Previewing Only: You cannot submit data from this form

Previewing at Level 1

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Title Review

Save to finish later | Submit Data

1. Does this article **potentially apply** to any of our key questions?

- **Potentially** eligible
- Ineligible
- Not in English
- Ineligible, but includes inflammatory markers
- Van de Laar/Salpeter article

Clear Selection

Save to finish later | Submit Data

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Previewing Only: You cannot submit data from this form

Previewing at Level 2

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Abstract Review

Keywords:
No keywords available

Increase Font Size
Decrease Font Size

Abstract:
The pharmacokinetic disposition of metformin in late pregnancy was studied together with the level of fetal exposure at birth. Blood samples were obtained in the third trimester of pregnancy from women with gestational diabetes or type 2 diabetes; 5 had a previous diagnosis of polycystic ovary syndrome. A cord blood sample also was obtained at the delivery of some of these women, and also at delivery of others who had been taking metformin during pregnancy but from whom no blood had been taken. Plasma metformin concentrations were assayed by a new, validated, reverse-phase HPLC method. A 2-compartment, extravascular maternal model with transplacental partitioning of drug to a fetal compartment was fitted to the data. Nonlinear mixed-effects modeling was performed in NONMEM using FOCE with INTERACTION. Variability was estimated using logarithmic interindividual and additive residual variance models; the covariance between clearance and volume was modeled simultaneously. Mean (range) metformin concentrations in cord plasma and in maternal plasma were 0.81 (range, 0.1-2.6) mg/L and 1.2 (range, 0.1-2.9) mg/L, respectively. Typical population values (interindividual variability, CV%) for allometrically scaled maternal clearance and volume of distribution were 28 L/h/70 kg (17.1%) and 190 L/70 kg (46.3%), giving a derived population-wide half-life of 5.1 hours. The placental partition coefficient for metformin was 1.07 (36.3%). Neither maternal age nor weight significantly influenced the pharmacokinetics. The variability (SD) of observed concentrations about model-predicted concentrations was 0.32 mg/L. The pharmacokinetics were similar to those in nonpregnant patients and, therefore, no dosage adjustment is warranted. Metformin readily crosses the placenta, exposing the fetus to concentrations approaching those in the maternal circulation. The sequelae to such exposure, eg, effects on neonatal obesity and insulin resistance, remain unknown.

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Save to finish later | Submit Data

1. Exclude article because… **(check one or more)**

- ☐ written in language other than **English**
- ☐ subjects **<18 years old**
- ☐ no **original data** (e.g., is a meeting abstract, review, commentary, etc.)
- ☐ study evaluates outcomes in **animals only** (no humans evaluated)
- ☐ not evaluating people with **type 2 diabetes**, NIDDM (non-insulin dependent diabetes mellitus), or adult onset diabetes
- ☐ evaluates markers of **inflammation only** (e.g., tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1), etc.)
- ☐ study only evaluates a **first generation sulfonylurea** (tolazamide, tolbutamide, chlorpropramide)
- ☐ evaluates none of the **medications** in our review (see medication list posted on trialstat to see which medications we have included in the review)
- ☐ does not apply to any of the **key questions**
- ☐ other: specify _____
- ☐ Undecided; retrieve full article to decide

Below are specific questions to determine inclusion/exclusion if did not exclude based on a reason above. Skip options under questions if the article does not apply to that particular question. **CHECK TO SEE IF ARTICLE APPLIES TO Q2-6 BEFORE MARKING EXCLUDE FOR Q1.**

2. Q1: **proximal clinical outcomes**: glycosylated hemoglobin, weight, systolic or diastolic blood pressure, serum lipid levels, and two hour postprandial glucose levels in adult patients with type 2 diabetes?

- ☐ exclude since study is **< 3 months**

- [ ] exclude since **NOT a randomized controlled trial**
- [ ] exclude since number of subjects in entire study is **< 40**
- [ ] include

3. Q2: **distal diabetes-related complications** including mortality and the following macrovascular and microvascular complications: coronary artery disease, myocardial infarction, stroke, transient ischemic attack, retinopathy, nephropathy, neuropathy, peripheral arterial disease (PAD), or amputations?

- [ ] exclude since study is **< 3 months**
- [ ] exclude since number of subjects in entire study is **< 40**
- [ ] include but mark if deals with **PAD, amputations, or neuropathy**
- [ ] include

4. Q3: other health outcomes including **quality of life** and **functional status**?

- [ ] exclude since study is **< 3 months**
- [ ] exclude since **NO comparison group**
- [ ] exclude since number of subjects in entire study **< 40**
- [ ] include

5. Old Q4&5: safety for the following life-threatening and non life-threatening **adverse events**: hypoglycemia, liver failure, congestive heart failure, lactic acidosis, cancer, anemia, thrombocytopenia, or leukopenia, allergic reactions requiring hospitalization or death, elevated aminotransferase levels, edema, hypervolemia, pancytopenia, weight gain and gastrointestinal problems and other adverse events?

See new revised Q4&5 below.

- [ ] (see below)
- [ ] (see below)
- [ ] (see below)
- [ ] (see below)
- [ ] (see below)

6. Q6: Are the safety and effectiveness different for particular adult populations such as those based on **demographic factors** (e.g., race/ethnicity, age>65 years, or gender) or **co-morbidities** (e.g., renal insufficiency, congestive heart failure, liver disease, obesity, depression, schizophrenia)?

- [ ] include

7. Evaluates an oral medication in our review and insulin. Check below if oral medication is compared to insulin (and there is **no** other oral comparison or placebo group). Examples to exclude are:

- oral + insulin compared to insulin
- oral + insulin compared to another oral medication **with no placebo or other oral medication arm**
- oral + insulin compared to oral + insulin
- oral compared to insulin **with no placebo or other oral medication arm**

☐ Exclude if oral medication is compared to insulin (and there is no other oral comparison or placebo group)

☐ Exclude for other reason (specify:)

8. Exclude if the following combinations are evaluated (and there is no other oral comparison groups and/or placebo groups).

☐ Exclude if study evaluates acarbose or miglitol added to any other oral medication in one arm

☐ Exclude if study evaluates nateglinide or repaglinide added to any other oral medication in one arm

☐ Exclude if study evaluates combinations of greater than 2 oral medications in one arm (e.g., metformin added to glyburide added to acarbose in one arm)

9. **Revised** Q4&5: safety for the following life-threatening and non life-threatening **adverse events**: hypoglycemia, liver failure, congestive heart failure, lactic acidosis, cancer, anemia, thrombocytopenia, or leukopenia, allergic reactions requiring hospitalization or death, elevated aminotransferase levels, edema, hypervolemia, pancytopenia, gastrointestinal problems and other adverse events? **Note: weight gain was removed from adverse events.**

☐ Include if **RCT** >3 months AND N>40 AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q1

☐ Include if **cohort** >3 months AND N>40 AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q2, 3

☐ Include if **case control study** AND N>40 AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract)

	☐ Exclude if **case report or case series** (i.e., a series of case reports) ☐ Other study design AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract) (specify:) ☐ Unable to tell study duration, number of subjects, or study design but is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract); retrieve full article to decide ☐ Exclude if does not meet any of the inclusion criteria for Q4&5, such as N<40 Save to finish later Submit Data

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Previewing Only: You cannot submit data from this form

Previewing at Level 3

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Article Review

Keywords:
No keywords available

Increase Font Size
Decrease Font Size

Abstract:
The pharmacokinetic disposition of metformin in late pregnancy was studied together with the level of fetal exposure at birth. Blood samples were obtained in the third trimester of pregnancy from women with gestational diabetes or type 2 diabetes; 5 had a previous diagnosis of polycystic ovary syndrome. A cord blood sample also was obtained at the delivery of some of these women, and also at delivery of others who had been taking metformin during pregnancy but from whom no blood had been taken. Plasma metformin concentrations were assayed by a new, validated, reverse-phase HPLC method. A 2-compartment, extravascular maternal model with transplacental partitioning of drug to a fetal compartment was fitted to the data. Nonlinear mixed-effects modeling was performed in NONMEM using FOCE with INTERACTION. Variability was estimated using logarithmic interindividual and additive residual variance models; the covariance between clearance and volume was modeled simultaneously. Mean (range) metformin concentrations in cord plasma and in maternal plasma were 0.81 (range, 0.1-2.6) mg/L and 1.2 (range, 0.1-2.9) mg/L, respectively. Typical population values (interindividual variability, CV%) for allometrically scaled maternal clearance and volume of distribution were 28 L/h/70 kg (17.1%) and 190 L/70 kg (46.3%), giving a derived population-wide half-life of 5.1 hours. The placental partition coefficient for metformin was 1.07 (36.3%). Neither maternal age nor weight significantly influenced the pharmacokinetics. The variability (SD) of observed concentrations about model-predicted concentrations was 0.32 mg/L. The pharmacokinetics were similar to those in nonpregnant patients and, therefore, no dosage adjustment is warranted. Metformin readily crosses the placenta, exposing the fetus to concentrations approaching those in the maternal circulation. The sequelae to such exposure, eg, effects on neonatal obesity and insulin resistance, remain unknown.

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Save to finish later | Submit Data

1. Exclude article because… **(check one or more)**

- ☐ not written in **English**
- ☐ subjects not **adults** (<18 years old)
- ☐ not an **original article** (e.g., is a meeting abstract, review, commentary, etc.)
- ☐ study evaluates outcomes in **animals only** (no humans evaluated)
- ☐ not evaluating people with **type 2 diabetes**, NIDDM (non-insulin dependent diabetes mellitus), or adult-onset diabetes (e.g. **exclude if** evaluates people with **impaired glucose tolerance, metabolic syndrome**, maturity onset diabetes of youth (MODY), gestational diabetes)
- ☐ evaluates **pregnant women** with diabetes only
- ☐ evaluates markers of **inflammation only** (e.g., tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1), etc.)
- ☐ study only evaluates a **first generation sulfonylurea** (tolazamide, tolbutamide, chlorpropramide) or is a head to head comparison with a first generation sulfonylurea only with no placebo or other comparison group to compare our medication of interest.
- ☐ evaluates none of the **medications** in our review (see medication list posted on trialstat to see which medications we have included in the review. Note: Exclude studies on **muraglitazar** unless data on other medications in the study. Exclude studies on **troglitazone, phenformin, and voglibose** even if its a head-to-head trial.)
- ☐ does not apply to any of the **key questions** (such as dealing with cost or adherence or results not broken down by type of medication or drug-drug interactions)
- ☐ **N<40**
- ☐ evaluates **acarbose or miglitol added** to any other oral medication in one arm (AND there is no other oral comparison or placebo groups)

☐ evaluates **nateglinide or repaglinide added** to any other oral medication in one arm (AND there is no other oral comparison or placebo groups)

☐ evaluates **combinations of greater than 2 oral medications in one arm** (e.g., metformin added to glyburide added to acarbose in one arm)

☐ oral medication is **compared or added to insulin** (AND there is no other oral comparison or placebo group). Examples to exclude are: oral + insulin compared to insulin, oral + insulin compared to another oral medication **with no placebo or other oral medication arm**, oral + insulin compared to oral + insulin, oral compared to insulin **with no placebo or other oral medication arm**

☐ the study is a **pharmacokinetic or dosing study** where there is no placebo or comparison group such as: acarbose 50mg compared to acarbose 100mg with no placebo or other oral medication comparison group.

☐ other: specify _____

2. Include:

☐ Include but do **NOT** review if this is a study with >2 trials reported in the article with **pooled results** eligible for one of the 6 questions.

Below are specific questions to determine inclusion/exclusion if did not exclude based on a reason above. Skip options under questions if the article does not apply to that particular question.
CHECK TO SEE IF ARTICLE APPLIES TO Q2-6 BEFORE MARKING EXCLUDE FOR Q1.

3.
Q1: **proximal clinical outcomes**: glycosylated hemoglobin, weight, systolic or diastolic blood pressure, serum lipid levels, and two hour postprandial glucose levels in adult patients with type 2 diabetes? (NOTE: if only evaluates another measure of post prandial glucose (e.g., study evaluates one hour post prandial glucose AND there is no other relevant outcome), then mark "does not apply to key question above.")

☐ exclude since study is **< 3 months**

☐ exclude since **NOT a randomized controlled trial**

☐ include - **CONSIDER FOR INCLUSION FOR OTHER QUESIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q1 & Q3 OUTCOMES FORM, AND QUALITY FORM.**

4.
Q2: **distal diabetes-related complications** including

mortality and the following macrovascular and microvascular complications: coronary artery disease, myocardial infarction, stroke, transient ischemic attack, retinopathy, nephropathy, neuropathy (microalbuminuria, urine albumin/creatinine ratio, serum creatinine, GFR, creatinine clearance, proteinuria/albuminuria, end stage renal disease, and renal replacement therapy or transplant), peripheral arterial disease (PAD), or amputations?

- exclude since study is **< 3 months**
- exclude if deals with **biological markers** of outcomes **such as vascular endothelial function or carotid intima media thickness**. (Mark "include" below if deals with clinical outcomes such as ventricular fibrillation, restenosis rates, or EKG abnormalities, such as QT prolongation.)
- include - **CONSIDER FOR INCLUSION FOR OTHER QUESIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q2 OUTCOMES FORM, AND QUALITY FORM**

5.

Q3: other health outcomes including **quality of life** and **functional status**?

- exclude since study is **< 3 months**
- exclude since **NO comparison group**
- include - **CONSIDER FOR INCLUSION FOR OTHER QUESIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q1 & Q3 OUTCOMES FORM, AND QUALITY FORM**

6.

Revised Q4&5: safety for the following life-threatening and non life-threatening **adverse events**: hypoglycemia, liver failure, congestive heart failure, lactic acidosis, cancer, anemia, thrombocytopenia, leukopenia, allergic reactions requiring hospitalization or death, elevated aminotransferase levels, edema, hypervolemia, pancytopenia, gastrointestinal problems and other adverse events? **Note: weight gain was removed from adverse events.**

- Include if **RCT** >3 months AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q1 - **CONSIDER FOR INCLUSION FOR OTHER QUESIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q4&5 OUTCOMES FORM, AND QUALITY FORM**
- Include if **cohort** >3 months AND is likely to have data on safety (i.e., those that mention safety or adverse events in the title or abstract) even if it does not have data on Q2, 3 - **CONSIDER FOR INCLUSION FOR OTHER QUESIONS THEN BEGIN DATA ABSTRACTION. COMPLETE**

ALL GENERAL FORMS, Q4&5 OUTCOMES FORM, AND QUALITY FORM

☐ Include if **case control study** AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract) - **CONSIDER FOR INCLUSION FOR OTHER QUESIONS THEN BEGIN DATA ABSTRACTION. COMPLETE STUDY DESIGN, ELIGIBILITY CRITERIA, POPULATION CHARACTERISTICS, Q4&5 CASE CONTROL OUTCOMES FORM**

☐ Exclude if **case report or case series** (i.e., a series of case reports)

☐ Include if other study design AND is likely to have data on safety (i.e., mentions safety or adverse events in the title or abstract) (specify:) - **CONSIDER FOR INCLUSION FOR OTHER QUESIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS, Q4&5 OUTCOMES FORM, AND QUALITY FORM**

_____

☐ Exclude if does not meet any of the inclusion criteria for Q4&5, such as N<40

7.

Q6: Are the safety and effectiveness different for particular adult populations such as those based on **demographic factors** (e.g., race/ethnicity, age>65 years, or gender) or **co-morbidities** (e.g., renal insufficiency, congestive heart failure, liver disease, obesity, depression, schizophrenia, etc…)?

☐ Include - **CONSIDER FOR INCLUSION FOR OTHER QUESTIONS THEN BEGIN DATA ABSTRACTION. COMPLETE ALL GENERAL FORMS AND QUALITY FORM**

Save to finish later | Submit Data

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Previewing Only: You cannot submit data from this form

Previewing at Level 4

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Study Design

Save to finish later | Submit Data

Oral Diabetes Medications

General Form

Study Design Characteristics

Fill out this form for ALL included studies.

1. In what country does the study occur? **(check all that apply)**

- [ ] United States
- [ ] Canada
- [ ] United Kingdom
- [ ] Other (specify:)

2. What study design is used? **(check only one response)**

- ( ) Randomized controlled trial
- ( ) Non-randomized trial
- ( ) Prospective or retrospective/non-concurrent cohort (e.g., post-marketing surveillance)
- ( ) Cross-sectional study
- ( ) Retrospective/non-concurrent case-control
- ( ) Nested case-control (e.g. conducted within a larger cohort study)
- ( ) Other

Clear Selection

3. If this is a trial, then please mark any of the following. **(check all that apply)**

- [ ] Factorial design
- [ ] Parallel arms
- [ ] Cross-over design
- [ ] Placebo-controlled
- [ ] Other (specify:)
- [ ] None of the above apply to the trial/Not applicable (not a trial)

4. If this is a crossover trial, was there a washout period? **(check only one response)**

- ( ) Yes (specify how long in days:)
- ( ) No
- ( ) Not reported

NA

Clear Selection

5. Is the source population of this study from one of the following studies? **(check only one response)**

UKPDS (United Kingdom Prospective Diabetes Study)

UGDP (University Group Diabetes Program)

DPP (Diabetes Prevention Program)

PROactive (Prospective pioglitazone clinical trial in macrovascular events)

Other (specify:)

None of the above

Clear Selection

6. Was pharmaceutical support (funding or drug given for free) received to conduct the study? **(check only one response)**

Yes

No

Not reported

Clear Selection

7. Study period recruitment was from:

Start year

End year

Not reported

The mean/median follow-up duration was: (Record your answer in weeks. If reported separately by groups then please list in other by group.)

	Weeks	Other (specify:)	Not reported
8. Mean			
9. Median			

10. Was a subgroup analysis conducted?

Yes (specify which subgroups were analyzed:)

No

Clear Selection

11. Comments:

Enlarge Shrink

Thank you very much!

Save to finish later Submit Data

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Previewing Only: You cannot submit data from this form

Previewing at Level 5

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Eligibility

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Oral Diabetes Medications

General Form

Eligibility Criteria

Fill out this form for ALL included studies. If the characteristic is listed as an exclusion criteria, please check the exclusion box. Otherwise, do not check the box. Please list all inclusion criteria as exclusions (i.e., if study includes patients with coronary artery disease, specify no coronary artery disease in "other" and click exclusion).

Eligibility criteria of participants (list as exclusion criteria)		
Characteristic	**Specify criteria for exclusion (e.g., age<30)**	**Exclusion**
Age	(Specify) Enlarge Shrink	☐
Male		☐
Female		☐
Any liver disease (such as elevated aminotransferases (ALT, AST, SGOT, SGPT))		☐
Any kidney disease (such as microalbuminuria, macroalbuminuria, or elevated creatinine, GFR, or creatinine clearance)		☐
History of cardiovascular disease (e.g., myocardial infarction, stroke, transient ischemic attack, coronary artery disease, angina)		☐
Treatment experienced (had been on oral hypoglycemics or insulin in the past)		☐
Neuropathy		☐
Retinopathy		☐
HgbA1c	(Specify HgbA1c criteria used)	☐

	Enlarge Shrink	
No type 2 diabetes		☐
Other	(Specify) Enlarge Shrink	☐
Other	(Specify) Enlarge Shrink	☐
Other	(Specify) Enlarge Shrink	☐
Other	(Specify) Enlarge Shrink	☐
Other	(Specify) Enlarge Shrink	☐
Other	(Specify) Enlarge Shrink	☐

26. Comments:

Enlarge Shrink

Thank you very much!

Save to finish later | Submit Data

Form took 1.28125 seconds to render

Previewing Only: You cannot submit data from this form

Previewing at Level 6

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Intervention

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Oral Diabetes Medications

General Form

Intervention Description

Fill out this form for ALL included RCT, cohort, and cross-sectional studies.

Please indicate the intervention or medication for each arm of the study. **(check all that apply)**

(For crossover studies, record each portion of the crossover as a separate group.)

(For cohort or cross-sectional studies, please record each medication exposure as a separate group.

(For case control studies, please fill out the Q4 & Q5 Case-Control Outcomes Form.)

	Group 1	Group 2
1. Placebo	☐	☐
Non medication intervention		
2. Diet	☐	☐
3. Exercise	☐	☐
4. Behavioral therapy	☐	☐
5. Education	☐	☐
6. Other non medication intervention (specify under checkbox)	☐	☐
7. Other non medication intervention (specify under checkbox)	☐	☐
Glucophage (metformin)		
8. metformin (Glucophage)	☐	☐
9. metformin extended release (Glucophage XR)	☐	☐
Second generation sulfonylureas		
10. glyburide (Micronase)	☐	☐
11. glyburide (Diabeta)	☐	☐
12. glyburide (Glynase PresTab)	☐	☐
13. glyburide (no trade drug specified)	☐	☐
14. glimepiride (Amaryl)	☐	☐

15. glipizide (Glucotrol)
16. glypizide XL (Glucotrol XL)
17. glibenclamide
18. glyclazide
19. unspecified sulfonylurea

Alpha glucosidase inhibitors

20. miglitol (Glyset)
21. acarbose (Precose)
22. voglibose
23. unspecified alpha-glucosidase inhibitor

Non-sulfonylurea secretagogues/metiglinides

24. nateglinide (Starlix)
25. repaglinide (Prandin)

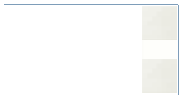
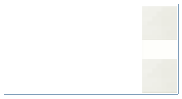
Thiazolidinediones

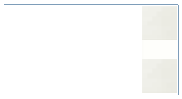
26. rosiglitazone (Avandia)
27. pioglitazone (Actos)
28. troglitazone
29. unspecified TZD

Combined medications in one pill

30. avandia + metformin (Avandamet)
31. glyburide + metformin (Glucovance)
32. metformin + glipizide (Metaglip)
33. Other (specify under checkbox)
34. Other (specify under checkbox)
35. Other (specify under checkbox)
36. Other (specify under checkbox)
37. Other (specify under checkbox)
38. Other (specify under checkbox)
39. Other (specify under checkbox)

	For each medication listed in Q1, please indicate the initial d	
Medication	**Group 1**	**Group 2**

Please select medication Please Select  Enlarge Shrink	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:
Please select medication Please Select  Enlarge Shrink	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:
	Initial dose:	**Initial** dose:

Please select medication Please Select  Enlarge Shrink	Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:	Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:
Please select medication Please Select Enlarge Shrink	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:
Please select medication Please Select	**Initial** dose: Unit: mg	**Initial** dose: Unit: mg

Enlarge Shrink	micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:	micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:
Please select medication Please Select Enlarge Shrink	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:	**Initial** dose: Unit: mg micronized tabs mcg IU Other Not specified Clear Selection Was the dose: fixed escalated other not reported Clear Selection If escalated, **maximum** dose:

Medication	Group 1	Group 2
Please select intervention or medication Please Select	1x/day 2x/day	1x/day 2x/day

Enlarge Shrink	3x/day Other (specify) Not specified Clear Selection	3x/day Other (specify) Not specified Clear Selection
Please select intervention or medication Please Select Enlarge Shrink	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection
Please select intervention or medication Please Select Enlarge Shrink	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection
Please select intervention or medication Please Select Enlarge Shrink	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection
Please select intervention or medication Please Select Enlarge Shrink	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection	1x/day 2x/day 3x/day Other (specify) Not specified Clear Selection
Please select intervention or medication Please Select	1x/day 2x/day 3x/day	1x/day 2x/day 3x/day

Enlarge Shrink	Other (specify) Not specified Clear Selection	Other (specify) Not specified Clear Selection

304. Please indicate if the duration of exposure to the medication was recorded as the mean duration or planned duration? **(If both, please on**

- Mean duration
- Planned duration
- Not reported
- Other

Clear Selection

For each intervention		
Medication	**Group 1**	
Please select intervention or medication Please Select Enlarge Shrink	weeks months years	weeks months years
Please select intervention or medication Please Select Enlarge Shrink	weeks months years	weeks months years
Please select intervention or medication Please Select Enlarge Shrink	weeks months years	weeks months years
Please select intervention or medication Please Select Enlarge Shrink	weeks months years	weeks months years
Please select intervention or medication Please Select Enlarge Shrink	weeks months years	weeks months years
Please select intervention or medication Please Select Enlarge Shrink	weeks months years	weeks months years

Group 1	Group 2	Gro
Indicate which medications group was on prior to starting the study. **(check all that apply)**	Indicate which medications group was on prior to starting the study. **(check all that apply)**	Indicate which medications starting the study. **(check a**
☐ placebo	☐ placebo	☐ placebo
☐ diet	☐ diet	☐ diet
☐ exercise	☐ exercise	☐ exercise
☐ behavioral therapy	☐ behavioral therapy	☐ behavioral therapy
☐ education	☐ education	☐ education
☐ metformin (Glucophage)	☐ metformin (Glucophage)	☐ metformin (Glucophage)
☐ metformin extended release (Glucophage XR)	☐ metformin extended release (Glucophage XR)	☐ metformin extended release (Glucophage XR)
☐ glyburide (Micronase)	☐ glyburide (Micronase)	☐ glyburide (Micronase)
☐ glyburide (Diabeta)	☐ glyburide (Diabeta)	☐ glyburide (Diabeta)
☐ glyburide (Glynase PresTab)	☐ glyburide (Glynase PresTab)	☐ glyburide (Glynase PresTab)
☐ glyburide (no trade drug specified)	☐ glyburide (no trade drug specified)	☐ glyburide (no trade drug specified)
☐ glimepiride (Amaryl)	☐ glimepiride (Amaryl)	☐ glimepiride (Amaryl)
☐ glipizide (Glucotrol)	☐ glipizide (Glucotrol)	☐ glipizide (Glucotrol)
☐ glipizide XL (Glucotrol XL)	☐ glipizide XL (Glucotrol XL)	☐ glipizide XL (Glucotrol XL)
☐ glibenclamide	☐ glibenclamide	☐ glibenclamide
☐ gliclazide	☐ gliclazide	☐ gliclazide
☐ miglitol (Glyset)	☐ miglitol (Glyset)	☐ miglitol (Glyset)
☐ acarbose (Precose)	☐ acarbose (Precose)	☐ acarbose (Precose)
☐ voglibose	☐ voglibose	☐ voglibose
☐ nateglinide (Starlix)	☐ nateglinide (Starlix)	☐ nateglinide (Starlix)
☐ repaglinide (Prandin)	☐ repaglinide (Prandin)	☐ repaglinide (Prandin)
☐ rosiglitazone (Avandia)	☐ rosiglitazone (Avandia)	☐ rosiglitazone (Avandia)
☐ pioglitazone (Actos)	☐ pioglitazone (Actos)	☐ pioglitazone (Actos)
☐ troglitazone	☐ troglitazone	☐ troglitazone
☐ avandia + metformin (Avandamet)	☐ avandia + metformin (Avandamet)	☐ avandia + metformin (Avandamet)
☐ glyburide +	☐ glyburide +	☐ glyburide +

metformin (Glucovance) ☐ metformin + glyburide (Metaglip) ☐ unspecified sulfonylurea ☐ unspecified alpha-glucosidase inhibitors ☐ unspecified TZD ☐ Other (specify below)	metformin (Glucovance) ☐ metformin + glyburide (Metaglip) ☐ unspecified sulfonylurea ☐ unspecified alpha-glucosidase inhibitors ☐ unspecified TZD ☐ Other (specify below)	metformin (Glucovance) ☐ metformin + glyburide (Metaglip) ☐ unspecified sulfonylurea ☐ unspecified alpha-glucosidase inhibitors ☐ unspecified TZD ☐ Other (specify below)

373. Comments:

Enlarge Shrink

374. If the dose is escalating, please record the mean dose for each medication for each group.

Enlarge Shrink

Thank you very much!

Save to finish later | Submit Data

Form took 8.28125 seconds to render

Previewing Only: You cannot submit data from this form

Previewing at Level 7

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Population

Save to finish later | Submit Data

Oral Diabetes Medications

General Form

Study Population Characteristics

Fill out this form for ALL included studies.

Please fill in the study population characteristics (age, gender, race/ethnicity, BMI, HgbA1c, and duration o need to record standard errors or standard deviations for these measures.

Total N at Enrollment

	Group 1	Group 2	Group 3	Group 4
1. Total N for **enrollment**				

Age

	Group 1	Group 2	Group 3	Group 4
2. Mean age				
3. Age range				
4. Age, other (specify age categories below in Q5 and record results under each group:)				

5. Specify other age classification for Q4.

Enlarge Shrink

Male

	Group 1	Group 2	Group 3	Group 4
6. N				
7. %				

Race/ethnicity

	Group 1	Group 2	Group 3	Group 4
8. African American (N)				
9. African American (%)				
10. Caucasian (N)				

	Group 1	Group 2	Group 3	Group 4
11. Caucasian (%)				
12. Asian or Asian American (N)				
13. Asian or Asian American (%)				
14. Hispanic/Latino (N)				
15. Hispanic/Latino (%)				
16. Other race/ethnicity (N) (specify other race/ethnicity below in Q20 and record results under each group)				
17. Other race/ethnicity (%) (specify other race/ethnicity below in Q20 and record results under each group)				
18. Other race/ethnicity (N) (specify other race/ethnicity below in Q21 and record results under each group)				
19. Other race/ethnicity (%) (specify other race/ethnicity below in Q21 and record results under each group)				

20. Specify other race/ethnicity cateogory for Q16 or Q17.

Enlarge Shrink

21. Specify other race/ethnicity category for Q18 or Q19.

Enlarge Shrink

BMI/Weight

	Group 1	Group 2	Group 3	Group 4
22. Mean BMI (kg/m2)				
23. Other BMI measures (specify other BMI measures below in Q26 and record results under each group:)				

	Group 1	Group 2	Group 3	Group 4
24. Mean weight (kg)				
25. Other weight measures (specify other weight measures below in Q27 and record results under each group:)				

26. Specify other BMI measures for Q23.

Enlarge Shrink

27. Specify other weight measures for Q25.

Enlarge Shrink

HgbA1c

	Group 1	Group 2	Group 3	Group 4
28. Mean HgbA1c(%)				
29. Other HgbA1c measures (specify HgbA1c measures below in Q33 and record results under each group:)				

	Group 1	Group 2	Group 3	Group 4
30. Mean HgbA1 (%)				
31. Other HgbA1 measures (specify other HgbA1 measures below in Q34 and record results under each group:)				
32. Other hemoglobin measures (specify other hemoglobin measures below in Q35				

and record results under each group:)

33. Specify other HgbA1c measures for Q29.

Enlarge Shrink

34. Specify other HgbA1 measures for Q31.

Enlarge Shrink

35. Specify other hemoglobin measures for Q32.

Enlarge Shrink

Duration of Diabetes

	Group 1	Group 2	Group 3	Group 4
36. Mean duration of diabetes (in years)				
37. Other duration of diabetes measures (specify other duration of diabetes measures below in Q38 and record results under each group:)				

38. Specify other duration of diabetes measures for Q37.

Enlarge Shrink

Other key characteristic that was different between randomized groups

	Group 1	Group 2	Group 3	Group 4
39. Other key characteristic (specify key characteristic below in Q43 and record results under each group) - mean				
40. Other key characteristic (specify key characteristic below in Q43 and record results under each group) - median				
41. Other key characteristic (specify key characteristic below in Q43 and record				

results under each group) - N				
42. Other key characteristic (specify key characteristic below in Q43 and record results under each group) - %				

43. Specify other key characteristic for Q39, Q40, Q41, or Q42.

Enlarge Shrink

44. Comments:

Enlarge Shrink

Thank you very much!

Save to finish later Submit Data

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Previewing at Level 8

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Q1 & Q3 Outcomes

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Oral Diabetes Medications

Q1 and Q3 (Proximal Clinical Outcomes and Quality of Life) Outcomes Form

Fill out this form only for proximal clinical outcomes and quality of life outcom

1. Outcome of interest being reported on this form: **(check only one response)**

- ○ LDL calculated
- ○ LDL measured
- ○ HDL
- ○ HgbA1c
- ○ Hemoglobin a1
- ○ Total glycated hemoglobin
- ○ Weight
- ○ BMI
- ○ Triglyceride
- ○ Systolic blood pressure
- ○ Diastolic blood pressure
- ○ 2 hour postprandial glucose Note: do not need to abstract area under the curve data or any other measure besides 2 hour ppg
- ○ Fasting plasma glucose (only report if 2 hour postprandial glucose is reported)
- ○ QOL (quality of life): treatment satisfaction, well-being, or functional status
- ○ Other (specify:) _____

Clear Selection

2. If quality of life assessed, what validated measure was used?

- ☐ Diabetes treatment satisfaction questionnaire from UKPDS
- ☐ Diabetes well-being questionnaire from UKPDS
- ☐ Medical outcomes study SF-36
- ☐ Euro-QoL (EQ-5D)
- ☐ ADL-activities of daily living
- ☐ IADL-instrumental activities of daily living
- ☐ WHO-DTSQ
- ☐ WHO-WBQ
- ☐ Other validated questionnaire or instrument (specify:)

☐ Other non-validated questionnaire or instrument (specify:)

3. What units were used? **(check only one response)**

- ○ mmol/L
- ○ umol/L
- ○ mg/dL
- ○ mmHg
- ○ %
- ○ kg/m2
- ○ pounds
- ○ kilograms
- ○ Other (specify:)

Clear Selection

Please fill in the results below.

(Note: Please record the N for analysis by group at the bottom.

Please report mean difference from placebo and/or mean difference from other group. If these measures a

You do not need to record the p-value if there are other measures of variability available (e.g., standard de

measure the p-value is for in Q27.)

	Group 1	Group 2	Group 3	Group 4
4. **Baseline Mean**				
5. Standard deviation (sd)				
6. Standard error (se)				
7. **Baseline Median**				
8. Lower limit of IQR (interquartile range) 25%				
9. Upper limit of IQR (interquartile range) 75%				

	Group 1	Group 2	Group 3	Group 4
10. **Final Mean**				
11. Standard deviation (sd)				
12. Standard error (se)				
13. **Final Median**				
14. Lower limit of IQR (interquartile range) 25%				
15. Upper limit of IQR (interquartile range) 75%				
16. Mean difference				

from baseline				
17. Mean difference from placebo				
18. Mean difference from other group (specify other group below:)				
19. 95% CI (lower limit)				
20. 95% CI (upper limit)				
21. p-value				
22. Other (specify below:)				
23. Other (specify below:)				
24. Other (specify below:)				
25. Other (specify below:)				

26. Specify other group for mean difference comparison.

Enlarge Shrink
27. Specify other measures.

Enlarge Shrink
28. Specify other measures.

Enlarge Shrink
29. Specify other measures.

Enlarge Shrink
30. Specify other measures.

Enlarge Shrink
31. Comments:

Enlarge Shrink

	Group 1	Group 2	Group 3	Group 4
32. **N for the analysis**				

Thank you very much!

Save to finish later Submit Data

Form took 1.984375 seconds to render

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Previewing at Level 19

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Q2 Outcomes

Save to finish later | Submit Data

Oral Diabetes Medications

Q2 (Distal Diabetes-Related Complications) Outcomes Form

Fill out this form only for distal diabetes-related complications (e.g., mortality, attack, retinopathy, and nephropathy). Fill out one form for each distal diabete

1. Outcome of interest being reported on this form: **(check only one response)**

- ○ All cause mortality
- ○ Cardiovascular disease mortality
- ○ Cardiovascular disease morbidity
- ○ Coronary heart diseases
- ○ Cerebrovascular diseases
- ○ Diabetic retinopathy
- ○ Diabetic nephropathy (e.g. urinary albumin, micro or macroalbuminuria, creatinine, kidney disease, GFR)
- ○ Peripheral arterial disease
- ○ Neuropathy
- ○ Other (specify:) _____

Clear Selection

2. **Outcomes of Interest: All cause mortality**

Indicate how the outcome was assessed. **(check all that apply)**

- ☐ Confirmed by National or State death certificate registry
- ☐ Other (Specify definition:) _____
- ☐ Other (Specify definition:) _____
- ☐ Present, but unclear definition

3. **Outcomes of Interest: Cardiovascular Disease Mortality**

Indicate how the outcome was assessed. **(check all that apply)**

- ☐ Fatal myocardial infarction
- ☐ Sudden cardiac death
- ☐ Fatal stroke
- ☐ Confirmed by death certificate registry
- ☐ Used ICD-9 codes to determine (specify:) _____

☐ Other (specify:) _____

☐ Other (specify:) _____

☐ Present, but unclear definition

Outcome(s) of Interest: C	
Outcome of Interest	**Indicate how the outcome was ass**
CVD Morbidity	☐ Use of nitrotryglycerine or oth
Coronary heart diseases	☐ Mycardial infarction (Non-fatal) ☐ In absence of percutaneous coronary intervention or CABG had at least 2 of: a)Symptoms suggestive of myo more, b) EKG evidence of MI, c) Elevated cardiac enzymes (CPK-MB, or troponin) serum levels d) Survived >24l ☐ Silent myocardial infarction ☐ Angina ☐ Ischemic heart disease ☐ Coronary artery bypass surgery ☐ Angioplasty or angiography showing at least 1 stenosis >50% ☐ Used ICD-9 codes 410-414 ☐ Used other ICD-9 codes (specify ICD-9 codes used:) ☐ Used Patient Self-Report ☐ Other (specify:) ☐ Other (specify:) ☐ Present, but unclear definition
Cerebrovascular diseases	☐ Stroke (defined as acute focal neurological deficit lasting for longer than 24h or resulting in death ☐ Transient ischemic attack (acute focal neurological deficit lasting for less than 24h) ☐ Carotid endarterectomy ☐ Used Patient self report ☐ Used ICD-9 codes (specify ICD-9 codes used:) ☐ Other (specify:) ☐ Other (specify:) ☐ Present, but unclear definition

10. **Outcomes of Interest: Diabetic Retinopathy**

Indicate how the outcome was assessed. **(check all that apply)**

☐ History of cataract extraction

☐ Macular edema

☐ Microaneurysms only

☐ Background retinopathy

- [ ] Proliferative retinopathy
- [ ] Mild non-proliferative diabetic retinopathy
- [ ] Moderate or severe non- proliferative diabetic retinopathy
- [ ] Visual Acuity
- [ ] ETDRS (Early Treatment Diabetic Retinopathy) criteria used
- [ ] Used ICD-9 codes: 362.0, 362.1, or 362.53
- [ ] Used other ICD-9 codes (specify ICD-9 codes used:)
- [ ] Used patient self-report
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Present, but unclear definition

11. **Outcomes of Interest: Diabetic Nephropathy**

Indicate how the outcome was assessed. **(check all that apply)**

- [ ] Proteinuria/Albuminuria
- [ ] Change in GFR/Creatinine clearance
- [ ] Change serum creatinine
- [ ] ESRD
- [ ] Renal Replacement Therapy or Transplant
- [ ] Used ICD-9 codes (specify ICD-9 codes used:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Present, but unclear definition

12. **Outcomes of Interest: PAD**

Indicate how the outcome was assessed. **(check all that apply)**

- [ ] Claudication
- [ ] Peripheral revascularization procedure – angioplasty, bypass surgery or stenting
- [ ] Gangrene
- [ ] Limb amputation
- [ ] Decreased ankle-brachial index
- [ ] Decreased systolic arm-toe gradient
- [ ] Patient self report of (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Present, but unclear definition

13. **Outcomes of Interest: Neuropathy**

Indicate how the outcome was assessed. **(check all that apply)**

- [ ] Peripheral, assessed by monofilament test
- [ ] Peripheral, assessed by other means (specify:)
- [ ] Autonomic (specify test:)
- [ ] Used ICD-9 codes 250.6 for peripheral
- [ ] Used other ICD-9 codes (specify ICD-9 codes used:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Present, but unclear definition

14. Is analysis adjusted for confounders?

- [ ] Yes
- [ ] No
- [ ] Not reported
- [ ] Not applicable (e.g., RCT)

15. What covariates/confounders were adjusted? **List all covariates here** **(Choose all applicable)**

- [ ] Age
- [ ] Gender
- [ ] Race
- [ ] BMI
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Not applicable (e.g., RCT)

Please report results of the most fully adjusted model if there is more than one model.

	Group 1	Group 2	Group 3	Group 4
16. **Number of people in the analysis for each group**				
17. Numerator: # of events				
18. Numerator: %				

with events				
19. Demoninator: # Time Unit				
20. Demoninator: Record the units that was used for Q19 (days, weeks, months, years, person-years)				
21. Incidence rate				
22. 95% CI: Lower limit				
23. 95% CI: Upper limit				
24. Difference in incidence rates				
25. 95% CI: Lower limit				
26. 95% CI: Upper limit				
27. p-value				
28. Relative risk				
29. Relative hazard/hazard ratio				
30. Odds ratio				
31. 95% CI: Lower limit				
32. 95% CI: Upper limit				
33. p-value				
34. Relative risk reduction				
35. Other (specify below:)				
36. Other (specify below:)				
37. Other (specify below:)				

38. Specify other analysis:

Enlarge Shrink

39. Specify other analysis:

Enlarge Shrink

40. Specify other analysis:

Enlarge Shrink
41. Comments:

Enlarge Shrink
Thank you very much!

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Previewing at Level 24

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Q4 & Q5 Outcomes

Save to finish later | Submit Data

Oral Diabetes Medications

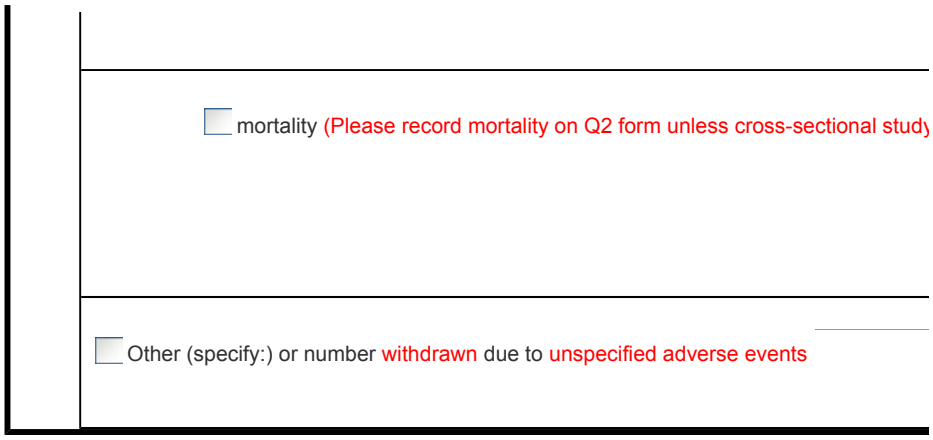
Q4 & Q5 (Safety & Adverse Events) Outcomes Form

Fill out this form only for safety & adverse events outcomes (e.g., hypoglycem thrombocytopenia, leukopenia, allergic reactions requiring hospitalization or d pancytopenia, gastrointestinal problems, and other adverse events). Fill out o

Choose the outcome of interest (choose one only) and then specify h

Adverse Event
☐ hypoglycemia
☐ elevated aminotransferase levels
☐ cholestatic abnormality
☐ liver failure
☐ congestive heart failure

- [ ] lactic acidosis
- [ ] cancer
- [ ] anemia
- [ ] thrombocytopenia
- [ ] leukopenia
- [ ] allergic reactions
- [ ] edema/hypervolemia
- [ ] gastrointestinal problems



Serious event = comprised any experience that was fatal, life-threatening, permanently or substantially d
ER visit, or an important medical event that jeopardized the patient or required intervention such as trans

	Group 1	Group 2	Group 3	Group 4
31. **Number of people in the analysis for each group**				
32. Number **WITHDRAWN** from study due to adverse events				
33. Numerator: # with **FIRST SERIOUS** event				
34. Numerator: % with **FIRST SERIOUS** events				
35. Numerator: # with **TOTAL FIRST** events				
36. Numerator: % with **TOTAL FIRST** events				
37. Numerator: Other (specify below in Q38)				
38. Specify other numerator.				
39. Numerator: Other (specify below in Q40)				
40. Specify other numerator.				
41. Demoninator: # Time Unit				
42. Demoninator: Record the				

units that was used for Q41 (days, weeks, months, years, person-years)				
43. Incidence rate				
44. 95% CI: Lower limit				
45. 95% CI: Upper limit				
46. Difference in incidence rates				
47. 95% CI: Lower limit				
48. 95% CI: Upper limit				
49. p-value				
50. Relative risk				
51. Relative hazard/hazard ratio				
52. Odds ratio				
53. 95% CI: Lower limit				
54. 95% CI: Upper limit				
55. p-value				
56. Relative risk reduction				
57. Other (specify below:)				
58. Other (specify below:)				
59. Other (specify below:)				

60. Specify other analysis:

Enlarge Shrink

61. Specify other analysis:

Enlarge Shrink

62. Specify other analysis:

Enlarge Shrink

63. Is analysis adjusted for confounders?

- [ ] Yes
- [ ] No

- [ ] Not reported
- [ ] Not applicable (e.g., RCT)

64. What covariates/confounders were adjusted? **List all covariates here** **(Choose all applicable)**

- [ ] Age
- [ ] Gender
- [ ] Race
- [ ] BMI
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Other (specify:)
- [ ] Not applicable (e.g., RCT)

65. Comments:

Enlarge Shrink

Thank you very much!

Save to finish later Submit Data

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Previewing Only: You cannot submit data from this form

Previewing at Level 33

Refid: 3597, Charles, B., Norris, R., Xiao, X., and Hague, W., Population Pharmacokinetics of Metformin in Late Pregnancy, *Ther Drug Monit*, 28(1), 2006, p.67-72
State: Excluded, Level: 1

Quality

Keywords:
No keywords available

Increase Font Size
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Abstract:
The pharmacokinetic disposition of metformin in late pregnancy was studied together with the level of fetal exposure at birth. Blood samples were obtained in the third trimester of pregnancy from women with gestational diabetes or type 2 diabetes; 5 had a previous diagnosis of polycystic ovary syndrome. A cord blood sample also was obtained at the delivery of some of these women, and also at delivery of others who had been taking metformin during pregnancy but from whom no blood had been taken. Plasma metformin concentrations were assayed by a new, validated, reverse-phase HPLC method. A 2-compartment, extravascular maternal model with transplacental partitioning of drug to a fetal compartment was fitted to the data. Nonlinear mixed-effects modeling was performed in NONMEM using FOCE with INTERACTION. Variability was estimated using logarithmic interindividual and additive residual variance models; the covariance between clearance and volume was modeled simultaneously. Mean (range) metformin concentrations in cord plasma and in maternal plasma were 0.81 (range, 0.1-2.6) mg/L and 1.2 (range, 0.1-2.9) mg/L, respectively. Typical population values (interindividual variability, CV%) for allometrically scaled maternal clearance and volume of distribution were 28 L/h/70 kg (17.1%) and 190 L/70 kg (46.3%), giving a derived population-wide half-life of 5.1 hours. The placental partition coefficient for metformin was 1.07 (36.3%). Neither maternal age nor weight significantly influenced the pharmacokinetics. The variability (SD) of observed concentrations about model-predicted concentrations was 0.32 mg/L. The pharmacokinetics were similar to those in nonpregnant patients and, therefore, no dosage adjustment is warranted. Metformin readily crosses the placenta, exposing the fetus to concentrations approaching those in the maternal circulation. The sequelae to such exposure, eg, effects on neonatal obesity and insulin resistance, remain unknown.

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Save to finish later | Submit Data

Oral Diabetes Medications

Quality Form

Fill out this form for all clinical trials.
Do not need to fill this out for cohort, case-control, or cross-sectional studies.

1. Was the study described as randomized (this includes the use of words such as randomly, random, and randomization)?

- Yes (1)
- No (0)
- Not Reported/Can't Tell (0)

Clear Selection

2. If yes to q1, was the randomization scheme described AND appropriate?

- Yes: (1) appropriate randomization is if each study participant is allowed to have the same chance of receiving each intervention and the investigators could not predict which treatment was next.
- No: (-1) randomization described AND inappropriate (e.g. methods of allocation using date of birth, date of admission, hospital numbers, or alteration should not be regarded as appropriate)
- No: (0) randomization methods not described

Clear Selection

3. Was the study described as double blind?

- Yes (1)
- No (0)
- Not reported/Can't tell (0)

Clear Selection

4. If yes to Q3, was the method of double blinding described AND appropriate?

- Yes: (1) appropriate double blinding is if neither the person doing the assessments nor the study participant could identify the intervention being assessed OR if the use of active placebos, identical placebos or dummies is mentioned
- No: (-1) the study was described as double blind AND inappropriate (e.g. comparison of tablet vs lifestyle with no double dummy or fake tablet given to the lifestyle group)

No: (0) no description of double blinding available and unable to tell if appropriate or not.

Clear Selection

5. Was there a description of withdrawals and drop-outs?

Yes: (1) the number and the reasons for withdrawals in each group must be stated or state that there were no withdrawals. If subjects were not included in the analysis, they must state the number and reasons for not including them in the analysis.

No (0)

Clear Selection

6. Comments:

Enlarge Shrink

Thank you very much!

Save to finish later | Submit Data

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