Lecture 06 - Contents

An overview of the parts in the clinical Chain-of-Thought lecture.

Part 1
Reasoning Fundamentals

Part 2
Advanced CoT Techniques

Part 3
Clinical Applications

Hands-on
CoT Implementation Hands-on

This outline is for guidance. Navigate the slides with the left/right arrow keys.

Lecture 6:

Chain-of-Thought: Teaching LLMs Clinical Reasoning

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Chain-of-Thought in Medical Context

CoT Prompting

- Step-by-step reasoning process
- Makes LLM thinking transparent
- Breaks complex problems into steps
- Intermediate reasoning shown explicitly

Medical Applications

- Diagnosis generation
- Treatment planning
- Clinical decision support
- Patient assessment

Standard vs CoT Comparison

Standard Prompting
Direct answer only

VS

CoT Prompting
Reasoning + Answer

Performance Improvement: **20-80% accuracy increase on complex medical reasoning tasks**

Lecture 6: Chain-of-Thought for Clinical Reasoning

Part 1
Reasoning Fundamentals

- Clinical Reasoning Process
- Diagnostic Reasoning Chains
- Zero-Shot CoT Medical
- Few-Shot CoT Examples
- Self-Consistency Voting
- Reasoning Path Selection
- Medical Knowledge Integration

Part 2
Advanced CoT Methods

- Tree of Thoughts Medical
- Graph of Thoughts
- Differential Diagnosis Trees
- Bayesian Reasoning Integration
- Uncertainty Propagation
- Counterfactual Reasoning

Part 3
Clinical Applications

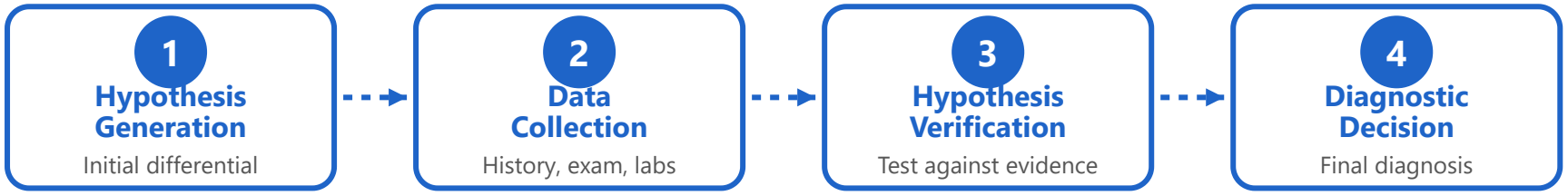
- Emergency Triage CoT
- Treatment Planning Chains
- Drug Interaction Reasoning
- Lab Result Interpretation
- Clinical Note Generation
- Error Analysis Patterns
- Reasoning Verification
- Performance Comparison
- Case Studies Analysis
- Hands-on Implementation
- Best Practices Guidelines

Part 1/3:

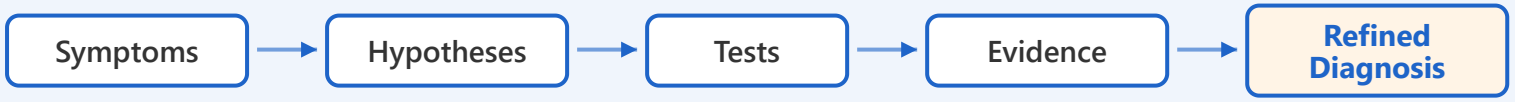
Clinical Reasoning Fundamentals

1. Clinical Reasoning Process
2. Diagnostic Reasoning Chains
3. Zero-Shot CoT in Medical Context
4. Few-Shot CoT Examples
5. Self-Consistency & Voting
6. Reasoning Path Selection
7. Medical Knowledge Integration

Clinical Reasoning Process

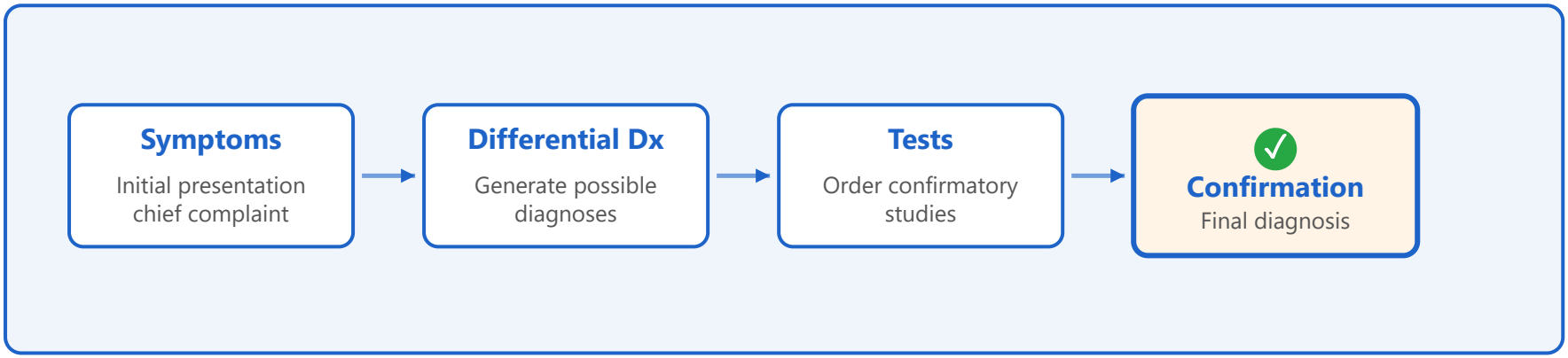


Iterative Clinical Reasoning Cycle



Key Insight: Clinical reasoning is iterative and hypothesis-driven, continuously updating based on new evidence

Diagnostic Reasoning Chains



Example: Chest Pain Evaluation

Symptoms:	65yo male, sudden chest pain, radiating to left arm, diaphoresis
Differential:	1) MI, 2) Angina, 3) GERD, 4) Costochondritis, 5) Pulmonary embolism
Key Tests:	ECG (ST elevation), Troponin (elevated), Cardiac enzymes
Diagnosis:	Acute ST-elevation myocardial infarction (STEMI)
Reasoning:	Classic presentation + ECG changes + elevated biomarkers → STEMI confirmed

Zero-Shot Chain-of-Thought in Medical Context

Standard Medical Query:

```
Patient presents with fever (39°C), productive cough, and pleuritic chest pain.
What is the most likely diagnosis?
```

"Let's think step by step"

Zero-Shot CoT Medical Prompt:

```
Patient presents with fever (39°C), productive cough, and pleuritic chest pain.
What is the most likely diagnosis? Let's think step by step.
```

✓ Success Case

Query: Fever + cough + pleuritic pain
With CoT: Systematic evaluation of symptoms → ruled out alternatives → pneumonia diagnosis
Accuracy: 85% → 92%

✗ Limitation Case

Query: Rare genetic syndrome
With CoT: Detailed reasoning but incorrect conclusion
Issue: Limited knowledge, not reasoning problem

Few-Shot Chain-of-Thought Examples

Few-Shot CoT Structure

2-5 Examples: Provide diverse medical cases

Show Reasoning: Include step-by-step clinical thinking

Format Consistency: Use same structure across examples

Example Template

Case: [Patient presentation]

Step 1: Identify key symptoms and risk factors

Step 2: Generate differential diagnosis list

Step 3: Determine discriminating tests

Step 4: Integrate results and reach conclusion

Diagnosis: [Final diagnosis]

Key: Examples teach the LLM both the format and the medical reasoning process

Self-Consistency & Voting Mechanism

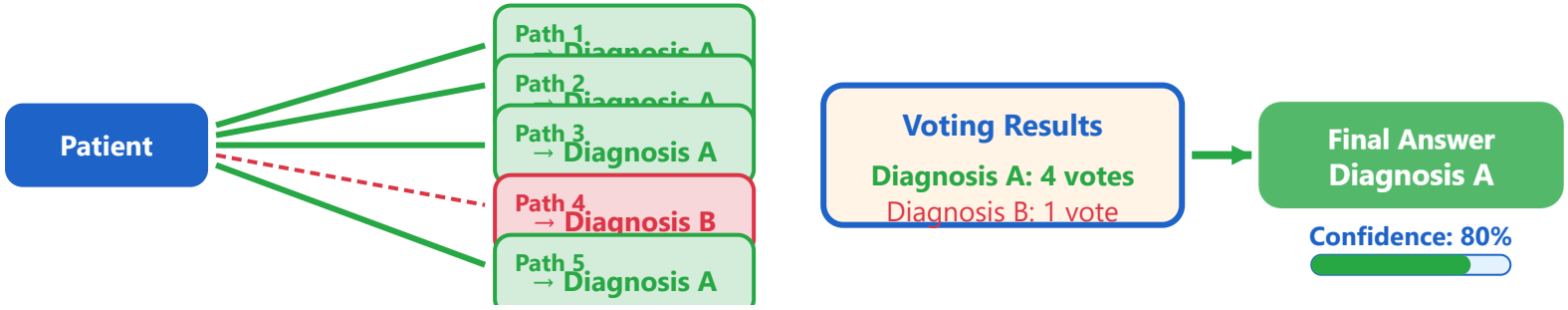
Multiple Reasoning Paths

Generate Multiple Solutions: Sample 5-10 different reasoning paths

Voting Mechanism: Select most consistent answer across paths

Confidence Boost: Agreement increases reliability

Example: 5 Reasoning Paths



Performance improvement: **5-15% accuracy gain** over single-path CoT

Reasoning Path Selection & Optimization

Path Quality Metrics

- Logical consistency
- Evidence alignment
- Medical accuracy
- Completeness of reasoning

Selection Strategies

- Confidence scoring
- Expert validation
- Guideline adherence
- Outcome verification

Pruning Strategy: Eliminate paths with logical contradictions or unsupported claims early

Medical Knowledge Integration

Knowledge Sources

- **Clinical Guidelines:** Evidence-based protocols (AHA, WHO, CDC)
- **Medical Literature:** PubMed, clinical trials, meta-analyses
- **Drug Databases:** Interactions, dosing, contraindications
- **Disease Knowledge:** Pathophysiology, diagnostic criteria

Integration Example

Patient Case: Hypertensive emergency

Guideline Reference: JNC-8 recommendations

Evidence Integration: BP targets, medication choice

Output: Treatment plan aligned with current guidelines

Critical: Always reference authoritative medical sources

Part 2/3:

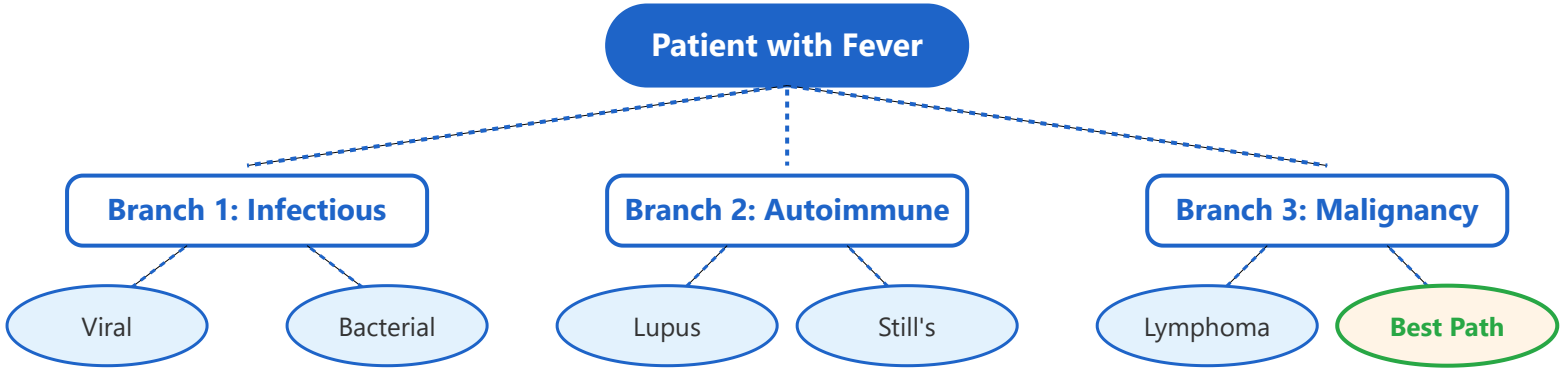
Advanced CoT Methods

1. Tree of Thoughts for Medical Reasoning
2. Graph of Thoughts
3. Differential Diagnosis Trees
4. Bayesian Reasoning Integration
5. Uncertainty Propagation
6. Counterfactual Reasoning

Tree of Thoughts (ToT) for Medical Reasoning

ToT Structure

- **Branching Exploration:** Multiple diagnostic pathways simultaneously
- **Depth-First/Breadth-First:** Systematic exploration strategies
- **Backtracking:** Return to earlier decision points if path fails
- **Evaluation:** Score each branch based on evidence



Advantage: Explores multiple hypotheses systematically before committing to one

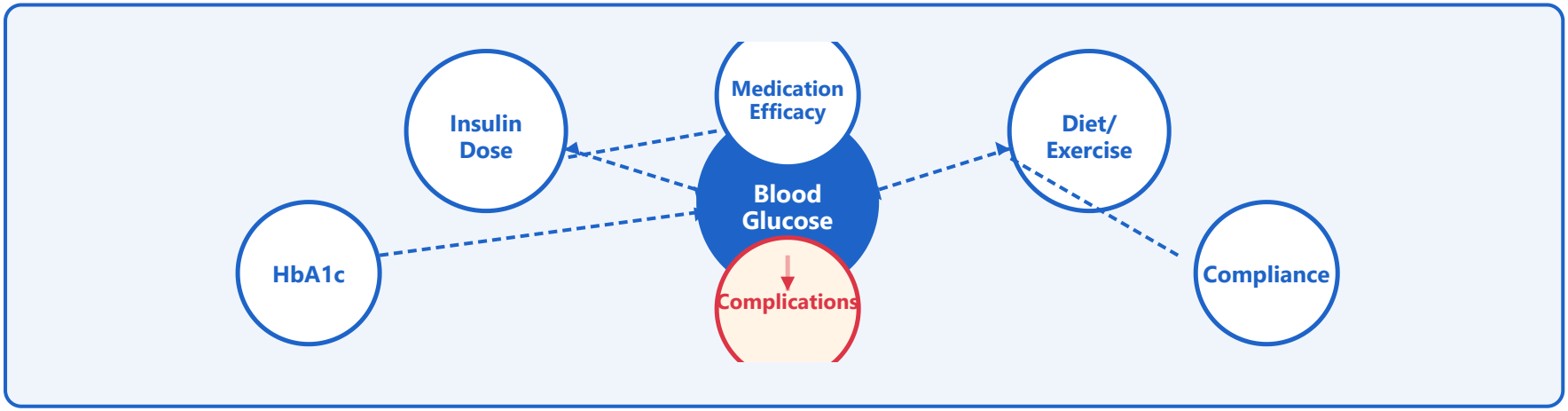
Graph of Thoughts (GoT)

Graph Structure

- Non-linear reasoning paths
- Cyclic relationships
- Bidirectional connections
- Complex interdependencies

Medical Applications

- Comorbidity interactions
- Drug-drug interactions
- Multi-system diseases
- Feedback loops in treatment



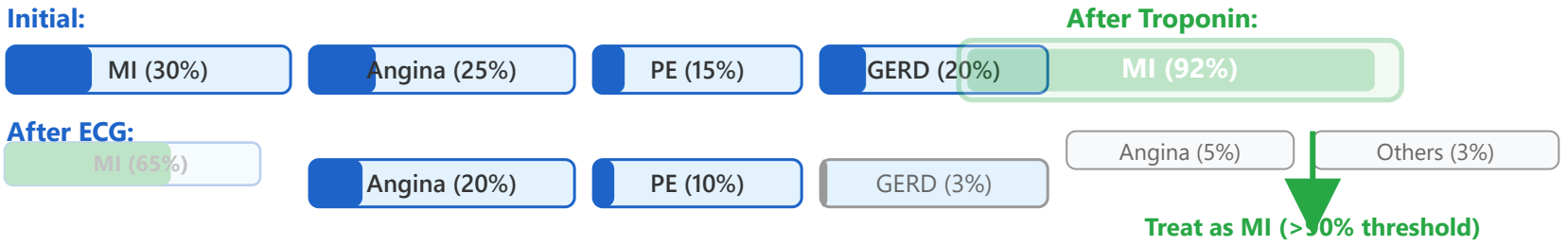
Key: Captures complex medical relationships beyond simple trees

Differential Diagnosis Trees

Probabilistic Branching

- **Prior Probabilities:** Based on prevalence and risk factors
- **Likelihood Ratios:** Each test updates probabilities
- **Bayesian Updates:** Continuous refinement with new data
- **Threshold Decision:** Diagnostic certainty level to act

Example: Chest Pain Differential



Quantitative reasoning: Numbers guide clinical decisions

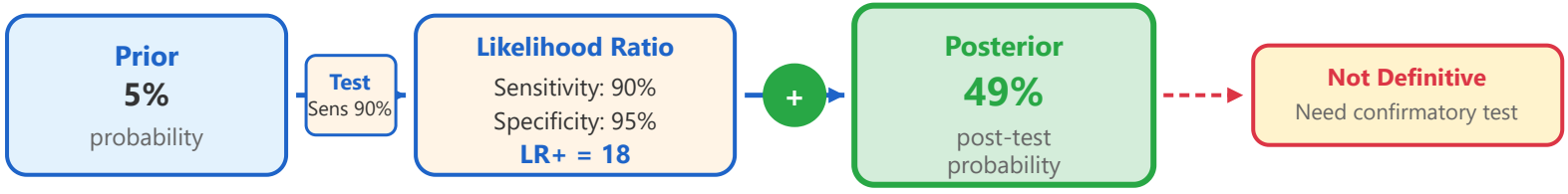
Bayesian Reasoning Integration

Bayesian Framework

- **Prior Probability:**Pre-test likelihood based on prevalence
- **Likelihood Ratio:**How much test changes probability
- **Posterior Probability:**Post-test diagnostic certainty
- **Sequential Testing:**Chain multiple tests together

Bayes' Theorem in Diagnosis

$$P(Disease|Test) = [P(Test|Disease) \times P(Disease)] / P(Test)$$



Critical: Integrating prevalence and test characteristics improves diagnostic accuracy

Uncertainty Propagation in Clinical Reasoning

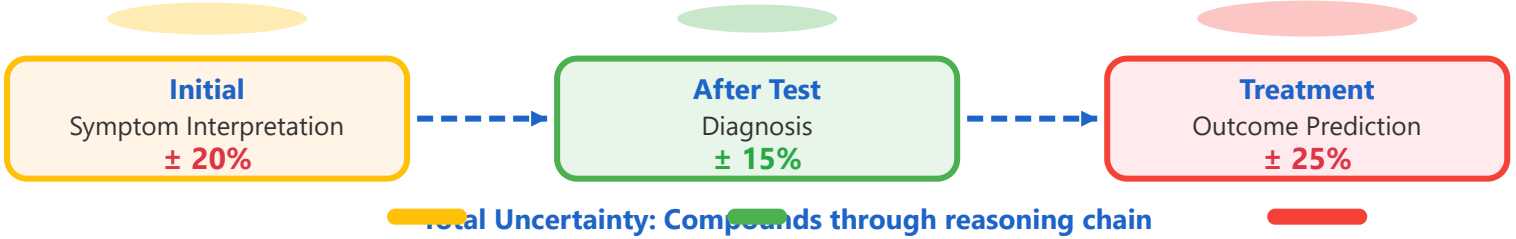
Sources of Uncertainty

- Incomplete patient history
- Test measurement error
- Diagnostic ambiguity
- Treatment response variability

Managing Uncertainty

- Confidence intervals
- Probability distributions
- Decision thresholds
- Risk-benefit analysis

Propagation Example



Action: Make decisions robust to uncertainty levels

Counterfactual Reasoning in Clinical Context

"What If" Scenarios

- **Alternative Treatments:** What if we chose treatment B instead of A?
- **Timing Variations:** What if intervention was earlier/later?
- **Diagnostic Paths:** What if initial diagnosis was different?
- **Risk Scenarios:** What if patient had different risk profile?

Example: Treatment Decision

Actual: Chose conservative management → symptom improvement in 2 weeks

Counterfactual 1: Surgery → faster recovery but higher risk

Counterfactual 2: Aggressive medication → potential side effects

Analysis: Conservative was appropriate given risk-benefit profile

Benefit: Exploring alternatives validates chosen approach and identifies improvements

Part 3/3:

Real Clinical Applications

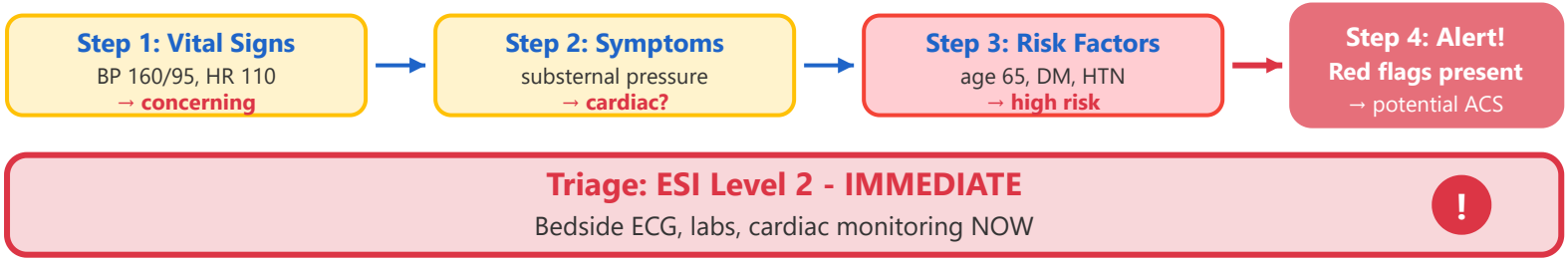
1. Emergency Triage with CoT
2. Treatment Planning Chains
3. Drug Interaction Reasoning
4. Lab Result Interpretation
5. Clinical Note Generation
6. Error Analysis & Verification
7. Performance & Case Studies
8. Hands-on Implementation

Emergency Triage with Chain-of-Thought

Triage CoT Process

- **Rapid Assessment:**ABC (Airway, Breathing, Circulation) first
- **Priority Scoring:**ESI (Emergency Severity Index) 1-5
- **Resource Prediction:**Anticipate needed tests/interventions
- **Time-Critical Flags:**STEMI, stroke, sepsis alerts

Example: Chest Pain Triage



Critical: CoT enables rapid, systematic prioritization under time pressure

Treatment Planning with CoT

Sequential Decision Process

- **Treatment Options:**List first-line, second-line alternatives
- **Risk-Benefit Analysis:**Weigh efficacy vs adverse effects
- **Patient Factors:**Consider comorbidities, preferences, adherence
- **Monitoring Plan:**Define follow-up and adjustment criteria

Example: Hypertension Management

Options: ACE-I, ARB, CCB, Diuretic, Beta-blocker

Patient: 55yo, DM, no CAD, eGFR 60, K+ 4.2

Reasoning: ACE-I preferred (DM protection) → check for contraindications (none) → assess tolerability risk (low)

Plan: Start Lisinopril 10mg daily

Monitoring: BP recheck 2 weeks, Cr/K+ 1 week, target BP <130/80

Guideline-based + personalized = optimal treatment

Drug Interaction Reasoning with CoT

Interaction Types

- Pharmacokinetic (absorption, metabolism)
- Pharmacodynamic (additive, antagonistic)
- Disease-drug interactions
- Food-drug interactions

Reasoning Steps

- Identify all medications
- Check known interactions
- Assess severity and mechanism
- Plan dose adjustment or alternative

Example: Warfarin Interactions

Patient on: Warfarin 5mg daily (INR target 2-3)

New Rx: Azithromycin for pneumonia

Reasoning: Azithromycin inhibits CYP3A4 → ↑ warfarin levels → ↑ bleeding risk

Action: Use alternative antibiotic (amoxicillin) OR ↓ warfarin dose + close INR monitoring

Safety First: CoT catches potential harms before they occur

Lab Result Interpretation with CoT

Interpretation Framework

- **Normal vs Abnormal:** Reference range comparison
- **Pattern Recognition:** Constellation of abnormalities
- **Clinical Context:** Integrate with symptoms and history
- **Differential for Findings:** What causes this pattern?

Example: Anemia Workup

Results: Hgb 8.5, MCV 68, Ferritin 8, TIBC ↑

Step 1: Anemia confirmed (low Hgb)

Step 2: Microcytic (low MCV) → think Fe, thalassemia, chronic disease

Step 3: Low ferritin + high TIBC → iron deficiency

Step 4: Cause? → GI loss, dietary, malabsorption

Diagnosis: Iron deficiency anemia → investigate source

Integration: Labs + clinical picture = complete assessment

Clinical Note Generation with CoT

SOAP Note Structure

- **Subjective:**Patient's symptoms and history
- **Objective:**Physical exam findings and lab results
- **Assessment:**Diagnosis and clinical reasoning
- **Plan:**Treatment and follow-up recommendations

CoT-Enhanced Assessment Section

Problem: Acute onset chest pain

Reasoning: Substernal pressure + radiation to arm + diaphoresis + troponin elevation + ECG changes → consistent with acute MI. Differential included angina (unstable vs stable ruled out by troponin), PE (low probability by Wells score), and GERD (atypical for severity). Given TIMI score 5 (high risk), urgent cardiology consultation and catheterization indicated.

Diagnosis: Acute STEMI, high risk

Documentation: CoT makes clinical reasoning explicit and auditable

Error Analysis in CoT Reasoning

Common Error Types

- Premature closure (stopping too early)
- Anchoring bias (fixation on initial diagnosis)
- Missing rare conditions
- Ignoring contradictory evidence

Improvement Strategies

- Force consideration of alternatives
- Explicit verification steps
- Checklist integration
- Human-AI collaboration

Error Pattern Analysis

Error: Misdiagnosed appendicitis as gastroenteritis

Root Cause: CoT stopped after matching 3 symptoms, missed fever + RLQ tenderness

Pattern: Premature closure (50% of diagnostic errors)

Fix: Add "Consider red flags" step before finalizing

Learning: Analyze failures to improve CoT prompting strategies

Reasoning Verification & Quality Control

Verification Steps

Logical Consistency: Check for contradictions in reasoning chain

Evidence Support: Verify each claim has supporting data

Completeness: Ensure all relevant factors considered

Guideline Adherence: Confirm alignment with clinical standards

Verification Checklist

✓ Are all steps logically connected?

✓ Is each conclusion supported by evidence?

✓ Were alternative diagnoses considered?

✓ Are contradictory findings explained?

✓ Does final answer match clinical guidelines?

✓ Are safety concerns addressed?

Quality Assurance: Systematic verification reduces errors by 30-40%

CoT vs Standard Prompting Performance

Standard Prompting

- Direct answer generation
- No intermediate steps
- Faster but less accurate
- Harder to debug errors

CoT Prompting

- Step-by-step reasoning
- Transparent logic
- Higher accuracy
- Auditable process

Benchmark Results

MedQA: 56% → 72% (+16% with CoT)

PubMedQA: 68% → 81% (+13% with CoT)

Clinical Diagnosis: 62% → 78% (+16% with CoT)

Treatment Planning: 70% → 84% (+14% with CoT)

Average Improvement: +15% accuracy across medical tasks

Trade-off: 2-3x slower but significantly more accurate and trustworthy

Real-World Case Studies

Case 1: Sepsis Detection

Presentation: 72yo, fever 39.2°C, confusion, HR 125, BP 85/50

CoT Process: SIRS criteria → infection source → SOFA score → sepsis diagnosis

Outcome: Early recognition → prompt antibiotics → improved survival

Case 2: Atypical Presentation

Presentation: 45yo female, fatigue, no chest pain, mild dyspnea

CoT Process: Atypical symptoms → considered MI (women present differently) → ECG → troponin → diagnosed NSTEMI

Outcome: CoT helped recognize atypical presentation, standard prompting missed it

Case 3: Complex Comorbidity

Presentation: DM + CKD + CHF patient with worsening shortness of breath

CoT Process: Multiple potential causes → systematically evaluated each → identified CHF exacerbation + UTI

Outcome: Treated both conditions appropriately, avoided missing secondary diagnosis

Lesson: CoT excels at complex, atypical cases requiring careful reasoning

Hands-on: Implementing CoT for Medical Tasks

Implementation Steps

1. Define Task: Diagnosis, treatment planning, triage, etc.

2. Design Prompt: Include "think step by step" or provide examples

3. Test & Iterate: Evaluate on sample cases, refine prompt

4. Validate: Compare to expert clinicians, measure accuracy

Code Example (Python)

```
prompt = f"""
Patient: {patient_info}
Task: Provide differential diagnosis.
Let's think step by step:
1. Key symptoms and signs
2. Possible diagnoses
3. Tests to discriminate
4. Most likely diagnosis
"""

response = model.generate(prompt)
```

Practice: Try implementing CoT for your own clinical scenarios

Best Practices for Clinical CoT

✓ DO

- Use clear, explicit step labels
- Reference clinical guidelines
- Verify reasoning logic
- Include safety checks
- Test on diverse cases

✗ AVOID

- Vague instructions
- Too many steps (>7-8)
- Ignoring contradictions
- Blind trust in output
- Skipping validation

Key Principles

1. **Clarity:** Each step should be clear and actionable
2. **Completeness:** Cover all critical decision points
3. **Safety:** Always include risk assessment
4. **Evidence:** Ground reasoning in medical literature
5. **Validation:** Human expert review essential

Remember: CoT is a tool to augment, not replace, clinical judgment

Thank you

Chain-of-Thought for Clinical Reasoning

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