

EMBRACE-II Variable Description

Version Date: November 04, 2025

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Quick Reference: All Added Variables EMBRACE-II

This document describes the custom variables added to the EMBRACE-II dataset during data processing. Variables are organized by functional categories.

1. Patient and Study Information

| Variable | Details |
|-------------------|--|
| age | <ul style="list-style-type: none">Patient age at diagnosisCalculation: histology_assessment_date – year_of_birthImplementation: add_age()Unit: Years |
| included_in_study | <ul style="list-style-type: none">Indicates whether a patient is included in the final study cohortCalculation: Based on the study's inclusion/exclusion criteria documented in the official study flowchartImplementation: load_embrace_ii()Values: TRUE = included in study, FALSE = excluded from study |
| withdrew_consent | <ul style="list-style-type: none">Indicates if a patient withdrew consent from the studyCalculation: Based on followup_*m columnsImplementation: add_lost_to_fu()Values: TRUE = consent withdrawn, FALSE = consent maintained |
| is_lost_to_fu | <ul style="list-style-type: none">Indicates if a patient was lost to follow-up during the studyCalculation: Based on followup_*m columnsImplementation: add_lost_to_fu()Values: TRUE = patient lost to followup, FALSE = patient not lost to followup |

2. Diagnostic Measurements

| Variable | Details |
|-------------------------------|--|
| max_tumor_dimension_sta_d | <ul style="list-style-type: none"> • Maximum tumor dimension at diagnosis • Calculation: Overall maximum value across both MRI and gynecological exam measurements (<code>mri_tumor_*_sta_d</code> and <code>gyn_tumor_*_sta_d</code>) • Implementation: <code>add_max_tumor_dimension()</code> • Unit: Millimeters |
| gyn_max_parametrium_sta_d | <ul style="list-style-type: none"> • Maximum parametrial involvement from gynecological examination at diagnosis • Calculation: Maximum value between left and right parametrial involvement (<code>gyn_left_parametrium_sta_d</code> and <code>gyn_right_parametrium_sta_d</code>) • Implementation: <code>add_parametrial_involvement()</code> • Values: 0 = Not involved, 1 = Proximal, 2 = Distal, 3 = To pelvic wall |
| gyn_max_tumor_dimension_sta_d | <ul style="list-style-type: none"> • Maximum tumor dimension from gynecological examination • Calculation: Maximum value across all gynecological tumor measurements (width, height, thickness) • Implementation: <code>add_max_tumor_dimension()</code> • Unit: Millimeters |
| mri_max_parametrium_sta_d | <ul style="list-style-type: none"> • Maximum parametrial involvement from MRI at diagnosis • Calculation: Maximum value between left and right parametrial involvement (<code>mri_left_parametrium_sta_d</code> and <code>mri_right_parametrium_sta_d</code>) • Implementation: <code>add_parametrial_involvement()</code> • Values: 0 = Not involved, 1 = Proximal, 2 = Distal, 3 = To pelvic wall |
| mri_max_tumor_dimension_sta_d | <ul style="list-style-type: none"> • Maximum tumor dimension from MRI • Calculation: Maximum value across all MRI tumor measurements (width, height, thickness) • Implementation: <code>add_max_tumor_dimension()</code> • Unit: Millimeters |

3. Brachytherapy Treatment and Technique

| Variable | Details |
|---------------------------|--|
| icis | <ul style="list-style-type: none"> Intracavitary/Interstitial classification Calculation: Based on <code>fraction_*_technique_tdvh</code> columns Implementation: <code>add_icis()</code> Values: Binary (1 = ICIS, 0 = IC) Note: Derived from technique values across fractions |
| icis_parallel_oblique | <ul style="list-style-type: none"> Detailed ICIS needle classification Calculation: Based on <code>fraction_*_technique_tdvh</code> columns Implementation: <code>add_parallel_oblique_needles()</code> Values: “no needles”, “parallel needles”, “oblique needles”, “other” |
| average_nr_active_needles | <ul style="list-style-type: none"> Average number of active needles Calculation: Mean of <code>fraction_*_active_needles</code> columns Implementation: <code>add_average_active_needles()</code> Unit: Number of needles |
| time_to_bt | <ul style="list-style-type: none"> Time from EBRT start to first BT fraction Calculation: <code>fraction01date_tdvh - ebrt_start_date_tdvh</code> Implementation: <code>add_time_to_bt()</code> Unit: Days |
| time_to_bt_percent | <ul style="list-style-type: none"> Relative timing of brachytherapy Calculation: <code>time_to_bt / ott_ebrt</code> Implementation: <code>add_time_to_bt()</code> Unit: Proportion |
| ott_ebrt | <ul style="list-style-type: none"> Overall treatment time of EBRT Calculation: <code>ebrt_end_date_tdvh - ebrt_start_date_tdvh</code> Implementation: <code>add_time_to_bt()</code> Unit: Days |
| ott | <ul style="list-style-type: none"> Overall Treatment Time from start of EBRT to last treatment Calculation: Time interval between <code>ebrt_start_date_tdvh</code> and <code>last_treatment_date</code> (which is the latest of EBRT end date and all fraction dates) Implementation: <code>emii_add_ott()</code> Unit: Days |
| last_treatment_date | <ul style="list-style-type: none"> Date of the last treatment received Calculation: Maximum date among EBRT end date (<code>ebrt_end_date_tdvh</code>) and all brachytherapy fraction dates (<code>fraction*date_tdvh</code>) Implementation: <code>emii_add_ott()</code> Unit: Date |

| Variable | Details |
|--|--|
| <code>fraction01hrctv_volume_bins</code> | <ul style="list-style-type: none"> • CTV-HR volume categories • Calculation: Based on <code>fraction01hrctv_volume_tdvh</code> • Implementation: <code>add_hrctv_volume_bins()</code> • Values: 0: < 30 cm³, 1: 30-45 cm³, 2: > 45 cm³, NA: missing |
| <code>trak_total_sum</code> | <ul style="list-style-type: none"> • Total Reference Air Kerma (TRAK) summed across all brachytherapy fractions • Calculation: Sum of all <code>fraction*trak_tdvh</code> values • Implementation: <code>emii_add_trak_absolute()</code> • Unit: cGy at 1m |
| <code>trak_needles_sum</code> | <ul style="list-style-type: none"> • Total TRAK contribution from needles across all brachytherapy fractions • Calculation: Sum of <code>fraction*_needles_abs</code> values, which are derived from percentage contributions (<code>trak * trak_needles_pct / 100</code>) • Implementation: <code>emii_add_trak_absolute()</code> • Unit: cGy at 1m |
| <code>trak_vaginal_applicator_sum</code> | <ul style="list-style-type: none"> • Total TRAK contribution from vaginal applicator across all fractions • Calculation: Sum of <code>fraction*_vaginal_applicator_abs</code> values, which are derived from percentage contributions (<code>trak * trak_vaginal_applicator_pct / 100</code>) • Implementation: <code>emii_add_trak_absolute()</code> • Unit: cGy at 1m |
| <code>trak_tandem_applicator_sum</code> | <ul style="list-style-type: none"> • Total TRAK contribution from tandem applicator across all fractions • Calculation: Sum of <code>fraction*_tandem_applicator_abs</code> values, which are derived from percentage contributions (<code>trak * trak_tandem_applicator_pct / 100</code>) • Implementation: <code>emii_add_trak_absolute()</code> • Unit: cGy at 1m |
| <code>imp1gyn_max_parametrium_sta_b</code> | <ul style="list-style-type: none"> • Maximum parametrial involvement from gynecological examination at first implant • Calculation: Maximum value between left and right parametrial involvement (<code>imp1gyn_left_parametrium_sta_b</code> and <code>imp1gyn_right_parametrium_sta_b</code>) • Implementation: <code>add_parametrial_involvement()</code> • Values: 0 = Not involved, 1 = Proximal, 2 = Distal, 3 = To pelvic wall |

| Variable | Details |
|--|---|
| <code>imp1image_max_parametrium_sta_b</code> | <ul style="list-style-type: none"> • Maximum parametrial involvement from imaging at first implant • Calculation: Maximum value between left and right parametrial involvement <code>(imp1image_left_parametrium_sta_b and imp1imaging_right_parametrium_sta_b)</code> • Implementation: <code>add_parametrial_involvement()</code> • Values: 0 = Not involved, 1 = Proximal, 2 = Distal, 3 = To pelvic wall |

4. External Beam Radiotherapy (EBRT)

| Variable | Details |
|---|---|
| <code>ebrt_elective_target_algorithm</code> | <ul style="list-style-type: none"> Algorithm-recommended treatment target volume for elective nodal irradiation Calculation: Determined based on EMBRACE-II protocol Implementation: <code>emii_add_elective_targets()</code> Values: ‘Small Pelvis’, ‘Large Pelvis’, ‘Large Pelvis + Para-aortic’, ‘Large Pelvis + Inguinal’, ‘Large Pelvis + Para-aortic + Inguinal’ |
| <code>elective_high_risk</code> | <ul style="list-style-type: none"> Indicates if high-risk criteria for nodal treatment are met Calculation: TRUE if pathological nodes present AND ≥ 3 nodes found, OR if any common iliac or para-aortic nodes present Implementation: <code>emii_add_elective_targets()</code> Values: TRUE/FALSE |
| <code>elective_inguinal</code> | <ul style="list-style-type: none"> Indicates if inguinal node irradiation criteria are met Calculation: TRUE if maximum vaginal involvement = 3 (distal third) OR any inguinal nodes present in right or left groin Implementation: <code>emii_add_elective_targets()</code> Values: TRUE/FALSE |
| <code>elective_low_risk</code> | <ul style="list-style-type: none"> Indicates if low-risk criteria for nodal treatment are met Calculation: TRUE if NO pathological nodes, tumor $\leq 40\text{mm}$, TNM stage 1/2/3/5, squamous cell histology, and no corpus uteri involvement on MRI Implementation: <code>emii_add_elective_targets()</code> Values: TRUE/FALSE |
| <code>any_node_ci_pa</code> | <ul style="list-style-type: none"> Indicates presence of any common iliac or para-aortic lymph nodes at diagnosis Calculation: TRUE if any node has anatomical position of “R com iliac”, “L com iliac”, or “Para Aortic” Implementation: <code>emii_add_elective_targets()</code> Values: TRUE/FALSE |

5. Lymph Nodes and Metastases

| Variable | Details |
|-------------------------------|---|
| nodal_classification | <ul style="list-style-type: none"> Classification of nodal involvement status Calculation: Based on pathological nodes present (<code>pathological_nodes_present</code>) and Para-Aortic lymph node involvement at diagnosis Implementation: <code>emii_add_nodal_classification()</code> Values: ‘N0’ (no pathological nodes), ‘N1PAN’ (pathological nodes with Para-Aortic involvement), ‘N1pelvic’ (pathological nodes without Para-Aortic involvement) |
| number_common_iliac_ln_stat_d | <ul style="list-style-type: none"> Count of common iliac lymph nodes at diag. Calculation: Sum of left and right common iliac lymph nodes from staging data Implementation: <code>emii_add_number_common_iliac_ln_stat_d()</code> Unit: Count |
| number_paraaortic_ln_stat_d | <ul style="list-style-type: none"> Count of para-aortic lymph nodes at diag. Calculation: Count of lymph nodes with “Para Aortic” anatomical position from staging data Implementation: <code>add_number_paraaortic_ln_stat_d()</code> Unit: Count |
| has_*_followup | <ul style="list-style-type: none"> Indicates lymph node involvement during follow-up by specific anatomical location Calculation: Checks if any lymph node documented during follow-up has this specific anatomical position Implementation: <code>emii_add_recurrent_nodes()</code> Example variables: <code>has_L.ext.iliac_followup</code>, <code>has_Para.Aortic_followup</code>, etc. Values: TRUE/FALSE |
| has_*_diagnosis | <ul style="list-style-type: none"> Indicates lymph node involvement at diagnosis by specific anatomical location Calculation: Checks if any lymph node documented at diagnosis has this specific anatomical position Implementation: <code>emii_add_diagnostic_nodes()</code> Example variables: <code>has_L.ext.iliac_diagnosis</code>, <code>has_Para.Aortic_diagnosis</code>, etc. Values: TRUE/FALSE |
| has_*_metastases | <ul style="list-style-type: none"> Indicates presence of specific metastatic disease sites Calculation: Checks if any follow-up visit reports metastasis at this site Implementation: <code>add_metastases()</code> Example variables: <code>has_liver_metastases</code>, <code>has_bone_metastases</code>, <code>has_brain_metastases</code>, <code>has_lung_metastases</code>, <code>has_other_metastases</code> Values: TRUE/FALSE |

| Variable | Details |
|---|---|
| <code>has_*_nodes</code> | <ul style="list-style-type: none"> • Indicates presence of distant nodal metastases • Calculation: Checks if any follow-up visit reports nodes at these sites • Implementation: <code>add_metastases()</code> • Example variables: <code>has_paraaortic_nodes_above_12</code>, <code>has_supraclavicular_nodes</code>, <code>has_mediastinal_nodes</code> • Values: TRUE/FALSE |
| <code>has_abdominal_carcinomatosis</code> | <ul style="list-style-type: none"> • Indicates presence of abdominal carcinomatosis • Calculation: Checks if any follow-up visit reports abdominal carcinomatosis • Implementation: <code>add_metastases()</code> • Values: TRUE/FALSE |

6. Event Endpoints

| Variable | Endpoint | Details |
|--|------------------------------------|---|
| <code>event_localfailure</code> | Local Control | <ul style="list-style-type: none"> Calculation: Triggered when any followup <code>disease_local_status_*</code> column has a value of 2, indicating recurrence/progression Implementation: <code>add_local_failure_event()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |
| <code>event_nodalfailure</code> | Nodal Control (lower PAO) | <ul style="list-style-type: none"> Calculation: Triggered when any followup <code>disease_nodal_status_*</code> column has a value of 2, indicating nodal recurrence or progression Implementation: <code>add_nodal_failure_event()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |
| <code>event_nodalcontrol_incl_pao</code> | Nodal control (incl. all PAO) | <ul style="list-style-type: none"> Calculation: Triggered when either nodal failure (<code>event_nodalfailure</code>) OR para-aortic nodal failure (<code>event_paraaortic_nodal</code>) occurs Implementation: <code>emii_add_nodalcontrol_incl_pao()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |
| <code>event_systemicfailure</code> | Systemic Control (incl. upper PAO) | <ul style="list-style-type: none"> Calculation: Triggered when any followup <code>disease_systemic_status_*</code> column has a value of 2, indicating systemic recurrence or progression Implementation: <code>add_systemic_failure_event()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |
| <code>event_systemic_excl_pao</code> | Systemic control (excl. PAO) | <ul style="list-style-type: none"> Calculation: All systemic failures (<code>event_systemicfailure</code>) MINUS cases where para-aortic nodes above L2 are the ONLY systemic failure. Cases with para-aortic nodes above L2 plus any other systemic metastasis remain included Implementation: <code>emii_add_systemic_excl_pao()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |

| Variable | Endpoint | Details |
|------------------------|--------------------------------|---|
| event_vitalstatus | Overall Survival | <ul style="list-style-type: none"> Calculation: Uses the value from <code>vital_status</code> when available; otherwise sets to 0 (alive) if a disease assessment date exists (<code>latest_assessment_date_disease</code>) Implementation: <code>add_vitalstatus_event()</code> Values: 1 = death (event occurred), 0 = alive (no event) |
| event_pelvic_nodal | Pelvic Nodal control | <ul style="list-style-type: none"> Calculation: Triggered when nodal failure (<code>event_nodalfailure</code>) occurs AND at least one node is positive in any pelvic location: external iliac, internal iliac, common iliac, or parametrial/paracervical regions (left or right), Other Implementation: <code>emii_add_pelvic_nodal_event()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |
| event_pelvic | Pelvic control (local + nodal) | <ul style="list-style-type: none"> Calculation: Triggered when either local failure (<code>event_localfailure</code>) OR pelvic nodal failure (<code>event_pelvic_nodal</code>) occurs Implementation: <code>emii_add_pelvic_event()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |
| event_paraaortic_nodal | Para-aortic nodal control | <ul style="list-style-type: none"> Calculation: Triggered when either para-aortic nodes above L2 (<code>has_paraaortic_nodes_above_l2</code>) OR para-aortic nodes below L2 (<code>has_Para.Aortic_followup</code>) is detected Implementation: <code>emii_add_paraaortic_nodal()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |
| event_locoregional | Locoregional (Pelvic/PAO) | <ul style="list-style-type: none"> Calculation: Triggered when either local failure (<code>event_localfailure</code>) OR nodal control including para-aortic (<code>event_nodalcontrol_incl_pao</code>) occurs Implementation: <code>add_locoregional_event()</code> Values: 1 = failure (event occurred), 0 = no failure (no event) |

| Variable | Endpoint | Details |
|--------------------------|------------------------------------|---|
| event_locoregional_alone | Locoregional alone (no metastases) | <ul style="list-style-type: none"> Calculation: Triggered when a locoregional failure occurs (<code>event_locoregional=1</code>) WITHOUT any concurrent distant metastases (<code>event_systemic_excl_pao=0</code>) Implementation: <code>add_locoregional_event()</code> Values: 1 = isolated locoregional recurrence, 0 = no recurrence or recurrence with distant metastases |
| event_cancer_specific | Cancer-Specific Survival | <ul style="list-style-type: none"> Calculation: Triggered when death occurs (<code>event_vitalstatus=1</code>) AND the main cause of death is primary cancer (codes 1 or 3 in <code>vital_status_cause_of_death_vital_status</code>) Implementation: <code>emii_add_cancer_specific()</code> Values: 1 = cancer death, 0 = alive or non-cancer death |
| event_disease_control | Disease Control | <ul style="list-style-type: none"> Calculation: Triggered when any failure occurs at any site: local failure OR nodal failure OR systemic failure Implementation: <code>emii_add_disease_control()</code> Values: 1 = any disease failure, 0 = disease controlled at all sites |
| event_progression_free | Progression-Free Survival | <ul style="list-style-type: none"> Calculation: Triggered when any disease event (<code>event_disease_control=1</code>) OR death occurs (<code>event_vitalstatus=1</code>) Implementation: <code>emii_add_progression_free_survival()</code> Values: 1 = progression or death, 0 = alive without progression |
| event_distant_alone | Distant Metastases Alone | <ul style="list-style-type: none"> Calculation: Triggered when systemic failure excluding para-aortic nodes (<code>event_systemic_excl_pao=1</code>) occurs AND no locoregional failure (<code>event_locoregional=0</code>) Implementation: <code>emii_add_distant_alone()</code> Values: 1 = isolated distant metastases, 0 = no distant metastases or concurrent locoregional disease |

| Variable | Endpoint | Details |
|---------------------------------------|---------------------------|---|
| <code>timetoevent_disease</code> | Time to Disease Event | <ul style="list-style-type: none"> Calculation: Time interval in months from histology assessment date to either the first disease event date or the latest assessment date if no event occurred Implementation: <code>add_time_to_diseaseevent()</code> Values: Number of months |
| <code>timetoevent_vitalstatus</code> | Time to Last Vital Status | <ul style="list-style-type: none"> Calculation: Time interval in months from histology assessment date to the latest vital status date Implementation: <code>add_time_to_last_vitalstatus()</code> Values: Number of months |
| <code>latest_vital_status_date</code> | Latest Vital Status Date | <ul style="list-style-type: none"> Description: The date of the latest available information on vital status, calculated from assessment dates, last info date, and date of death when available Implementation: <code>add_time_to_last_vitalstatus()</code> Values: Date format |

7. Late Toxicity and Morbidity (only followup assessments)

| Variable | Details |
|-----------------------------|---|
| max_value_* | <ul style="list-style-type: none"> • Maximum grade of a specific toxicity or morbidity across all follow-up time points • Calculation: Maximum CTCAE grade value observed for the specific toxicity across all follow-up assessments • Implementation: <code>get_max_side_effects()</code> • Values: 0-5 (CTCAE grade scale) • Example variables: <ul style="list-style-type: none"> – <code>max_value_bladder_cystitis</code> – <code>max_value_vagina_stenosis</code> – <code>max_value_fistula</code> – <code>max_value_gastro_proctitis</code> |
| max_timepoint_* | <ul style="list-style-type: none"> • Follow-up timepoint at which the maximum grade of toxicity was observed • Calculation: Time point (e.g., “3m” for 3 months) at which maximum CTCAE grade was observed for each specific toxicity • Implementation: <code>get_max_side_effects()</code> • Values: Time point indicators (e.g., “3m”, “6m”, “12m”, etc.) • Example variables: <ul style="list-style-type: none"> – <code>max_timepoint_bladder_cystitis</code> – <code>max_timepoint_vagina_stenosis</code> – <code>max_timepoint_fistula</code> – <code>max_timepoint_gastro_proctitis</code> |
| overall_max_morbidity_grade | <ul style="list-style-type: none"> • Overall maximum morbidity grade across all toxicity endpoints and all time points • Calculation: The maximum value across all <code>max_value_*</code> variables for each patient • Implementation: <code>emii_add_max_morbidity()</code> • Values: 0-5 (CTCAE grade scale) • Purpose: Represents the highest toxicity experienced by a patient regardless of specific type or timepoint |

The toxicity and morbidity data include various organ systems and toxicity types:

1. **Bladder toxicity:** Cystitis, frequency, incontinence, urgency, stenosis/stricture, bleeding
2. **Gastrointestinal toxicity:** Abdominal pain/cramping, constipation, diarrhea, incontinence, proctitis, bleeding (at different sites), stenosis/stricture
3. **Vaginal toxicity:** Bleeding, discharge, dryness, mucositis, stenosis
4. **Fistula:** Grading and localization (bladder, rectum, vagina, etc.)
5. **Lymphatic complications:** Edema (limb, trunk/genital), lymphocele, thromboembolic events
6. **Muscle/skeletal toxicity:** Fibrosis, fracture, back/pelvic pain
7. **Other toxicities:** Fatigue, hot flashes, insomnia, and other patient-specific issues