

Unleashing the potential of AI: a deeper dive into GPT prompts for medical research

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I read the article by Haemmerli *et al* on the performance of ChatGPT-3.5 in generating treatment recommendations for central nervous system (CNS) tumours, which were then evaluated by tumour board (TB) experts. While the study did illuminate promising aspects of the Artificial Intelligence (AI) model, the design of the prompt used to interact with ChatGPT warrants further consideration.

In the study, the prompt employed was a brief patient history, followed by two questions, which appears to have limited the model's performance. As a sophisticated

large language model (LLM), GPT-3.5 relies heavily on the context and specificity of the provided prompt.^{1 2} Based on cited literature, an alternative prompt structure could have included context, specific intent, a question and an expected response format. Moreover, pretraining the LLM with examples of the expected answer significantly improves the quality of the answer.^{2 3} Finally, the introduction of GPT-4 in early March 2023 has shown considerable improvement in understanding and generating responses when compared with ChatGPT-3.5.^{4 5}

Table 1 ChatGPT-3.5 from the paper's online supplemental material S1 (6), chatGPT-3.5 and GPT-4 adapted output

ChatGPT-3.5 with simple prompt (from the study ⁶)	ChatGPT-3.5 with pretraining and structured prompt	GPT-4 with pretraining and structured prompt
Patient 9 '(...)the patient has a malignant brain tumour known as an astrocytoma. These tumours are typically treated with a combination of surgery, radiation therapy and chemotherapy.(...)'	'Oncological diagnosis: Glioblastoma (WHO grade IV) right precentral lesion(...) Proposed treatment: Palliative care, supportive management. Discussion: Considering the patient's age, comorbidities and postoperative complications, the panel recommends a palliative approach.(...)'	'Oncological diagnosis: Glioblastoma (WHO grade IV) Right precentral Lobe(...) Proposed treatment: Due to the poor general condition and advanced age of the patient,(...)focus should be on symptomatic relief, quality of life, and palliative care. Discussion: (...)The tumour board suggests a supportive and palliative care approach(...). Regular follow-ups with palliative care and neurology teams should be established(...).'
Patient 10 '(...)the patient likely has a grade III or IV astrocytoma. The best adjuvant treatment for this type of tumour would likely be a combination of radiation therapy and chemotherapy with temozolomide It is also important to note that the patient has IDH-1 wild type, which is associated with poor outcome and less response to chemotherapy and radiation therapy.'	'Oncological diagnosis: Glioblastoma (WHO grade IV) left frontotemporal lesion Proposed treatment: Radiotherapy and chemotherapy. Discussion: In the case of a gross total resection of a left frontotemporal glioblastoma, the neurotumour board recommends adjuvant treatment with radiotherapy and chemotherapy. (...)Close monitoring and follow-up will be essential to assess treatment response(...)'	'Oncological diagnosis: Glioblastoma (WHO grade IV) left frontotemporal lobe proposed treatment: (...)Standard adjuvant radiotherapy and chemotherapy using temozolomide according to the STUPP protocol(...) Discussion: (...)an unmethylated MGMT promoter suggests a less favourable response to temozolomide chemotherapy, however, given the patient's overall good health status, adjuvant radiochemotherapy remains the standard of care.(...)'
MGMT, O6-methylguanine-DNA methyltransferase; IDH-1, isocitrate dehydrogenase 1; STUPP protocol, temozolomide + radiotherapy according to Roger Stupp's regimen		



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With the application of these techniques, researchers could have guided the predictive capabilities of the LLM to generate more relevant and contextually nuanced responses. This could have particularly helped in areas where the model underperformed, such as precision in glioma subtypes and considerations of patient functional status.

As an illustration, both ChatGPT-3.5 and GPT-4 were pretrained with eight examples (patients 1–8, patient history followed by TB response) from online supplemental material of the study. A more context-specific prompt was then used with the history of patients 9 and 10. [Table 1](#) displays main output obtained using this technique, revealing enhanced precision in oncological diagnosis, treatment discussions and patient functional status from ChatGPT-3.5 compared with what was presented in the paper. GPT-4 seemed to align even more closely with the board's opinion, which was defined as the gold standard. Full discussion with the chatbot is available in online supplemental material 1.

It is critical to acknowledge that the efficiency of LLMs applications heavily depends on the prompt used and the quality of the data given. Future research needs to employ a refined, context-driven approach in interacting with these models and the development and sharing of prompt engineering techniques should continue to be prioritised.

In conclusion, the exploration of LLM in CNS oncology research is commendable, but it is essential to optimise the methodology to fully unlock the true potential of AI tools in such a complex and challenging clinical landscape.

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Supplementary material 1 : full discussion with GPT-4 and ChatGPT-3.5**PATIENT 9****Prompt used :**

[8 examples for pre-training removed for visibility]

I'm a neurosurgeon in a university hospital. Here is the story of a patient with a brain tumor. His story will be discussed at the neurotumor board. What is the best adjuvant treatment for the patient? According from all the examples I gave you before, give an answer equivalent to a tumor board answer. Answer with oncological diagnosis, oncological medical history, surgery, proposed treatment, discussion. *[patient history removed]*

GPT-4's answer :

Local CNS tumor board's answer:

Oncological Diagnosis:

Glioblastoma (WHO Grade IV) Right precentral Lobe

Oncological Medical History:

An 83-year-old male patient, with a medical history of MGUS, polymyalgia rheumatica, and chronic kidney failure, presented with a central facial paresis on the left side. MRI revealed a right precentral lesion with contrast enhancement and perifocal edema. Despite his limited condition and advanced age, a gross total resection was performed. Unfortunately, the patient suffered from a postoperative hemorrhage at the surgical site and woke up with hemiplegia. His Karnofsky Performance Status is evaluated at 40%. The pathological examination revealed proliferative cerebral tumor cells of astrocytic phenotype with observable mitoses and apoptotic cells, and necrotic areas characterized as pseudopalisades. The immunohistochemistry analysis showed GFAP positive tumor cells, IDH-1 wild type, and MGMT unmethylated.

Surgery and postoperative condition:

Gross total resection was performed, followed by a postoperative hemorrhage. The patient awoke with hemiplegia.

Proposed Treatment:

Due to the poor general condition and advanced age of the patient, aggressive therapies such as standard radiotherapy or chemotherapy may not be suitable. The focus should be on symptomatic relief, quality of life, and palliative care.

Discussion:

Given the aggressive nature of glioblastoma, advanced age, and overall poor health status, treatment decisions must be made in consideration of the patient's quality of life. As the patient's Karnofsky index is only 40% and he suffers from multiple comorbidities, aggressive therapy may lead to further decline in the patient's functional status and overall quality of life. Therefore, the tumor board suggests a supportive and palliative care approach, aimed at managing symptoms and optimizing the patient's comfort and quality of life. Regular follow-ups with palliative care and neurology teams should be established, alongside family

discussions for advanced care planning. It's essential to individualize the care plan to respect the patient's goals, needs, and preferences.

ChatGPT-3.5's answer:

Oncological Diagnosis: Glioblastoma (WHO Grade IV) Right Precentral Lesion

Oncological Medical History: An 83-year-old male with a history of MGUS, polymyalgia rheumatica, and chronic kidney failure.

Surgery: Gross total resection with postoperative hemorrhage and subsequent hemiplegia.

Proposed Treatment: Palliative care, supportive management.

Discussion: Considering the patient's age, comorbidities, and postoperative complications, the panel recommends a palliative approach with supportive care to manage symptoms and optimize the patient's quality of life. The treatment focus will be on comfort measures and addressing any potential complications that may arise.

Second prompt: What is the standard regimen for chemotherapy and radiotherapy for this patient ?

GPT-4's answer:

Given the age and condition of the 83-year-old patient with a diagnosed glioblastoma and a Karnofsky index of 40%, a less aggressive and more palliative approach would likely be more appropriate. The focus would be on managing symptoms, ensuring the patient's comfort, and maintaining the best possible quality of life.

However, if treatment is decided to be beneficial and aligns with the patient's wishes, a regimen of hypofractionated radiotherapy or chemotherapy with Temozolomide may be considered.

Hypofractionated Radiotherapy: This regimen delivers a higher dose of radiation per treatment but over a shorter course of treatment, typically over two to three weeks. This is often used for elderly patients or those in poor health.

Chemotherapy: If the patient can tolerate it, chemotherapy with Temozolomide could be considered. However, given the patient's advanced age and frail health, it might be administered at a lower dose or less frequently than the standard regimen.

It's essential to note that any treatment decision should be made in a multidisciplinary setting, involving a comprehensive discussion with the patient and their family about the potential benefits, side effects, and impact on the patient's quality of life. Palliative and supportive care measures should be included regardless of the decision to pursue disease-directed therapy.

ChatGPT-3.5's answer:

Based on the patient's age, comorbidities, and postoperative complications, the standard regimen for chemotherapy and radiotherapy may not be recommended in this case. Instead, a palliative approach with supportive care is typically favored to manage symptoms and improve the patient's quality of life. The treatment plan will focus on providing comfort measures and addressing specific needs as they arise.

PATIENT 10 (same prompt used as for patient 9)**GPT-4's answer:**

Local CNS tumor board's answer:

Oncological Diagnosis:

Glioblastoma (WHO Grade IV) Left fronto-temporal Lobe

Oncological Medical History:

A 60-year-old right-handed female presented with progressive psychomotor retardation and speech disturbance. An MRI showed a left fronto-temporal lesion with contrast enhancement, suggestive of a primary brain tumor. A temporal pole craniotomy was performed leading to gross total resection, but postoperatively, some residual tumor with contrast enhancement was noted at the resection cavity's border. The postoperative course was uncomplicated and the patient was able to undergo neurorehabilitation. The pathological examination revealed small tumor cells infiltrating the cortex, with astrocytic phenotype, frequent mitoses, necrosis, and microvascular proliferation. Immunohistochemical analysis showed the tumor cells were GFAP positive, IDH-1 wild type, and ATRX preserved with unmethylated MGMT.

Surgery and postoperative condition:

The patient underwent a gross total resection with some residual contrast-enhancing tumor seen postoperatively at the border of the resection cavity. The postoperative period was without complications.

Proposed Treatment:

The tumor board recommends standard adjuvant radiotherapy and chemotherapy using temozolomide according to the STUPP protocol. The treatment aims at the residual tumor and to prevent or delay recurrence.

Discussion:

The patient's diagnosis of glioblastoma, WHO Grade IV, with an unmethylated MGMT promoter suggests a less favorable response to temozolomide chemotherapy, however, given the patient's overall good health status, adjuvant radio-chemotherapy remains the standard of care. The presence of residual tumor postoperatively is a concern for potential early recurrence, reinforcing the need for adjuvant therapy. The patient's functional status post-rehabilitation, and her involvement in decision-making processes, will be crucial factors in managing this aggressive condition. Regular follow-ups with imaging and monitoring of clinical symptoms are needed to evaluate the effectiveness of the treatment and manage any potential side-effects.

Second prompt: What would be the regimen of radiotherapy and chemotherapy for this patient?

GPT-4's answer :

The standard regimen of radiotherapy and chemotherapy for a glioblastoma patient, according to the STUPP protocol, is as follows:

Radiotherapy:

The patient would undergo radiotherapy for six weeks, five days per week. The total dosage usually delivered is approximately 60 Gy, typically divided into 30 fractions of about 2 Gy each.

Chemotherapy:

Concurrently with radiotherapy, the patient would also start taking the oral chemotherapy drug Temozolomide. This is typically administered daily at a dose of 75 mg/m² body surface area during the entire period of radiotherapy.

Following a 4-week break after the completion of the concurrent radiotherapy and chemotherapy, the patient would then enter the adjuvant phase, where they would receive Temozolomide alone. This is usually given at a higher dose of 150-200 mg/m² for five consecutive days during each 28-day cycle, for up to 6-12 cycles, depending on the patient's tolerance and response to treatment.

The patient's condition, performance status, and any side effects of treatment will be continuously monitored and evaluated during this period to adjust the treatment plan as needed. Please note that this regimen might vary depending on the individual patient's health condition, age, and potential comorbidities.

chatGPT-3.5's answer:

Oncological Diagnosis: Glioblastoma (WHO Grade IV) Left Fronto-temporal Lesion

Oncological Medical History: A 60-year-old female with progressive psychomotor retardation and speech disturbance.

Surgery: Gross total resection with residual rest with contrast enhancement at the border of the cavity.

Proposed Treatment: Radiotherapy and chemotherapy.

Discussion: In the case of a gross total resection of a left fronto-temporal glioblastoma, the neurotumor board recommends adjuvant treatment with radiotherapy and chemotherapy. This standard approach aims to target any remaining tumor cells and improve patient outcomes. The specific treatment regimen will be determined based on the patient's overall health, tolerance, and individual factors. Close monitoring and follow-up will be essential to assess treatment response and manage potential side effects.

Second prompt : What would be the regimen of radiotherapy and chemotherapy for this patient?

GPT-4's answer:

The standard regimen of radiotherapy and chemotherapy for a glioblastoma patient, according to the STUPP protocol, is as follows:

Radiotherapy:

The patient would undergo radiotherapy for six weeks, five days per week. The total dosage usually delivered is approximately 60 Gy, typically divided into 30 fractions of about 2 Gy each.

Chemotherapy:

Concurrently with radiotherapy, the patient would also start taking the oral chemotherapy drug Temozolomide. This is typically administered daily at a dose of 75 mg/m² body surface area during the entire period of radiotherapy.

Following a 4-week break after the completion of the concurrent radiotherapy and chemotherapy, the patient would then enter the adjuvant phase, where they would receive Temozolomide alone. This is usually given at a higher dose of 150-200 mg/m² for five consecutive days during each 28-day cycle, for up to 6-12 cycles, depending on the patient's tolerance and response to treatment.

The patient's condition, performance status, and any side effects of treatment will be continuously monitored and evaluated during this period to adjust the treatment plan as needed. Please note that this regimen might vary depending on the individual patient's health condition, age, and potential comorbidities.

chatGPT-3.5's answer:

The standard regimen for chemotherapy and radiotherapy in the case of a gross total resection of a left fronto-temporal glioblastoma typically follows the Stupp protocol. This involves concurrent chemoradiotherapy followed by adjuvant chemotherapy. The specific details and duration of the treatment regimen will be determined by the patient's oncologist, taking into account various factors such as overall health, treatment response, and potential side effects. Regular monitoring and follow-up will be essential throughout the treatment process.

PRE-TRAINING TECHNIQUE USED WITH PATIENT 1 TO 8**Prompt used :**

I'm a neurosurgeon in a university hospital. Here is the story of a patient with a brain tumor:
"[patient's history from paper's supplementary material]"

His story was discussed at the neurotumor board. Here is the tumor board response :

"[TB's proposition from paper's supplementary material]"

Read the information and keep it, but don't answer. Just say "read" when your done.

ChatGPT's answer:

Read.