

## Supplementary materials

### Cost assumptions based on:

1. Hospital visits
  - a. One hospital stay visit = \$2,137 (from the document of Charge Description Master [CDM])
    - i. The CDM contains charges for services provided at all of the hospitals. These charges are the same for all patients, regardless of coverage; however, the charges appearing in the document do not reflect any adjustments that may be made based on your insurance program or coverage. The amount you are required to pay will vary as a result of negotiated reimbursement rates by health plans and other payers and your specific plan details. If you are not covered by Kaiser Foundation Health Plan or Kaiser Permanente Insurance Company, or your insurance coverage does not include services received at a Kaiser Foundation Hospital, the charges contained in the CDM will be applicable. However, each medical procedure is made up of numerous charges and this document should not be used to accurately estimate the total charges or final patient cost of a given hospital stay. It is provided for information only.
  - b. Calculation is length of stay (days) × \$2,137 = total cost of the hospital stay  
Example: admission date January 2, 2008 and discharge date January 5, 2008 = LOS  
LOS is 4 days × \$2,137 = \$8,548 = total cost of this hospital stay
2. Outpatient visit (see sample fee schedule)
  - a. If a patient has outpatient visit only for that encounter = \$91 (average of all visits below)
    - i. Established patient visit level 1 (low severity) = \$25
    - ii. Established patient visit level 2 = \$50
    - iii. Established patient visit level 3 = \$85
    - iv. Established patient visit level 4 = \$125
    - v. Established patient visit level 5 (high severity) = \$170

Assumption: We took the average of all the visits  $([25+50+85+125+170]/5) = \$91$  since the severity of the outpatient visit was unknown (checkups, follow-up appointments, etc).
  - b. If a patient has an outpatient visit and then went to emergency room (ER) or admitted to Hospital from outpatient, then we applied the following calculation:
    - i. Established patient visit level 5 (high severity) = \$170
3. ER Visit (see sample fee schedule)
  - a. If a patient has an ER visit only we applied \$250 (average of all ER visits)
    - i. Emergency care by a physician level 1 (low severity) = \$125
    - ii. Emergency care by a physician level 2 = \$185
    - iii. Emergency care by a physician level 3 = \$275
    - iv. Emergency care by a physician level 4 (high severity) = \$415

Assumption: We took the average of all the visits from level 1 to level 4  $([125+185+275+415]/4) = \$250$  since severity of an ER visit was unknown.
  - b. If a patient has an ER visit and then was admitted to the Hospital we applied the following calculation:
    - i. Emergency care by a physician level 4 (high severity) = \$415

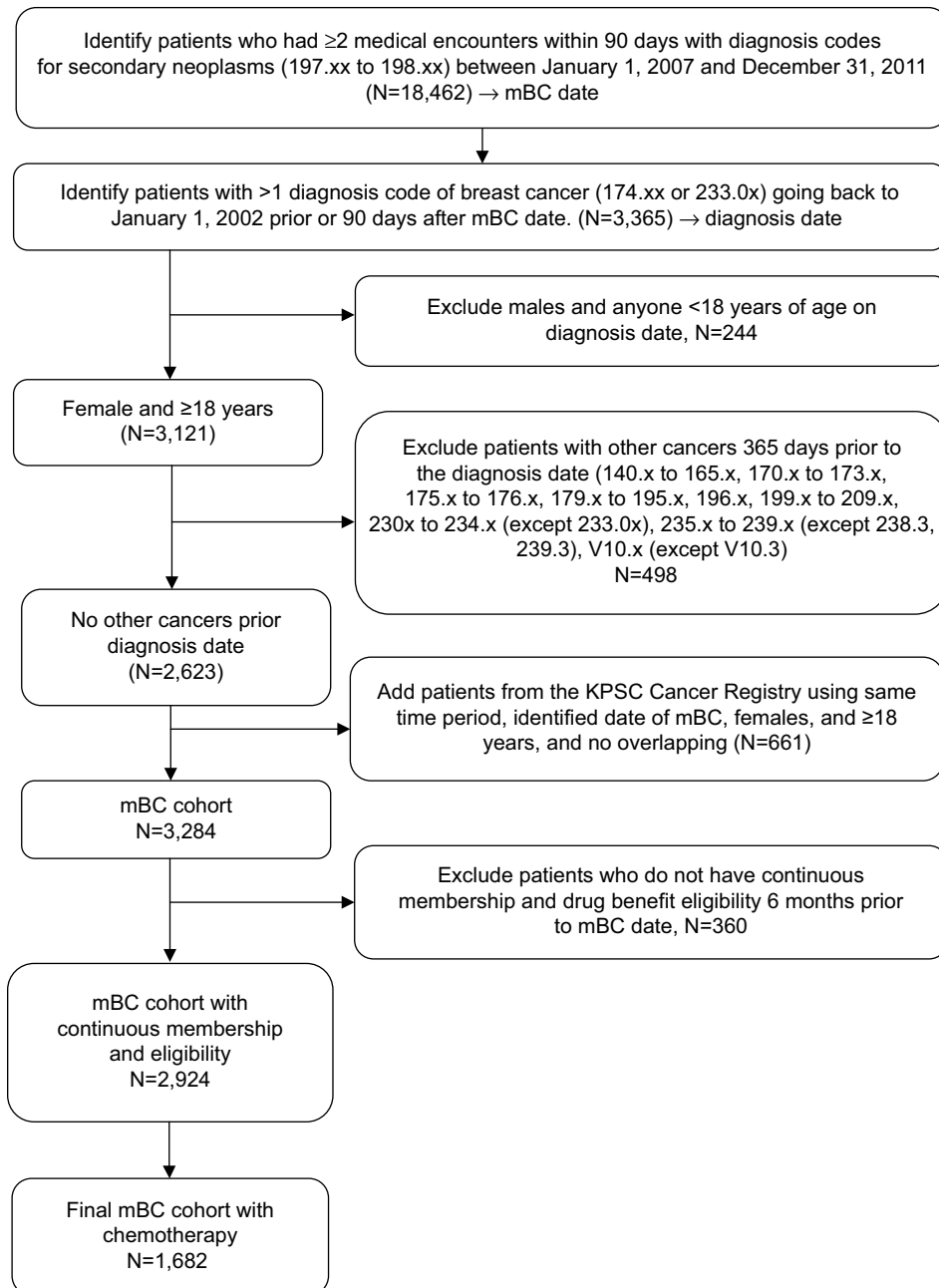
Examples:  
Outpatient only: \$91  
Outpatient + ER: \$170 + 195 = \$365  
Outpatient + hospital = \$170 + the length of stay of the hospital (\$2,137 per day)  
ER + hospital = \$415 + the length of stay of the hospital (\$2,137 per day)

### Medication for adverse event treatments:

Using the Redbook, we used average wholesale price (AWP) and AWP unit fee. We gathered an extensive list with medications that would be used for these various AE, and pulled all these medications during index date to end of first line of chemotherapy. We categorized by inpatient dispensed and outpatient dispensed.

1. Inpatient
  - a. If a patient had an EOC that was hospitalized and the medication from the list was identified, it was extracted. We identified the medication using dispense date on or between the admission date of the EOC to the discharge date of the EOC.
    - i. Step 1: pull name of drug, NDC, sig, direction
    - ii. Step 2: located NDC in the red book

- iii. Step 3: read the whole script, how many tabs given
  - iv. Step 4: identified AWP package price
  - v. Step 5: identified AWP unit price
2. Outpatient dispensed medications
- a. We obtained all the outpatient medications from the list during first-line chemotherapy.
  - b. We use GPI codes at Kaiser Permanente Southern California Region (KPSC), and because Red Book does not have GPI as a filter, we used generic name to identify the medication.
  - c. Follow steps above as for inpatient.



**Figure S1** mBC study population diagram.

**Abbreviations:** mBC, metastatic breast cancer; KPSC, Kaiser Permanente Southern California Region.

**Table S1** Adverse events identified using the following diagnosis and procedure codes

<b>Adverse event</b>	
<b>Dermatological</b>	
Alopecia	704.0x
Injection site reaction	999.39
Rash	693.0x, 708.8x, 708.9x, 782.1x
Dehydration	276.5x
Dyspnea	786.xx
Edema	782.3x, 514.xx, 518.4x
<b>Gastrointestinal</b>	
Constipation	564.0x
Decreased appetite	783.0x, 783.2x
Diarrhea	558.9x, 564.5x, 787.91, 007.xx, 009.xx
Nausea	787.0x, 787.01, 787.02, 787.03, 536.20
Stomatitis	528.0x
<b>Hematological</b>	
Anemia	280.xx, 281.xx, 283.xx, 284.xx, 285.xx
Leukopenia	288.5x, 288.8x, 288.9x
Neutropenia	288.xx
Thrombocytopenia	287.3x, 287.4x, 287.5x, 444.6x, 289.84, 99.05
<b>Hepatic</b>	
ALP, ALT, AST increased	790.4x, 790.5x; CPT: 84450
Bilirubin increased	277.4x, CPT: 81000, 81001, 81002, 81003, 82248, 82247
<b>Infection or pyrexia</b>	
Infection	001.xx-018.xx, 030.xx-041.xx, 045.xx-049.xx, 050.xx-057.xx, 110.xx-118.xx, 070.xx-079.xx, 130.xx-136.xx, 460.xx-466.xx, 480.xx-488.xx, 038.0x, 038.19, 038.80, 038.9x, 995.91, 995.92
Pyrexia	780.6x
Musculoskeletal/pain related	
Arthralgia	719.4x, 524.62
Myalgia	729.1x
Peripheral Neuropathy	356.xx, 357.xx, 337.0x, 337.1x

**Abbreviations:** ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase.

**Table S2** Medications used to identify treatment for during EOC

Adverse event category	Treatment	Drug class	Specific drugs
<b>Dermatological</b>			
Alopecia	Scalp cooling, minoxidil	Hair growth agents	
Injection site reaction	Corticosteroid, benadryl, antihistamine	Oral and topical antihistamines, anti-inflammatory, antipruritics	Generic name: diphenhydramine
Rash	Corticosteroid creams, antihistamines, analgesics	Analgesic or combos, topical antihistamines	
<b>Hematological</b>			
Anemia	Erythropoiesis-stimulating agents	Hematopoietic agents, hemostatics, misc hematological agents, iron, FeSo <sub>4</sub>	Generic name: epoetin, filgrastim, sargramostim, darbepoetin, pegfilgrastim, erythropoietin (Epo); • epoetin alfa (Procrit/Epogen); • epoetin beta (NeoRecormon); • darbepoetin alfa (Aranesp)
Leukopenia	Epoetin alfa, Darbepoetin, iron supplement, multivitamin, red blood cell transfusion	Hematopoietic agents, hemostatics, misc hematological agents	Generic name: filgrastim, sargramostim, pegfilgrastim
Neutropenia	Antibiotics/antifungal medications, and GCSF	Hematopoietic agents, hemostatics, misc hematological agents	Generic name: filgrastim, pegfilgrastim,
Thrombocytopenia	Corticosteroids, red blood cell transfusion	Hematopoietic agents, hemostatics, misc hematological agents	Corticosteroids
<b>Hepatic</b>			
ALP, ALT, AST increased	N/A	N/A	
Bilirubin	N/A	N/A	
Edema			
Edema	Diuretic	Diuretics	
Dehydration			
Dehydration	IVF, electrolytes	Vitamins, multivitamins, minerals, electrolytes, nutrients	
<b>Gastrointestinal</b>			
Constipation	Laxatives	Laxatives	
Decreased appetite	Appetite stimulants, such as to help with anorexia, cachexia	Appetite stimulants	Generic name: megestrol, dronabinol
Diarrhea	Imodium, Kaopectate, Maalox, Pepto, Lomotil, tincture of opium	Antidiarrheals	
Nausea/vomiting	Aprepitant, ondansetron, granisetron, dolasetron, palonosetron, anti-nausea medications	Antiemetics	Generic name: aprepitant, ondansetron, granisetron, dolasetron, palonosetron
Stomatitis	Mouth washes, oral corticosteroids, antiseptic	Mouth and throat (local). Antispetics-mouth/throat, lozenges, mouthwashes, anesthetics topical oral	
Infection or pyrexia			
Infection	Sulfamethoxazole, fluconazole, itraconazole, other antibiotics, other antimicrobials	Anti-infective agents	
Pyrexia	Antifever meds, acetaminophen, NSAIDs	Analgesics, NSAIDs, APAP	
MUSC neurological			
Arthralgia	Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs (DMARD), corticosteroids	NSAIDs, corticosteroids, narcotics	
Myalgia	Antidepressants, corticosteroids, narcotics	NSAIDs, corticosteroids, narcotics, muscle relaxants	
Peripheral neuropathy	Analgesics, antidepressants, antiseizure medications, physical therapy, occupational therapy, acupuncture		Generic name: gabapentin, duloxetine, pregabalin

**Notes:** HCRU For EOC costs related to adverse events were defined as all visits that a patient had from index date to end of their initial chemotherapy during post index. The visits were categorized into EOC as described earlier.

**Abbreviations:** EOC, episode of care; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; N/A, not applicable.