetic selection should reflect patient risk, clinical context, and recovery priorities.

The Environmental Footprint of Inhaled Anesthetics

A substantial proportion of inhaled anesthetic is exhaled and released through the anesthetic gas scavenging system.

Reported 100-year global warming potentials (GWP100; CO_2 = 1): sevoflurane ≈ 144; isoflurane ≈ 539; desflurane ≈ 2,540.

Approximate atmospheric lifetimes: sevoflurane 1–2 years; isoflurane 3–4 years; desflurane 14 years.

By mass emitted, sevoflurane has a lower direct warming impact than isoflurane and desflurane.

Lower impact does not mean zero impact; the advantage is relative.

More Sustainable Use: Practical Priorities

Avoid unnecessary desflurane use when a clinically appropriate alternative is available.

Use the lowest fresh-gas flow compatible with patient needs, equipment limitations and safety requirements.

Limit unnecessary exposure and discontinue volatile agents at the appropriate time.

Environmental considerations should inform—but never compromise—anesthetic adequacy or patient safety.

Reduce avoidable emissions while preserving clinical safety.

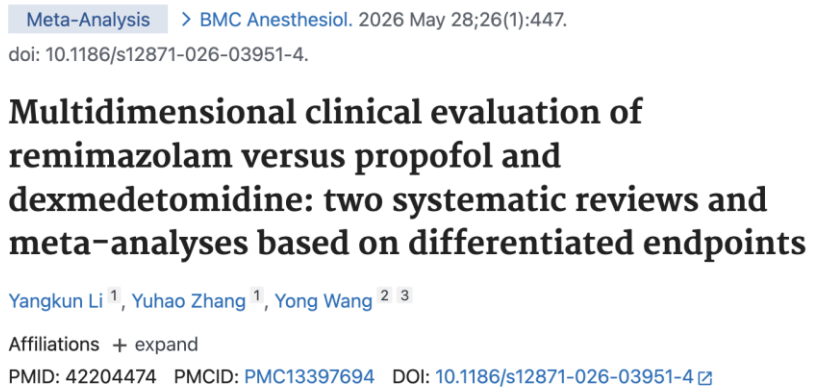
Remimazolam: Better Pharmacology, Better Recovery?

Pharmacological advantages

- Ultra-short-acting benzodiazepine; GABA-A receptor modulation
- Rapid esterase-mediated metabolism
- Flumazenil reversibility
- Lower incidence of intraoperative hypotension than propofol

Recent evidence — 2026 Meta-analysis

- Hypotension: OR 0.35 (95% CI 0.29–0.43)
- Postoperative delirium: OR 1.06 (95% CI 0.78–1.45)


Meta-Analysis > BMC Anesthesiol. 2026 May 28;26(1):447.
doi: 10.1186/s12871-026-03951-4.

Multidimensional clinical evaluation of remimazolam versus propofol and dexmedetomidine: two systematic reviews and meta-analyses based on differentiated endpoints

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Affiliations + expand

PMID: 42204474 PMCID: PMC13397694 DOI: 10.1186/s12871-026-03951-4

➢ Improved hemodynamic tolerability does not establish superior postoperative recovery

Knowledge gaps: Long-term functional recovery, high-risk populations, resedation after reversal, and cost-effectiveness

Xenon

Distinct pharmacology

- Noble gas with anesthetic properties
- Predominantly noncompetitive NMDA receptor inhibition
- Extremely low blood–gas partition coefficient ≈ 0.12–0.14
- MAC approximately 63–71%
- **Potential advantages**
- Very rapid emergence and early neurological responsiveness
- Minimal metabolism; elimination through exhalation
- Relatively stable BP and HR → Hemodynamic stability
- Potential neuroprotective and cardioprotective effects
- Environmental consideration: Xenon has zero ozone depletion potential

limitations

- Higher PONV incidence: 34.4% vs 19.9% (RR 1.72)
- High acquisition cost and limited availability
- Specialized equipment

Xenon is a anesthetic in terms of clinical performance, but its high MAC and limited availability make its routine use challenging.

Dexmedetomidine

Pharmacological characteristics

- Selective α2-adrenergic agonist
- Arousable sedation with relatively limited respiratory depression
- Analgesic- and opioid-sparing properties

Recent evidence — 2026

- Delirium prevention: 22 RCTs, 4,161 patients
- Postoperative delirium: RR 0.56 (95% CI 0.47–0.66)
- Reduced PONV: RR 0.79 (95% CI 0.62–0.99)
- Increased bradycardia and hypotension

❖ Dexmedetomidine may improve specific recovery outcomes.

Review > Eur Geriatr Med. 2026 Oct 30. doi: 10.1007/s41999-026-01636-2.
Online ahead of print.

Effects of perioperative dexmedetomidine on postoperative delirium in older surgical patients: an updated meta-analysis of randomized controlled trials

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Knowledge gaps: Optimal dosing, patient selection, long-term cognitive outcomes, and cardiovascular tradeoffs

Ketamine & Esketamine

- **Pharmacological profile**
  - •NMDA receptor antagonism and antihyperalgesic effects
  - •Analgesic and opioid-sparing properties
  - •Potential effects on psychological recovery

- **Recent evidence — 2026**
  - •Esketamine meta-analysis: 35 RCTs, 3,831 patients
  - •Improved early postoperative pain scores; long-term functional benefit remains uncertain
  - •RCT in patients with pre-existing depressive symptoms (n=435):
    - Depression remission at day 3: 28.3% vs 11.3%
    - OR 3.12 (95% CI 1.79–5.55)

❖ Analgesic benefits are supported; broader psychological and functional recovery benefits require further validation.

- **Limitations:** Dissociation, hallucinations, dizziness, and variable psychomimetic effects



Meta-Analysis > J Clin Anesth. 2026 Sep:114:112278. doi: 10.1016/j.jclinane.2026.112278. Epub 2026 Jul 23.

Efficacy of intraoperative low dose intravenous Esketamine for acute postoperative pain control: Meta-analysis of randomized controlled trials

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Opioid-Sparing Anesthesia Without Undertreating Pain

Opioids remain important for acute surgical pain, but unnecessary exposure can contribute to PONV, sedation, respiratory depression, ileus and delayed mobilization.

Complete opioid avoidance is not appropriate for every patient; poorly controlled pain can itself impair recovery.

Build a procedure- and patient-specific multimodal plan: acetaminophen, NSAIDs when appropriate, local anesthetics and regional techniques.

Selected adjuncts may include dexmedetomidine (consider bradycardia and hypotension) or low-dose ketamine, particularly in painful surgery or opioid-tolerant patients.

The goal: the least pain, the fewest adverse effects and the best possible function.

PONV: A Preventable Barrier to Recovery

PONV can delay oral intake, mobilization and discharge—even when consciousness and respiratory function have recovered.

Risk factors include previous PONV, motion sickness, female sex, non-smoking status, perioperative opioid use and volatile anesthetic exposure.

For high-risk patients, consider propofol-based TIVA when appropriate, opioid reduction, fluid balance and prophylaxis using different antiemetic classes.

Dexamethasone and a 5-HT_3 antagonist (e.g., ondansetron) are common components; an NK_1 antagonist (Aprepitant) may be considered in selected high-risk patients.

If prophylaxis fails, rescue treatment should preferably come from a different drug class.

PONV prevention is part of recovery design—not an optional add-on.

Neuromuscular Recovery: A Safety-Critical Endpoint

A patient may be awake and breathing spontaneously yet still have clinically important residual neuromuscular weakness.

Residual block can impair pharyngeal function, promote airway obstruction and hypoventilation, and increase respiratory complications.

The 2023 ASA guidance recommends quantitative monitoring when neuromuscular blockers are used, with a train-of-four ratio of at least 0.9 at the adductor pollicis before extubation.

Sugammadex can provide rapid, predictable reversal of rocuronium- or vecuronium-induced block; choice depends on block depth, patient factors, access and cost.

Fast extubation without confirmed adequate reversal is not successful recovery.

Sugammadex Versus Neostigmine: Interpreting Outcomes

In the 2026 SNaPP trial (3,498 patients):

Postoperative pulmonary complications or death were reported in 19.0% with sugammadex and 21.5% with neostigmine (RR 0.88).

The result was statistically significant; the reduction was mainly attributable to atelectasis.

No clear difference in pneumonia was observed.

The findings are encouraging, but do not imply that sugammadex eliminates postoperative pulmonary complications.

Promising risk reduction is not risk elimination.

EEG-Guided Anesthesia: Individualizing Drug Delivery

Dose, end-tidal volatile concentration, blood pressure and heart rate are indirect indicators; none alone defines an individual brain's response.

Two patients with similar age, weight and end-tidal sevoflurane concentrations may have different electroencephalographic responses.

Frontal EEG and processed indices such as BIS provide additional information—but a processed number is not the same as reviewing the raw EEG.

Raw waveform, spectral features and burst suppression may add clinically relevant context.

The aim is not to drive every patient to one number, but to avoid both inadequate anesthesia and unnecessary anesthetic exposure.

Interpret EEG as a clinical signal—not a target number in isolation.

What Does the Evidence Say About EEG Guidance?

A 2025 meta-analysis in the International Journal of Surgery included 12 randomized trials and 4,523 patients.

Processed EEG-guided anesthesia was associated with a 19% relative reduction in postoperative delirium (RR 0.81; 95% CI 0.69–0.95).

A separate 2025 meta-analysis of 12 studies involving 7,441 older adults also reported reduced postoperative delirium.

EEG monitoring alone does not prevent delirium. Avoiding prolonged hypotension, hypoxemia, metabolic disturbances and excessive drug exposure remains essential.

Delirium prevention is multifactorial; EEG may be one component.

A Practical Five-Question Recovery Algorithm

1. What is the recovery goal? Rapid emergence, pain control, PONV prevention, cognitive recovery or same-day discharge

2. Which anesthetic best fits this patient? Sevoflurane, remimazolam or propofol-based TIVA, considering procedure, PONV risk, hemodynamics and available resources

3. How will pain be controlled? Avoid unnecessary opioids, use multimodal analgesia and regional techniques when indicated.

4. Has physiological function recovered? Confirm quantitative neuromuscular recovery, adequate ventilation, hemodynamic stability and normothermia.

5. Is the patient truly discharge-ready? Assess consciousness, pain, nausea, vital signs and formal discharge criteria.

Recovery begins before induction and continues beyond extubation.

Take-Home Messages

Sevoflurane remains a valuable, controllable option in modern adult anesthesia; propofol-based TIVA may offer an advantage in patients at high risk of PONV.

Remimazolam expands the available options, but promising findings should not be mistaken for proven superiority in overall recovery.

Optimal recovery is not achieved by changing one drug alone: it requires rational drug selection, individualized dosing, multimodal analgesia, PONV prevention, appropriate depth monitoring and complete neuromuscular recovery.

Future Perspective: Optimal recovery is achieved through: individualized anesthesia, multimodal strategies, and evidence-based clinical decision-making.

The goal is not to wake patients faster; it is to return them to normal life sooner and more safely.

Key Message

Beyond waking up faster,
Let's help patients recover better.

Thank You for Your Attention

Questions and Discussion